REVIEW ARTICLE

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Meta analysis of the treatment-related factors of external apical root resorption

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Structured Abstract

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Objective – To elucidate possible treatment-related etiological factors – such as, duration of treatment and apical displacement – for external root resorption.

Design – Meta-analysis of the available English-language literature.

Inclusion & Exclusion Criteria – Papers with a sample size >10, fixed appliances, pre- and post-operative radiographs, and apical displacement recorded were included. History of trauma, prior root resorption and endodontic treatment were excluded. Appropriateness of these selections was tested with a 'funnel plot' analysis.

Outcome Measure – Correlations between root resorption, apical displacement, and treatment duration.

Results – Mean apical root resorption was strongly correlated with total apical displacement ($r = 0.822$) and treatment duration ($r = 0.852$).

Conclusion – The treatment-related causes of root resorption appear to be the total distance the apex had moved and the time it took.

Key words: external root resorption; orthodontics

Introduction

Orthodontic treatment is known to be the most common cause of apical root resorption. Patients who receive orthodontic treatment are much more likely to experience severe apical root shortening than individuals who do not (1). Factors that are associated with the onset and extent of external apical root resorption

(EARR) are not clearly understood. These factors can be patient-related or treatment-related. Several patient-related factors, such as genetics and trauma, have long been known to be associated with increased levels of root resorption (2,3) A consensus on treatment-related causes of apical root resorption, however, cannot be found in the literature. Treatment-related factors can be frequency of force application, magnitude of the forces applied, duration of treatment, types of teeth, direction of tooth movement, character of the supporting bone, and the like. One can find reports that support or refute these claims in equal numbers.

Regardless of genetic or treatment-related factors the maxillary incisor consistently averages more apical root resorption than any other tooth (2–9). The maxillary incisor is also moved greater distances than any other tooth. For this reason, more emphasis has been placed, by some, on the duration a tooth is subjected to forces that produce hyalinization as opposed to overall force levels (10).

For obvious ethical considerations, no human studies on EARR can be prospective, randomized clinical trials. Consequently, published reports differ significantly in terms of their study designs, methodology, type of controls, and treatment assignment. Inaccuracy of the radiographic technique, lack of standardization of image acquisition, and a minimal sample size are common features that may lead a study to produce erroneous results. A significant number of studies fail to adjust for potential confounding effects of patient or treatment characteristics, such as, history of trauma, age, presence of extractions, appliance type, overjet and overbite.

Despite the unpredictable nature of EARR, blame is usually attributed to the orthodontist. A recent study demonstrated that many general dentists and other dental specialists perceive apical root resorption to be an avoidable phenomenon, and hold the orthodontist responsible for its manifestation (11). It is not uncommon for an orthodontist to be sued for allegedly inflicting apical root resorption (12). Nonetheless, severe EARR is of clinical significance, especially when it is coincident with alveolar bone loss. The purpose of this study was to establish treatment-related etiological factors of EARR through meta-analytic assessment of studies published in the literature. The study was limited to the maxillary incisor, in particular, the displacement of its apex.

Methods and materials

Meta-analysis is the statistical analysis of a sample of analysis results from individual studies for the purpose of integrating findings to produce a single estimate (13,14). The fundamental objective of this analytic method is to achieve an overall conclusion from a compilation of independent studies for the purpose of guiding future treatment (15). It allows the findings of disparate studies to be combined for greater statistical power than the independent studies alone can provide (16). Over the past decade, meta-analysis has been increasingly popular in the health sciences as a structural alternative to the narrative literature review.

This meta-analysis was designed to resolve the conflict among the reports of etiological factors responsible that produce external apical root resorption. A computerized search using the MEDLINE database was conducted with ‘root resorption’ as the subject heading. The initial sample of over 1900 articles was reduced by combining terms such as ‘orthodontics’ and ‘incisors’, and limiting the search to ‘English language’, and ‘human subjects’. Citations of the remaining studies were examined in order to find publications not located in the MEDLINE database. A total of 150 studies were selected, and subjected to strict exclusion/inclusion criteria. Of the 150 articles, only nine met the initial inclusion/exclusion criteria (Table 1).

The inclusion criteria required that each publication consisted of a clinical trial in the English language and was conducted on human subjects. The studies had to have a sample of more than 10 individuals that had undergone orthodontic therapy with fixed appliances.

Table 1. **Exclusion/inclusion criteria**

Exclusion criteria	Inclusion criteria
History of trauma	English language
History of prior root resorption	Human subjects
History of prior endodontic treatment	Sample size >10
	Fixed appliance therapy
	Pre-operative and post-operative X-rays
	Root resorption recorded on maxillary incisors
	Root apex used as reference to measure total apical displacement

Both pre-operative and post-operative X-rays had to be available for the study to be considered. In order to be included, each publication had to have measured external apical root resorption in maxillary incisors. Studies were not ruled out if they also measured root resorption in other tooth types. Finally, it was essential that each study has to measure incisal displacement with the apex of the root as the reference. Studies that measured apical displacement, but did not record their data were included. Exclusion criteria applied to studies that included a sample with a history of trauma, prior root resorption, or endodontic treatment (Table 2).

Table 2. **Resultant sample used for meta analysis**

Study ID no.	Bibliographic reference
24	DeShields R. A study of root resorption in treated class II, division I malocclusions. AJOD. 1969;39:231–244.
22	Costopoulos G, Nanda, R. An evaluation of root resorption incident to orthodontic intrusion. Am J Orthod Dentofac Orthop 1996;109:543–548.
108	Sameshima G, Sinclair P. Predicting and Preventing Root Resorption: Part II. Treatment Factors. Am J Orthod Dentofac Orthop 2001;119:511–515.
44	Horiuchi A, Hotokezaka H, Kobayashi K. Correlation between cortical plate proximity and apical resorption. Am J Orthod Dentofac Orthop 1998;114:311–8.
122	Goldin B. Labial root torque: effect on the maxilla and incisor root apex. Am. J.Orthodd. Dentofac. Orthop 1989;95:208–218.
97	Parker R, Harris E. Directions of orthodontic tooth movements associated with external apical root resorption of the maxillary central incisor. Am J Orthod Dentofac Orthop 1998;114:677–683.
144	Phillips J. Apical root resorption under orthodontic therapy. Angle Orthod. 1955;25:1–22.
77	Mirabella A., Artun J. Risk factors for apical root resorption of maxillary anterior teeth in adult orthodontic patients. Am J Orthod Dentofac Orthop 1995;108:48–55.
12	Baumrind S, Korn E, Boyd R. Apical root resorption in orthodontically treated adults. Am J Orthod Dentofac Orthop 1996;110:311–320.

Three investigators participated in the coding of variables and grading of articles selected for the meta-analysis. They were blinded with respect to authorship, and journal of publication. Each investigator was provided with a copy of the blinded studies and instructed to provide an evaluation and overall grade for the each individual article using a pre-determined coding template. After assigning individual scores, the three investigators convened and negotiated final coding figures and an assessment of methodologic soundness for each individual study. Scores were summed up and multiplied by the individual article's grade for methodologic soundness. Using this method, a cumulative 'Meta-analysis factor' was computed for each study. Final coding figures are summarized in Table 3.

An attempt was made to evaluate each study in an objective manner in order to minimize the degree of bias. For each study, assessments of methodology were governed by the basic principles of research and orthodontic tooth movement. The selected articles were evaluated based on the characteristics of study design, population sample, treatment assignment, documentation of statistics, and the accuracy of root resorption measurement, and apical displacement of incisor roots.

In addition to scoring each article, we thought it important to discuss our sample for a number of reasons. For example, because genetic pre-disposition influence on the onset of apical root resorption (17), it is preferable for studies to have large samples in order to reduce variability. Random assignment is also critical. Clinicians with a pre-conceived notion of what causes root resorption, may be biased when obtaining their patient sample. Certain measurement methods of root resorption are clearly less accurate than others. In cephalometric X-rays, incisors are superimposed, which often results in distortion at the root apex. This may lead to inaccuracies in apical root resorption measurements, and can be misleading. Also, age may influence the amount of recorded EARR. Patients under 11 years of age often have not completed root formation of their maxillary incisors, and thus, it may be difficult to measure the overall root loss. Because we measured the contribution of apical displacement on overall EARR, it is important that incisors are moved significant distances in order to determine if a relationship exists. Studies that recorded greater levels of mean apical displacement were given higher scores for

Table 3. **Coding categories and meta-analysis evaluation factors**

Categories	Meta analysis evaluation factors					
Study design	Retrospective	Prospective				
	1	2				
Control group	Control unnecessary	Untreated	Alternative Tx			
	1	1	2			
Sample size	10–30	31–100	101–200	201–300	301–401	400+
	5	6	7	8	9	10
Treatment assignment	Non-random	Random				
	2	3				
Mean Tx duration						
Mean RR						
Mean age and SDs						
Methods of data collection						
Standardized	Yes	No				
	2	1				
Types of X-ray	Cephalometric	Panoramic	FMX			
	1	2	3			
Statistics						
Error analysis: was it done?	Yes	No				
	2	1				
Age	Equal or <11	Mixed	>11			
	1	2	3			
Distance Apex moved and Statistics available	Apex distance mentioned		Apex distance measured			
	2		3			
Total apical distance moved in mm	Total apical distance (TAD xTAD)		No linear measurements/no correlation			
Methodological soundness	(+ or −) 0.5, 1, 2		1			
Appliance described						
Statistics provided						
Methods of measuring total apical displacement						
Meta-analysis factor						

that particular category. There are many methods of measuring apical displacement, and some are far more accurate than others. This factor was taken into account to measure a study's methodological soundness.

The final numerical value obtained from each study was termed the 'meta-analysis factor.' Scorings as outlined in Table 4 were used in the development of a weighting scheme that reflected the association between overall apical displacement of incisor roots, and treatment duration with mean apical root resorption.

The presence of publication bias is always possible in meta analyses, but it can be examined in a funnel plot analysis. These graphs represent scatter plots in which treatment effects estimated from individual studies on the horizontal axis are plotted against a measure of study precision on the vertical axis (18). Treatment effects from smaller studies should scatter more widely at the bottom of the graph, with the spread narrowing as precision increases from larger studies. In the absence of bias, the graph should resemble an inverted funnel. If the plot appears asymmetrical, then bias may be present. This can occur as a result of smaller studies overestimating treatment effects, or a publication bias in which smaller studies that don't show significant findings remain unpublished.

In this study a funnel plot was generated by plotting standard deviation as a function of mean root resorption. This can be seen in Fig. 1. Several studies did not

Table 4. **Individual meta-analysis evaluation scores**

Categories	Divisions and meta-analysis factors								
	Study ID no. 97	Study ID no. 144	Study ID no. 77	Study ID no. 12	Study ID no. 24	Study ID no. 22	Study ID no. 108	Study ID no. 44	Study ID no. 122
Study design	1	1	1	1	1	2	1	1	1
Control group	1	1	1	1	1	2	1	1	1
Sample size	7	6	9	6	6	5	10	7	5
Sample selection bias	2	2	2	2	2	2	2	2	1
Treatment assignment	2	2	2	2	2	2	5	5	2
Mean Tx duration	2.7 years	12.5 months (1.04 years)	2 years	3 years	21.7 months (2.3 years)	4.6 months (0.38 years)	1.47 years	*Not available	1.57 years
Mean root resorption	1.4 mm	1.33 mm	1.5 mm	1.36 mm	2.25 mm	0.6 mm	1.44 mm	*Not available	1.36 mm
Mean age and SDs	13.4 years	13.7 years	34.5 ± 9.0 years	33.3 ± 8.5 years	12.38 ± 0.86 years	11.9 years	*Not available	15 years	11.8 years
Methods of data collection									
Standardized	2	2	2	2	2	2	1	2	2
Types of X-rays	1	1	3	3	1	3	3	1	1
Statistics									
Error analysis: was it done?	2	1	2	2	1	1	2	2	1
Age	3	2	3	3	3	3	2	3	2
Distance apex moved and available statistics	3	3	3	3	3	3	3	3	3
Total apical distance moved in mm	(1 mm^2 = 1 mm^2)	(1.7 mm^2 = 2.89 mm^2)	(1 mm^2 = 1 mm^2)	(1.9 mm^2 = 3.61 mm^2)	(1.51 mm^2 = 2.28 mm^2)	(3 mm^2 = 9 mm^2)	(3 mm^2 = 9 mm^2)	(1 mm^2 = 1 mm^2)	(3.18 mm^2 = 10.11 mm^2)
Methodological soundness	1	0.5	2	2	0.5	1.5	2	1	0.5
Appliance described	Tweed, Begg, Roth Edgewise therapy	Edgewise fixed therapy	Multi-bracketed appliance	Fully banded/bonded Edgewise therapy	Edgewise fixed therapy	Burstone Intrusion Arch and Full Arch fixed therapy	Edgewise fixed therapy	Multi-bracketed therapy	Edgewise appliance therapy
Meta-analysis factor	25	12	62	57	12	51	78	28	15

include data on standard deviations of mean apical root resorption. These three studies were not included in the funnel plot. For each experimental point, upper and lower 95% confidence limits are presented. The presence of asymmetry is not observed in the funnel plot, and thus, one can assume an absence of bias among the selected articles.

Results

Of the nine articles that met the initial inclusion/exclusion criteria, one did not include data on mean root resorption and was subsequently not included in the statistical analysis. There were two articles that did not include data on mean apical displacement and thus, correlations between mean EARR and mean apical displacement could not be calculated for these studies.

As mentioned earlier, Table 4 contains the coding categories. The meta evaluation scores and a final meta-analysis factor for each study. The mean meta-analysis factor was 39, ranging from the lowest score of 12 to a high of 78. Table 5 displays the outcome data, including weighted and unweighted data. The mean root resorption for eight studies was 1.421 ± 0.448. The mean apical displacement was 2.382 ± 0.756.

Table 6 contains the calculated correlations among the variables studied. The unweighted correlation between mean root resorption and apical displacement (columns B and D) is −0.548. The weighted correlation between these two variables is 0.822. The unweighted correlation between mean root resorption and treatment duration (columns B and C) is 0.564. The weighted correlation is 0.852.

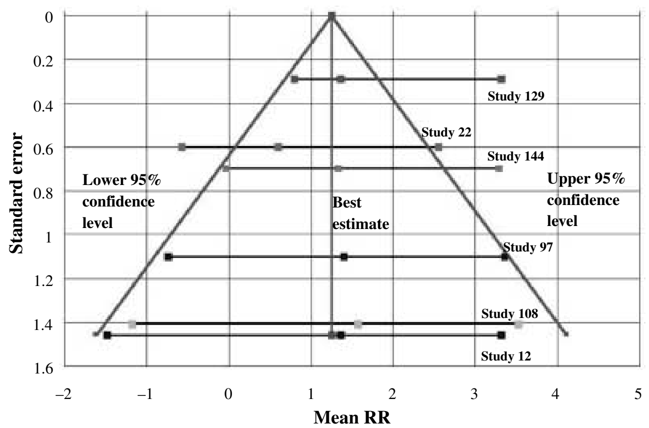

Fig. 1. Funnel plot analysis.

Discussion

Most recently, it was reported that variations in the IL-1β allele 1 cytokine is strongly associated with an increased risk of EARR (17). Patients who were homozygous for IL-1β allele 1 had a 95% chance of having root resorption greater than 2 mm. The demonstration that susceptibility to EARR is largely

Table 5. **Outcome data**

Study ID no.	A MA factor	B Mean RR (mm)	C Mean Tx duration (years)	D Mean total apical displacement (mm)	E B weighted (A × B)=	F C weighted (A × C)=	G D weighted (A × D)=
24	12	2.25	2.30	1.51	27.0	27.6	18.1
22	51	0.60	0.38	3.00	30.6	19.4	153.0
108	78	1.57	1.47	3.00	112.3	114.7	234.0
44	15	1.36	1.57	3.18	20.4	23.6	47.7
122	25	1.40	2.70	N/A	35.0	67.5	N/A
97	12	1.33	1.04	1.70	15.9	12.5	20.4
77	62	1.50	2.00	N/A	93.0	124.0	N/A
12	57	1.36	3.00	1.90	77.5	171.0	108.3
Average		1.421	1.808	2.382	51.475	70.021	96.920
SD		0.448	0.807	0.756	37.106	59.695	85.502

Table 6. **Correlation matrix data**

	B Mean RR	C Mean Tx duration	D Mean distance of apical displacement	E Weighted mean RR	F Weighted mean Tx duration	G Weighted mean distance of apical displacement
B Mean RR	1.000	**0.564**	**–0.548**	0.112	0.103	–0.361
C Mean Tx duration		1.000	–0.504	0.249	0.606	–0.205
D Mean distance of apical displacement			1.000	0.224	–0.053	0.605
E Weighted mean RR				1.000	**0.852**	**0.822**
F Weighted mean Tx duration					1.000	0.515
G Weighted mean distance of apical displacement						1.000

intrinsic to the patient carries important implications. These findings suggest that variation in outcome associated with EARR is largely beyond the practitioner's control. In contrast to this revolutionary finding, despite decades of work there is no conclusive evidence that implicates a definitive treatment-related factor for EARR. This paper attempts to quantitate statistical data from disparate findings to examine etiologic factors of EARR. It is tempting to suggest that the use of weighted data to reach a single estimate is more powerful than the individual findings in any of the original studies.

Etiologic factors of EARR

The observation that EARR is always preceded by hyalinization has prompted many to investigate the association between active treatment duration and subsequent root loss (19–21). Of all the treatment-related variables, treatment duration is most often correlated with apical root loss. Still, several recent publications report no association between treatment duration and EARR (20,21). There are several possible explanations for these disparate findings. Prolonged duration of treatment does not necessarily coincide with extended periods 'active' treatment. A patient that repeatedly misses appointments may be in treatment for a prolonged period despite limited periods of activation. Certain clinicians prefer lengthy periods between appointment intervals. This could increase the likelihood that a patient will experience diminished force levels between appointments.

Total apical displacement might represent a better marker for overall treatment activation. A tooth that is moved greater distances through bone, is subjected to longer durations of activation. There is no way to move a tooth between two points with fixed appliances, without causing hyalinization. Perhaps, this is why maxillary incisors are most likely to exhibit severe levels of EARR. The results of this study show that total apical displacement is highly correlated with mean apical root resorption ($r = 0.822$). There was a higher correlation between treatment duration and mean apical root resorption ($r = 0.852$). It should be noted that study no. 2 was conducted over a very short time span (mean of 4.6 months), and this may be the reason that the extent of root resorption was minimal. After all, the total active treatment time is ultimately more critical than the total apical displacement. If this study is eliminated, the correlation between apical displacement and mean apical root resorption becomes staggeringly more significant ($r = 0.97$).

The greatest challenge has been the measurement of total apical displacement. It makes sense to measure overall displacement of a tooth from the root apex, as this is where the pathology is occurring. Surprisingly, there is a paucity of studies that use the apex as a reference point to determine the overall distance a tooth has moved. A number of studies use angles such as SN to U1, or FH to U1 in order to determine overall apical displacement (22,23). This can result in inaccurate findings. For example, proclination of upright incisors might yield significant changes in angulation, with only slight displacement of the apex. In addition, bodily movement of incisors may produce no angular changes but significant apical displacement.

The most obvious reason clinicians do not measure overall displacement from the root apex is because it is difficult to pinpoint this landmark on the cephalometric X-ray film. Most studies report a mean apical displacement between 1.5 and 3 mm, and therefore, a 1-mm discrepancy in measurement can significantly alter the findings of a study. Also, as studies on EARR are retrospective in nature; authors do not have the luxury of re-taking the radiographs. Increased accuracy in the acquisition of radiographic images will resolve this dilemma in the future.

Conclusions

When the data were weighted, apical displacement and total treatment duration proved to be highly correlated with mean apical root resorption. Prior to this study the only conclusive evidence related to root resorption was patient-related factors. We now can suggest a specific treatment-related etiological factor of EARR: factors that are associated with the duration of active treatment might result in increased levels of apical root resorption in the pre-disposed individual.

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