CLINICAL INVESTIGATIONS

Predicting Severe Pain after Root Canal Therapy in the National Dental PBRN

A.S. Law[1,2], D.R. Nixdorf[3,4,5]*, A.M. Aguirre[6], G.J. Reams[7], A.J. Tortomasi[8], B.D. Manne[9], D.R. Harris[10], and National Dental PBRN Collaborative Group[11]

Abstract: *Some patients experience severe pain following root canal therapy (RCT) despite advancements in care. We sought to identify factors, which can be measured preoperatively, that predict this negative outcome so that future research may focus on preemptive steps to reduce postoperative pain intensity. Sixty-two practitioners (46 general dentists and 16 endodontists) who are members of the National Dental Practice-Based Research Network enrolled patients receiving RCT for this prospective observational study. Baseline data collected from patients and dentists were obtained before treatment. Severe postoperative pain was defined based on a rating of ≥7 on a scale from 0 (no pain) to 10 (pain as bad as can be) for the worst pain intensity experienced during the preceding week, and this was collected 1 wk after treatment. Multiple logistic regression analyses were used to develop and validate the model. A total of 708 patients were enrolled during a 6-m period. Pain intensity data were collected 1 wk postoperatively from 652 patients (92.1%), with 19.5% (n = 127) reporting severe pain. In multivariable modeling, baseline factors predicting severe postoperative pain included current pain intensity (odds ratio [OR], 1.15; 95% confidence interval [CI], 1.07 to 1.25;* P = *0.0003), number of days in the past week that the subject was kept from their usual activities due to pain (OR, 1.32; 95% CI, 1.13 to 1.55;* P = *0.0005), pain made worse by stress (OR, 2.55; 95% CI, 1.22 to 5.35;* P = *0.0130), and a diagnosis of symptomatic apical periodontitis (OR, 1.63; 95% CI, 1.01 to 2.64;* P = *0.0452). Among the factors that did not contribute to predicting severe postoperative pain were the dentist's specialty training, the patient's age and sex, the type of tooth, the presence of swelling, or other pulpal and apical endodontic diagnoses. Factors measured preoperatively were found to predict severe postoperative pain following RCT. Practitioners could use this information to better inform patients about RCT outcomes and possibly use different treatment strategies to manage their patients (Clinicaltrials.gov NCT01201681).*

Key Words: predictors, endodontics, evidence-based dentistry/health care, clinical outcomes, clinical studies/trials, patient outcomes.

Introduction

Initial orthograde root canal therapy (RCT) is a common treatment in the United States (American Dental Association Survey Center 2007). Severe postoperative pain following RCT, a negative outcome of treatment (Pak and White 2011; Law et al. 2014), continues to occur despite improvements in care. If risk factors for severe postoperative pain could be identified that are measurable before initiation of treatment, dentists could use this information to preoperatively identify patients at increased risk and implement preemptive steps to minimize the pain and reduce patient suffering.

Predictors of severe pain following RCT have been explored in several studies that were succinctly reviewed in Hargreaves and Cohen's *Pathways of the Pulp* (2011; see Keiser and Byrne 2011). They listed 12 predictors from 38 studies, including presenting factors (i.e., patient specific, tooth specific, and diagnoses) and procedural factors (i.e., retreatment, intracanal medicament, apical patency, and 1-step procedures versus multiple appointments). This body of literature, however, is subject to the following major limitations: 1) retrospective

DOI: 10.1177/0022034514555144. [1]Private Practice, The Dental Specialists, Lake Elmo, MN; [2]Division of Endodontics, School of Dentistry, University of Minnesota, Minneapolis, MN; [3]Division of TMD and Orofacial Pain, School of Dentistry, University of Minnesota, Minneapolis, MN; [4]Department of Neurology, Medical School, University of Minnesota, Minneapolis, MN; [5]HealthPartners Institute for Education and Research, Bloomington, MN; [6]Private Practice, Endodontic Associates, Coon Rapids, MN; [7]PDA Permanente Dental Associates, Tigard, OR; [8]Private Practice, Sumiton Dental, Sumiton, AL; [9]Private Practice, Ormond Beach, FL; [10]Westat, Rockville, MD; and [11]the National Dental PBRN Collaborative Group includes practitioner, faculty, and staff investigators who contributed to this activity (a complete list is at http://nationaldentalpbrn.org); *corresponding author, nixdorf@umn.edu

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study design, 2) small sample sizes, 3) important predictors were not included in the model (e.g., psychosocial variables), 4) difficult-to-interpret outcome measures (e.g., composite of pain and office visit), and 5) less-than-ideal analyses (e.g., only bivariate analyses). Because of these limitations, it is difficult to draw clear conclusions, as reflected by the conflicting results for all predictors except for 2 (hyperalgesia and swelling presenting preoperatively).

This area of research would benefit greatly from a large prospective study using a multivariable analysis. Using data from a large, multisite, prospective observational cohort study, conducted in a practice-based setting, we performed a multivariable logistic regression analysis to identify predictors of severe postoperative pain intensity associated with initial orthograde RCT.

Methods

Brief Overview of the Study

This research was conducted within the National Dental Practice-Based Research Network (Gilbert et al. 2008, 2013); details are provided online at http://nationaldentalpbrn.org. Ethical review board approval from each region and from the University of Minnesota was obtained prior to initiation of this research. The study methods have been previously reported (Nixdorf et al. 2012), as have details regarding the outcome of "severe" postoperative pain following RCT (Law et al. 2014), and they conform to Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines.

Study Design and Setting

This prospective observational cohort study included 62 member dentists (46 general practitioners [GPs] and 16 endodontic specialists [ESs]) from 5 geographical regions: Alabama–Mississippi, Florida–Georgia, Minnesota, Oregon–Washington, and Denmark–Sweden. Dentists enrolled their patients seeking dental care throughout a 6-month period. Informed consent was obtained from patients, and study procedures were conducted in accordance with institutional oversight. Project staff met with each dentist to explain the study protocol. Data collection occurred 1) immediately before initiation of treatment to assess the preoperative state, 2) immediately following treatment to assess the intraoperative experience, and 3) 1 wk after treatment to assess the postoperative state. Patients who had more than 1 appointment to complete RCT received a postoperative questionnaire after each appointment to complete 1 wk later.

Patient Eligibility and Recruitment

Dentists approached consecutive eligible patients for participation in this study. Inclusion criteria were patients who were 19 to 70 y of age and had a permanent tooth requiring RCT. Exclusion criteria were 1) iatrogenic pulpal exposure (cases of carious pulp exposure were included); 2) patient previously enrolled in this study (i.e., each patient could contribute only 1 tooth to the study); 3) previous endodontic treatment (i.e., in patients with a prior RCT, it could be unclear whether pain was associated with the prior treatment or the study treatment); 4) obvious cognitive impairments (e.g., prior stroke with communication deficits, dementia, or mental disability); 5) inability to read, understand, and complete the baseline patient questionnaire provided in English (or 1 of 2 Scandinavian languages for the relevant geographic region); and 6) anticipated lack of availability to provide 6-mo follow-up information for additional research that was planned. Participation was voluntary, and refusal to participate did not affect care.

Measurement of Predictive Factors

Prior research suggests that many factors can play a role in the outcome of severe postoperative pain, some being specific to RCT (Keiser and Byrne 2011) and others related to surgery in general (Ip et al. 2009). For descriptive purposes, the variables from this study were grouped into 12 domains; study region and practitioner specialty status, demographics, socioeconomic status, pain intensity, pain qualities, pain sensitivity, pain interference, psychosocial characteristics, systemic health characteristics, pulpal diagnoses, apical diagnoses, and tooth characteristics. The individual factors investigated as predictors were collected before initiation of RCT from both the patients and the dentists, and the questionnaires used are available online (please see reference at http://nationaldentalpbrn.org/peer-reviewed-publications.php).

Measure of Severe Postoperative Pain

The Graded Chronic Pain Scale was used to measure pain intensity using a 0 (*no pain*) to 10 (*pain as bad as could be*) rating scale (Von Korff et al. 1992). The dependent outcome of severe postoperative pain corresponded to a rating of ≥7 for worst pain intensity experienced during the preceding week, collected 1 wk after RCT. If more than 1 appointment was required to complete the root canal, the highest pain level reported among the appointments was captured for this variable.

Statistical Procedures

Bivariate associations of putative predictors with severe worst postoperative pain were used as the basis for screening variables for possible inclusion in the multivariable logistic regression modeling; the Student's *t* test and nonparametric Wilcoxon rank sum test were used for continuous scaled measures, and the Fisher's exact test or Fisher–Freeman–Halton test was used for categorical measures (see the Appendix for details). Variables associated with severe worst postoperative pain at an alpha ≤0.1 level were considered as possible candidates for inclusion in the modeling. Certain covariates were forced into the model, regardless of their significance, to adjust for potential bias that they might otherwise introduce to the analyses if not included (i.e., dentist training specialty, patient age, and patient sex). Covariates that have been reported to be predictors of postoperative pain in other studies (i.e., pain duration, medications taken, diagnoses of necrotic pulp, the presence of swelling, the

presence of apical radiolucency, maxillary tooth, posterior tooth, and the number of appointments to complete treatment) were explored in the modeling.

A series of models were fit to the data to derive the final model, starting with forward selection to identify variables that contribute significantly. Subsequently, backward elimination was used to assess model stability as a validation step. Both modeling approaches were carried out with and without the forced variables used for adjustment purposes. The fit of the final model was assessed using the Hosmer–Lemeshow test.

All analyses were performed using the SAS software system, version 9.3. No imputation for missing values was undertaken.

Results

Characteristics of the 708 patients enrolled in the study are given in Table 1. Mean (standard deviation) age was 47.8 y (13.0), 58.6% were female, and a majority were white (90.6%) and college educated (51.4%); 58.9% of treated teeth were maxillary, and 89.1% posterior. Among the 708 patients, 1-wk worst-pain data were available from 652 (92.1%) (655 returned forms, but 3 did not list pain ratings). There were 127 subjects with worst-pain intensity in the past week ≥7, 525 with worst-pain intensity <7, and 56 who were missing a response for this variable. The overall prevalence of severe worst postoperative pain was 19.5%; the exact (Clopper–Pearson) confidence limits (CIs) for this proportion were 16.5% to 22.7%.

Dentist training specialty, patient's age, and patient's sex did not make a significant contribution to the modeling ($P > 0.4$) (Table 2). Current pain intensity at baseline (preoperative) was significantly associated with the development of severe worst postoperative pain ($P = 0.0003$); for each unit increase in baseline pain, the risk of developing severe worst postoperative pain increased by 15% (odds ratio [OR], 1.15; 95% confidence interval [CI], 1.07 to 1.25). The number of days in the past week in which the subject was kept from their usual activities due to pain was also significantly associated with severe postoperative pain ($P = 0.0005$); the risk of developing severe postoperative pain increased by 32% for each 1-d increase in the number of days in the past week

Table 1.
Patient, Tooth, and Procedure Characteristics ($N = 708$)

Characteristic	Overall
Patient-Related Characteristics	
Age, y, mean (SD)	47.8 (13.0)
Number missing	13
Female sex, *n* (%)	409 (58.6)
Number missing	10
Ethnicity, *n* (%)	
Hispanic/Latino	29 (4.2)
Non-Hispanic/Latino	663 (95.8)
Number missing	16
Race, *n* (%)	
White	633 (90.6)
Black/African American	38 (5.4)
Other	28 (4.0)
Number missing	9
Highest level of education completed, *n* (%)	
Less than a college degree	340 (48.6)
College degree or more advanced degree	359 (51.4)
Number missing	9
Tooth-Related Characteristics	
Maxillary tooth, *n* (%)	417 (58.9)
Number missing	0
Posterior tooth, *n* (%)	631 (89.1)
Molar	434 (68.8)
Premolar	197 (31.2)
Number missing	0
Pulpal endodontic diagnoses, *n* (%)	
Necrotic pulp	377 (53.7)
Normal pulp or reversible pulpitis	68 (9. 7))
Irreversible pulpitis	257 (36.6)
Number missing	6
Apical endodontic diagnoses, *n* (%)	
Normal apical tissue	163 (24.3)
Symptomatic apical periodontitis	364 (54.2)
Asymptomatic apical periodontitis	42 (6.3)
Acute apical abscess	45 (6.7)
Chronic apical abscess	57 (8.5)
Number missing	37

the subject was kept from their usual activities (OR, 1.32; 95% CI, 1.13 to 1.55). Participants indicating that their pain was made worse by stress were more than 2.5 times more likely to develop severe worst postoperative pain intensity (OR, 2.55; 95% CI, 1.22 to 5.35; $P = 0.0130$) than those whose pain was not worsened with stress. A diagnosis of symptomatic apical periodontitis significantly increased the likelihood of developing severe worst postoperative pain intensity (OR, 1.63, 95% CI, 1.01 to 2.64; $P = 0.0452$).

The Hosmer–Lemeshow test, used to assess goodness-of-fit for logistic regression models, indicated that the model was a good fit to the data ($P = 0.26$). Further exploration of the Hosmer–Lemeshow test result showed that the model generally fit the data very well among all deciles of risk, with observed and predicted outcomes differing only modestly.

A model was also fit to the data that included covariates that were identified in the literature to be related to postoperative pain intensity (Table 2). None of these additional covariates contributed significantly to the model ($P > 0.08$). The marginally significant finding for diagnosis of symptomatic apical periodontitis observed in the final model ($P = 0.0452$) was no longer significantly associated with predicting severe worst postoperative pain intensity in the presence of these added covariates. The addition of this relatively large number of nonsignificant covariates adds unnecessary "noise" to the model, however, which tends to increase variance estimates, leading to wider CIs for the estimated parameters and consequently larger P values.

Discussion

Frequency of Severe Postoperative Pain

We found that 19.5% of patients reported severe pain in the first week following their root canal treatment. This percentage is higher than that reported by other endodontic studies, which range from 0% to 9% (Harrison et al. 1983; Oliet 1983; Genet et al. 1986; Genet et al 1987; Trope 1991; Walton and Fouad 1992; Imura and Zuolo 1995; Albashaireh and Alnegrish 1998; Eleazer and Eleazer 1998). This is likely because we asked patients to self-report their worst pain in the week following treatment, as opposed to requiring them to contact the practitioner's office about their pain and/or swelling (Georgopoulou et al. 1986; Trope 1991; Walton and Fouad 1992; Imura and Zuolo 1995), experience pain that was unrelieved by pain medications (Harrison et al. 1983; Genet et al. 1986; Georgopoulou et al. 1986; Genet et al. 1987; Albashaireh and Alnegrish 1998; Eleazer and Eleazer 1998), or experience swelling associated with the treated tooth (Walton and Fouad 1992). Because we used pain as the only outcome, our findings are not directly comparable with those of studies that used pain and/or swelling or an unscheduled office visit as the outcome(s).

Current Pain Intensity as a Predictor

Our finding that pretreatment pain predicts posttreatment pain is consistent with several endodontic studies (Seltzer et al. 1961; Genet et al. 1987; Walton and Fouad 1992; Torabinejad et al. 1994; Imura and Zuolo 1995; Glennon et al. 2004). This suggests that this factor is an important predictor of severe posttreatment pain and should be considered when discussing treatment outcomes with patients. Furthermore, it seems logical that future clinical trials focusing on reducing severe postoperative pain following RCT should address this predictor, such as by implementing preemptive analgesia strategies before the initiation of treatment.

Days Kept from Usual Activities and Pain Made Worse with Stress as Predictors

The factors *number of days in the past week kept from usual activities due to pain* and *pain made worse with stress* were found to be predictors of severe posttreatment pain. Neither of these factors has been previously explored as a predictor of severe postoperative pain following RCT. This finding suggests that these factors should be included in future studies that assess posttreatment pain and that collection of this information prior to treatment might be important for prediction and management of posttreatment pain.

Diagnosis of Symptomatic Apical Periodontitis as a Predictor

The diagnosis of symptomatic apical periodontitis was found to be a predictor of severe posttreatment pain. This finding is consistent with Walton and Fouad (1992), who reported that the frequency of flare-ups was higher in patients with diagnoses of acute apical periodontitis and acute apical abscess, and Imura and Zuolo (1995), who found that flare-ups were positively correlated with periradicular pain prior to treatment. Other studies have found no relationship (Harrison et al. 1979). Given that apical periodontitis could include symptomatic and asymptomatic cases in these reports and we found only symptomatic apical periodontitis to predict posttreatment pain, this may account for the inconsistent results in previous studies. Differences in study outcome criteria, patient populations, and study analyses could also contribute to these differences. Furthermore, we found that the presence of an apical radiolucency alone did not predict severe posttreatment pain, providing further support that the symptom of pain associated with symptomatic apical periodontitis is the most important component of the predictor.

Forced Covariates as Adjustors

Dentist Training

There is a paucity of findings related to the relationship between dentist specialty status and posttreatment pain. Walton and Fouad (1992) reported that patients treated by undergraduate students had fewer flare-ups than those treated by residents and faculty, and they suggested that the difference may be the longer time that undergraduate students spent cleaning and shaping the canals. Conversely, Glennon et al. (2004) found no significant difference in postpreparation pain between

Table 2.
Multivariable Logistic Regression Modeling for Predicting Severe Worst Postoperative Pain Intensity ($N = 652$)

	Final Model		Final Model with Literature-Based Risk Factors Included	
Covariate	**OR (95% CI)**	***P* Value**	**OR (95% CI)**	***P* Value**
Sample size	$n = 592$		$n = 575$	
Dentist's training specialty				
General practitioner	1.17 (0.75–1.83)	0.49	0.95 (0.59–1.53)	0.82
Endodontist	1.0		1.0	
Participant's age (1-y increase)	1.00 (0.98–1.01)	0.61	1.00 (0.98–1.02)	0.70
Participant's sex				
Male	0.97 (0.61–1.53)	0.88	1.05 (0.65–1.69)	0.85
Female	1.0		1.0	
Current pain intensity preoperative (1-unit increase)	1.15 (1.07–1.25)	0.0003	1.15 (1.06–1.24)	0.0006
Number days in past week kept from usual activities due to pain (1-d increase)	1.32 (1.13–1.55)	0.0005	1.31 (1.18–1.54)	0.0009
Pain made worse with stress				
Yes	2.55 (1.22–5.35)	0.0130	2.44 (1.14–5.24)	0.0219
No	1.0		1.0	
Diagnosis of symptomatic apical periodontitis				
Yes	1.63 (1.01–2.64)	0.0452	1.52 (0.88–2.61)	0.13
No	1.0		1.0	
Literature-Based Risk Factors				
Diagnosis of necrotic pulp				
Yes	NA		1.25 (0.67–2.34)	0.48
No			1.0	
Swelling with tooth				
Yes	NA		0.77 (0.28–2.12)	0.61
No			1.0	
Apical radiolucency				
Yes	NA		0.67 (0.35–1.29)	0.23
No			1.0	
Maxillary tooth				
Yes	NA		0.67 (0.43–1.06)	0.08
No			1.0	
Posterior tooth				
Yes	NA		1.06 (0.49–2.27)	0.89
No			1.0	
Number of appointments to complete RCT				
≥2	NA		1.34 (0.78–2.28)	0.29
1			1.0	

OR, odds ratio; CI, confidence interval; RCT, root canal therapy; NA, not applicable.

patients treated by general dentists and those treated by endodontists. Given that data about other factors that may be influencing outcomes (e.g., differences in patient referral patterns due to differences in case difficulty) were not present in these reports, it is difficult to assess how training affects the outcome of severe postoperative pain. Furthermore, technical measures of successful treatment (e.g., length of final obturation and treatment misadventures) were not included in these analyses and may be important predictors.

Patient Age

Older patients have been reported to experience more pain following endodontic treatment in several studies (Seltzer et al. 1961; Balaban et al. 1984), whereas many studies have shown no relationship between age and posttreatment pain and exacerbations (Maddox et al. 1977; Georgopoulou et al. 1986; Genet et al. 1987; Mor et al. 1992; Imura and Zuolo 1995). Given that older patients may not have an increased propensity for postoperative pain, in general (Ip et al. 2009), it seems that the impact that age likely has on increased risk for the development of severe postoperative pain is small and should be explored further.

Patient Sex

Females have been shown to have higher levels of posttreatment pain in some studies (Genet et al. 1987; Morse et al. 1987; Torabinejad et al. 1994; Albashaireh and Alnegrish 1998; Al-Negrish and Habahbeh 2006), although other studies have not shown a difference by sex (Clem 1970; Maddox et al. 1977; Oliet 1983; Georgopoulou et al. 1986; Genet et al. 1987; Mor et al. 1992). Given that females may have an increased propensity for postoperative pain in general (Ip et al. 2009), this relationship should be further explored.

Forced Covariates from the Literature

We found that the diagnosis of necrotic pulp, swelling associated with the tooth, tooth type, and the number of appointments did not influence posttreatment pain. Each of these factors has been shown to be related to severe posttreatment pain in some studies; however, none of these factors has consistently been associated with an increased likelihood of severe pain following endodontic treatment (Keiser and Byrne 2011). The lack of association between these factors and severe posttreatment pain suggests that other patient, tooth, and treatment factors may play more important roles in determining posttreatment pain. The differences between our findings and those of previous reports may also reflect differences in study design between our study and previous studies.

Limitations

Worst-pain intensity rating was based on recall, as opposed to obtaining a pain intensity measure each postoperative day. Although subject to potential recall bias, it is unlikely to have played an important role in the study because worst-pain intensity is often best remembered (Haythornthwaite and Fauerbach 2001), and the period of recall was rather brief (only 1 wk). We did not comprehensively assess psychosocial factors. Research exploring postoperative pain in other types of surgery has repeatedly demonstrated their significance as predictors (Ip et al. 2009), so their absence could be influencing the study findings.

Conclusions

Our findings suggest that preoperatively measured factors—preoperative pain intensity, pain interfering with daily activities, pain made worse with stress, and diagnosis of symptomatic apical peridodontitis—are independent predictors of severe pain intensity following RCT. Given that information on these factors could be collected preoperatively, practitioners could use this information to better inform patients about their possibility of developing postoperative pain in the days following treatment and use different pain management strategies for patients more likely to experience severe pain.

Author Contributions

A.S. Law, D.R. Nixdorf, contributed to conception, design, data acquisition, analysis, and interpretation, drafted and critically revised the manuscript; A.M. Aguirre, G.J. Reams, A.J. Tortomasi, B.D. Manne, contributed to data acquisition and interpretation, critically revised the manuscript; D.R. Harris, contributed to data analysis and interpretation, drafted and critically revised the manuscript. All authors gave final approval and agree to be accountable for all aspects of the work.

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