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*Corresponding author

Christine Peters, School of Dentistry, The University of Queensland, Oral Health Centre, Herston, Qld, Australia

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Research Article

Cross-Sectional Study Correlating Findings from Full-Mouth Radiographs to Patients' Epidemiologic and System Health Data

Byung K Choi[1], Christine I Peters[1,2], Aparna Nidamarthi[1], Ana Arias[3] and Ove A Peters[1,2]

[1]*Department of Endodontics, University of the Pacific, Arthur A. Dugoni School of Dentistry, USA*

[2]*School of Dentistry, The University of Queensland, Brisbane, Australia*

[3]*Department of Conservative Dentistry, School of Dentistry, Complutense University, Spain*

Abstract

This study correlated radiographic findings to epidemiologic data and systemic health records. A representative sample of full mouth radiographs (n=1545) was analysed. Systemic health information regarding Diabetes Mellitus (DM), Human Immunodeficient Virus (HIV) infection, neuropathy, Cardiovascular Disease (CVD), corticosteroid consumption, chemotherapy, and bisphosphonate consumption was collected by reviewing charts and multivariate regression analyses were performed. Patients with crestal bone loss had fewer teeth, more implants, Root-Canal Filled Teeth (RFT), and more teeth with radiolucent areas (PRRL). Prevalence of crestal bone loss increased with age; HIV-positive patients had fewer teeth while patients with neuropathy had more implants and RFT. Presence of DM, CVD, or history of corticosteroid, bisphosphonates, or chemotherapy did not affect numbers of teeth, implants, RFT and PRRLs. The presence of PRRLs and crestal bone loss was not significantly associated with any of the systemic factors. Radiographic endodontic outcomes may not be negatively impacted by the systemic conditions investigated.

Introduction

Since the promotion of the focal infection theory in the early nineteen-hundreds [1], attempts have been made to link localized oral infection to the general health of a patient. Research in the last few decades has often led to inconclusive results, some showing supporting evidence while others denied the association of general health issues with periodontal disease [2]. The current general consensus appears to be that, while there is a statistical association between "periodontal health" variables and "cardiovascular health" variables, a cause-and-effect relationship has not been conclusively demonstrated [2]. Systemic diseases such as Diabetes Mellitus (DM) type 1 and 2 affect wound healing mainly due to a negative impact on microcirculation. Patients with DM and marginal periodontitis displayed impaired healing, worse periodontal destruction and increase in insulin resistance [3]. Neuropathy is a common clinical sequalae of type 1 DM and associations between periodontal disease and neuropathy exist [4]. Patients with Human Immunodeficiency Virus (HIV) infection present accelerated clinical attachment loss compared to healthy individuals [5]. Moreover, certain systemic drugs cause a higher incidence of marginal periodontitis. For example, individuals with chronic inflammatory diseases or cancers receive drugs that dampen inflammation by reducing cytokine production or by acting as antiangiogenics. Antirheumatic drugs such as methotrexate suppress neutrophil activities and inhibit productions of proinflammatory cytokines. Conversely, bisphosphonate treatment impedes bone turnover and thus may modulate healing of apical periodontitis. Conceivably, these pharmacological effects modulate the immunological response of the periodontium in primary periodontal conditions and in primary endodontic periapical pathosis [6,7]. Data on an potential association between periradicular inflammation and systemic health is relatively sparse [8], but research is currently laying the groundwork in the area. Assiri et al. [9] assessed fifteen medical conditions, correlated these to an oral health index based on ten oral-health related variables observed on panoramic radiographs and found significantly poorer oral health in patients with a medical history of systemic diseases such as diabetes mellitus and hypertension [9]. Studies recorded increased levels of systemic inflammatory markers in patients with apical periodontitis in the absence of marginal periodontitis [10].

A positive association between periapical pathosis and elevated systemic oxidative stress has been identified [11]. Both a Brazilian study and a US study discovered a higher risk of developing Cardiovascular Disease (CVD) in patients with apical periodontitis [12,13]. Pulps from patients with DM displayed a limited collateral circulation compared to healthy controls, which resulted in a compromised immune response with increased risk of pulp infection and necrosis [14]. In a cross-sectional study, apical periodontitis was significantly more prevalent in untreated teeth in type 2 diabetics [15]. There is conflicting evidence for the effect of an HIV infection on the development of endodontic disease or the healing of the disease after treatment; Quesnell et al (2005) did not find evidence for inferior outcomes after root canal treatment in HIV positive patients, compared to healthy controls. Conversely, a recent study (14) found that compromised immune status in HIV positive patients may lead to a higher prevalence of the disease and poorer prognoses of root canal treatments, due to the reduced number of functional T cells [16]. Several clinical studies indicated that there was no statistical difference in the prevalence of periapical lesions [17] and in the degree of healing [18] after endodontic treatment between HIV infected patients and the immunocompetent controls. Associations between certain systemic drugs and periradicular healing were also investigated. Patients with past medical history of organ transplant, Sjögren disease, or cancer treatment often are prescribed immunosuppressants such as cytostatic drugs or corticosteroids. These medications reduce the ability to contain infections. For example, Cotti et al. [19] reviewed the effects of TNF alpha inhibiting drugs on periapical disease and concluded that modulation in cytokine levels may influence the rate of periapical healing when root canals were simultaneously disinfected [19]. A lack of interventional studies limits our understanding of the implication of periradicular pathosis on systemic health, but more information must be gathered before designing such studies. One obstacle is the highly variant rate of periradicular pathosis and systemic disease among different populations. More cross-sectional studies of different populations with larger sample sizes have been advocated [20]. Therefore, the aim of this study was two-fold: i) to assess full-mouth radiographs for the numbers of existing teeth, implants, Root Filled Teeth (RFT), the Presence of Periradicular Radiolucencies (PRRLs) and crestal bone loss in an adult population,

and ii) to associate the radiographic findings to epidemiologic data and systemic health of the patients.

Materials and Methods

The protocol for this study was approved by the Institutional Review Board at the University (IRB Approval No.10-28.7).

Case Selection

Between January 2006 and July 2012, over 9000 full mouth series of digital radiographs were obtained during regular intake assessment for patients at the University Dental School. For the present investigation, each patient was sequentially allocated into a ten-year age bracket and was assigned a random number. Patients were listed in ascending order in their age subgroup, based on their random numbers. The age groups were: 21-30, 31-40, 41-50, 51-60, 61-70, 71-80, and 81-90 years old. Patients younger than 21 or older than 90 years of age were excluded from this study. Based on a preliminary feasibility study, random representative subsamples of 250 patients each were extracted per age group, except for the oldest group where only 188 patients were available. Randomisation was based on adding a random number from random.org to each data set. Patient inclusion criteria required all preexisting radiographs be captured in the last five years from the day of the reading, yielding a total of 1592 patients. Full mouth series from the initial 1592 patients were further screened for record completeness. Forty data sets were excluded due to incomplete intake record and seven due to lacking demographic information. A total of 1545 patients with complete records who met the inclusion criteria remained for this study.

Radiographic Recording and Analysis

Preexisting full mouth series for each included patient consisted of 14 periapical images and 4 bitewings. All radiographs were captured with a "GSX 700" x-ray unit (Gendex Corporation, Milwaukee, Wisconsin, USA), using the paralleling technique, and adhering to the manufacturer's recommended exposure settings for size and age. All images were stored in MiPACs (Medicor Imaging, Charlotte, NC, USA). Bitewing radiographs were assessed for the presence or absence of radiographic crestal bone loss. The periapical status for all teeth with PRRL or root filling was assessed using the 5-score periapical index (PAI) system developed by Ørstavik et al. [21]; the assessors were endodontists-specialists (CIP, OAP) with>20 years clinical experience. Prior to the evaluation of radiographs for the study, the observers participated in a standard calibration process for PAI. Calibration was performed as described by Ørstavik et al. [21], using 100 sample radiographs until an agreement of 60% or better was reached. Periapical radiolucency was later classified as "absent" if PAI ≤ 2, or "present" if PAI ≥ 3. The highest score of all roots was considered for multi-rooted teeth. Descriptions of each score level were as follows: 1) normal periapical structures; 2) small changes in bone structure; 3) changes in bone structure with some mineral loss; 4) periodontitis with well-defined radiolucent area; 5) severe periodontitis with exacerbating features. Two calibrated observers (AN & CP) independently examined the radiographs. In equivocal cases, a discussion ensued, and consensus was reached. All results were entered directly into an input mask.

General Health Variables

The following health variables were obtained from each patient's Axium chart record and registered: presence of DM, HIV infection, neuropathy, CVD, and medications including corticosteroids, chemotherapy drugs, and bisphosphonates. The World Health Organization defines CVD as a group of disorders of the heart and blood vessels that include coronary heart disease, cerebrovascular disease, peripheral arterial disease, rheumatic heart disease, congenital heart disease, deep vein thrombosis and pulmonary embolism. In addition, patients with a history of hypertension, artificial heart valve or stent placement, and bypass surgery were also included in this category [22].

Data tabulation

The university's Informational Technology department designed an input mask for this study. The following information was collected for each patient: Randomized patient number, patient age, sex, date of full mouth radiographs, number of teeth in the radiographs, number of RFT, number of teeth with PRRL, location of PRRL noted as periapical, and/or lateral and furcal, number of implants, presence of crestal bone loss, history of systemic diseases, history of systemic medications, and PAI score (Figure 1).

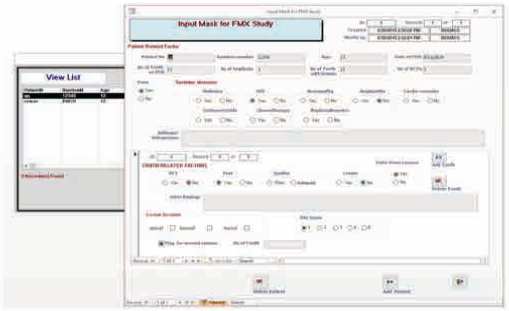

Figure 1: Mask used for data entry into the database.

Statistical analysis

Associations among demographic factors, including age and sex, and systemic health factors with the numbers of existing teeth, implants, RFT, and teeth with PRRL, were assessed with linear regression analysis. A logistic regression analysis was also performed to assess the impact of demographic and systemic health factors on the presence of crestal bone loss and PRRLs. For patients with multiple teeth, the highest PAI scoring tooth was used for later analysis. All statistical analyses were performed with SPSS, version 10 (SPSS Inc., Chicago, IL, USA) and p value was considered significant at 0.05.

Results

Demographic, systemic and radiographic findings

The average patient age (standard deviation, SD) included in the study sample was 54.57 (19.15) years; 56.5% of the patients were male and 43.5% were female. The average (SD) numbers of existing teeth, implants, RFT, and teeth with PRRL were 24.9 (5.5), 0.13 (0.53), 1.32 (1.7), and 0.43 (0.85), respectively (Table 1). A total of 432 PRRLs were detected in 28.0% of the patients. Radiographic crestal bone loss was detected in 996 patients or 62.5% of study subjects (Table 1). The percentage of patients with at least one tooth with PRRL among different age groups ranged between 17.2-36.0% (Figure 2). PRRLs were further categorized as periapical, lateral, and furcal types. Of all teeth assessed radiographically, 19.34% showed periapical, 2.11% showed lateral, and 2.34% furcal radiolucency (Figure 3). In a total of 798 (51.7%) patients at least one of the health variables queried on data collection was present. From those, 500 patients reported one systemic health factor, 230 reported two, 55 reported three, 10 reported four, and 3 reported five (Figure 4). Of all patients with one or more systemic health factors, 231 (53.3%) patients had at least one or more PRRLs (Table 2).

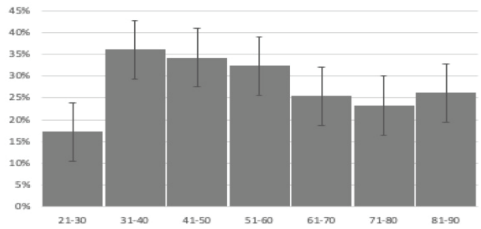

Figure 2: Percentages (and 95% confidence intervals) of patients with at least one tooth with periradicular radiolucencies.

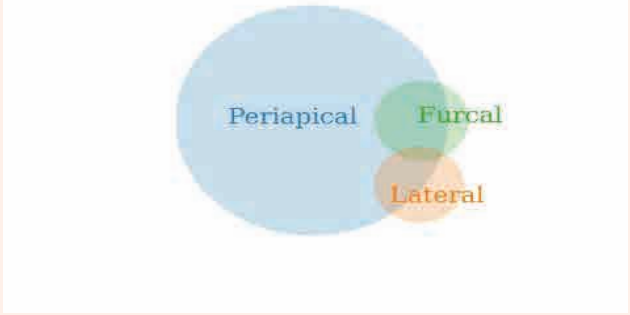

Figure 3: Periradicular radiolucency subclassification.

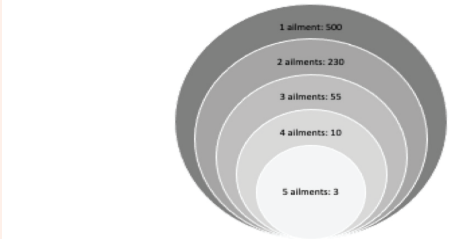

Figure 4: Numbers of reported systemic health factors.

Table 1: Distribution of patients with regards to age, sex, average numbers of existing teeth, implants, root filled teeth, teeth with periradicular radiolucencies, and presence of cresta bone loss.

Age Group	Female (%)*	Male (%)*	No. of patients (%)‡	Average no. of existing teeth (SD)	Average no. of implants (SD)	Average no. of root filled teeth (SD)	Average no. of teeth with periradicular radiolucency (SD)	No. of patients with at least one tooth with periradicular radiolucency (%)*	Presence of radiographic crestal bone loss (%)*
21-30	125 (56.6)	96 (43.4)	221 (14.3)	28.1 (1.9)	0.03 (0.21)	0.58 (1.2)	0.25 (0.65)	38 (17.2)	7 (3.2)
31-40	106 (47.1)	119 (52.9)	225 (14.6)	27.4 (2.7)	0.10 (0.42)	1.13 (1.6)	0.63 (1.07)	81 (36.0)	32 (14.2)
41-50	70 (29.2)	170 (70.8)	240 (15.5)	26.6 (3.1)	0.10 (0.44)	1.32 (1.7)	0.45 (0.78)	82 (34.2)	105 (43.8)
51-60	81 (34.9)	151 (65.1)	232 (15.0)	25.4 (4.4)	0.18 (0.58)	1.31 (1.7)	0.53 (0.98)	75 (32.3)	202 (87.1)
61-70	90 (39.5)	138 (60.5)	228 (14.8)	24.0 (5.5)	0.14 (0.45)	1.82 (1.9)	0.37 (0.81)	58 (25.4)	226 (99.1)
71-80	101(47.9)	110 (52.1)	211 (13.7)	22.5 (5.8)	0.29 (0.96)	1.70 (1.7)	0.34 (0.72)	49 (23.2)	208 (98.6)
81-90	94 (50.0)	94 (50.0)	188 (12.2)	20.2 (7.4)	0.04 (0.22)	1.38 (1.9)	0.38 (0.75)	49 (26.1)	186 (98.9)
Total	672 (43.5)	873 (56.5)	1545 (100)	24.9 (5.5)	0.13 (0.53)	1.32 (1.7)	0.43 (0.85)	432 (28.0)	966 (62.5)

Table 2: Prevalence of periradicular radiolucencies in patients with a systemic health factor.

	Patients with periradicular radiolucencies / total patients with systemic health factor (%)	Patients with periradicular radiolucencies / total patients lacking systemic health factor (%)
DM	95/329 (28.9%)	337/1216 (27.7%)
HIV	60/218 (27.5%)	372/1327 (28.0%)
Neuropathy	5/14 (25.7%)	427/1531 (27.9%)
CVD	132/482 (27.4%)	300/1063 (28.2%)
Corticosteroid consumption	7/36 (19.4%)	425/1509 (28.2%)
History of chemotherapy	13/61 (21.3%)	419/1484 (28.2%)
Bisphosphonate consumption	12/40 (30.0%)	420/1505 (27.9%)
Total	231/798 (28.9%)	201/747 (26.9%)

Association of radiographic findings to epidemiologic data and systemic health

The number of existing teeth significantly decreased with age ($p < 0.001$), in patients presenting with radiographic crestal bone loss ($p = 0.02$), and in HIV-seropositive patients ($p = 0.008$). The number of implants was significantly higher in patients with radiographic crestal bone loss ($p = 0.01$) and in patients with neuropathy ($p = 0.025$). The number of RFT was significantly higher in females ($p = 0.049$), patients with radiographic crestal bone loss ($p < 0.001$), and patients with neuropathy ($p = 0.026$). The number of teeth with PRRLs significantly increased with age ($p < 0.001$) and with the presence of radiographic crestal bone loss ($p < 0.001$) but showed no significant association with any of the systemic health factors considered. Consumption of corticosteroids, bisphosphonates, and history of chemotherapy did not show statistically significant difference in the numbers of existing teeth, implants, RFT, and teeth with PRRLs (Table 3). Presence of radiographic crestal bone loss showed significant association with age (OR: 1.21, 95% CI: 1.18-1.23). Presence of radiographic crestal bone loss and presence of one or more PRRLs were associated with neither sex nor any of the systemic health factors considered (Table 4).

T able 3: Regression analysis investigating association among demographic, dental and systemic health factors.

	No. of teeth			No. of implants			No. of root filled teeth			No. of teeth with periradicular radiolucencies		
	β§	95% CI	p*	β§	95% CI	p*	β§	95% CI	p*	β§	95% CI	p*
Age	-0.39	-0.13, -0.09	<0.001			n.s.			n.s.	-0.24	-0.14, -0.01	<0.001
Sex			n.s.			n.s.	-0.05	-0.36, 0	0.049			n.s.
Presence of crestal bone loss	-0.08	-1.62, -0.12	0.023	0.1	0.03, 0.19	0.011	0.19	0.41, 0.95	<0.001	0.27	0.34, 0.61	<0.001
DM			n.s.			n.s.			n.s.			n.s.
HIV	-0.06	-1.61, -0.24	0.008			n.s.			n.s.			n.s.
Neuropathy			n.s.	0.06	0.04, 0.59	0.025	0.06	0.12, 1.91	0.026			n.s.
CVD			n.s.			n.s.			n.s.			n.s.
Corticosteroid medication			n.s.			n.s.			n.s.			n.s.
History of chemotherapy			n.s.			n.s.			n.s.			n.s.
Bisphosphonate medication			n.s.			n.s.			n.s.			n.s.

Source: § Standardized coefficient
CI, Confidence interval
*The significance level is set to p = 0.05.

Table 4: Logistic regression analyses for presence of crestal bone loss and periradicular radiolucencies as dependent variables.

	Presence of crestal bone loss		Presence of periradicular radiolucencies	
	Adjusted OR (95% CI)	p-value*	Adjusted OR (95% CI)	p-value*
Age	1.21 (1.18-1.23)	<0.001	1.00 (0.99-1.01)	0.82
Sex	0.73 (0.49-1.10)	0.271	1.17 (0.92-1.49)	0.19
DM	1.23 (0.80-1.89)	0.759	1.03 (0.78-1.37)	0.84
HIV	0.95 (0.58-1.56)	0.657	0.98 (0.70-1.36)	0.89
Neuropathy	0.15 (0.01-1.60)	0.339	1.43 (0.47-4.34)	0.53
CVD	1.01 (0.63-1.64)	0.954	0.98 (0.74-1.29)	0.87
Corticosteroid consumption	0.45 (0.12-1.64)	0.524	0.66 (0.28-1.55)	0.34
History of chemotherapy	1.25(0.36-4.33)	0.512	0.72 (0.38-1.36)	0.32
Bisphosphonate consumption	0.26 (0.01-5.29)	0.3	1.26 (0.62-2.57)	0.53

Source: OR, Odds ratio
CI, Confidence interval
* The significance level is set to p = 0.05.

Discussion

Out of 9000 full mouth series of digital radiographs taken during new patient assessment at the University Dental School, 1592 patients between 21 and 90 years old were randomly selected. Radiographic assessment occurred for the numbers of existing teeth, implants, root filled teeth (RFT), the presence of periradicular radiolucencies (PRRLs) and crestal bone loss. The radiographic findings were analysed regarding epidemiologic data and systemic health affected by DM, HIV infection, neuropathy, CVD, and medications including corticosteroids, chemotherapy drugs, and bisphosphonates. CVD accounts for nearly one-third of deaths worldwide annually. Approximately 32-50% of US population [23], or roughly one in three American adults, has high blood pressure and is at risk of coronary heart disease and cerebrovascular disease [24]. The implications of the data are alarming and the WHO has set an action plan for 25% reduction of hypertension by 2020 [23]. This plan has recently been extended to 2025. Reportedly, Hippocrates claimed more than 2000 years ago that curing systemic disease by pulling out infected teeth [25] was possible, and since that time, clinicians and scientists have sought to understand the impact of oral health on systemic health such as CVD. The vast majority of current studies are cross-sectional and look at snapshots of patients [26], but a few cohort studies also have contributed to the research Endeavor [27]. A randomized controlled trial assessed the effect of periodontal treatment on low birth weight of newborns [28]. In the current cross-sectional study, we investigated the associations between prevalence of PRRL and systemic health factors using full mouth radiographs and chart records. According to the Centers for Disease Control (CDC) and Prevention Report from 2005, the mean number of teeth in the permanent dentition among adults 20 years of age or older is 23.95 [29]. The numbers of existing teeth in the current study in corresponding age groups were slightly higher than the CDC report, possibly because the need for full mouth radiographs is more biased towards dentate patients. Previous studies demonstrated an increasing number of root canal treatments and higher prevalence of periapical radiolucency with age [26].

The regression analysis from the current study, on the other hand, did not show association between the number of RFT and age while the number of teeth with PRRL diminished with age. The decreasing trend with age may be explained by the fact that teeth with the worst diagnosis are generally the earliest to get extracted, leaving fewer teeth to consider. The results of the logistic regression analysis also found a similar rate of prevalence of PRRL in all age groups although the total number of teeth changed. In other words, without any information about previously extracted teeth, it is difficult to determine a true association between prevalence of PRRL and age in cross-sectional studies. Since the rate of osseointegration with implants decreases with increasing age [30], less implant survival has been anticipated with advancing age. In contrast, the current investigation found no variation in the number of implants with increasing age. It is, however, important to note that this study did not assess the quality of osseointegration. While sex caused no difference in the numbers of remaining teeth, implants, or teeth

with PRRL, female patients had greater number of RFT compared to males. This may indicate that female patients are more inclined to seek root canal treatments, and this observation is consistent with a previous study [31]. In the current study, the presence of HIV infection was associated with a lower number of remaining teeth when compared to the healthy patients. Yeung et al. found a higher chance of developing periodontal conditions that can lead to tooth loss in HIV-positive patients [5]. On the other hand, Engeland et al. [32] investigated the association between HIV infection and tooth loss and concluded that the rate of tooth loss in HIV sero-positive individuals was not different from that of the healthy group regardless of the severity of the disease progression. These conflicting outcomes should be interpreted with caution. Only sparse data on the matter exists, and sample populations are widely different from one another. The latter study recruited HIV sero-positive patients from an existing pool of patients, who had undergone periodontal maintenance with periodic assessment for CD4+ cell count and viral load. The current study, on the other hand, relied on new patients' self-report of HIV status, and the history of periodontal maintenance was unknown. Moreover, it should be noted the Dental School Clinic cares for HIV-patients enrolled in a special program and these patients may have certain co-morbidities not specifically assessed in the current study. Indeed, a previous report noted a similar success rate of root canal treatments in an HIV-positive group compared to a healthy group [18]. In our data, both the HIV positive and the healthy groups presented similar prevalence of PRRL and number of RFT. These findings substantiate the claim that HIV status of a patient has little to no effect on healing after endodontic treatment.

Endodontists are faced with diagnostic challenges daily, e.g., to distinguish odontogenic pain from non-odontogenic pain. Estimates claim that 3.4% of endodontic treatments are performed as a consequence of misdiagnosed non-odontogenic pain [33]. We found an association between neuropathy and increasing number of implants and root canal treatments. This could indicate that some treatments were the consequences of misdiagnosed non-odontogenic pain. A longitudinal study should be carried out to elucidate the effect of misdiagnosed neuropathy on a treatment decision. Several authors agree that presence of CVD is correlated with higher prevalence of endodontic pathosis. In Khalighinejad et al.'s systematic review of the topic [34], the majority of investigators showed a positive correlation with varying degrees of odds ratio [12,13]. In regard to CVD's correlation with endodontic pathosis, the results of the current study differ from the general consensus found in the literature in that no correlation was noted. Conversely to the effect of CVD, there is no consensus in the literature on correlation between DM and endodontic pathosis. Marotta et al. reported a positive correlation between endodontic pathosis and DM [15], but Britto et al., in line with the results of the current investigation, reported no significant association between the two [35]. Reasons for discrepancies between the studies may be due to variations in the inclusion criteria and samples. For instance, the current investigation included hypertension in the definition of CVD, and hypertension was the most common type of CVD factor noted in our investigation, but most other studies did not include hypertension as a CVD.

A recent systematic review associated periapical pathoses to three autoimmune disorders (rheumatoid arthritis, diabetes mellitus Type I, and inflammatory bowel disease) [36]. Bender and Bender showed difference in the success rate of an endodontic treatment between the patients with controlled and uncontrolled DM [37], but the current investigation did not distinguish the two. In our analysis, radiographic crestal bone loss was correlated with a lower number of remaining teeth, more implants, more RFT, more teeth with PRRL, and older age. With respect to age-related prevalence of marginal periodontitis, a positive association was explained in NHANES' report [38]. Assuming that the radiographic crestal bone loss is generally due to a periodontal disease, the correlation results found in the current investigation are consistent with other studies. Khalighinejad et al. showed teeth with mild periodontitis are twice as likely to get extracted than periodontally healthy teeth; hence, the lower number of natural dentition in patients with periodontitis [39]. If there are more missing teeth in patients with periodontitis, it naturally follows that the patients would be more inclined to replace these teeth with implants and preserve remaining teeth by receiving root canal treatments. Ruiz et al. showed that the risk of developing apical periodontitis in endodontically treated teeth is 5.2 times greater for patients with periodontal disease [40], while Jansson's study of 1,152 dentate patients showed that the relative frequency of root canal treated teeth with apical periodontitis was significantly higher in patients with more marginal bone loss [41]. The results of these studies are consistent with the current investigation with radiographic bone loss. In contrast to the findings from previous studies [19,42], the current investigation did not find significant difference in the prevalence of periapical radiolucency in patients with a history of corticosteroid or bisphosphonate consumption. With regards to the effect of neuropathy and history of chemotherapy, the current investigation also did not find significant difference in the prevalence of apical periodontitis, but no research study was found in the literature to compare our results.

Conclusion

Presence of periradicular radiolucencies and presence of crestal bone loss were not associated with any of the systemic factors considered. Crestal bone loss was associated with older age, fewer teeth, more implants, more root filled teeth, and more teeth with periradicular radiolucencies. Human immunodeficient virus infection was associated with fewer teeth, and neuropathy was associated with a greater volume of implants and root canal treatments. Considering the paucity of literature on the topic and the limitations of a cross-sectional study, future longitudinal study designs would be advantageous in confirming the associations found in the current study.

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