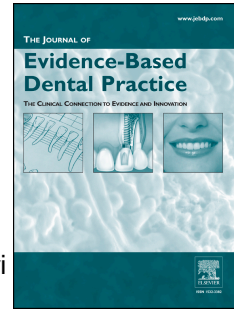


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In-vivo and in-vitro effectiveness of rotary nickel-titanium versus manual stainless steel instruments for root canal therapy: systematic review and meta-analysis

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REVIEW

In-vivo and in-vitro effectiveness of rotary nickel-titanium versus manual stainless steel instruments for root canal therapy: systematic review and meta-analysis

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Running head: Rotary nickel-titanium vs manual stainless steel files

KEYWORDS

Key words (MeSH): Bacteria; Dental Pulp Cavity; Meta-analysis; Root Canal Preparation; Stainless Steel; titanium nickelide.

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Authors' contributions

MDF, contributed to design of the review, the data analysis and has written the manuscript.; KIA, contributed to the data acquisition and interpretation and critically revised the manuscript; SC, contributed to the data acquisition; AE, contributed to the data acquisition and draft of the manuscript; IP, contributed to the design of the review; ST is the head of the project and developed the project. All authors gave final approval and agree to be accountable to all aspects of the work.

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INTRODUCTION

Over the years, a number of techniques have been described to obtain a tapered preparation, mostly using conventional manual stainless steel (mSST) instruments. Although different designs and mechanical procedures have been proposed, they have all suffered from intrinsic problems, mainly attributed to the intrinsic stiffness of conventional stainless steel (SST) instruments, such as zipping, stripping, ledging, perforation, canal transportation and broken instruments, especially in severely curved canals.¹

The development of rotary nickel-titanium (rNiTi) instrumentation in the past decade has modified the root canal preparation.²⁻⁴ Nickel-titanium (NiTi) endodontic files have a remarkable ability of adequately shaping root canals.¹ The characteristic of NiTi alloys to alter their crystalline state gives them exceptional flexibility. Super-elasticity, high resilience, excellent cutting efficiency, shaping ability and fatigue resistance are peculiar features of NiTi endodontic files.⁵⁻¹⁰

Accordingly, NiTi instruments have gained rapid acceptance among endodontists,^{1,11} suggesting that they outperform mSST instruments in most of the parameters related to root canal treatment success. However, the available evidence on this topic has not been systematically assessed to date. Therefore, the aim of this systematic review was to evaluate and compare the effectiveness (outcome) of using rNiTi (intervention) versus mSST (comparison) files in root canal-treated teeth (population).

MATERIALS AND METHODS

A systematic review was conducted and reported adhering to the PRISMA statement¹² and the quality standards proposed by AMSTAR on therapies.¹³ This was done to obtain an adequate transparency, quality methodology and reporting, thus, minimize potential bias in the review process.¹⁴

Search method

Two experienced clinician scientists conducted a systematic search of four electronic databases (MEDLINE via PubMed ([http:// www.ncbi.nlm.nih.gov/sites/pubmed](http://www.ncbi.nlm.nih.gov/sites/pubmed)), EMBASE via Ovid, Scopus, and Cochrane Central Register of Controlled Trials (CENTRAL) via the Cochrane Library) up to February 2016 with no language restriction. The following search string was used for MEDLINE database: ((endodontic* or "root

canal*" or orthograd* or "dental pulp devitali*") and ((nickel and titanium) or nickel-titanium or niti or "ni ti" or ni-ti or nitinol)). This search strategy was adapted to the three remaining databases. Additionally, a manual search was performed in the reference list of the selected articles, and in the following 13 journals: *International Endodontic Journal*, *Journal of Endodontics*, *Oral Surgery Oral Medicine Oral Pathology Oral Radiology and Endodontology*, *Journal of Dental Research*, *Journal of Dentistry*, *Australian Endodontic Journal*, *Caries Research*, *Dental Traumatology*, *European Journal of Oral Science*, *International Dental Journal*, *Oral Diseases*, *Oral Microbiology and Immunology*, and *Endodontic Practice Today*.

Types of studies and selection criteria

For this review, prospective and retrospective clinical studies as well as randomized in vitro studies were considered by two independent review authors (AMK, ST) for answering our research question. When disagreements were not resolved, a third author was consulted (MD). A protocol was designed a priori (Appendix S1). For studies appearing to meet the inclusion criteria or for which there was insufficient information in the title and abstract to make a clear decision the full-text was obtained. Reports were included if they compared rNiTi to mSST files for orthograde root canal therapy. Reports were excluded if they evaluated: only one type of the files of interest, and engine driven SST files or manual NiTi files were used. All studies meeting the inclusion criteria underwent data extraction and risk of bias assessment. In addition, clinical studies were excluded if they were not comparative (e.g. case reports or case series), or if they considered root canal retreatment cases.

In vitro studies were considered when they were on extracted human teeth and randomized. Thus, the excluded in vitro studies consisted of: using resin blocks, creating glide path only, or extracted endo-treated teeth undergoing retreatment.

- Outcomes of interest

Primary outcomes were all variables used to identify any advantage brought in by the use of a given type of instrumentation in root canal treatment that may imply a clinically relevant benefit for the patient (e.g. pain reduction, symptoms resolution and healing, improvement of quality of life, occurrence of complications, tooth retention and function, incidence of relapse of the condition).

Secondary outcomes were directly measured parameters such as cleansing of the root canal, microbial load reduction, apical debris extrusion, transportation and centring ability. Technical quality of root canal filling, based on the canal length, density (presence of voids) and width (tapering), was also considered. Such variables may aid the operator to choose the most accurate technique for management of difficult clinical scenarios (e.g. exceptionally curved root canals).

Data extraction

The following data were extracted and recorded by two review authors (AMK, IP) independently into a specifically designed electronic spreadsheet: dates in which the study was performed, study type, year of publication, country of origin, source of study funding, type and location of teeth, type of materials and instruments used for root canal system management, details of the outcomes reported. Only for clinical trials: the details of the participants including demographic characteristics, the method of outcome assessment and the time intervals after intervention. Any disagreement was resolved by consensus, and a third review author (MD) was consulted when necessary, and a fourth reviewer (KIA) verified the information.

Quality assessment and risk of bias

- Clinical studies

Three review authors (MD, KIA, ST) graded the selected clinical trials following the domain-based evaluation, described in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011). The evaluations were compared and any inconsistencies between the review authors were resolved by consensus. The following domains were assessed as 'low risk of bias', 'unclear' (i.e. uncertain risk of bias) or 'high risk of bias': sequence generation, allocation concealment, blinding of outcome assessment, incomplete outcome data, and selective outcome reporting. Assessment of blinding of participants and personal, comparability of groups at entry, clear definition of selection criteria, clear definition of outcomes assessment, recall rate (it was assumed adequate if dropout <10%), sample size calculation, and number of operators involved, were also considered.

The overall risk of bias of each included study was categorized according to the following: low risk of bias if all criteria are met; unclear risk of bias if one or more criteria are assessed as unclear; or high risk of bias if one or more criteria are not met.

- In vitro studies

The included in vitro studies were assessed based on the following information: overall and group-specific sample size calculation, randomization, reporting reasons of exclusion or withdrawals. If the number of in vitro samples undergoing the experimental procedure was clearly documented and matched the number of samples reported, the study reporting of withdrawals was classified as adequate or low risk of bias.

Data synthesis

For each study, the mean difference and the standard deviation (SD) in the primary and/or secondary outcome variable was extracted or calculated to estimate the effect of interventions. Heterogeneity was assessed by examining the types and the number of samples, the type of endodontic file used, and the outcomes in each study. A meta-analysis was attempted only if studies that performed similar comparisons, and reporting the same outcome measures, were found. The only difference between groups had to be the type of file used for orthograde root canal treatment. The primary or secondary outcome variables from each study were combined for continuous data using a random-effects model. Standardized mean differences were calculated for each study. The analysis was performed using the software Review Manager (RevMan, Version 5.3, The Nordic Cochrane Center, The Cochrane Collaboration, Copenhagen, Denmark, 2014) and the results were graphically presented by means of Forest plots.

RESULTS

This systematic review focuses on the root canal treatment success when using two intracanal preparation instruments only: NiTi rotary files compared to SST hand files. Other factors that influence survival and success of root canal treatments will have to be assessed in future systematic reviews. Examples of these may be host-dependant (age, gender, health status, parafunction, presence of antagonists, number of canals), operator-dependant factors (level of experience, training, dexterity, knowledge), other root canal treatment-factors (type of intracanal medicaments when used, irrigation solution and technique, single- and multiple-visit endodontics, condensation technique) and clinical setting.¹⁵

The electronic and hand search strategies yielded 1155 references of studies after removal of duplicates (Fig. 1). After examination of titles and abstracts, 80 potentially relevant references reporting on

the success of endo-treated teeth when shaping root canals with rNiTi compared to mSST files were examined in full-text, and 58 of these references were excluded (Appendix S2). From the 22 references that fulfilled the proposed inclusion criteria (Table 1; Appendices S3-S5), six were included for further quantitative assessment (Fig. 2). All included articles were published between 1995 and 2013.

Clinical studies

Four clinical studies were included in this review (Table 1). Of these, two were randomized clinical trials (RCTs) and two were retrospective studies. The RCTs demonstrated that rNiTi files were as efficient as mSST files for intracanal bacterial reduction.^{16,17} Two studies retrospectively evaluated the endodontic success rate.^{18,19} One study reported that teeth treated with rNiTi files achieved higher success rate than mSST files concerning periapical healing.¹⁸ The other study reported that there was no statistically significant difference between the two endodontic files groups with regard of tooth success rate.¹⁹

- Quality and risk of bias assessment of included clinical studies

One RCT¹⁶ was judged at low risk of bias as it met all the evaluation criteria, while the other RCT¹⁷ was at high risk as it had two high risk of bias items (Fig. 2). The two retrospective studies^{18,19} were judged at high risk of bias, mainly due to their study design (Fig. 2). Additional information regarding the full quality assessment can be found at the Appendices S6-S8.

A meta-analysis of two RCTs^{16,17} quantifying the bacteria present after treatment did not suggest a difference between the rNiTi and the mSST group (Fig. 3a).

In vitro studies

Eighteen in vitro were included. All of these studies allocated samples in a random sequence, and the sample size was considered adequate in most studies. The overall methodology of the included studies was considered adequate, as most studies had a low risk of bias.

Due to different experimental set-ups and parameters investigated, a direct comparison of all the results was unfeasible. The operator expertise, the sample size, the type of teeth used, the degree of curvature of the canal varied among different studies. Moreover, the rotary systems under evaluation were used according to different protocols, and the number, sequence, and taper were also different.

- Cleansing ability

Nine studies were classified in this category. Of these, three considered the cleansability outcome in terms of

removal of bacterial biofilm.²⁰⁻²² other four studies assessed the removal of the smear layer and debris after treatment,²³⁻²⁶ and two studies measured the removal of the dye injected in the root canal before instrumentation (Appendix S3).^{27,28}

Four studies found no statistically significant difference between the two groups.^{20,21, 24, 27} Four studies reported that the cleaning was better when mSST files were used instead of rNiTi files.^{23,25,26,28} Only one study reported that rNiTi files were significantly more effective than mSST files in removing the bacterial biofilm.²²

A meta-analysis of two RCTs^{20,22} quantifying the bacteria present after treatment did not suggest a difference between rNiTi and mSST group (Fig. 3b).

- Apical extrusion of intracanal debris

Two studies performed by the same research group evaluated the weight of dentine debris and the volume of irrigant apically extruded in mandibular premolar teeth during initial treatment (Appendix S4).^{29,30} Both studies reported that rNiTi files extrude significantly less intracanal debris than mSST files.^{29,30} However, given the differences in the operative protocol among the two studies, no meta-analysis was performed.

- Transportation and centring ability

Seven studies were classified in this category (Appendix S5). Two out of the three studies that evaluated transportation using standardized radiographs, reported that rNiTi files produce significantly less canal transportation and display better centring ability than mSST files,^{31, 32} while the third study³³ and the study that examined digital radiographs³⁴ found no statistically significant difference between the two groups.

The remaining three studies evaluated transportation by using computed tomography. Two of them reported that rNiTi files cause less canal transportation and have better centring ability than mSST files.^{35,56} Conversely, the other study reported opposite results.³

Meta-analysis was performed on these three studies which provided similar quantitative outcomes regarding the amount of canal transportation.³⁵⁻³⁷ Such analysis showed that rNiTi files produce significantly less canal transportation than mSST endodontic files (Fig. 3).

DISCUSSION

The present review evaluated the currently available evidence that compared the performance between rNiTi

and mSST files for root canal treatment in both clinical and *in-vitro* studies. Though the methodological quality of the included studies was adequate in *in vitro* studies, the considerable heterogeneity and the limited number of clinical studies available for meta-analyses prevented to drawing reliable conclusions about the topics investigated. Additionally, it is questionable that randomised controlled studies will be carried out using manual preparation techniques when in clinical practice these have been super-seeded by NiTi instruments.

In spite of using broad selection criteria, only four comparative clinical studies relevant to the aim of the present review could be included. Two of these reported data regarding a large cohort of patients and one of the primary outcomes (i.e. healing rate after treatment).^{18,19} However, since selection bias may have occurred due to their retrospective nature, they were judged at high risk of bias. Each of the outcomes of interest of this review is described below.

- *Intra-canal bacterial reduction.* The elimination or reduction of intracanal bacteria remains a primary objective for successful treatment of apical periodontitis.³⁸ This is accomplished by a combination of mechanical instrumentation, various irrigation solutions, and antibacterial medicaments or dressings placed into the canal.³⁹ Chemo-mechanical instrumentation is often the first means of bacterial reduction during root canal treatment.¹⁶ The finding of the current review was similar to what reported in previous studies showing that rNiTi files are as efficient as mSST files in reducing root canal flora.^{16,17} A previous review concluded that mSST files and rNiTi files showed no difference in their respective ability to eliminate residual intracanal infection after instrumentation.⁴⁰ The substantial bacterial reduction was achieved with progressive filing, regardless of file type, and neither of the techniques could predictably render canals free of bacteria.

- *Success rate after treatment.* The goal of root canal treatment is to eliminate diseased pulpal tissue and to create an environment that will allow for healing of periapical tissues and prevent the development of apical periodontitis.⁴¹ Through the removal of diseased tissue, sealing of the canal system, and subsequent restoration of the coronal tooth structure, affected teeth may be retained.¹⁴ An extensive literature has been published on the success of root canal treatment, but considerable variability exists among study protocols as well as among reported outcomes.⁴² Differences include the length of recall, radiographic interpretation, experience of practitioners, success criteria adopted and methods for assessment of treatment outcomes.³⁹ Thus, treatment outcomes and success rates differ significantly, and their comparison is often unfeasible. Some studies define treatment success based upon strict radiographic healing, whereas others consider a root canal-treated tooth a

success if it remains still present and functioning in the oral cavity.⁴²⁻⁴⁴ In the current review, rNiTi files proved to be as efficient as mSST endodontic files regarding tooth success.¹⁹ However, rNiTi files achieved better success rate than mSST files concerning periapical healing.¹⁸

A more recent review that evaluated success rates after preparation with NiTi instruments⁴⁵ had the following findings. Evidence from two studies suggested that the use of NiTi, either hand or rotary, instruments significantly increased success rates of primary root canal treatment compared with the use of mSST instruments.^{18,46} Conversely, other three investigations failed to show any significant difference in treatment outcomes between NiTi and SST instruments.^{19,47,48} Schäfer & Bürklein (2012)⁴⁵ acknowledged that such contradictory results might be due to heterogeneity in the investigations' design, and provided a qualitative description of the included studies. Thus, all studies were classified as having the same level of evidence (2b [Individual cohort study (including low-quality RCT; e.g., <80% follow-up)] according to the classification proposed by the Oxford Center for Evidence-based Medicine). As opposed to the present review, the authors⁴⁵ did not evaluate the risk of bias for each study, failing to evidence potential flaws of the included studies. Nevertheless, the authors concluded that there is not sufficient evidence to adopt NiTi files instead of continuing using the traditional instruments. This is also aligning with the present review's findings.

- *Technical quality.* In light of the undergraduate students' performance using NiTi instruments and techniques, systematic incorporation of these systems into the preclinical and clinical curriculum and education regarding newer technologies and instruments seemed promising and advocated to improve root canal treatment quality.^{18,49,50} Also, rNiTi is backed up by its low incidence of fracture.⁵¹

- *Cleansing of the root canal.* The conclusions of this systematic review were similar to the narrative review from Vaudt *et al.* (2007),⁵² which also showed that there is no clear advantage in reducing the remaining amount of bacteria after treatment and all outcomes may be considered satisfactory with any of the techniques used. This may also suggest the need for using irrigants and intracanal medicaments, especially in necrotic teeth.⁵³

- *Apical extrusion of debris.* Pain is a frequent complication associated with orthograde root canal treatment,⁵⁴ as it has a significant impact on the quality of life.⁵⁵ Post-treatment pain may be caused by the apical extrusion of infected debris during chemo-mechanical instrumentation (Fig. 4), which can generate an acute inflammatory response.^{56,57} A recent randomized study reported that postoperative pain was significantly lower

in patients undergoing root canal instrumentation with rotary instruments as compared with the reciprocating single-file technique.⁵⁸ The amount of extruded debris may be primarily affected by the device movement (i.e. rotary vs. translational) and by the relationship between canal size and instrument size (e.g. such as crown down vs. early preparation to length). A study investigated the quantity of apical debris produced in vitro using two manual and two rotary instrumentation techniques reported that manual rotational movement produces less extrusion than with the step-back technique.⁵⁹ In a review by Nair *et al.* (2005),⁶⁰ it was concluded that all instrumentation techniques provide apical extrusion of debris even when the preparation is maintained at the apical terminus, the difference lies in the ability of some techniques to extrude less debris than others. Findings from the present review are in line with other studies^{61,62} that also showed that rNiTi instruments, especially when combined with copious irrigation, may extrude less debris than methods based on mSST instruments. This may also be attributed to the greater elasticity of the NiTi files that enables a more centered canal preparation with less transportation and incidence of canal aberrations as compared to mSST files.⁶³ Hence, to decrease the amount of apical extrusion of debris, the use of rNiTi instrumentation may be recommended. Nevertheless, NiTi files display a slightly higher incidence of instrument breakage or rupture than mSST instruments.⁶⁴ Though there is no clear evidence that a retained fragment into the canal may jeopardize the outcomes of the treatment,⁶⁵ nor that may cause pain. The presence of a broken instrument may increase the risk for postoperative discomfort to the patients only in case an additional operative procedure is performed for its removal from the root canal.⁶⁶

- *Transportation and centring ability.*

In endodontic research, evaluation of the mean centering ratio is a measure of the ability of the instrument to stay centered in the canal; the smaller the ratio, the better the instrument remained centered in the canal (Fig. 5). The extent and direction of canal transportation are determined by measuring the greatest distance between the edge of each instrumented canal and the corresponding edge of the uninstrumented canal. The formula used for the centering ratio calculation is $(X_1 - X_2) / (Y_1 - Y_2)$, and for the transportation is $(X_1 - X_2) - (Y_1 - Y_2)$. If the result obtained from the latter calculation is 0, then no canal transportation is assumed.⁶⁷ All root canal preparation techniques considered in the current review produced canal transportation. However, rNiTi instruments showed less canal transportation and a better centring ability than techniques based on mSST files, a finding which is also supported by a narrative review.⁵² This may be attributed to the increased

flexibility of the NiTi files as compared with SST instruments and to the different preparation techniques. The centring ability varied amongst the different NiTi systems, possibly due to the different flexibility, size, and taper of each system. On the other hand, though NiTi files might lead to a more centred canal shape that is very close to the original shape, they have a tendency of straightening the root canal when the instrument is left too long within the canal, causing reduction of the dentine wall thickness in the apical direction which can increase the risk of root fracture.⁶⁸

CONCLUSIONS

The present systematic review found no clear evidence to recommend one file type versus another concerning cleansing of the root canal when instrumentation is associated with irrigation regimen. Conversely, there was *in vitro* evidence suggesting that NiTi instruments may achieve better results than SST ones when considering apical extrusion of debris and centring ability.

There were only two randomized clinical studies that investigated the effect of using rNiTi versus mSST files, and there was no significant difference between both groups. The rNiTi was superior to mSST when *in vitro* studies compared the canal transportation and apical extrusion. However, all the meta-analyses were based on an insufficient number of cases. Thus, the results emerged should be interpreted with caution. Furthermore, direct comparisons among the various studies are difficult, due to different experimental set-up, aims and investigated parameters. With no reason of doubt, more standardized homogenous clinical studies are needed.

The choice of a particular type of endodontic file for the preparation of the root canal should take into account that any type of instrument has its specific indications, advantages, and limitations, which means that rNiTi and mSST files systems are not completely interchangeable.

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LEGENDS

Figure legends

Figure 1. Flowchart of the study selection process.

Figure 2. Risk of bias summary: reviewers' judgements about each risk of bias item for each included study.

Figure 3. Forest plots comparing the following endodontic success outcomes between manual nickel-titanium versus control group: bacteria remaining after clinical treatment between (a), bacteria remaining after in vitro treatment (b), and in vitro canal transportation (c).

Figure 4. Apical extrusion of intracanal debris during root canal preparation aided by an endodontic file.

Figure 5. Radiographic cross-sectional tooth image displaying the landmarks used for calculation of canal transportation and centering ratio. Uninstrumented canal (a), instrumented canal (b). Where X and Y are the shortest mesial and distal distance, respectively, from the root surface to the canal surface. 1, uninstrumented canal measurement; 2, instrumented canal measurement; M, mesial; D, distal; B, buccal; P, palatal.

Table legend

Table 1. Clinical studies comparing rotary nickel-titanium versus manual stainless steel instruments.

Supporting information

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Proposed Protocol.

Appendix S2. Full-text excluded articles and reasons for the exclusion.

Appendix S3. Articles evaluating the cleansing capacities with rotary nickel-titanium versus manual stainless steel instruments on extracted human teeth.

Appendix S4. Articles evaluating the amount of apical extrusion of debris with rotary nickel-titanium versus manual stainless steel instruments on extracted human teeth.

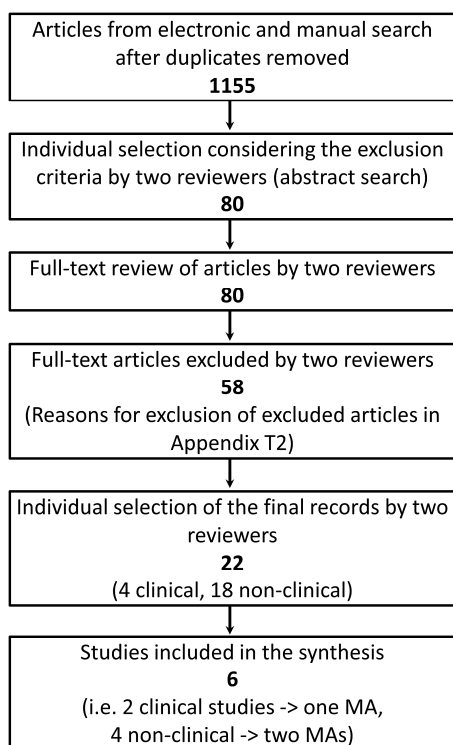
Appendix S5. Articles evaluating transportation and centering ability with rotary nickel-titanium versus manual stainless steel instruments on extracted human teeth.

Appendix S6. Further risk of bias summary: reviewers' judgements about each risk of bias item not included in Figure 2 for each included study.

Appendix S7. Risk of bias summary: reviewers' judgements about each risk of bias item presented as percentages across the two randomized control trials (Dalton *et al.* 1998, Subramaniam *et al.* 2013) reporting intracanal bacterial reduction outcome.

Appendix S8. Risk of bias summary: reviewers' judgements about each risk of bias item presented as percentages across the two retrospective studies (Cheung & Liu 2009, Fleming *et al.* 2010) reporting success outcome.

FIGURES

Figure 1. Flowchart of the study selection process.**Figure 2.** Risk of bias summary: reviewers' judgements about each risk of bias item for each included study.

- + Low risk
- High risk
- ? Unclear
- Not applicable

	Random sequence generation	Allocation concealment	Blinding of outcome assessment	Incomplete outcome data	Selective reporting
Dalton et al 1998	+	+	+	+	+
Subramaniam et al 2013	-	-	+	+	+
Cheung & Liu 2009	—	—	-	+	+
Fleming et al 2010	—	—	?	+	+

Figure 3. Forest plots comparing the following endodontic success outcomes between manual nickel-titanium versus control group: bacteria remaining after clinical treatment between (a), bacteria remaining after in vitro treatment (b), and in vitro canal transportation (c).

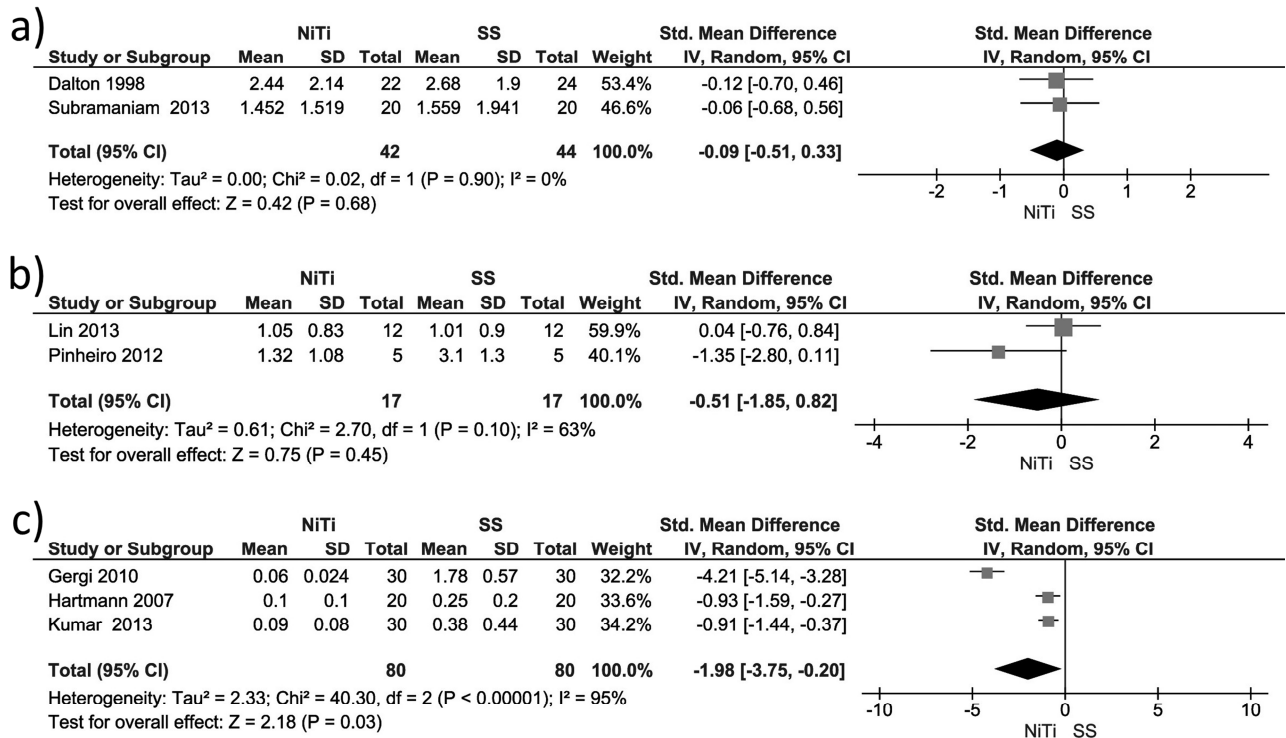
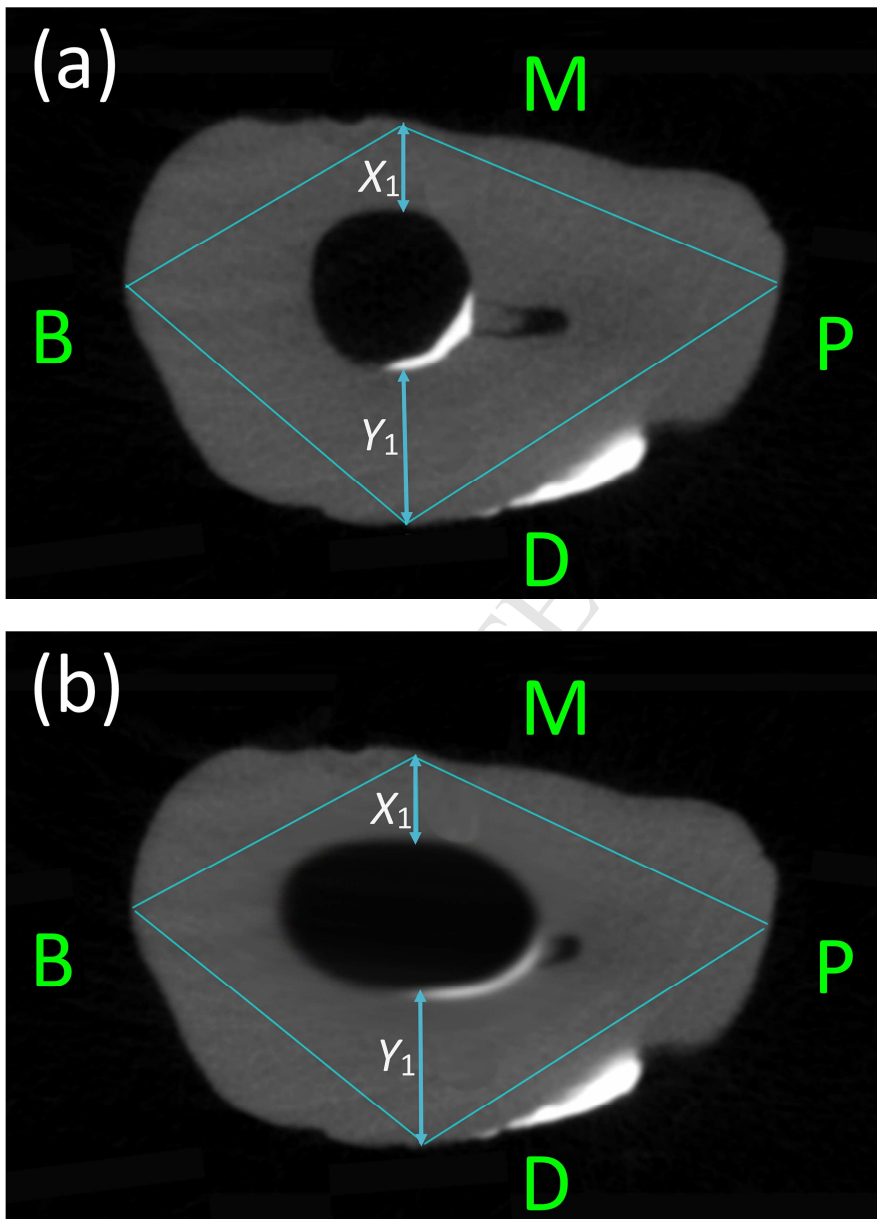


Figure 4. Apical extrusion of intracanal debris during root canal preparation aided by an endodontic file.



Figure 5. Radiographic cross-sectional tooth image displaying the landmarks used for calculation of canal transportation and centering ratio. Uninstrumented canal (a), instrumented canal (b). Where X and Y are the shortest mesial and distal distance, respectively, from the root surface to the canal surface. 1, uninstrumented canal measurement; 2, instrumented canal measurement; M, mesial; D, distal; B, buccal; P, palatal.



TABLES

Table 1. Clinical studies comparing rotary nickel-titanium versus manual stainless steel instruments

Study ID	Study design	# rNiTi-treated teeth	# mSST-treated teeth	Type of irrigant	Outcomes of interest	Study risk of bias
<i>Intracanal bacterial reduction</i>						
Dalton <i>et al.</i> 1998 ¹⁶	RCT	24	24	1% NaOCl, 5% sodium thiosulfate solution and sterile saline irrigation	Both groups presented similar ability to reduce intracanal bacteria.	Low
Subramaniam <i>et al.</i> 2013 ¹⁷	RCT	20	20	1% NaOCl	Both groups presented similar ability to reduce intracanal bacteria.	High
<i>Success rate after treatment</i>						
Cheung & Liu 2009 ¹⁸	Retrosp	110	115	1- 2.5% NaOCl and 17% EDTA	Teeth root canals prepared with rNiTi system presented higher success in terms of signs of periapical healing compared to teeth prepared with mSST.	High
Fleming <i>et al.</i> 2010 ¹⁹	Retrosp	525	459	Interchanging 5.25% NaOCl and 3% H2O2	Both groups presented similar tooth success.	Unclear

Study ID, First author and year of publication; RCT, randomized clinical trial; Restrosp, retrospective; rNiTi, rotary nickel-titanium; SST, stainless-steel; mSST, manual stainless-steel. NaOCl, Sodium Hypochlorite.

Supplementary data

Appendix S2. Full-text excluded articles and reasons for the exclusion

Main reason of exclusion (n)	Articles excluded
Clinical (3)	
Missing a mSST files group (1)	Rocas & Siqueira 2013
Missing a rNiTi files group (1)	Pettiette <i>et al.</i> 1999
A questionnaire-based study (1)	Abu-Tahun <i>et al.</i> 2014
In vitro (55)	
Non randomized study (35)	Gambill <i>et al.</i> 1996; Harlan <i>et al.</i> 1996; Samyn <i>et al.</i> 1996; Tharuni <i>et al.</i> 1996; Coleman & Svec 1997; Ferraz <i>et al.</i> 2001; Garip & Günday 2001; Park <i>et al.</i> 2001; Schäfer & Schlingemann 2003; Hulsmann & Bluhm 2004; Guelzow <i>et al.</i> 2005; Tasdemir <i>et al.</i> 2005; Zmener <i>et al.</i> 2006; Gergi & Sabbagh 2007; Khadivi Nia Javan <i>et al.</i> 2007; Matwychuk <i>et al.</i> 2007; Gu <i>et al.</i> 2008; Hammad <i>et al.</i> 2008; Kustarcı <i>et al.</i> 2008; Somma <i>et al.</i> 2008; Unal <i>et al.</i> 2009; Madhusudhana <i>et al.</i> 2010; Yin <i>et al.</i> 2010; Ghivari <i>et al.</i> 2011; Madan <i>et al.</i> 2011; Nordmeyer <i>et al.</i> 2011; Rhodes <i>et al.</i> 2011; Zmener <i>et al.</i> 2011; Jayasenthil <i>et al.</i> 2012; Mollo <i>et al.</i> 2012; Rodig <i>et al.</i> 2012; Celik <i>et al.</i> 2013; Zuolo <i>et al.</i> 2013; Rödig <i>et al.</i> 2014a; Rödig <i>et al.</i> 2014b
Study on orthograde endo-retreatment (13)	Barrieshi-Nusair 2002; Masiero <i>et al.</i> 2005; Kosti <i>et al.</i> 2006; Schirrmeister <i>et al.</i> 2006; Saad <i>et al.</i> 2007; Giuliani <i>et al.</i> 2008; Pirani <i>et al.</i> 2009; Duarte <i>et al.</i> 2010; Fenoul <i>et al.</i> 2010; Fariniuk <i>et al.</i> 2011; Akpınar <i>et al.</i> 2012; Khalilak <i>et al.</i> 2013; Yadav <i>et al.</i> 2013
Use of resin blocks (3)	Schäfer <i>et al.</i> 2001; Schäfer & Florek 2003; Perez <i>et al.</i> 2005
Use of mNiTi files (2)	Goldberg <i>et al.</i> 2002; Pataký <i>et al.</i> 2002
Only creating glide path (1)	D'Amario <i>et al.</i> 2013
Use of animal teeth (1)	Bueno <i>et al.</i> 2006
rNiTi, rotatory nickel-titanium; SST, stainless-steel; mSST, manual stainless-steel.	

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Appendix S3. Articles evaluating the cleansing capacities with rotary nickel-titanium versus manual stainless steel instruments on extracted human teeth

Study ID	Study risk of bias	# extracted teeth in total	Teeth characteristics	Type of files	Cleansing techniques outcome
Smear layer and debris *					
Manjunatha <i>et al.</i> (2013) ²³	Low	30	Premolar, single-rooted	ProFile rNiTi mSST K-Fexofiles	The manual technique was superior in cleaning the canals compared to the rotary instrument.
Bechelli <i>et al.</i> (1999) ²⁴	Low	20	Anterior, single-rooted	LightSpeed rNiTi mSST Hedstroem	No significant differences between the two groups.
Ahlquist <i>et al.</i> (2001) ²⁵	Low	30	20–25 degree curved canals	ProFile rNiTi mSST S-files	The manual technique was significantly superior than the rotary technique.
Schäfer & Lohmann (2002) ²⁶	Low	48	25-35 degrees curved canals	rNi-Ti Flex Master mSST K-Flexofiles	The manual technique cleaned significantly better than the rotary technique. The rotary instruments maintained the original curvature significantly better.
Biofilm *					
Pinheiro <i>et al.</i> (2012) ²⁰	Unclear	15 (45 root canals)	primary molars, moderate root angulation	ProTaper rNiTi mSST K-files Hybrid technique	No significant differences between the rotary and manual techniques to reduce bacteria. The rotary technique produced the lowest amount of smear layer and required shorter instrumentation time.
Chuste-Guillot <i>et al.</i> (2006) ²¹	Low	64	Single-rooted	ProFile rNiTi HERO 642 rNiTi GT rNiTi mSST K-Flexofiles	The rNiTi techniques were as efficient to reduce the bacterial rate as the mSST instrumentation.
Lin <i>et al.</i> (2013) ²²	Low	36 (6 received no treatment)	Single-rooted with oblong canals	ProFile rNiTi SAF compressible rNiTi mSST K-file	All techniques equally removed bacteria in the main canal. SAF reduced significantly more bacteria than the other two techniques within the standardized apical groove.
Dye *					
Azar <i>et al.</i> (2011) ²⁷	Low	140	70 primary 70 permanent	Mtwo rNi-Ti mSST K-files	No significant differences between the two groups to cleaning the canals.
Nazari Moghaddam <i>et al.</i> (2009) ²⁸	Low	23 (68 canals)	primary posterior	rNi-Ti Flex Master mSST K-files	Manual technique was significantly better to clean than the rotary technique only at the coronal third. The rotary technique was significantly less time consuming.

Study ID, Frist author and year of publication; rNiTi, rotary nickel-titanium; mSST, manual stainless-steel; SAF, self-adjusting file.

*Type of substrate tested

Appendix S4. Articles evaluating the amount of apical extrusion of debris with rotary nickel-titanium versus manual stainless steel instruments on extracted human teeth

Study ID	Study risk of bias	# extracted teeth in total	Teeth characteristics	Type of irrigant	Type of files	Apical extrusion outcome
Kustarci <i>et al.</i> (2008) ²⁹	Low	45	Mandibular premolars, single-rooted	9 ml of 0.9% NaOCl	ProTaper rNiTi K3 rNiTi mSST K-files	Rotary systems extruded significantly less apical debris than manual technique. Among rotary systems, ProTaper was the superior.
Kustarci <i>et al.</i> (2008) ³⁰	Low	60	Mandibular premolars, single-rooted, 0-10 degrees curved canals	7 mL of 2.5% NaOCl	RaCe rNiTi K3 rNiTi FlexMaster rNiTi mSST K-file	There was no significant difference among all groups regarding debris or irrigant extrusion. The rotary systems were associated with less apical extrusion and irrigant.

Study ID, First author and year of publication; rNiTi, rotatory nickel-titanium; mSST, manual stainless-steel; SAF, self-adjusting file.

Appendix S5. Articles evaluating transportation and centering ability with rotary nickel-titanium versus manual stainless steel instruments on extracted human teeth



















Study ID	Study risk of bias	# extracted teeth in total	Teeth characteristics	Type of files	Transportation and centering outcome
Computed Tomography*					
Kumar <i>et al.</i> (2013) ³⁵	Low	90	Mandibular premolar, single-rooted, 10-20 degrees curved canals	Twisted rNiTi Hyflex CM rNiTi mSST K-flexofile	Manual technique showed highest transportation and less centered when compared to rotary systems.
Gergi <i>et al.</i> (2010) ³⁶	Low	90	Single-rooted, 25-35 degrees curved canals	Twisted rNiTi Pathfile-ProTaper rNiTi mSST K-file	The manual technique showed significantly higher transportation. Among rotary systems, Twisted rNiTi performed significantly better.
Hartmann <i>et al.</i> (2007) ³⁷	Low	60	Maxillary molars, 20-40 degrees curved canals	mSST K-file oscillatory SST K-file rNiTi ProTaper	The manual technique produced significantly less canal transportation than the oscillatory and rotary techniques.
Standardized radiographs*					
Alves Vde O <i>et al.</i> (2012) ³³	Low	45	Mandibular first and second molars, 25-35 degrees curved canals	PathFile rNiTi Mtwo rNiTi mSST K-file	All groups had no effect on apical transportation.
Pereira <i>et al.</i> (2012) ³¹	Low	60	Mandibular incisors	mSST K-Flexofile mNiTi ProTaper Universal rNiTi ProTaper Universal	Rotatory technique showed significantly less apical deformation than the manual techniques.
Esposito & Cunningham (1995) ³²	Low	45	20-45 degrees curved canals	mSST K-Flex mNiTi Mac rNiTi	Nickel-titanium instruments significantly maintained the original canal path compared with stainless steel files when the apical preparation was enlarged to size 35 or higher.
Digital radiographs*					
Mikrogeorgis <i>et al.</i> (2006) ³⁴	Low	40	Mandibular incisors	rNiTi ProFile mSST Hedström	No significant difference in terms of configuration and enlargement of the canals.

Study ID, First author and year of publication; rNiTi, rotatory nickel-titanium; mNiTi, manual nickel-titanium; mSST, manual stainless-steel.

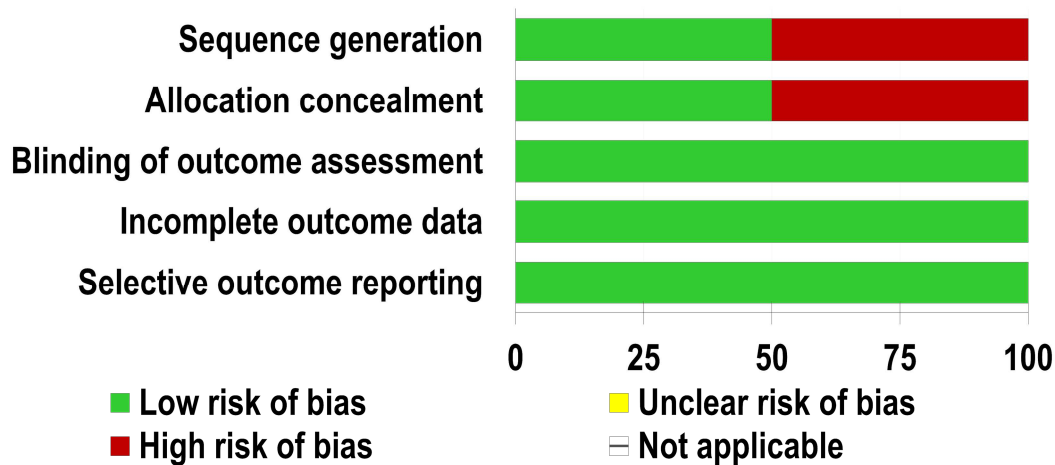
*Scanning method

Appendix S6. Further risk of bias summary: reviewers' judgements about each risk of bias item not included in Figure 2 for each included study.

-  Low risk
-  High risk
-  Unclear
- Not applicable

	Blinding of participants and personnel	Comparability of control and treatment group	Clear definition of inclusion and exclusion criteria	Clear definition of outcome assessment and success criteria	Recall rate	Sample size calculation	Number of endodontists involved
Dalton et al 1998	—				—		
Subramaniam et al 2013	—				—		
Cheung & Liu 2009	—				—	—	
Fleming et al 2010	—				—	—	

Appendix S7. Risk of bias summary: reviewers' judgements about each risk of bias item presented as percentages across the two randomized control trials (Dalton et al. 1998, Subramaniam et al. 2013) reporting intracanal bacterial reduction outcome.



Appendix S8. Risk of bias summary: reviewers' judgements about each risk of bias item presented as percentages across the two retrospective studies (Cheung & Liu 2009, Fleming *et al.* 2010) reporting success outcome.

