Treatment Outcome in Endodontics: The Toronto Study—Phase 4: Initial Treatment

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Abstract

Outcome 4–6 years after initial treatment was assessed for Phase 4 (2000–2001) of the Toronto Study. Of 582 teeth treated, 430 were lost to follow-up (99 discontinuers, 331 dropouts), 15 were extracted, and 137 (32% recall minus 15 extracted teeth) were examined for outcome: healed (no apical periodontitis, signs, symptoms) or diseased. When pooled with Phases 1–3, 439 of 510 teeth (86%) were healed. Logistic regression identified 2 significant ($P \leq .05$) preoperative outcome predictors: radiolucency (odds ratio [OR], 2.86; confidence interval [CI], 1.56–5.24; healed: absent, 93%; present, 82%) and number of roots (OR, 2.53; CI, 1.25–5.13; healed: single, 93%; multiple, 84%). In teeth with radiolucency, intraoperative complications (OR, 2.27; CI, 1.05–4.89; healed: absent, 84%; present, 69%) and root-filling technique (OR, 1.89; CI, 1.01–3.53; healed: lateral, 77%; vertical, 87%) were additional outcome predictors. A better outcome was suggested for teeth without radiolucency, with single roots, and without mid-treatment complications. The predictive value of root-filling technique in teeth with radiolucency requires validation from randomized controlled trials. *(J Endod 2008;34:258–263)*

Key Words

Apical periodontitis, endodontic treatment, prognosis, prospective study, root canal therapy, treatment outcome

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The general objective of endodontic initial (first-time) treatment is to retain the treated tooth in normal function, and the specific goal is to prevent or heal apical periodontitis (1). Because other treatment modalities are available to replace the affected tooth and restore function, patients frequently have to select among the available modalities by weighing the risks and benefits associated with each treatment alternative (2). The main benefit considered in making the selection is the desired outcome—healing and functional retention of the treated tooth. The potential outcome taken into account should be supported by sound evidence from current clinical studies. Several reviews (3–5) of the many studies reported over the years on the outcome of endodontic initial treatment have identified 20 studies (6–25) as providing better evidence than others, and an additional randomized clinical trial was published recently (26). The treatment techniques used in several of these selected studies (6–10) are not consistent with the current ones (3, 4), reducing the evidence base for current initial treatment to 15 studies (12–26). Three of these current studies (19, 22, 25) have reported on the first 3 phases of the Toronto Study project.

The Toronto Study Project was established in 1993 with the intention to augment the evidence supporting endodontic treatment by prospectively investigating the 4- to 6-year outcome of treatment provided by endodontic residents. The modular design included recall of treated subjects in 2-year phases and pooling of successive samples to improve the power of statistical analysis and the resulting ability to identify significant predictors of outcome. In the successive reports on initial treatment in Phases 1 (19), 2 (22), and 3 (25), the number of predictors of persistent apical periodontitis identified by multivariate analysis increased with each added phase from 1 to 3. Preoperative apical periodontitis was identified as an outcome predictor in all 3 phases (19, 22, 25), as in the majority of previous studies (6, 7, 13, 18, 21, 23, 24). More than 1 root in the treated tooth was identified in the latter 2 phases (22, 25), and occurrence of a mid-treatment complication was identified in the most recent phase (25).

The pattern demonstrated in the previous phases suggested that addition of the next phase of the Toronto Study might identify additional outcome predictors. Thus, the purpose of this study was twofold: (1) to systematically assess the 4- to 6-year outcome of endodontic initial treatment in Phase 4 of the Toronto Study and (2) to examine outcome predictors in the samples of Phases 1–4.

Materials and Methods

Study Cohort

The potential study population comprised all patients referred to the Graduate Endodontic Clinic at the University of Toronto for initial treatment during the period from January 2000–December 2001. All the patients were informed about the indications for endodontic treatment, the benefits and risks associated with treatment, and the alternative of extraction and replacement. Individual subjects were included in the study if they selected endodontic treatment and signed an informed consent form. The study protocol and the informed consent forms were approved by the University of Toronto Health Sciences Research Ethics Board. The inception cohort consisted of 582 teeth in 511 patients subjected to initial treatment.

Intervention

The protocol adhered to in this study was established before the recruitment of subjects and has been described previously (19, 22, 25). Graduate endodontics students performed the treatments under supervision by qualified endodontists. Teeth requiring apexification were excluded. All treatments were performed with the aid of dental operating microscopes (Global Surgical Corporation, St Louis, MO). All preoperative and intraoperative data were coded and recorded in real-time by each treatment provider and subsequently entered into the Toronto Study database.

Teeth were anesthetized, caries were removed, and the coronal structure was reconstructed as required for proper isolation. After isolation, teeth were surface-disinfected and accessed following conventional procedures. Cleaning and shaping were performed in a crown-down or modified step-back manner, with hand files and engine-driven nickel titanium instruments of different designs. Canals were irrigated with 2.5% NaOCl and, on occasion, also with 2% chlorhexidine. Smear layer was removed with 17% ethylenediaminetetraacetic acid (Smear Clear; SybronEndo Corporation, Orange, CA). Canals of teeth treated in more than 1 session were medicated with a calcium hydroxide slurry (Pulpdent; Pulpdent Corporation, Watertown, MA), applied with a lentulo spiral (Dentsply Maillefer, Ballaigues, Switzerland). Root fillings were performed with gutta-percha and a variety of sealers. Different root-filling techniques were performed in various treatment sessions during the week according to a predetermined schedule, and subjects selected treatment sessions according to their convenience. Lateral compaction (LC) was carried out with finger spreaders (Dentsply Tulsa Dental, Tulsa, OK). Vertical compaction of warm gutta-percha (VC) was carried out with heat generators (Touch 'n Heat or System-B; SybronEndo Corporation) for down-packing and an injectable gutta-percha device (Obtura II; Obtura Spartan, Fenton, MO) for back-filling. In a few teeth, a single gutta-percha cone was used with a glass ionomer cement sealer (Ketac-Endo; 3M ESPE, St Paul, MN), or injectable gutta-percha was used from the apex coronally. Any perforations that occurred were sealed with mineral trioxide aggregate (MTA) (Dentsply Tulsa Dental). Access cavities were temporized, and subjects were referred back to their dentists or undergraduate students for definitive restoration.

Preoperative, intraoperative, and postoperative radiographs were exposed with the aid of Rinn XCP film holders (Dentsply Rinn, Elgin, IL). They were appended to the data sheets that were kept on file for each subject.

Outcome Assessment

Subjects were recalled 4–6 years after treatment. They were contacted by letter and telephone, encouraged to attend a follow-up examination, and offered compensation for time lost and travel expenses. Attempts were made to locate and contact subjects whose letters were returned. If the subject reported the tooth had been extracted, the subject's chart at the Faculty of Dentistry was examined to establish the reason for extraction, or for externally referred subjects, the subject was questioned about the reason for extraction.

Follow-up examinations were performed by one examiner (C. de C.) who was blinded to the preoperative data. Symptoms and clinical signs were recorded, and radiographs were exposed to assign a Periapical Index (PAI) score (27). The examiner was calibrated for the use of PAI with the standard calibration kit, and the reproducibility of scores was assessed by using Cohen kappa statistics (28) in 2 calibration sessions 1 month apart.

Teeth were classified as either healed (PAI $\leq$2, no symptoms or clinical signs other than tenderness to percussion) or diseased (PAI $\geq$3, presence of symptoms or clinical signs other than tenderness to percussion). The evaluated unit was the whole tooth, with multi-rooted teeth assigned the highest score of all roots. Teeth were recorded as functional when absence of any signs or symptoms was noted independently of the PAI score.

Analysis

Statistical analysis was performed on the Phase 4 sample, as well as on the pooled samples from all 4 Phases. It included univariate description to characterize the study material, bivariate analysis of outcome associations with preoperative, intraoperative, and postoperative variables (χ^2 or Fisher exact test) to identify potential outcome predictors and multivariate analysis (logistic regression models) to identify significant outcome predictors. The complete dataset was analyzed first, followed by stratified analysis of the subsamples of teeth without and with preoperative radiolucency. All tests were performed as two-tailed with the SPSS 15.0 software (SPSS Inc, Chicago, IL) and interpreted at the 5% significance level. A total of 17 variables were investigated (Table 1).

Results

The intraexaminer reliability scores established with Cohen kappa statistics for both calibration sessions were 0.84, indicating very good agreement (28). The interobserver reliability scores between the Phase 4 examiner (C. de C.) and the examiners of Phases 1 (S.A.), 2 (M.F.), and 3 (V.M.) ranged from 0.63–0.78, indicating good agreement (28).

Phase 4

The inception cohort of 582 teeth in 511 subjects was considerably eroded during the time period of the study. Ninety-nine teeth from subjects who could not be contacted and one deceased subject (discontinuers) were excluded from the study, because their absence was not related to the treatment provided or the outcome of interest. An additional 331 teeth could not be examined because the subjects either declined the recall or did not respond (dropouts). The responding population included 152 teeth (32% recall), of which 15 teeth were extracted for restorative (12 teeth), periodontal (2 teeth), or unknown (1 tooth) considerations. The remaining 137 teeth were examined for outcome (study sample). The inception cohort and study sample are compared in Table 1. Characteristics of the lost-to-follow-up population and the study sample were compared to identify possible response bias. The analysis (not shown) revealed that the study sample was significantly older (mean age, 52 vs 44 years) and had a significantly lower proportion of teeth root-filled with VC (71% vs 81%), compared with the lost-to-follow-up population including dropouts and discontinuers.

At the end point of the Phase 4 study, 121 of 137 teeth (88%) were classified as healed and 16 of 137 teeth (12%) as diseased. Among the latter, 5 teeth had larger lesions than before treatment (or new lesions), 7 had unchanged lesions, 2 had smaller lesions, and 2 had no lesions (PAI $\leq$2). Of the entire study sample of 137 teeth, symptoms or any clinical signs were found in only 8 teeth; 6 of 121 teeth classified as healed presented with slight tenderness to percussion, whereas 2 of 16 teeth classified as diseased presented with pain. Thus, a total of 129 of 137 teeth (94%) were fully functional, being free of any clinical signs or symptoms.

Pooled Phases 1–4

The characteristics of the samples of Phases 1, 2, and 3 were reported previously (19, 22, 25). The pooled inception cohort included 1952 teeth, of which 537 were from discontinuers and 829 from dropouts. The pooled responding population of 586 teeth (41% recall) included 76 extracted teeth and 510 examined teeth (pooled study sample). The inception cohort and study sample are compared in

TABLE 1. Univariate Distribution of Investigated Variables in the Study Population

Variables	Phase 4		Pooled Phases 1–4	
	Inception cohort, % (n = 582)	Study sample, % (n = 137)	Inception cohort, % (n = 1952)	Study sample, % (n = 510)
Preoperative				
Age				
≤45 y	45	34	48	28
>45 y	55	66	52	73
Gender				
Female	55	54	55	54
Male	45	46	45	46
Tooth type				
Anterior	19	18	18	18
Posterior	81	82	82	82
Tooth location				
Maxilla	57	57	53	52
Mandible	43	43	47	48
No. of roots				
1	29	24	29	29
≥2	71	76	71	71
Signs and symptoms				
Absent	35	41	36	39
Present	65	59	64	61
Radiolucency				
Absent	43	39	43	42
Present	57	61	57	58
Pulp status				
Responsive	30	33	33	35
Nonresponsive	70	67	67	65
Intraoperative				
Treatment sessions				
1	30	31	21	21
≥2	70	69	79	79
Filling technique				
LC	20	28	42	45
VC	77	71	55	52
Other*	3	1	3	3
Root-filling length				
Adequate	83	83	80	78
Short	7	9	8	8
Long	10	8	12	14
Root-filling voids				
Absent	93	94	88	87
Present	7	6	12	13
Sealer extrusion				
Absent	56	50	48	47
Present	44	50	52	53
Complications				
Absent	86	88	84	84
Present	14	12	16	16
Coronal seal material				
Temporary†	60	61	43	43
Definitive‡	40	39	57	57
Postoperative				
Restoration at follow-up				
Temporary†		9		7
Definitive filling		26		29
Crown		65		64
Post				
Absent		68		61
Present		32		39

*Single gutta-percha cone with glass ionomer cement sealer.

†Cavit, zinc oxide–eugenol, intermediate restorative material.

‡Amalgam, composite resin, glass ionomer cement, crown.

Table 1. The response bias analysis (not shown) revealed that the study sample was significantly older than the lost-to-follow-up population (mean age, 53 vs 42 years).

In total, 439 of 510 teeth (86%) healed, and 71 of 510 teeth (14%) were classified as diseased. Four teeth (1 healed and 3 diseased) were fractured and subsequently excluded from further analysis to avoid confounding of other variables, leaving 506 teeth for analysis. Of the remaining 68 diseased teeth, 23 had larger lesions than before treatment (or new lesions), 17 had unchanged lesions, 23 had smaller lesions, and 5 had no lesions (PAI ≤2). Of the 506 teeth in the pooled

TABLE 2. Significant Associations between Variables and the Healed Rate 4–6 Years after Initial Treatment in the Pooled Phases 1–4 (n = 506, fractured teeth excluded)

Variables	n	Healed (% n)	*P* value
Preoperative			
Radiolucency			
Absent	214	93	<.001
Present	292	82	
No. of roots			
1	147	93	.005
≥2	359	84	

Bivariate analysis with χ^2.

TABLE 4. Significant Predictors of 4- to 6-Year Outcome of Initial Treatment Assessed in the Pooled Phases 1–4 (n = 506, fractured teeth excluded)

Predictor	OR for disease	95% Confidence interval	*P* value
Preoperative			
Radiolucency (0, absent; 1, present)	2.86	1.56–5.24	<.001
No. of roots (0, single; 1, multiple)	2.53	1.25–5.13	.010

Multivariate analysis with logistic regression.

study sample (4 fractured teeth excluded), 27 teeth were associated with symptoms or any form of clinical signs; 18 of 438 healed teeth (1 fractured tooth excluded) had slight tenderness to percussion, and 9 of 68 diseased teeth (3 fractured teeth excluded) had symptoms. Thus, in total, 479 of 506 teeth (95%) were completely asymptomatic and fully functional.

The bivariate analysis of the pooled sample (Table 2) identified statistically significant differences in the healed rate, associated with preoperative radiolucency ($P < .001$) and the number of roots ($P = .005$). Healed rate differentials associated with all other variables were smaller than 10% and nonsignificant. Without preoperative radiolucency, 199 of 214 teeth (93%) remained free of disease, and 94% were functional. Stratified bivariate analysis of this subsample identified no significant associations with any of the examined variables. Among teeth with preoperative radiolucency, 239 of 292 (82%) healed, and 96% were functional. Stratified bivariate analysis of this subsample (Table 3) identified statistically significant differences in the healed rate, associated with the number of roots ($P < .04$), root-filling technique ($P < .04$), and mid-treatment complications ($P = .02$). Note that without complications, 84% of the teeth healed.

The multivariate analysis (Table 4) identified 2 preoperative significant predictors of disease persistence, presence of radiolucency (odds ratio [OR], 2.86), and 2 or more roots (OR, 2.53). Stratified multivariate analysis of the subsample of teeth with preoperative radiolucency (Table 5) identified 2 significant predictors of disease, mid-treatment complications (OR, 2.27) and root-filling by using LC (OR, 1.88).

Discussion

Current, methodologically sound clinical studies are essential to demonstrate the benefit of endodontic treatment—the potential of teeth affected by endodontic disease to heal and to be retained in function.

TABLE 3. Significant Associations between Variables and the Healed Rate 4–6 Years after Initial Treatment in the Pooled Phases 1–4, Stratified for Teeth with Preoperative Radiolucency (n = 292, fractured teeth excluded)

Variables	n	Healed (% n)	*P* value
Preoperative			
No. of roots			
1	78	90	.035
≥2	214	79	
Intraoperative			
Root-filling technique			
LC	122	77	.037
VC	157	87	
Complications			
Absent	250	84	.020
Present	42	69	

Bivariate analysis with χ^2.

The demonstrated benefit is the key consideration when patients have to weigh treatment vis-à-vis extraction and replacement of the affected tooth. This prospective cohort study assessed the 4- to 6-year outcome of initial treatment in Phase 4 and in the pooled samples of Phases 1–4 of the modular Toronto Study project. The sequential increase in the number of significant outcome predictors identified by pooling successive samples of the first 3 phases of the project (19, 22, 25) suggested that addition of Phase 4 might identify new outcome predictors.

As discussed in the previous reports (19, 22, 25, 29, 30), the methodology of this study conformed to strict criteria related to the cohort, intervention, outcome assessment and analysis. Thus, methodologically the study was consistent with the second highest level of evidence; however, because its recall rate fell below the 80% required for the highest level of evidence (31), the validity of the results was undermined (31). Monetary compensation was offered with the hope to incentivize the subjects to respond to the recall, and exhaustive efforts had been made to contact all subjects and to encourage them to attend the follow-up examination. However, the large proportion of discontinuers (28%) who could not be reached and the even larger proportion of dropouts (42%) who had not responded to the numerous letters and phone messages were consistent with the previous Toronto Study reports on nonsurgical treatment (19, 22, 25, 29). Nevertheless, the attending population of the Phase 4 study was the largest of all 4 phases reported to date. A response bias analysis was performed to examine whether the large loss to follow-up could have skewed the results. Age was suggested as the only characteristic in which the attending population differed from the lost-to-follow-up population. Because age was not identified as an outcome predictor, the suggested difference in characteristics between the examined and lost populations was unlikely to affect the results. Another factor that limited the external validity of the results was the specific referral pattern of the study cohort. Because the cohort included dental school patients, the results of the study might not be generalized, even though the characteristics of cases included in the study, treatment decisions, and procedures performed were typical of an endodontic specialty practice.

TABLE 5. Significant Predictors of 4- to 6-Year Outcome of Initial Treatment in Teeth with Preoperative Radiolucency, Assessed in the Pooled Phases 1–4 (n = 292, fractured teeth excluded)

Predictor	OR for disease	95% Confidence interval	*P* value
Intraoperative			
Complications (0, absent; 1, present)	2.27	1.05–4.89	.037
Root filling technique (0, vertical; 1, lateral)	1.88	1.01–3.53	.049

Multivariate analysis with logistic regression.

In the Phase 4 sample, 88% of the teeth healed, compared with 81% in Phase 1 (19), 87% in Phase 2 (22), and 86% in Phase 3 (25). When all 4 phases were pooled, 439 of 510 teeth (86%) were assessed as healed, reflecting the potential to attain the treatment goal of complete healing (2). However, reduction of pathologic lesions (occasionally described as incomplete healing) and functional retention of treated teeth might also be considered benefits by individual patients who are weighing endodontic treatment against extraction and restoration of function with a prosthetic device (2). In the pooled study sample, diminished radiolucent lesions were observed in 23 of 506 teeth (5%, 4 fractured teeth excluded), and functional retention (absence of any clinical signs and symptoms) was recorded in 479 of 506 teeth (95%, 4 fractured teeth excluded). Therefore, patients who are considering initial treatment and alternative extraction and replacement should be informed of the 86% chance for the treated tooth to heal completely, an additional 5% chance for incomplete healing, and 95% chance for functional retention 4–6 years after initial treatment.

Unlike the previous 3 phases (19, 22, 25), each of which added a new significant outcome predictor, this study confirmed the same 4 predictors identified in Phase 3 (25). The significant outcome predictors identified by the multivariate analysis included preoperative apical periodontitis, identified in Phases 1, 2, and 3 (19, 22, 25), and the number of roots, identified in Phases 2 and 3 (22, 25). Mid-treatment complications, identified in Phase 3 (25), were a significant predictor only among teeth with apical periodontitis, as was root-filling technique, identified in Phases 2 and 3 (22, 25).

Preoperative apical periodontitis was the dominant outcome predictor as in all 3 previous phases (19, 22, 25), associated with a difference of 11% in the healed rate (absent, 93%; present, 82%). In teeth without apical periodontitis, the 93% healed rate was in the middle of the range (88%–97%) reported in methodologically compatible previous studies (6–8, 10, 12, 13, 18, 19, 21–23, 25, 26). This excellent outcome was unaffected by any of the analyzed variables, suggesting that clinical outcome research related to initial treatment should focus on teeth with apical periodontitis. In teeth with apical periodontitis, the 82% healed rate varied from the 74%–80% recorded in Phases 1–3 (19, 22, 25), and it was in the middle of the range (73%–90%) reported in methodologically compatible previous studies (6–9, 11–23, 25). This healed rate might have been compromised by the presence of 42 teeth with mid-treatment complications, of which only 69% healed. In teeth treated without complications, the 84% healed rate best reflects the prognosis. Another important consideration for teeth with apical periodontitis is the slow dynamics of the healing process that might affect individual teeth and require longer than 4–6 years for completion. Indeed, in a study spanning 27 years of follow-up (32), approximately 6% of teeth appeared healed only during the second or third decade after treatment. In the present study, 5% of all the teeth had persistent but diminished lesions; if some of these teeth exhibited slower than usual healing dynamics, the healed rate might improve with time.

The finding of a better healed rate in single-rooted teeth than in multi-rooted teeth (one, 93%; two or more, 84%) was not surprising, considering that the evaluated unit was the tooth, not the individual root. In multi-rooted teeth, the risk for persistence of disease is proportional to the number of roots. Therefore, the results might have been inherent to the method of analysis, but they might also reflect the greater challenge encountered when the anatomically complex, multi-rooted teeth are treated. In any event, clinicians should consider the 11% difference in outcome when projecting the prognosis for single-rooted and multi-rooted teeth.

Mid-treatment complications, including iatrogenic occurrences such as perforations, untreated canals, fractured instruments, and massive sealer extrusion, but also objective observations such as cracks and aberrant anatomy, were recorded in 42 of 292 teeth with apical periodontitis (14%, 4 fractured teeth excluded). The presence of complications lowered the healed rate by 15%, in agreement with several previous studies (6, 12, 25). By their nature, these complications can either promote infection or interfere with its elimination; therefore, iatrogenic complications should be avoided to maximize the outcome of treatment in teeth with apical periodontitis.

The smallest OR among the significant outcome predictors in teeth with apical periodontitis was associated with root-filling technique, where the difference in the healed rate was 10% (LC, 77%; VC, 87%), as compared with 16% observed in Phase 3 (25). Even though this variable has been repeatedly identified as an outcome predictor from Phase 2 (22) on, its importance should be considered as suggestive at best. Indeed, interventions such as treatment techniques should best be compared in well-planned randomized controlled trials and not in cohort studies such as this one (31, 33). Thus, the outcome predictive role of the root-filling technique in teeth with apical periodontitis requires confirmation from randomized controlled trials.

In summary, 4–6 years after endodontic initial treatment, 86% of teeth healed, and 95% remained asymptomatic and functional. Addition of Phase 4 of the Toronto Study did not identify additional significant outcome predictors to those identified in Phases 1–3. Absence of preoperative apical periodontitis, single-rooted teeth, and the absence of intraoperative complications in teeth with apical periodontitis were all significant predictors of better outcome in initial endodontic treatment. Treatment technique also appeared as a significant outcome predictor for teeth with apical periodontitis, but its importance requires confirmation from properly designed randomized controlled trials.

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