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SYSTEMATIC REVIEW

Treatment Outcomes and Prognostic Factors of Direct Pulp Capping in Permanent Teeth: A Systematic Review and Meta-analysis

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ABSTRACT

This study aimed to evaluate the overall treatment outcomes of direct pulp capping in permanent teeth and investigate the prognostic factors. MEDLINE via Ovid, EMBASE, PubMed, Cochrane Library, and manual search methods were used to select the included studies. After thorough screening, the criteria for quality assessment and data extraction were determined. Meta-analysis was performed using the random-effects model and meta-regression analysis. This systematic review included 33 studies, 11 prospective cohort studies, 9 retrospective cohort studies, and 13 randomised clinical trials. After applying the quality assessment criteria, 26 articles were included in the meta-analysis. The weighted pooled success rate was 83%, with a 95% confidence interval of 79-87% in studies that ranged from 6 months to 10 years. The meta-regression analysis showed that rubber dam isolation throughout all procedures was significantly more effective than other techniques (risk ratio=1.44; 95% confidence interval 1.06-2.16, $p<0.05$). This study provides evidence of successful treatment outcomes in direct pulp capping of permanent teeth, with "adequate tooth isolation" identified as a significant prognostic factor.

Keywords: Direct pulp capping, meta-analysis, prognosis, systematic review, treatment outcomes

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HIGHLIGHTS

- This systematic review and meta-analysis showed an 83% success rate of DPC.
- It was recommended that DPC be performed on vital teeth when asymptomatic and normal apical conditions are present.
- Adequate tooth isolation with a rubber dam during all treatment procedures, including the aseptic technique, was the key to success.

INTRODUCTION

Pulp exposure due to caries, trauma, or mechanical preparation can lead to pulp inflammation and microbial infection (1, 2). The two main treatment options for irreversible pulpitis are (i) pulpectomy or (ii) vital pulp therapy (VPT), i.e. direct pulp capping (DPC), partial pulpotomy (PP), and complete pulpotomy (FP). DPC is a procedure that is used when vital pulp tissue is exposed. A suitable dental material is placed on the non-inflamed pulp to facilitate healing and preservation of the remaining vital pulp (3). The prerequisites for a successful outcome in VPT were outlined as follows: healthy condition of the pulp tissue, controlled bleeding, non-toxic pulp capping materials, and bacteria-tight sealing (4). In addition, accurate diagnosis, appropriate case selection, and appropriate treatment contribute to favourable outcomes (5). Previous systematic reviews showed a high success rate for PP (99.4%) and FP (99.3%) in permanent teeth (6). Although several studies reported satisfactory treatment outcomes for DPC, the indicators and clinical factors influ-

encing outcomes varied and were highly controversial (5–9). Conducting a systematic review and meta-analysis of relevant articles can provide a higher level of evidence-based data to make more accurate clinical decisions.

This systematic review and meta-analysis aimed to evaluate the overall treatment outcomes of DPC in permanent teeth and to investigate and identify the significant prognostic factors influencing treatment outcomes.

MATERIALS AND METHODS

The systematic process was conducted using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines published in 2020 (10). The question, "What clinical factors affect the treatment outcomes of DPC in vital permanent teeth?" was used to construct the PICOS framework as follows:

- Population (P): vital, pulp-exposed permanent teeth.
- Intervention (I): direct pulp capping.
- Comparison (C): preoperative, intraoperative, and postoperative factors.
- Outcome (O): successful outcome, defined as an asymptomatic tooth with normal apical tissues on the radiographic examination.
- Study design (S): non-randomised studies of interventions and randomised clinical trials.

Literature Search

In this meta-analysis, four electronic databases (MEDLINE via Ovid, EMBASE, PubMed and Cochrane Library) were used to systematically search for studies published before January 2022 using the following 7 keywords (vital pulp therapy, vital pulp treatment, direct pulp capping, permanent teeth, success rate, treatment outcome, prognosis). In PubMed, MEDLINE and the Cochrane Library, the keywords were searched directly in the medical subject headings, while the search for MeSH terms was conducted via the National Centre of Biotechnology Information (NCBI). Each keyword and MeSH term was used for the initial search and combined with the Boolean operators (Appendix 1). In addition, the references of five Endodontic textbooks, including Pathways of the Pulp (Hargreaves and Cohen, 11th ed., 2016), Endodontics (Ingle and Bakland, 7th ed., 2019), Textbook of Endodontology (Bergenholtz, Horsted-Bindslev, and Reit), Endodontics: Principles and Practice (Torabinejad and Walton, 5th ed, 2015) and Essential Endodontology (Ørstavik, 3rd ed., 2020) as well as seven public journals (Journal of Endodontics, International Endodontic Journal, Australian Endodontic Journal, Dental Traumatology, Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology and Endodontics, Endodontic topics and Iranian Endodontic Journal) were searched manually. Unpublished studies, such as records of ongoing research or conference proceedings, were also identified as potential reference material for this study.

Study Selection

The literature from the electronic and manual search was checked for relevance using the titles and abstracts of all reports. Once all relevant articles were found, the complete articles were selected based on the defined selection criteria. The eligible studies were required to meet all of the following inclusion criteria. The reasons for rejection at various stages were also reported.

Inclusion Criteria

- Studies of DPC treatment.
- Evaluation of treatment outcomes based on both clinical and radiographic examination.
- Sample size was provided.
- The success rate was available or at least calculable from the data provided.
- Description of the preoperative data, treatment procedure, and outcome assessment.
- A minimum of a six-month follow-up period.
- Articles published in the English language.

Exclusion Criteria

- Studies of case reports or case series.
- Studies conducted on animal or human deciduous teeth.

Quality Assessment

The modified Downs and Black quality checklist for non-randomised studies was used to provide scores in the three domains: (i) reporting bias, (ii) validity of the study, and (iii) statistical power (11). The above criteria were used to determine the total score for each checklist of the study: excellent (26–28), good (20–25), fair (15–19) and poor quality (≤14) (12).

For the randomised trials included in this study, we used the Cochrane Risk of Bias 2.0 tool (RoB2) to determine the risk of bias in the five individual study domains: randomisation, performance, missing data, outcome assessment, and reporting bias. The levels of risk bias for each trial were determined as follows: (i) "low risk" (when having "low risk" in all domains), (ii) "some concerns" (when having at least "some concerns" in one domain without "high risk"), and (iii) "high risk" (when having at least "high risk" in one domain or "some concerns" in multiple domains) (13). Studies considered of poor quality or at "high risk of bias" were not included in the meta-analysis.

Data Extraction

The selected studies were processed for data extraction. The preoperative, intraoperative and postoperative factors were collected and recorded using the following data points: Age, tooth type, pulp status, periapical status, root development, cause of exposure, tooth isolation, site of exposure, size of exposure, controlled bleeding time, haemostatic agents, haemostatic method, pulp capping material, liner or base, restorative material, timing of restoration, use of magnification, treatment provider, and recall period. The entire process of systematic review and data extraction was performed independently by three different authors. Any discrepancies were discussed, and final decisions were made.

Meta-analysis

All statistical analyses were performed using STATA version 16.0 (Stata Corp, College Station, TX, USA). The heterogeneity of the study was measured using Cochran's Q-test and

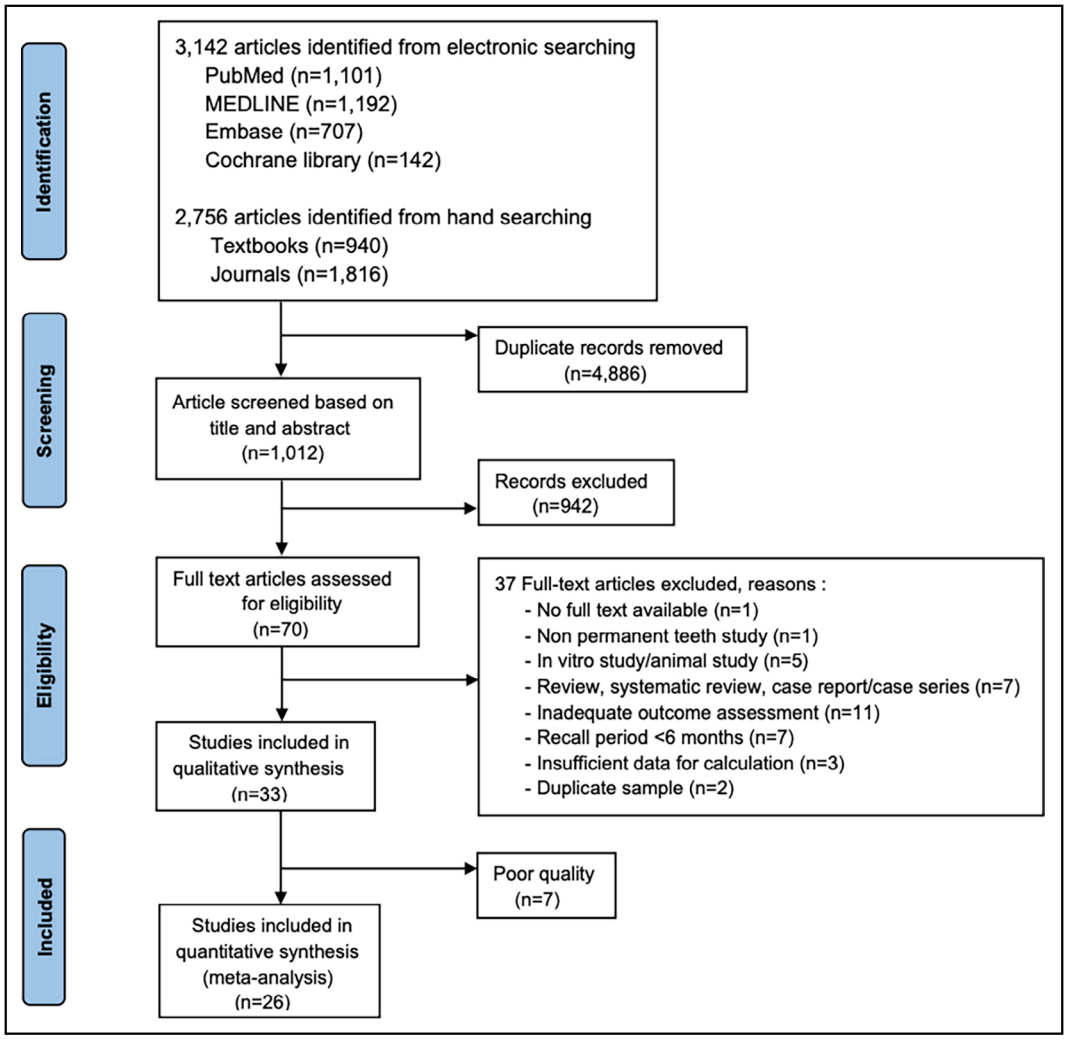

Figure 1. The PRISMA flow diagram

the I-squared (I^2) statistic. A Q-test $p<0.10$ was considered significant heterogeneity. An I2 value of more than 75% was interpreted as high heterogeneity among studies. If the presence of high heterogeneity was detected, a subgroup analysis of the initial study was performed. The DerSimonian and Laird random effects model was used to analyse the weighted pooled success rate. Prognostic factors were assessed using the univariable meta-regression models.

Multiple sensitivity analyses based on the different conditions were used to evaluate the robustness of pooled results accurately. An alteration of the weighted pooled success rate of more than 5% was interpreted as lacking result robustness.

Publication bias was assessed from the visual inspection of the funnel plot with Egger's regression asymmetry test. The asymmetrical shape of the funnel plot or Egger $p<0.05$ indicated publication bias. As a result, the source of the funnel plot asymmetry required further investigation.

RESULTS

Study Selection

In the initial search, 5,898 studies were screened, of which 1,012 studies remained after all duplicates had been removed. The titles and abstracts of each study were screened, and the relevant studies were selected for the initial full-text review. Of the 70 studies that underwent a full review, only 33 articles were selected for this study based on the inclusion and exclusion criteria. Following a quality assessment, 26 of the 33 studies were included in the meta-analysis. The subsequent results of the systematic search, including study identification, screening, inclusion, and reasons for exclusion, were presented in the PRISMA flowchart (Fig. 1).

Study Characteristics

The general characteristics of the 33 studies were considered (5, 9, 14–44) and summarised using the following details: Author, year of publication, country, study design, follow-up period, sample size, recall rate (%), and reported success rate (%) (Table 1). The selected articles were published in several different countries between 1985 and 2019. The most relevant articles were from the non-randomised design group, which consisted of 11 prospective cohort studies (5, 15–17, 22, 24, 26, 30, 35, 41, 42), 9 retrospective cohort studies (9, 14, 18–20, 29, 34, 37, 43), and only 13 studies were randomised clinical trials (21, 23, 25, 27, 28, 31–33, 36, 38–40, 44). In all included studies, the reported success rate of DPC ranged from 5.9% to 100%.

TABLE 1. General characteristic of 33 included studies

No	Study	Year	Setting	Design	Age (year)	Follow up	Sample size	Recall rate (%)	Success rate (%)
1	Hørsted et al. (14)	1985	Denmark	RC	10–79	5 Y	245	48	90.2
2	Matsuo et al. (5)	1996	Japan	PC	Mean 41.9	3 Y	44	9	100
3	Barthel et al. (9)	2000	Germany	RC	10–70	10 Y	123	30.7	13
4	Farsi et al. (15)	2006	Saudi Arabia	PC	9–12	2 Y	30	100	93
5	Olivi et al. (16)	2007	Italy	PC	Mean 14.5	4 Y	34	100	73.5
6	Bogen et al. (17)	2008	USA	PC	Mean 16.6	Mean 3.94 Y	49	92.5	97.96
7	Miles et al. (18)	2010	USA	RC	Mean 42±15.6 SD	2 Y	51	68	60.78
8	Willershausen et al. (19)	2010	Germany	RC	Mean 37.1±15.3 SD	1 Y	1075	49.7	80.1
9	Cho et al. (20)	2013	Korea	RC	<40, >40	Mean 13.7 Y	175	71.4	78.9
10	Hilton et al. (21)	2013	USA	RCTs	Mean 37.9	2 Y	358	95.2	81
11	Bansal et al. (22)	2014	India	PC	18–42	2 Y	30	93.75	83.33
12	Yazdanfar et al.(23)	2014	Germany	RCTs	Mean 26	1 Y	10	100	80
13	Mente et al. (24)	2014	Germany	PC	Median 44	4 Y	229	74	75
14	Jang et al. (25)	2015	Korea	RCTs	Median 42	1 Y	41	89.13	85.36
15	Marques et al. (26)	2015	Netherland	PC	Mean 36.1	Mean 3.6 Y	46	71.8	91.3
16	Cengiz et al. (27)	2016	Turkiye	RCTs	Mean 28	6 M	60	100	85
17	Bjøndal et al. (28)	2017	Denmark	RCTs	Median 29	5 Y	17	100	5.9
18	Caliskan et al. (29)	2017	Turkiye	RC	Mean 29.7±10.59 SD	24–72 M	152	88.4	82.24
19	Daniele et al. (30)	2017	Italy	PC	14–68	10 Y	80	100	92.5
20	Hegde et al. (31)	2017	India	RCTs	18–40	6 M	24	100	87.5
21	Katge et al. (32)	2017	India	RCTs	7–9	1 Y	42	72.4	100
22	Kundzina et al. (33)	2017	Norway	RCTs	Mean 30.2	3 Y	65	92.8	67
23	Linu et al. (34)	2017	India	RC	15–30	18 M	26	86.67	88.5
24	Lipski et al. (35)	2017	Poland	PC	Median 44	Median 14.7 M	86	76.8	82.6
25	Parinyaprom et al. (36)	2017	Thailand	RCTs	Mean 10±2 SD	Mean 18.9 M	55	93.2	94.5
26	Wang et al. (37)	2017	China	RC	6–16	Median 23 M	28	100	42.9
27	Brizuela et al. (38)	2017	Chile	RCTs	Mean 11.3	1 Y	69	40.8	91.3
28	Asgary et al. (39)	2018	Iran	RCTs	Mean 28.15	1 Y	57	78	94.7
29	Awawdeh et al. (40)	2018	Jordan	RCTs	Mean 32.5	3 Y	15	88.24	93.33
30	Oz et al. (41)	2019	Turkiye	PC	18–60	Mean 62 M	65	97	60
31	Kusumvalli et al. (42)	2019	India	PC	15–40	1 Y	7	100	85.7
32	Paula et al. (43)	2019	Portugal	RC	Mean 32.2	6 M	21	100	95
33	Suhag et al. (44)	2019	India	RCTs	Mean 21.8	1 Y	56	87.5	80.4

RC: Retrospective cohort study, PC: Prospective cohort study, RCTs: Randomised clinical trials, SD: Standard deviation, Y: Year, M: Month

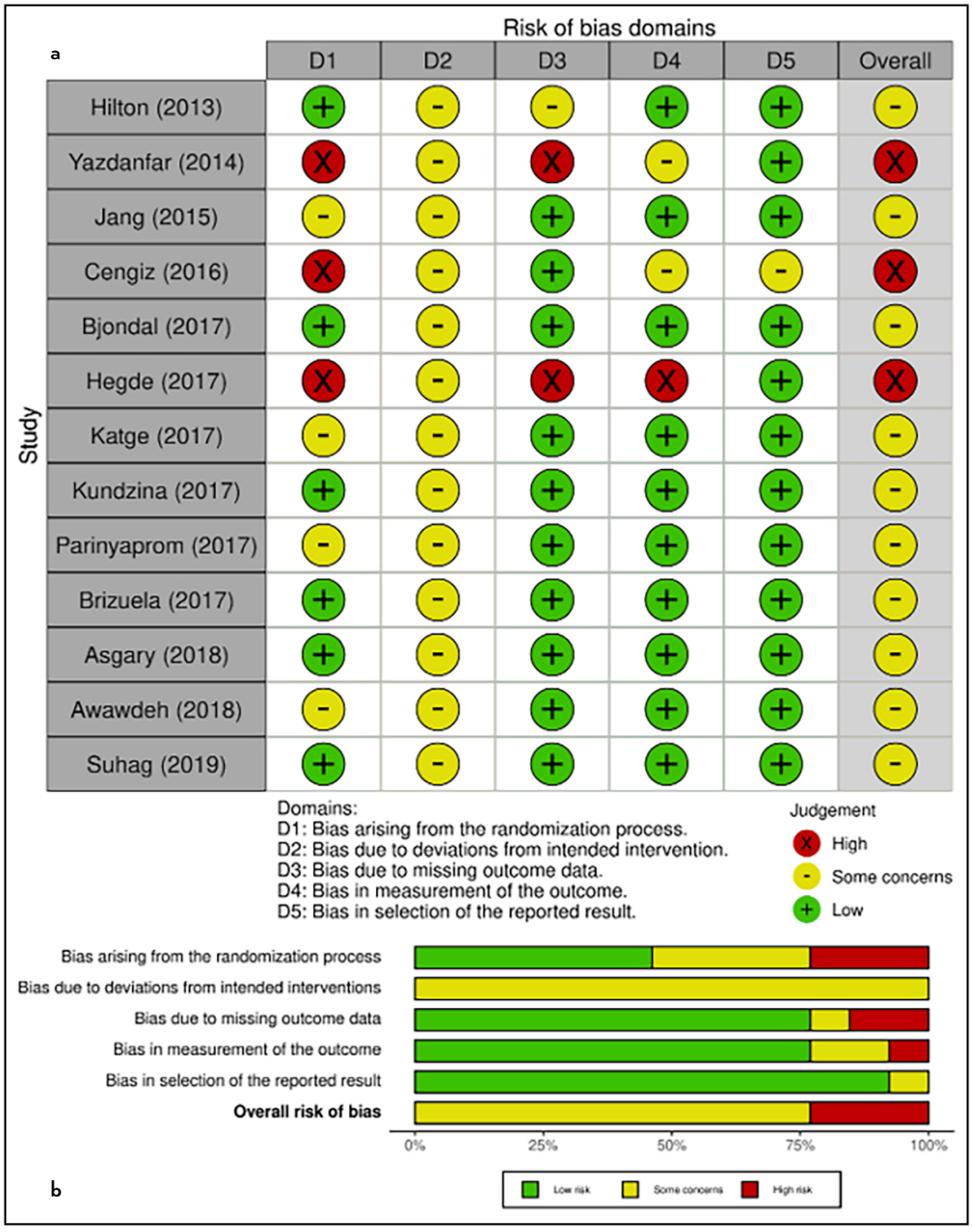

Figure 2. (a) A summary of the risk of bias in the randomised studies. (b) A review of the risk of bias domain presented as percentages

Quality Assessment

In the non-randomised studies, the mean Downs score was 18.55±3.27 (Mean±standard deviation (SD)) (between 10 and 23). A total of 9 studies were classified as being of good quality (14, 18, 24, 26, 29, 30, 34, 35, 41), 7 with fair quality (15, 17, 19, 20, 22, 37, 43), and 4 indicating poor quality (5, 9, 16, 42) (Appendix 2). For the remaining randomised clinical trials, most articles were assessed as having Some concerns of bias (21, 25, 28, 32, 33, 36, 38–40, 44), and 3 randomised trials were evaluated as having an overall high risk of bias (23, 27, 31) (Fig. 2). All seven studies considered as poor quality and at high risk of bias were excluded (5, 9, 16, 23, 27, 31, 42), and 26 remaining studies were considered for the quantitative synthesis (14, 15, 17–22, 24–26, 28–30, 32–41, 43, 44).

Meta-analysis

Study heterogeneity & pooled results

The overall I2 value was 87.93%, and the Q test p<0.01, indicating significant heterogeneity among all studies. The weighted pooled success rate of DPC was 83% (95% confidence interval [CI], 79%–87%), and the pooled effect size forest plot is shown in Figure 3. The most of studies had recall period under 5 years as shown in Figure 4.

Exploring the source of study heterogeneity

Subgroup analysis was performed based on various preoperative, intraoperative and postoperative factors (Table 2). These factors included tooth type, cause of exposure, isolation

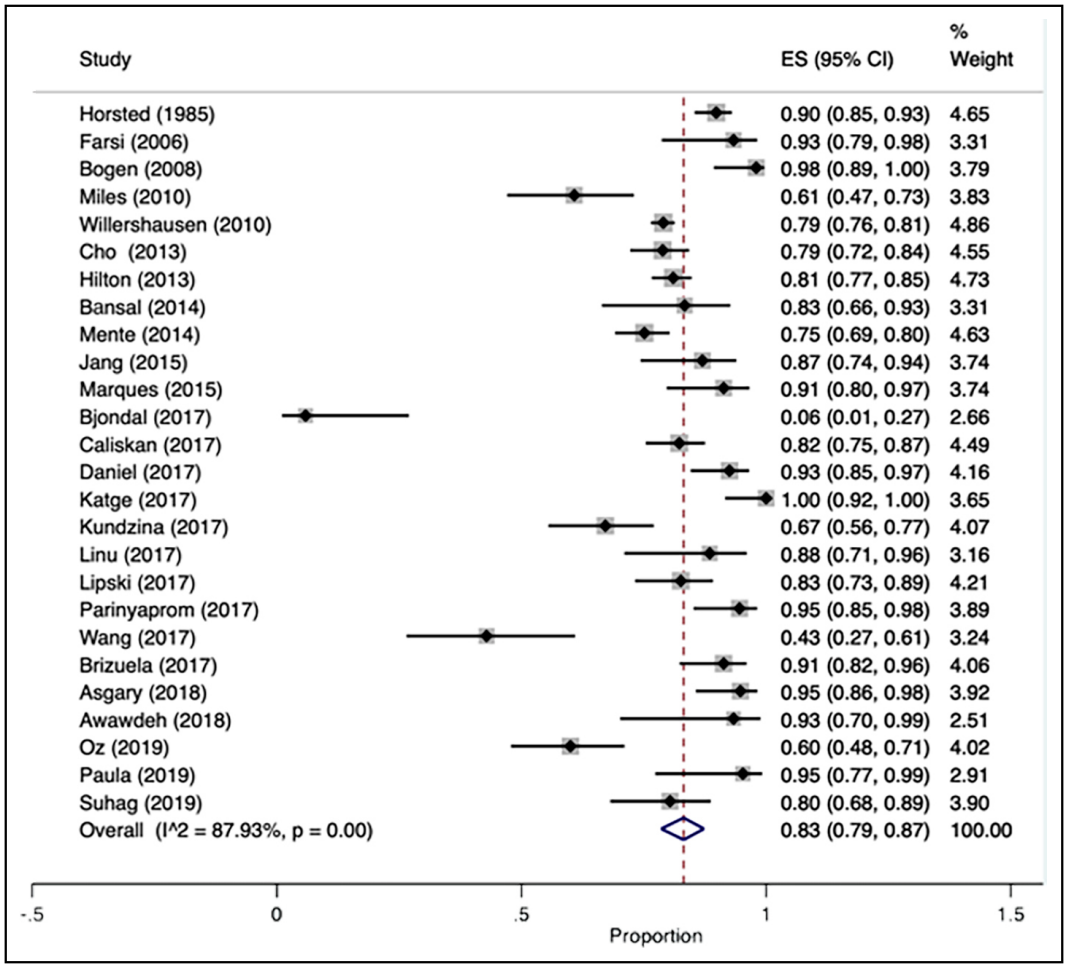

Figure 3. The forest plot of pooled effect size from 26 included studies

ES: Effect size; CI: Confidence interval

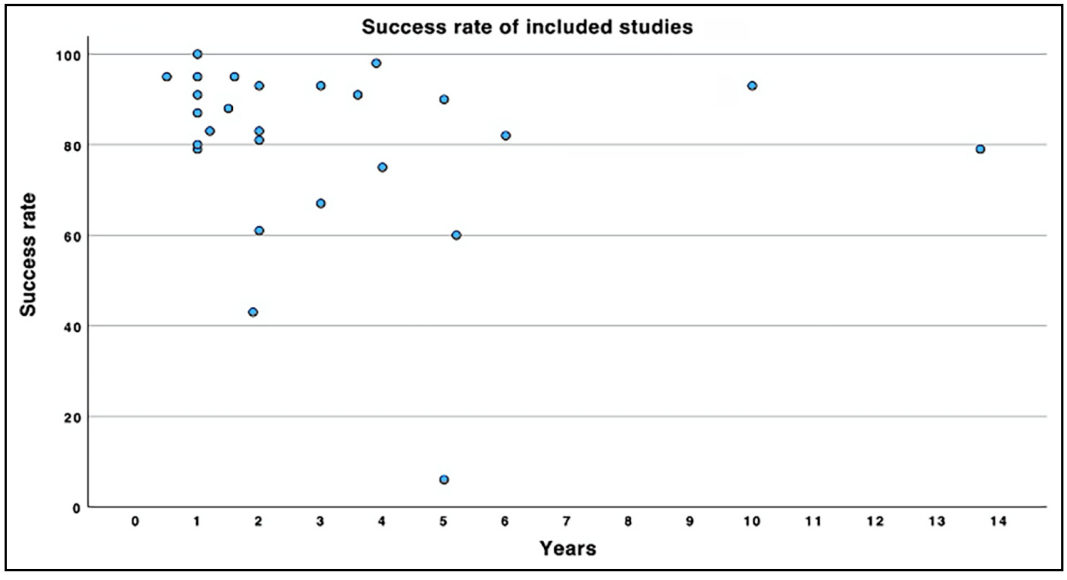

Figure 4. The success rates of included studies

of the tooth, haemostatic agents, haemostatic method, pulp capping material, and use of magnification, which were the suspected sources of heterogeneity based on I2 percentage and Q-test p-value. In all studies, the possible sources of high heterogeneity were differences in these factors.

Assessment of significant prognostic factors

The univariable meta-regression analysis showed tooth isolation was a significant prognostic factor (Table 3). The relative risk (RR) for rubber dam isolation in all treatment steps was 1.44 (95% CI, 1.06–2.16, p<0.05). The increased risk for a fa-

TABLE 2. Subgroup analysis based on the preoperative, intraoperative, and postoperative factors

Prognostic factors	No. of study	Sample size	Pooled success rate (%) [95% CI]	Weight (%)	Q test p-value	I square (%)
Preoperative factors						
Age					0.27	86.99
≤20 years	7	287	91 (79–98)	26.31		87.46
21–40 years	10	1,691	80 (71–87)	37.88		87.26
>40 years	8	427	82 (76–87)	35.81		80.13
Tooth type					0.06*	83.24
Anterior teeth	6	244	78 (70–86)	30.86		87.21
Posterior teeth	15	1,387	87 (82–91)	69.14		81.58
Pulpal status					0.11	87.43
Asymptomatic#	17	2,396	91 (84–96)	89.81		88.14
Symptomatic	2	56	84 (79–89)	10.19		–
Periapical status					0.56	87.95
Normal	17	2,450	84 (79–89)	81.27		89.64
Uncertain##	4	268	87 (78–94)	18.73		72.06
Root development					0.55	89.32
Open apex	4	118	88 (62–100)	35.33		93.15
Close apex	7	376	80 (69–90)	64.67		85.70
Cause of exposure					<0.01*	89.06
Caries	18	1,269	85 (79–90)	77.95		86.56
Non-caries	5	520	79 (61–92)	22.05		94.49
Intraoperative factors						
Rubber dam isolation (throughout all procedures)					0.01*	88.18
Yes	16	1,170	88 (83–92)	61.46		81.04
No	10	2,003	74 (64–82)	38.54		92.49
Location of exposure					0.59	63.09
Occlusal surface	9	453	83 (79–87)	51.43		57.21
Axial surface	8	409	85 (80–90)	48.57		71.37
Size of exposure					0.99	88.18
≤1 mm	7	1,596	86 (78–93)	77.35		90.03
>1 mm	2	54	86 (81–91)	22.65		–
Controlled bleeding time					0.12	90.97
<5 min	4	508	90 (82–96)	46.95		81.43
5–10 min	5	363	74 (50–93)	53.05		93.74
Haemostatic agents					<0.01*	88.89
NaOCl	11	653	85 (78–91)	52.70		82.28
Non-NaOCl	8	820	82 (71–92)	38.06		91.72
None	2	93	55 (45–65)	9.24		–
Haemostatic method					0.04*	83.01
Pressing with soaked cotton	13	1,431	86 (81–91)	61.15		86.34
Pressing with dry cotton	2	1,121	80 (77–82)	10.6		–
Irrigation & cotton pressing	6	475	86 (80–92)	28.25		68.66
Pulp capping material					0.01*	85.19
Calcium hydroxide	11	1,916	76 (70–82)	39.52		89.49
Calcium-silicate based material	19	1,179	86 (82–90)	60.48		80.59
Liner or base					0.23	88.18
Yes	17	1,763	85 (80–89)	66.83		83.33
No	9	1,410	78 (65–89)	33.17		92.74
Restorative material					0.34	86.98
Amalgam	4	109	89 (81–95)	17.66		64.65
Resin composite	29	1,117	84 (78–90)	82.34		88.61
Timing of restoration					0.201	89.38
Immediate	8	1,625	79 (69–87)	37.96		91.20
Delayed ≤3 weeks	9	498	88 (81–93)	39.88		75.59
Delayed >3 weeks	5	317	78 (54–94)	22.17		94.75

TABLE 2. Cont.

Prognostic factors	No. of study	Sample size	Pooled success rate (%) [95% CI]	Weight (%)	Q test p-value	I square (%)
Use of magnification					<0.01*	88.18
Yes	4	244	93 (90–96)	15.58		–
No	2	2,929	81 (76–86)	84.42		88.23
Treatment provider					0.39	89.63
Undergraduate student	4	547	73 (57–87)	24.33		93.13
Postgraduate student	4	355	87 (78–93)	23.39		75.94
General practitioner	5	614	81 (73–87)	30.62		80.63
Specialist dentist	4	298	75 (46–96)	21.65		95.70
Postoperative factor						
Recall period					0.60	88.26
6 months-1 year	9	511	80 (64–92)	34.18		92.63
Over 1 year-2 years	6	585	87 (81–91)	23.6		51.43
Over 2 years-3 years	3	136	76 (53–93)	12.15		–
Over 3 years	7	1,845	86 (77–92)	30.07		89.43

#: Presence of short-lived thermal sensation or absence of symptoms; ##: No radiographic information was described; *: Q test p-value<0.10 was considered as evidence of significant heterogeneity. CI: Confidence interval; NaOCl: Sodium hypochlorite

TABLE 3. Univariable meta-regression analysis

Prognostic factors	Risk ratio	95% CI	p
Preoperative factors			
Age			
≤20 years	1.28	0.73–2.23	0.367
21–40 years	1	–	–
>40 years	1.21	0.72–2.06	0.447
Tooth type			
Anterior teeth	1	–	–
Posterior teeth	1.05	0.93–1.19	0.351
Pulpal status			
Asymptomatic	1.21	0.46–3.18	0.678
Symptomatic	1	–	–
Periapical status			
Normal	1	–	–
Uncertain	1.17	0.6–2.29	0.62
Root development			
Open apex	1.04	0.66–1.62	0.852
Close apex	1	–	–
Cause of exposure			
Caries	1.06	0.59–1.92	0.828
Non-caries	1	–	–
Intraoperative factors			
Rubber dam isolation (throughout all procedures)			
Yes	1.44	1.06–2.16	0.046*
No	1	–	–
Location of exposure			
Occlusal surface	1	–	–
Axial surface	1.01	0.91–1.12	0.871
Size of exposure			
≤1 mm	1	–	–
>1 mm	1.04	0.82–1.32	0.709
Controlled bleeding time			
<5 min	1.76	0.43–7.27	0.378
5–10 min	1		
Haemostatic agents			
NaOCl	1.63	0.63–4.21	0.294
Non-NaOCl	1.28	0.48–3.39	0.605
None	1	–	–

TABLE 3. Cont.

Prognostic factors	Risk ratio	95% CI	p
Haemostatic method			
Pressing with soaked cotton	1.02	0.89–1.18	0.726
Pressing with dry cotton	1	–	–
Irrigation & cotton pressing	1.05	0.89–1.23	0.551
Pulp capping material			
Calcium hydroxide	1	–	–
Calcium-silicate based material	1.30	0.92–1.82	0.513
Liner or base			
Yes	1.35	0.88–2.07	0.166
No	1	–	–
Restorative material			
Amalgam	1.19	0.63–2.26	0.575
Resin composite	1	–	–
Timing of restoration			
Immediate	1.60	0.83–3.01	0.15
Delayed ≤3 weeks	1.36	0.70–2.66	0.346
Delayed >3 weeks	1	–	–
Use of magnification			
Yes	1.14	0.99–1.31	0.068
No	1		
Treatment provider			
Undergraduate student	1	–	–
Postgraduate student	1.22	0.46–3.25	0.672
General practitioner	1.23	0.45–2.85	0.786
Specialist dentist	0.68	0.25–1.84	0.421
Postoperative factor			
Recall period			
6 months-1 year	1.20	0.54–2.67	0.644
Over 1 year-2 years	0.86	0.41–1.84	0.690
Over 2 years-3 years	1	–	–
Over 3 years	1.15	0.53–2.49	0.721

*: p<0.05 was considered statistically significant. CI: Confidence interval; NaOCl: Sodium hypochlorite

TABLE 4. Multiple sensitivity analysis for robustness assessment of pooled results

Groups	Number of study	Pooled success rate (%) [95% CI]	Q test p-value	I square (%)
All included studies	26	83 (79–87)	<0.01	87.93
Statistical analytic model				
Random-effects model	26	83 (79–87)	<0.01	87.93
Fixed-effects model	26	82 (81–83)	–	–
Study design				
Observational studies	16	82 (77–87)	<0.01	85.26
Interventional studies	10	84 (77–87)	<0.01	91.18
Retrospective cohort studies	8	79 (72–86)	<0.01	86.24
Prospective cohort studies	8	86 (77–93)	<0.01	85.98
Randomised clinical trials	10	84 (73–93)	<0.01	91.18

CI: Confidence interval

vourable treatment outcome of DPC in this group was 44% compared to the other group. No additional significant prognostic factors were found in the meta-analysis.

Robustness test of pooled results

The sensitivity analysis of the pooled results in various conditions was evaluated. The change in success rate was less than 5%. Therefore, the pooled results of the meta-analysis were robust and were not affected by the statistical analysis model or study design (Table 4).

Test of publication bias

The Egger p=0.448 and the funnel plot were asymmetric on visual inspection, indicating the presence of publication bias (Fig. 5a). A contoured funnel plot was created and analysed to investigate the source of the asymmetry. The results showed

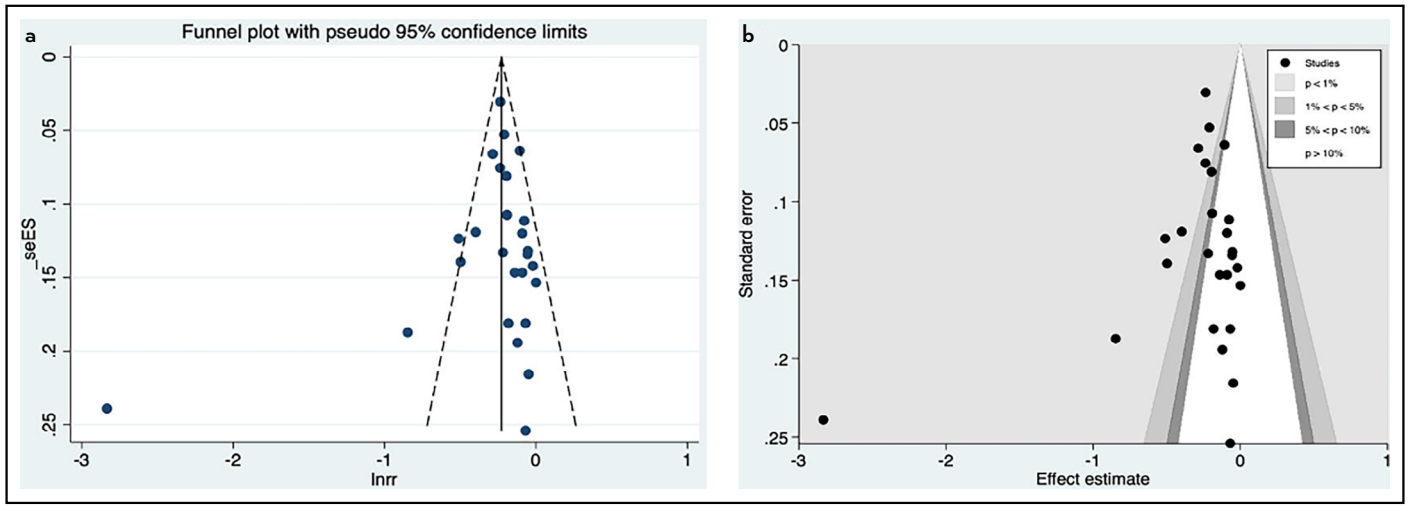

Figure 5. (a) Funnel plot showed asymmetrical shape suggesting publication bias. (b) The contour-enhanced funnel plot showed the number of included studies was approximately close in both the region of high statistical significance (p<0.01) and the region of low statistical significance (p>0.1)

that the number of included studies in both areas was relatively close to each other with high statistical significance (p<0.01) and the area of low statistical significance (p>0.10) (Fig. 5b). Therefore, it was concluded that the asymmetry of the funnel plot was not caused by publication bias.

DISCUSSION

The 33 articles selected from 70 articles for this systematic review were based on the predefined inclusion and exclusion criteria. The most common exclusion was inadequate treatment outcome assessment, as the criteria were unclear and only the clinical or radiographic examinations were reported. The successful outcomes of VPT should be evaluated without clinical symptoms on the tooth and with normal radiographic findings (45). Therefore, clinical and radiographic assessments in published studies should be included for relevance. Other article exclusions were due to the following reasons: recall period of fewer than six months, review article or case report/case series, laboratory or animal study, insufficient data, full text unavailable, study on deciduous teeth, and duplicate samples as shown in the PRISMA flow.

Methodological quality was assessed for all selected studies. To exclude the effect of "low study quality" in the statistical analysis, studies with "poor quality" and "high risk of bias" were not included. The modified Downs & Black checklist for non-randomised studies was used in this systematic review due to its overall simplicity and was more than sufficient for the critical appraisal (11). The mean Downs score was 18.55, indicating that the quality of the non-randomised studies was (on average) good. However, 4 studies were considered poor quality and were excluded from the statistical analysis (5, 9, 16, 42). In addition to the scores, the other reasons for exclusion were high drop-out rates at the endpoint (5), high confounding factors (9, 16), and small sample sizes (42).

For the randomised studies, the Cochrane Risk of Bias 2.0 tool (RoB2) was used to assess the risk of bias in each trial. All randomised trials were found to have "some concern of bias" in the second domain (bias due to deviation from the intended intervention). The lack of blinding of operators to the closure materials could lead to bias in the results, and blinding participants and operators was not possible during the study. Therefore, the effect on the estimated results of blinding the outcome assessors was considered. Three studies were classified as having an overall "high risk of bias" and had to be excluded from the meta-analysis. The most common problem encountered in the studies was randomisation bias. The details of the randomisation method or concealment were not available or not adequately described in these studies (23, 27, 31).

To date, no meta-analysis of the total weighted, pooled results of all included studies has been conducted. The pooled results showed that DPC's overall weighted pooled success rate was 83%, based on studies ranging from 6 months to 10 years, indicating a highly successful treatment outcome based on the available clinical evidence. This result is consistent with the conclusions of the meta-analysis by Aguilar et al. (6), in which the weighted pooled success rate of DPC was between 72.5 % and 95.4 %, and the pairwise meta-analysis by Cushley et al. (46), in which the success rate of the DPC was between 59% and 91%.

There was evidence that the weighted pooled success rate was influenced by high study heterogeneity. Subgroup analysis examined clinical heterogeneity caused by differences in participant characteristics and intervention. The following factors—tooth type, cause of exposure, tooth isolation, haemostatic agent, haemostatic method, pulp capping material, and use of magnification—were identified as possible sources of clinical heterogeneity. The high heterogeneity of the studies was a possible cause for the funnel plot asymmetry when testing for publication bias. Due to this limitation, the random effects model, which accounts for heterogeneity between studies, was used to analyse the data in all statistical analyses. However, in multiple subgroup analyses where more groups were analysed, it was more likely that a statistically significant effect was found by chance alone. Therefore, all significant prognostic factors that emerged from the subgroup analyses were carefully reviewed and interpreted in the results.

This study shows that the pulpal and periapical status of the tooth has no significant influence on the treatment outcome of DPC. However, it is important to note that almost all studies primarily included teeth with asymptomatic irreversible pulpitis and normal apical tissues. Asymptomatic clinical conditions may reflect normal pulp tissue or reversible pulpitis that may return to normal (47). While previous studies indicated that DPC could be successful in teeth with periapical lesions due to neurogenic inflammation (48, 49), the treatment was more evidently successful in the group with normal apical tissues (14, 15, 17, 19, 21, 25, 28–30, 32–36, 40, 41, 44). In addition, other conditions, such as the appearance of the exposed pulp tissue and adequate haemostasis, had to be assessed as part of the clinical procedure.

In the past, carious pulp exposure was not considered an indicator of DPC (4, 50). A possible explanation was an unpredictable degree of pulp inflammation (51, 52). The clinical success rate varied and remained inconclusive. However, over the past two decades, DPC in teeth with carious pulp exposure has demonstrated increased success rates (15, 22, 26, 30, 34, 38–40, 44). Aguilar et al. (6) reported DPC success rates in teeth with carious pulp exposure ranging from 72.9% to 95.4%. In our study, the cause of pulp exposure was not identified as a significant prognostic factor, with a weighted pooled success rate of 85% in the group of caries-exposed teeth. The indicators for using a DPC procedure in teeth with caries-exposed pulp should be re-evaluated. According to the results of this meta-analysis, the success rate was higher with caries exposure than with non-carious exposure. The lower success rate in the non-carious exposure group could be due to the presence of dental trauma, which has a direct impact on treatment outcomes.

Based on the meta-regression analysis, using rubber dam isolation in all treatment procedures was a significant prognostic factor for DPC. The weighted pooled success rate was higher for the group where all procedures were performed under rubber dam isolation. In addition, the relative risk (RR) was 1.44 (95% CI, 1.06–2.16) with statistical differences ($p<0.05$), indicating a 44% increased risk of a favourable treatment outcome for DPC in this group compared to the other group. Isolation of teeth with gauze, cotton rolls and rubber dams after caries removal or pulp exposure increases the possibility of bacterial contamination of the pulp, which may lead to treatment failure due to progressive infection and pulp inflammation (53). Therefore, ensuring adequate tooth isolation with a rubber dam in all treatment steps and the aseptic technique were key factors responsible for the success rate of the DPC.

Magnification was found to improve some DPC outcomes; however, it did not reach statistical significance ($p=0.068$). Despite the lack of statistical significance, the group using magnification had a higher weighted pooled success rate. Assessing the clinical appearance of the pulp tissue at the exposure site is crucial for decision-making in DPC procedures. Exposed pulp tissue that is considered suitable for DPC has characteristics such as sound surrounding dentin, a red, homogeneous, blood-filled surface of the pulp tissue, the absence of yellowish or dark, non-bleeding areas and no dentine chips at the wound when observed under the microscope (51). Magnification can be particularly beneficial for directly observing the exposure site during and after haemostasis.

In addition to the appearance of the pulp tissue, proper haemostasis is another important factor in assessing non-inflamed pulp. Various factors have been reported, including the time of haemostasis, haemostatic agents, and haemostatic methods (14, 15, 17, 18, 20–22, 24, 25, 28–30, 34, 36, 38–40, 44). The limited data shows that a haemostasis time of less than 5 minutes and using haemostatic agents have a higher weighted pooled success rate in the subgroup analysis. A high degree of pulpal haemorrhage and the difficulty in controlling the bleeding may be due to severe inflammation of the remaining pulp (54–56), which is the reason for the contraindication for DPC. Haemostatic agents such as sodium hypochlorite are preferred due to their haemostatic and antimicrobial properties (54). However, these factors did not show increased significance compared to all factors in the univariable analysis.

Although pulp capping material was not a significant prognostic factor in the meta-regression analysis, a higher pooled success rate was observed in the group using calcium silicate-based materials compared to the group using calcium hydroxide. This result is consistent with previous meta-analyses that indicated that mineral trioxide aggregate (MTA) and Biodentine had a higher success rate than calcium hydroxide (6, 46). The improved outcomes can be attributed to better results in forming calcified bridges and the excellent sealing properties of calcium silicate-based materials (57, 58). Nevertheless, some reference studies reported direct comparative outcomes between the two groups of different coating materials (20, 21, 24, 29, 32–34, 36, 38, 44). Given this, an additional network meta-analysis of the DPC treatment outcomes with different pulp coating materials should be considered to obtain more relevant results.

While other factors were not identified as predictors of treatment outcomes in this meta-analysis, some showed a high tendency for clinical success in DPC, such as young age and incomplete root development. However, the weighted pooled success rate of some factors did not differ between groups due to the limited data available and the different number of studies for each factor. It is important to note that overall, there was high clinical and statistical heterogeneity across all studies used in this article.

It is important to acknowledge the limitations of our study, particularly the fact that most of the included studies used a non-randomised design and about one-third were retrospective cohort studies, each with different treatment protocols. Due to these limitations, future research, especially randomised clinical trials, is crucial for developing more definitive guidelines for DPC case selection and treatment protocols.

CONCLUSION

In conclusion, this systematic review and meta-analysis of the existing evidence showed a weighted pooled success rate of 83% for DPC. This is based on the results of the 26 studies included in this review. The analysis identifies adequate tooth isolation as a prognostic factor significantly influencing treatment outcomes.

Disclosures

Appendix File: https://jag.journalagent.com/eurendodj/abs_files/EEJ-93723/EEJ-93723_(0)_EEJ-2023-07-097_apendix.pdf

Ethics Committee Approval: The study was approved by the Institutional Review Board of the Faculty of Dentistry/Pharmacy, Mahidol University (no: MU-DT/PY-IRB 2020/067.2512, date: 25/12/2020).

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