Factors Associated with Apical Periodontitis: A Multilevel Analysis

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Abstract

Introduction: Ignoring the cluster effect is a common statistical oversight that is also observed in endodontic research. The aim of this study was to explore the use of multilevel modeling in investigating the effect of tooth-level and patient-level factors on apical periodontitis (AP). **Methods:** A random sample of digital panoramic radiographs from the database of a dental hospital was evaluated. Two calibrated examiners ($\kappa \geq 0.89$) assessed the technical quality of the root fillings and the radiographic periapical health status by using the periapical index. Descriptive statistical analysis was carried out, followed by multilevel modeling by using tooth-level and patient-level predictors. Model fit information was obtained, and the findings of the best-fit model were reported. **Results:** A total of 6409 teeth were included in the analysis. The predicted probability of a tooth having AP was 0.42%. There was a statistically significant variability between patients ($P < .05$). Approximately 53.16% of the variability was accounted for by the patients, leaving 46.84% of the variability to teeth or other factors. Posterior tooth, inadequate root filling, and age were found to be significantly associated with AP ($P < .05$). **Conclusions:** Multilevel modeling is a valid and efficient statistical method in analyzing AP data. The predicted probability of a tooth having AP was generally small, but there was great variation between individuals. Posterior teeth and those with poor quality root filling were found to be more frequently associated with AP. On the patient level, advancing age was a factor significantly associated with AP. *(J Endod 2016;■:1–5)*

Key Words

Apical periodontitis, endodontic, periapical status, radiographic evaluation, risk factors

Significance

Understanding the epidemiology of AP aids clinicians in identifying and treating patients or teeth at risk of the disease. Furthermore, it will facilitate the targeted distribution of valuable resources, alignment, and planning of dental, especially endodontic, manpower and training.

Apical periodontitis (AP) is an inflammatory disease of endodontic origin (1); it can develop and persist without obvious clinical signs. Therefore, radiologic examination, confirming the presence of a periapical radiolucency, is essential for the diagnosis of AP (2). In epidemiologic research, the periapical index (PAI) is commonly used to categorize the radiographic presentation of the extent of disease (3). Epidemiologic studies permit a disease of interest such as AP to be put in a wider and multifactorial context, thereby complementing our understanding of experimental and controlled studies (4). Although there are many prevalence reports on AP, the efficient use of cross-sectional design in identifying the predictors of the disease is lacking (5).

In the existing prevalence reports, risk factors analysis of AP was done primarily by using bivariate analysis (6–16). Periapical radiolucencies were found more frequently in molar teeth (6–8). Root-filled teeth were consistently found to be associated with AP, especially if the quality of the root filling was inadequate (6, 7, 9–14). At the other extreme, overfilling the canal may likewise compromise periapical health (15, 16). Radiologic assessment indicated that post placement (16) and defective coronal restoration (13, 14) were associated with the presence of periapical radiolucencies. Although these tooth-level variables are useful indicators, patient-level variables such as age and gender have been identified as confounders and adjusted by using multivariate analysis (17).

However, analyzing AP data at a single level assumes each tooth is an independent entity, ignoring the fact that teeth are clustered and correlated within patients, and the risk factors operate differently at each level (18). This can increase the type I error rates and lead to incorrect conclusions (19). Also, it does not explain the variability at different levels, hence reducing its validity (20). Alternatively, the number of teeth with AP can be aggregated and analyzed for each individual, but this approach undermines the statistical power of the study and overlooks important clinical details at tooth level (21).

To date, multilevel modeling was proven useful in understanding periodontal (22) and caries (23) data, particularly in optimizing the use of tooth and surface

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specific information, as well as addressing issues such as estimating variances and detecting covariate effects. Adoption of such statistical approach in endodontics can potentially give new insights in the epidemiology of AP. Epidemiology and public health are closely intertwined; the data will be relevant to everyday clinical practice. Furthermore, it will facilitate the targeted distribution of valuable resources, alignment, and planning of dental, especially endodontic, manpower and training. Therefore, the aim of this study was to explore the use of multilevel modeling in investigating the effect of tooth-level and patient-level factors on AP. Specifically, the research questions posed were as follows:

1. What is the predicted probability of a tooth having AP?
2. Does the predicted probability of having AP vary between patients?
3. What is the association between each variable and the likelihood of having AP while controlling for other tooth and patient characteristics?

Materials and Methods

A retrospective study was conducted by using digital panoramic radiographs taken from patients attending the dental clinics at Faculty of Dentistry, Universiti Kebangsaan Malaysia, Kuala Lumpur. Ethical approval for this study was obtained from the Universiti Kebangsaan Malaysia Research Ethics Committee (UKM 1.5.3.5/244/DD/2014/004(1)). All of the digital panoramic radiographs were taken by 3 trained and qualified radiographers who used Sirona Orthophos (Sirona Dental System GmbH, Bensheim, Germany) and Kodak 9000/9000D (Dental Systems Group, Carestream Health Inc, Kodak Dental Systems, Marne-la-Vallée, France).

Sample size estimation was calculated by using the following formula (24):

$$n = \frac{Z^2 P\,(1-P)}{d^2}$$

The prevalence (P) of AP found on radiographic assessment was estimated at 13.6% (25). The Z value was 1.96 for 95% confidence interval, and the precision level (d) was determined at 0.05. From the above formula, the sample size required was 184 patients. Assuming that 25% of the panoramic radiographs could not be used because of inadequate quality, the sample size was increased by 25%. Therefore, the minimum number of patients required was 230.

The sampling frame consisted of collated prescription forms for digital panoramic radiographs taken during 2011–2012. From the prescription forms, information regarding the patients' gender and age as well as the reason/s the panoramic radiographs were taken was recorded in chronological order; this then provided guidance as to the suitability of a particular radiograph. The inclusion criterion was a digital panoramic radiograph taken on a patient 18 years or older. If multiple radiographs for a patient were available, only the earliest dated radiograph was used. To avoid overestimation of disease prevalence, radiographs taken for the sole purpose of diagnosing AP were excluded. Radiographs of fully edentulous patients were also excluded. Random sampling was then performed by using the computer-generated random number. Once selected, the corresponding digital panoramic radiograph was retrieved.

Radiographic Evaluation

The radiographic periapical health status and technical quality of the root fillings were assessed by 2 examiners who viewed on a 19-inch computer screen calibrated for medical imaging and used Digora for Windows 2.6 (Soredex, Tuusula, Finland). The periapical health status of each tooth was assessed by using the PAI (3). For a multirooted tooth, the worst PAI score was recorded. Teeth were classified as root-treated if they contained a radiopaque material in the pulp chamber and/or in 1 or more root canals (12). The root filling was considered adequate if it terminated within 0–2 mm from the radiographic apex and without any visible void (26). Teeth that were not possible to assess radiographically because of superimposition of anatomic structures were excluded from the study. Additional periapical radiographs, if available, were used to confirm the presence of periapical radiolucencies. The films were examined in a darkened room on an illuminated viewer box by using the PAI.

The 2 examiners were calibrated beforehand by using 10 digital panoramic radiographs that were not part of the randomized sample. Both examiners viewed the panoramic radiographs independently, and intra-examiner and inter-examiner agreement was determined by using Cohen kappa coefficient (κ). For intra-examiner assessment, a second reading was scored 1 month later. The κ for intra-examiner agreement was 0.91 for the evaluation of the periapical health status and 0.95 for technical quality of root canal filling. Similarly, inter-examiner agreement of $\kappa = 0.95$ and $\kappa = 0.89$ was achieved for the detection of AP and the categorization of the quality of the root fillings, respectively. These results indicated a high intra-examiner and inter-examiner agreement.

Data Analysis

Multilevel modeling was carried out by using PROC GLIMMIX and the Laplace estimation method in SAS 9.4 (SAS Institute, Cary, NC). Hierarchical generalized linear models were built to investigate the association between AP and risk indicators at both levels.

The PAI score was dichotomized and used as the outcome variable. A PAI score of more than 2 was considered a sign of periapical disease. Suppose y_{ij} is the dichotomized PAI outcome for tooth i in patient j and x_{ij} is an explanatory variable at the tooth level. The probability of having AP is represented as $p_{ij} = Pr(y_{ij} = 1)$, where y_{ij} follows a binomial distribution. First, a simple tooth-level model was estimated by using the logit link function.

$$\log\left[\frac{p_{ij}}{\left(1-p_{ij}\right)}\right] = \beta_{0j} + \beta_{1j}x_{1ij} + \beta_{2j}x_{2ij} + \beta_{3j}x_{3ij} + \beta_{4j}x_{4ij} \qquad \text{(Equation 1)}$$

In Equation 1, β_{0j} represents the intercept, the average log odds of a tooth having AP. The binary predictors are anteroposterior location of the tooth (x_1), maxilla-mandibular location of the tooth (x_2), root-filling adequacy (x_3), and root-filling inadequacy (x_4). β_{ij} represents the coefficient of tooth-level predictor x_i. The error variance is not estimated separately at tooth level because it is determined directly by the population mean (27).

$$\beta_{0j} = \gamma_{00} + \gamma_{o1}W_{1j} + \gamma_{o2}W_{2j} + u_{0j} \qquad \text{(Equation 2)}$$

$$\beta_{ij} = \gamma_{i0}$$

Equation 2 represents a simple patient-level model, in which γ_{00} is the log odds of a patient having AP, W_{1j} is the age (continuous variable), and W_{2j} is the gender of the patient. γ_i represents the coefficient of patient-level predictor W_i, and u_{0j} is the patient-level error term. Each of the coefficients of tooth-level predictor (β_{ij}) is equal to the

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