

Pulpotomy for carious pulp exposures in permanent teeth: A systematic review and meta-analysis

Yuanyuan Li^a, Bingdong Sui^{a,b}, Christian Dahl^c, Brian Bergeron^c, Peter Shipman^d, Lina Niu^{a,c,**}, Jihua Chen^{a,c,**}, Franklin R. Tay^{a,c,*}

^a State Key Laboratory of Military Stomatology & National Clinical Research Center for Oral Diseases & Shaanxi Key Laboratory of Oral Diseases, Department of Prosthodontics, School of Stomatology, The Fourth Military Medical University, 145 Changle West Road, Xi'an, Shaanxi 710032, PR China

^b State Key Laboratory of Military Stomatology & Center for Tissue Engineering, School of Stomatology, The Fourth Military Medical University, 145 Changle West Road, Xi'an, Shaanxi 710032, PR China

^c Department of Endodontics, The Dental College of Georgia, Augusta University, 1430, John Wesley Gilbert Drive, Augusta, GA 30912-1129, USA

^d Greenblatt Library, Augusta University, 1430, John Wesley Gilbert Drive, Augusta, GA 30912-1129, USA

ARTICLE INFO

Keywords:

Cost-benefit analysis
Dental caries
Meta-analysis
Pulpotomy
Pulpitis
Systematic review

ABSTRACT

Objectives: The most commonly-accepted strategy for managing irreversible pulpitis, an irreversible condition of dental pulp inflammation, is root canal treatment, which is limited by high costs and complex techniques. High success rates have been reported for the use of pulpotomy in managing pulp exposure resulting from extensive caries. The objective of the present work was to evaluate the effectiveness and cost-effectiveness of pulpotomy and associated medicaments in saving permanent teeth with pulp exposure resulting from extensive caries.

Sources: Multiple databases were searched on January 12, 2019, without limitations on the language or year of publication.

Study selection: Randomized controlled trials comparing pulpotomy with alternative treatments, or comparing two or more medicaments in pulpotomy for permanent teeth with carious pulp exposure were included.

Data: Seventeen studies reported in 21 articles were included. Intention-to-treat analyses on studies comparing pulpotomy and other treatment modalities tended to favor pulpotomy. Meta-analysis was not performed on comparisons of pulpotomy and other treatments because of the limited number of studies. Most evidence on comparisons among different pulpotomy medicaments was found in trials comparing mineral trioxide aggregate (MTA) and calcium hydroxide, with the results of meta-analyses favoring MTA. Data were insufficient to determine the cost-effectiveness of successful modality.

Conclusions: Pulpotomy is a prospective substitute for root canal treatment in managing permanent teeth with carious pulp exposures, even in permanent teeth with irreversible pulpitis. Large, well-designed trials comparing pulpotomy with other treatments in terms of cost-effectiveness should be informative.

Clinical significance: The success of pulpotomy in managing irreversible pulpitis challenges the rhetoric that irreversible pulpitis can only be managed by root canal treatment. Cost-effectiveness analysis rather than analysis on effectiveness of treatment outcome alone should be considered in all health care domains to evaluate the benefits of alternative treatment options.

1. Introduction

Untreated decay in permanent teeth is the most prevalent disease globally [1]. According to the Global Burden of Disease Study 2015, the age-standardized prevalence of untreated carious permanent teeth is 34.1%, with 2.5 billion people affected annually [1]. Deep caries and extensive restorative procedures with exposure or near-exposure of the

dental pulp invariably result in irreversible pulpitis, an irreversible condition of pulpal inflammation [2]. Irreversible pulpitis is commonly accompanied by spontaneous intermittent pain or continuous pain, although no symptoms may be found in some cases [2]. Vital pulp therapy comprises modalities such as direct pulp capping, pulpotomy, and an emerging family of regenerative pulp therapy; judicious application of these procedures enables apical closure and root development

* Corresponding author at: The Dental College of Georgia, Augusta University, 1430, John Wesley Gilbert Drive, Augusta, GA 30912-1129, USA.

** Corresponding authors at: School of Stomatology, The Fourth Military Medical University, 145 Changle West Road, Xi'an, Shaanxi 710032, PR China.

E-mail addresses: niulina831013@126.com (L. Niu), jhchen@fmmu.edu.cn (J. Chen), ftay@augusta.edu (F.R. Tay).

in immature permanent teeth by preserving the vitality of pulp tissues [3]. The primary difference between pulpotomy and direct pulp capping lies in the amount of pulp tissues removed: the coronal pulp tissues are removed in the former procedure, while considerably less pulp tissues are removed in the latter procedure. Pulpectomy followed by root canal treatment, in which all the pulp tissues are removed and replaced with biologically-inert materials, is the most commonly-accepted strategy for managing irreversible pulpitis in mature permanent teeth. Nevertheless, these procedures are costly and technically demanding [3]. Recent advancements in biomaterials research and knowledge on pulp biology have significantly improved the success rates of pulpotomy on inflamed dental pulps [4], even for treatment of irreversible pulpitis in permanent teeth [5,6]. Previous systematic reviews reported that the success rates of pulpotomy in the treatment of carious pulp exposure in permanent teeth were higher than 90% [7,8]. Those success rates were pooled primarily from data derived from case series. Regrettably, such information is ranked Level 4 according to the Oxford Center for Evidence-Based Medicine [9]. There was also no comparison with other treatment modalities.

Bioactive medicaments are placed on the exposed pulp in vital pulp therapy for the purposes of resolving inflammation and tissue formation. Calcium hydroxide is the earliest medicament employed in pulpotomy that possesses the ability to stimulate tertiary dentinogenesis. This is attributed to its high alkalinity after mixing with water [10]. Mineral trioxide aggregate (MTA) is a more recent, biocompatible and bioactive tricalcium silicate-based inorganic material utilized in vital pulp therapy. The effect of MTA on pulp tissues is analogous to calcium hydroxide because the primary soluble constituent of MTA is calcium hydroxide [11]. However, tooth discoloration, long setting time, difficult handling characteristics and high cost have emerged as its potential drawbacks [11]. Several medicaments have been developed and used in pulpotomy of permanent teeth, such as calcium-enriched mixture (CEM) cement, platelet-rich fibrin, and Biodentine (Septodont Inc., Saint-Maur-des-Fossés, France) [12]. Previous meta-analyses comparing these medicaments indicated that MTA is the most effective pulpotomy medicament in primary teeth with extensive decay [10]. For permanent teeth, indirect evaluation of weighted assembled success rates showed that calcium hydroxide was superior to MTA in partial pulpotomy (partial removal of coronal pulp tissues), while no difference was found between these two medicaments in full pulpotomy (removing all coronal pulp tissues) [8]. That analysis was handicapped by the inclusion of observational studies, which rendered the results inconclusive. Systematic review of randomized controlled trials, ranked Level 1 according to Oxford Center for Evidence-Based Medicine [9], is highly desirable in providing robust evidence on the effectiveness of pulpotomy and associated medicaments in permanent teeth.

Accordingly, a systematic review was conducted to evaluate the efficacy and cost-effectiveness of pulpotomy and associated medicaments in saving permanent teeth with pulp exposure resulting from extensive caries.

2. Methods

The present work adhered to the preferred reporting items for systematic reviews and meta-analyses [13].

2.1. Study selection

Databases including Embase, MEDLINE, Web of Science, Trip Pro, Cochrane Library, the International Clinical Trials Registry Platform and ClinicaTrials.gov were searched to identify randomized controlled trials on January 12, 2019, without limitations on the language or year of publication. Medical subject headings associated with pulpotomy were identified using keywords and relevant studies. The search strategy was developed by a librarian (PS) (Supplementary methods). Open Grey online database was used to search grey literatures. The

references of relevant articles were manually searched for further relevant studies.

Inclusion criteria included: 1) randomized or quasi-randomized controlled trials comparing pulpotomy with other treatments or no treatment, or comparing two or more medicaments in pulpotomy; 2) human permanent teeth with carious pulp exposures or pulpitis associated with caries; 3) studies reporting clinical, radiographic, or overall success rates with at least 12-month follow-up; 4) proper descriptions of success. Clinical success was described as devoid of clinical manifestations such as pain on percussion/palpation and spontaneous pain, and devoid of need for further root canal treatment [7]. Radiographic success was defined as healing or resolution of radiographic periapical lesions, and devoid of need for further root canal treatment [7]. Overall success was defined as achievement of both clinical and radiographic success [7].

Exclusion criteria were: 1) non-randomized controlled trials, non-comparative designs, qualitative studies, case studies, reviews, systematic reviews, observational studies, or animal studies; 2) glutaraldehyde or formocresol pulpotomy; 3) studies on primary teeth; 4) one treatment arm of fewer than 10 participants. Non-randomized controlled trials, non-comparative studies and observational studies were excluded because the high risk of bias associated with those studies could compromise the results of meta-analysis. Glutaraldehyde and formocresol pulpotomy were excluded because of the toxicity of the medicaments. Studies with fewer than 10 participants in one treatment arm were considered non-representative.

Two investigators (YL and CD) screened all the searched titles and abstracts independently and evaluated the retrieved full texts of potentially qualified studies. When the same results of the same subjects were reported in more than one paper, the study with the maximum subjects was included.

2.2. Data collection

Data were extracted separately by two investigators (YL and CD). The following data were collected from each included paper: study characteristics (year of publication, country), population characteristics (age of participants, condition of teeth before treatment, number of teeth allocated, number of teeth at follow-ups), treatments and associated medicaments, and results (overall, clinical, and radiographic success rates, root growth, apical closure). For studies reporting cost-effectiveness, the following data were also collected: study characteristics (currency, perspective) and results (incremental cost effectiveness ratios). Authors of eligible studies were contacted for usable but unreported data.

2.3. Quality evaluation

Two investigators (YL and BB) evaluated the quality of the included studies independently, in accordance with the Cochrane Handbook for Systematic Reviews of Interventions 5.1.0 [14] and the Grading of Recommendations Assessment, Development and Evaluation [15]. Details of criteria used in the present work are included in Supplementary Table 1.

All disagreements during study selection, data extraction, and quality assessment were discussed with a third investigator (FT) to arrive at a consensus.

2.4. Data synthesis and statistical analyses

Primary outcomes formulated after data collection included overall, clinical or radiographic success at 12 months. Secondary outcomes included: 1) overall, clinical, or radiographic success at longer follow-up periods; and 2) root growth or apical closure (for immature permanent teeth only). Success rates were evaluated using two dissimilar definitions: 1) all the subjects allocated were evaluated and drop-outs were

regarded as failure; 2) only subjects who were examined at follow-ups were evaluated. Meta-analyses were subsequently conducted on all the subjects allocated, by following the intention-to-treat principle, to calculate more conservative figures of success rates. The different types of MTA were combined. When two or more articles reported the same outcome, data were pooled using the Mantel-Haenszel tests. The meta-analyses focused on the outcomes at 12 months. Odds ratios were calculated in the meta-analyses. If two or more articles reported the same outcome at longer follow-up periods, the data were also pooled. Fixed-effect analysis was performed because of the small number of studies [10]. Heterogeneity of the studies was analyzed using the I^2 statistic. The origins of heterogeneity were delved by the following pre-specified subgroup analyses: 1) type of teeth (immature versus mature teeth); 2) sample size (< 200 versus ≥ 200 subjects). Sensitivity analyses were performed by pooling the data with large studies omitted (if identified) to detect their effect on the outcomes. Egger's test was applied to funnel plots to identify publication bias [16] when sufficient studies (> 10) existed [17]. The RevMan 5.2 (Nordic Cochrane Centre) software was used for all analyses.

3. Results

3.1. Search results

The logistics for study selection are depicted in Fig. 1. After title and abstract screening, 88 articles were considered potentially relevant and retrieved for eligibility assessment. Seventeen studies reported in 21 articles were included in the systematic review: four studies comparing

pulpotomy and other treatment modalities (three trials reported in six articles [18–23] and one ongoing trial from the trial registry [24]) and 13 studies comparing pulpotomy using different medicaments (nine trials reported in ten articles [25–34] and four ongoing trials from the trial registries [35–38]). Reasons for exclusion of each full-text article are listed in Supplementary Table 2.

3.2. Studies comparing pulpotomy and other treatment modalities

All studies were performed on mature permanent teeth with carious pulp exposures. Three articles reported outcomes from follow-ups at different time points of the same trial [20–22]. Two articles reported outcomes from follow-ups at different time points of another trial [18,19]. Three studies compared the efficacy of pulpotomy with root canal treatment [20–24]. One study compared pulpotomy with direct pulp capping [18,19]. Data retrieved from these studies are included in Table 1 and Supplementary Table 3.

The risk of bias of each evaluated trial is included in Supplementary Table 4. Overall, no trial was considered low risk of bias in all items. All trials had high risk with regard to performance bias resulting from the lack of blinding of participants and/or clinicians. Three trials [18–23] that reported details of randomization and allocation concealment were considered as low risk of selection bias. Reporting bias, attrition bias, and other kinds of bias were not detected in the three trials [18–23].

Intention-to-treat pair-wise analyses based on reported data from one trial [19] showed that pulpotomy using calcium hydroxide had higher radiographic success rate at 60 months compared with direct pulp capping (odds ratio, 3.58, 95% confidence interval (CI), 1.05 to

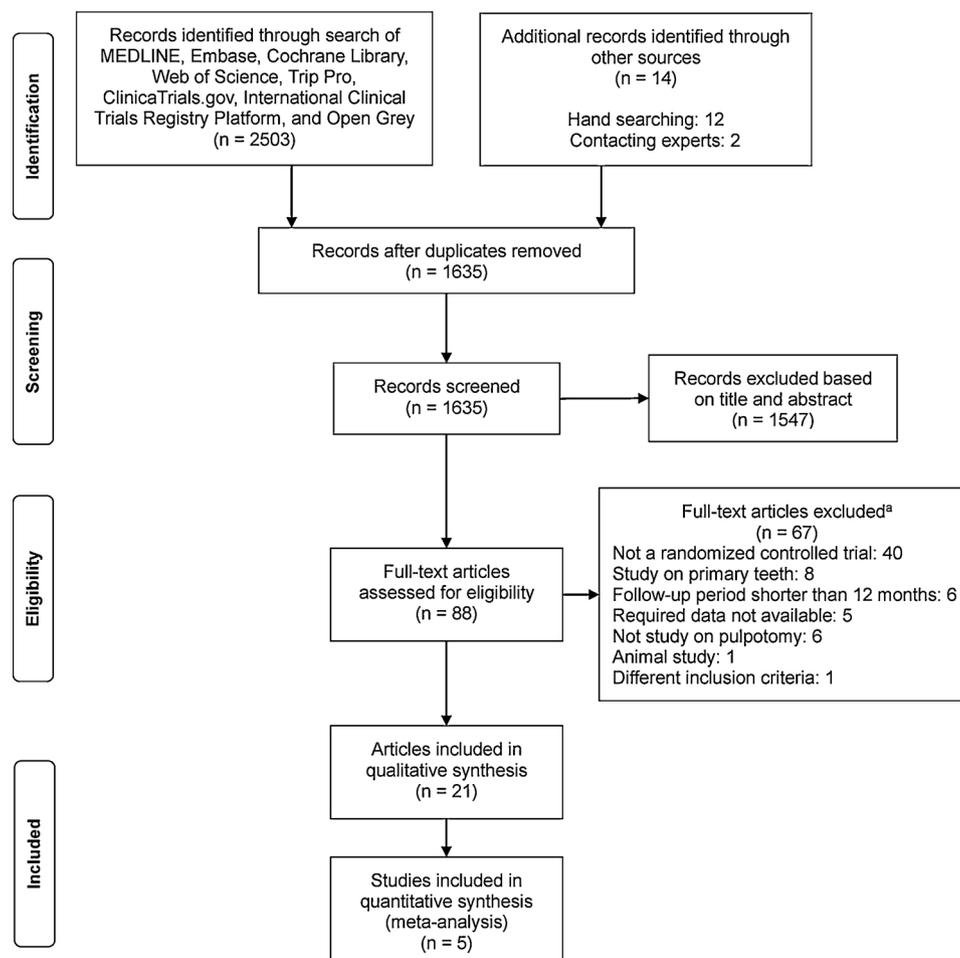


Fig. 1. Flowchart of study selection.

^aSome studies were excluded for more than one reason.

Table 1
Characteristics of studies comparing pulpotomy and other treatment modalities for permanent teeth with carious pulp exposures.

Study, year	Country	Condition of teeth before treatment	Mean age (range)	Type of pulpotomy	Medicaments (number of teeth treated)	Restoration	Follow-up period (months)
Asgary et al. [20,21,22], 2013, 2014, 2015	Iran	Mature permanent molars with irreversible pulpitis associated with extensive caries	NA	Complete coronal pulpotomy	Pulpotomy using calcium-enriched mixture cement, root canal treatment (205, 202)	Amalgam	6, 12, 24, 60
Björndal et al. [18,19], 2010, 2017	Denmark, Sweden	Mature permanent teeth with carious pulp exposures	NA	Partial pulpotomy	Pulpotomy using calcium hydroxide, direct pulp capping using calcium hydroxide (31, 27)	Resin composite	12, 60
Galani et al. [23], 2017	India	Mature permanent molars with carious pulp exposures	22 (12–50)	Complete coronal pulpotomy	Pulpotomy using white mineral trioxide aggregate, root canal treatment (27, 27)	Resin composite	3, 6, 9, 12, 15, 18
NCT02727088 [24], ongoing	France	Mature permanent molars with carious pulp exposures or pulpitis associated with extensive caries	≥18	Complete coronal pulpotomy	Pulpotomy using tricalcium silicate cement ^a , root canal treatment (113, 113) ^b	Resin composite	6, 12, 24

NA = not available.

^a Based on data provided by the authors.

^b Target sample size.

12.19, $P = 0.04$; Supplementary Table 5). No difference was detected in the other outcomes of this trial (Supplementary Table 5). Intention-to-treat pair-wise analyses based on reported data from the other trials (pulpotomy with CEM cement versus root canal treatment; pulpotomy using MTA versus root canal treatment) found no difference in clinical, radiographic or overall success at 12 months (Supplementary Table 5). Because different medicaments were applied in those studies, heterogeneity across studies was presumed and no meta-analysis was performed. No study conducted cost-effectiveness analyses.

3.3. Studies comparing pulpotomy using different medicaments

Two studies reported outcomes from follow-ups at different times of the same trial [26,27]. Four studies were performed on mature permanent teeth [25–28,36]. Eight studies were performed on immature permanent teeth [29–33,35,37,38]. One study was performed on both mature and immature permanent teeth [34]. Data retrieved from these studies are summarized in Table 2 and Supplementary Table 6.

The risk of bias of each evaluated trial is included in Supplementary Table 7. Only one trial was considered low risk of bias for all domains [26,27]. The other studies had unclear or high risk with regard to selection, performance and/or detection bias. One trial was identified with a high risk with regard to attrition bias as a result of the high drop-out rate (28% (9/32)) of one treatment arm [34]. Reporting bias and other sorts of bias were not identified in all the completed trials. Ongoing trials were excluded from the meta-analysis because insufficient data were available.

Five trials compared MTA and calcium hydroxide [25,28,29,32,34]. When the data on both immature and mature permanent teeth from these five trials were pooled following the intention-to-treat principle, MTA had higher success rates in all items at 12 months and higher overall and radiographic success rates at 24 months compared with calcium hydroxide (12 months: clinical success, odds ratio, 2.23, 95% CI, 1.16 to 4.29, $P = 0.02$, $I^2 = 0\%$, Fig. 2; radiographic/overall success, odds ratio, 2.19, 95% CI, 1.16 to 4.14, $P = 0.02$, $I^2 = 0\%$, Fig. 3; 24 months: radiographic/overall success, odds ratio, 2.20, 95% CI, 1.15 to 4.20, $P = 0.02$, $I^2 = 47\%$, Fig. 4). There was no difference between MTA and calcium hydroxide in clinical success at 24 months (Supplementary Fig. 1). The quality of the evidence, however, is moderate or low (Supplementary Table 8). When the data were stratified by the type of teeth (immature and mature permanent teeth), intention-to-treat analyses identified that MTA had higher clinical and overall success rates than calcium hydroxide at 24 months in mature permanent teeth (Supplementary Table 9) [25]. There was no difference between MTA and calcium hydroxide in the other outcomes for mature permanent teeth (Supplementary Table 9). For immature permanent teeth, no difference was observed between MTA and calcium hydroxide in all treatment outcomes (Supplementary Table 10). Two trials compared MTA and CEM cement: one in immature permanent teeth [33] and one in mature permanent teeth [26,27]. Intention-to-treat pair-wise analyses based on the reported data found that MTA had higher radiographic success rate at 24 months than CEM cement in mature permanent teeth (odds ratio, 1.88, 95% CI, 1.19 to 2.97, $P = 0.007$) [27], while no difference was detected in the other outcomes (Supplementary Tables 9 and 10). The effectiveness of MTA and platelet-rich fibrin was also compared in two trials: one in immature permanent teeth [31] and one in mature permanent teeth [28]. One trial compared calcium hydroxide and platelet-rich fibrin in mature permanent teeth [28]. One trial compared MTA, triple antibiotic paste, and abscess remedy (polyoxymethylene, cresol, excipient ad, and oil of cinnamon) in immature permanent teeth [30]. Intention-to-treat pair-wise analyses based on the reported data from those trials showed no difference among the medicaments for pulpotomy in all outcomes derived from immature or mature permanent teeth (Supplementary Tables 9 and 10). Publication bias across studies included in meta-analyses could not be evaluated because of the small number of studies [17]. No study

Table 2
 Characteristics of studies comparing pulpotomy using different medicaments for permanent teeth with carious pulp exposures.

Study, year	Country	Condition of teeth before treatment	Mean age (range)	Type of pulpotomy	Medicaments (number of teeth treated)	Restoration	Follow-up period (months)
Asgary et al. [26,27], 2013, 2017	Iran	Mature permanent molars with irreversible pulpitis associated with extensive caries	NA	Complete coronal pulpotomy	Tooth-colored mineral trioxide aggregate, calcium-enriched mixture cement (208, 205)	Amalgam	12, 24, 60
Chailertvanitkul et al. [32], 2013	Australia	Immature permanent molars with carious pulp exposures and irreversible pulpitis	8.5 ^a (7–10)	Partial pulpotomy	Mineral trioxide aggregate, calcium hydroxide (44, 40)	Amalgam	3, 6, 12, 24
Eppa et al. [30], 2018	India	Immature permanent teeth with carious pulp exposures	NA (6–14)	Complete coronal pulpotomy	Mineral trioxide aggregate, triple antibiotic paste, abscess remedy (20, 20, 20)	Stainless steel crown	1, 3, 6, 9, 12, 18, 24
Keswani et al. [31], 2014	India	Immature permanent molars with carious pulp exposures	8 (6–12)	Complete coronal pulpotomy	White mineral trioxide aggregate, platelet-rich fibrin (31, 31)	Stainless steel crown	6, 12, 24
Kumar et al. [28], 2016	India	Mature permanent molars with carious pulp exposures and irreversible pulpitis	21.2 (14–32)	Complete coronal pulpotomy	Mineral trioxide aggregate, calcium hydroxide, platelet-rich fibrin (19, 18, 17)	Resin composite	6, 12
NCT03119779 [39], ongoing	Egypt	Immature permanent molars with carious pulp exposures	NA (6–9)	Partial or complete coronal pulpotomy	Mineral trioxide aggregate, resin-modified calcium silicate (TheraCal) (11, 11) ^b	Resin composite	12
NCT03166748 [38], ongoing	Egypt	Immature permanent molars with carious pulp exposures	NA (6–9)	NA	Mineral trioxide aggregate, polycarboxylate cement (25, 25) ^b	NA	3, 6, 12
NCT03426046 [35], ongoing	Turkey	Immature permanent molars with carious pulp exposures	NA (6–13)	Partial pulpotomy	Mineral trioxide aggregate, Biodentine, calcium hydroxide (18, 18, 18) ^b	Stainless steel crown	12
Nosrat et al. [33], 2013	Iran	Immature permanent molars with carious pulp exposures	8.3 (6–10)	Complete coronal pulpotomy	Mineral trioxide aggregate, calcium-enriched mixture cement (25, 26)	Amalgam or stainless steel crown ^a	6, 12
Özgür et al. [29], 2017	Turkey	Immature permanent molars with carious pulp exposures	NA (6–13)	Partial pulpotomy	White mineral trioxide aggregate, calcium hydroxide (40, 40)	Resin composite	6, 12, 18, 24
Qudeimat et al. [34], 2007	Jordan	Mature and immature permanent molars with carious pulp exposures	10.3 (6.8–13.3)	Partial pulpotomy	Grey mineral trioxide aggregate, calcium hydroxide (32, 32)	Amalgam or metal crown	12, 24
Taha et al. [25], 2017	Jordan	Mature permanent molars with carious pulp exposures and irreversible pulpitis	30.3 (20–52)	Partial pulpotomy	White mineral trioxide aggregate, calcium hydroxide (27, 23)	Amalgam or resin composite	6, 12, 24
TCTR20171228003 [36], ongoing	Thailand	Mature permanent molars with carious pulp exposures	≥ 18	Partial pulpotomy	Mineral trioxide aggregate, Biodentine (32, 32) ^b	Resin composite ^a	12

NA = not available.

^a Based on data provided by the authors.

^b Target sample size.

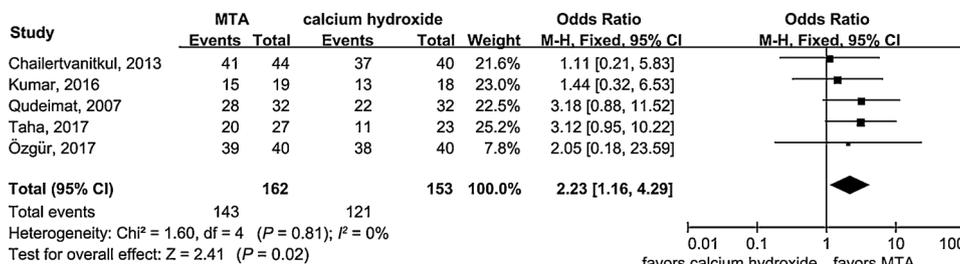


Fig. 2. Mineral trioxide aggregate versus calcium hydroxide for clinical success at 12 months. CI = confidence interval; MTA = mineral trioxide aggregate.

conducted cost-effectiveness analyses.

4. Discussion

The present work is the first systematic review of randomized controlled trials on pulpotomy of carious pulp exposures in permanent teeth. In the present systematic review, 17 randomized controlled trials were included: 13 trials reporting comparisons among different pulpotomy medicaments [25–38], three trials reporting comparisons between pulpotomy and root canal treatment [20–24], and one trial reporting comparisons between pulpotomy and direct pulp capping [18,19].

Intention-to-treat analyses on studies comparing pulpotomy and other treatment modalities tended to favor pulpotomy. However, each comparison included only one trial and the treatment effects were not different except for the comparison between pulpotomy using calcium hydroxide and direct pulp capping. Pulpotomy using calcium hydroxide had higher radiographic success rate at 60 months compared with direct pulp capping in mature permanent teeth [19].

The bulk of the evidence on comparisons among different pulpotomy medicaments was found in trials comparing MTA and calcium hydroxide [25,28,29,32,34]. Intention-to-treat analyses showed that MTA increased clinical and overall success rates at 24 months in mature permanent teeth [25]. Other outcomes tended to favor the use of MTA. For other comparisons of medicaments, each comparison included only one trial and no difference was detected except for the comparison between MTA and CEM cement. Mineral trioxide aggregate had a higher odds ratio of radiographic success at 24 months in treating mature permanent teeth, compared with CEM cement [27].

Most studies were considered low risk of bias for all domains except for high risk of performance bias associated with blinding of clinicians. Although performance bias does have an effect on evaluation of treatment outcomes, it is difficult to accomplish blinding of clinicians: for studies comparing pulpotomy and other treatment modalities, different procedures are performed; for studies comparing pulpotomy using different medicaments, diverse observable properties of different medicaments impede the fulfillment of blinding. In some studies [25,28], the clinicians (operators) were blinded prior to medicament placement. However, once they were given certain medicaments, blinding was unlikely to be continued.

The limitations of small numbers of included trials and the moderate/low quality of the evidence are offset by the comprehensive search of literature and rigorous implementation of predefined criteria. Within those limitations, pulpotomy is a prospective alternative to root canal treatment for the treatment of inflamed pulps. Pulpotomy appears to bridge the gap between root canal treatment and direct pulp capping. All the pulp tissues are removed and replaced with biologically-inert materials during root canal treatment while most of the pulp tissues are retained during direct pulp capping. In contrast, only the coronal pulp tissues are removed with the remnant pulp tissues remaining vital in the canals during pulpotomy. It has long been assumed that the success of pulpotomy depends on proper evaluation of pulpal inflammation [2]. The rhetoric that pulpotomy is contraindicated in teeth with irreversible pulpitis has been challenged by recent studies that reported long-term success of pulpotomy in managing irreversible pulpitis [5,6].

One large-scale multicentre trial included in the present review reported that in addition to a non-inferior success rate, significantly-reduced treatment time and costs were also identified in pulpotomy using CEM cement, compared with root canal treatment in managing irreversible pulpitis of permanent teeth [21]. Health technology assessment in this trial by a specialist committee concluded that pulpotomy using CEM cement outweighs root canal treatment because of the less stringent technique and apparatus requirements, lower direct and indirect costs, shorter visiting time, fewer complications and lower risk of tooth fracture [39]. Some equipment required in root canal treatment such as radiography units are not available in some poverty-stricken areas [39]. In addition, the high cost of root canal treatment is not covered by public health insurance programs in some countries [39]. A large number of patients have to forfeit their inflamed tooth or endure a painful toothache. Successful application of pulpotomy for irreversible pulpitis is an exciting challenge of the currently-accepted paradigm that the only available treatment alternatives for irreversible pulpitis are root canal treatment and tooth extraction [39]. More importantly, pulpotomy maintains vascularization and nutrition of the dental pulp, which are important in the maintenance of tooth integrity [40]. Pulpotomy in permanent teeth means more for children in that pulp vitality and function can be maintained and shorter appointments reduce concerns on children's compliance [40]. The goal of health care lies in improving welfare. Economic evaluation provides scientific evidence on costs and effectiveness of each alternative management

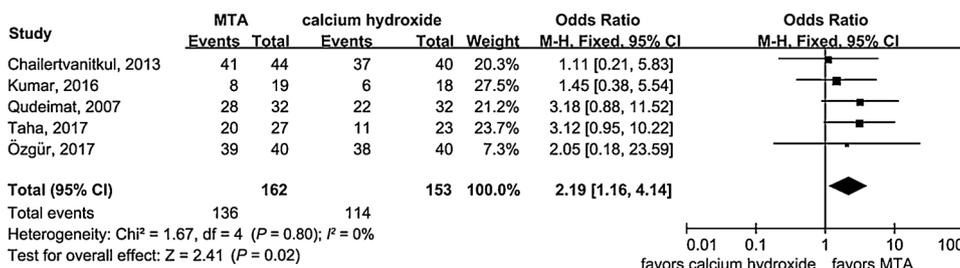


Fig. 3. Mineral trioxide aggregate versus calcium hydroxide for radiographic/overall success at 12 months. CI = confidence interval; MTA = mineral trioxide aggregate.

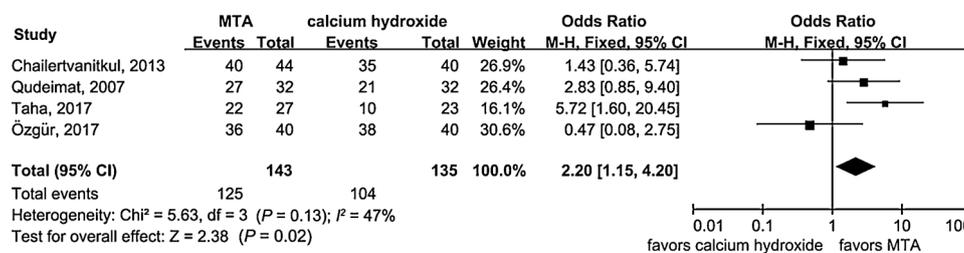


Fig. 4. Mineral trioxide aggregate versus calcium hydroxide for radiographic/overall success at 24 months. CI = confidence interval; MTA = mineral trioxide aggregate.

plan [41]. Such evidence of economic evaluation on pulpotomy is lacking in the literature. Large, unbiased, well-designed trials comparing pulpotomy with other treatment modalities in terms of cost-effectiveness should be informative.

Although evidence is scanty for other pulpotomy medicaments, MTA appears to be the best pulpotomy medicament in carious permanent teeth with pulp exposures. Previous reviews that included both observational studies and randomized controlled trials either favored calcium hydroxide over MTA or found no difference among the various medicaments employed in pulpotomy of carious permanent teeth with pulp exposures [7,8]. The disparities in criteria for study inclusion may have contributed to the different results. Drawbacks of MTA, such as high cost and long setting time, are still road blocks in the large scale deployment of MTA pulpotomy. Several recently-introduced tricalcium silicate cements with MTA-like properties such as Biodentine have been claimed to overcome the shortcomings of MTA [12]. Clinical trials show that the outcome for using Biodentine in pulpotomy is similar to MTA in carious primary teeth [42] as well as in sound permanent teeth [43]. There are ongoing trials comparing the clinical efficacy of MTA with Biodentine in managing carious permanent teeth with pulp exposures [35,36].

5. Conclusions

Data derived from currently available studies indicate that pulpotomy is a prospective substitute for root canal treatment in managing permanent teeth with carious pulp exposures, even in permanent teeth with irreversible pulpitis. Large, well-designed, long-term trials are required to provide more convincing evidence. While current evidence suggests MTA as the most promising medicament for pulpotomy of permanent teeth, several ongoing trials aim to determine the clinical efficacy of some novel tricalcium silicate cements that may overcome the drawbacks of MTA.

Like the yin and yang in Chinese philosophy, cost and effectiveness are two opposing yet complementary entities important in decision-making. Whether the cost of a decision in health care is justifiable based on the health benefits gained necessitates an evaluation of the after-effects of the opportunity costs and the fringe benefits gained [41]. To achieve authentic welfare of society and individuals, cost-effectiveness analysis rather than analysis based on treatment outcome alone should be considered in future studies to evaluate the benefits of alternative treatment options [41]. This dogma is applicable to all health care domains, and not exclusively to the decision-making in the management of inflamed pulps. Future advancement in medicine may rely on recognizing the optimal treatment modality that yields the maximum health benefits without being restricted by costs.

Declarations of interest

None.

Acknowledgments

The authors thank the assistance of Richard McGowan, NYU Health Sciences Library in the literature search and the authors that provided usable but unreported data of the studies included in the present work. This work was supported by the National Key Research & Development Program of China (Nos. 2017YFC0840100 and 2017YFC0840109), National Natural Science Foundation of China (Nos. 81720108011, 81470773, 81722015 and 81870805), and Changjiang Scholar Program of Chinese Ministry of Education (No. IRT13051). The funding sources had no involvement in the design, conduct or interpretation of the present work or in the decision to submit the manuscript for publication.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.jdent.2019.03.010>.

References

- [1] N.J. Kassebaum, A.G.C. Smith, E. Bernabé, T.D. Fleming, A.E. Reynolds, T. Vos, et al., Global, regional, and national prevalence, incidence, and disability-adjusted life years for oral conditions for 195 countries, 1990–2015: a systematic analysis for the global burden of diseases, injuries, and risk factors, *J. Dent. Res.* 96 (4) (2017) 380–387.
- [2] K. Gulabivala, Y. Ng, *Endodontics*, 4th ed., Mosby, St. Louis, Missouri, 2014.
- [3] A.B. Fuks, B. Peretz, *Pediatric Endodontics: Current Concepts in Pulp Therapy for Primary and Young Permanent Teeth*, Springer International Publishing, Switzerland, 2016.
- [4] S. Simon, M. Perard, M. Zanini, A.J. Smith, E. Charpentier, S.X. Djole, et al., Should pulp chamber pulpotomy be seen as a permanent treatment? Some preliminary thoughts, *Int. Endod. J.* 46 (1) (2013) 79–87.
- [5] N.A. Taha, M.A. Khazali, Partial pulpotomy in mature permanent teeth with clinical signs indicative of irreversible pulpitis: a randomized clinical trial, *J. Endod.* 43 (9) (2017) 1417–1421.
- [6] M.A. Qudeimat, A. Alyahya, A.A. Hasan, Mineral trioxide aggregate pulpotomy for permanent molars with clinical signs indicative of irreversible pulpitis: a preliminary study, *Int. Endod. J.* 50 (2) (2017) 126–134.
- [7] H. Alqaderi, C.T. Lee, S. Borzangy, T.C. Pagonis, Coronal pulpotomy for cariously exposed permanent posterior teeth with closed apices: a systematic review and meta-analysis, *J. Dent.* 44 (2016) 1–7.
- [8] P. Aguilar, P. Linsuwanont, Vital pulp therapy in vital permanent teeth with cariously exposed pulp: a systematic review, *J. Endod.* 37 (5) (2011) 581–587.
- [9] OCEBM Levels of Evidence Working Group. The Oxford Levels of Evidence 2. Oxford Centre for Evidence-Based Medicine. <https://www.cebm.net/index.aspx?o=5653>. (Accessed 11 July 2018).
- [10] V. Small-Faugeron, A.M. Glenn, F. Courson, P. Durieux, M. Muller-Bolla, H. Fron Chabouis, Pulp treatment for extensive decay in primary teeth, *Cochrane Database Syst. Rev.* 5 (2018) CD003220.
- [11] M. Parirokh, M. Torabinejad, Mineral trioxide aggregate: a comprehensive literature review - part III: clinical applications, drawbacks, and mechanism of action, *J. Endod.* 36 (3) (2010) 400–413.
- [12] M. Parirokh, M. Torabinejad, Mineral trioxide aggregate and other bioactive endodontic cements: an updated overview - part I: vital pulp therapy, *Int. Endod. J.* 51 (2) (2018) 177–205.
- [13] D. Moher, A. Liberati, J. Tetzlaff, D.G. Altman, P. Group, Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement, *BMJ* 339 (2009) b2535.
- [14] J.P.T. Higgins, S. Green (Eds.), *Cochrane Handbook for Systematic Reviews of Interventions* 5.1.0, The Cochrane Collaboration, 2011 (updated March 2011).
- [15] H.J. Schünemann, A.D. Oxman, G.E. Vist, J.P.T. Higgins, J.J. Deeks, P. Glasziou, et al., Chapter 12: interpreting results and drawing conclusions, in: J.P.T. Higgins,

- S. Green (Eds.), *Cochrane Handbook for Systematic Reviews of Interventions* 5.1.0, The Cochrane Collaboration, 2011 (updated March 2011).
- [16] M. Egger, G. Davey Smith, M. Schneider, C. Minder, Bias in meta-analysis detected by a simple, graphical test, *BMJ* 315 (7109) (1997) 629–634.
- [17] J.A. Sterne, A.J. Sutton, J.P. Ioannidis, N. Terrin, D.R. Jones, J. Lau, et al., Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials, *BMJ* 343 (2011) d4002.
- [18] L. Bjørndal, C. Reit, G. Bruun, M. Markvart, M. Kjældgaard, P. Nasman, et al., Treatment of deep caries lesions in adults: randomized clinical trials comparing stepwise vs. Direct complete excavation, and direct pulp capping vs. Partial pulpotomy, *Eur. J. Oral Sci.* 118 (3) (2010) 290–297.
- [19] L. Bjørndal, H. Fransson, G. Bruun, M. Markvart, M. Kjældgaard, P. Nasman, et al., Randomized clinical trials on deep carious lesions: 5-year follow-up, *J. Dent. Res.* 96 (7) (2017) 747–753.
- [20] S. Asgary, M.J. Eghbal, J. Ghoddusi, S. Yazdani, One-year results of vital pulp therapy in permanent molars with irreversible pulpitis: an ongoing multicenter, randomized, non-inferiority clinical trial, *Clin. Oral Investig.* 17 (2) (2013) 431–439.
- [21] S. Asgary, M.J. Eghbal, J. Ghoddusi, Two-year results of vital pulp therapy in permanent molars with irreversible pulpitis: an ongoing multicenter randomized clinical trial, *Clin. Oral Investig.* 18 (2) (2014) 635–641.
- [22] S. Asgary, M.J. Eghbal, M. Fazlyab, A.A. Baghban, J. Ghoddusi, Five-year results of vital pulp therapy in permanent molars with irreversible pulpitis: a non-inferiority multicenter randomized clinical trial, *Clin. Oral Investig.* 19 (2) (2015) 335–341.
- [23] M. Galani, S. Tewari, P. Sangwan, S. Mittal, V. Kumar, J. Duhan, Comparative evaluation of postoperative pain and success rate after pulpotomy and root canal treatment in cariously exposed mature permanent molars: a randomized controlled trial, *J. Endod.* 43 (12) (2017) 1953–1962.
- [24] NCT02727088. Pulpotomy vs pulpectomy outcome. <https://www.clinicaltrials.gov/ct2/show/NCT02727088>. (Accessed 12 January 2019).
- [25] N.A. Taha, M.A. Khazali, Partial pulpotomy in mature permanent teeth with clinical signs indicative of irreversible pulpitis: a randomized clinical trial, *J. Endod.* 43 (9) (2017) 1417–1421.
- [26] S. Asgary, M.J. Eghbal, Treatment outcomes of pulpotomy in permanent molars with irreversible pulpitis using biomaterials: a multi-center randomized controlled trial, *Acta Odontol. Scand.* 71 (1) (2013) 130–136.
- [27] S. Asgary, M.J. Eghbal, A.A. Bagheban, Long-term outcomes of pulpotomy in permanent teeth with irreversible pulpitis: a multi-center randomized controlled trial, *Am. J. Dent.* 30 (3) (2017) 151–155.
- [28] V. Kumar, R. Juneja, J. Duhan, P. Sangwan, S. Tewari, Comparative evaluation of platelet-rich fibrin, mineral trioxide aggregate, and calcium hydroxide as pulpotomy agents in permanent molars with irreversible pulpitis: a randomized controlled trial, *Contemp. Clin. Dent.* 7 (4) (2016) 512–518.
- [29] B. Özgür, S. Uysal, H.C. Güngör, Partial pulpotomy in immature permanent molars after carious exposures using different hemorrhage control and capping materials, *Pediatr. Dent.* 39 (5) (2017) 364–370.
- [30] H.R. Eppa, R. Puppala, B. Kethineni, S. Banavath, P.K. Kanumuri, G.V.S. Kishore, Comparative evaluation of three different materials: mineral trioxide aggregate, triple antibiotic paste, and abscess remedy on apical development of vital young permanent teeth, *Contemp. Clin. Dent.* 9 (2) (2018) 158–163.
- [31] D. Keswani, R.K. Pandey, A. Ansari, S. Gupta, Comparative evaluation of platelet-rich fibrin and mineral trioxide aggregate as pulpotomy agents in permanent teeth with incomplete root development: a randomized controlled trial, *J. Endod.* 40 (5) (2014) 599–605.
- [32] P. Chailertvanitkul, J. Paphangkorakit, N. Sooksantisakoonchai, N. Pumas, W. Pairojamornyoot, N. Leela-Apiradee, et al., Randomized control trial comparing calcium hydroxide and mineral trioxide aggregate for partial pulpotomies in cariously exposed pulps of permanent molars, *Int. Endod. J.* 47 (9) (2014) 835–842.
- [33] A. Nosrat, A. Seifi, S. Asgary, Pulpotomy in caries-exposed immature permanent molars using calcium-enriched mixture cement or mineral trioxide aggregate: a randomized clinical trial, *Int. J. Paediatr. Dent.* 23 (1) (2013) 56–63.
- [34] M.A. Qudeimat, K.M. Barrieshi-Nusair, A.I. Owais, Calcium hydroxide vs mineral trioxide aggregates for partial pulpotomy of permanent molars with deep caries, *Eur. Arch. Paediatr. Dent.* 8 (2) (2007) 99–104.
- [35] NCT03426046. Treatment of immature permanent teeth with three different pulp capping materials with partial pulpotomy. <https://www.clinicaltrials.gov/ct2/show/NCT03426046>. (Accessed 12 January 2019).
- [36] TCTR20171228003. Partial pulpotomy comparing two tricalcium silicate cement as pulp capping material in permanent teeth with cariously exposed pulp in adult patients. <http://www.clinicaltrials.in.th/index.php?tp=regtrials&menu=trialsearch&smenu=fulltext&task=search&task2=view1&id=3075>. (Accessed 12 January 2019).
- [37] NCT03166748. Clinical and radiographic assessments of potassium nitrate in polycarboxylate versus mineral trioxide aggregate as pulpotomy biomaterials in immature mandibular first permanent molars. <https://clinicaltrials.gov/show/NCT03166748>. (Accessed 12 January 2019).
- [38] NCT03119779. Effect of pulpotomy using TheraCal versus MTA on survival rate of cariously-exposed vital permanent molars. <https://clinicaltrials.gov/show/NCT03119779>. (Accessed 12 January 2019).
- [39] S. Yazdani, M.P. Jadidifard, B. Tahani, A. Kazemian, O. Dianat, L. Alim Marvasti, Health technology assessment of CEM pulpotomy in permanent molars with irreversible pulpitis, *Iran. Endod. J.* 9 (1) (2014) 23–29.
- [40] H.E. Alqaderi, S.A. Al-Mutawa, M.A. Qudeimat, MTA pulpotomy as an alternative to root canal treatment in children's permanent teeth in a dental public health setting, *J. Dent.* 42 (11) (2014) 1390–1395.
- [41] M.F. Drummond, M.J. Sculpher, K. Claxton, G.L. Stoddart, G.W. Torrance, *Methods for the Economic Evaluation of Health Care Programmes*, 4th ed., Oxford University Press, New York, NY, 2015.
- [42] C. Cuadros-Fernández, A.I. Lorente Rodríguez, S. Sáez-Martínez, J. García-Binimelis, I. About, M. Mercadé, Short-term treatment outcome of pulpotomies in primary molars using mineral trioxide aggregate and Biodentine: a randomized clinical trial, *Clin. Oral Investig.* 20 (7) (2016) 1639–1645.
- [43] H. Bakhtiar, M.H. Nekoofar, P. Aminishakib, F. Abedi, F. Naghi Moosavi, E. Esnaashari, et al., Human pulp responses to partial pulpotomy treatment with TheraCal as compared with Biodentine and ProRoot MTA: a clinical trial, *J. Endod.* 43 (11) (2017) 1786–1791.