Title	Long-term outcome of primary non-surgical root canal treatment
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Citation	Clinical Oral Investigations, 2012, v. 16 n. 6, p. 1607-1617
Issued Date	2012
URL	http://hdl.handle.net/10722/147135
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ORIGINAL ARTICLE

Long-term outcome of primary non-surgical root canal treatment

A. H. C. Lee · G. S. P. Cheung · M. C. M. Wong

Abstract

Aim The aim of this study is to examine the survival distributions of primary root canal treatment using interval-censored data and to assess the factors affecting the outcome of primary root canal treatment, in terms of periapical healing and tooth survival.

Materials and methods About one tenth of primary root canal treatment performed between January 1981 and December 1994 in a dental teaching hospital were systematically sampled for inclusion in this study. Information about the patients' personal particulars, medical history, pre-operative status, treatment details, and previous review status of the treated teeth, were obtained from dental records. Patients were recalled for examination clinically and radiographically. Treatment outcomes were categorized according to the status for periapical healing and tooth survival. The event time was interval-censored and subjected to survival analysis using the Weibull accelerated failure time model.

Results A total of 889 teeth were suitable for analysis. Survival curves of both outcome measures (periapical healing and tooth survival) declined in a non-linear fashion with time. Median survival of the treated teeth was 119 months (periapical healing) and 252 months (tooth survival). Age, tooth type, pre-operative periapical status, occlusion, type of final restoration, and condition of the tooth/restoration margin were significant factors affecting both periapical healing and tooth survival. Apical extent and homogeneity of root canal fillings had a significant impact towards periapical healing ($p < 0.05$), but not tooth survival.

Conclusion The longevity of treated teeth based on tooth survival was considerably greater than that of periapical healing. Both outcome measures were affected by a number of socio-demographic, pre-, intra-, and post-operative factors.

Clinical relevance Root canal-treated teeth may continue to function for a considerable period of time even though there may be radiographic periapical lesion present. Decision for extraction may be due to reasons other than a failure of the periapical tissues to heal.

Keywords Endodontic treatment · Survival analysis · Longevity · Periapical healing · Extraction · Tooth loss

Introduction

In endodontics, the outcome of root canal treatment is an important event of interests. From a clinician's perspective, outcome in terms of *periapical healing* or *post-treatment disease* is probably the most important as the periapical status of a treated tooth determines whether the ultimate goal of endodontic treatment has been achieved or not [1]. On the other hand, a relatively new measure, known as *tooth survival*, is considered to be more patient-centered [2], and is more consistent with and comparable to that used in outcome studies of other treatment modalities, such as the implant-supported restorations [3, 4]. Presumably, prognosis of root canal-treated teeth measured by these two different but somehow overlapping treatment outcomes might be influenced by different sets of factors.

Weiger et al. [5] and Cheung [6] have commented that simple calculation of a percentage value for the *healed* or *survival rate* does not accurately reflect the prognosis of the

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root canal-treated teeth. Indeed, it only reflects a snap-shot experience at a certain point in time and can be misleading because it does not reflect the change in healing or survival pattern over a longer observation period [7]. Although an "adjusted rate" has been reported in an attempt to factor the observation time into the calculation (to produce a certain percentage of failure occurrence per year) to provide, hopefully, a more realistic estimation of the prognosis, this assumption of a constant rate of deterioration of treatment effect with time still hardly reflects the truth [5]. In order to gain a more complete picture of the longevity of a treatment modality over time, survival analysis is considered more appropriate [7].

Survival analysis is a statistical method employed for analyzing the time to an event occurrence, to compute the cumulative survival probability up to a certain time point [8]. In dentistry, an "event" can only be known to have occurred when a diagnosis is made at a dental visit. It follows the occurrence time of that event, typically, is less than or equal to the time when it is first observed. Therefore, the actual time of event falls between two review visits, hence a so-called *interval-censored observation*. An observation is said to be *right-censored* when the event has not occurred, but is unknown whether it will occur in the future [8, 9].

Patients who are regularly reviewed at frequent intervals would be suitable for survival analysis using the Life-Table approach. This is not always practicable, especially when one would like to keep the amount of radiation to the patient as low as possible. An alternative approach, the Kaplan–Meier (K–M) product-limit estimator that calculates the survival probability of the subject (or treatment) as a function of time, is a widely used statistical method for survival analysis in dentistry. Survival studies using Kaplan–Meier approach have been reported for primary non-surgical root canal treatment [6, 10, 11] and for dental restorations. As the K–M analysis requires the entry of an exact event date into the data set to produce a statistically meaningful result, the date of the last recall was often needed [8]. Another approach is by taking linear time estimates between two dental visits as the date of event [6]. However, these practices might lead to bias, error, and misleading result [9].

Over the years, a variety of methods for *interval-censored* data have been developed [9, 12, 13]. Such methods take into account the uncertainty as to the exact time when the event occurs within two consecutive reviews for a reliable and valid result [13]. Therefore, the aim of the present study was to examine the long-term outcome of primary non-surgical root canal treatment performed in a dental teaching hospital, with the specific objectives to evaluate the survival distributions of treatment outcome in terms of *periapical healing* and *tooth survival* with *interval-censored* data, and to identify factors that might affect these outcomes.

Materials and methods

Sample

A total sample of 999 teeth in 950 patients was obtained from a stratified random sample of patients treated in a dental teaching hospital. Some interim results have been reported previously [6, 10]. Briefly, the sample population constituted about one tenth of all teeth that have been root canal treated between January 1981 and December 1994. The routine practice during that period included rubber dam isolation, manual preparation with stainless steel K-files using the Step-back or Step-down Technique, irrigation with a bland (sterile saline) or dilute (0.5%) hypochlorite solution, and obturation using cold lateral compaction of gutta-percha with AH26 (Dentsply DeTrey, Konstanz, Germany) as sealer. The treatment, typically, were completed in two or more visits.

Collection of data

A data collection form was used to collate information about the patients' personal particulars and medical history, as well as the pre-operative status, treatment details, and documented review status of the treated teeth. Information was extracted from the treatment records for the clinical and radiographic findings.

When a sampled tooth has been retreated or extracted, the date of such treatment was recorded. Such information was obtained from the patient's record, if the treatment had been provided within the hospital, or by asking the patient over the phone for the relevant details. Attempt was made to contact the dental practitioner who provided the (remedial) treatment for the necessary information after obtaining consent from the patient for information release. Those who received pre-planned endodontic surgery as part of the initial endodontic treatment plan were excluded.

Of all samples, 277 teeth had been recorded as either retreated or extracted. In addition, 32 teeth had shown clinical signs or symptoms (as was recorded in the patient record), indicating *post-treatment disease* and loss of *tooth survival* (according to the definition by Friedman and Mor [2]). These 309 teeth were deemed to have "failed". The remaining 653 patients (690 teeth) were invited to return for a review appointment.

All patients who attended the review were examined by one operator (AL) for the presence of any clinical signs or symptoms, including spontaneous pain, swelling, sinus tract, temperature sensitivity, increased mobility, and tenderness to palpation, percussion, or pressure. The integrity of the selected tooth and its restoration were examined for (recurrent) caries, fracture, and the presence of any marginal opening and occlusal interference. It was advised that ethics approval was not required because the clinical and radiographic procedures

constituted a routine check-up and did not expose the patients to any unnecessary or additional risk(s). Patients who required further treatment were scheduled to be seen in another appointment.

For those patients who were unwilling or did not attend the recall, as well as those who were unable to be contacted (collectively called "discontinuers"), but the sampled teeth had been reviewed on at least one occasion after the primary treatment, the clinical and radiographic status were evaluated based on that (the most recent) review. To reduce the problem associated with too many early *right-censored* data [7], any discontinuer with the last review appointment that fell within 4 years after treatment but showing no adverse clinical signs or symptoms was excluded.

Radiographic evaluation

Paralleling periapical radiographs were taken using either one of the two methods: (1) conventional radiography—a size 2 dental X-ray film (Insight; Eastman Kodak, Rochester, NY, USA) with the use of a positioning device (XCP holder; Rinn, Elgin, IL, USA), and then developed in an automated processing machine (Velopex Intra XE; Medivance Instruments, London, UK); or (2) digital radiography—an intraoral sensor (Visualix HDI; Gendex, Milan, Italy) with a positioning device (Endo Bite Senso, Kerr; Sybron Dental Specialties, Bioggio, Switzerland) to produce a paralleling image.

Film-based radiographs were evaluated over a light box aided by a 2× magnifying viewer (X-ray Viewer; Directa AB, Upplands Väsby, Sweden) that would exclude extraneous light. Digital radiographic images were evaluated on a computer screen in a room with dimmed ambient lighting. Contrast and brightness of the digital images were adjusted, if required, to aid visualization of image details. All radiographs were coded and then evaluated by one operator (AL), with one fifth of the samples re-evaluated by the same operator after 4 weeks to check for intra-examiner variability. Any uncertain cases were evaluated by a second examiner independently; the examiners were calibrated beforehand. Then, any disagreement on the findings was discussed between the two examiners. If an agreement could not be reached, a third examiner was recruited to resolve the disagreement. Any disagreement cases that remained so were excluded from the study [14]. Radiographs were evaluated for the periapical status (see below), quality of the root canal filling (i.e., apical extent, presence of voids, profile in relation to original canal curvature), radiographic apical seal (apical to the post, if applicable), and presence of recurrent caries.

Periapical status

Given that all treatments had been provided for more than 4 years before this radiographic examination, the periapical status of the selected teeth was categorized, in accordance to the strict criteria [15], dichotomously into (1) *healed*—no periapical rarefaction, except widening of periodontal ligament space around an overextended filling, or (2) presence of periapical rarefaction.

The size of the periapical lesion, if present, was measured in two dimensions: vertical or length-wise (L), and transverse or width (W). The length-wise dimension (L) was measured as the diameter of the radiolucent area along an imaginary axis that was an extension of the apical (curved) portion of the root. The transverse dimension (W) was measured in a similar manner but along another imaginary axis drawn perpendicular to the length-wise diameter. In the presence of more than one focal area of rarefaction (as might be found with multi-rooted teeth), the largest radiolucent area was selected for measurement. Comparison of the size of radiolucent lesion would form the basis to determine if progressive disease was present for teeth with a pre-operative periapical radiolucency.

Outcome measures

When there was an absence of clinical signs, symptoms, or periapical radiolucency, the tooth was deemed to have achieved complete *periapical healing*. Teeth that had been extracted, retreated (surgically or non-surgically), or associated with any clinical signs, symptoms or periapical radiolucency were categorized as *post-treatment disease*.

Another outcome measure examined in this study was *functional retention* [2]; some refer to it as *tooth survival* [3, 16]. It was defined as the continuous function of the tooth in the mouth with absence of clinical symptoms, but regardless of their radiographic periapical status.

The recorded reasons for the failures (due to either *post-treatment disease* or loss of *tooth survival*) were noted. To eliminate any possible systemic influence or clustering, due to the inclusion of multiple teeth from one patient, a single-level modeling was used in this study. That is, only one tooth was randomly selected from each patient for entry into the statistical analysis if multiple teeth had previously been included in the initial sample.

Statistical analysis

The events of interest included the onset of *post-treatment disease* and the loss of *tooth survival*. For the latter, diagnosis might be easier, as the patient would be more likely to make a complaint when clinical symptoms have developed. On the other hand, *post-treatment disease* usually develops over time and may not be observed until a diagnosis is made on the basis of clinical and radiographic findings at a recall, or until acute symptoms or catastrophes such as tooth fracture set in [6, 10]. The actual date of event (onset of *post-treatment disease*) would lie between the last known date

when such condition was not observed (denoted as *Dnodisease*), and the date when it was first diagnosed (denoted as *Ddisease*). That is, the onset of *post-treatment disease* was *interval-censored* (Fig. 1). The same applied to the time measurement for *tooth survival*, which lied between the last known date that the tooth was still surviving (denoted as *Dsurvival*) and the date when the tooth was not (denoted as *Dnosurvival*) (Fig. 1). Note that *Ddisease* did not necessarily coincide with *Dnosurvival*, especially for asymptomatic teeth.

In this context, a review appointment served to update the status of the treated teeth, confirming *Ddisease* or *Dnosurvival*, if such event was noted, or resetting the period (*Dnodisease* or *Dsurvival*) up to this new date of examination. In the present analysis, date of obturation (*D0* in Fig. 1) was used as the origin of time measurement.

The survival probability of the treated teeth was computed for the two outcome measures, using the Weibull accelerated failure time (WAFT) model for *interval-censored* data [12]. One limitation of this model was that it could not analyze the data for an event (*post-treatment disease* or loss of *tooth survival*) observed at the first review, i.e., samples with data available only for *Ddisease* or *Dnosurvival*, but no information for *Dnodisease* or *Dsurvival* [17]. An assumption had to be made for these cases ($n=172$ and 73 for *post-treatment disease* and loss of *tooth survival*, respectively). From a clinician's point of view, it is reasonable to assume that the root canal-treated teeth would function for at least 2 weeks (being the typical time required for construction of the final restoration, especially for the sample population concerned in this study) before any problems may develop. Thus, the date of last review, *Dnodisease* or *Dsurvival*, was set to 2 weeks for those without any data for the first review.

Twenty-one factors, categorized as socio-demographic, pre-operative, intra-operative, or post-operative (Table 1), were examined statistically using the WAFT model individually at first. To examine any confounding or interdependence of factors, those factors with $p <0.2$ when tested individually (see p values in Table 1) were re-entered into the overall analysis, until they were eliminated in a

Fig. 1 Schematic diagrams illustrating the survival time of a tooth from date of obturation (*D0*) leading up to (*a*) the development of *post-treatment disease* and (*b*) loss of *tooth survival*. Note that the actual date of *post-treatment disease* and loss of *tooth survival* should lie between (*a*) *Dnodisease–Ddisease* and (*b*) *Dsurvival–Dnosurvival*

backward stepwise method. Those factors that remained ($p<0.05$) after the stepwise analysis formed the basis for calculating the hazard ratio (that is, the relative risk of developing an adverse reaction, compared with the reference group that was assigned a value of 1) and the 95% confidence intervals. All analysis was performed using PROC LIFEREG in the software SAS/STAT 9.2 (SAS Institute Inc. 2008, Cary, NC, USA).

Results

Of the 999 teeth in 950 patients, 110 teeth in 59 patients were excluded from this study due to various reasons (Table 2). The final sample for analysis involved 889 teeth from 889 patients.

The survival curves of both outcome measures declined in a non-linear fashion, consistently showing an initial rapid drop up to about 40 months which then slowed down with longer observation time (Fig. 2). The cumulative survival computed for *periapical healing* and *tooth survival* after 25 years was 0.29 and 0.46, respectively (Fig. 2). That is, complete periapical healing was expected in 29% of root canal-treated teeth, and that 46% of all treated teeth would still be present in the mouth some 25 years after treatment. The median time for the onset of *post-treatment disease* was about 119 months, and for loss of *tooth survival* was approximately 252 months.

Reasons for failure

The reasons for failure due to either *post-treatment disease* or loss of *tooth survival* for short- (<40 months) versus long-term (≥40 months) observations are summarized in Table 3. Presence of persistent or progressive apical periodontitis was the most prevalent reason of adverse outcomes. At the end of the study, 26.5% of teeth ($n=236$) were recorded as extracted with known reasons. Of these, almost one third ($n=74$) were carried out within the first 40 months after primary treatment. Nearly half of all the extraction ($n=116$) was due to fracture of the crown or root.

Factors affecting outcome

Of the 21 factors examined, 19 were included for further analysis as they were found to have $p <0.2$ with either one or both of the outcome measures when tested individually (Table 1); only "pre-operative (clinical) signs or symptoms" and "acute flare-up during treatment" were eliminated. After backward stepwise examination, nine factors were found to be significant in their effect on either *post-treatment disease* or *tooth survival* in the final model (Table 4).

Factors that showed a positive favorable influence (i.e., hazard ratio less than 1; see Table 4) on *periapical healing*
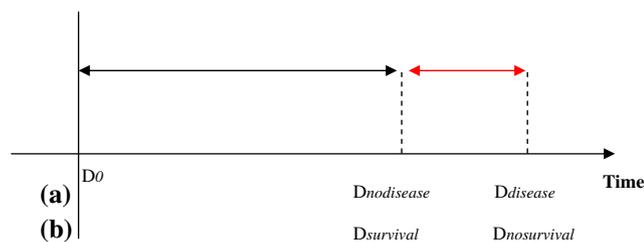
Table 1 Factors examined in this study ($N=889$)

Category	Covariables	Subgroups	N (%)	p value from individual test on covariable	
				Healing outcome	Tooth survival
Socio-economic	Age	Below 25 years	247 (27.8)	<0.001	<0.001
		25–50 years	444 (50.0)		
		Above 50 years	198 (22.2)		
	Gender	Male	358 (40.3)	0.003	0.032
		Female	531 (59.7)		
Pre-operative	General health ($N=863$; missing 26)	Healthy	580 (67.2)	0.428	0.027
		Not healthy	283 (32.8)		
	Tooth location	Maxilla	512 (57.6)	0.026	0.089
		Mandible	377 (42.4)		
	Tooth type	Anteriors	336 (37.8)	<0.001	0.005
		Premolars	268 (30.1)		
		Molars	285 (32.1)		
	Pre-operative signs or symptoms	Absent	401 (45.1)	0.248	0.653
		Present	488 (54.9)		
	Pre-operative pulpal status	Non-vital	548 (65.6)	0.010	0.026
		Vital	288 (34.4)		
	Pre-operative periapical status	No radiolucency	516 (58.0)	<0.001	0.002
		≤5 mm	266 (29.9)		
		>5 mm	107 (12.1)		
Intra-operative	Operator status	Undergraduate students	629 (70.8)	0.029	0.054
		Qualified dentists	260 (29.2)		
	Number of visits ($N=888$; missing 1)	1 visit	27 (3.0)	<0.001	<0.001
		2 visits	301 (33.9)		
		3 visits	301 (33.9)		
		≥4 visits	259 (29.2)		
	Acute flare-up during treatment ($N=846$; missing 43)	Absent	792 (93.6)	0.892	0.490
		Present	54 (6.4)		
	Extent of root filling ($N=870$; missing 19)	Flush (0–2 mm)	675 (77.6)	<0.001	<0.001
		Short (>2 mm)	107 (12.3)		
		Overextension	88 (10.1)		
	Extrusion of root filling; including sealer ($N=855$; missing 34)	Absent	721 (84.3)	<0.001	0.006
		Present	134 (15.7)		
	Homogeneity of root filling ($N=883$; missing 1)	No apparent voids	432 (48.9)	<0.001	0.009
		Voids in apical third	252 (28.5)		
		Voids in middle or coronal third	199 (22.6)		
	Root filling profile ($N=882$; missing 7)	Follow original canal form	721 (81.7)	<0.001	0.101
		Sign(s) of ledging, transportation, deviation, broken instrument, or perforation	161 (18.3)		
Post-operative	Function ($N=875$; missing 14)	Presence of both proximal contacts	576 (65.8)	0.003	<0.001
		Presence of ≤1 proximal contact	128 (14.6)		
		Cantilever/fixed-fixed/fixed-movable bridge abutment	68 (7.8)		
		Denture/overdenture abutment	103 (11.8)		
	Occlusion ($N=860$; missing 29)	No opposing teeth, or opposing denture	76 (8.9)	0.112	0.017
		Opposing natural teeth	733 (85.2)		

Table 1 (continued)

Category	Covariables	Subgroups	N (%)	p value from individual test on covariable	
				Healing outcome	Tooth survival
		Opposing fixed prosthesis	51 (5.9)		
	Post (N=885; missing 4)	Absent	342 (38.6)	<0.001	<0.001
		Present	543 (61.4)		
	Type of final restoration (N=831; missing 58)	Amalgam	189 (22.7)	<0.001	<0.001
		Composite resin or GIC	151 (18.2)		
		Indirect cuspal coverage restoration	476 (57.3)		
		Others	15 (1.8)		
	Time to the placement of final restoration (N=700; missing 189)	≤2 months	270 (38.6)	0.002	<0.001
		>2–10 months	284 (40.6)		
		>10 months	146 (20.8)		
	Condition of tooth/restoration margin	Satisfactory	679 (76.4)	<0.001	<0.001
		Unsatisfactory	210 (23.6)		

Missing values referred to those cases where the relevant information could not be identified in the patient records. *Unhealthy* included any known systemic diseases, immunosuppressive medication, or history of radiotherapy in the head and neck regions. *Unsatisfactory* tooth/restoration margin included the presence of recurrent caries, fracture, and/or marginal opening

included patient's age (50 years old or younger; $p<0.001$), anterior teeth and premolars ($p=0.007$), absence of pre-operative periapical lesion ($p<0.001$), tooth without any opposing or with opposing denture teeth ($p=0.028$), root canal filling that appeared "flush" (0–2 mm) with the radiographic apex ($p=0.041$), homogenously filled root with no radiographic void ($p=0.008$), and those restored with a cuspal coverage restoration ($p<0.001$) and with satisfactory tooth/restoration margin ($p<0.001$).

A slightly different set of factors were found to affect *tooth survival*. Patient aged 50 years old or younger ($p<0.001$), premolars ($p<0.001$), absence of pre-operative periapical lesion ($p=0.003$), tooth opposing a fixed prosthesis ($p=0.004$), treatment completed in two visits (compared with that completed in four or more visits; $p=0.036$), and tooth with a cuspal coverage restoration ($p<0.001$) and with satisfactory tooth/restoration margin ($p<0.001$) were found to enjoy a greater longevity, with significantly lower hazard

Table 2 Number of cases and reasons for exclusion from statistical analysis

Reasons for exclusion	No. of teeth	Remarks
Mismatch of information with patients' records	7	Entry errors in the original patient records
Periapical surgery pre-planned as part of root canal treatment	6	
Patient never returned for any review	9	
Retreatment cases, instead of primary root canal treatment	4	Entry errors
Right censoring <4 years	31	Last available review date <4 years without any observation of *post-treatment disease* or loss of *tooth survival*; and patient never returned again
Multiple teeth treated for a patient	49	Only one tooth, randomly selected, was included for each patient
Incomplete review information, including *uncertain healing*	2	
Teeth survived for less than 2 weeks after root canal treatment	2	Observation of *post-treatment disease* or loss of *tooth survival* within 2 weeks
Total number of teeth excluded (initial sample=999)	110	A total of 889 teeth were suitable for analysis

Fig. 2 Weibull survival curves for *periapical healing* and *tooth survival* outcome
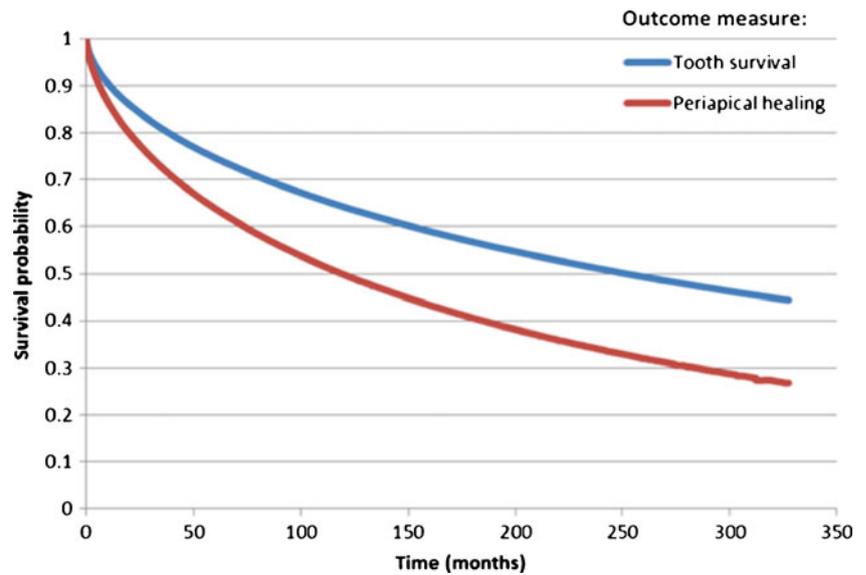
ratios compared to their respective reference subgroups (Table 4).

Discussion

Methodology

This study has the inherent limitations of any cohort clinical study. That is, the number of dropouts tends to increase with an extended observation period. A high dropout rate would jeopardize the precision of survival estimates from the analysis [18]. Fortunately, the present WAFT model takes into account not only those complete (*interval-censored*) but also incomplete (*right-censored*) observations, which should improve the reliability of the survival estimates. Information was extracted from the clinical documentation for the patients over the years. In the case when some entries were unavailable (e.g., due to patient not returning to the hospital for further treatment or review), retrospective information provided by the patient over the phone would become the only source of data. Such self-reported data could be subjected to prevarication, especially for the date of such events as retreatment, extraction, or incidence of pain.

Another limitation of the present study is related to the use of radiographs, as they only represented a two-dimensional image of the three-dimensional structures of the jaw [19]. It is commonly accepted that lesions limited to the cancellous bone are almost impossible to detect with conventional radiographic technique [20], although other studies showed the opposite [21, 22]. Cone-beam computerized tomography is a relatively new technique that produces a three-dimensional image of the bony structures and might be a useful tool to detect periapical lesions and for assessing endodontic healing outcome in the future [23].

Table 3 Summary of reasons for failure due to either *post-treatment disease* or loss of *tooth survival* for short- (<40 months) vs. long-term (≥40 months) observations

Outcome measure	Reasons	≤40 months	≥40 months	Total (% of total 889 cases)
Post-treatment disease (clinical plus radiographic)	Periapical periodontitis	180	466	646 (72.2)
	Emerging	38	98	136 (15.3)
	Persistent or progressive	142	368	510 (57.4)
Loss of tooth survival	Clinical signs and symptoms	85	170	255 (28.7)
	Extraction	74	162	236[a] (26.5)
	Failed RCT	19	19	38 (4.3)
	Fractures—root	26	54	80 (9.0)
	Fractures—crown	9	27	36 (4.0)
	Periodontal reasons	10	19	29 (3.3)
	Others	10	43	53 (6.0)

[a] Total number of teeth extracted was actually 255 (same as those that developed signs and symptoms). Of these, the date or reason for extraction was unavailable for 19 teeth; thus, only 236 extracted teeth were listed here

Table 4 Factors found to be significant ($p<0.05$) after backward stepwise analysis using the Weibull accelerated failure time model for periapical healing and tooth survival outcome

Factors	Periapical healing		Tooth survival	
	Hazard ratio[a] (95% CI)	p value	Hazard ratio[a] (95% CI)	p value
Age		<0.001		<0.001
<25 years	0.48 (0.36, 0.64)		0.39 (0.27, 0.55)	
25–50 years	0.64 (0.50, 0.82)		0.60 (0.45, 0.79)	
>50 years	1		1	
Tooth type		0.007		<0.001
Anteriors	0.71 (0.53, 0.95)		0.72 (0.52, 1.00)	
Premolars	0.66 (0.50, 0.86)		0.52 (0.38, 0.71)	
Molars	1		1	
Pre-operative periapical status		<0.001		0.003
No lesion	0.60 (0.44, 0.80)		0.63 (0.44, 0.89)	
≤5 mm	0.84 (0.61, 1.14)		0.92 (0.64, 1.33)	
>5 mm	1		1	
Occlusion		0.028		0.004
Non-opposing/opposing denture	1		1.66 (0.82, 3.33)	
Opposing (natural teeth)	1.61 (1.12, 2.32)		2.45 (1.35, 4.46)	
Opposing (fixed prosthesis)	1.30 (0.77, 2.19)		1	
Extent of root filling		0.041	Not significant	NS
Flush	0.68 (0.49, 0.93)			
Short	0.84 (0.57, 1.23)			
Overextended	1			
Homogeneity of root filling		0.008	Not significant	NS
No voids, apparently Homogenous	0.76 (0.59, 0.98)			
Voids in apical third	1.08 (0.83, 1.41)			
Voids in middle/coronal third	1			
Number of visits	Not significant	NS		0.036
1			0.63 (0.29, 1.39)	
2			0.64 (0.47, 0.88)	
3			0.86 (0.65, 1.14)	
4 or more			1	
Type of final restoration		<0.001		<0.001
Amalgam	1		1	
Composite/GIC	0.69 (0.49, 0.97)		0.70 (0.47,, 1.03)	
Indirect cuspal coverage Restoration	0.51 (0.40, 0.65)		0.41 (0.31, 0.55)	
Others	1.73 (0.85, 3.52)		1.36 (0.65, 2.84)	
Condition of the tooth/restoration margin		<0.001		<0.001
Satisfactory	0.63 (0.51, 0.79)		0.47 (0.36, 0.60)	
Unsatisfactory	1		1	

[a] Hazard ratio is the relative risk of having adverse reaction when compared with the reference group (which was assigned an value of 1). A hazard ratio greater than 1 indicates a higher risk of developing an adverse outcome (i.e., failure to achieve periapical healing, or loss of tooth survival) relative to the reference group

With the use of the WAFT model for *interval-censored* data [12, 13], one could expect to get a reliable and valid result. The problem of early *right-censored* data (i.e., last review being made shortly after the treatment with no adverse outcome but then patient never returned again), which tends to introduce more errors in survival analysis [7], was

mostly eliminated in this study because those *right-censored* observations with less than 4 years of review were excluded. This is in line with the recommendation that root canal treatment (with uncertain outcome) should be reviewed for 4 years before a definite decision of failure (to heal) is made [1]. Inevitably, this would also exclude some cases that might have exhibited signs of favorable *periapical healing* before that period but were not reviewed further. Thus, there was a possibility of underestimating the survival outcomes for the first 4 years of observation. Fortunately, only a small number of samples (*n*=31 or 3.1% of total sample) were excluded from the initial sample due to such early *right-censoring* (Table 2). On the other hand, it was not uncommon to find cases that were condemned as "failed" and retreated (surgical or non-surgically) within the first 4 years after treatment, often without obvious symptoms or signs of disease progression documented. This might truly have resulted in the "unfair" inclusion of the failure cases for both outcome measures especially in the early post-treatment periods.

In an epidemiologic survey of (the insurance records of) over 1.4 million teeth, Salehrabi and Rotstein [24] reported that 97% of teeth *survived* some 8 years after primary non-surgical root canal treatment. Similar studies by Lazarski et al. [25] and Chen et al. [26] also reported high *survival* rates of 94% (3.5 years of observation) and 93% (5 years), respectively. However, these studies were done on dental insurance records of patients without reference to the clinical conditions of the tooth, especially for the presence of any symptoms on the date of study. Our results suggested a somewhat lower *tooth survival* rate at those corresponding periods of observation (Fig. 2). The difference may be due to a number of reasons: (1) criteria for failure—our study here also included clinical signs or symptoms as an unfavorable outcome for *tooth survival*; (2) sample selection—patients in the above epidemiologic studies were recruited from population enrolled in dental insurance plans, who might possess a different attitude and awareness towards dental health and tooth retention from the sample (mostly walk-in patients on a need basis) in the present study; and (3) treatment providers—treatment for patients in the epidemiologic studies were provided by either qualified dentists or endodontists, as opposed to that by undergraduate students in the majority of cases here.

Factors affecting the outcome of primary root canal treatment

While many studies failed to find any association between *patient age* and *periapical healing* after primary root canal treatment [27–29], we found that patients above 50 years of age seemed to have a significantly higher chance of developing *post-treatment disease*. Presumably, the healing process in older patients is slower and not as effective due to physiological aging process [30]. The increased incidence of secondary or tertiary dentine deposition, pulp stones, and internal/dystrophic calcification with age could result in canal obliteration, posing a challenge to optimal root canal preparation with a negative effect on healing outcome. The finding of a lower chance of *tooth survival* for older individuals corroborated with that of other studies [31, 32].

Some systematic reviews have concluded that while *tooth type* does not affect the *periapical healing* after primary root canal treatment [33], molar teeth were associated with a lower chance of *survival* [4]. Our results, indeed, showed that molars were associated with the greatest risk (or highest hazard ratio) of developing *post-treatment disease* and fared the shortest *tooth survival* time. This may be attributable to the complex anatomy of molars, accessibility and technical difficulties in treating them, as well as to heavy occlusal stresses acting on these teeth [34]. It should be mentioned that the unit of measurement was the tooth, not root, in the present study. The status of a multi-rooted tooth was represented by the worst-appearing root and, thus, molars would have multiple chances for *post-treatment disease*, compared with single-rooted teeth. Another situation may exist; for instance, the root with a grossly overextended root filling might not be the root associated with the largest periapical rarefaction. In other words, confounding of the true effect of a factor may exist for *post-treatment disease* for multi-rooted teeth.

A periapical lesion tends to develop more or less concentrically around the root apex with the apical foramen acting as the "source" of irritation that is situated in the center of the (radiographic) lesion. Some authors refer the apical foramen as the "portal of exit" for irritants to escape into the apical periodontium [35, 36]. Although an attempt was made to quantify the size of radiographic lesions, in this study, the vertical (length-wise) dimension was not considered as it may be constrained by anatomic borders, such as the maxillary sinus or mandibular canal. The vertical angulation of the X-ray beam is also more likely to vary, compared with the horizontal angulation, when a film-holder is in use. Teeth with a pre-operative lesion especially those with a transverse diameter greater than 5 mm had the highest odd to fail (i.e., high hazard ratio) in either outcome measure. The result was consistent with that of studies carried out in other countries [11, 16, 37]. This reflects the difficulties in effective disinfection of the root canal system of teeth with an established infection [36]. No significant difference was found between lesions of size greater or smaller than 5 mm in diameter. As healing is a function of time, an outcome similar to smaller-sized lesions should be applicable to larger-sized lesions, if sufficient time was allowed for healing to take place [37].

This study reiterated the importance of homogenous root canal fillings (absence of apparent voids) [16] and the

extension within 2 mm of the radiographic apex (or "flush") for optimal *periapical healing* [10, 11, 16, 37]. Both results were confirmed by a recent systematic review [33]. However, these two factors did not seem to affect *tooth survival*. Although root fillings of insufficient quality in terms of length and seal should increase the risk of tooth loss due to the development of apical periodontitis, neither the quality of root filling nor the presence of apical periodontitis is easily noticeable by the patient [38]. In the absence of clinical symptoms, the treatment need may not be translated into demand.

Root canal-treated teeth opposing the natural tooth/teeth were consistently found to be associated with a significantly lower survival rate for both outcome measures, when compared to those opposing a denture, fixed prosthesis, or without any opposing dentition. It might be related to the damaging effects of premature contacts or occlusal stresses during function. This might translate into an increased risk of tooth fracture, leading to a need for tooth extraction. It has been suggested that occlusal trauma was associated with increased chance of unfavorable *periapical healing* [39].

The presence of cuspal coverage restorations was associated with an increased chance of *periapical healing* and of *tooth survival*, a finding supported by numerous other studies [10, 11, 24, 34, 40–42] as well as systematic reviews [4, 43]. The importance of cuspal protection for root canal-treated teeth to prevent cuspal flexure cannot be overemphasized. Without such protection, the (micro-)flexure may lead to breakdown of the marginal seal of simple intracoronal restoration and result in (coronal-to-apical) microleakage which hampers *periapical healing* [44]. Tooth fracture is also prevented, especially for molars which were the tooth type associated with the least favorable outcomes in this study. Aquilino and Caplan [34] have reported that root canal-treated teeth without a crown suffered six times greater rate of tooth loss than those with one.

Exposure of the root canal filling to saliva and bacteria is a serious challenge to the seal provided by the obturation material [45, 46]. A good-quality coronal restoration is important to ensure long-term success of root canal treatment [47, 48]. Indeed, the result of this study indicated that teeth presented with unsatisfactory tooth/restoration margin (due to marginal defects, fractures, or recurrent caries) would suffer from a less favorable outcome than those with satisfactory margins.

The number of visits to complete the treatment did not affect the *periapical healing*, but a lower number was associated with more favorable *tooth survival* compared to those completed in four or more visits. Protracted treatment may be a reflection of increased technical difficulties or problems in treatment, hence reducing the chance for survival or healing. Apical periodontitis would resolve upon thorough disinfection and elimination of microorganisms from the infected root canal system [49], regardless of the number of treatment visits.

Conclusions

For both *periapical healing* and *tooth survival* after primary root canal treatment, the survival curves declined in a non-linear pattern, showing a steep drop up to about 40 months which then slowed down over longer observation periods. The median time of *tooth survival* (approximately 252 months) was considerably greater than those without *post-treatment disease* (approximately 119 months). Persistence or progression of periapical periodontitis was the most prevalent reason for adverse treatment outcomes. Age, tooth type, pre-operative periapical status, occlusion, type of final restoration, and the quality of tooth/restoration margin significantly affected the long-term *periapical healing* and *tooth survival*. The apical extent and homogeneity of the root canal fillings only contributed significantly towards *periapical healing*, but did not seem to affect *survival* of the treated teeth.

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