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Research Article

TOOTH SURVIVAL FOLLOWING REGENERATIVE ENDODONTIC TREATMENT: A REVIEW

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Abstract

Based on published studies of regenerative endodontic treatment (RET), an attempt was made to draw conclusion about the survival outcome of RET treated teeth. PubMed searches were conducted using the terms "survival", "functional retention", "outcome", "regenerative endodontic treatment" and "revascularization therapy" as well as combinations of these terms and other related ones. After full-text evaluation, twelve papers fulfilled the inclusion criteria. Traumatized nonvital incisors were the most commonly RET treated teeth followed by premolars. There was wide variability in the follow-up timings across the studies. Intracanal irrigation was performed in all studies with sodium hypochlorite with variable concentrations. In addition, a considerable variation of intracanal medication was observed, with the use of double, triple antibiotic paste (DAP-TAP), and Ca(OH)2. Based on the best available evidence, RET has an excellent tooth survival rate. The tooth survival ranged from 81.3% - 100%. The most commonly reported late-stage effects were pulp canal obliteration and tooth discoloration. This review revealed excellent success rates in terms of tooth survival after RET. However, there is a paucity of well-documented long-term prospective studies that report on long- term tooth survival outcomes beyond 18 months and the prognostic factors. Thus, well-designed standardized long-term prospective studies should be conducted to provide more concise and safe information.

Keywords: Regenerative endodontic treatment, Survival, Functional retention.

INTRODUCTION

Since the first case of revascularization of an immature permanent tooth with apical periodontitis and a sinus tract was reported by Iwaya et al in 2001 (Iwaya *et al.,* 2001), many more case reports and case series of such treatments have been published (Diogenes *et al.,* 2013). Unlike apexification therapy, thickening of the canal walls and continued root maturation are sometimes observed after regenerative endodontic treatment (RET) (Bose *et al.,* 2009; Jeeruphan *et al.,* 2012); therefore, the treatment procedure is currently widely accepted for the management of endodontic pathology when treating immature permanent necrotic teeth. The outcome of RET is largely measured by the possibility to attain primary, secondary, and tertiary goals (American Association of Endodontists, 2018):

1) Primary goal: The elimination of symptoms and the evidence of bony healing.

2) Secondary goal: Increased root wall thickness and/or increased root length.

3) Tertiary goal: Positive response to vitality testing.

Regardless of substantial heterogeneity in the reporting of outcomes among studies, such as the report of pre- and postoperative clinical factors as well as the quantification and report of radiographic outcomes. In addition to the variability between clinical protocols, several publications suggest that RET has positive outcomes (Luiz Alexandre Chisini *et al.,* 2018). However, there is a striking paucity of high-quality evidence regardingfunctional survival, as defined by Friedman &Mor 2004 (Friedman and Mor, 2004), of RET treated teeth.

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MATERIALS AND METHODS

PubMed search was conducted for the last 10 years to identify all peer-reviewed English language papers using the terms "survival", "functional retention", "outcome", "regenerative endodontic treatment" and "revascularization therapy" as well as combinations of these terms and other related ones. In this review, studies with randomized controlled clinical trials design as well as prospective or retrospective clinical trials were included. To be included, studies should investigate the survival rate following revascularization therapy of nonvital immature permanent teeth. However, studies in vitro, case reports and series, letters to editor and reviews were not included in the present review. The type of teeth reported, etiology of pulp necrosis, follow-up range, intracanal medication, irrigation solution, survival rate and late stage effects were collected (Table 1).

RESULTS

Included studies and study design: The initial research found 83 records. The titles of the studies were evaluated and 17 were selected for abstract evaluation. After full-text evaluation, twelve papers fulfilled the inclusion criteria. In relation to study design, eight studies were retrospective (Jeeruphan *et al.,* 2012; Alobaid *et al.,* 2014; Silujjai and Linsuwanont, 2017; Mittmann *et al.,* 2014; Pereira *et al.,* 2020; Peng *et al.,* 2017; Elfrink *et al.,* 2020; Chrepa *et al.,* 2020) and four prospective (Chan *et al.,* 2017; Li *et al.,* 2017; Saoud *et al.,* 2014), of which only one is a randomized controlled study (Lin *et al.,* 2017).

Type of teeth reported and etiology of pulp necrosis: Traumatized nonvital incisors were the most commonly RET treated teeth followed by premolars, while only three studies reported the use of RET on molar teeth (Silujjai and Linsuwanont, 2017; Chrepa *et al.,* 2020; Chan *et al.,* 2017).

Table 1. Characteristics of included studies

Study	Follow up (months)	Number of Teeth (type)	Etiology forpulp necrosis	Intracanal medication	Irrigation	Tooth Survival n (%)	Late stage effects
Jeeruphan *et al.* (2012)	21 ± 12	20 (Incisors & premolars)	Caries, Dens evaginatus, Trauma	TAP	2.5% NaOCl	20 (100%)	Not reported
Alobaid *et al.* (2014)	15 ± 9	19 (Anteriors)	Trauma, Caries, dens evaginatus	$Ca(OH)_2$/TAP/ DAP	NaOCl and chlorhexidine	18 (95%)	PCO &Discoloration
Silujjai *et al.* (2017)	12–93	17 (Incisors, premolars & molars)	Trauma, Caries, dens evaginatus	TAP	1.5%—2.5% NaOCl and 17% EDTA	15 (88.24%)	PCO
Mittmann *et al.* (2014)	Mean 22	16 (Incisors)	Trauma	Ledermix	1% NaOCl and 17% EDTA	13 (81.3%)	Root resorptions, Ankylosis & Discoloration
Cardoso *et al.* (2020)	9 - 36	16 (Incisors)	Trauma	$Ca(OH)_2$ and 2% chlorhexidine gel	6% NaOCl, 2% chlorhexidine and 17% EDTA	15 (93.75%)	Discoloration
C. Peng *et al.* (2017)	37 □ 12	60 (Anteriors & premolars)	Caries, Anomaly, Trauma	TAP	5.25% NaOCl	59 (98.3%)	PCO & Discoloration
Elfrink *et al.* (2020)	Mean 35	47 (Incisors)	Trauma	TAP	2% NaOCl	46 (97.9%)	Ankylosis, Discoloration & New apical rarefaction
Chrepa *et al.* (2020)	12-96	51 (Anteriors, premolars & molars)	Trauma, Caries, dens evaginatus	$Ca(OH)_2$/TAP/ DAP	1.5% or 6% NaOCl & 2% chlorhexidine	47 (92%)	Discoloration
Chan *et al.* (2017)	30	28 (Incisors, premolars & molars)	Trauma, Caries, dens evaginatus	TAP	5.25% NaOCl	27 (96.4%)	Discoloration
Li *et al.* (2017)	12	20 (Premolars)	dens evaginatus	$Ca(OH)_2$	2.5% NaOCl	20 (100%)	Not reported
Saoud *et al.* (2014)	12	20 (Incisors)	Trauma	TAP	2.5% NaOCl	20 (100%)	Hard tissue bridge formation (not at apex)
Lin *et al.* (2017)	12	80 (Incisors & Premolars)	Trauma & dens evaginatus	TAP	1.5%NaOCl and 17% EDTA	80 (100%)	Root resorptions, PCO & Discoloration

Seven studies had mixed etiologies for the loss of pulp vitality (caries, trauma, and developmental anomaly). Only 4 studies specified the trauma as the only cause for necrosis (Mittmann *et al.,* 2014; Pereira *et al.,* 2020; Elfrink *et al.,* 2020; Saoud *et al.,* 2014) and one study had the developmental anomaly as the primary etiology (Li *et al.,* 2017).

Follow-up Range: There was wide variability in the follow-up timings across the studies, with eight studies having a minimum review of 12 months. Two studies had a minimum follow up of 10 and 9 months respectively ((Mittmann *et al.,* 2014; Pereira *et al.,* 2020), while Alobaid *et al.* (2014) and Elfrink *et al.* (2020) had 6 months as a minimum follow up period.

Intracanal irrigation and medication: Intracanal irrigation was performed in all studies with sodium hypochlorite with variable concentrations 1% - 6%, whilst three studies (Alobaid *et al.,* 2014; Pereira *et al.,* 2020; Chrepa *et al.,* 2020) also used chlorhexidine in the first visit. Four studies (Silujjai and Linsuwanont, 2017; Mittmann *et al.,* 2014; Pereira *et al.,* 2020; Lin *et al.,* 2017) reported that they used 17% EDTA in the second visit. In addition, a considerable variation of intracanal medication was observed, with the use of double (Alobaid *et al.,* 2014; Chrepa *et al.,* 2020) and triple antibiotic paste (DAP-TAP), even as $Ca(OH)_2$ (Alobaid *et al.,* 2014; Chrepa *et al.,* 2020; Li *et al.,* 2017). Mittmann et al. (2014) used ledermix as an intracanal medicament in traumatized immature incisors to inhibit external root resorption. Cardoso and colleagues (Pereira *et al.,* 2020) used calcium hydroxide associated with 2% chlorhexidine gel as the only intracanal medication in their study. This association allows the increase of antimicrobial activity against some bacteria found in endodontic infections and diffusion into dentinal tubules, without interfering in the chemical and biological properties of calcium (Gomes *et al.,* 2006 & 2009).

Survival rate: Based on the best available evidence, RET has an excellent tooth survival rate (Table 1). The tooth survival ranged from 81.3% - 100%. Four studies revealed that all RET treated teeth were present and functioning throughout the study period (100%). Only one study [10] reported survival rate less than 88%. However, the main cause of extraction was serious root resorption resulting from trauma.

Late stage effects: Late-stage effects after RET were reported inconsistently across articles (Table 1). The most commonly reported late-stage effects were Pulp Canal Obliteration (PCO) and tooth discoloration. Discoloration was correlated with tetracycline antibiotics or MTA use.

Conclusion

This review revealed excellent success rates in terms of tooth survival after RET. However, there is a paucity of well-documented long-term prospective studies that report on long-term tooth survival outcomes beyond 18 months and the prognostic factors. Thus, well-designed standardized long-term prospective studies should be conducted to provide more concise and safe information.

Conflict of interest: The author has no conflicts of interest to disclose.

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