Outcomes of Regenerative Endodontic Treatment

Dr. Pedram Iranmanesh

DDS, MSc (Endodontics), PhD

Department of Endodontics, Isfahan University of Medical Sciences

Goals

AAE Clinical Considerations for a Regenerative Procedure
Revised 4/1/2018

These considerations should be seen as one possible source of information and, given the rapid evolving nature of this field, clinicians should also actively review new findings elsewhere as they become available.

Case Selection:

- Tooth with necrotic pulp and an immature apex.
- Pulp space not needed for post/core, final restoration.
- Compliant patient/parent.
- Patients not allergic to medicaments and antibiotics necessary to complete procedure (ASA 1 or 2).

Informed Consent

- Two (or more) appointments.
- Use of antimicrobial(s).
- Possible adverse effects: staining of crown/root, lack of response to treatment, pain/infection.
- Alternatives: MTA apexification, no treatment, extraction (when deemed non-salvageable).

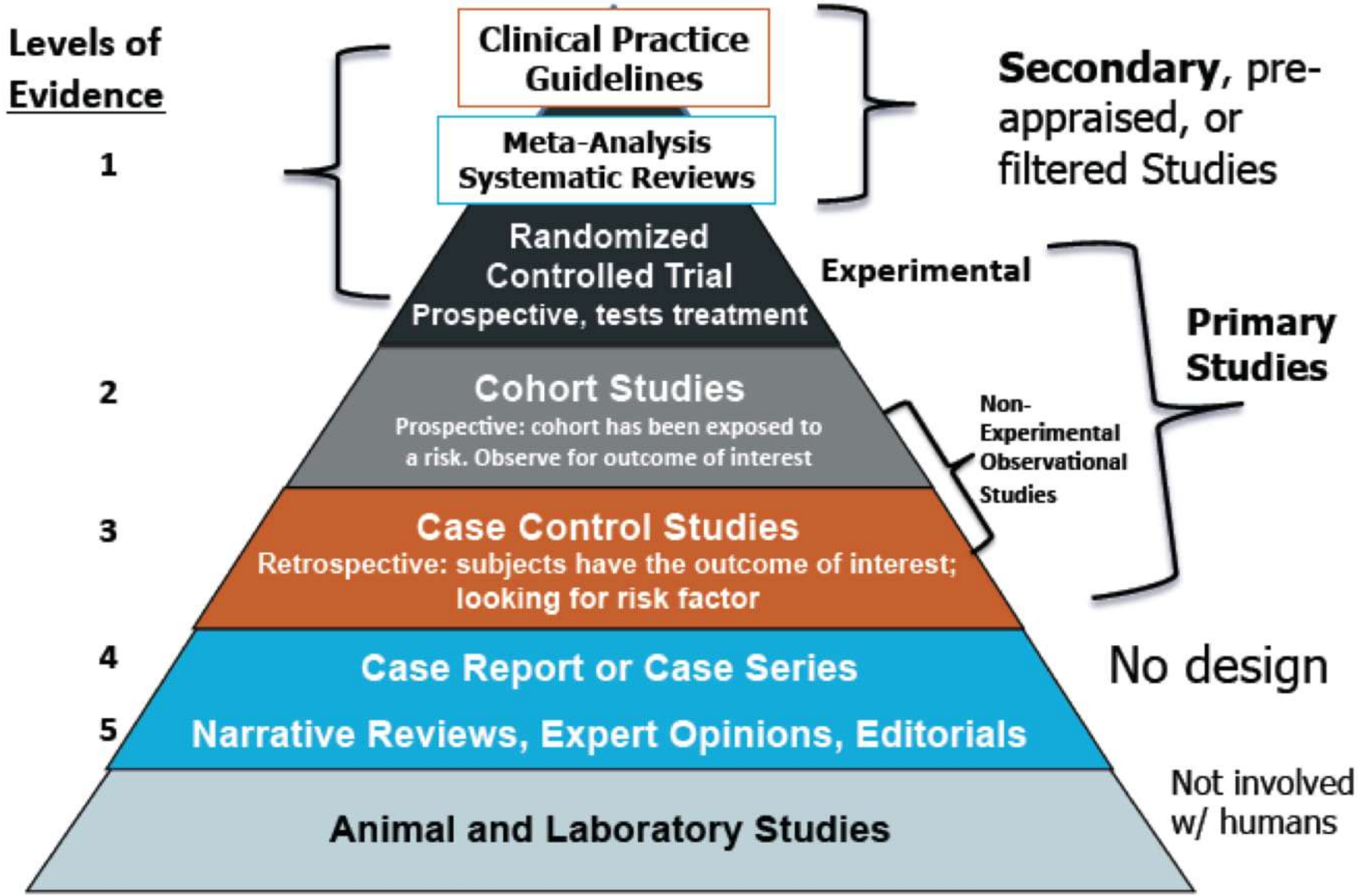
Collatape/Collaplug and restoring with 3mm of MTA, followed by RMGI, composite or alloy.

Follow-up (6-, 12-, 24-months)

- Clinical and Radiographic exam
  - No pain, soft tissue swelling or sinus tract (often observed between first and second appointments).
  - Resolution of apical radiolucency (often observed 6-12 months after treatment)
  - Increased width of root walls (this is generally observed before apparent increase in root length and often occurs 12-24 months after treatment).
  - Increased root length.
  - Positive Pulp vitality test response
  - Recommended yearly follow-up after the first 2 years
  - CBCT is highly recommended for initial evaluation and follow-up visits

- The degree of success of Regenerative Endodontic Procedures is largely measured by the extent to which it is possible to attain primary, secondary, and tertiary goals:
  - Primary goal: The elimination of symptoms and the evidence of bony healing.
  - Secondary goal: Increased root wall thickness and/or increased root length (desirable, but perhaps not essential)
  - Tertiary goal: Positive response to vitality testing (which if achieved, could indicate a more organized vital pulp tissue)

Scientific Landscape


Levels of Evidence
1
2
3
4
5
Clinical Practice Guidelines
Meta-Analysis Systematic Reviews
Randomized Controlled Trial
Prospective, tests treatment
Cohort Studies
Prospective: cohort has been exposed to a risk. Observe for outcome of interest
Case Control Studies
Retrospective: subjects have the outcome of interest; looking for risk factor
Case Report or Case Series
Narrative Reviews, Expert Opinions, Editorials
Animal and Laboratory Studies
Secondary, pre-appraised, or filtered Studies
Experimental
Primary Studies
Non-Experimental Observational Studies
No design
Not involved w/ humans

Regenerative Endodontics: A Scientometric and Bibliometric Analysis

Sayna Shamszadeh, DDS, Saeed Asgary, DDS, MS,† and Ali Nosrat, DDS, MS, MDS†‡*

Abstract

Introduction: Scientometric analyses outline the research output in a field and, therefore, help researchers and funding agencies to focus more on under-investigated areas and make more efficient decisions related to public health. The aim of this study was

1. to perform a scientometric analysis to characterize the status of the research and publications in the field of regenerative endodontics and
2. to identify the most effective actors (authors, countries, and journals) and to examine their role in the development of science using a bibliometric analysis.

Methods: Electronic searches were done in MEDLINE and Scopus databases using specified search criteria. articles with LOE 1 is low. The research groups around the globe are encouraged to focus their collaborative efforts on higher-quality and clinically oriented research. *(J Endod 2019;45:272–280)*

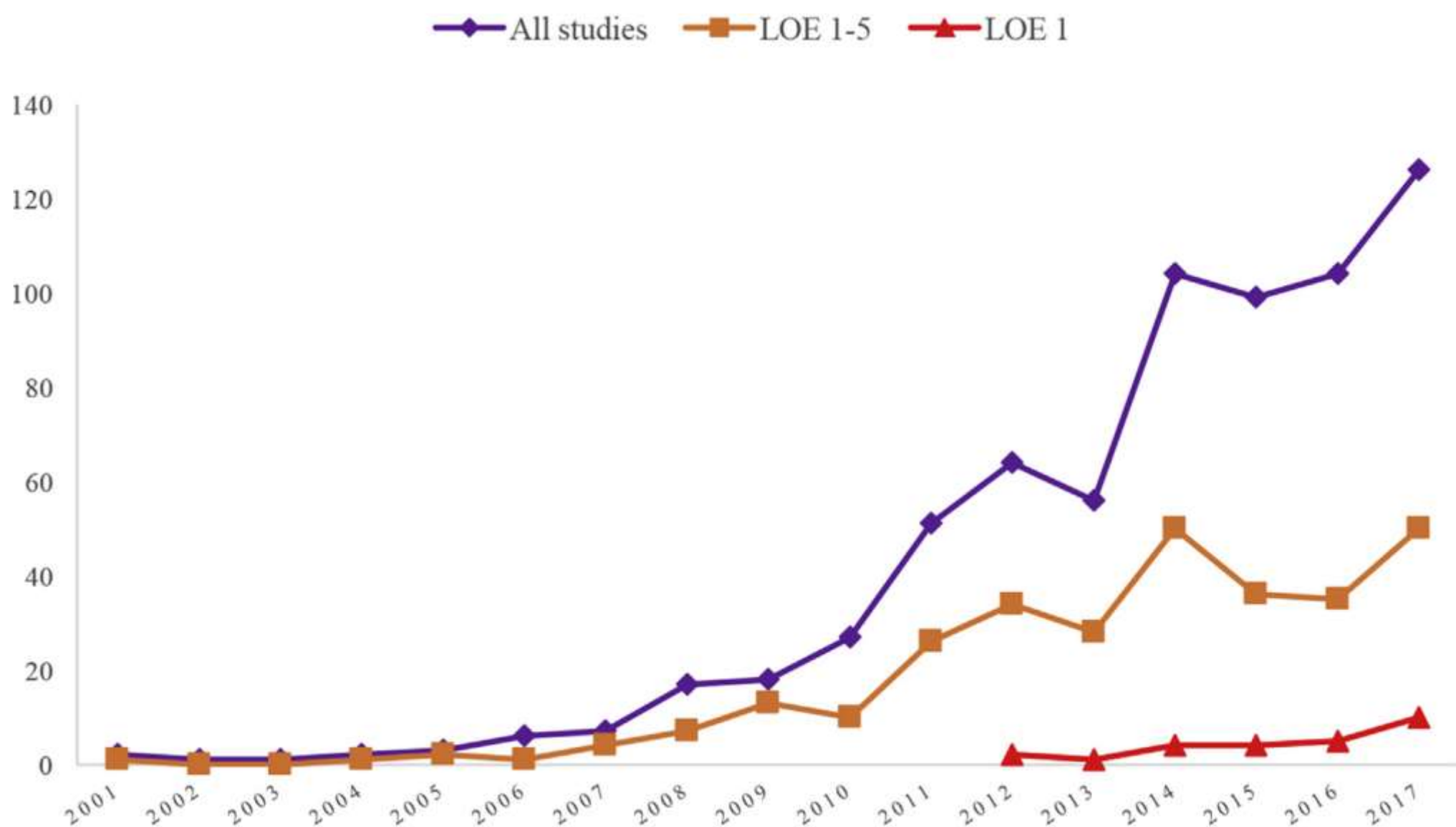
Key Words

Bibliometric analysis, pulp regeneration, regenerative endodontics, scientometric analysis

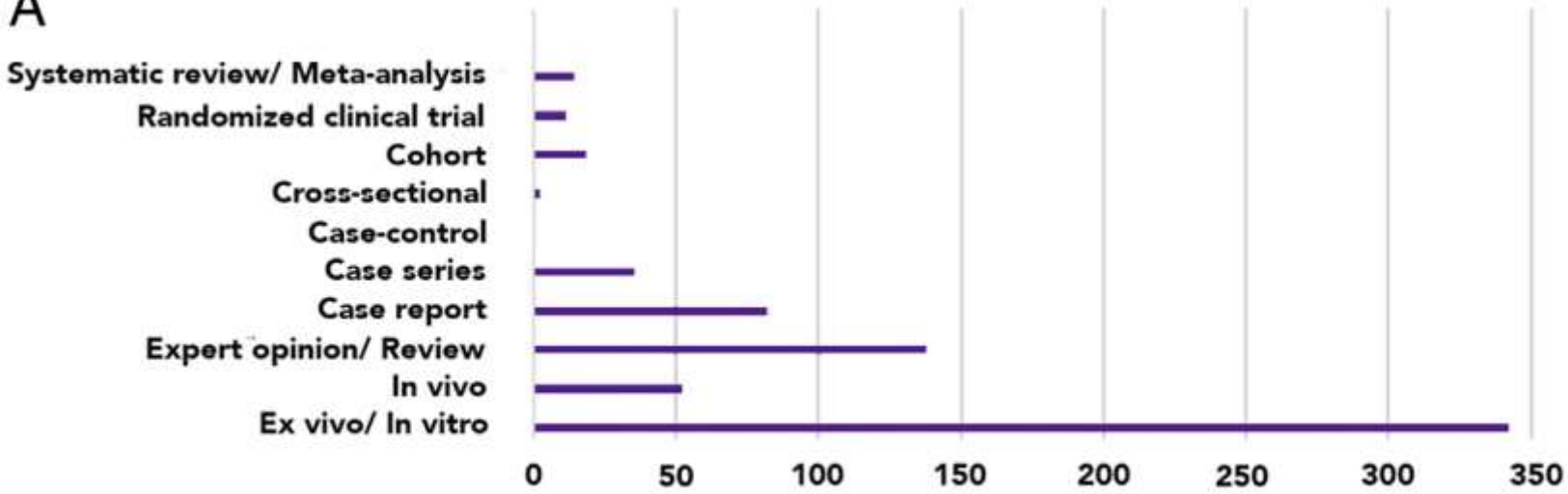
Scientometrics, also known as science mapping, is often used in conjunction with information visualization to study a large body of bibliographic materials as well

Significance

The total number of publications in the field of regenerative endodontics shows exponential growth. The overall ratio of articles with LOE 1 is low. A total of 1820 authors in 53 countries contributed to the research in this field. Research groups


All studies
LOE 1-5
LOE 1
140
120
100
80
60
40
20
0
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017

A


Systematic review/ Meta-analysis
Randomized clinical trial
Cohort
Cross-sectional
Case-control
Case series
Case report
Expert opinion/ Review
In vivo
Ex vivo/ In vitro
0
50
100
150
200
250
300
350

B


Systematic review/ Meta-analysis
Randomized clinical trial
Cohort
Cross-sectional
Case-control
Case series
Case report
Expert opinion/ Review
%4.67
%3.67
LOE 1
%6.00
LOE 2
%0.66
%0
LOE 3
%11.67
LOE 4
%27.33
%46.00
LOE 5

RET vs MTA plug

Regenerative Endodontic Treatment or Mineral Trioxide Aggregate Apical Plug in Teeth with Necrotic Pulps and Open Apices: A Systematic Review and Meta-analysis

Mahmoud Torabinejad, DMD, MSD, PhD, Ali Nosrat, DDS, MS, MDS,† Prashant Verma, DDS, MS, FAGD,† and Oyoyo Udochukwu, MPH‡*

Abstract

Introduction: A mineral trioxide aggregate (MTA) apical plug (MAP) and regenerative endodontic treatment (RET) have shown acceptable clinical outcomes. However, comparative studies are scarce. The aims of this study were to examine the level of evidence for both treatments, conduct a systematic review of the literature on MAP and RET, and run a meta-analysis on the survival and success rates of teeth treated with these procedures. **Methods:** Electronic searches were performed

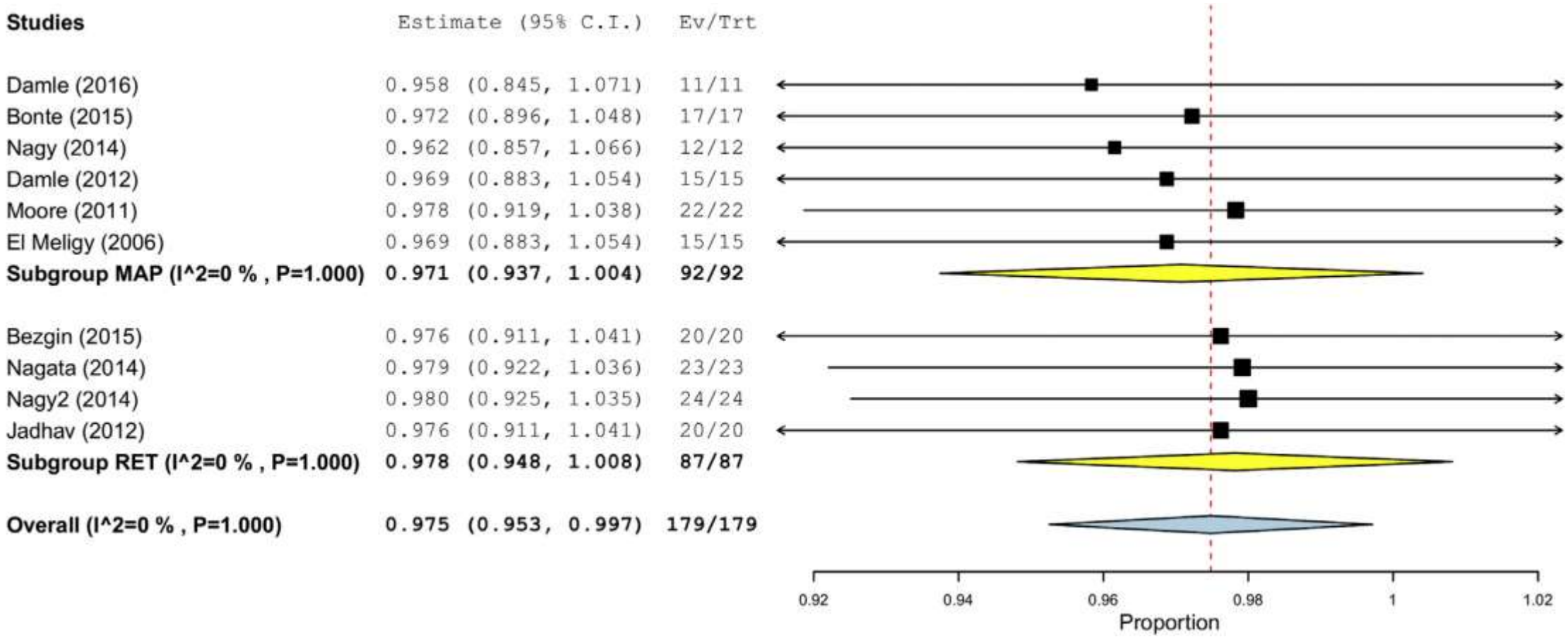
Key Words

Immature tooth, meta-analysis, mineral trioxide aggregate apical plug, necrotic pulp, open apex, outcome, regenerative endodontic treatment, success, survival, systematic review

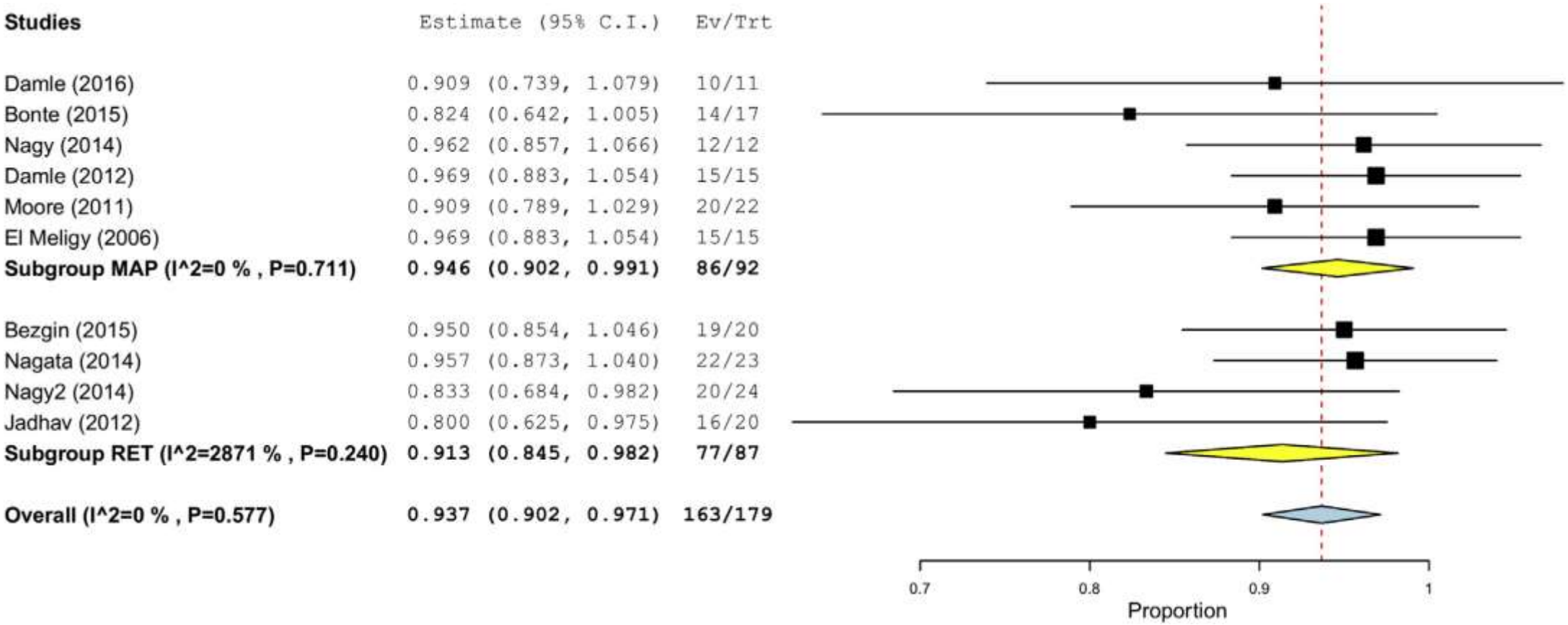
The preservation of natural dentition has long been the main objective in root canal treatment

Significance

The treatment of immature teeth with pulp necrosis using an MTA apical plug or regenerative endodon-



A forest plot of subgroup analysis of survival rates.



A forest plot of subgroup analysis of success rates.

Significance

The treatment of immature teeth

with pulp necrosis using an MTA apical plug or regenerative endodontic treatment results in

high survival and success rates

RET vs Apexification

Pulp Revascularization or Apexification for the Treatment of Immature Necrotic Permanent Teeth: Systematic Review and Meta-Analysis

Gabriel Ferreira Nicoloso*/ Gabriela Maltz Goldenfum**/Tatiane da Silva Dal Pizzol***/ Roberta Kochenborger Scarparo****/ Francisco Montagner*****/ Jonas de Almeida Rodrigues******/ Luciano Casagrande*******

This systematic review and meta-analysis assessed clinical, radiographic and functional retention outcomes in immature necrotic permanent teeth treated either with pulp revascularization or apexification after a minimum of three months to determine which one provides the best results. The literature was screened via PubMed/MEDLINE and Embase databases up to June 2017 to select observational studies that compared pulp revascularization and apexification treatments assessing clinical, radiographic and functional retention outcomes. Two reviewers independently performed screening and evaluation of articles. A total of 231 articles were retrieved from databases, wherein only four articles were selected for full-text analyses. After exclusion criteria, three studies remained in quantitative and qualitative analyses. Pooled-effect estimates were obtained comparing clinical and radiographic outcomes ('overall outcome') and functional retention rates between apexification and pulp revascularization treatment. The meta-analysis comparing apexification vs. revascularization for 'overall outcome' (Z=0.113, p=0.910, RR=1.009, 95%CI:0.869-1.171) and functional retention rates (Z=1.438, p=0.150, RR=1.069, 95%CI:0.976-1.172) showed no statistically significant differences between the treatments. All studies were classified as high quality. The current literature regarding the clinical, radiographic and functional retention outcomes in immature necrotic permanent teeth treated either with pulp revascularization or apexification is limited. Based on our meta-analysis, the results do not favor one treatment modality over the other.

Keywords: Pulp revascularization, apexification, immature necrotic permanent teeth

From the Federal University of Rio Grande do Sul (UFRGS), Porto Alegre–RS, Brazil.

Gabriel Ferreira Nicoloso, DDS, MS, PhD, School of Dentistry, Inedi College - CESUCA, Cachoeirinha, RS, Brazil.

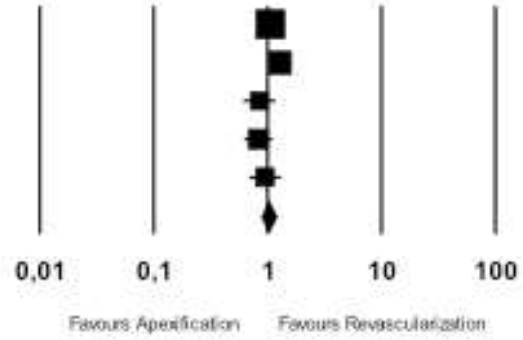
Gabriela Maltz Goldenfum, DDS, MS, School of Dentistry, Post-Graduate Program in Pediatric Dentistry.

Tatiane da Silva Dal Pizzol, MS, PhD, Faculty of Medicine, Post-Graduate

INTRODUCTION

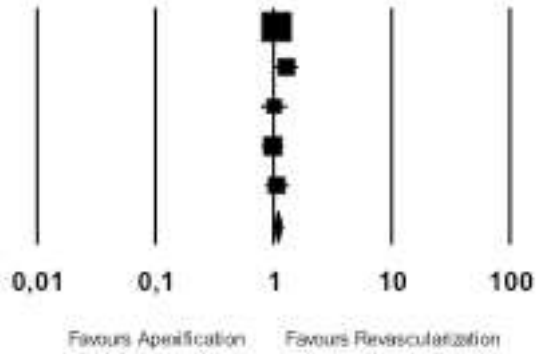
Pulp necrosis in children and adolescents, mainly due to trauma or caries, may arrest permanent tooth root development, resulting in thin dentinal walls, wide-open apexes and inadequate crown-root ratio[1,2]. These features may hamper the endodontic treatment and its protocol for cleaning, shaping and

Study name	Risk ratio	Lower limit	Upper limit	Z-Value	p-Value
Jeeruphan et al (2012) (MTA)	1,055	0,916	1,216	0,746	0,456
Jeeruphan et al (2012) (CH)	1,283	1,011	1,629	2,047	0,041
Alobaid et al (2014) (MTA)	0,845	0,603	1,185	-0,975	0,330
Alobaid et al (2014) (CH)	0,827	0,615	1,112	-1,259	0,208
Silujjai & Linsuwanont (2017) (MTA)	0,947	0,685	1,309	-0,331	0,740
Meta Analysis	1,009	0,869	1,171	0,113	0,910



'Overall outcomes' (clinical and radiographic) comparing BC revascularization to MTA and CH apexification

Study name	Statistics for each study					Risk ratio and 95% CI
	Risk ratio	Lower limit	Upper limit	Z-Value	p-Value	
Jeeruphan et al (2012) (MTA)	1,055	0,916	1,216	0,746	0,456	
Jeeruphan et al (2012) (CH)	1,283	1,011	1,629	2,047	0,041	
Alobaid et al (2014) (MTA)	1,009	0,769	1,324	0,065	0,948	
Alobaid et al (2014) (CH)	0,957	0,793	1,227	-0,121	0,904	
Silujjai & Linsuwanont (2017) (MTA)	1,066	0,838	1,356	0,523	0,601	
	1,069	0,976	1,172	1,438	0,150	



Meta Analysis

Functional retention outcomes comparing BC revascularization to MTA and CH apexification

Significance

Do not favor one treatment modality over the other

More clinical studies are necessary

Regenerative Endodontics Versus Apexification in Immature Permanent Teeth with Apical Periodontitis: A Prospective Randomized Controlled Study

Jiacheng Lin, PhD, Qian Zeng, PhD,† Xi Wei, PhD,† Wei Zhao, PhD,* Minyi Cui, PhD,‡ Jing Gu, PhD,§ Jiaxuan Lu, PhD,* Maobin Yang, DMD, MDS, PhD,‖ and Junqi Ling, PhD¶*

Abstract

Introduction: The aim of the study was to compare the outcomes of regenerative endodontic treatment (RET) and apexification on immature permanent teeth with pulp necrosis and apical periodontitis. **Methods:** A total of 118 patients (118 teeth) were recruited and randomly assigned to either RET or apexification treatment. Each treatment group was divided into 2 subgroups according to the etiology: dens evaginatus or trauma. Clinical symptoms and complications were recorded, and cone-beam computed tomographic imaging with a limited field of view was used to measure the change of root length, root thickness, and apical foramen size at the 12-month follow-up. The *t* test/rank sum test and Fisher exact test were applied to compare the

Key Words

Apexification, apical periodontitis, cone-beam computed tomography, immature teeth, regenerative endodontics

Significance

This clinical randomized controlled study compared the outcomes of RET and apexification. The results showed a high success rate of the RET group at the 12-month follow-up. Dens evaginatus cases showed better prognoses than trauma cases upon RET treatment.

Immature teeth with pulp necrosis and apical periodontitis have been a challenge for endodontic treatment because of the thin root wall and open apex. These cases are usually caused by trauma, caries, or a developmental

Significance

Comparable outcome
resolution of symptoms and apical healing.

RET showed a better outcome
increased root thickness and root length.

Immature Teeth

Regenerative Endodontic Therapy in the Management of Nonvital Immature Permanent Teeth: A Systematic Review—Outcome Evaluation and Meta-analysis

Huei Jinn Tong, BDS, MDentSci, MPaedDent RCS, [*]
Sadna Rajan, BDS, MDSc, MDentSci, MPaedDent RCS, [†]
Nabina Bhujel, BDS, MFDS RCPS, MPaedDent RCPS, D Clin Dent, FDSRCS, [‡]
Jing Kang, PhD, [§] *Monty Duggal, BDS, MDS, FDS, PhD,* [*] *and*
Hani Nazzal, BDS, MFDS RCS Ire, FRCD Can Paed Dent, PhD Paed Dent, MPaed Dent RCS Glas, FDS Paed Dent [¶]

Abstract

Introduction: Although the protocols in previously published studies appeared to be largely similar, there were inadequate evidence-based guidelines to support a single protocol. Using a meta-analysis, this systematic review aimed to summarize and quantitatively evaluate the outcomes for nonvital immature permanent teeth treated using the regenerative endodontic technique (RET) as well as critically appraise the level and quality of evidence of the existing publications. **Methods:** Risk of bias assessment and level of evidence grading were performed on

Key Words

Level of evidence, meta-analysis, outcomes, regenerative endodontic therapy

Although several publications suggest that treatment using the regenerative endodontic technique (RET) has positive outcomes, the results of such studies should be interpreted with

Significance

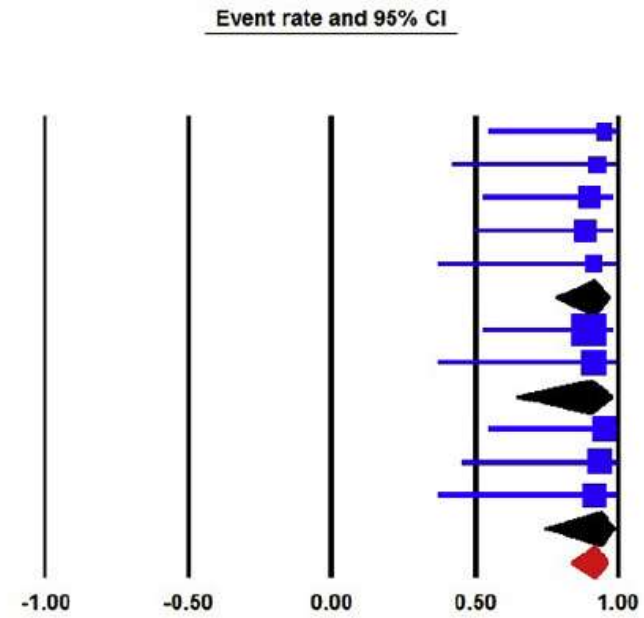
The review summarizes systematically the clinical and radiographic outcomes of existing clinical studies on regenerative endodontic therapy. It also aims to help clinicians evaluate the levels of evidence of published articles and identify addi-

A

Heterogeneity: tau^2= 1.28, Q = 12.58, df = 2, I^2= 0.00, p = 0.92

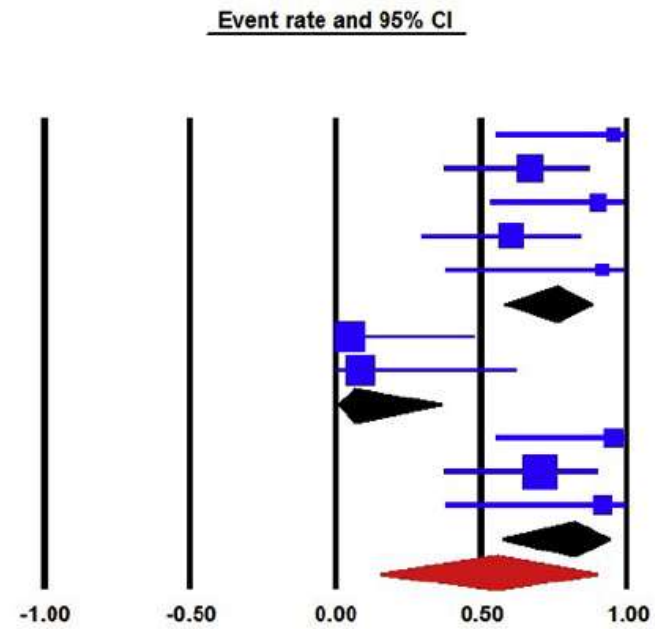
PA healing

Group by Subgroup within study	Study name	Subgroup within study	Outcome	Event rate	Lower limit	Upper limit
BC	Jadhav 2012	BC	PA healing	0.955	0.552	0.997
BC	Nagata 2014	BC	PA healing	0.929	0.423	0.996
BC	Nagy 2014	BC	PA healing	0.900	0.533	0.986
BC	Bezgin et al 2015	BC	PA healing	0.889	0.500	0.985
BC	Narang 2015	BC	PA healing	0.917	0.378	0.995
BC				0.915	0.782	0.970
Control	Nagy 2014	Control	PA healing	0.900	0.533	0.986
Control	Narang 2015	Control	PA healing	0.917	0.378	0.995
Control				0.906	0.642	0.981
PRP	Jadhav 2012	PRP	PA healing	0.955	0.552	0.997
PRP	Bezgin et al 2015	PRP	PA healing	0.938	0.461	0.996
PRP	Narang 2015	PRP	PA healing	0.917	0.378	0.995
PRP				0.938	0.744	0.988
Overall				0.919	0.836	0.962



Apical Closure

Group by Subgroup within study	Study name	Subgroup within study	Outcome	Event rate	Lower limit	Upper limit
BC	Jadhav 2012	BC	Apical closure	0.955	0.552	0.997
BC	Nagata 2014	BC	Apical closure	0.667	0.376	0.869
BC	Nagy 2014	BC	Apical closure	0.900	0.533	0.986
BC	Bezgin et al 2015	BC	Apical closure	0.600	0.297	0.842
BC	Narang 2015	BC	Apical closure	0.917	0.378	0.995
BC				0.756	0.577	0.875
Control	Nagy 2014	Control	Apical closure	0.050	0.003	0.475
Control	Narang 2015	Control	Apical closure	0.083	0.005	0.622
Control				0.064	0.009	0.355
PRP	Jadhav 2012	PRP	Apical closure	0.955	0.552	0.997
PRP	Bezgin et al 2015	PRP	Apical closure	0.700	0.376	0.900
PRP	Narang 2015	PRP	Apical closure	0.917	0.378	0.995
PRP				0.816	0.569	0.937
Overall				0.552	0.152	0.894



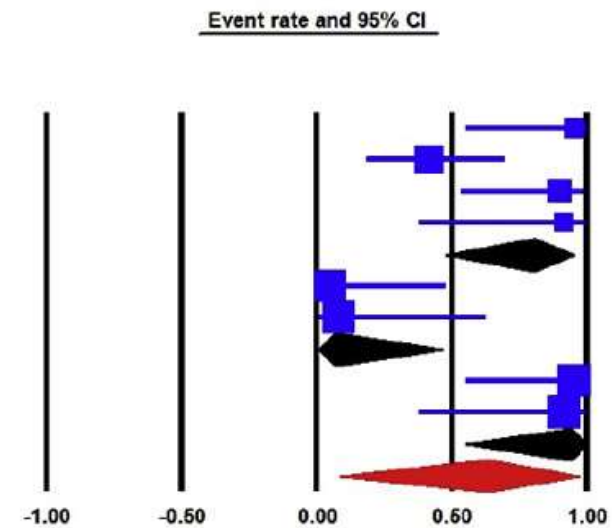
Heterogeneity: $tau^2 = 3.3$, $Q = 10.14$, $df = 2$, $I^2 = 70.32$, $p = 0.006$

estimated success rate

C Heterogeneity: tau^2= 3.3, Q = 10.14, df = 2, I^2= 70.32, p = 0.006

Root Length

Group by Subgroup within study		Subgroup within study	Outcome	Event rate	Lower limit	Upper limit
BC	Jadhav 2012	BC	Rooth Length	0.955	0.552	0.997
BC	Nagata 2014	BC	Rooth Length	0.417	0.185	0.692
BC	Nagy 2014	BC	Rooth Length	0.900	0.533	0.986
BC	Narang 2015	BC	Rooth Length	0.917	0.378	0.995
BC				0.802	0.475	0.948
Control	Nagy 2014	Control	Rooth Length	0.050	0.003	0.475
Control	Narang 2015	Control	Rooth Length	0.083	0.005	0.622
Control				0.065	0.006	0.462
PRP	Jadhav 2012	PRP	Rooth Length	0.955	0.552	0.997
PRP	Narang 2015	PRP	Rooth Length	0.917	0.378	0.995
PRP				0.939	0.551	0.995
Overall				0.631	0.083	0.970



estimated success rate

D Heterogeneity: tau^2= 3.3, Q = 10.14, df = 2, I^2= 70.32, p = 0.006

Root Dentine Formation

Group by Subgroup within study		Subgroup within study	Outcome	Event rate	Lower limit	Upper limit
BC	Jadhav 2012	BC	Root dentine formation	0.955	0.552	0.997
BC	Nagata 2014	BC	Root dentine formation	0.417	0.185	0.692
BC	Nagy 2014	BC	Root dentine formation	0.900	0.533	0.986
BC	Narang 2015	BC	Root dentine formation	0.917	0.378	0.995
BC				0.802	0.475	0.948
Control	Nagy 2014	Control	Root dentine formation	0.050	0.003	0.475
Control	Narang 2015	Control	Root dentine formation	0.083	0.005	0.622
Control				0.065	0.006	0.462
PRP	Jadhav 2012	PRP	Root dentine formation	0.955	0.552	0.997
PRP	Narang 2015	PRP	Root dentine formation	0.917	0.378	0.995
PRP				0.939	0.551	0.995
Overall				0.631	0.083	0.970

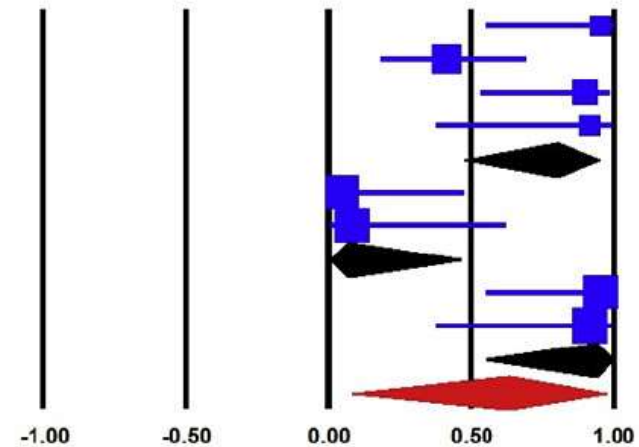


TABLE 4. I^2 Values for Each Subgroup

I^2 (P value)	PA healing	Apical closure	Increased root length	Increased dentin thickness
Control	0.00 ($P = 0.863$)	67.49 ($P = 0.046$)*	48.083 ($P = 0.165$)	48.083 ($P = 0.165$)
BC	0.00 ($P = 0.946$)	36.7 ($P = 0.176$)	70.366 ($P = 0.034$)*	70.366 ($P = 0.034$)*
PRP	20.163 ($P = 0.286$)	0.00 ($P = 0.387$)	0.00 ($P = 0.755$)	0.00 ($P = 0.755$)

BC, blood clot; PA, periapical; PRP, platelet-rich plasma.

*Significant, indicative of high heterogeneity.

Significance

- Success rates for tooth survival and resolution of periapical pathosis were excellent;
- Results for apical closure and continued root development were inconsistent

REGENERATIVE ENDODONTICS

Teng Kai Ong, BDS, FRCD(C), Ghee Seong Lim, BDS, MClinDent, ITF RCS,† Maharaj Singh, PhD,‡ and Alissa V. Fial, MA, MLIS§*

Quantitative Assessment of Root Development after Regenerative Endodontic Therapy: A Systematic Review and Meta-Analysis

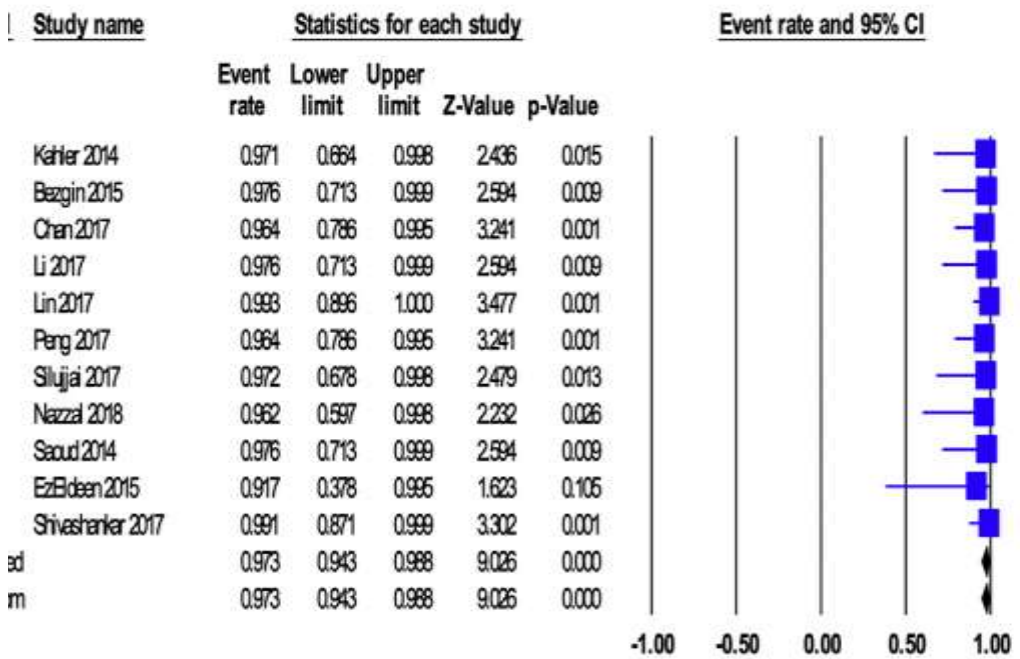
SIGNIFICANCE

Regenerative endodontic therapy on necrotic immature permanent teeth was shown to have high survival and healing rates with a good root development rate. However, the existing literature failed to show predictable clinical meaningful root development after regenerative endodontic therapy.

ABSTRACT

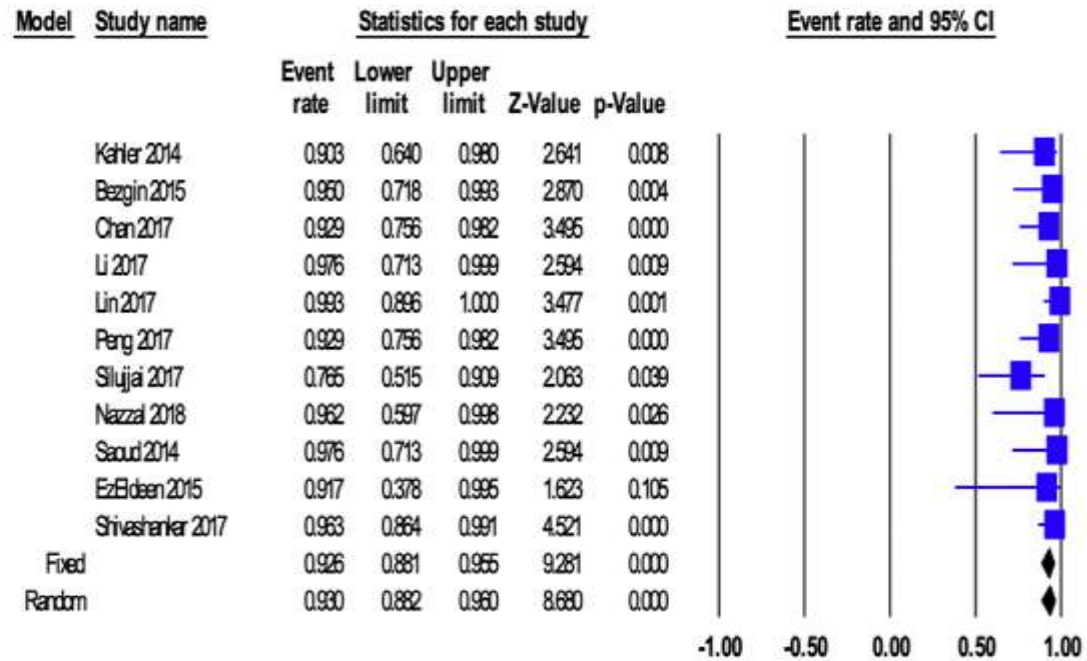
Introduction: The purposes of this review were to appraise the level of evidence of the existing regenerative endodontic therapy (RET) publications, perform a meta-analysis on the survival and healing rates of necrotic immature permanent teeth treated with RET, and run a meta-analysis on the quantitative assessment of the root development of those teeth. **Methods:** Electronic searches were performed in Web of Science, PubMed, CINAHL (Cumulative Index to Nursing and Allied Health Literature), and Cochrane Library databases. Two authors independently screened the titles and abstracts for eligibility. The analyses were performed on the clinical outcomes (ie, survival, healing, and root development) of the procedure. **Results:** Eleven articles were included in the qualitative and quantitative syntheses. Three studies were randomized controlled trials, 6 were prospective cohort studies, and 2 were retrospective cohort studies. The pooled survival and healing rates were 97.3% and 93.0%, respectively. The pooled rates of root lengthening, root thickening, and apical closure were 77.3%, 90.6%, and 79.1%, respectively. However, if 20% radiographic changes were used as a cutoff point, there were only 16.1% root lengthening and 39.8% root thickening. **Conclusions:** Within the limitations of the present study, it can be concluded that RET yielded high survival and healing rates with a good root development rate. However, clinical meaningful root development after RET was unpredictable. *(J Endod 2020;46:1856–1866.)*

Survival



D

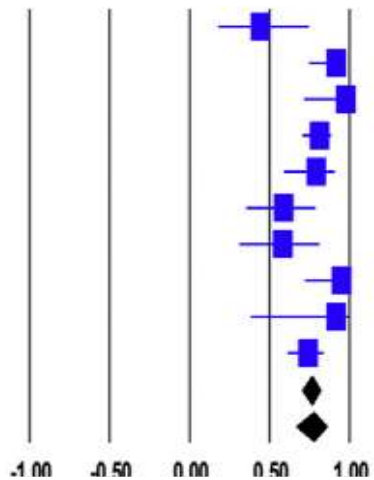
Healing



C

Root Lengthening

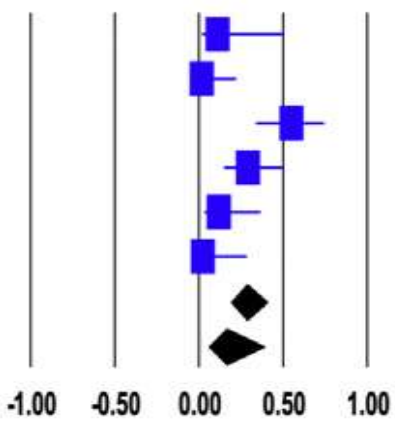
Model	Study name	Event rate	Lower limit	Upper limit	Z-Value	p-Value
	Kahler 2014	0.444	0.177	0.748	-0.335	0.737
	Chan 2017	0.917	0.743	0.977	3.507	0.000
	Li 2017	0.976	0.713	0.999	2.594	0.009
	Lin 2017	0.812	0.702	0.888	4.748	0.000
	Peng 2017	0.792	0.587	0.911	2.669	0.008
	Silujjai 2017	0.588	0.362	0.789	0.722	0.470
	Nazzal 2018	0.583	0.307	0.815	0.572	0.567
	Saoud 2014	0.950	0.718	0.993	2.870	0.004
	EzEldeen 2015	0.917	0.378	0.995	1.623	0.105
	Shivashanker 2017	0.741	0.609	0.840	3.384	0.001
Fixed		0.762	0.700	0.815	7.184	0.000
Random		0.773	0.663	0.854	4.402	0.000



D

Root Lengthening (>20%)

Model	Study name	Event rate	Lower limit	Upper limit	Z-Value	p-Value
	Kahler 2014	0.111	0.015	0.500	-1.961	0.050
	Chan 2017	0.017	0.001	0.223	-2.834	0.005
	Li 2017	0.550	0.336	0.747	0.446	0.655
	Peng 2017	0.292	0.146	0.499	-1.973	0.049
	Silujjai 2017	0.118	0.030	0.369	-2.676	0.007
	Saoud 2014	0.024	0.001	0.287	-2.594	0.009
Fixed		0.283	0.188	0.402	-3.425	0.001
Random		0.161	0.056	0.384	-2.751	0.006



-1.00 -0.50 0.00 0.50 1.00

E

Root Thickening

Model	Study name	Event rate	Lower limit	Upper limit	Z-Value	p-Value
	Kahler 2014	0.889	0.500	0.985	1.961	0.050
	Lin 2017	0.826	0.718	0.898	4.905	0.000
	Peng 2017	0.917	0.722	0.979	3.247	0.001
	Silujia 2017	0.706	0.458	0.872	1.646	0.100
	Nazzal 2018	0.500	0.244	0.756	0.000	1.000
	Saoud 2014	0.900	0.676	0.975	2.948	0.003
	EzEldeen 2015	0.917	0.378	0.995	1.623	0.105
	Shivashanker 2017	0.815	0.689	0.897	4.231	0.000
Fixed		0.805	0.742	0.855	7.707	0.000
Random		0.806	0.715	0.873	5.544	0.000

Statistics for each study

Event rate and 95% CI

-1.00 -0.50 0.00 0.50 1.00

F

Root Thickening (>20%)

Model	Study name	Event rate	Lower limit	Upper limit	Z-Value	p-Value
	Kahler 2014	0.556	0.252	0.823	0.335	0.737
	Chan 2017	0.017	0.001	0.223	-2.834	0.005
	Peng 2017	0.583	0.383	0.759	0.809	0.418
	Silujai 2017	0.294	0.128	0.542	-1.646	0.100
	Saoud 2014	0.450	0.253	0.664	-0.446	0.655
Fixed		0.447	0.335	0.565	-0.876	0.381
Random		0.398	0.220	0.608	-0.952	0.341

Statistics for each study

Event rate and 95% CI

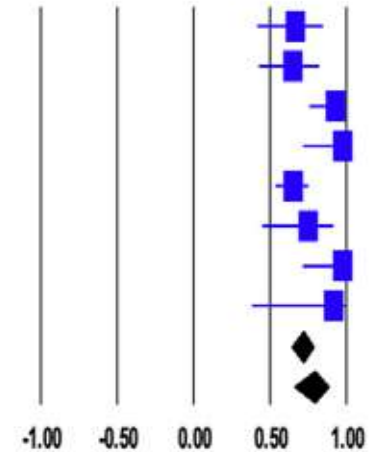
-1.00 -0.50 0.00 0.50 1.00

G

Apical Narrowing

Model	Study name	Event rate	Lower limit	Upper limit	Z-Value	p-Value
	Kahler 2014	0.666	0.414	0.849	1.302	0.193
	Bezgin 2015	0.650	0.426	0.823	1.320	0.187
	Chen 2017	0.929	0.756	0.982	3.495	0.000
	Li 2017	0.976	0.713	0.999	2.594	0.009
	Lin 2017	0.652	0.533	0.755	2.484	0.013
	Nazzal 2018	0.750	0.448	0.917	1.648	0.099
	Saoud 2014	0.976	0.713	0.999	2.594	0.009
	EzEldeen 2015	0.917	0.378	0.995	1.623	0.105
Fixed		0.716	0.637	0.783	4.997	0.000
Random		0.791	0.655	0.882	3.796	0.000

Event rate and 95% CI

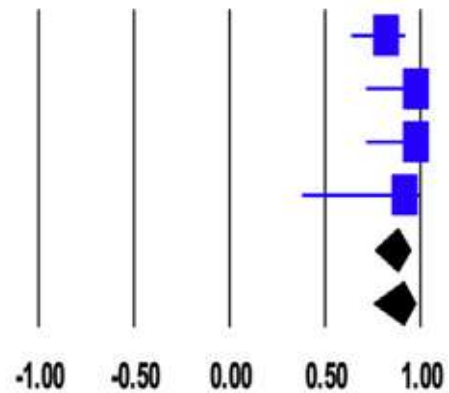


H

Apical Narrowing (>20%)

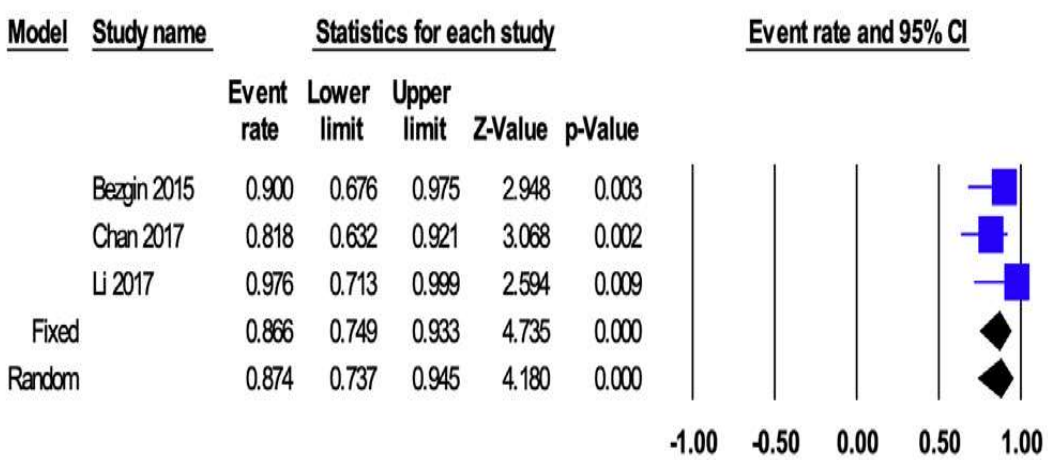
Model	Study name	Event rate	Lower limit	Upper limit	Z-Value	p-Value
	Chen 2017	0.820	0.635	0.923	3.083	0.002
	Li 2017	0.976	0.713	0.999	2.594	0.009
	Saoud 2014	0.976	0.713	0.999	2.594	0.009
	EzEldeen 2015	0.917	0.378	0.995	1.623	0.105
Fixed		0.878	0.758	0.943	4.658	0.000
Random		0.907	0.753	0.969	3.830	0.000

Event rate and 95% CI



I

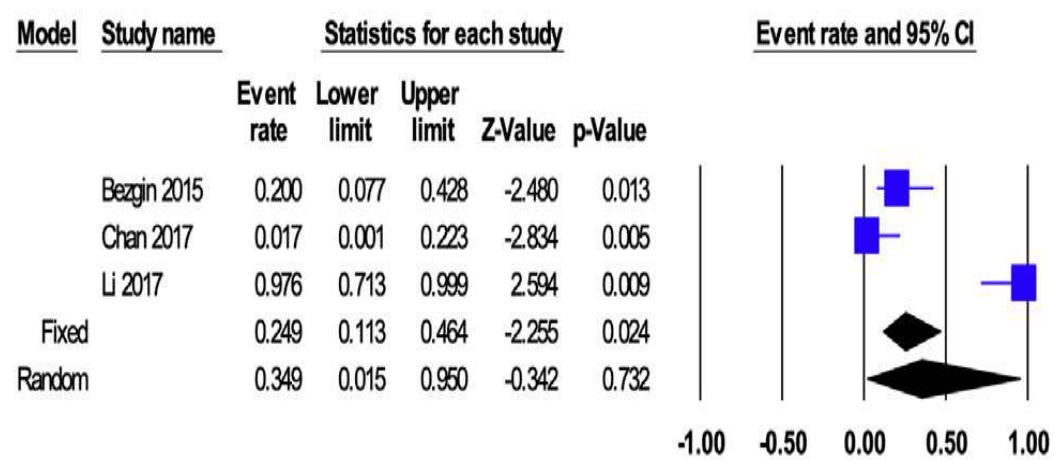
Radiographic Root Area



Model	Study name	Event rate	Lower limit	Upper limit	Z-Value	p-Value
	Bezgin 2015	0.900	0.676	0.975	2.948	0.003
	Chan 2017	0.818	0.632	0.921	3.068	0.002
	Li 2017	0.976	0.713	0.999	2.594	0.009
Fixed		0.866	0.749	0.933	4.735	0.000
Random		0.874	0.737	0.945	4.180	0.000

J

Radiographic Root Area (>20%)



Model	Study name	Event rate	Lower limit	Upper limit	Z-Value	p-Value
	Bezgin 2015	0.200	0.077	0.428	-2.480	0.013
	Chan 2017	0.017	0.001	0.223	-2.834	0.005
	Li 2017	0.976	0.713	0.999	2.594	0.009
Fixed		0.249	0.113	0.464	-2.255	0.024
Random		0.349	0.015	0.950	-0.342	0.732

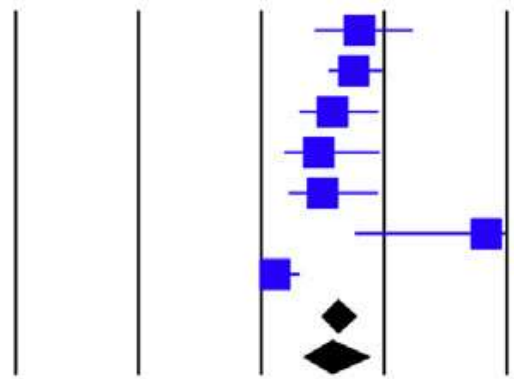
K

Calcific Barrier or Intracanal Calcification

Model	Study name	Event rate	Lower limit	Upper limit	Z-Value	p-Value
	Bezgin 2015	0.400	0.214	0.620	-0.888	0.374
	Lin 2017	0.377	0.271	0.496	-2.022	0.043
	Peng 2017	0.290	0.153	0.480	-2.150	0.032
	Silujjai 2017	0.235	0.091	0.485	-2.063	0.039
	Saoud 2014	0.250	0.108	0.478	-2.127	0.033
	EzEldeen 2015	0.917	0.378	0.995	1.623	0.105
	Shivashanker 2017	0.056	0.018	0.159	-4.773	0.000
Fixed		0.308	0.243	0.380	-4.929	0.000
Random		0.284	0.170	0.434	-2.757	0.006

Statistics for each study

Event rate and 95% CI



Significance

Regenerative endodontic therapy on necrotic immature permanent teeth was shown

to have high survival and healing rates with a good root development rate.

failed to show predictable clinical meaningful root development after regenerative endodontic therapy.

Review Article

Regenerative Endodontic Therapy in the Management of Immature Necrotic Permanent Dentition: A Systematic Review

Faisal T. Alghamdi[1] **and Alaa E. Alqurashi**[2]

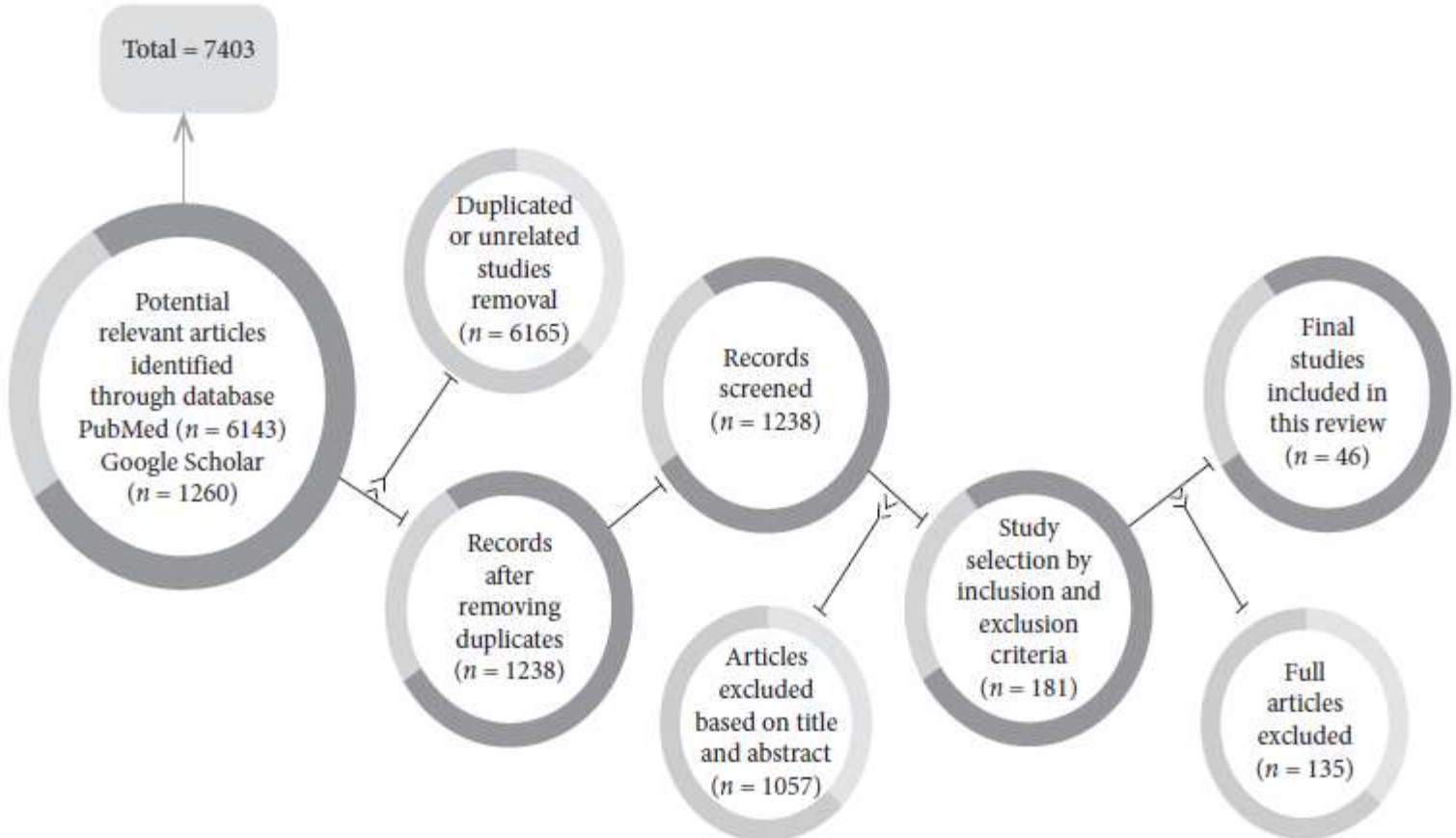
[1]*Department of Oral Biology, Faculty of Dentistry, King AbdulAziz University, Jeddah 80209, Saudi Arabia*
[2]*Ibn Sina National College for Medical Studies, Dental College, Jeddah 22421, Saudi Arabia*

Correspondence should be addressed to Faisal T. Alghamdi; dr.faisal2020@hotmail.com

Received 6 May 2020; Revised 22 June 2020; Accepted 27 June 2020; Published 13 July 2020

Academic Editor: Gianandrea Pasquinelli

Background and Objective. Management of immature permanent teeth exhibiting necrotic pulp is clinically challenging. An appropriate diagnosis, case selection, and good management ensure good outcomes. The objective of this review reviews all up-to-date data in regard to endodontic regeneration therapy in the management of immature permanent teeth with necrotic pulp and which conducts are most used and appropriate for this procedure in human and animal investigations. *Materials and Methods.* The electronic databases PubMed and Google Scholar were used to search the literature for relevant studies after applying specific inclusion and exclusion criteria


Total = 7403
Potential relevant articles identified through database PubMed (n = 6143) Google Scholar (n = 1260)
Duplicated or unrelated studies removal (n = 6165)
Records after removing duplicates (n = 1238)
Records screened (n = 1238)
Articles excluded based on title and abstract (n = 1057)
Study selection by inclusion and exclusion criteria (n = 181)
Final studies included in this review (n = 46)
Full articles excluded (n = 135)

Significance

Endodontic regenerative therapy showed better results in certain parameters such

- as increase in root wall lengthening and thickening,
- acute/chronic periapical lesions healing,
- and improved apical closure formation

However, more clinical trials with a standardized protocol and defined clinical, radiographic, and histopathological outcomes with longer follow-up periods are warranted.

LITERATURE REVIEW

Histological assessment of human regenerative endodontic procedures (REP) of immature permanent teeth with necrotic pulp/apical periodontitis: A systematic review

Digka Anna, DDS, PhD; Sakka Dimitra, DDS; and Lyroudia Kleoniki, DDS, PhD

Department of Endodontology, School of Dentistry, Aristotle University of Thessaloniki, Thessaloniki, Greece

Keywords
histology, human, immature permanent teeth, regenerative endodontic procedures, systematic review.

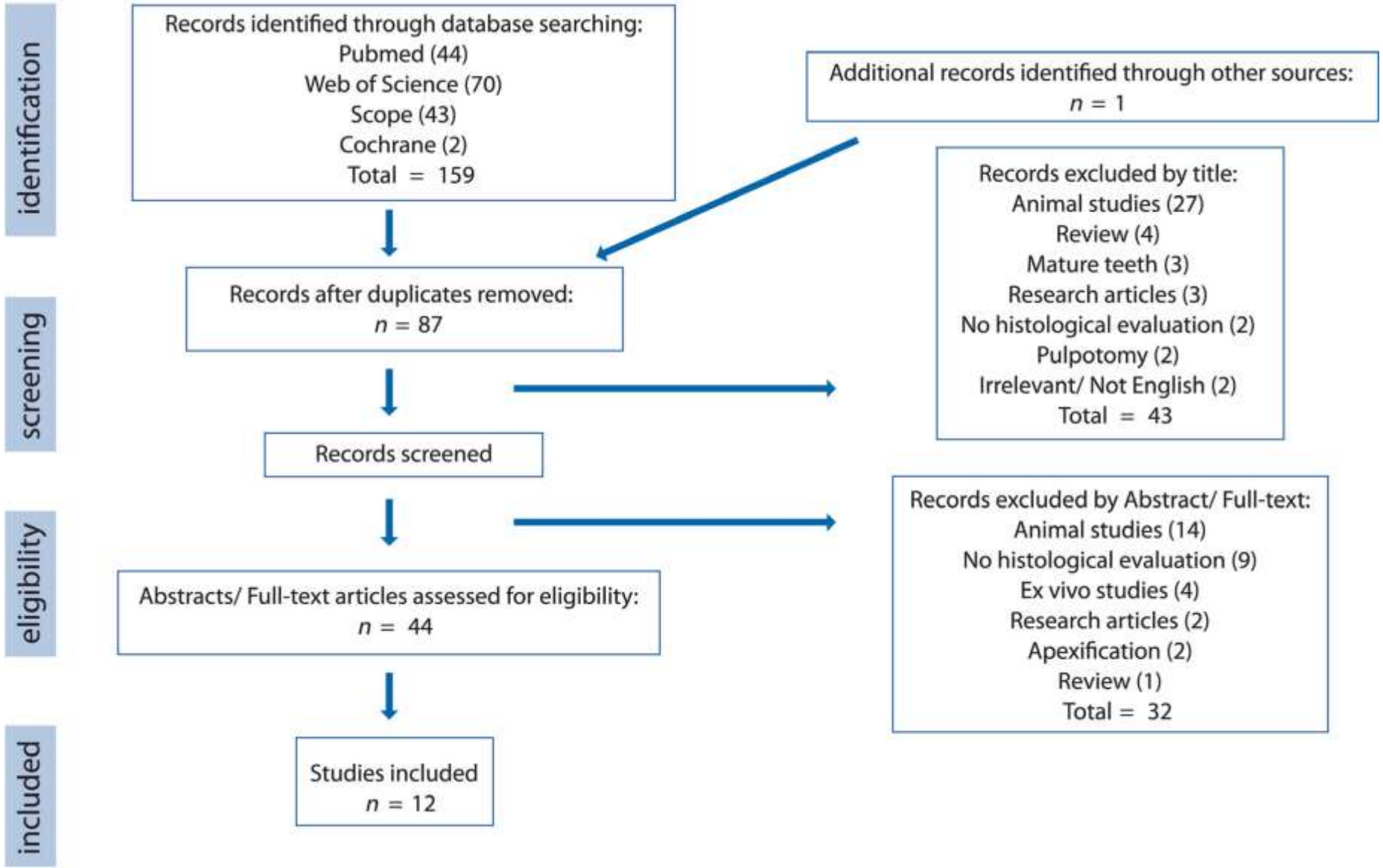
Correspondence
Dr Digka Anna, Department of Endodontology, School of Dentistry, Aristotle University of Thessaloniki, Ermou 36, 54623 Thessaloniki, Greece. Email: annadiga@hotmail.com

doi: 10.1111/aej.12371

(Accepted for publication 31 July 2019.)

Abstract

The aim of this study was to systematically review the histological evidence of the neo-formed tissues inside the root canals of human teeth having previously received regenerative endodontic treatment. An electronic research was performed in the MEDLINE, Web of Science, Scopus and Cochrane Library databases using controlled vocabulary. The retrieved studies were screened by two reviewers according to the predetermined inclusion and extrusion criteria and were full-text-evaluated. Research resulted in 160 studies. Among them, twelve fitted the inclusion criteria and were critically appraised. The tissues formed in the root canals of immature human teeth treated with REP indicate repair or a combination of repair and regeneration. Pulp remnants and healthy periapical tissues seem to improve regeneration. The level of available evidence was low. Further clinical studies are needed in order to establish the appropriate treatment protocol related to the pretreatment status of the dental pulp and the periapical tissues.


identification
screening
eligibility
included
Records identified through database searching:
Pubmed (44)
Web of Science (70)
Scope (43)
Cochrane (2)
Total = 159
Additional records identified through other sources:
n = 1
Records after duplicates removed:
n = 87
Records excluded by title:
Animal studies (27)
Review (4)
Mature teeth (3)
Research articles (3)
No histological evaluation (2)
Pulpotomy (2)
Irrelevant/ Not English (2)
Total = 43
Records screened
Records excluded by Abstract/ Full-text:
Animal studies (14)
No histological evaluation (9)
Ex vivo studies (4)
Research articles (2)
Apexification (2)
Review (1)
Total = 32
Abstracts/ Full-text articles assessed for eligibility:
n = 44
Studies included
n = 12

Significance

- In immature permanent human teeth treated with REP,
    - the newly formed tissues indicate tissue repair or a combination of repair and regeneration.
    - Pulp remnants and healthy periapical tissues seem to improve regeneration, and the status of the dental pulp and the periapical tissues are imperative for case selection for the treatment.
    - Further clinical and histological research is necessary in order to establish

Procedures

Contents lists available at ScienceDirect

Journal of Oral Biology and Craniofacial Research

journal homepage: www.elsevier.com/locate/jobcr

Research Paper

"Meta-analysis of regenerative endodontics outcomes with antibiotics pastes and calcium hydroxide. The apex of the iceberg"☆

Viviana Báez [a,b,*], Lorena Corcos [a], Florencia Morgillo [a], Lorena Imperatrice [a], Ariel Félix Gualtieri [c]

[a] Universidad de Buenos Aires. Facultad de Odontología. Cátedra de Endodoncia. Buenos Aires, Argentina
[b] Centro de Educación Médica e Investigaciones Clínicas CEMIC, Departamento de Odontología. Buenos Aires, Argentina
[c] Universidad de Buenos Aires. Facultad de Odontología. Cátedra de Biofísica y Bioestadística. Buenos Aires, Argentina

ARTICLE INFO

Keywords:
Regenerative endodontics
Disinfection
Immature tooth
Antibiotics
Calcium hydroxide
Outcomes

ABSTRACT

Porpose: The aim of this study was to evaluate, through a meta-analysis, the predictability of Regenerative Endodontic therapies with antibiotic pastes and calcium hydroxide [$Ca(OH)_2$], related to four variables as follows: root dentin wall thickening, apical closure, apical repair and root lengthening.

Methods: Literature electronic searches were performed in Pubmed - MEDLINE, Scopus and Lilacs-BVS platforms using appropriate search terms, Mesh (Medical Subject Headings), DeCS (Health Sciences Descriptors) and Boolean operators comprising articles published between 2009 and 2020. Thirty-two original indexed papers

Response variable	Treatment	Number of studies	Model (Fixed/Random effects)	Succes rate (CI95)	I^2 (CI95)
Root dentin wall thickening	Antibiotic Paste	23	Random	66% (58% - 73%)	61% (38% - 75%)
	$Ca(OH)_2$	8	Random	53% (26% - 78%)	80% (60% - 90%)
	Total	31	Random	64% (55% - 71%)	68% (53% - 78%)
Apical Closure	Antibiotic Paste	25	Random	66% (58% - 73%)	61% (40% - 75%)
	$Ca(OH)_2$	6	Fixed	88% (80% - 93%)	13% (0% - 78%)
	Total	31	Random	70% (63% - 77%)	64% (48% - 76%)
Periapical Repair	Antibiotic Paste	26	Random	91% (87% - 94%)	30% (0% - 57%)
	$Ca(OH)_2$	7	Fixed	88% (79% - 94%)	9% (0% - 74%)
	Total	33	Fixed	89% (86% - 92%)	24% (0% - 51%)
Root lenghtening	Antibiotic Paste	26	Random	68% (60% - 74%)	57% (33% - 72)
	$Ca(OH)_2$	9	Random	80% (60% - 92%)	70% (41% - 85%)
	Total	35	Random	70% (63% - 76%)	60% (43% - 73%)

Significance

Antibiotic pastes
higher percentage of root dentin wall thickening

Calcium hydroxide
higher percentage of apical closure

Regenerative Endodontic Therapy in the Management of Nonvital Immature Permanent Teeth: A Systematic Review—Outcome Evaluation and Meta-analysis

Huei Jinn Tong, BDS, MDentSci, MPaedDent RCS, [*]
Sadna Rajan, BDS, MDSc, MDentSci, MPaedDent RCS, [†]
Nabina Bhujel, BDS, MFDS RCPS, MPaedDent RCPS, D Clin Dent, FDSRCS, [‡]
Jing Kang, PhD, [§] *Monty Duggal, BDS, MDS, FDS, PhD,* [*] *and*
Hani Nazzal, BDS, MFDS RCS Ire, FRCD Can Paed Dent, PhD Paed Dent, MPaed Dent RCS Glas, FDS Paed Dent [¶]

Abstract

Introduction: Although the protocols in previously published studies appeared to be largely similar, there were inadequate evidence-based guidelines to support a single protocol. Using a meta-analysis, this systematic review aimed to summarize and quantitatively evaluate the outcomes for nonvital immature permanent teeth treated using the regenerative endodontic technique (RET) as well as critically appraise the level and quality of evidence of the existing publications. **Methods:** Risk of bias assessment and level of evidence grading were performed on

Key Words

Level of evidence, meta-analysis, outcomes, regenerative endodontic therapy

Although several publications suggest that treatment using the regenerative endodontic technique (RET) has positive outcomes, the results of such studies should be interpreted with

Significance

The review summarizes systematically the clinical and radiographic outcomes of existing clinical studies on regenerative endodontic therapy. It also aims to help clinicians evaluate the levels of evidence of published articles and identify addi-

TABLE 4. I^2 Values for Each Subgroup

I^2 (P value)	PA healing	Apical closure	Increased root length	Increased dentin thickness
Control	0.00 ($P = 0.863$)	67.49 ($P = 0.046$)*	48.083 ($P = 0.165$)	48.083 ($P = 0.165$)
BC	0.00 ($P = 0.946$)	36.7 ($P = 0.176$)	70.366 ($P = 0.034$)*	70.366 ($P = 0.034$)*
PRP	20.163 ($P = 0.286$)	0.00 ($P = 0.387$)	0.00 ($P = 0.755$)	0.00 ($P = 0.755$)

BC, blood clot; PA, periapical; PRP, platelet-rich plasma.

*Significant, indicative of high heterogeneity.

Thank you