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Modified pulpotomy procedure in immature permanent teeth with apical periodontitis: a randomised controlled trial

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ABSTRACT

Objectives The objective of this study was to evaluate the effectiveness of a modified pulpotomy (MP) procedure in immature permanent teeth with apical periodontitis (AP).

Design Randomised controlled trial.

Setting One public hospital in Shanghai, China

Participants A total of 33 teeth (31 patients) with a definitive diagnosis of AP with radiographic periapical radiolucency were recruited in this study. All the patients (teeth) completed the study accordingly.

Methods and intervention Patients were randomly assigned to either MP or apexification treatment groups and were followed up for 12 months. Clinical symptoms and complications were recorded, and parallel periapical radiographic images were used to measure changes in root length and apical diameter. Wilcoxon's rank sum test and Fisher's exact test were used to compare the clinical and radiographic outcomes between MP and apexification, and analysed with analysis of variance.

Main outcome measure The primary outcome was increase in root length at 12 months. The secondary outcomes included tooth survival, clinical success and decrease in apical diameter.

Results MP group showed a significant increase in root length (10.05%±2.14% vs 1.16%±0.79%, p<0.05) at 12 months and a decrease in apical diameter (48.88%±10.42% vs 15.90%±8.88%, p<0.05) as compared with the apexification group. The tooth survival rate was 100%, and 90.91% (30/33) of teeth were asymptomatic with apical healing in both treatment groups (p>0.05).

Conclusions MP can be an option for treating immature permanent teeth with AP. MP showed better performance in terms of continued root maturation than apexification. MP and apexification achieved comparable outcomes with regard to the resolution of clinical symptoms and apical healing.

Trial registration number ChiCTR-INR-17012169.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This was a randomised controlled trial that evaluated the effectiveness of clinical and radiographic outcomes of modified pulpotomy (MP) in immature permanent teeth with apical periodontitis (AP), with strict inclusion and exclusion criteria.
⇒ Clinical and radiographic outcomes of MP procedure as compared with apexification were quantitatively analysed.
⇒ In radiographic outcomes, cone-beam CT was substituted by parallel periapical X-ray films because of human ethical consideration; and radiographs were aligned using the TurboReg plug-in to minimise any dimensional changes that occurred as a result of angulation differences at the time of image taken.
⇒ The limitation of this clinical trial is that long-term observation is needed to confirm the long-term success of the MP procedure.
⇒ Subgroup analysis and histological examination of the apical canal space in the MP procedure are needed in future studies.

INTRODUCTION

Pulpotomy is one of the vital pulp therapy, and the aims of pulpotomy include the maintenance of vitality and preservation of the remaining pulp for adequate structural and functional healing of the pulp-dentin complex.[1] Apical periodontitis (AP) is characterised by an inflammatory response and bone destruction in the periapical tissues caused by microbial infection in the dental pulp.[2] Historically, the consensus is that the pulp should be regarded as irreversibly inflamed in immature permanent teeth with a presumptive diagnosis of AP, and pulpal inflammation has reached a level at which its elimination is not possible without removal of the entire pulp.[3] The use of pulpotomy is discouraged in these cases[4]; and the majority recommendation is pulpectomy, such as apexification.[5] However, apexification is considered a nonconservative and nonbiological treatment since it removes the entire infected and inflamed pulp and leads to loss in regenerative potential.[6]

Significant improvements have been made in the understanding of pulp biology. Clinical signs and symptoms, such as the degree and characteristics of pain or periapical radiolucency (PARL) do not reflect the actual histological status and subsequently the healing potential of the inflamed pulp,[7] and final diagnosis can be reached only after histological examination. Therefore, it is doubtful

that radical treatment is performed for teeth only by clinical diagnosis.[8] Moreover, it has been reported that in immature permanent teeth with PARL and bone destruction, residual vital pulp tissues are inflamed but not infected (infection is restricted to the necrotic coronal pulp).[9] Histological studies have shown that early periapical pathosis may not necessarily be associated with total pulp necrosis,[10] and periapical immune responses to root canal infection, including immune cell infiltration and bone resorption, can take place long before the pulp is totally necrotic.[11] Wigler *et al*[12] reported that during root canal exploration, the following conditions appeared, indicating that there was residual vital pulp tissue in the root canals: (1) when inserting a file or gutta-percha cone into the canal, a little resistance caused by the presence of tissue was felt; (2) the patient reported a sensation of pain and (3) the patient still felt uncomfortable even under local anaesthesia. Surviving apical papilla cells (APCs) and dental pulp stem cells (DPSCs) have the potential to resume proliferation and differentiation after eliminating inflammation and restoring pulp function.[13] Additionally, compared with mature teeth, the pulp tissue of immature permanent teeth has a rich vascular supply, which carries cellular and molecular components of the immune system through the large foraminal opening and may delay the process of total pulp necrosis.[14–16] All these events make it seem reasonable to conserve the residual vital pulp tissue and eliminate the infection to induce root maturation.

Based on the experience of our previous cases of immature permanent teeth with AP after a modified pulpotomy (MP) procedure, pulpotomy can be offered as an option with a modified procedure. The concept of the MP procedure was consequently developed to conserve the residual vital pulp tissue and potentially promote continued root development. In the MP procedure, after gently exploring the canal and marking the level of vital remaining pulp tissue, chemical debridement with 2.5% sodium hypochlorite (NaOCl), 3% hydrogen peroxide solution and 0.9% sterile saline solution (NS) was introduced to remove necrotic tissue and to disinfect the residual vital pulp tissue, instead of using high-speed diamond bur to amputate the pulpal tissue.

In the past years, convergent results from literature suggest that pulpotomy may improve the Periapical Index (PAI) score,[17–20] achieve good prognosis of clinical symptom regression and even continue root maturation.[21] However, previous investigations were case series or cases reports, and there was a lack of clinical trials. Furthermore, the clinical and radiographic changes in the MP procedure have not yet been quantitatively analysed. Therefore, the purpose of this prospective study was to assess the effectiveness of the MP procedure in immature permanent teeth with AP, and then quantitatively analyse the outcomes as compared with apexification.

MATERIALS AND METHODS

This study was registered at the Chinese Clinical Trial Registry (www.chictr.org.cn), ID: ChiCTR-INR-17012169 on 28 July 2017. Our research was conducted in accordance with the World Medical Association Declaration of Helsinki. The trial was a 12-month randomised, parallel-group to assess the effectiveness of MP and apexification in immature permanent teeth with AP.

Patients/subject participants

Patients were recruited from the Department of Pediatric Dentistry, Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine, China, from July 2017 to October 2018.

The inclusion criteria were as follows: (1) children in good general health with no systemic diseases and aged 7–12 years at the time of treatment; (2) immature permanent teeth (stage 7–9 according to Nolla's criteria[22]) diagnosed with AP with periapical pathology at the initial appointment; (3) operator gently explored the root canal and evaluated there was remnant vital pulp tissue remained in the canal. The exclusion criteria were as follows: (1) patients with chronic systemic disease, or allergic to the medicine used in the study; (2) teeth with periodontal disease; (3) teeth with excessively dental defect that the post core crowns were needed in future restoration; (4) cases wherein radiographic examination of the teeth with apical cysts and (5) teeth with radiographic evidence of root fracture.

Practitioner participants

Practitioner participants of the trial were three experienced pediatric dentists of the Department of Pediatric Dentistry, Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine, China. They also had special training in endodontics. They received a training standard operating procedure of MP and apexification methods, resin-bonded restoration to guarantee standardisation among practitioners.

Sample size calculation

The mean increase in root length for MP was approximately 28% with an SD of approximately 16% according to the retrospective analysis of 13 cases collected from June 2015 to June 2016,[23] while the change rate for apexification was approximately 5% according to the published RCT research.[24] The Mann-Whitney-Wilcoxon test, based on Monte Carlo simulation in PASS 2019, was used to estimate the sample size. With α=0.05 (bilateral), β=0.1 and considering a 10% loss rate, 16 cases in each group were needed in this study.

Randomisation/allocation concealment mechanism/implementation/blinding

An independent statistician generated a random allocation sequence. A computer-generated random allocation sequence was used to allocate patients to the treatment group in a 1:1 ratio. Envelopes containing information on MP or apexification were randomly assigned to the

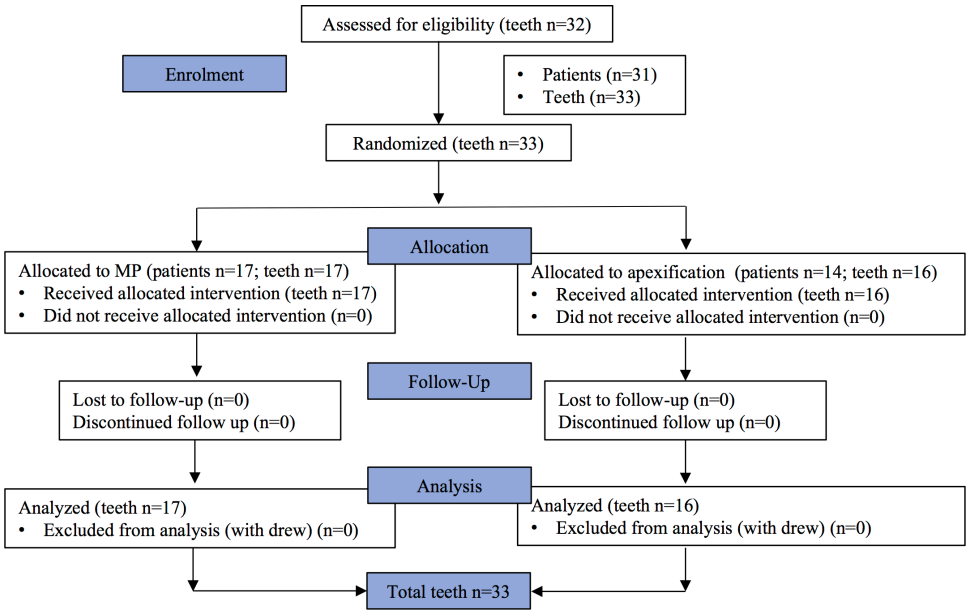

Figure 1 Participant flow through the trial. MP, modified pulpotomy.

patients. After the patients signed the written informed consent, they received these envelopes from the dentists. The patients were blinded to the procedures in this single-blind trial.

Interventions

MP procedure

After clinical and radiographic examination, the tooth was locally infiltration anaesthetised (lidocaine 2%) on the surrounding mucosa avoiding abscess, avoiding the root canal injection or periodontal ligament injection. Then the tooth was isolated with a rubber dam, and access was gained to the pulp chamber under strict aseptic conditions. The pulp chamber was irrigated with 2.5% NaOCl to remove the necrotic tissue. Then, a size #20 hand K-file was used to gently explore the root canal. The depth where the patient reported discomfort or the operator felt the soft tissue was recorded as the level of residual vital pulp tissue. Then the canal 1 mm above the vital tissue was irrigated with copious amounts of 2.5% NaOCl, 3% hydrogen peroxide solution, and NS without mechanical debridement (NS as terminal irrigating solution). After irrigating and achieving hemostasis (application of a 2.5% NaOCl cotton pellet) within 5 min, the root canal above the vital tissue was dried with sterile paper points and dressed with calcium hydroxide (CH) paste (CALXYL, OCO Praparate, Dirmstein, Germany), which was placed up to the level of the root canal orifice. Next, the access cavity was sealed with glass ionomer cement (GlasIonomer FX-II; Shofu, Kyoto, Japan) for 2 weeks.

At the second visit, if the tooth was asymptomatic, the access cavity was reopened and the CH paste was removed with copious amounts of irrigation. The canal above the vital tissue was dried with paper points without inducing intracanal bleeding from the periapical tissues. At least 1.5 mm thickness i-Root BP Plus (Innovative BioCeramix, Burnaby, Canada) was gently placed over the residual vital pulp tissue using appropriate Buchanan hand plungers (SybronEndo, Orange, California, USA) to prevent extrusion into the vital tissues, and radiography was performed to check its placement. The access cavity was sealed with a conventional glass ionomer cement and resin composite (Z350; 3M ESPE, St Paul, Minnesota, USA). If the tooth was symptomatic, another round of chemical debridement and CH paste intracanal dressing was performed until the tooth became asymptomatic before completion of the MP procedure. Postoperative radiographs were obtained accordingly during the follow-up visit.

Apexification procedure

After clinical and radiographic examination, the tooth was locally infiltration anaesthetised same as MP procedure, then isolated with a rubber dam and performed the pulp access. Standard irrigants and instrumentation were used for the procedure.[24] Working length was determinated by diagnostic radiograph, canal was chemomechanical prepared with K-files and copious irrigation to remove the necrotic pulp tissue. Minimal root canal preparation to avoid damage to APCs. The canal was dried with sterile paper points, the intracanal dressing paste was CH paste and the tooth was temporarily sealed with glass ionomer cement.

Two weeks later, the tooth was reaccessed and isolated with a rubber dam. The CH paste was removed using irrigating solution. We dried the root canal with sterile paper points, and filled the root canal with the Vitapex paste (Neo Dental International, Tokyo, Japan), the tooth was sealed with glass ionomer cement and resin composite in the crown. Postoperative radiographs were taken to confirm the extension of Vitapex paste apical plug in root canals.

Table 1 Baseline demographic and clinical characteristics for cases recruited in the MP and apexification groups

Variable	N (%)	
	MP (n=17)	Apexification (n=16)
Age (years)		
7–8	3 (17.65)	2 (12.50)
9–10	9 (52.94)	8 (50.0)
11–12	5 (29.41)	6 (37.50)
Gender		
Male	9 (52.94)	9 (56.25)
Female	8 (47.06)	7 (43.75)
Tooth type		
Incisor	4 (23.53)	4 (25.00)
Premolar	9 (52.94)	8 (50.00)
Molar	4 (23.53)	4 (25.00)
Stage of root development (Nolla)		
7	3 (17.65)	1 (6.25)
8	8 (47.06)	4 (25.00)
9	6 (35.29)	11 (68.75)
Etiology		
Trauma	3 (17.65)	3 (18.75)
Developmental malformation	10 (58.82)	8 (50.00)
Caries	4 (23.53)	5 (31.25)
Apical periodontitis		
Present	17(100)	16(100)
Percussion, swelling or sinus tract		
Percussion positive only	4 (23.53)	4 (25.00)
Percussion with swelling or sinus tract	13 (76.47)	12 (75.00)

Frequency of all categorical variables is presented as teeth number (N) and percentage (%).
MP, modified pulpotomy.

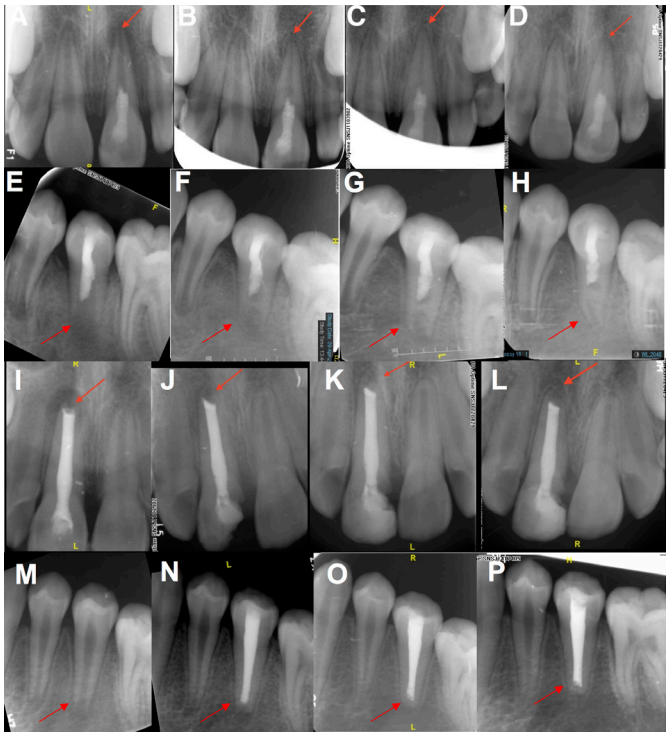

Figure 2 Two representative cases of MP procedure and apexification. (A–D) MP case 1 #21and (E–H) MP case 2 #35, (I–L) apexification case 1 #11and (M–P) apexification Case 2 #35. (A, E, I) immediate postoperation, (M) preoperation, (B, F, J, N) follow-up at 3 months. (C, G, K, O) follow-up at 6 months. (D, H, L, P) follow-up at 12 months. MP, modified pulpotomy. Arrows mark the significant changes of the roots.

Postoperative radiographs were obtained during the follow-up visit. When the apical barrier was formed, root canal was reaccessed and performed definitive root canal was filled with sealer and worm gutta-percha.

Outcomes/follow-up observation and measurement

Parallel periapical radiographic images were taken to examine the periapical tissue and root development. The patients were scheduled for follow-up at 3, 6 and 12 months after the completion of therapy. Follow-up included clinical assessment (pain, swelling, sinus tract and mobility) and acquisition of a periapical radiograph.

The primary outcome in this trial was an increase in root length 12 months after therapy. In this study, cone-beam CT was substituted by parallel periapical X-ray films because of human ethical consideration. Preoperative and postoperative radiographs were evaluated by study investigators who were blinded to the research purpose. Changes in root length were quantitatively analysed from both the preoperative and recall images, which were modified from the procedure as described by Alobaid *et al*.[25] The periapical films were taken using the paralleling technique and the after-image standardisation was performed by using TurboReg (Biomedical Imaging Group, Swiss Federal Institute of Technology, Lausanne, Vaud, Switzerland) to minimise any dimensional changes that occurred as a result of angulation differences at the time of image acquisition. Root length was measured using NIH Image J software (V.1.41; National Institutes of Health, Bethesda, Maryland, USA). For root length, the measurements were performed on a straight line from the midpoint of the CEJ to the midpoint of the radiographic apex from both mesial and distal, and the average of both measurements was thus calculated. According to Bose *et al*,[26] we presented the data as a percentage (%) change from preoperative values rather than the actual millimetric data to eliminate one potential source of systematic error in the overall analysis of treatment outcomes. If the change was larger than 20%, the cases had achieved clinically meaningful changes.[27] All measurements were collected by the same investigator and repeated after 1 week, and the mean of the two replicates was considered the final value.

Secondary outcomes included a decrease in apical diameter at 12 months after therapy, and clinical outcomes were evaluated on the basis of both survival and clinical success. The apical diameter was measured as a straight line across the apical foramen. Changes in apical diameter were quantitatively calculated, similar to the method used for changes in root length. Survival was defined as

Table 2 Survival rate, clinical success and outcomes of clinical evaluation in the MP and apexification groups at 12-month follow-up

	Total (n=33)	MP (n=17)	Apexification (n=16)	P value	OR
Survival rate	33 (100)	17 (100)	16 (100)	/	/
Absent of clinical symptoms	30 (90.91)	14 (82.35)	16 (100)	0.227	0.82 (0.68,1.03)
Resolution of radiolucency	30 (90.91)	14 (82.35)	16 (100)	0.227	0.82 (0.68,1.03)
Type					
I	15 (45.45)	12 (70.59)	3 (18.75)	0.002	4.25 (1.46,12.33)
II	15 (45.45)	2 (11.76)	13 (81.25)	0.001	0.16 (0.04,0.61)
III	3 (9.1)	3 (17.65)	0 (0)	0.103	0.81 (0.64,1.03)

Date are teeth number (N) and percentage (%).
MP, modified pulpotomy.

the remaining tooth in the arch throughout the study period. Clinical success was defined as a tooth without clinical symptoms and resolution of the PARL. The failed cases were recorded, and additional endodontic treatment was required for these patients.

For additional analysis, we referenced the AAE (American Association of Endodontists) clinical consideration for the degree of success to better evaluate treatment outcomes.[28] Root morphology and clinical symptoms were both considered, and we classified the cases into the following three types: type I, the cases were asymptomatic and had continued root maturation; type II, the cases were asymptomatic, but had no significant root maturation; type III, one of the following was present: the presence of clinical symptoms (spontaneous pain, swelling or sinus tract), recurrence of AP and external root resorption. We regarded types I and II as clinical success, and type III as failure.

Statistical methods

The data were collected, tabulated and analysed by a professional statistician using SPSS V.25.0 statistical software (SPSS).

The changes in root length and apical diameter were expressed as mean±SE of the mean. The Wilcoxon rank sum test for unpaired data was used to investigate the changes in root length and apical diameter between the MP and apexification groups. The changes in root length were submitted to a two-way repeated-measure analysis of variance (ANOVA) with time (3, 6 and 12 months) and group (MP or apexification). The Fisher's exact test was used to compare clinical success and additional analyses.

Statistical significance was set at $p<0.05$. Graphs were generated using GraphPad Prism V.8 (GraphPad Software, La Jolla, California, USA).

Patient and public involvement statement

Immature permanent teeth with definitive diagnosis of AP with PARL were recruited for this study. After patients signed the written informed consent, they were randomly assigned to either MP or apexification treatment and followed up for 12 months. During the follow-up period, they had the priority of treatment and traffic allowance.

RESULTS

The patients in this study were recruited from July 2017 to October 2018 with a 12-month follow-up period. A total of 31 patients (33 teeth) were recruited for this study. Patients were randomly assigned to the MP group (17 patients, 17 teeth) and the apexification group (14 patients, 16 teeth). All patients in the groups completed the study (figure 1). The age of the patients ranged from to 7–12 years old at the initial appointment, with an average age of 10.00 years (SD=1.35). Developmental malformations were the most common etiology in both groups. Gingival swelling or sinus tract occurred in 76.47% (13/17) and 75.00% (12/16) of cases in the MP and apexification groups, respectively. Baseline demographic and clinical characteristics of each group are shown in table 1.

The radiographic images of the two representative cases of the MP procedure and apexification are presented in figure 2.

For the primary outcome, as compared with the apexification group, the MP group showed a significant increase in the change of root length at 12 months after therapy (10.05%±2.14% vs 1.16%±0.79%, $p<0.05$). The change in root length at 3 months and 6 months also showed statistically significant differences (3 months, 2.06%±0.68% vs 0%; 6 months, 7.41%±1.86% vs 0.79%±0.53%, $p<0.05$, figure 3A). Repeated-measures ANOVA also demonstrated that there was significant between MP procedure and apexification ($F=13.184$, $p<0.001$).

For secondary outcomes, the decreases in apical diameter compared with the apexification group were also significant (3 months, 16.66%±5.26% vs 2.08%±1.44%; 6 months, 36.13%±9.39% vs 6.47%±3.63%; 12 months, 48.88%±10.42% vs 15.90%±8.88%, $p<0.05$, figure 3B). All teeth survived after the 12-month follow-up. The asymptomatic rate and resolution of radiolucency rate for the MP and apexification groups were 82.35% (14/17) and 100%, respectively ($p>0.05$) (table 2). The results showed

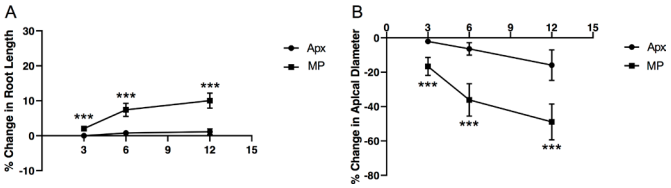

Figure 3 Radiographic changes of root length and apical diameter during the study period. (A) Root length (B) Apical diameter. Error bars represent mean±SE of the mean. ***p<0.05 means statistically significant difference. Apx, apexification; MP, modified pulpotomy.

that when treated with the MP procedure, type I was the most common outcome, 70.59% (12/17), whereas types II and III were rare (11.76% (2/17) and 17.65% (3/17), respectively). In the apexification group, type II was the most common outcome (81.25%,13/16), whereas types I and III were rare (18.75% (3/16) and 0%, respectively). A significant difference was found between these two groups in types I and II (p<0.05), with no statistical difference in type III (table 2). At 12 months, in the MP group, 23.53% (4/17) of cases achieved clinically meaningful changes in root length, while there were no cases in the apexification group. Meanwhile, in the MP group, 70.59% (12/17) of cases met this criterion for apical diameter, and in the apexification group, the number was 18.75% (3/16) (online supplemental figure 1S).

DISCUSSION

The present trial evaluated the effectiveness of the MP procedure in the management of immature permanent teeth with AP. This is the first randomised controlled trial comparing the clinical and radiographic outcomes of MP procedure and apexification. All patients (teeth) completed the study, which is above the minimum 80% recall rate required for a high level of evidence.[29] Clinical decision-making should be based on the best available evidence. Based on the results of this trial, the MP procedure can be recommended for the management of immature permanent teeth with AP.

According to the AAE recommendation,[28] the primary goal of success is the elimination of symptoms and evidence of bony healing, and the secondary goal is continuing root maturation. In this study, 82.35% (14/17) of the cases in the MP group achieved the primary goal, comparable with the apexification group (p>0.05, table 2). Moreover, PARL significantly resolved at the 3-month follow-up (online supplemental figure S2). Similar to previous literature, full pulpotomy may improve the PAI score.[17–20] Our infection control measurement of the inflamed residual vital pulp tissue using chemical debridement and CH intracanal medication was effective.

Evaluating the condition of the residual pulp played a significant role in the success of the MP procedure, which seemed challenging in practice. Infection and inflammation of the pulpal-periapical tissue complex were controlled so that the APCs and DPSCs could resume their biological function, and the residual pulp would have the potential to continue to develop.[13 30] Continuing maturation of roots is evidenced by increased root length and decreased apical diameter.[31] The results of this study indicated that MP showed a significantly better outcome than apexification in continuing root development (figure 3 and online supplemental figure S1, p<0.05), and that radiographic apical closure was significantly different at the 12-month follow-up (online supplemental figure S2), achieving a secondary successful goal.[26] There are the most important clinical difference. The majority of MP cases (70.59%, 12/17) achieved root maturation (type I), and 35.29% (6/17) of MP cases achieved apical closure. Apexification cases (81.25%, 13/16) had an apical calcification barrier (type II) (table 2, p<0.05). In the current study, an apical calcification barrier might occur during apexification, but further maturation usually does not.[24 32] With the recent development of new materials and improved understanding of pulp biology and reparative processes,[33] the following biocompatibility considerations were considered in the MP procedure.[34] A reduced concentration of NaOCl solution (2.5%) and NS was used as the final irrigation solution, followed by low toxicity disinfection in order to protect vital remnants of APCs and DPSCs.[35] CH was used as an intracanal and interappointment medicament for the greatest viable bacterial reduction[36] and a higher number of APCs attached to the root dentin surface.[35] IRoot-BP Plus, a biocompatible material,[37] was used as a pulp capping material to induce the release of growth factors and stimulate differentiation of odontoblast-like cells that modulate the inflammatory process and induce repair.[20]

The limitation of this clinical trial is that the diagnosis of residual vital pulp tissue in the MP procedure is subjective, and most failed cases are identified after more than 2 years of follow-up,[38] hence, longer follow-up periods should be performed in order to provide a better evaluation of success rate, survival rate and complications. However, due to the influence of COVID-19, data from the second-year follow-up cannot be obtained for these patients. Another limitation is that because only two patients had correlated teeth, we did not consider carrying out the statistical methods that were used to analyse the correlated outcome, such as generalised estimating equation or mixed model.

In future studies, a subgroup analysis is needed. Proper case selection is crucial for the long-term success of pulpotomy.[20] There is an effect of severe trauma and long-standing periapical infections subsequent to pulpal necrosis on the viability of the APCs and Hertwig's epithelial root sheath cells.[25] Therefore, it was hypothesised that the aetiology and persistence of periapical pathology may have impacts on the outcome of MP. Moreover, Nolla's stage of root development may have another impact.[14–16] In addition, the type of tissue formed on the apical canal walls and in the apical canal space in the MP procedure in this study is not known without histological examination. We assumed that after inflammation was controlled, the

APCs and DPSCs had the potential to resume proliferation and differentiation, differentiating into cementoblasts, osteoblasts or odontoblasts. To achieve continuous root maturation, the apical canal space is formed with pulp-like tissue, in contrast to the regenerative endodontic procedure formed in the canals, mineralised tissue and some fibrous connective tissue.[39]

CONCLUSION

Our results suggest that, with the MP procedure, the indication for pulpotomy may be greater than that as previously thought. With the help of canal exploration, proper case selection, strict aseptic conditions, suitable solution irrigation lotion, and intracanal and pulp capping materials, MP showed better achievements in continued root maturation than apexification. MP can be offered to the patient as an alternative to apexification in immature permanent teeth with AP. A longer follow-up period should be performed to provide a better evaluation of the success rate, survival rate and complications.

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Contributors WX and JW conceived the project; JW procured the project funding; WX, ZC and JW coordinated the trial. WX and JW assisted with protocol design. WX and JW recruited the participants and managed the project. WX wrote the first draft of this manuscript. WS performed the statistical analyses. WX and JW are acting as guarantors.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not applicable.

Ethics approval This randomised controlled trial was approved by the Ethics Committee of Human Research Ethics at the Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine (Ref: 2017-341-T250). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request. Individual deidentified participant data and related documents will be made available 1 year after publication of the primary manuscript. Data requests should be submitted to the corresponding author. Request for data sharing will be handled in line with the relevant regulations for data access and sharing in China and will need the approval of the trial steering committee, Ethics Committee of Human Research Ethics at the Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine.

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