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ORIGINAL ARTICLE

What ultimately matters in root canal treatment success and tooth preservation: A 25-year cohort study

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Abstract

Aim: There are currently no prospective studies evaluating the long-term outcomes of non-surgical root canal treatments beyond 5 years, both in terms of treatment success and tooth preservation, and identifying factors predictive of treatment outcome. The aim of the present work was therefore to fill this gap by assessing these outcomes over time and identifying predictive variables based on systematic data collection over a 25-year period.

Methodology: Data concerning the treatments ($N = 2500$) were systematically collected since 1990. Information was recorded among clinical, technical, radiographic and patient-related characteristics, i.e., approximately 150 variables for each treatment. The data were analysed regarding both treatment success and tooth preservation by multivariable Cox proportional hazards model, and survival curves were generated. The statistical significance level was set at 0.0125.

Results: In total, 56.4% of the treatments could be followed over time (0–25 years, mean = 6.5 years, median = 5 years). Survival probability decreased almost linearly for treatment success, with about 85% after 5 years and 60% after 20 years, and for tooth preservation, with about 90% at 5 years and 50% at 20 years. The variables significantly associated with treatment failure were: pre-operative pain (Hazard Ratio—HR = 1.56 [95% CI 1.23–1.97]), persistent pain (HR = 2.63 [95% CI 1.44–4.80]), good operator rating of treatment prognosis (HR = 0.46 [95% CI 0.36–0.58]), size of periapical bone radiolucency (HR = 1.88 [95% CI 1.67–2.11]), and tooth type (p = .0006). For tooth extraction, they were: combined endodontic-periodontal lesion (HR = 3.37 [95% CI 1.88–6.05]), pre-existing complication before treatment (HR = 1.67 [95% CI 1.26–2.21]), good operator rating of treatment prognosis (HR = 0.45 [95% CI 0.33–0.60]), clinical failure of root canal treatment (HR = 2.78 [95% CI 1.98–3.89]) and tooth type (p = .0012).

Conclusion: Root canal treatment success and tooth preservation on the arch are not static outcomes, but evolve with time. Among a substantial set of potential predictors, only a small proportion was significantly predictive of treatment success and tooth preservation, most of them being disease and patient characteristics, and not technical aspects, except pre-existing complications. These observations challenge the importance frequently given to byzantine considerations related to the numerous technical details of endodontic procedures, as opposed to general concepts of good clinical practice.

KEYWORDS

dental pulp diseases, periapical diseases, prospective studies, root canal therapy, treatment failure, treatment outcome

INTRODUCTION

According to Wennberg (1990), there is a critical need to develop a system to ensure that key clinical theories are systematically tested, which is rarely the case apart from the evaluation of new drugs.

The consequence of the lack of consideration of outcome assessment is an insufficient scientific basis for clinical decision-making (Wennberg, 1990). This resonates with a statement made in a call for improved research efforts in endodontics, underlining that the treatment methods currently in use rely on inadequate scientific data, i.e., scarcely any randomized clinical trials or prospective cohort studies with sufficiently large sample size are available (Bergenholtz & Kvist, 2013). The authors also pointed out that while randomized trials are the standard of excellence for comparing the effect of treatments over time, it may not necessarily answer all clinical interrogations, particularly because of the large number of clinical variables that potentially influence the outcome. A more appropriate option would be large prospective cohort studies (Bergenholtz & Kvist, 2013; Duncan et al., 2016), in which dentists can work in their usual way (Bergenholtz & Kvist, 2014). This study design also takes into account the evolution of treatment protocols over time, such as materials or technologies, provided that these variables are properly recorded as potential influencing variables. The inclusion of a large number of variables and the use of multivariate statistical methods are indeed essential to reduce the risk of confounding bias (Leprince & Van Nieuwenhuysen, 2020).

Unfortunately, large prospective cohort studies with an extensive collection of variables are costly, time-consuming and require careful attention to detail (Bergenholtz & Kvist, 2014; Duncan et al., 2016). Therefore, very few prospective long-term evaluations of root canal treatment success, including multivariate analyses, are available (Ng et al., 2011b; Ricucci et al., 2011), and these have a relatively limited follow-up time (≤5 years). Longer-term prospective data are required for appropriate information and informed consent of patients, as well as for public health considerations.

Moreover, while the treatment of dental pulp and periapical bone inflammatory diseases is very important to maintain or restore the quality of life of patients over the long term (Dugas et al., 2002; Leong & Yap, 2020; Neelakantan et al., 2020), other considerations have been shown as important to patients. The preservation of a functional root canal treated tooth on the arch has notably been shown to be what matters most to patients undergoing root canal treatment, being their second most frequent expectation, after communication and trust in the practitioner (Azarpazhooh et al., 2016). Hence, tooth preservation is a major outcome that must be considered along with root canal treatment success. However, as mentioned in the influential work by Ng et al. (2010), the prognostic factors for treatment success and tooth survival following root canal treatment have so far not been investigated using the same patient and tooth dataset, which prevents the identification of commonality between prognostic factors for the two outcome measures.

These various key points highlight a major need for prospective long-term follow-up of non-surgical root canal treatments in a large cohort study, allowing to identify predictors of treatment outcome among a substantial set of variables. This was the objective of the present work, presenting the results of a systematic data collection over a 25-year period, with treatment success and tooth preservation as measured outcomes.

MATERIALS AND METHODS

Sample

The present study was carried out at the Dental School of Cliniques universitaires St-Luc, UCLouvain, Brussels, Belgium. All the patients who received an endodontic treatment (limited in the context of this work to root canal treatment) by a single practitioner (J.-P. V.N.) between 1990 and 2016 were included in the prospective data collection, with informed consent. The evaluations were performed at the university clinics until 30 September 2017. The present work conformed to STROBE guidelines, and the use of the data for retrospective analysis of the database was approved by the ethical committee of the Cliniques universitaires Saint-Luc, Brussels, Belgium (#2020/13JAN/019).

Pre-operative and follow-up radiographs

A periapical radiograph was taken prior to treatment initiation, except when one was provided by the referring dentist. The post-operative radiograph was considered as the baseline for follow-up. Radiographs were taken using conventional radiographic films between 1990 and 2005, and digital sensors or plates, after 2005. For teeth with multiple root canals, additional radiographs were taken using mesial-to-distal angulations.

Variables

The variables were recorded prior to and during the intervention in a predetermined FilemakerPro template (available on demand, example in Figure S1). Data collected before, during and after the endodontic procedure include clinical, technical, radiographic, patient-related characteristics, as well as follow-up assessments; these are described in detail in the Tables S1–S5.

Treatment procedures

The indication of performing endodontic treatments was conditioned by the possibility of placing a quality coronal restoration after treatment completion. Given the long-term span of the present data collection, there have been some changes in equipment and materials over time. Regardless of these technical variations (all of which being documented in the FilemakerPro file and considered as potential explanatory variables), the treatments were always performed based on similar state-of-the-art biological and technical concepts, which happened to be later on summarized in the quality guidelines recommended by the European Society of Endodontology, (2006). Treatment of vital teeth was performed under local anaesthesia, in contrast to non-vital teeth, where anaesthesia was applied when necessary to reduce patient discomfort. The vital or non-vital pulp status was confirmed upon pulp chamber access by the presence or absence of bleeding. Whenever possible, the treatment was completed in one appointment; the reasons for multiple appointment treatments were either lack of time due to technical difficulties, and/or impossibility to dry the canal(s). In those instances, temporary intra-canal medications were used, mostly calcium hydroxide.

Outcome assessment

Two outcomes were considered in the present work, first, the root canal treatment success and second, the tooth preservation on the arch. The *global* success of root canal treatment was defined as the combination of *clinical* and *radiographic* success (Figure 1). The former includes the absence of clinical signs (sinus tract, swelling, etc.) and symptoms (pain, sensitivity to percussion or chewing, etc.), and the latter requires a periapical

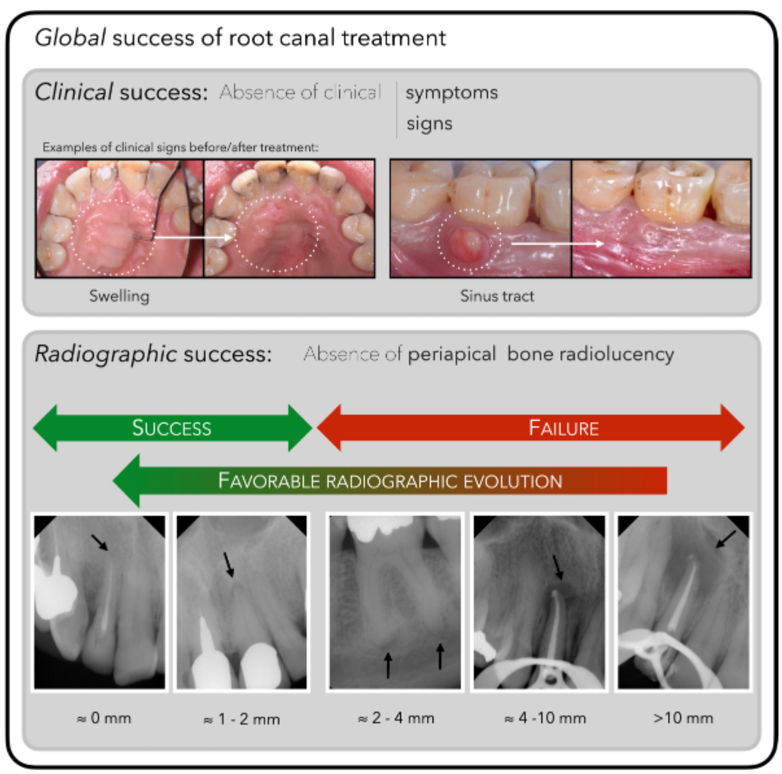

FIGURE 1 Criteria chosen for outcome assessment of root canal treatment success, which combines clinical and radiographic success criteria; examples intraoral radiographs are provided as representative examples of each size category of periapical radiolucency (indicated by black arrows).

bone radiolucency <2 mm on the intraoral radiograph (Figure 1). A periapical space <2 mm was considered to be within a normal physiological range, while radiolucencies >2 mm were considered diseased. In multi-rooted teeth, when various periapical statuses were observed, the worst-case scenario was considered, i.e., the larger radiolucency among the different roots was recorded. The evaluation of the size of the radiolucency has to be considered as estimation since any practitioner in a normal clinical setting must be able to easily reproduce it. An intra-examiner Kappa coefficient was calculated (J.-P. V.N.) on 10% of the sample to evaluate the reliability of the estimation. When several controls were performed for a given tooth, only the last one was eligible for analysis. Hence, a case for which improvement was observed clinically or radiographically, but was later followed by deterioration, was classified as a failure. By contrast, failure of the root canal treatment was defined as the presence of at least one of the following: clinical signs, symptoms and periapical bone radiolucency (>2 mm).

The tooth preservation on the arch was defined as the lack of tooth extraction during the follow-up period. Any tooth classified as a failure of root canal treatment—whether it required non-surgical or surgical retreatment or no further treatment was carried out for medical reasons or by the patient's decision—was still taken into account for the tooth preservation outcome.

Statistical analyses

The variables related to time (age of the patient, year of the treatment) required the stratification in groups, which was performed based on quartile distribution. The data were analysed using SAS software (SAS 9 release, Linux platform), by performing univariate analyses, followed by multiple logistic regression with stepwise selection. The lost to follow-up data were analysed in a similar fashion. The significant variables were then introduced into a Cox proportional hazard model, and Cox model-derived survival curves (with mean values of covariates as reference set) were generated to illustrate long-term treatment outcome. Due to the number of candidate predictors, statistical significance level was set at 0.0125 to limit type I errors (Bonferroni correction for four different outcomes considered combining treatment success—*global*, *radiographic* and *clinical* success—and tooth preservation). In the present paper, only *global* treatment success and tooth preservation were taken into account for readability and conciseness; *clinical* and *radiographic* success outcomes will be covered in a separate work.

RESULTS

The present cohort included 1545 patients for 2500 root canal treatments, among which 1063 were primary treatments and 1437 retreatments. The latter were in large majority retreatments of failed cases performed by other practitioners, only 34 of them (=1.3%) being failed cases of the present cohort performed by (J.-P. V.N.). The number of treated cases in each variable category is indicated in Tables S1–S5. The distribution was symmetrical between left and right patient sides in each tooth type category (Figure 2a). The sample was dominated by molars, representing 46% of the treated teeth. A Gaussian distribution (mean 48.2 years; SD 14.9 years) was observed relative to patient age (Figure 2b).

The sample included 20% vital teeth, half of which were associated with pain, and 80% non-vital teeth, 28% of which were associated with clinical signs and/or symptoms, and 50% with periapical bone resorption visible on the radiograph.

Treatment follow-up period ranged from 0 to 25 years; the mean and median were 6.5 and 5 years for treatment success, respectively, and 7.1 and 5.7 years for tooth preservation. Complete data collection was achieved for 56.4% of the treatments (Figure 3a). The distribution of the recall period for treatments with follow-up is illustrated in Figure 3b. The percentage of follow-up was relatively similar for each age group (Figure 2b) and root canal number category (Figure 2c), which is illustrative of the balanced nature of the cohort between the lost to follow-up and the global sample. In this regard, the C-statistics was close to 0.5 (0.586), which stresses that there does not seem to be major variables explaining why these patients dropped out (details available on request). Hence, the analysed fraction of the cohort was considered as representative of the global sample. Regarding the classification into size categories of periapical radiolucencies, the intra-examiner kappa coefficient was 0.78 for film and 0.75 for digital radiographs.

Out of the initial set of about 150 possible predictors of treatment outcome, univariate analyses performed for all outcomes revealed certain number of significant variables ($p < .05$), which were then used for the multiple logistic regression modelling and finally introduced in the Cox proportional hazards model. Only a limited number of variables remained significantly associated ($p < .0125$) with root canal treatment failure (5 variables) and tooth extraction (5 variables) after multivariate Cox analysis (Table 1). By exclusion, any variable not listed in Table 1 was not identified as significant in the multivariate Cox model, for example, primary treatment or re-treatment, presence of sinus tract, flare-up, presence or removal of the post, treatment period, single or multiple visits, type or size of instrumentation, type of root canal filling,

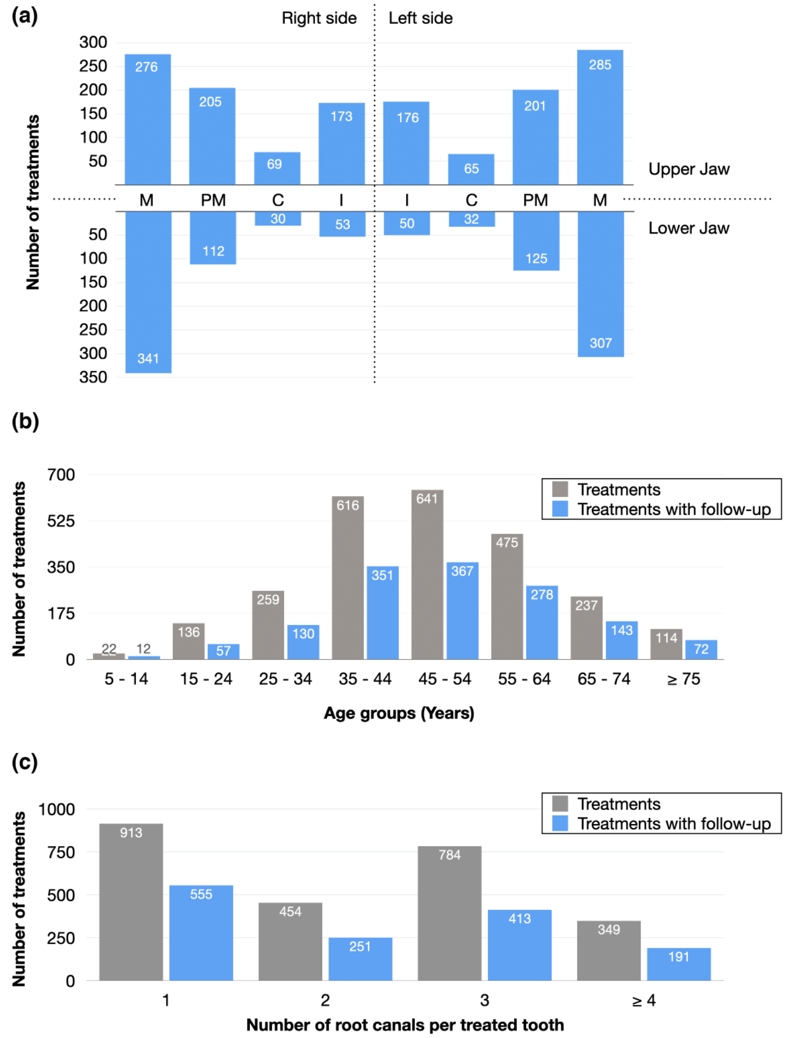

FIGURE 2 (a) Distribution of treatments by tooth type (upper and lower jaw, left and right patient side); (b) Distribution of treatments by age category (total number in grey and with follow-up in blue); (c) Distribution of treatments by the number of root canals (total number in grey and with follow-up in blue).

etc. The other non-significant variables can be found in Tables S1–S5.

The goodness of fit of the multivariate logistic regression models can be illustrated by R_N^2 (Nagelkerke pseudo-R^2), which is 0.2943 for treatment success and 0.1407 for tooth preservation. It is worth mentioning that the introduction of additional variables into the model resulted in negligible increase (<1%) in R_N^2 (additional details in Figure S2).

Of the significant variables included in the Cox models (Table 1), most were disease and patient characteristics; the only technical variable remaining significant was the presence of existing complications before treatment (e.g., perforation, canal transportation, fractured instruments, etc. – Table S2) for tooth extraction.

Following multivariate analysis, survival curves were generated with Cox regression to illustrate the long-term probability for treatment success (Figure 4a) and tooth preservation on the arch (Figure 4b). For example, the probability of treatment success and tooth preservation at 20 years was approximately 60% and 50%, respectively. Tooth type was significantly associated with both outcomes, incisors being the least successful group regarding treatment success (Figure 4c), while it was the molars regarding tooth preservation (Figure 4d). Finally, the size of the periapical radiolucency was highly associated with treatment failure ($p < .0001$, Table 1); the larger the size of the periapical radiolucency, the higher the probability of failure with time (Figure 4e).

This leads to consider the fate of teeth after failure of root canal treatment, and the main reason for tooth loss (Table 2). The majority of treatment failures underwent retreatment (either non-surgical or surgical), with only one-third of failures leading to tooth extraction. This corresponds to only 12% of tooth loss due to root canal treatment failure, most extractions being related to non-restorable tooth fractures (>50%) or to prosthetic or periodontal considerations (25%).

DISCUSSION

Our data clearly establish that the evaluation of the success of root canal treatment, as well as the preservation

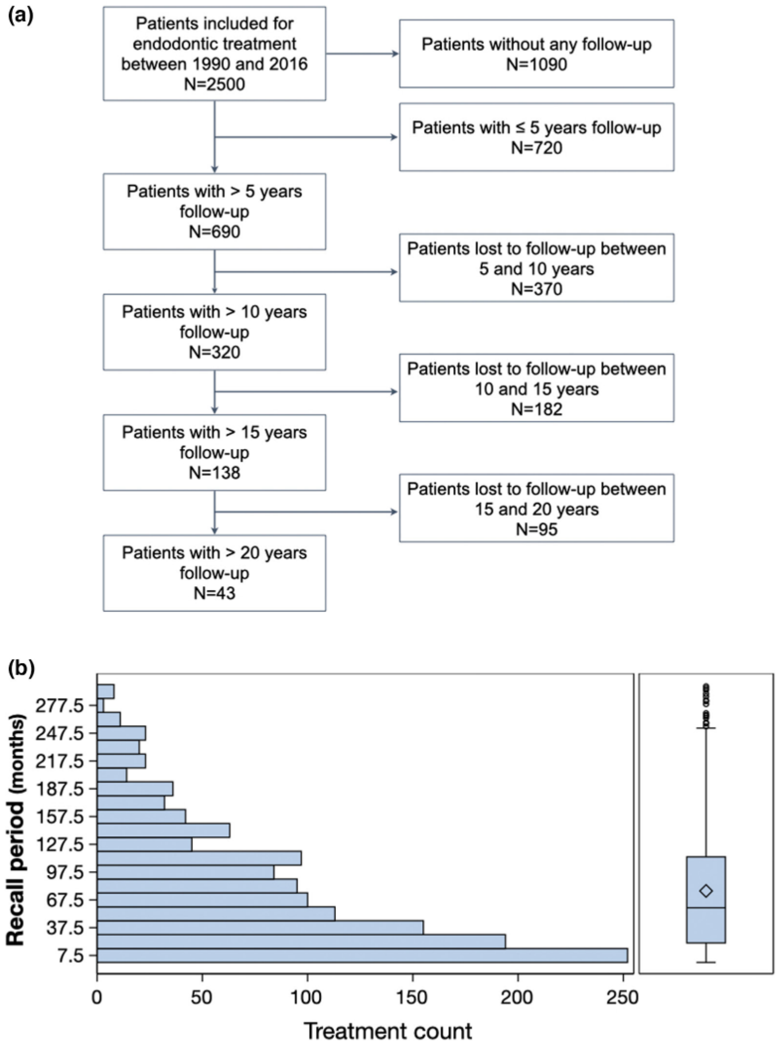

FIGURE 3 (a) Global flowchart with lost to follow-up and number of treatments followed by 5-year periods after treatment; the last data were censored at 298 months (last 3 controls); (b) Distribution of treatments by recall period; mean = 77 months, median = 59 months, quartile 1 = 21 months, quartile 3 = 114 months.

of treated teeth in the arch, is a dynamic process in which the probability of treatment success and tooth preservation progressively decreases over time. Paraphrasing the French writer Louis Aragon, this shows that nothing can be taken for granted for the endodontist ("Rien n'est jamais acquis à l'homme..."). It demonstrates once again the need for quality follow-up in endodontics, and in dental medicine in general.

Regarding treatment success, the short-term success rates measured in the present investigation (about 85% at 5 years) were in the same range as those put forth in the few prospective works available so far and being based on a multivariate analysis, i.e., between 70 and 90% at ≤5 years (Ng et al., 2011b; Ricucci et al., 2011). Similar ranges of success rates were also reported in two systematic reviews and meta-analyses (Ng et al., 2007, 2008). However, the disadvantage of those studies is the consideration of treatment success over a limited follow-up period, which gives the artificial impression of a fixed success rate over time. It is demonstrated here that success rates continue to decline to about 60% after 20 years, which further emphasizes that time is an essential aspect when describing the dynamics of endodontic status and disease (Kirkevang et al., 2012). Nevertheless, such long-term success rates remain quite satisfactory, and justify root canal treatment as a procedure that brings lasting relief to patients.

Similarly to treatment success, the probability of preservation in the dental arch of a root canal treated tooth decreases steadily with time. The probability of tooth preservation on the arch at 10 years (about 80%) is in good agreement with the few recent studies providing a comparable follow-up time (Landys Boren et al., 2015; Skupien et al., 2013; Yee et al., 2018) as well as with a meta-analysis including older works (8–10 years pooled percentage of tooth survival rate = 87%, CI 82%–92%) (Ng et al., 2010). Our data provide an additional 10+ years of perspective on the fate of these teeth, with a probability of about 50% of the teeth retained 20 years after treatment.

Overall, this work demonstrates the long-term reliability of root canal treatments with respect to two main patient-centred outcomes, i.e., first, the absence of clinical signs and symptoms, combined with the absence of

TABLE 1 Factors associated with root canal treatment success and tooth preservation on the arch in Cox Proportional Hazards regression ($N = 1410$).

Variables	Hazard ratio	95% confidence limits		*p*-Value
For the outcome "*global* success of root canal treatment":				
Pre-operative pain	1.56	1.23	1.97	.0002
Persistent pain	2.63	1.44	4.80	.0016
Good operator rating of treatment prognosis	0.46	0.36	0.58	<.0001
Size of periapical bone radiolucency	1.88	1.67	2.11	<.0001
Tooth type				
Tooth type "incisor" versus Tooth type "molar"	1.41	1.09	1.84	.0006
Tooth type "canine" versus Tooth type "molar"	0.69	0.39	1.22	
Tooth type "premolar" versus Tooth type "molar"	0.71	0.51	0.98	
For the outcome "tooth preservation on the arch":				
Combined endodontic-periodontal lesion	3.37	1.88	6.05	<.0001
Presence of existing complication before treatment	1.67	1.26	2.21	.0004
Good operator rating of treatment prognosis	0.45	0.33	0.60	<.0001
Clinical failure of root canal treatment	2.78	1.98	3.89	<.0001
Tooth type				
Tooth type "incisor" versus Tooth type "molar"	0.49	0.33	0.75	.0012
Tooth type "canine" versus Tooth type "molar"	0.48	0.25	0.91	
Tooth type "premolar" versus Tooth type "molar"	0.72	0.52	0.99	

periapical radiolucencies, and second, the preservation of a functional tooth on the dental arch.

A comparison of the survival rates of root canal treated teeth with those of titanium implants is often made. In total, 10-year implant survival rates ranging from 80% to more than 95% were reported, depending on the consideration of initial implant loss prior to loading and on the type of restoration supported by the implant (Holm-Pedersen et al., 2007; Rabel et al., 2018; von Stein-Lausnitz et al., 2019). These rates, compared with those reported in the present work, are in agreement with the statement by Holm-Pedersen et al. (2007) that the longevity of oral implants is in the same range as that of conservatively treated natural teeth. Nevertheless, it has also been stated that natural tooth preservation and implant placement should be considered as complementary rather than competing approaches (Setzer & Kim, 2014), meaning that an implant should be seen as a way to replace only irreversibly damaged teeth.

Root canal treatment is, therefore, a predictable treatment strategy, with good success and tooth preservation on the arch, and can be recommended as long-term strategy in comparison with very costly alternatives such as implants. Only a small proportion of the variables were significantly associated with root canal treatment failure and tooth extraction, most of which were disease and patient characteristics, rather than technical variables.

Regarding the predictors of treatment success, the size of the periapical radiolucency was significantly and negatively associated with treatment success, which is consistent with the two available prospective studies mentioned earlier, comparable to the present study in design (Ng et al., 2011b; Ricucci et al., 2011). While the latter works and the present work used millimetres to assess the size of radiolucency, another frequently used classification is the periapical index (PAI) (Orstavik et al., 1986; Rechenberg et al., 2021). The first two size categories of this study (0 and 0–2 mm, Figure 1) can be assimilated to PAI1 and

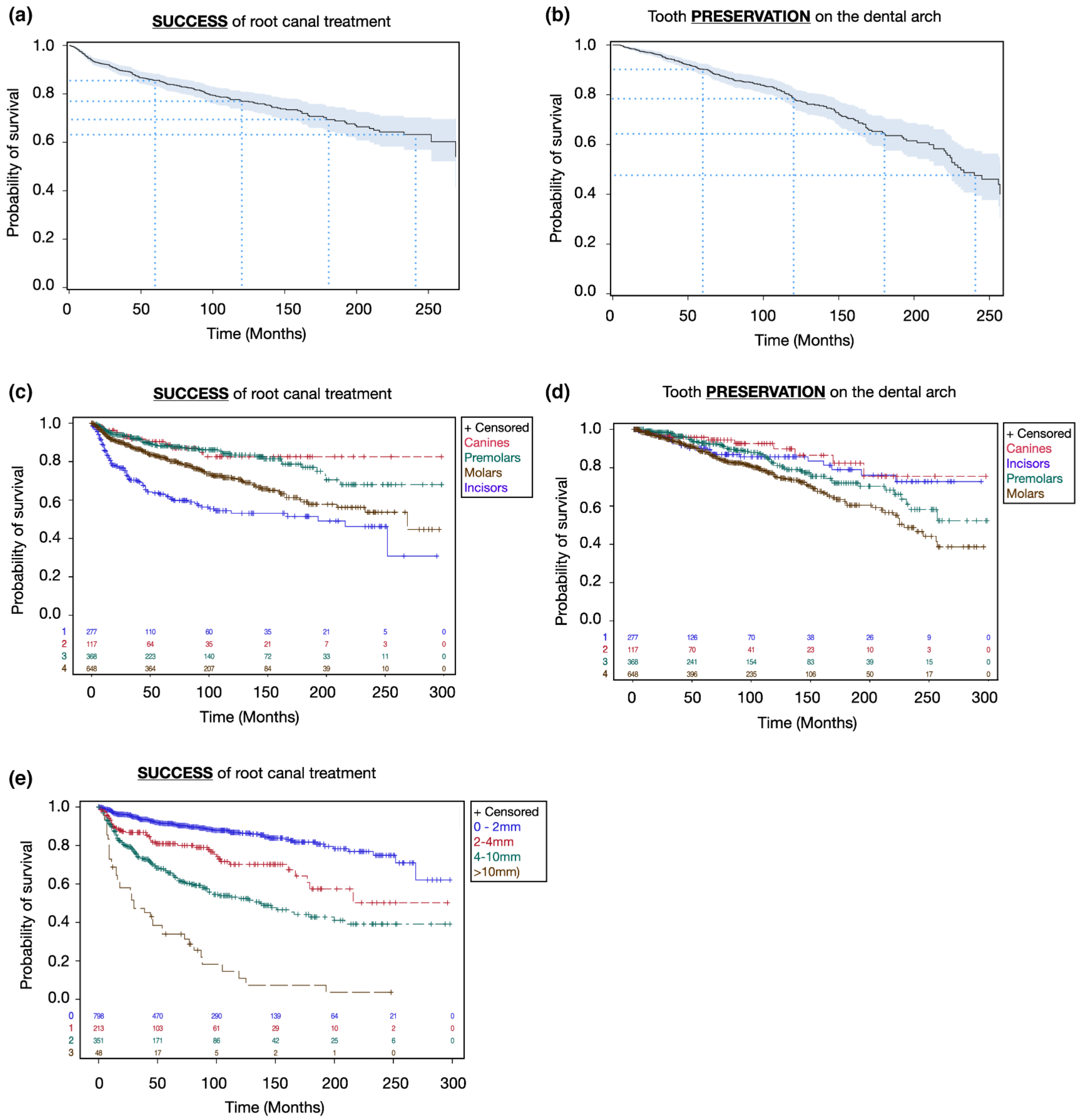

FIGURE 4 (a, b) Cox regression survival curves (black) with 95% confidence interval (blue), respectively, for treatment success and tooth preservation on the dental arch (the covariates were those identified as statistically significant, $p < .0125$, in the Cox proportional hazards regression in Table 1); (c, d) Kaplan–Meier curves according to tooth types, respectively regarding root canal treatment success and tooth preservation on the dental arch; (e) Kaplan–Meier curves according to the four size categories of periapical bone radiolucencies regarding treatment success.

PAI2, hence with a relatively comparable threshold between a healthy and diseased periapical space.

The presence of radiolucency indicates a bacterial infection of the root canal space (Moller et al., 1981; Sundqvist, 1976). It corresponds to a local bone resorption triggered by the recognition by toll-like receptors of bacterial components such as lipopolysaccharide or lipoteichoic acid (Sasaki & Stashenko, 2012). Cells of the innate and adaptative immune system accumulate at the site of bone resorption, in order to prevent the spread of the intracanal infection (Sasaki & Stashenko, 2012). The latter is organized in a multi-species biofilm, making its elimination all the more difficult, and requiring a combination of antiseptic agents (generally sodium hypochlorite) and mechanical instrumentation with endodontic files (Neelakantan et al., 2017; Siqueira et al., 2010). In light of the present data, a larger lesion size may be seen as a more advanced state of the disease, and requires a particular attention in the post-treatment follow-up due to the higher failure risk.

The significant impact of pre-operative pain on treatment outcome is in accordance with the results of a previous large cohort (Ricucci et al., 2011), while the effect of persistent pain is a new observation, since it was, to our knowledge, not considered in previous long-term outcome

TABLE 2 Management of failed root canal treatments ($N = 91$) and reasons for the loss of root canal treated teeth ($N = 228$).

Management of failed root canal treatments: Types of re-intervention	Number	Percentage
Non-surgical root canal retreatment	34	37
Surgical root canal retreatment (including apicoectomy)	29	32
Tooth extraction	28	31

Reasons for the loss of root canal treated teeth	Number	Percentage
Non-restorable tooth fracture	117	51
For prosthetic reasons	33	14
For endodontic reasons	28	12
For periodontal reasons	24	11
Non-restorable carious lesion	13	6
Unknown reason	7	3
For orthodontic reasons	2	1
Upon patient demand	3	1
For medical reasons	1	<1

studies. Persistent pain is understood here as chronic pain, defined classically as persisting beyond the usual recovery period, typically more than 3–6 months. In terms of prevalence, the rate of persistent pain (28/1410 = 2%) is in the same range as those documented in a recent work (Jonsson Sjogren et al., 2019) as well as in a systematic review on the subject (Nixdorf et al., 2010), i.e., around 5%. This highlights the need to give more importance to pain considerations rather than to technical aspects, and to better investigate pain outcome rather than the usual dichotomous measure (pain present or absent) in the previous long-term works such as the present paper or others (Ricucci et al., 2011), which represents a limitation. Due to the inherent subjective component of the pain experience, other tools shall be implemented in routine practice to better characterize the patient's pain experience. Such tools can range from the use of a simple numerical rating pain scale for the measurement of pain intensity and its evolution over time (Beauquis et al., 2021) to the innovative use of pain drawings to improve the characterization of pain in complex symptomatology (Pitance et al., 2021).

Regarding the protective effect of the good operator rating of treatment prognosis upon treatment completion, it is hazardous and beyond the scope of the present work to make speculations at this stage, but this aspect is currently under investigation by the authors to determine the process for decision-making based on data mining statistical methods.

Finally, the significant influence of tooth type on treatment outcome is more controversial, particularly the lower success rate observed for incisors. It is particularly difficult to compare rigorously with the other long-term prospective studies available (Ng et al., 2011b; Ricucci et al., 2011), due to a different grouping of teeth for analysis and/or a statistical analysis performed at the root rather than the tooth level. However, when looking at the raw numbers, incisors have in both works a tendency of being associated with lower success rates, particularly for maxillary incisors (Ricucci et al., 2011). The reason for that is unclear, but one could speculate on a possible different aetiology leading to root canal treatment, with trauma as the leading cause when compared with caries for other tooth types. In any case, as mentioned by Ricucci et al. (2011), those teeth require particular attention. The fact that molars represent almost half of the sample is interesting to assess the impact of treatment complexity on the outcome. Despite the fact that molars are considered by practitioners as an indicator of treatment complexity (Ree et al., 2003), they have a better success rate than incisors. A selection bias cannot be excluded in the process of transferring the patient to the specialist in a tertiary setting.

Regarding the predictors of tooth preservation on the dental arch, cases where periapical lesion was combined with periodontal involvement was significantly associated with an increased risk of tooth loss, in accordance with another prospective study with 4-year follow-up (Ng et al., 2011a). This highlights the importance of considering a multidisciplinary approach when dealing with periapical diseases. Besides periodontal aspects, the type of restoration was identified in the past as an important factor regarding tooth preservation (Ng et al., 2010). However, it was not recorded in the present work since the patients were returned to the referring dentists for restoration, and the variable could, therefore, not be considered in the prospective design.

Another important finding is the negative impact of a pre-operative complication on tooth preservation on the arch, which constitutes the only technical variable identified as significant in the multivariate model. All pre-existing complications were grouped in a similar category in order to avoid losing statistical power with too small subgroups. However, the message for clinicians is clearly that caution must be an important aspect of performing root canals, as complications precipitate tooth extraction, as was shown previously for pre-operative perforations (Ng et al., 2011a).

Like for treatment success, tooth type was a variable significantly affecting tooth preservation, with molar teeth being more prone to extraction, in agreement with a meta-analysis on the subject (Ng et al., 2010). This can be explained by a combination of several factors, i.e., molars withstand most of the masticatory forces (Hidaka et al., 1999), are the most affected by caries (Luan et al., 2000; Sheiham & Sabbah, 2010) and the most susceptible to cracks (Kang et al., 2016).

The major reasons reported for extraction of root canal treated teeth are tooth fracture, unrestorable caries lesions and periodontal diseases (Axelsson et al., 2004; Landys Boren et al., 2015; Ng et al., 2010; Riis et al., 2018; Toure et al., 2011; Vire, 1991; Zadik et al., 2008), depending on the quality of maintenance care in the population. Here, the vast majority of tooth extractions are due to fracture (51%), only a minor proportion of teeth being lost for endodontic reasons (12%). From an endodontic perspective, it can be explained by the possibility of re-intervention upon treatment failure, either by non-surgical or surgical endodontic retreatment, which allowed to prolong the preservation on the dental arch of 69% of the teeth considered as failed treatments (Table 2). Nevertheless, the persistence of pain and symptoms (*clinical* treatment failure) does increase the probability of tooth extraction, as was reported previously for persistent pain (Ng et al., 2011a).

Regarding the choice of management of failed root canal treatments, two objective elements could be identified as potentially involved in the decision-making, i.e., tooth type and the cumulated number of failure criteria. Specifically, extraction was preferred in molar teeth with a combination of clinical signs, symptoms and the presence of a periapical radiolucency. The same can be said for surgical retreatment, but this time with a majority of single-rooted teeth. Non-surgical retreatment was undertaken more often for teeth with less symptomatology. However, decision-making is a complex process (Kvist, 2018), involving not only objective criteria, but also other aspects, such as the implications of treatment costs or patient preferences, which were not recorded here.

Concerning tooth preservation, the lack of systematic recording of the type of restoration placed following root canal treatment may certainly be considered as a limitation of the present work. It can, however be mentioned that one recorded variable was that root canal treatment was requested by the referring dentist for the placement of a fixed prosthetic restoration; this variable did not appear as a significant in the multivariate model.

Despite its limitations, the present data fills a gap identified in a major report by Swedish Council on Health and Technology Assessment (SBU, 2010). The latter indeed highlighted the need to identify the factors influencing long-term preservation of root canal-treated teeth.

The present cohort study provides the first work available to date, including a large number of patients (n = 1545), a high number of treated teeth (n = 2500) followed prospectively for an extended period (up to 25 years) with a satisfactory follow-up rate (56.4% of treatments). The data also enables, for the first time to generate survival curves based on the variables identified by multivariable analyses, for both treatment success and tooth preservation.

The distribution of the teeth in the sample reflects both the left–right symmetry and the preferential location of carious lesions in the mouth. As reported in classical works of cariology for a global population, there is a hierarchy of caries susceptibility by tooth type, with molars being the most susceptible to decay, followed by upper premolars as the level of carious involvement increases; canines and incisors are only affected at higher levels of caries, lower anterior teeth being the least susceptible to caries (Luan et al., 2000; Sheiham & Sabbah, 2010). This nicely fits with the pattern of treated teeth in the present work, except for upper incisors, which represent a more substantial proportion of treated teeth than accounted for by caries only. This can be explained by the other aetiology of dental pulp and periapical bone inflammation, namely, dental trauma (Petti et al., 2018), which involves frequently the upper incisors (Lam, 2016). The present sample is actually an overlap of teeth most commonly affected by both dental caries and trauma, and therefore is representative of a global patient population. The balanced nature of the sample is further supported by the gaussian age distribution, and is unique to the present data. In addition, the follow-up rate was equivalent regardless of the age category or number of root canals per tooth.

The fact that all the treatments and evaluations were carried out by the same operator may be considered as a risk of bias, but corresponds to the reality of each practitioner in a real-life clinical setting. As stated by Bergenholtz & Kvist, (2013), a cohort study design allows dentists to work clinically in their usual manner. It was considered literally in our study, by considering that clinical work includes both treatment and evaluation of the outcome. It is indeed the practitioner's responsibility in a practice routine to evaluate the efficiency of the treatment and to deal with the consequences in case of failure. Also, the other side of the coin of the evaluation of the radiographs by a single person was that the bias – if there is one—is constant between observations, and the reliability is thereby increased. A practitioner evaluating his own treatment may be either too harsh or too complacent, but the error—if there is one—is *a priori* systematic, as demonstrated by the Kappa, which was reasonable. Also, any error in one direction or the other is compensated by the large sample size.

A single operator may also be seen as a limitation regarding the possibility to extrapolate the conclusions to a larger population of dentists, but it was not initially the objective here. Nevertheless, the success and survival rates, at short-term are in the same range as those of other studies, including multiple operators.

It could be argued that despite the large number of predicting variables considered, the resulting explained variability of the logistic regression models tested (R^2) were rather low (30%). However, this rate is in the same range as those reported for other oral pathoses, such as caries (25%–50%) (Granath et al., 1991; Holbrook et al., 1993) or tooth erosion (15%) (Holbrook et al., 2009). There are several reasons why a poor R^2 is observed. First, the array of predictors considered could be incomplete, and the consideration of others, such as host-related ones, could contribute to increase R^2, e.g., biomarkers, gene polymorphism, epigenetics or patients affected by systemic diseases (de Souza et al., 2019; Ideo et al., 2022; Marending et al., 2005; Peddis et al., 2019; Torres et al., 2020). These factors have nevertheless rarely been included so far, possibly due to the difficulty of measuring them. The use of artificial intelligence assistance in the analysis of large databases will possibly bring new possibilities in the study of these diseases (Schwendicke, Samek, & Krois, 2020). Finally, from a purely theoretical aspect, an intrinsically random phenomenon, having no identified causation, cannot be excluded.

The present data are useful both for clinicians and patients to get a clear idea on the long-term probability of success and tooth preservation, and thus facilitate decision-making regarding a given treatment and its impact on the quality of life. This work also emphasizes that, as long as the concepts of good clinical practice (Endodontology, 2006) are followed by prioritizing pragmatic concepts over Byzantine details (Leprince & Van Nieuwenhuysen, 2020), root canal treatment is a reliable long-term option for the preservation of teeth with pulpal and periapical disease.

Also, it seems important to underline that such work confirms the long-term efficacy of antibiotic-free treatments for such pathoses. Antibiotic over-prescription remains a problem in dental practice, globally and in the country of the present investigation in particular (Mainjot et al., 2009; Struyf et al., 2019). In the global attempt to reduce the rise in antibiotic resistance (Hernando-Amado et al., 2019), the long-term evidence provided here further support the need to avoid prescription outside the few exceptional situations specified in the latest guidelines (Leroy et al., 2020).

Finally, from a more global perspective, it can be reminded that in 2015, dental diseases ranked third in expenditures in the EU, behind diabetes and cardiovascular diseases (Peres et al., 2019). Looking ahead, projections by 2030 predict a reduction of missing teeth but an increase of decayed teeth per individual (Jordan et al., 2019). As a result, an increase of endodontic treatment can be expected, and the present data can help to better predict the need for dental services in the future (Schwendicke, Krois, & Jordan, 2020).

In conclusion, what ultimately matters in root canal treatment success and tooth preservation in this 25-year cohort study is first, the importance of follow-up time, and second a small proportion of predictive variables, most of them being disease and patient characteristics. Despite its limitations, notably the fact that treatments were performed by a single operator in secondary care, the present work contributes to providing a medical and long-term perspective on the treatment of pulp and periapical pathoses. It thus responds to recent articles (Peres et al., 2019; Watt et al., 2019) deploring the dominance of high technology and aesthetics in dental care, motivated by profit and consumerism, at the expense of fundamental public health objectives. This work can also impact significantly the public health considerations of such treatments, since it gives ground to calculations of public health expenditures in the long term. Finally, the results allow to better inform patients on the rationale of performing root canal treatments with a long-term perspective.

AUTHOR CONTRIBUTIONS

JPVN conceptualized the study and collected the data. JPVN, WD, and JL analysed and interpreted the data. JL drafted the manuscript, JPVN and WD critically revised the manuscript. All the authors approved the final version for submission and publication.

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None.

CONFLICT OF INTEREST

No authors declare any conflict of interests.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICAL APPROVAL

The use of the data was approved by the ethical committee of the Cliniques universitaires Saint-Luc, Brussels, Belgium (#2020/13JAN/019).

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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