

# Management of Carious Pulp Exposure in Vital Permanent Teeth: An Evidence-Based Clinical Practice Guideline

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**Introduction:** Annually ~2 million permanent teeth are lost in public dental clinics in Iran. Many of these losses are caused by difficulties in provision of timely root canal treatment (RCT) or their low quality. The present guideline aimed to find and recommend the best treatment options for management of vital permanent teeth with carious exposure. **Materials and Methods:** The guideline domain was examined and treatment options were determined as scenarios comprised of indications and possible interventions. Two main indications including carious pulp exposure with or without irreversible pulpitis in open-apex and in closed-apex permanent teeth were included. Nine treatment options were found for each indication based on the available literature. Exhaustive search was performed to find the current evidence and the retrieved studies were critically reviewed. Treatment options and their supporting evidence were extracted. Search for the side effects and benefits of each treatment option was also performed. The expenses regarding each treatment were then determined and treatment options with Level of Evidence (LOE) I and II evidence were presented to an expert panel for each indication. Each clinical scenario was examined and rated by each member considering six aspects: effectiveness of the intervention, costs, side effects, side benefits, applicability of the scenario and generalizability of the treatment. The best scenarios were chosen based on the expert panel ratings and the recommendations were extracted. **Results:** Based on the present guideline, full pulpotomy with calcium enriched mixture (CEM) cement is recommended in vital permanent teeth with open- or closed-apex, with or without irreversible pulpitis, following carious pulp exposure (Grade A recommendation). **Conclusion:** Adherence to the present guideline may help preserve pulp vitality and decrease the risk of loss of vital permanent teeth with carious pulp exposure.

**Keywords:** Calcium enriched mixture; Dental pulp exposure; Evidence-based practice; Guideline; Pulpotomy; Dentition, Permanent

## Introduction

Annually two million teeth are lost in public dental clinics in Iran. The average number of lost teeth in 35-44 year-old adults in Iran is 6.6 teeth (1). A great deal of these losses is related to problems in provision of timely root canal treatment (RCT) for permanent teeth with pulpal involvement. Some barriers are inaccessibility to root canal treatment facilities and RCT expenses. Low-quality RCTs further add to this value.

Irreversible pulpitis is a clinical diagnosis based on subjective and objective findings. It is characterized by an inflamed pulp that is no longer capable of healing and returning to its normal state. This condition has a wide range of forms and symptoms. The current treatment for

irreversible pulpitis is root canal treatment, pulpectomy or extraction of the affected tooth (2). However, reversibility of pulp inflammation is controversial. From a clinical perspective, it is not possible to accurately determine the state of pulpitis in all cases. Currently, differentiating between reversible and irreversible pulpitis is largely done on an empirical basis. It is also not known if all pulps with inflammation could recover if conservative treatment strategies were used. This question requires further research to establish an answer (2). In their recent systematic review, Mejare *et al.*, suggested that research should focus on exploring methods that can reveal whether a vital but injured pulp can be maintained, or whether it should be removed and replaced with a root filling material (3). Considering the fact that infection is often the cause of inflammation, an inflamed pulp should be able

to heal if the source of infection is eliminated, as is often the case in other body organs. Therefore, caries-induced pulpitis should be reversible and the pulp should be able to heal if caries is removed. However, no study of sufficient quality was found that assessed the relationship between markers of pulp infection and the outcome of conservative treatment, aimed at preserving the exposed pulp (3-5).

An evidence-based clinical practice guideline is a "systematically developed statement to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances" (6) and includes the best current recommendations for health care providers concerning the most appropriate care for patients.

The present guideline aimed to find and recommend the best treatment options for management of vital permanent teeth with carious exposure, with or without irreversible pulpitis to general dental practitioners of I.R. Iran, based on the best current evidence.

## Materials and Methods

On April 2012, Clinical Knowledge Management Unit of Research Institute of Dental Sciences of Shahid Beheshti University of Medical Sciences accepted the mission of developing an evidence-based clinical practice guideline on management of pulp exposure in vital permanent teeth with or without irreversible pulpitis assigned by deputy of Medical Care, Ministry of Health and Medical Education. The following steps were taken in this regard:

- The guideline domain was examined.
- The guideline questions were determined.
- Exhaustive search was done to find the current evidence (See details in the next section).
- The retrieved relevant studies were critically reviewed and their findings were analyzed and their methodological quality was assessed by a newly developed tool, which is a modification of van Tulder's checklist (7) (Table 1).

The level of evidence for each study was then determined (Table 2). Level of evidence was adapted from the Scottish Intercollegiate Guidelines Network (SIGN) (6) and Oxford Centre for Evidence-based Medicine (CEBM) (8) leveling systems.

- Treatment options and their supporting evidence were then extracted.
- Search for side effects and benefits of each treatment option was also performed.
- The expenses regarding each treatment option were then determined.

- Treatment options for each question with LOE (Level of Evidence) I and II evidence were presented to the expert panel.
- Clinical scenarios were evaluated and rated by an expert panel, comprised of:
  - Full professors of endodontics from all medical universities of I.R. Iran,
  - Full professors of pedodontics from all medical universities of Tehran,
  - Representatives of oral health office of the Ministry of Health and Medical Education,
  - Representative of health insurance office of the Ministry of Health and Medical Education,
  - Representatives of health and medical care deputies of selected medical universities,
  - Representative of the Ministry of Labor and Social Affairs,
  - Representative of the Medical Council of I.R. Iran,
  - Representative of the Iran Dental Association,
  - Representative of the 'health-oriented dentistry' project and Director of Clinical Knowledge Management Unit

Each clinical scenario was examined for six aspects by each member of the expert panel:

**Effectiveness of intervention** based on the best current evidence

**Intervention expenses** extracted from the relative values of diagnostic and therapeutic dental services booklet (Ministry of Labor and Social Affairs, 2009)

**Intervention side effects** according to the published reports

**Intervention side benefits** are the positive effects of an intervention not expressed in effectiveness studies; e.g. decreased need for radiography, increased tooth survival following preservation of tooth vitality and decreased post-operative pain.

**Applicability of the scenario** is determined by three criteria: Accessibility of facilities, instruments and materials in all dental care provision centers, possibility of acquiring knowledge and skills of treatment by all dental care providers, and affordability of the treatment for all socioeconomic classes in the society.

**Generalizability of the scenario** is also determined by three criteria: Similarity of biological properties of the target population with the studied populations, similarity of disease properties of the target population with studied populations, and similarity of the quality of care provision of target care providers with studied care providers.

- The best scenarios were chosen based on expert panel ratings and the recommendations were extracted.



**Table 1.** Modified van Tulder's list (9)

		Yes/No/Don't Know
i)	Was an appropriate method of randomization performed?	
ii)	Treatment allocation: Was the treatment allocation concealed?	
iii)	Were the groups similar at baseline regarding the most important prognostic indicators?	
iv)	Was the outcome assessor(s) blinded?	
v)	Was the care provider(s) blinded?	
vi)	Was the patient(s) blinded?	
vii)	Was the outcome assessor(s) calibrated?	
viii)	Were the co-interventions avoided?	
ix)	Was the follow-up period adequate?	
x)	Were withdrawal and dropout rates described and acceptable? (>85%)WCA	
xi)	Was the timing of the outcome assessment comparable in all groups?	
xii)	Were relevant outcomes used?	
xiii)	Was the sample size adequate?	
xiv)	Were the outcome measures objective?	
xv)	Did the analysis include an intention-to-treat analysis?	

**Table 2.** Level of evidence(9)

Level of evidence	Study design
I	High quality meta-analyses or systematic reviews of randomized controlled trials, OR Randomized controlled trials with a very low risk of bias / high quality randomized controlled trials
II	High-quality semi-experimental studies, OR High-quality systematic reviews of cohort studies, OR High-quality cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal, OR High-quality systematic reviews of semi-experimental studies, OR Randomized controlled trials with a moderate-high risk of bias (low-quality randomized controlled trials) Ecological studies or outcome research studies
III	High-quality systematic reviews of case-control studies, OR High-quality case-control studies with a low risk of confounding or bias and a moderate probability that the relationship is causal, OR Low-quality semi-experimental studies
IV	Case series, OR Case-control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
V	Expert opinion, case reports, narrative reviews

Accumulation of expert panel ratings for each clinical scenario was done based on Rand/UCLA appropriateness method (10). The summary of the method is as follows:

Each clinical scenario was reviewed by each member of the expert panel. Each scenario was eventually rated from 1 to 9; where 1-3 was inappropriate, 4-6 was partially appropriate and 7-9 was appropriate. After accumulation of ratings, the statistical median was determined. The consensus on ratings was then determined based on the algorithm mentioned in Table 3.

When ratings are not included in either of the categories, it is called incomplete consensus.

- Grades of recommendations were determined based on three

factors of LOE, Scenario Appropriateness and Panel Consensus on each scenario (Table 4).

### Search Strategy

Treatment options were determined as scenarios comprised of indications and possible interventions. Two main indications of carious pulp exposure with or without irreversible pulpitis in open apex permanent teeth and carious pulp exposure with or without irreversible pulpitis in closed apex permanent teeth were included in this guideline. Nine treatment options were found for each indication based on available literature.

Searches were done from May to November 2012.



**Table 3.** Expert panel rating analysis

Number of members of the expert panel	Absolute consensus Number of members whose ratings are not in the median range	Lack of consensus Number of members whose ratings are in any of extreme ranges
8-10	2 or less	3 or more
11-13	3 or less	4 or more
14-16	4 or less	5 or more
19-17	5 or less	6 or more
20-22	6 or less	7 or more
23-25	7 or less	8 or more

**Table 4.** Grade of recommendation

Grade of recommendation	Description
A	Absolute appropriateness of the scenario based on evidence rated as level I or II <b>and</b> absolute consensus of the expert panel
B	Absolute appropriateness of the scenario based on evidence rated as level I or II <b>and</b> incomplete consensus of the expert panel; OR Absolute appropriateness of the scenario based on evidence rated as level III <b>and</b> absolute consensus of the expert panel
C	Absolute appropriateness of the scenario based on evidence rated as level III <b>and</b> incomplete consensus of the expert panel; OR Partial appropriateness of the scenario based on evidence rated as level III <b>and</b> absolute consensus of the expert panel
D	Partial appropriateness of the scenario based on evidence rated as level I or II <b>and</b> incomplete consensus of the expert panel; OR Partial appropriateness of the scenario based on evidence rated as level III <b>and</b> incomplete consensus of the expert panel; OR Absolute appropriateness of the scenario based on evidence rated as level I or II <b>and</b> lack of consensus of the expert panel
Good Practice Points <input checked="" type="checkbox"/>	Recommended best practice based on the clinical experience of the guideline development group

**First Question**

Which treatment option is mostly recommended for management of carious pulp exposure with or without irreversible pulpitis in “open-apex” permanent teeth based on the best current evidence?

Medline was searched using the following queries through PubMed:

- (systematic[sb] AND (“Pulpotomy”[Mesh])
- (Therapy/Broad[filter]) AND (“pulpotomy”[MeSH] AND permanent [Text Word])
- (Therapy/Broad[filter]) AND (“pulpotomy”[Mesh] AND apexogenesis[Text Word])
- (Therapy/Broad[filter]) AND (“Calcium hydroxide”[MeSH] AND “pulpotomy”[MeSH] AND permanent [Text Word])
- (“Calcium hydroxide”[MeSH] AND “pulpotomy”[MeSH] AND permanent [Text Word])
- (“Mineral trioxide aggregate” [Supplementary Concept]AND “pulpotomy”[MeSH] AND permanent [Text Word])
- (“Calcium enriched matrix” [All fields]AND “pulpotomy”[MeSH] AND permanent [Text Word])
- (Systematic[sb] AND (“Dental Pulp Capping”[Mesh]))
- (Therapy/Broad[filter]) AND (“Dental Pulp Capping”[Mesh] AND permanent [Text Word])
- (Therapy/Broad[filter]) AND (“Calcium hydroxide”[MeSH] AND “Dental Pulp Capping”[Mesh] AND permanent [Text Word])
- (“Calcium hydroxide”[MeSH] AND “Dental Pulp Capping”[Mesh] AND permanent [Text Word])
- (“Mineral trioxide aggregate” [Supplementary Concept]AND “Dental Pulp Capping”[Mesh] AND permanent [Text Word])
- (“Calcium enriched matrix” [All fields]AND “Dental Pulp Capping”[Mesh] AND permanent [Text Word])

TRIP database was searched by the *pulp* keyword and the Cochrane Library with *pulp\** keyword and the search results were reviewed. “Clinicaltrials.gov” was also searched for ongoing clinical trials.

The following search queries were used for searching the side effects of pulpotomy:

- (Prognosis/Broad[filter]) AND (“Pulpotomy/adverse effects”[Mesh])



2. (Prognosis/Broad[filter]) AND ("Pulpotomy"[Mesh])
3. (((("Pulpotomy"[MeSH]) AND ("Calcium Hydroxide/adverse effects"[Mesh] OR "Calcium Hydroxide/poisoning"[Mesh] OR "Calcium Hydroxide/toxicity"[Mesh]))) - Limits: Prognosis/ Therapy/ Etiology
4. "Mineral trioxide aggregate" [Supplementary Concept]AND "Tooth Discoloration"[Mesh]
5. ("Calcium hydroxide"[MeSH] AND "pulpotomy"[MeSH] AND "internal root resorption" [Text word])
6. ("Calcium hydroxide"[MeSH] AND "pulpotomy"[MeSH] AND "Dental Pulp Calcification"[Mesh])
7. ("Calcium Hydroxide"[Mesh]) AND "Dental Pulp Calcification"[Mesh]
8. (Calcification AND "pulpotomy" [MeSH]) AND "Calcium Hydroxide"[Mesh]
9. ("Calcium enriched matrix" [All fields]AND "pulpotomy"[MeSH] AND adverse effect[Text Word])
10. ("Calcium enriched matrix" [All fields]AND "adverse effects" [Subheading])

### Second Question

Which treatment option is mostly recommended for management of carious pulp exposure with or without irreversible pulpitis in "closed-apex" permanent teeth based on the best current evidence?

Medline was searched using the following queries through PubMed:

1. "Pulpotomy"[MeSH] AND permanent [Text Word]
2. Systematic [sb] AND ("Root Canal Therapy"[Mesh])
3. (Systematic[sb] AND ("Pulpotomy"[Mesh])
4. ("Mineral trioxide aggregate" [Supplementary Concept]AND "pulpotomy"[MeSH] AND permanent [Text Word])
5. ("Calcium enriched matrix" [All fields]AND "pulpotomy"[MeSH] AND permanent [Text Word])
6. "Dental Pulp Capping"[Mesh] AND permanent [Text Word]
7. (Systematic[sb] AND ("Dental Pulp Capping"[Mesh]))
8. ("Mineral trioxide aggregate" [Supplementary Concept]AND "Dental Pulp Capping"[Mesh] AND permanent [Text Word])
9. ("Calcium enriched matrix" [All fields]AND "Dental Pulp Capping"[Mesh] AND permanent [Text Word])

TRIP database was searched by the *pulp* keyword and the Cochrane Library with *pulp\** keyword and the search results were reviewed. Clinicaltrials.gov was also searched for ongoing clinical trials.

The following search queries were used for searching the side effects of pulpotomy and RCT:

1. ((Prognosis/Broad[filter]) AND ("Pulpotomy/adverse

effects"[Mesh])

2. (Prognosis/Broad[filter]) AND ("Pulpotomy"[Mesh])
3. (((("Pulpotomy"[MeSH]) AND ("Calcium Hydroxide/adverse effects"[Mesh] OR "Calcium Hydroxide/poisoning"[Mesh] OR "Calcium Hydroxide/toxicity"[Mesh]))) - Limits: Prognosis/ Therapy/ Etiology
4. "Mineral trioxide aggregate" [Supplementary Concept]AND "Tooth Discoloration"[Mesh]
5. ("Calcium hydroxide"[MeSH] AND "pulpotomy"[MeSH] AND "internal root resorption" [Text word])
6. ("Calcium hydroxide"[MeSH] AND "pulpotomy"[MeSH] AND "Dental Pulp Calcification"[Mesh])
7. ("Calcium Hydroxide"[Mesh]) AND "Dental Pulp Calcification"[Mesh]
8. (Calcification AND "pulpotomy" [MeSH]) AND "Calcium Hydroxide"[Mesh]
9. ("Calcium enriched matrix" [All fields]AND "pulpotomy"[MeSH] AND adverse effect[Text Word])
10. ("Calcium enriched matrix" [All fields]AND "adverse effects" [Subheading])
11. (Prognosis/Broad[filter]) AND ("Root Canal Therapy/adverse effects"[Mesh])
12. (Prognosis/Broad[filter]) AND ("Root Canal Therapy" [Mesh])

The general term of mineral trioxide aggregate (MTA) was searched not mentioning the commercial brands and the ProRoot MTA was found in the retrieved studies. Other brands of MTA are however available in dental market. Thus, randomized controlled trials on the use of Angelus MTA (Brazil) and Root MTA (Iran) for carious pulp exposure in vital permanent teeth were also searched in PubMed and Google search engines.

## Results

### Systematic reviews on effectiveness of different treatment options

Miayshita *et al.*, reviewed randomized controlled trials to assess the effectiveness of techniques used to treat asymptomatic carious teeth and maintain pulp vitality in a Cochrane systematic review. Reviewers expressed no consensus on the effectiveness of different treatment modalities and suggested that further well designed RCTs are needed to investigate the potential of contemporary materials, which may be suitable for the management of carious teeth (11). In 2010, a systematic review was conducted by Swedish Council on Health Technology Assessment on methods of diagnosis and treatment in



endodontics. Their first conclusion was that "because of the lack of studies, it is not possible to determine which diagnostic methods can disclose whether a vital but injured pulp can be maintained or whether it should be removed and replaced with a root filling. The available research provides limited direction as to what distinguishes a treatable from a non-treatable pulpal inflammation (pulpitis)". Another important conclusion of the review is that "there is no scientific basis for assessment of which method, indirect pulp capping, step-wise excavation, direct pulp capping, partial pulpal amputation or pulpal amputation gives the most favorable conditions for maintaining the pulp in a vital and asymptomatic condition". The authors have suggested studies to be conducted in order to answer the question of whether a pulp exposed by caries or other causes is best treated by measures intended to preserve the pulp or pulpectomy and root filling and also, studies to investigate whether root filled teeth survive in long-term and what factors influence the loss of endodontically treated teeth (4). In 2011, Aguilar and Linsuwanont conducted a systematic review to illustrate the outcome of vital pulp therapy, namely direct pulp capping, partial pulpotomy, and full pulpotomy, in vital permanent teeth with cariously exposed pulp. According to this review, no significant statistical difference was evident between treatment results of calcium hydroxide and MTA. The results of this review, however, were based on pooling success rates of the two materials in studies with different levels of evidence and different methodological quality levels. No comparison was found between different vital pulp therapy techniques. Authors also expressed no consensus on definition of reversible and irreversible pulpitis. Well-designed randomized controlled trials have been suggested to compare the effectiveness of different vital pulp therapy techniques and their indications (5).

### Review of original literature

**First question:** Which treatment option is mostly recommended for management of carious pulp exposure with or without irreversible pulpitis in "open-apex" permanent teeth based on the best current evidence?

#### Full pulpotomy

In 1993, Caliskan treated 24 permanent teeth of individuals aged 10-22 years diagnosed with hyperplastic pulpitis by pulpotomy with calcium hydroxide. The treatment was successful in 22 teeth. The follow-up period was 12-48 months. From 24 studied teeth, one had shown failure at the 4-month follow-up and one at the 6-month follow-up. This study lacked a control group (LOE III) (12). In 1995, Caliskan treated

permanent vital molars of 10-24 year olds with carious pulp exposures and periapical involvement presenting as radiolucencies or radiopacities on radiographic examination with calcium hydroxide. The follow-up period was 16-72 months. From 26 studied teeth, one had shown failure at the 2-week follow-up and one at the 6-week follow-up. This study lacked a control group (LOE III) (13). Waly compared the results of calcium hydroxide-glutaraldehyde and calcium hydroxide pulpotomies of 20 cariously exposed first permanent molars. The studied teeth were followed for five years. All 10 samples of calcium hydroxide-glutaraldehyde group were successful. However, two cases out of 10 showed failure at 24 months and 36 months in calcium hydroxide group. Random allocation into two study groups had not been mentioned (LOE III) (14). Teixeira *et al.*, followed 41 permanent mandibular molars with deep carious lesions and/or exposed pulps that were treated with pulpotomy and dressed with calcium hydroxide. The overall success rate of pulpotomies with calcium hydroxide was 83% (LOE III) (15). Witherspoon *et al.*, followed 23 symptomatic permanent teeth for 6-53 months after MTA pulpotomy. Nineteen teeth were available for recall. Of these, 15 were healed i.e. the apex had been closed, three were healing i.e. the apex was closing and one had failed to heal. This study also lacked a control group (LOE III) (16). El-Meligy and Avery randomly allocated 15 children, each with at least two immature permanent teeth requiring pulpotomy (apexogenesis), to either MTA or calcium hydroxide group. Follow-up visits were done at three, six and 12 months. Among 15 pulpotomized teeth with MTA, no failure was reported; whereas two failures were noted in the calcium hydroxide group after 12 months. Power of this randomized controlled trial was low because of small sample size (LOE II) (17). In a randomized controlled trial, Nosrat *et al.*, compared CEM cement and MTA in carious exposed vital immature permanent first molars. Closure of apex was evident in 41 and 45 roots out of 55 roots treated with CEM and 35 and 44 roots out of 54 roots treated with MTA at six- and 12-month follow-up visits. All other apices were closing in both study groups and no clinical and radiographic failures were reported in either group. No significant statistical difference was shown between the study groups (LOE I) (18).

Studies on the effectiveness of partial pulpotomy and direct pulp capping for treatment of cariously exposed permanent teeth have been done simultaneously on both open- and closed-apex teeth.

#### Partial pulpotomy

Baratieri *et al.*, followed 26 treated permanent teeth with



carious exposure, which had received partial pulpotomy with calcium hydroxide. Over an average follow-up period of 18 months, they reported no failures (LOE III) (19). Mejare and Cvek monitored 37 young posterior teeth with deep carious lesions and exposed pulps, which received partial pulpotomy with calcium hydroxide. After an average observation time of 56 months, failure occurred in two of 31 asymptomatic teeth and two of six symptomatic teeth (LOE III) (20). Barreishi-Nusair and Qudeimat treated 31 first permanent molars of seven- to 13-year-old patients with a carious exposure using partial pulpotomy with gray MTA. Twenty-eight teeth were available in the follow-up period with an average of 17.5 months. They reported that 22 teeth did not show any clinical or radiographic signs of failure. Although six teeth did not respond to vitality tests, no radiographic signs of failure were identified (LOE III) (21). In a randomized clinical trial, Qudeimat *et al.* performed partial pulpotomy on first permanent molars with either MTA or calcium hydroxide. All teeth were exposed by a carious lesion and 79% were open-apex. In an average follow-up period of 34.5 months, 13 of 64 teeth had left the study (loss to follow-up >20%). Two failures were reported in each group (success rate: 91% and 93%) (LOE II) (22). Mass and Zilberman treated 49 young permanent molars with a carious exposure by partial pulpotomy with calcium hydroxide. After an average observation time of 49 months, three failures were reported out of 49 teeth. Six molars that had received apexogenesis were also successfully treated (LOE III) (23).

### Direct pulp capping

Haskell *et al.*, reported a success rate of 78.3% in 149 permanent teeth with carious exposure, which were treated with direct pulp capping with calcium hydroxide or penicillin crystals; 23.8% of patients were available after 5-22 years (LOE IV) (24). In a study reported by Gallien and Schuman, the investigators treated 40 cariously exposed teeth with formocresol pulpotomy (for primary teeth) or direct pulp capping with calcium hydroxide (for permanent teeth). All patients were followed for one-three years and three failures were reported out of 17 direct pulp capping cases (LOE III) (25). Matsuo *et al.*, evaluated the success rate of direct pulp capping with calcium hydroxide for cariously exposed permanent teeth. The cases were followed for three-36 months and four teeth remained in the study. The success rate after a nine-month follow-up was 82.8% with 35% loss of samples (LOE III) (26). In a retrospective study, Santucci investigated

the efficacy of direct pulp capping in permanent teeth with Nd:YAG laser and Vitrebond compared to calcium hydroxide over intervals of up to 54 months; 29 cases received calcium hydroxide direct pulp capping and the cumulative proportion surviving declined from 89.7% at one month to 43.6% after 54 months (LOE III) (27). Barthel *et al.*, studied the treatment outcome of pulp capping in permanent teeth with carious exposures after five and 10 years; 123 pulp-capped teeth were followed-up out of 401 cases. The results showed 37% success rate at five years and 13% success rate in 10 years (LOE IV) (28). Farsi *et al.*, evaluated the results of direct pulp capping with MTA in 30 young cariously exposed permanent teeth; 22 teeth had open apices. The follow-up period was 24 months and all patients were available. Root-end closure occurred in all open-apex teeth and success rate was reported to be 93% (LOE III) (29). Bogen *et al.*, examined the long-term success rate of direct pulp capping with MTA in permanent teeth with carious exposure. Over an observation period of nine years, 49 of 53 teeth were available for recall appointments and 97.96% had favorable outcomes. All teeth that initially had open apices (15/15) showed complete root formation (LOE IV) (30). Mente *et al.*, determined the clinical success of direct pulp capping using MTA (53 cases) or calcium hydroxide (69 cases) in permanent teeth with carious exposure. The observation time was 12–80 months (median: 27 months) with 72.5% recall rate. A significant difference in success rates was recorded between the MTA group (78%) and the calcium hydroxide group (60%) (LOE III) (31).

The expert panel came to the decision that the treatment outcomes of one randomized controlled trial with LOE I (18) was absolutely appropriate regarding the local factors, and enjoyed the absolute consensus of the expert panel.

**Recommendation: Full pulpotomy with CEM cement is recommended in vital permanent teeth with open apex –with or without irreversible pulpitis- following carious pulp exposure (Grade A).**

**Second question:** Which treatment option is mostly recommended for management of carious pulp exposure with or without irreversible pulpitis in “closed-apex” permanent teeth based on the best current evidence?

### Root canal therapy

In 2000, Kirkevang *et al.*, performed an epidemiologic study on



773 endodontically treated teeth in Denmark; 52.3% of the teeth had apical periodontitis and were considered as failure (LOE II) (32). In a meta-analysis and systematic review, Kojima *et al.*, reported a success rate of 82.8% for root canal treatments in vital teeth (LOE II) (33). Caplan *et al.*, conducted a retrospective matched cohort study and demonstrated that root canal filled (RCF) teeth -especially molars- had significantly worse survival than their non-RCF counterparts. Adjusted hazard ratio for loss of RCF versus non-RCF molars was 7.4 (LOE III) (34).

Another systematic review by Ng *et al.* demonstrated that success rates of root canal treatments ranged between 68% and 85%. The review also revealed that there was no improvement in success rates over the last four or five decades (LOE III) (35). Sunay *et al.*, investigated the quality of root canal treatment in an adult Turkish population in an epidemiologic study. The periapical status of 8,863 teeth was evaluated and 53.5% of root-filled teeth presented apical periodontitis, 91% of which were determined to have inadequate root fillings (LOE II) (36). In a 2010 epidemiologic study in Iran, Asgary *et al.* showed that 52% of the endodontically treated teeth presented with apical periodontitis. Only 42.3% of endodontically treated teeth fulfilled the criteria of an acceptable RCT (LOE II) (37). In a randomized clinical trial, Asgary *et al.*, randomly treated 407 teeth with irreversible pulpitis with either root canal therapy or vital pulp therapy with calcium-enriched mixture cement (VPT/CEM). Six- and 12-month follow-ups did not show statistical difference in clinical success rates; but the results of radiographic evaluation illustrated that the radiographic success rate of VPT/CEM was significantly greater than that of RCT at both follow-ups. At 12-month follow-up, the radiographic success rate in VPT/CEM and RCT groups was 92% and 70%, respectively (LOE I) (38). Pak *et al.*, carried out a systematic review and meta-analysis in 2012 to investigate the prevalence of periapical radiolucencies and root canal treatment in cross-sectional studies. From 300,861 teeth, 5% had periapical radiolucency and 10% were root-filled. An interesting finding of the study was that 36% of all endodontically treated teeth showed periapical radiolucency. The authors of 24 of the 33 included studies found the RCTs to be of low quality (LOE II) (39).

#### Full pulpotomy

In a randomized clinical trial, Asgary *et al.*, randomly treated 407 teeth with irreversible pulpitis with either root canal therapy or VPT/CEM. Six- and 12-month follow-ups did not show statistical difference in clinical success rates; however, the results of radiographic evaluation illustrated that the

radiographic success rate in VPT/CEM was significantly greater than in RCT at both follow-ups. At 12-month follow-up, the radiographic success rate in VPT/CEM and RCT was 92% and 70%, respectively (LOE I) (38). In another randomized clinical trial, Asgary and Eghbal randomly allocated 413 permanent molars with irreversible pulpitis into two study arms: MTA pulpotomy and CEM pulpotomy. At 12-month follow-up, the clinical and radiographic success rates were 98% and 95% for MTA; and 97% and 92% for CEM, respectively. No significant differences in clinical ( $P=0.7$ ) and radiographic ( $P=0.4$ ) success rates were found between the two groups (LOE I) (40).

Studies on the effectiveness of partial pulpotomy and direct pulp capping for treatment of cariously exposed permanent teeth have been done simultaneously on both open- and closed-apex teeth (20-32).

It should be mentioned that no randomized controlled trial was found on the use of Angelus MTA (Brazil) and Root MTA (Iran) for pulpotomy or direct pulp capping of carious pulp exposures in vital permanent teeth.

The expert panel came to the decision that the treatment outcomes of the two randomized controlled trials with LOE I (38, 40) were absolutely appropriate regarding the local factors, and enjoyed the absolute consensus of the expert panel.

#### Recommendation

**Full pulpotomy with CEM cement is recommended in vital permanent teeth with closed apex -with or without irreversible pulpitis- following carious pulp exposure (Grade A).**

## Discussion

Irreversible pulpitis can be a very painful condition with a severe impact on the quality of life. To relieve the pain, many patients choose tooth extraction over RCT because of financial considerations or no access to advanced dental facilities (38). Moreover, from a technical point of view, RCT is one of the most demanding dental procedures. Epidemiologic studies carried out in different countries have shown a high prevalence of apical periodontitis following RCT (32, 34, 35, 37). With recent progress in tissue management methods, VPT/CEM might be an affordable alternative to RCT with the main advantage of maintaining tooth vitality and therefore an increase in tooth survival (41).



It also enjoys a simple technique and requires minimal equipment. Recent studies have demonstrated dental pulp stem cells with tissue regenerative potential in permanent teeth with irreversible pulpitis and the fact that such teeth can be successfully managed by VPT (5, 42). Since in VPT the vitality of the pulp is preserved, the remaining pulpal tissue is stimulated to continue healing. The response of the pulp depends on creating a biological seal, which eliminates the connection between the pulp and the oral environment, preventing the main cause of failure, which is bacterial recontamination (43).

The aim of the current study was to implement an exhaustive review of the best current evidence on treatment options of carious pulp exposures in vital permanent teeth with or without irreversible pulpitis. The retrieved evidence was critically reviewed and used for development of an evidence-based clinical practice guideline.

The search queries were formulated using the Medical Subject Headings (MeSH terms) and clinical filters of PubMed were extensively used. The strategy was broad and sensitive in order not to miss any relevant evidence. TRIP database, the Cochrane Library and Clinicaltrials.gov were also searched for increasing search coverage.

Relevant retrieved evidence was then reviewed critically using a novel methodological quality assessment tool (9), which is a modification of van Tulder's checklist.

The most recent systematic review on the focus of the current study, done by Aguilar and Linsuwannont has reviewed original clinical studies of vital pulp treatment of human vital permanent teeth with cariously exposed pulp with at least 6-month follow-up (5). The VPT agents reviewed were calcium hydroxide or MTA used for direct pulp capping, partial pulpotomy and full pulpotomy. All the studies reviewed in this systematic review were analyzed and critically reviewed again in addition to studies retrieved from our search.

Since development of evidence-based clinical recommendations for guidelines is a multiple-criteria decision making process, the efficacy of each intervention extracted from the best current evidence and potential side effects and benefits of treatment options should be considered in line with other criteria relevant to local clinical practice i.e. treatment expenses, applicability and generalizability of scenarios and thus were proposed to the expert panel for rating the scenarios' appropriateness. This brings about local concerns and limitations to be taken into account on deciding on the

treatment options.

The SIGN has stated that the panel composition has considerable influence on the guideline recommendations (6). One favorable feature of this guideline was the diversity of the expert panel. Our multidisciplinary expert panel comprised of ALL full professors of endodontics nationwide, in addition to selected expert pedodontists along with representatives of different organizations involved in dental public health, insurance and social affairs, and dental association representatives who led to involvement of all potential stakeholders. Although this diversity brought us some difficulties in arrangements, we believe that for a guideline to become nationally implemented, it plays a critical role to engage all involved people/organizations in the process of development, which allows for many potential obstacles of implementation to be identified and addressed in advance.

Adding Panel Consensus to the grading system in line with Level of Evidence and Scenario Appropriateness was another feature of this guideline development process. This means that even when there is evidence of high level, if the panel does not *agree* on a recommendation, it gets a lower grade. This approach to grading is for addressing all possible applicability limitations, which might have been ignored. The same approach can be found in other guideline development organizations such as SIGN by including the applicability to target population as a criterion for grading and European Society of Cardiology by including the agreement on scenarios as a criterion for grading (44). This could have complicated the choice of recommendations, as a scenario supported by high-level evidence could have been appropriate, but incomplete consensus was reached in this regard. This, however, was not the case in the present guideline. The major recommendations of the guideline were based on studies at the top of the hierarchy of study design and methodological quality (high levels of evidence) as well as absolute consensus of the expert panel. This demonstrates the strength of supporting evidence and that the proposed scenario can and should be confidently recommended.

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