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Cross-sectional associations of impaired glucose metabolism measures with bleeding on probing and periodontitis

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Abstract

Aim—This study assessed the associations of prediabetes and insulin resistance with bleeding on probing (BOP) and periodontitis among adults.

Materials and methods—We included 1,191 Hispanic adults aged 40-65 years, free of diabetes, enrolled in the San Juan Overweight Adults Longitudinal Study. Pre-diabetes was defined as impaired fasting glucose (IFG), impaired glucose tolerance (IGT), or impaired glycated hemoglobin. Impaired one-hour plasma glucose (1hPG) was defined as levels>155 mg/dL. Insulin resistance was defined using the study population-specific 75th percentile (HOMA-IR≥3.13). High BOP was defined as percentage of teeth with bleeding ≥30%. Periodontitis was defined according to the CDC/AAP definition.

Results—After multivariable adjustment for age, gender, education, smoking status, alcohol consumption, physical activity, obesity, HDL-C, and plaque index, prediabetes with and without 1hPG, IFG, impaired 1hPG, IGT, and HOMA-IR were significantly associated with high BOP; prediabetes, IFG, and impaired 1hPG were significantly associated with severe periodontitis. Most of these associations remained significant when the analyses were restricted to non-smokers.

Conclusions—This study suggests associations between prediabetes and insulin resistance with BOP and periodontitis. Given the high prevalence of impaired glucose metabolism and

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periodontitis, the assessment of the temporal sequence of these associations are of utmost importance.

Keywords

Periodontitis; bleeding on probing; impaired fasting glucose; impaired glucose tolerance; impaired glycated hemoglobin; prediabetes; insulin resistance

Introduction

Systematic reviews of epidemiologic studies suggest a bidirectional association between type 2 diabetes and periodontitis (Borgnakke et al., 2013; Taylor et al., 2013). Very few prospective cohort studies have shown positive associations of baseline periodontitis with incident type 2 diabetes (Miyawaki et al., 2016; Chiu et al., 2015; Demmer et al., 2008). However, two recent reviews of clinical trials assessing the effect of periodontitis treatment on HbA1c levels among subjects with type 2 diabetes showed very modest reductions (Li et al., 2015; Simpson et al., 2015). Conversely, type 2 diabetes has also been associated longitudinally with an elevated risk of periodontitis (Chiu et al., 2015; Jimenez et al., 2012) and tooth loss (Jimenez et al., 2012). Relative to diabetes-free participants, both uncontrolled type 1 and type 2 diabetes have been associated with clinical attachment loss progression and tooth loss, whereas only uncontrolled type 2 diabetes was associated with pocket depth changes (Demmer et al., 2012).

Few cross-sectional studies (Arora et al., 2014; Choi et al., 2011; Hong et al., 2016; Islam et al., 2015; Song et al., 2016) and only three longitudinal studies (Chiu et al., 2015; Demmer et al., 2010; Saito et al., 2004) have found significant associations between prediabetes states and periodontitis. However, other cross-sectional studies have found no association between prediabetes states and periodontitis (Arora et al., 2014; Demmer et al., 2015; Kowall et al., 2015; Noack et al., 2000; Saito et al., 2005). Thus, there is insufficient evidence regarding the associations of pre-clinical stages of type 2 diabetes with periodontitis.

Furthermore, little work has been done in examining the associations of HbA1c and insulin resistance. Demmer et al. (2010) found that periodontitis was associated with five-year glycated hemoglobin (HbA1c) progression among diabetes-free participants. A pilot case-control study found that mean HbA1c was significantly higher in periodontitis cases than in healthy controls (Wolff et al., 2009). The insulin resistance-periodontitis association has been investigated in six cross-sectional studies (Song et al., 2016; Demmer et al., 2012; Islam et al., 2015; Benguigui et al., 2010; Lim et al., 2014; Timonen et al., 2011) and one longitudinal study (Timonen et al., 2013) and have produced mixed results. The one-hour post-load plasma glucose (1hPG) concentration during the oral glucose tolerance test has been shown to correlate strongly with predictors of diabetes and abnormal glucose homeostasis (Abdul-Ghani et al., 2008; Joshipura et al., 2011). To the best of our knowledge, the association of 1hPG with periodontitis has not been examined thus far.

Studies examining the associations of prediabetes states and insulin resistance with bleeding on probing (BOP), an indicator of periodontal inflammation, have also yielded mixed results. Two of these studies have been cross-sectional (Andriankaja & Joshipura, 2014;

Noack et al., 2000), one used a case-control study design (Javed et al., 2012), and one performed a cross-sectional analysis within a longitudinal study (Cherry-Peppers & Ship, 1993), all of which have been limited by small sample sizes.

The present study assessed the cross-sectional associations between several glucose metabolism measures (fasting plasma glucose (FPG), 1hPG, two-hour post-load glucose (2hPG) concentration, HbA1c, and insulin resistance) with BOP and periodontitis among diabetes-free individuals of Hispanic origin enrolled in the San Juan Overweight Adults Longitudinal Study (SOALS). We hypothesized that impaired glucose metabolism measures would be associated with higher odds of BOP and periodontitis.

Materials and Methods

Study sample

The SOALS was initiated in 2011 to evaluate the bi-directional, longitudinal association between periodontitis and glucose abnormalities over a three-year period. Detailed descriptions of the study have been published elsewhere (Andriankaja et al., 2015, Rivera et al., 2016). Briefly, we recruited individuals aged 40-65 years who were overweight or obese (body mass index (BMI)≥25 kg/m^2) and free of clinically diagnosed diabetes from the San Juan municipality area. People were excluded if they had less than four natural teeth, a history of conditions that increase the risk of systemic complications during a periodontal exam, or inability to complete study procedures. Participants were also excluded if they met any of the American Diabetes Association criteria for diabetes (2011).

Of 2,626 adults screened to determine eligibility, 695 were excluded based on the criteria described above. Once the screening process concluded, 1,931 adults were deemed eligible, 1,610 agreed to be scheduled for the baseline visit, and 1,451 adults attended the visit. During the baseline visit, additional eligibility criteria were further assessed and an additional 245 participants were excluded. Of the remaining 1,206 participants, 15 were excluded due to missing data on key variables for analyses; thus, the final sample size comprised 1,191 diabetes-free participants. The University of Puerto Rico Institutional Review Board approved the study, and all participants gave written consent prior to completing the study procedures. For the current study, a completed STROBE checklist is provided as a supplementary file (see Additional File 1).

Assessment of glucose measures

All participants were asked to fast for 10 hours prior to the appointment and through the two-hour blood drawing. FPG and insulin levels were determined at baseline and 30, 60, and 120 minutes after administration of a 75-g glucose load, using an enzymatic colorimetric assay. Plasma insulin concentrations were analyzed using an immunochemiluminometric assay, and HOMA-IR was calculated as [FPG (mg/dL) × fasting insulin (μg/dL)]/405]. HbA1c was measured with an assay based on a latex immunoagglutination inhibition method (DCA 2000+ Analyzer, Siemens Healthcare Diagnostics, Tarrytown, NY, USA). Participants were classified as having IFG (FPG 100-125 mg/dl), IGT (2hPG 140-199 mg/dl), impaired glycated hemoglobin (HbA1c 5.7%-6.4%), or normal glucose tolerance (FPG

<100 mg/dl, 2hPG <140 mg/dl, and HbA1c <5.7%) following the American Diabetes Association criteria (2011). Pre-diabetes was defined as having at least one of these diagnostic criteria. A modified definition of prediabetes based on the American Diabetes Association glucose thresholds for prediabetes and/or 1hPG concentration >155 mg/dl (Abdul-Ghani et al., 2008) was also assessed. Since there is no consensus on a cut point to define HOMA-IR, the study population-specific 75th percentile was used (HOMA-IR ≥3.13).

Ascertainment of periodontitis—Periodontitis was assessed by clinical measurements of probing pocket depth (PPD) and clinical attachment loss (CAL) at six sites (disto-buccal, mid-buccal, mesio-buccal, disto-lingual, mid-lingual, and mesio-lingual buccal) for all teeth excluding the third molars. All measurements were taken with a periodontal probe (Hu-Friedy, Chicago, IL, product number PCP2) and rounded off upwards to the nearest millimeter. Periodontitis was defined according to the Centers for Disease Control and Prevention/American Academy of Periodontology (CDC/AAP) (Eke et al., 2015). Severe periodontitis was defined as having at least two interproximal sites with CAL≥6 mm (not on the same tooth) and at least one interproximal site with PPD≥5 mm. Moderate periodontitis was defined as having at least two interproximal sites with CAL≥4 mm (not on the same tooth) or at least two interproximal sites with PPD≥5 mm (not on the same tooth). Mild periodontitis was defined as having at least two interproximal sites with CAL≥3 mm and at least two interproximal sites with PPD≥4 mm (not on the same tooth) or one site with PPD≥5 mm. Full mouth clinical exams were conducted by three examiners who had been previously calibrated by the National Health and Nutrition Examination Survey (NHANES) reference examiner (Dr. Bruce Dye).

During the measurement of PPD, a periodontal probe was inserted to the base of the sulcus or pocket with a maximum force of 20 g. BOP was present if the probed site bled about 20 seconds after probing the lingual and buccal surfaces of each tooth. BOP was classified as high if 30% or more teeth showed bleeding on probing, and as low otherwise (Lang et al., 1986). The Silness and Loe Plaque Index, a measure of oral hygiene status, was determined by visual assessment of presence of bacterial plaque after passing a periodontal probe around the tooth surface of six pre-selected Ramfjörd teeth. Plaque index was coded as 0 if no plaque present, 1 if dental plaque was present after passing the periodontal probe around the tooth, 2 if plaque was visible along the gingival margin, and 3 if the tooth surface was covered with abundant plaque.

Ascertainment of covariates

Sociodemographic characteristics, health behaviors, and general health were collected by in-person interviews and physical and laboratory assessments. Covariates included age, gender, education (less than high school, high school or more), annual income (<$20,000, ≥ $20,000), smoking status (never, past, current), number of cigarettes per week, alcohol consumption (grams per week), and frequency and type of physical activity converted to metabolic equivalent of task (MET) in hours per week. Fruit and vegetable consumption was assessed as the number of servings per week. Waist circumference (WC) was measured at the umbilical level and recorded to the nearest 0.1 cm. High-density lipoprotein cholesterol

(HDL-C) was determined using a commercially available enzymatic assay (Roche Diagnostics, Indianapolis, IN). High-sensitivity C reactive protein (hs-CRP) levels were considered high if they exceeded 3 mg/L (Ridker and Morrow, 2003). The number of dental visits in the past year (none, at least one) and tooth brushing and dental flossing frequency (at least twice a day, once a day or less) were recorded.

Statistical analysis

Differences in baseline characteristics of participants across BOP status were assessed using Student's t test or Mann Whitney's test for continuous variables and Pearson's chi square test for categorical variables. Similarly, these characteristics were compared across periodontitis status using ANOVA or Kruskal-Wallis test for continuous variables and Pearson's chi square test for categorical variables.

Binary logistic regression models were fit to assess the relationship of each glucose metabolism measure with BOP as outcome. Multinomial logistic regression was used to assess the associations of each glucose metabolism measure with the CDC/AAP definition of periodontitis as outcome, using adults with no or mild periodontitis as the reference group. Odds ratios (OR), their 95% confidence intervals (CI), and p values derived from the Wald chi-square test were reported.

Potential confounders were selected a priori based on their hypothesized associations with impaired glucose metabolism measures, BOP, and periodontitis status. The first multivariable model adjusted for age and the second model additionally adjusted for sex, smoking status, education, grams of alcohol consumption, WC, HDL-C, MET, and plaque index. We also assessed whether hs-CRP might mediate the associations of interest. In exploratory analyses, we stratified the logistic regression models by smoking status to evaluate whether associations of impaired glucose metabolism measures with BOP and periodontitis status differed across smoking status categories.

Several diagnostics were performed in all multivariable logistic models (Hosmer et al., 2013). The test of nonlinearity supported treating age, grams of alcohol, WC, MET, HDL-C, and plaque index as linear in the logit of all models (all p values>0.05). Multicollinearity diagnostic statistics showed that most variables (except annual income) had tolerance values greater than 0.1 and variance inflation factors less than 10. Finally, all the logistic regression models showed no evidence of lack of fit according to the Hosmer-Lemeshow statistic (all p values>0.05). Statistical analyses were performed using Stata (StataCorp LP, College Station, Texas, USA) for Windows version 14.

Results

Of 1,191 participants, 450 were classified as having high BOP, 407 had no or mild periodontitis, 502 had moderate periodontitis, and 282 had severe periodontitis (Table 1). Participants with high BOP were more likely to be older, males, have a lower education and an annual income, have more abdominal obesity, have no dental check-ups within the past year and to floss their teeth less than once per day, have a higher plaque index, and have impaired glucose metabolism. This pattern was similar across periodontitis severity.

However, current smoking, alcohol intake, fewer teeth, and BOP were also higher among those with severe periodontitis.

After multivariable adjustment for age, gender, education, smoking status, physical activity, alcohol consumption, WC, HDL-C, and plaque index, both definitions of prediabetes (OR=1.51, 95% CI: 1.15-1.97; OR=1.43, 95% CI: 1.08-1.91, respectively), IFG (OR=1.50, 95% CI: 1.10-2.06), impaired 1hPG concentration (OR=1.39, 95% CI: 1.07-1.80), IGT (OR=1.54, 95% CI: 1.11-2.13), and HOMA-IR (OR=1.55, 95% CI: 1.14-2.12) were significantly associated with high BOP (Table 2).

Relative to participants with no/mild periodontitis, prediabetes with or without 1hPG (OR=1.67, 95% CI: 1.17-2.40; OR=1.84; 95% CI: 1.24-2.73; respectively), IFG (OR=1.62, 95% CI: 1.06-2.48), and impaired 1hPG concentration (OR=1.46, 95% CI: 1.03-2.07) were significantly associated with severe periodontitis after controlling for confounders (Table 3). There was a trend for IGT (OR=1.53, 95% CI: 0.99-2.36) and HOMA-IR (OR=1.51, 95% CI: 0.99-2.32) to increase the odds of severe periodontitis. In contrast, IFG (OR=1.45, 95% CI: 1.01-2.08) was the only glucose metabolism measure significantly associated with moderate periodontitis relative to participants with no/mild periodontitis. There was a trend for individuals with prediabetes to have greater odds of moderate periodontitis (OR=1.31, 95% CI: 0.98-1.74). There was no association between impaired HbA1c and BOP or periodontitis status, either age-adjusted or in multivariable-adjusted models. Additional adjustment for number of natural teeth and hs-CRP and replacement of WC for other obesity measures (BMI, WHR, and percent body fat modeled as continuous) did not meaningfully change the effect estimates in the models for BOP and periodontitis status (data not shown).

Table 4 shows the results of the models for BOP and periodontitis status stratified by smoking status. Among non-smokers, the associations of prediabetes, IFG, and IGT remained significantly associated with BOP, whereas a trend was observed for prediabetes with 1hPG, impaired 1hPG concentration, and HOMA-IR. Moreover, IFG and IGT were significantly associated with severe periodontitis among non-smokers, whereas a trend was observed for prediabetes with and without 1hPG and HOMA-IR.

Discussion

This study assessed the cross-sectional associations between several glucose metabolism measures (fasting plasma glucose (FPG), 1hPG, two-hour post-load glucose (2hPG) concentration, HbA1c, and insulin resistance) with BOP and periodontitis among diabetes-free individuals of Hispanic origin enrolled in the San Juan Overweight Adults Longitudinal Study (SOALS). Prediabetes with and without 1hPG, IFG, impaired 1hPG concentration, IGT, and HOMA-IR were significantly associated with high BOP after extensive multivariable adjustment for confounders. Moreover, prediabetes, IFG, and impaired 1hPG concentration were significantly associated with severe periodontitis. Most of these associations remained significant or borderline significant when the analyses were restricted to non-smokers. This is among the first studies to show significant associations relating impaired glucose metabolism with BOP and severe periodontitis.

The associations of prediabetes, IFG, and IGT with severe periodontitis were consistent with few cross-sectional studies that have assessed the associations similar to the way they were modeled in this study. For example, Hong et al. (2016) found that individuals with IFG (111-125 mg/dL) had an increased odds of periodontitis (OR=1.33, 95% CI: 1.01-1.75) compared with subjects with normal fasting glucose (<90 mg/dL). Similarly, Saito et al. (2005) found that IGT was significantly associated with quintiles of mean PPD among Japanese women. However, Kowall et al. (2015) found that prediabetes was neither associated with mean CAL and PPD in a large, population-based study. Other cross-sectional studies that have modeled the associations in the opposite direction have found positive findings. For example, Choi et al. (2011) reported that participants in the top quintile category of CAL and PPD had significantly higher odds of IFG (OR=1.55, 95% CI: 1.16-2.07; OR=1.39, 95% CI: 1.00-1.92; respectively). Arora et al. (2014) found that severe periodontal infection was significantly associated with IGT (OR=1.93; 95% CI: 1.18-3.17) but not with IFG. However, Demmer et al. (2015) found that higher tertiles of specific periodontal microbiota, but not moderate or severe periodontitis, were significantly associated with prediabetes.

While we observed a trend for HOMA-IR to increase the odds of severe periodontitis, findings from other cross-sectional studies are mixed. Benguigui et al. (2010) found that only HOMA-IR was associated with severe periodontitis and greater number of sites with CAL≥4 mm, CAL≥5 mm, and PPD≥4 mm; however, these associations disappeared among non-smokers. Lim et al. (2014) found that postmenopausal women who were in the highest quartile of HOMA-IR were more likely to have periodontitis; however, the association was not seen among men nor premenopausal women. Timonen et al. (2011) found that the association between HOMA-IR and periodontitis disappeared after controlling for BMI. A longitudinal study by Timonen et al. (2013) found that participants in the highest HOMA-IR tertile (RR=1.6, 95% CI: 1.0-2.6) and those in the highest HOMA-β tertile (RR=1.5, 95% CI: 0.9-2.4) had higher risk of PPD≥4 mm during a four-year follow-up period. Two cross-sectional studies that modeled the associations in the opposite direction also found mixed results. While Demmer et al. (2012) found that quartiles of mean PPD were associated with HOMA-IR in the presence of elevated hs-CRP and white blood cell values, Islam et al. (2015) found that Korean adults with and without periodontitis had similar HOMA-IR.

One notable inconsistency with two prior studies is the null association of HbA1c with periodontitis. A longitudinal study by Demmer et al. (2010) found that elevated levels of periodontitis and progression of periodontitis predicted five-year HbA1c progression in diabetes-free participants. Wolff et al. (2009) found slightly higher HbA1c levels in periodontitis cases than in controls (5.66% and 5.51%, p=0.046). Our preliminary analysis suggests that the HbA1c test, relative to plasma glucose criteria (fasting glucose and 2hPG), has low specificity and sensitivity, especially for the pre-diabetes diagnosis. Further studies are needed to clarify the role of HbA1c levels on periodontitis among diabetes-free participants.

Novel findings on the associations of prediabetes, IFG, IGT, 1hPG, and HOMA-IR with high BOP using a large sample have rarely been reported and should be replicated. Few studies, with limited sample sizes, have investigated these associations and have yielded

conflicting results. One pilot study by our group found that prediabetes (based on IFG and/or IGT) was strongly associated with high BOP (Andriankaja et al., 2014). Javed et al. (2012) found that clinical periodontal inflammation was more severe in patients with prediabetes as compared with controls. In contrast, Cherry-Peppers & Ship (1993) did not find a difference in the percentage of sites with gingival bleeding between patients with impaired glucose tolerance and normal controls. Similarly, Noack et al. (2000) did not find a significant difference in the percentage of sites showing BOP in individuals with IGT compared to normoglycemic individuals. Further studies are needed to clarify the longitudinal associations between glucose metabolism and BOP as this measurement, along with assessment of other clinical periodontal parameters, could enhance knowledge about the risk of disease progression.

Several biological mechanisms of the bidirectional connection between impaired glucose metabolism and periodontitis have been proposed. Periodontal pathogens and an ensuing inflammatory response lead to collagen destruction resulting in periodontitis, characterized by a deepening of the pockets around the teeth and loss of attachment and alveolar bone. Periodontal pathogens activate cytokines which are associated with increased levels of inflammatory markers and endothelial dysfunction, and altered lipid metabolism, which in turn could lead to increased glucose abnormalities, insulin resistance, and increased risk of diabetes (Demmer et al., 2015, Genco et al., 2005, Taylor et al., 2013). While increasing evidence supports systemic inflammation as one mechanistic link explaining the effects of periodontitis on diabetes, the Diabetes and Periodontal Therapy Trial showed that non-surgical periodontal treatment was not associated with six-month changes in serum biomarkers in patients with type 2 diabetes and chronic periodontitis (Geisinger et al., 2016). In contrast, a recent meta-analysis supports the hypothesis that periodontal therapy reduces systematic inflammation (hs-CRP and TNF-α) in people with type 2 diabetes (Artese et al., 2015). On the other hand, it is hypothesized that hyperglycemia induces oxidative stress through increased intracellular formation of advanced glycation end products and increased proinflammatory cytokine production by monocytes, which can contribute to periodontal tissue destruction (Taylor et al., 2013). Thus, cross-sectional study findings can reflect either or both directions regardless of what is modeled as the outcome and exposure. Longitudinal studies are needed to better understand the bidirectional relationship between periodontitis and insulin resistance and glucose abnormalities and to assess potential mediators of these relationships.

This study has several notable strengths, including collection of several measures of glucose metabolism and high-quality clinical data on periodontitis. All three dental examiners were trained according to NHANES criteria, showing excellent agreement with the reference examiner. Although residual confounding cannot be ruled out, it is unlikely to explain the observed effects given the minimal attenuation of the effect measures after extensive multivariable adjustment for potential confounders. One inherent limitation of this cross-sectional analysis is the inability to distinguish the temporal sequence of events. As with many etiologic studies, a non-probability sampling strategy was used to select and recruit the study group. While this would limit our ability to generalize the distribution of impaired glucose metabolism measures and periodontitis, the non-random sample would not affect the validity or generalizability of the associations to other overweight and obese populations, as

there is no reason to expect that the relationship between these two conditions and biological pathways would be different in our sample.

In summary, this cross-sectional analysis indicates the potential role of prediabetes and insulin resistance in high BOP and severe periodontitis. Given the high prevalence of impaired glucose metabolism and periodontitis, the replication of these findings and assessment of the temporal sequence of these associations in longitudinal studies could have substantial implications in the prevention of these chronic conditions.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Kaumudi J. Joshipura, Cynthia M. Pérez, and Christine S. Ritchie contributed to conception and design of the study; Francisco Muñoz performed the statistical analyses with the advice of Cynthia M. Pérez, Kaumudi J. Joshipura, and Oelisoa M. Andriankaja; and Cynthia M. Pérez wrote the manuscript and had primary responsibility for the final content. All other authors made substantial contributions to data acquisition and interpretation and revised the manuscript critically for important intellectual content. All authors read and approved the final version of the manuscript. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

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Clinical relevance

Scientific rationale for study: Current studies suggest a bidirectional relationship between periodontitis and diabetes. However, there is a paucity of data examining the relationship of insulin resistance and pre-clinical stages of diabetes with BOP and periodontitis.

Principal findings: Prediabetes, IFG, impaired 1hPG concentration, IGT, and HOMA-IR were associated with high BOP; prediabetes, IFG, and impaired 1hPG were significantly associated with severe periodontitis. Most of these associations remained significant when the analyses were restricted to non-smokers.

Practical implications: These findings, if further confirmed in longitudinal studies, could have substantial implications in the prevention of these chronic conditions.

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Table 1

Baseline characteristics (Mean ± SD or %) of SOALS participants across BOP and periodontitis status (n=1,191)

	BOP			Periodontitis status*			
	<30% (n=741)	**≥30% (n=450)**	**P value**	**None/Mild (n=407)**	**Moderate (n=502)**	**Severe (n=282)**	**P value for trend**
Age (y)	49.3±6.5	51.0±6.9	<0.001	49.2±6.7	51.0±6.9	51.0±6.5	<0.001
Male gender	25.2	30.4	0.05	18.9	26.3	40.8	<0.001
Less than high school education	8.9	16.7	<0.001	9.6	10.6	17.4	<0.001
Annual income below $20,000	50.8	64.4	<0.001	44.4	59.1	66.7	<0.001
Smoking status			0.49				<0.001
Never	62.8	63.6		71.1	63.4	51.1	
Former	17.8	15.3		15.7	16.9	18.4	
Current	19.4	21.1		13.3	19.7	30.5	
Number of cigarettes smoked/week	67.4±61.7	65.5±54.8	0.81	55.6±52.1	60.5±61.8	80.7±57.6	0.019
Current alcohol intake	44.8	42.4	0.43	41.5	42.8	49.3	0.11
Alcohol intake (grams/day)	2.2±5.9	2.6±5.7	0.19	1.6±5.4	2.5±6.0	3.0±6.0	0.006
Physical activity (METS/week)	21.9±38.0	20.3±39.5	0.47	20.4±35.3	21.9±41.2	21.6±38.3	0.83
Fruit and vegetable consumption (servings/week)	7.3±4.0	6.9±4.0	0.05	7.2±4.0	7.2±4.0	7.0±4.0	0.82
BMI (kg/m^2)	33.1±6.1	33.8±6.6	0.07	33.2±6.1	33.3±6.5	33.5±6.3	0.83
WC (cm)	105.3±14.1	107.8±14.7	0.003	105.1±13.9	106.6±14.8	107.4±14.2	0.09
Number of teeth			0.51				0.001
25-32	49.5	47.6		55.3	48.0	40.8	
4-24	50.5	52.4		44.7	52.0	59.2	
No dental visits in past 12 months	34.1	46.0	<0.001	31.7	39.6	46.8	<0.001
Tooth brushing once or less per day	8.5	9.3	0.62	7.1	10.2	8.9	0.28
Dental flossing less than once per day	53.6	65.3	<0.001	54.3	57.6	64.2	0.034
Plaque index	0.7±0.6	1.1±0.7	<0.001	0.6±0.4	0.9±0.6	1.2±0.7	<0.001
BOP≥30%	-	-	-	17.7	38.3	66.0	<0.001
hs-CRP>3.0 (mg/L)	56.4	61.9	0.17	58.6	56.9	61.2	0.63
FPG (mg/dL)	92.0±9.0	93.8±8.9	0.001	91.3±8.6	93.2±9.1	93.8±9.1	<0.001
1hPG concentration (mg/dL)	150.6±40.2	158.9±41.7	<0.001	147.7±40.6	156.4±40.9	157.7±40.6	0.001
2hPG concentration (mg/dL)	113.5±28.8	118.3±30.1	0.006	114.0±28.7	115.0±28.9	117.7±31.1	0.25

	BOP			Periodontitis status*			
	<30% (n=741)	**≥30% (n=450)**	**P value**	**None/Mild (n=407)**	**Moderate (n=502)**	**Severe (n=282)**	**P value for trend**
Pre-diabetes†	55.1	61.1	0.041	51.6	59.0	62.8	0.009
Modified definition of prediabetes†	66.7	71.6	0.08	63.4	68.9	75.2	0.005
Fasting insulin (mIU/L)	10.3±6.5	11.6±7.8	0.003	10.6±6.9	10.8±7.0	11.2±7.2	0.52
HbA1c (%)	5.7±0.3	5.7±0.3	0.76	5.7±0.3	5.7±0.3	5.7±0.3	0.33
HOMA-IR	2.4±1.6	2.7±1.9	0.001	2.4±1.7	2.5±1.7	2.6±1.8	0.24
HDL-C (mg/dL)	48.0±12.8	49.2±13.6	0.15	49.0±12.7	48.3±13.6	48.1±13.1	0.64

*Periodontitis was defined according to CDC/AAP definition.

†Pre-diabetes was defined as having at least one ADA diagnostic criterion; the modified definition used ADA glucose thresholds for prediabetes plus 1hPG concentration >155 mg/dl.

Table 2

Multivariable odds ratios for BOP status by glucose metabolism measures (n=1,191)

	OR	95% CI	P value‡
Prediabetes			
Model 1*	1.44	1.13-1.84	0.004
Model 2†	1.51	1.15-1.97	0.003
Prediabetes + impaired 1hPG concentration			
Model 1	1.42	1.09-1.84	0.009
Model 2	1.43	1.08-1.91	0.013
IFG			
Model 1	1.55	1.16-2.07	0.003
Model 2	1.50	1.10-2.06	0.010
Impaired 1hPG concentration			
Model 1	1.44	1.13-1.83	0.003
Model 2	1.39	1.07-1.80	0.013
IGT			
Model 1	1.58	1.17-2.14	0.003
Model 2	1.54	1.11-2.13	0.010
Impaired HbA1c			
Model 1	1.01	0.79-1.28	0.95
Model 2	1.06	0.81-1.38	0.66
HOMA-IR			
Model 1	1.51	1.16-1.98	0.002
Model 2	1.55	1.14-2.12	0.006

*Model 1 adjusted for age.

†Model 2 additionally adjusted for gender, education, smoking status, physical activity (METs), alcohol consumption (grams/week), WC, HDL-C, and plaque index.

‡P value derived from the Wald chi-square statistic.

Table 3

Multivariable odds ratios for periodontitis status by glucose metabolism measures (n=1,191)

	No or mild periodontitis[‡]	Moderate periodontitis			Severe periodontitis		
		OR	95% CI	P value[§]	OR	95% CI	P value[§]
Prediabetes							
Model 1[*]	1.0	1.24	0.95-1.62	0.12	1.46	1.07-2.00	0.018
Model 2[†]	1.0	1.31	0.98-1.74	0.07	1.67	1.17-2.40	0.005
Prediabetes + impaired 1hPG concentration							
Model 1	1.0	1.17	0.88-1.55	0.28	1.61	1.14-2.27	0.006
Model 2	1.0	1.22	0.90-1.65	0.19	1.84	1.24-2.73	0.002
IFG							
Model 1	1.0	1.52	1.08-2.14	0.017	1.87	1.28-2.74	0.001
Model 2	1.0	1.45	1.01-2.08	0.042	1.62	1.06-2.48	0.027
Impaired 1hPG concentration							
Model 1	1.0	1.14	0.87-1.48	0.35	1.54	1.13-2.10	0.006
Model 2	1.0	1.10	0.83-1.46	0.50	1.46	1.03-2.07	0.035
IGT							
Model 1	1.0	1.04	0.73-1.49	0.81	1.43	0.97-2.10	0.07
Model 2	1.0	1.06	0.73-1.53	0.75	1.53	0.99-2.36	0.06
Impaired HbA1c							
Model 1	1.0	0.95	0.72-1.24	0.70	1.04	0.76-1.42	0.81
Model 2	1.0	0.99	0.74-1.32	0.95	1.23	0.85-1.76	0.27
HOMA-IR							
Model 1	1.0	1.27	0.93-1.74	0.13	1.58	1.11-2.25	0.010
Model 2	1.0	1.20	0.84-1.71	0.31	1.51	0.99-2.32	0.06

[*] Model 1 adjusted for age.

[†] Model 2 additionally adjusted for gender, education, smoking status, physical activity (METs), alcohol consumption (grams/week), WC, HDL-C, and plaque index.

[‡] Reference category

[§] P value derived from the Wald chi-square statistic.

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Table 4

Multivariable odds ratios [*] for BOP and periodontitis status by glucose metabolism measures among never (n=751) and ever (n=440) smokers.

	BOP		Moderate periodontitis[†]		Severe periodontitis[†]	
	OR	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
Prediabetes						
Never-smokers	1.55	1.10-2.20[‡]	1.19	0.84-1.69	1.53	0.95-2.45[§]
Ever smokers	1.47	0.95-2.27[§]	1.53	0.92-2.52	1.91	1.08-3.39[‡]
Prediabetes + impaired 1hPG concentration						
Never-smokers	1.39	0.96-2.01[§]	1.19	0.82-1.73	1.63	0.97-2.74[§]
Ever smokers	1.56	0.98-2.49[§]	1.26	0.75-2.11	2.16	1.16-4.00[‡]
IFG						
Never-smokers	1.52	1.01-2.30[‡]	1.43	0.92-2.23	1.85	1.06-3.23[‡]
Ever smokers	1.58	0.96-2.58[§]	1.58	0.84-2.96	1.53	0.77-3.05
Impaired 1hPG concentration						
Never-smokers	1.33	0.95-1.85[§]	1.07	0.76-1.52	1.23	0.78-1.95
Ever smokers	1.53	1.00-2.36[§]	1.12	0.67-1.86	1.92	1.08-3.39[‡]
IGT						
Never-smokers	1.60	1.07-2.38[‡]	1.04	0.67-1.61	1.86	1.09-3.17[‡]
Ever smokers	1.38	0.78-2.45	1.02	0.51-2.06	1.03	0.47-2.23
Impaired HbA1c						
Never-smokers	1.05	0.74-1.47	0.95	0.67-1.36	1.13	0.70-1.82
Ever smokers	1.16	0.75-1.78	1.09	0.66-1.80	1.63	0.92-2.91
HOMA-IR						
Never-smokers	1.49	0.99 -2.24[§]	1.13	0.73-1.74	1.74	0.99-3.07[§]
Ever smokers	1.69	1.04-2.77[‡]	1.32	0.72-2.42	1.42	0.73-2.78

[*] Models adjusted for age, gender, education, physical activity (METs), alcohol consumption (grams/week), WC, HDL-C, and plaque index.

[†] Relative to none/mild periodontitis.

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‡P value <0.05

§0.05≤P value<0.10