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Periodontal Disease and Incident Venous Thromboembolism: The Atherosclerosis Risk in Communities Study

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Abstract

Aim—Periodontal disease is a cardiovascular disease (CVD) risk factor but few studies have considered the relationship between periodontal disease and venous thromboembolism (VTE). We hypothesized that periodontal disease is independently associated with increased risk of incident VTE.

Materials and Methods—We used data from 8,092 participants of the Atherosclerosis Risk in Communities (ARIC) study to examine periodontal disease in 1996–1998 and incident VTE through 2011. Periodontal disease was determined using self-reported tooth loss due to gum disease and dental exams. Cox-proportional hazards regression models were used to estimate hazard ratios for VTE and 95% confidence intervals adjusted for relevant confounders.

Results and Conclusions—Participants were on average 62.7 years old at baseline and 13.9% self-reported tooth loss from gum disease. Over a mean of 12.9 years of follow-up there were 313 incident VTE events. Self-reported tooth loss due to gum disease was associated with 30% higher VTE risk (HR = 1.29 (0.96, 1.73) after adjusting demographic factors, SES, periodontal risk factors, oral hygiene, and access to dental care variables. No statistically significant associations between clinical measures of periodontitis and VTE were observed after adjustment. Further research is needed to elucidate if a relationship between periodontal disease and VTE exists.

Introduction

Periodontal disease is a chronic inflammatory disease caused by bacterial infection of the supporting tissues around the teeth.(Offenbacher, 1996) Periodontitis is common with 46% of US adults having any periodontitis and 9% having severe periodontitis.(Eke et al., 2015) It is a significant contributor to tooth loss among adults in the United States.(Ong, 1998)

Periodontitis may be related to venous thromboembolism (VTE) through infection-induced systemic inflammation that contributes to platelet aggregation and hypercoagulability. (Blaizot, Vergnes, Nuwwareh, Amar, & Sixou, 2009) Existing studies have shown that periodontitis is associated with higher levels of systemic inflammatory markers including interleukin-6 (IL-6)(Loos, Craandijk, Hoek, Wertheim-van Dillen, & van der Velden, 2000), C-reactive protein (CRP)(D'Aiuto et al., 2004; Loos et al., 2000), fibrinogen,(Chandy et al., 2017; Kweider, Lowe, Murray, Kinane, & McGowan, 1993) and soluble intercellular adhesion molecule-1 (sICAM-1).(Hannigan, O'Connell, Hannigan, & Buckley, 2004) Higher levels of inflammatory markers have also been associated with increased risk of VTE.(Folsom, Lutsey, Astor, & Cushman, 2009)

VTE, comprising deep vein thrombosis (DVT) and pulmonary embolism (PE), is a common, life-threatening disease in the United States with over 500,000 hospitalized cases annually. (Centers for Disease & Prevention, 2012) Previous epidemiologic research has identified numerous VTE risk factors including immobilization, surgery, trauma, cancer, older age, family history of VTE, genetically-determined hypercoagulable states, oral contraceptive use, and obesity.(Anderson & Spencer, 2003; Mahmoodi et al., 2017) Though multiple individual studies and meta-analyses have reported an association between periodontal infection and increased risk of atherosclerotic CVD,(Blaizot et al., 2009; Leng, Zeng, Kwong, & Hua, 2015) to date only one study has explored a possible association between periodontitis and VTE. Sanchez-Siles et al. found that periodontitis was more prevalent among 97 VTE patients compared to 100 healthy controls in an unadjusted analysis (OR = 3.33 (95% CI 1.83, 6.06)), thus supporting a potential association between periodontal disease and VTE risk.(Sanchez-Siles, Rosa-Salazar, Camacho-Alonso, Salazar-Sanchez, & Cozar-Hidalgo, 2013)

The prospective Atherosclerosis Risk in Communities (ARIC) cohort has ancillary studies that conducted dental exams and validated VTE events. Using these data we examined the relationship between periodontal disease and risk of incident VTE. We hypothesized that periodontal disease is independently and positively associated with incident VTE risk and that the risk is graded such that the association between periodontal disease and VTE is strongest among those with more severe periodontal disease.

Methods

LITE is a prospective study of VTE occurrence in 2 pooled, multicenter, longitudinal population-based cohort studies: the Atherosclerosis Risk in Communities (ARIC) study and the Cardiovascular Health Study (CHS). The LITE study design, methods, and VTE incidence rates have been described in detail elsewhere.(Tsai et al., 2002) For these analyses, only ARIC data were included due to the availability of dental information collected at visit 4 during the dental ancillary study (D-ARIC). The ARIC study is a multi-center population-based prospective cohort study designed to investigate the etiology and natural history of atherosclerosis.(The ARIC investigators, 1989) At baseline in 1987–1989 (visit 1), 15,792 predominantly white and black men and women aged 45–64 years were selected from 4 US communities: Forsyth County, North Carolina; Jackson, Mississippi; suburbs of Minneapolis, Minnesota; and Washington County, Maryland.(The ARIC investigators, 1989)

Subsequent ARIC exams took place with ARIC study participants during 1990 to 1992 (visit 2), 1993 to 1995 (visit 3), 1996 to 1998 (visit 4), 2011 to 2013 (visit 5), and 2016 to 2017 (visit 6). (The ARIC investigators, 1989)

The purpose of D-ARIC was to determine the prevalence, extent, and severity of periodontal conditions in the dentate ARIC population and describe the association between those conditions and prevalent CHD and atherosclerosis. (Elter, Champagne, Offenbacher, & Beck, 2004) The D-ARIC study was an ARIC ancillary study that took place among ARIC participants at all study sites during visit 4 (1996–1998). All ARIC participants who had natural teeth, no contraindications, and did not require antibiotic prophylaxis for periodontal probing were eligible to participate in D-ARIC. Details of the D-ARIC study objectives and methodology have been described in a previous publication. (Beck et al., 2001)

For the present analyses, we used a prospective cohort study design. Visit 4 (1996–1998) which was attended by 11,656 total ARIC participants was used as the baseline for these analyses. All ARIC participants who reported being edentulous at visit 4 (n=1,651) and those who completed the D-ARIC exam (n=6,793) were included. We excluded those of races other than black and white (n=27), African-Americans from the Minnesota or Maryland field centers (n = 27) due to the small numbers recruited from these sites, those with prevalent VTE (n=218) as determined by self-report at study entry or adjudicated VTE events occurring prior to visit 4, and those taking anticoagulants at visit 4 (n=80) leaving a final sample of n=8,092.

Periodontal Disease Ascertainment

The exposure of interest was periodontitis determined using self-reported tooth loss due to gum disease, two clinical periodontal disease classifications, and four continuous measures of periodontal disease. Self-reported tooth loss due to gum disease was based on the question “Did you lose any teeth because of gum disease?” Two clinical case definitions of periodontitis were assessed using clinical measures collected during the D-ARIC oral examination including probing pocket depth and gingival recession on 6 sites for all teeth. Attachment level was calculated from the sum of pocket depth and gingival recession scores.

The first clinical case definition used was the CDC Periodontal Disease Surveillance workgroup in collaboration with the American Academy of Periodontology (CDC/AAP) definition. (Eke, Page, Wei, Thornton-Evans, & Genco, 2012) This 4-level definition is as follows:

- No periodontitis: Not meeting the definition of mild, moderate, or severe periodontitis
- Mild periodontitis: 2 interproximal (between teeth) sites with attachment loss 3mm, and 2 interproximal sites with probing depth 4 mm (not on same tooth) or one site with probing depth 5 mm
- Moderate periodontitis: 2 interproximal sites with attachment loss 4 mm (not on same tooth), or 2 interproximal sites with probing depth 5 mm (not on same tooth)

- Severe periodontitis: 2 interproximal sites with attachment loss ≥ 6 mm (not on same tooth) and 1 interproximal site with probing depth ≥ 5 mm

The second clinical periodontal disease classification used was the Periodontal Profile Class (PPC) proposed by Morelli et al. (Morelli et al., 2016). This uses 7 tooth-level clinical parameters (interproximal attachment level, probing depth, bleeding on probing, gingival inflammation index, plaque index, the presence/absence of full prosthetic crowns for each tooth, and tooth status presence) to identify seven distinct periodontal profile classes (PPC). This 7-level definition is as follows:

- PPC-A: Health
- PPC-B: Mild Disease
- PPC-C: High Gingival Inflammation
- PPC-D: Tooth Loss
- PPC-E: Posterior Disease
- PPC-F: Severe Tooth Loss
- PPC-G: Severe Disease

We performed sensitivity analyses using four continuous measures of periodontal disease including mean periodontal inflamed surface area (PISA), mean attachment loss (AL), mean periodontal probing depth (PPD), and proportion of tooth sites with bleeding on probing (BOP). Periodontal probing depth and bleeding on probing were assessed on 6 sites for all teeth during the D-ARIC exam. Attachment level was calculated from the sum of pocket depth and gingival recession scores. PISA was estimated using the average surface area of each tooth type along with periodontal measures using the methodology of Neese et al. (Neese et al., 2008).

Covariate Ascertainment

Education (some high school or less, high school diploma, college degree or higher) was assessed at study entry (visit 1) while income (<\$25,000/year, \$25,000 – <\$50,000/year, \$50,000 – <\$75,000/year, ≥\$75,000/year) was assessed at visit 4. Common risk factors including smoking (current, former, never), alcohol consumption (grams/week), BMI (Kg/M^2) calculated from measured height and weight, and statin use (yes/no) were assessed at visit 4. Finally, oral hygiene and access to care variables were collected during the dental history questionnaire administered at visit 4. These included medical insurance status (private insurance, Medicare/Medicaid only, none), last dental visit (<6 months ago, 6 months – <2 years ago, 2 – <5 years ago, ≥5 years ago), dental visit frequency (regularly, only for discomfort or repair, do not regularly visit the dentist), and having a current dentist (yes/no).

Outcome Ascertainment

The outcome of interest was incident VTE, defined as PEs and DVTs occurring in the legs (n=755) from 1996–98 through 2011. Potential hospitalized incident VTE events were identified using ICD-9CM discharge diagnosis codes (415.1x, 451.1x, 451.2, 451.8x,

451.9, 453, 453.0, 453.1, 453.2, 453.8, 453.9, 996.7x, 997.2, 999.2, 38.7), and ARIC staff obtained materials from the hospital records, including physician and consultant reports, discharge summaries, and imaging reports.(Cushman et al., 2004) Hospital records were independently reviewed and adjudicated by two study physicians to determine the VTE case status.(Cushman et al., 2004) The hospital admission date abstracted from the patient medical record was considered the VTE date.

Statistical Analysis

Descriptive statistics were calculated for study participant characteristics at baseline (visit 4) by periodontal disease category. Cox-proportional hazards regression models were used to estimate hazard ratios and 95% confidence intervals of VTE associated with periodontal disease classification. Those who reported being edentulous and those with different levels of periodontal disease were compared to those without periodontal disease (referent). The proportional hazards assumption was assessed by visual inspection of the Kaplan-Meier (KM) survival curves and by testing the interaction between periodontal disease status and follow-up time.

Crude (unadjusted) models and those adjusting for potential confounding variables were constructed via assessments performed at the ARIC visit 4 exam modeled according to the descriptions in the covariate ascertainment section. Model 1 included demographic and SES variables, including age, sex, race/center, education, and income. Model 2 added adjustment for relevant periodontal risk factors that also may be associated with VTE including smoking, alcohol consumption, BMI, and statin use. Finally, model 3 additionally included adjustment for variables related to oral hygiene and access to care including medical insurance status, last dental visit, dental visit frequency, and having a current dentist.

We performed a sensitivity analysis using self-reported tooth loss due to gum disease stratified by median number of teeth at baseline to see if the association between self-reported tooth loss due to gum disease and VTE risk differed by baseline number of teeth. We also performed a sensitivity analysis in which we excluded participants who reported a history of endodontic therapy (n=3,314) since endodontic infection may trigger an inflammatory response similar to that triggered by periodontal infection. Finally, we also performed a sensitivity analysis in which we excluded secondary (provoked) VTE since periodontal disease may more strongly associated with VTE not provoked by a transient risk factor.

For all analyses, follow- up time began at entry into the D-ARIC study (visit 4) and extended to the incident VTE, dropping out of the study, death, or else, December 31, 2011.

Results

Baseline (ARIC visit 4) characteristics are provided in Table1 and Supplementary Tables 1 and 2 for study participants by self-reported periodontal disease status, CDC/AAP clinical periodontal disease status, and PPC periodontal disease classification respectively. Across exposure classifications, periodontal disease was more common among males compared to females, among blacks compared to whites, and among those of low SES status compared to

those of high SES status. Those with periodontal disease were more likely to be smokers and less likely to have medical insurance, a current dentist, and visited the dentist regularly compared to those without periodontal disease.

Over a mean of 12.9 years of follow-up (range 15.8 years), 313 incident VTE events were identified in the ARIC cohort at risk. Overall, the VTE incidence rate was 3.00 events per 1,000 person-years of follow-up. Those who self-reported tooth loss due to gum disease had a VTE incidence rate of 4.53 per 1,000 person-years of follow-up compared to an incidence rate of 2.79 per 1,000 person-years of follow-up among those who did not self-report tooth loss due to gum disease. The VTE incidence rates overall and by periodontal disease status are reported in Figure 1.

The KM curves revealed no significant departures from proportionality (data not shown). Further, no significant interactions between exposure and follow-up time were observed (all p-values > 0.05).

Table 2 contains the results of the Cox proportional hazards regression models. Self-reported tooth loss due to periodontal disease was associated with higher risk of VTE in the crude model. This association remained significant or borderline significant after adjustment for potential confounders. In the fully adjusted model (model 3), self-reported tooth loss due to gum disease was associated with 30% higher VTE risk compared to those who did not report past tooth loss due to gum disease (HR = 1.29 (0.96, 1.73)). Associations between both CDC/AAP and PPC periodontal disease classifications and VTE risk were not statistically significant in adjusted models.

Results from the sensitivity analyses using continuous measures of periodontal disease showed no significant associations between any of the continuous measures of periodontal disease and VTE after adjustment for confounders and are presented in Supplementary Table 3. The association between self-reported tooth loss due to gum disease and VTE did not differ by median number of teeth at baseline and the results of this sensitivity analysis are presented in Supplementary Table 4. Results from the sensitivity analysis in which we excluded participants who reported a history of endodontic therapy were not materially different from the primary results and are presented in Supplementary Table 5. Similarly, the sensitivity analysis in which only unprovoked VTE events were considered did not differ significantly from the primary results and are presented in Supplementary Table 6.

Discussion

In this prospective cohort study on periodontal disease and incident VTE, we found that self-reported tooth loss due to gum disease may be associated with 30% higher VTE risk than no tooth loss due to gum disease, and this association remained significant or borderline significant after adjustment for confounding variables. Associations between CDC/AAP and PPC clinical periodontal disease classifications and VTE as well as continuous measures of periodontal disease and VTE were not statistically significant in adjusted models.

Our results differ from the previous study evaluating periodontal disease and VTE.(Sanchez-Siles et al., 2013) In that study, Sanchez-Siles et al. found that periodontitis was more

prevalent among 97 VTE patients than in the 100 healthy controls (OR = 3.33 (95% CI 1.83, 6.06)). The case-control study design which is unable to verify temporality between the exposure and the outcome and the lack of adjustment for relevant confounding may make these results prone to bias. The discordant findings suggests that further research on the association between periodontal disease and VTE is needed.

The discrepancy between our self-reported periodontal disease and clinical periodontal disease results is worth exploring. Self-reported tooth loss due to gum disease may indicate more severe periodontal disease over a longer period of time compared to the clinical disease classifications which were categorized based on measures taken at a single point in time. If periodontal disease is in fact a risk factor for VTE, the potential greater lifetime duration and severity of periodontal disease among those who reported tooth loss may explain why a stronger result was found for self-reported periodontal disease compared to one-time clinical characterizations in those who still have natural teeth.

Our study has a number of strengths, including a large sample size from a community cohort with lengthy follow-up and rigorous methodology to adjudicate VTE events. It also has limitations. Since we are assessing exposure at only a single time point, our study could suffer from measurement error since a participant's periodontal disease status could change after baseline assessment. Changes in periodontal disease status after baseline could not be accounted for and could create misclassification of our exposure. This potential time lag between exposure and the outcome of interest would most likely lead to non-differential misclassification which could bias our results towards the null and may explain the absence of significant findings. Further, there could be measurement error associated with self-reported tooth loss due to gum disease. Social and behavioral risk factors may be a common causes of both tooth loss and VTE. We attempted to isolate the impact of self-reported tooth loss due to gum disease on VTE risk by including relevant SES and access to dental care variables in our adjusted models but residual confounding may persist and may explain the association between self-reported periodontal disease and VTE. In addition, those who had all teeth removed would have been counted in the periodontitis group, even though tooth removal should have removed their oral inflammatory burden that was hypothesized to be the mechanism between periodontitis and VTE. The vast majority of VTE events were symptomatic events captured via hospital records. Although we did not capture VTEs treated in an outpatient setting, pilot studies have indicated that the aging ARIC cohort had few outpatient VTEs through 2011. VTE results from a combination of predisposing factors (genetic predisposition, increased coagulability with aging, obesity, etc.) as well as precipitating factors (recent trauma, immobilization, surgery, cancer, etc.).(Rosendaal, 1999) Chronic periodontal disease or other chronic inflammation, generally, would be hypothesized to be a predisposing factor for VTE. This study was unable to incorporate precipitating factors for VTE and other unmeasured confounders in the analysis, which could have led to biased HRs.

Traditional risk factors for atherosclerotic CVD (e.g., smoking, hypertension, dyslipidemia, and diabetes) are generally considered weak risk factors for VTE. However, systemic inflammation is believed to predispose to both atherosclerotic CVD (Ridker, Hennekens, Buring, & Rifai, 2000) and VTE. (Folsom et al., 2009) While studies investigating the

periodontal disease treatment as a primary prevention strategy of CVD are lacking, a number of studies have investigated the impact of periodontal treatment on atherosclerotic CVD risk factors.(Li et al., 2014) Most relevant to VTE, a recent meta-analysis of clinical trials investigating the impact of periodontal treatment on CVD risk factors found that periodontal treatment was effective at reducing systemic inflammatory marker levels in subjects with periodontitis.(Teeuw et al., 2014) Further research is needed to determine if periodontal treatment reduces VTE risk.

Conclusion

Self-reported tooth loss due to periodontal disease may be associated with a 30% increase in VTE risk compared to no tooth loss due to periodontal disease. Objectively measured periodontitis, as categorized by the CDC/AAP and PPC clinical periodontal disease classifications and continuous measures of periodontal disease were not associated with VTE risk. Further research is needed to elucidate whether there is truly any relation between periodontal disease and VTE.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Clinical Relevance**Scientific Rationale**

Periodontal disease is a known cardiovascular disease risk factor but little is known regarding the impact of periodontal disease on venous thromboembolism (VTE) risk.

Principal Findings

Self-reported tooth loss due to gum disease was associated with 30% higher VTE risk compared to those without past tooth loss due to gum disease. No significant associations between clinical periodontal disease classifications and VTE risk were observed.

Practical Implications

The impact of periodontal disease on VTE risk remains unknown. Further research is needed to determine if periodontal treatment reduces VTE risk.

Figure 1.

VTE incidence rates per 1,000 person-years of follow-up overall and by periodontal disease status in the ARIC cohort, 1996–98 to 2011

* - PPC-A: Health

† - PPC-B: Mild Disease

‡ - PPC-C: High Gingival Inflammation

§ - PPC-D: Tooth Loss

|| - PPC-E: Posterior Disease

¶ - PPC-F: Severe tooth Loss

- PPC-G: Severe Disease

Table 1.

Visit 4 (1996–1998) characteristics of ARIC participants by self-reported periodontal disease status

	Tooth Loss from Gum Disease	No Tooth Loss from Gum Disease
Total, count (%)	1,095 (13.9)	6,761 (86.1)
Age (years), mean $\pm$ SD	63.5 (5.7)	62.6 (5.6)
Sex, count (%)		
Male	490 (44.8)	3,046 (45.1)
Female	605 (55.3)	3,715 (55.0)
Race, count (%)		
White	725 (66.2)	5,484 (81.1)
Black	370 (33.8)	1,277 (19.0)
Education, count (%)		
Some High School	331 (30.3)	1,160 (17.2)
High School Diploma	439 (40.2)	2,904 (43.0)
College Degree	322 (29.5)	2,687 (39.8)
Income, count (%)		
<\$24,999	462 (43.6)	1,838 (27.7)
\$25,000–\$50,000	356 (33.6)	2,344 (35.3)
\$50,000–\$74,999	139 (13.1)	1,260 (19.0)
>\$75,000	83 (7.8)	1,047 (15.8)
Refused	20 (1.9)	147 (2.2)
Smoker, count (%)		
Current	245 (22.6)	914 (13.6)
Former	508 (46.8)	2,876 (42.7)
Never	333 (30.7)	2,940 (43.7)
Statin Use, count (%)		
No	931 (85.3)	6,055 (89.8)
Yes	161 (14.7)	687 (10.2)
BMI (Kg/M ²), mean $\pm$ SD	29.3 (5.7)	28.7 (5.5)
Alcohol (g/week), mean $\pm$ SD	36.4 (86.4)	32.8 (77.7)
Medical Care Payment, count (%)		
Health Plan	836 (76.9)	5,902 (87.6)
Medicare/Medicaid Only	162 (14.9)	485 (7.2)
None	89 (8.2)	347 (5.2)
Number of Teeth, mean $\pm$ SD	16.6 (7.7)	22.4 (6.8)
Current Dentist, count (%)		
Yes	761 (70.0)	5,635 (83.6)
No	326 (30.0)	1,109 (16.4)
Last Dental Visit, count (%)		
Within last 6 months	428 (39.4)	3,708 (54.9)

	Tooth Loss from Gum Disease	No Tooth Loss from Gum Disease
6 months to 2 years ago	200 (18.4)	1,511 (22.4)
2 to 5 years ago	172 (15.8)	662 (9.8)
More than 5 years ago	287 (26.4)	869 (12.9)
When do you visit Dentist, count (%)		
Regular Basis	437 (40.0)	4,363 (64.5)
Discomfort/Something Fixed	566 (51.9)	2,116 (31.3)
Don't go to Dentist	78 (7.2)	216 (3.2)
Other	10 (0.9)	61 (0.9)

Table 2.

Association (HR and 95% CI) between self-reported and clinical periodontal disease and incident VTE in the ARIC cohort, 1996–98 to 2011

	Events	N	Crude	Model 1	Model 2	Model 3
<u>Self-Report</u>						
No	245	6,761	Ref	Ref	Ref	Ref
Yes	61	1,095	1.65 (1.25, 2.18)	1.36 (1.02, 1.82)	1.31 (0.98, 1.75)	1.29 (0.96, 1.73)
CDC/AAP						
Healthy	31	749	Ref	Ref	Ref	Ref
Mild	51	1,972	0.61 (0.39, 0.95)	0.59 (0.37, 0.92)	0.60 (0.38, 0.94)	0.60 (0.38, 0.95)
Moderate	103	2,699	0.93 (0.62, 1.39)	0.89 (0.59, 1.33)	0.86 (0.57, 1.29)	0.86 (0.57, 1.29)
Severe	40	1,131	0.90 (0.56, 1.44)	0.76 (0.47, 1.22)	0.72 (0.44, 1.16)	0.70 (0.43, 1.14)
Edentulous	88	1,541	1.59 (1.06, 2.40)	1.09 (0.71, 1.68)	1.00 (0.65, 1.55)	1.02 (0.64, 1.64)
PPC						
A [*]	53	1,799	Ref	Ref	Ref	Ref
B [†]	34	1,007	1.17 (0.76, 1.79)	1.00 (0.64, 1.55)	0.94 (0.61, 1.46)	0.91 (0.58, 1.41)
C [‡]	28	674	1.45 (0.92, 2.29)	0.83 (0.49, 1.42)	0.74 (0.43, 1.25)	0.70 (0.41, 1.20)
D [§]	25	766	1.15 (0.72, 1.85)	0.85 (0.52, 1.39)	0.75 (0.46, 1.22)	0.72 (0.44, 1.18)
E	25	962	0.91 (0.57, 1.47)	0.86 (0.53, 1.40)	0.79 (0.49, 1.31)	0.78 (0.47, 1.27)
F [¶]	35	861	1.47 (0.96, 2.25)	0.96 (0.60, 1.52)	0.82 (0.51, 1.31)	0.76 (0.47, 1.23)
G [#]	25	482	1.91 (1.19, 3.08)	1.20 (0.71, 2.03)	1.05 (0.62, 1.78)	0.92 (0.53, 1.59)
Edentulous	88	1,541	2.29 (1.63, 3.22)	1.31 (0.88, 1.96)	1.10 (0.73, 1.66)	1.05 (0.65, 1.68)

Model 1: Included age, sex, race/center, education, income

Model 2: Added smoking, alcohol consumption, BMI, and statin use

Model 3: Added health insurance status, last dental visit, dental visit frequency, and having a current dentist

^{*}PPC-A: Health

[†]PPC-B: Mild Disease

[‡]PPC-C: High Gingival Inflammation Index

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PPC-D: Tooth Loss
PPC-E: Posterior Disease
PPC-F: Severe tooth Loss
PPC-G: Severe Disease