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Preoperative Factors Analysis on Root Development after Regenerative Endodontic Procedures: a Retrospective Study of 116 Cases

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Research Article

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Abstract

Background Regenerative endodontic procedures (REPs) has achieved clinical success on the immature permanent teeth with pulp necrosis, and can promote root development. However, preoperative factors and their effects on root development of REPs have not been definitely concluded. The aim of this study was to investigate the preoperative factors that may influence the root development of REPs.

Methods A total of 116 teeth in 110 patients treated with REPs in the Paediatric Dentistry Department and Endodontics Department from 2013 to 2017 were included in this study. Factors including aetiology, age, preoperative diagnosis and initial root morphology were collected retrospectively, and the associations between these factors and root development after REPs were analysed by Fisher's exact test and multivariate logistic regression model.

Results The overall rate of root development after REPs was 89.7%. The dens evaginatus group showed a higher rate (98.8%) in root development than the trauma group (67.6%) ($P<0.01$). There was no significant difference among the different age groups (7-13 years old) or among different preoperative diagnoses regarding root development ($P>0.05$). And it showed in the trauma group that the teeth with apical foramen sizes larger than 3 mm obviously continued root development than those smaller than 3 mm ($P<0.01$). Multivariate logistic regression indicated that aetiology was significantly correlated with root development of REPs (OR: 1.31, 95% CI: 0.007, 0.627, $P<0.05$).

Conclusions Within the limitation of the present study, aetiology was correlated with the root development of REPs and the REPs achieved better outcomes in the cases caused by dens evaginatus than the trauma cases.

Background

The occurrence of trauma, developmental malformation or caries in young permeant teeth can cause pulp necrosis and hinder root development. Regenerative endodontic procedures (REPs), a biologically based treatment, have been widely used to treat the above cases since Banchs and Trope introduced the modified clinical regenerative endodontic protocol in 2004 [1]. The recommendations of the American Association of Endodontists (AAE) for REPs have been revised several times due to the rapid advancement in research findings in this field. Nevertheless, the goals of REPs according to AAE consistently include the following: primary goal (resolve symptoms and promote apical healing), secondary goal (root development), and tertiary goal (obtain a positive response to vitality testing) [2].

Numerous cases of REPs have achieved clinical success, defined as the disappearance of periapical lesions (primary goal) and continued root development (secondary goal) [3–6]. Several clinical studies have also shown the success rate of REPs ranging from 83.3–100% [7–10]. However, the root development of teeth after REPs is still unpredictable. Thus the prognostic factors that would influence the outcome of REPs have drawn dramatic attention. Up till now, the prognostic factors influencing the success rate of REPs have been reported in a few studies. It has been reported that age and the preoperative stage of root morphology, such as foramen diameter, could be associated with the success of the REPs [11–13]. Our previous study showed that dens evaginatus cases had a higher success rate than trauma cases at 12 months after receiving REPs [8], suggesting that the aetiology could also be a prognostic factor. However, due to the limitation of sample size and study design, no definite conclusion has been drawn about the influence of the above factors on the root development of REPs. The present retrospective study aimed to analyse the preoperative factors for the root change outcomes of REPs on the basis of a large sample size.

Methods

Patient samples

Patients receiving REPs on immature permanent teeth with pulp necrosis or apical periodontitis from January 2013 to April 2017 were included. This study was approved by the Ethics Committee of the Affiliated Hospital of Stomatology, Sun Yat-sen University. All cases were treated at the Paediatric Dentistry Department and Endodontic Department of Hospital of Stomatology, Sun Yat-sen University, with at least one year follow-up. The treatment were performed by two dentists who had special training in paediatric dentistry and endodontics.

The REPs was performed according to the procedures described in a previous study [8]. At the first visit, limited field of view cone beam computed tomography (FOV CBCT) (PHT-6500; VATECH Co., Ltd., Korea, 90 kV, 7.0 mA) was taken. After local anaesthesia with 2% lidocaine without epinephrine (Lidocaine Hydrochloride Injection, Tianshengkangdi Pharmaceutical Co. LTD, China), isolation with a rubber dam and cavity access were performed. The canals were irrigated with 20 mL 1.5% sodium hypochlorite (NaOCl) (Tanxiao Fenwei Pharmaceutical Co. LTD, China), and 20 mL 17% EDTA (Zhongnan Reagent Industry Co. LTD, China). Ciprofloxacin (Sigma Chemical Company, USA), metronidazole (Sigma Chemical Company, USA) and clindamycin hydrochloride (Sigma Chemical Company, USA) were mixed with sterile water into 0.1 mg/mL triple antibiotic paste and delivered into the canals, followed by temporary sealing with Caviton (GC Corporation, Tokyo, Japan). At the recall of 3 weeks after the first visit, the asymptomatic teeth proceeded to local anaesthesia with 2% lidocaine (no epinephrine) and rubber dam isolation. The triple antibiotic paste was removed and the canals were irrigated by 20 mL 17% EDTA. After a blood clot formation, an absorbable collagen barrier (Heal-all Biological Membrane; Zhenghai Biological Technology Co. LTD, China) was placed on top of the blood clot, followed by WMTA (ProRoot white MTA; Dentsply International, Inc., Germany) and glass-ionomer cement (GlasIonomer FX-II, Shofu Inc., Japan) sealing. Permanent restoration with composite resin (Z350, 3 M, USA) was finished 1 week later. The patients were recalled at 3, 6, 12, and 24 months and then yearly after treatment.

Data collection

The following variables were retrospectively collected from the electronic medical records: (a) age when the REPs were initiated, (b) tooth type, (c) aetiology, (d) preoperative diagnosis, and (e) preoperative root morphology. The root morphology data from FOV CBCT taken before REPs and 1 year after REPs was analysed, and the root morphology data, including root length, root wall thickness and apical foramen diameter, were measured by one experienced oral radiologist using Ez3D2009 software according to a previous study [8]. Briefly, axial planes X, Y, and Z were used to determine the central location of the measurement. The X axial plane was parallel to the long axis of the teeth with Y axial plane perpendicular to the X axial plane and crossed the maximum diameter of the pulp from the mesio-distal direction. The Z axial plane was perpendicular to both the X and Y axial planes and connected the top of the alveolar ridge crest mesial and distal to the teeth. The distance between the cemento-enamel junction (CEJ) and the apical endpoint was measured distally, mesially, buccally and lingually, which were then averaged as the root length. The size of the apical foramen was averaged from the diameters of the buccolingual and mesiodistal directions. The root thickness was the average value of the thickness at 4 mm, 6 mm and 8 mm from the CEJ and from the bucco-lingual and mesio-distal directions (Supplementary 1).

Root development was classified into four types according to the postoperative CBCT results at one year follow-up. Type I was defined as an increase in root length and a decrease in apical foramen length. Type II and Type III were defined as only increases in root length or decreases in the apical foramen, respectively, while Type IV was regarded as unchange in root length and apical foramen [8]. Outcomes of Type I, Type II and Type III were regarded as continued root development after REPs.

The success of REPs was defined as elimination of symptoms and disappearance of apical radiolucency (AAE primary goal). The failure of REPs was defined as one of the following: the presence of clinical symptoms (pain, swelling or sinus tract), root fracture or recurrence of apical periodontitis.

Statistical analysis

All data were analysed using IBM SPSS 25.0 software, and a p-value of 0.05 or less was considered to indicate statistical significance. Demographics and clinical data were expressed as percentages for categorical variables, means with standard deviations (SDs) and median for continuous variables.

For univariate analysis, Fisher's exact test was used for categorical variables. A multivariate logistic regression model was used to identify the preoperative factors influencing the root development of REPs. Gender, age, tooth type, aetiology, preoperative diagnosis and preoperative root morphology (apical foramen size, root length, and root canal wall thickness) were included in the regression model according to the professional and univariate outcomes using the type IV group as a reference. For the logistic regression model, the odds ratio (OR) and 95% confidence interval (95% CI) were used to describe the results. The Hosmer–Lemeshow test was used to evaluate the goodness of fit of the model.

Results

From 2013 to 2017, 121 young permanent teeth in 115 patients were treated with REPs. By June 2019, 4 patients with 4 teeth were lost within one year follow-up, and 1 tooth was extracted because of orthodontic requirements within 1 year after REPs. Therefore, a total of 116 teeth in 110 patients were included in this study. The included patients' demographic and clinical details were shown in Supplementary 2 and 3, and Table 1 summarized the demographic and clinical data of the study population. The age of the patients ranged from 7 to 13 years old. The average age of trauma group was 8.9 ± 0.5 years old and that of dens evaginatus group was 10.9 ± 0.8 years old.

Table 1
Demographics and Clinical Data of the Study Population

Variables	Categories	N (%)
Age	Years (mean ± SD)	10.3 ± 0.7
Gender	Male	52 (47.3%)
	Female	58(52.7%)
Tooth type	Maxillary central incisors	32 (27.6%)
	Maxillary lateral incisors	2 (1.7%)
	Maxillary second premolars	3 (2.6%)
	Mandibular second premolars	76 (65.5%)
	Mandibular first premolars	3 (2.6%)
Aetiology	Dental trauma	34 (29.3%)
	Dens evaginatus	82 (70.7%)
Preoperative diagnosis	Asymptomatic apical periodontitis	77 (66.4%)
	Symptomatic apical periodontitis	18 (15.5%)
	Chronic apical abscess	16 (13.8%)
	Acute apical abscess	5 (4.3%)
Apical foramen size in trauma group	mm (median)	3.00
Apical foramen size in dens evaginatus group	mm (median)	2.65
Root length in trauma group	mm (median)	12.9
Root length in dens evaginatus group	mm (median)	11.50
Root thickness in trauma group	mm (median)	1.41
Root thickness in dens evaginatus group	mm (median)	1.41

Among all 116 cases, only 1 case was retreated with apexification due to infection recurrence 3 months after REPs, and 115 cases achieved apical healing and were clinically asymptomatic, reaching a success rate of 99.1% by the primary goal of AAE. Root development was analysed by comparing the CBCT images at the 1-year follow-up (Supplementary 4) to the preoperative CBCT images. A total 104 out of 116 teeth achieved root development (Type I, II or III), with a rate of 89.7% by the secondary goal of AAE. The dens evaginatus group had Type I 86.6% (71/82 cases), Type II 9.8% (8/82 cases), Type III 2.4% (2/82 cases), and Type IV 1.2% (1/82 cases), while the trauma group had Type I 44.1% (15/34 cases), Type II 2.9% (1/34 cases), Type III 20.6% (7/34 cases) and Type IV 32.4% (11/34 cases). The statistical analysis showed a significant difference in the outcome distribution between the dens evaginatus group and trauma group ($P < 0.001$) (Table 2), indicating that aetiology may affect the root development of REPs.

Next, whether preoperative periapical diagnosis would influence the outcomes of REPs was evaluated. Table 2 showed that most cases achieved Type I outcomes despite different preoperative diagnoses, and overall, no significant difference was found among the four types of distribution of treatment outcomes based on the preoperative diagnosis ($P > 0.05$), suggesting that preoperative diagnosis may not influence root development of REPs.

The effect of age on REPs outcomes was also analysed. Considering that the overall range of patients' ages was relatively small (7 to 13 years old), we first analysed the effect of each age subgroup on the outcome of REPs (7, 8, 9, 10, 11, 12, 13 years old) and found no significant difference among all age groups within each aetiology group. Next, the average ages of the dens evaginatus group and trauma group (10.9 and 8.9 years old, respectively) were used for further statistical analysis, and there was no significant difference among them (≥ 10.9 years old. vs. <10.9 years old in the dens evaginatus group and ≥ 8.9 years old vs. <8.9 years old in the trauma group) ($P > 0.05$) (Table 3).

Statistical analysis was also performed to determine whether preoperative root morphology (apical foramen size, root length and thickness) affected outcomes of REPs. First, we analysed whether there was any difference in REPs outcomes among each range of apical foramen size (1, 2, 3 mm), root length (8, 9, 10, 11, 12 mm) and root wall thickness (1.2, 1.3, 1.4 mm) and found no significant difference among each range. Thus, the median values of these three indexes were calculated for statistical analysis. In the dens evaginatus group, preoperative root morphology did not affect the root development of REPs ($P > 0.05$) (Table 4). In the trauma group, only the teeth with apical foramen sizes larger than 3 mm achieved significant root development than those smaller than 3 mm ($P < 0.01$) (Table 4).

To further confirm the above results, multivariate logistic regression was also conducted and the results demonstrated that aetiology was correlated with root development of REPs with a regression coefficient of -2.687, OR 1.31, and 95% CI (0.007, 0.627) ($P = 0.018$) (Table 5).

Table 2
The influence of aetiology and preoperative diagnosis on root changes after REPs

Factors	Categories	Type I n = 86	Type II n = 9	Type III n = 9	Type IV n = 12	In total n = 116	*P*
Aetiology	Dens Evaginatus	71 (86.6%)	8 (9.8%)	2 (2.4%)	1 (1.2%)	82 (70.7%)	<0.001***
	Trauma	15 (44.1%)	1 (2.9%)	7 (20.6%)	11 (32.4%)	34 (29.3%)	
Diagnosis	Symptomatic apical periodontitis	14 (77.8%)	0 (0.0%)	3 (16.7%)	1 (5.6%)	18 (15.5%)	0.608
	Asymptomatic apical periodontitis	56 (72.7%)	6 (7.8%)	6 (7.8%)	9 (11.7%)	77 (66.4%)	
	Acute apical abscess	4(80.0%)	1(20.0%)	0(0.0%)	0(0.0%)	5 (4.3%)	
	Chronic apical abscess	12(75.0%)	2 (12.5%)	0 (0.0%)	2 (12.5%)	16 (13.8%)	

** P<0.05, ** P<0.01, *** P<0.001,△Fisher's exact test*

Table 3
The influence of age on root changes after REPs

Aetiology	Age	Type I n = 86	Type II n = 9	Type III n = 9	Type IV n = 12	In total n = 116	*p*
Dens evaginatus	< 10.9	32 (84.2%)	4 (10.5%)	2 (5.3%)	0 (0.0%)	38 (46.3%)	0.413
	≥ 10.9	39 (88.6%)	4 (9.1%)	0 (0.0%)	1 (2.3%)	44 (53.7%)	
Trauma	< 8.9	8 (47.1%)	0 (0.0%)	3 (17.6%)	6 (35.3%)	17 (50.0%)	1.000
	≥ 8.9	7 (41.2%)	1 (5.9%)	4 (23.5%)	5 (29.4%)	17 (50.0%)	
** P<0.05, ** P<0.01, *** P<0.001, △Fisher's exact test*							

Table 4
The influence of preoperative root morphology on root changes after REPs

Aetiology	Root morphology	(mm)	Type I	Type II	Type III	Type IV	In total n = 116	p
Dens evaginatus	Apical foramen size	<2.65	31 (81.6%)	4 (10.5%)	2 (5.3%)	1 (2.6%)	38 (46.3%)	0.319
		≥ 2.65	40 (90.9%)	4 (9.1%)	0 (0.0%)	0 (0.0%)	44 (53.7%)	
	Root length	<11.50	35 (87.5%)	5 (12.5%)	0 (0.0%)	0 (0.0%)	40 (48.8%)	0.486
		≥ 11.50	36 (85.7%)	3 (7.1%)	2 (4.8%)	1 (2.4%)	42 (51.2%)	
	Root thickness	<1.41	39 (81.3%)	7 (14.6%)	1 (2.1%)	1 (2.1%)	48 (58.5%)	0.182
		≥ 1.41	32 (94.1%)	1 (2.9%)	1 (2.9%)	0 (0.0%)	34 (41.5%)	
Trauma	Apical foramen size	<3.00	13 (52.0%)	1 (4.0%)	1 (1.0%)	10 (40.0%)	25 (73.5%)	0.001**
		≥ 3.00	2 (22.2%)	0 (0.0%)	6 (66.7%)	1 (11.1%)	9(26.5%)	
	Root length	<12.90	8(42.1%)	1 (5.3%)	4 (21.1%)	6 (31.6%)	19 (55.9%)	1.000
		≥ 12.90	7 (46.7%)	0 (0.0%)	3 (20.0%)	5 (33.3%	15 (44.1%)	
	Root thickness	<1.41	4 (40.0%)	0 (0.0%)	2 (20.0%)	4 (40.0%)	10 (29.4%)	0.921
		≥ 1.41	11 (45.8%)	1 (4.2%)	5 (20.8%)	7 (63.6%)	(70.6%)	

** P<0.05, ** P<0.01, *** P<0.001, △Fisher's exact test*

Table 5
Multivariate analysis of root changes after REP

Factors	Regression coefficient	Standard error	OR 95% CI	p△
Aetiology	-2.687	1.133	(0.007, 0.627)	0.018*

** P<0.05,* △multivariate logistic regression

Discussion

Endodontic treatment of immature permanent teeth with necrotic pulp consistently challenges clinicians due to the weak root wall and divergent apical foramen. To date, the REPs has been widely used to treat the above cases because they allow further increases in root length and root wall thickness, leading to the closure of the apical foramen [6, 14–17]. Although the literature has demonstrated the efficacy of REPs in healing apical lesion, the outcome of continued root development is still unpredictable. A few studies have investigated the prognostic factors affecting the outcomes of REPs to guide clinical work [10–12]. However, the sample size of these studies was relatively small and no conclusion has been drawn [10–12]. To understand the possible prognostic factors influencing the outcome of REPs, we designed this retrospective study based on our REPs database with a relative large sample size of 116 patients from 2013–2017. As we know, preoperative factors and treatment protocols may affect the outcomes of REPs. In the present study, we focused on the influence of preoperative factors on the root development of REPs due to the standard operative procedure for the included patients.

Dens evaginatus and trauma are two major causes of immature permanent teeth with necrotic pulp and apical periodontitis. A meta-analysis reported that there was no evidence of a difference in aetiology for the outcomes of REPs, in which success was defined as teeth being asymptomatic and teeth not requiring any other endodontic treatment after REPs (primary goal of AAE) [18]. However, our previous prospective study found that REPs cases with dens evaginatus had significantly better outcomes than those with an aetiology of dental trauma in achieving root development [8]. Chrepa et al also reported that aetiology was a significant predictor of failure as well as root development [10]. Our present study confirmed that dens evaginatus cases showed a better prognosis than trauma cases in terms of root development, which was verified by multivariate logistic regression. This may be because dental trauma induces damage to the apical papilla and Hertwig epithelial root sheath, which might lead to failure of continued root maturation. From the above studies, we may conclude that aetiology would affect root development rather than apical healing after REPs.

The preoperative diagnosis was evaluated as a potential prognostic factor in this study. We used current AAE diagnostic terminology and divided the cases into four clinical categories according to periapical status: asymptomatic apical periodontitis, symptomatic apical periodontitis, chronic apical abscess, and acute apical abscess [19]. The retrospective study by Chrepa et al stated that preoperative apical diagnosis based on AAE criteria was considered a significant predictor for radiographic root area (RRA) change after REPs, indicating that the status of infection/inflammation at the apical area could influence the regulation of root development [10]. In contrast, our results showed that the preoperative diagnosis did not significantly affect root development after REPs defined by our study, suggesting that the preoperative clinical diagnosis may not be used as case selection for REPs. The opposite outcomes may be due to the different variables and statistical approaches used in the studies. In our opinion, regardless of the preoperative diagnosis, microbial control is the foundation for regenerative endodontic treatment, and appropriate disinfection of the canal is needed to achieve apical healing. Once the infection is well controlled, root development would be possible.

It has been reported that younger patients have a better healing ability in terms of dental pulp regeneration [10]. Bishoy et al explored the influence of age on the success of REPs and found that compared to the older age group (14–18 years old), the younger age group (9–13 years old) showed a significant increase in length independent of the preoperative size of apical diameter [12]. In the study of Chrepa et al., age was one of the significant predictors of failure and RRA change [10]. However, our results showed no significant difference between ages on root development of REPs. This could be because the age range of patients in this study was relatively small (7–13 years old). Including samples with a wider age range should be considered for future studies to achieve more specific outcomes.

Preoperative root status/root morphology has also been evaluated as a prognostic factor of REPs. The study from Bishoy et al. found that teeth with preoperatively wider diameters (≥ 1 mm) demonstrated greater increases in root thickness, length, and apical narrowing [12]. Fang et al conducted a literature search and concluded that teeth with apical diameters < 1.0 mm achieved clinical success after REPs, and teeth with apical diameters of 0.5–1.0 mm attained the highest clinical success rate [13]. Lei et al. posited that dental roots shorter than 17 mm might achieve a higher success rate of REPs [20]. In our study, the initial apical foramen size in the trauma group impacted the root development of REPs. The larger apical foramen achieved more Type I outcomes after REPs, which may be due to the abundant blood supply provided via the large apex.

Conclusion

In the limitation of the present study, we demonstrated that aetiology and initial apical foramen size in the trauma group may correlate with root development after REPs. The REPs achieved more root development in the cases caused by dens evaginatus than in those caused by trauma. The present retrospective study provides additional evidence for the preoperative factors affecting the root development of REPs and will help clinicians make decisions when choosing the treatment plan for immature permanent teeth with necrotic pulps. Future studies should implement longer follow-up times and larger sample sizes to obtain more solid evidence-based conclusions that can guide clinical decision-making.

Abbreviations

REPs: Regenerative endodontic procedures

AAE: American Association of Endodontists

NaOCL: sodium hypochlorite

CI: confidence interval

FOV CBCT: field of view cone beam computed tomography

SDs: standard deviations

CEJ: Cemento-Enamel Junction

Declarations

Ethical approval and consent to participate

All procedures performed in studies involving human participants were in accordance with the ethical standards of Ethics Committee of the Affiliated Hospital of Stomatology (KQEC-2019-19), Sun Yat-sen University, Guangzhou, Guangdong, China. All procedures were in accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent Informed consent was obtained from all participants and their parents included in this study.

Consent for publication

Not applicable.

Availability of data and materials

All data generated or analysed during this study are included in this published article and its supplementary information files.

Competing interests

The authors declare that they have no Competing interests.

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Author contributions

LJC and YMB involved in conceptualization, methodology, investigation. ZQ involved in methodology, resources, and writing— original draft preparation. ZHJY involved in methodology and writing— original draft preparation. GJ involved in resources, writing— review and editing, and supervision. LSHY involved in formal analysis, writing— review and editing. All authors read and approved the final manuscript.

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