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ABSTRACT

Studies have suggested an association between clinical/subclinical atherosclerosis and periodontal status. The purpose of this study was to investigate the association among maximal carotid intima–media thickness (cIMT), atherosclerotic plaque, and periodontal status in Chinese elderly patients. A cross-sectional study was conducted of 847 participants (age, 70.64 ± 9.03 yr) with ≥10 teeth. A questionnaire survey, routine biochemical tests, a periodontal examination, and maximal cIMT measurement were performed for each. Traditional risk factors for atherogenesis were considered in the statistical analysis. Mean plaque index, which reflects oral hygiene, was correlated with maximal cIMT and atherosclerotic plaque in the study sample overall (β = 0.068, $p < .001$; OR = 2.051, $p < .001$) and in euglycemic participants (β = 0.066, $p = .008$; odds ratio = 2.122, $p = .009$). In hyperglycemic participants, multiple linear regression analysis ($p = .006$) and multivariate logistic regression analysis ($p = .025$) revealed a linear and dose-dependent association between mean clinical attachment loss and maximal cIMT after adjustment for traditional risk factors. Each 1-mm increase in mean clinical attachment loss corresponded to a 0.018-mm increase in maximal cIMT. The risk of atherosclerotic plaque increased by 18.3% with each 1-mm increase in mean clinical attachment loss. Other indicators of periodontal exposure, including percentage of sites with attachment loss ≥ 3 to 5 mm (3%-5%), were also correlated with cIMT and atherosclerotic plaque in hyperglycemic patients. In this elderly population, a linear and dose-dependent association among mean clinical attachment loss, attachment loss 3% to 5%, maximal cIMT, and atherosclerotic plaque was verified in those with hyperglycemia. Poor oral hygiene was correlated with maximal cIMT and atherosclerotic plaque in all participants, including those with normal blood glucose.

KEY WORDS: atherosclerosis, periodontitis, periodontal attachment loss, oral hygiene, hyperglycemia, cardiovascular diseases.

INTRODUCTION

Atherosclerosis is involved in several disorders with high mortality, including cardiovascular, cerebrovascular, and peripheral arterial disease. The condition usually starts in the vascular intima, progressing to the medial arterial wall. Thickening of the arterial wall due to deposition of lipid and glycocomponents is associated with chronic inflammation around the vessel and can develop into a proliferation of fibers and calcium deposition known as atherosclerotic plaque (Libby *et al.*, 2011). Carotid intima–media wall thickness (cIMT) is an indicator of the risk of vascular disease (Kablak-Ziembicka *et al.*, 2005; Rosvall *et al.*, 2005). Increased cIMT and presence of atherosclerotic plaque are considered subclinical atherosclerosis and can be used for

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cardiovascular risk assessment in asymptomatic adults (Kadota *et al.*, 2013).

Atherosclerosis is a multifactorial disorder with numerous risk factors. Chronic inflammatory reaction has been found to occur throughout atherogenesis (Paquette *et al.*, 2007). Studies have shown a possible association between clinical/subclinical atherosclerosis and chronic periodontitis, epidemiologically and microbiologically (Ford *et al.*, 2006; Hayashida *et al.*, 2013; Jung *et al.*, 2013; Tonetti and Van Dyke, 2013). This hypothesis is reasonable considering that chronic periodontitis is a chronic multifactorial inflammatory disease surrounding the root of a tooth. Possible links between the 2 disorders have been suggested (Tonetti and Van Dyke, 2013; Bullon *et al.*, 2014), but mechanisms remain to be determined. Hyperglycemic individuals are at higher risk of atherosclerosis and chronic periodontitis, which is further evidence for a link between the 2 and may be a consequence of a widespread inflammatory response (Chistiakov *et al.*, 2012; Southerland *et al.*, 2012).

There has been little research into the relationship of atherosclerosis with chronic periodontitis in China, where the latter is a public oral health problem. The purpose of this study was to investigate the association between subclinical atherosclerosis and periodontal status in China.

MATERIALS & METHODS

The recruitment was performed from May to July 2005. Residents served by a community hospital (Gucheng Hospital) were invited to participate in the study. Of the individuals who were eligible for inclusion in the study, 1,058 (18.9%) volunteered to participate and signed informed written consent. None of the participants had a history of carotid artery surgery. The study was approved by the Institutional Review Board and Ethics Committee of the Peking University Health Science Center. A cross-sectional study conforming to STROBE guidelines was conducted. All participants underwent routine biochemical tests and ultrasonography to measure cIMT. They also completed a questionnaire concerning their medical history and lifestyle. In sum, 1,001 underwent periodontal examination. Further inclusion criteria were as follows: complete results available for all of the examinations and at least 10 remaining teeth. Fifty-seven participants without results for periodontal examination were excluded. Reasons included inability to cooperate with dental examination, use of antibiotics for >1 wk in the past 6 mo, and a diagnosis of any condition for which prophylactic antibiotic treatment is required. In addition, 154 were excluded due to having <10 remaining teeth. As such, 847 (434 men and 413 women) met criteria and were included in the study.

Patient Assessment

A standardized questionnaire was given to collect information about participants' history of systemic diseases, such as hypertension, diabetes, and hyperlipidemia. Participants were classified as smokers (ever smoked, including those who had quit) or never smokers. Educational level was classified as middle school or below (≤9 yr) or high school or above (>9 yr). Family income was classified as low (≤US$120.85), average (US$120.86–US$362.54), or high (≥US$362.55). Sitting blood pressure was measured 3 times using a mercury sphygmomanometer after 5 min of rest. The average of 3 measurements of systolic blood pressure and diastolic blood pressure was used. Weight, height, and waist and hip circumference were measured after an overnight fast while participants were not wearing overcoats or shoes. Body mass index (kg/m^2) and waist:hip ratio were calculated. Peripheral blood samples were collected after an overnight fast. Serum was separated within 2 hr and stored in liquid nitrogen until required. Triglycerides, high-density lipoprotein, low-density lipoprotein, fasting blood glucose, and postprandial blood glucose were measured with an automatic analyzer (Model 7060; Hitachi, Tokyo, Japan). High-density lipoprotein was measured by a direct method; low-density lipoprotein was calculated by the Friedewald equation. Blood glucose was measured via the glucose-hexokinase method.

The definition of hyperglycemia was as follows:

Impaired fasting glucose: 6.1 ≤ fasting plasma glucose < 7.0 mmol/L

Impaired glucose tolerance: 7.8 ≤ postprandial blood glucose < 11.1 mmol/L; or

Diabetes: fasting plasma glucose ≥ 7.0 mmol/L and/or postprandial blood glucose ≥ 11.1 mmol/L and/or ever diagnosed with diabetes.

Hypertension was defined as follows: systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mm Hg and/or ever diagnosed with hypertension.

Periodontal Examination

One specially trained dentist from Peking University School of Stomatology, China, performed all periodontal examinations. Plaque index (PLI), probing depth, clinical attachment loss (AL), and bleeding index were measured and recorded at mesiobuccal and distal-lingual sites for all teeth, excluding the third molars, with a Williams probe (Hu-Friedy, Chicago, IL, USA). The odds of total identity and error range within 1 or 2 mm were used. Eighty-one sites of 3 randomly selected periodontal patients were examined twice to test the reproducibility of the examiners' findings. The values were 85.2%, 98.8% and 100% for probing depth and 74.1%, 80.2%, and 97.5% for AL. Number of lost teeth and mean PLI, probing depth, AL, and bleeding index were used. The percentages of sites with AL ≥ 3-6 mm (AL 3%-6%) were also analyzed in the study.

Assessment of Atherosclerotic Plaque

Internal carotid artery, common carotid artery (CCA), and carotid bifurcation thickness are commonly used to measure cIMT. The CCA is used in most studies because of its convenience and high repeatability. We used CCA thickness to detect subclinical atherosclerosis.

cIMT was assessed by M-mode ultrasonography via a Vivid 7 system with a 7- to 10-MHz linear transducer (GE Medical Systems, Horten, Norway) with participants in the supine

position. The carotid artery was scanned bilaterally on longitudinal two-dimensional planes. Images were obtained at the level of the distal 1.0 cm of the left and right CCAs. When an optimal image was obtained, it was frozen on the R wave of the electrocardiogram and stored on videotape. For each segment, the cIMT of the posterior wall was measured automatically over 200 pixels with computer-assisted electronic calipers. The examination was performed by 1 of 3 radiologists from the Cardiology Department of Peking University First Hospital, China. Maximal right and left CCA thickness was measured and used for analysis. The intra- and intersonographer correlation coefficients of variability were 0.90 and 0.98, respectively.

Most studies use cIMT ≥ 1 mm as evidence of arterial thickening (Cheng *et al.*, 2012). However, there is controversy regarding the cutoff point for atherosclerotic plaque. According to previous studies, we defined the presence of atherosclerotic plaque as maximal cIMT≥ 1.2 mm (Kablak-Ziembicka *et al.*, 2005; Rosvall *et al.*, 2005).

Statistical Analysis

For continuous variables, results were presented as the mean ± standard deviation. For categorical variables, results were expressed as frequencies and/or percentages. Differences in means were assessed by Student's *t* test; differences in prevalence were assessed by the chi-square test. For multivariate analysis, multiple linear regression and multivariate logistic regression were used. Traditional risk factors were adjusted for in the analysis, including sex, age, family income, educational level, body mass index, waist:hip ratio, blood lipid level, hypertension, diabetes, and smoking. Multicollinearity was examined by tolerance and a variance inflation factor for each variable. We found tolerance to be >0.5 and variance inflation factor to be <2.5 in all models. Hence, multicollinearity was not a concern. SPSS 20 for MacBook (IBM, Armonk, NY, USA) was used for statistical analysis; $p < .05$ was considered statistically significant.

RESULTS

Patient Background and Clinical Characteristics

In sum, 847 participants (434 men and 413 women) met the inclusion criteria. Table 1 lists their characteristics. Among the total sample, 245 (28.93%) were regarded as having atherosclerotic plaque (maximal cIMT ≥ 1.2 mm), and 602 (71.07%) were regarded as being free from plaque (maximal cIMT < 1.2 mm). Sex ratio, age, high-density lipoprotein, fasting blood glucose, body mass index, waist:hip ratio, systolic blood pressure, hypertension, and smoking status differed significantly. All periodontal parameters, excluding mean bleeding index, were considered significantly different between those with and without atherosclerotic plaque. The participants were further divided into 2 groups: hyperglycemic and euglycemic. Their characteristics are shown in Table 2. Among hyperglycemic participants, 165 (34.45%) had atherosclerotic plaque, in which the following were significantly higher: number of lost teeth; mean PLI and AL; and AL 3%, 4%, 5%, and 6%. Among euglycemic participants, 80 (21.74%) had atherosclerotic plaque. Regarding their periodontal status, only mean PLI differed significantly.

Periodontal Status and Subclinical Atherosclerosis

Partial correlation analysis results for maximal cIMT and other variables after adjustment for age and sex are shown in Appendix Table 1. Multiple linear regression results for maximal cIMT and periodontal parameters are shown in Table 3. Over the whole sample, cIMT was significantly correlated with mean PLI ($p < .001$) after adjusting for sex, age, body mass index, waist:hip ratio, educational level, family income, blood lipid level, hypertension, diabetes, and smoking, with a nonstandardized coefficient of 0.068 (95% confidence interval [CI]: 0.033, 0.103). A similar correlation was found in euglycemic participants ($p = .008$); the nonstandardized coefficient was 0.066 (95% CI: 0.017, 0.115). Among hyperglycemic participants, a significant correlation was found between mean AL and cIMT ($p = .006$). Each 1-mm increase in mean AL corresponded to a 0.018-mm increase in maximal cIMT after adjustment (95% CI: 0.005, 0.031). Other periodontal exposures, including AL 3% ($\beta = 0.001$, $p = .004$), AL 4% ($\beta = 0.001$, $p = .011$), and AL 5% ($\beta = 0.001$, $p = .033$), were also correlated with maximal cIMT, although AL 6% ($p = .489$) did not show such a correlation (Table 4). Regression line displaying the association between maximal cIMT and mean AL in hyperglycemic subjects is shown in the Appendix Figure.

Multiple logistic regression results for atherosclerotic plaque were in accord with the above linear regression analysis (Table 5). The whole sample showed a greater risk of atherosclerotic plaque with increased mean PLI (adjusted odds ratio [OR] = 2.051; 95% CI: 1.410, 2.982) after adjusting for the above traditional risk factors. This was also the case for euglycemic participants (adjusted OR = 2.122; 95% CI: 1.204, 3.741). In hyperglycemic participants, the prevalence of atherosclerotic plaque was significantly correlated with mean AL (adjusted OR = 1.183; 95% CI: 1.021, 1.371; $p = .025$). AL 3% (adjusted OR = 1.013; $p = .001$), AL 4% (adjusted OR = 1.009; $p = .016$), AL 5% (adjusted OR = 1.008; $p = .047$) were also correlated with increased risk of atherosclerotic plaque (Table 4).

DISCUSSION

In this study, mean PLI, which is an important indicator of oral hygiene, was correlated with cIMT and atherosclerotic plaque in the study sample as a whole and in euglycemic participants. Previous studies have demonstrated a relationship between oral hygiene and atherosclerotic disease. Using the DMFT method (*i.e.*, decayed, missing, filled teeth) and the Silness-Löe index, Schillinger *et al.* (2006) showed that dental status and oral hygiene are associated with degree of carotid stenosis, finding that both DMFT and Silness-Löe were predictors for atherosclerosis severity. Other studies have confirmed a relationship among oral hygiene, cIMT, and atherosclerosis (Hoke *et al.*, 2011; Uyar *et al.*, 2013). After 4 wk of ligature-induced periodontitis, accumulation of lipid representing early atherosclerosis occurred in the rat aorta (Ekuni *et al.*, 2009).

A role for periodontitis in the pathogenesis of atherosclerosis has been noticed on the basis of various indicators of periodontitis severity to investigate the relationship. Beck *et al.* (2001) were the first to suggest that periodontitis might play a role in subclinical atherosclerosis. Severe periodontitis characterized

Table 1. Characteristics of the Total Sample

	Total Sample (*n* = 847)		
	cIMT ≥ 1.2 (*n* = 245)	cIMT < 1.2 (*n* = 602)	*p*
Sex			
Men	150 (34.6)	284 (65.4)	<.001*
Women	95 (23.0)	318 (77.0)	
Age, yr	73.05 ± 8.24	69.66 ± 9.16	<.001*
Educational level, yr			
≤ 9	148 (29.7)	350 (7.3)	.543
> 9	97 (27.8)	252 (72.2)	
Family income			
Low	18 (25.0)	54 (75.0)	.517
Average	191 (28.8)	473 (71.2)	
High	36 (32.7)	74 (67.3)	
Triglycerides	2.33 ± 1.29	2.40 ± 2.09	.651
Lipoprotein			
High density	1.28 ± 0.30	1.37 ± 0.34	<.001*
Low density	2.96 ± 0.95	2.84 ± 0.94	.080
Fasting blood glucose	6.79 ± 2.47	6.20 ± 2.16	.001*
Body mass index	26.40 ± 3.33	25.59 ± 3.91	.005*
Waist:hip ratio	0.92 ± 0.06	0.90 ± 0.09	<.001*
Hypertension			
Yes	137 (37.0)	233 (63.0)	<.001*
No	108 (22.6)	369 (77.4)	
Smoking status			
Yes	107 (37.3)	180 (62.7)	<.001
No	138 (24.6)	422 (75.4)	
No. of lost teeth	4.62 ± 4.87	3.60 ± 4.34	.004*
Plaque index	1.83 ± 0.52	1.62 ± 0.50	<.001*
Probing depth	2.85 ± 0.85	2.72 ± 0.78	.038*
Bleeding index	2.02 ± 0.54	2.03 ± 0.56	.925
Attachment loss	2.98 ± 1.73	2.42 ± 1.57	<.001*
3%	54.20 ± 27.79	44.66 ± 27.92	<.001*
4%	37.75 ± 28.96	29.59 ± 26.27	<.001*
5%	26.29 ± 26.58	19.16 ± 22.44	<.001*
6%	15.21 ± 21.88	9.93 ± 16.49	.001*
Blood pressure			
Systolic	138.66 ± 17.79	131.32 ± 17.70	<.001*
Diastolic	81.40 ± 11.45	79.94 ± 10.72	.077
Maximal cIMT	1.38 ± 0.17	0.97 ± 0.14	<.001*

Values in *n* (%) or mean ± SD.
cIMT, carotid intima–media wall thickness.

by extensive clinical AL was found to increase the likelihood of greater cIMT, and further studies have demonstrated such an association (Pinho *et al.*, 2013). Other indicators, such as number of lost teeth and bleeding on probing, have been associated with increased cIMT (Jung *et al.*, 2013). A systemic review and meta-analysis demonstrated that periodontal treatment could improve endothelial function as well as reduce indicators of atherosclerosis, such as high-sensitivity C-reactive protein, interleukin 6, tumor necrosis factor, fibrinogen, high-density lipoprotein, and hemoglobin A1c (Teeuw *et al.*, 2014).

In the present study, clinical AL, which reflects the extent of periodontal tissue destruction, was found to be associated with maximal cIMT and atherosclerotic plaque in hyperglycemic participants. After adjustment, each 1-mm increase in mean AL corresponded to a 0.018-mm increase in maximal cIMT. The risk of atherosclerotic plaque increased by 18.3% with each 1-mm increase in mean AL. Other indicators reflecting the extent of periodontal tissue destruction, including AL 3%, 4%, and 5%, were found to be associated with subclinical atherosclerosis. It is reasonable to assume that this was a consequence of a relationship between diabetes and periodontitis; thus, presence of diabetes was considered a confounding factor in our statistical analysis. Our results are consistent with other studies that have demonstrated an association between periodontal status and atherosclerosis in

Table 2. Characteristics of the Hyperglycemic and Euglycemic Group

	Hyperglycemic Group (*n* = 479)			Euglycemic Group (*n* = 368)		
	cIMT ≥ 1.2 (*n* = 165)	cIMT < 1.2 (*n* = 314)	*p*	cIMT ≥ 1.2 (*n* = 80)	cIMT < 1.2 (*n* = 288)	*p*
Sex						
Men	98 (41.7)	137 (58.3)	.001*	52 (26.1)	147 (73.9)	.027*
Women	67 (27.5)	177 (72.5)		28 (16.6)	141 (83.4)	
Age, yr	73.04 ± 8.34	70.68 ± 8.63	.004*	73.07 ± 8.07	68.55 ± 9.03	<.001*
Educational level, yr						
≤9	94 (33.7)	185 (66.3)	.681	54 (24.7)	165 (75.3)	.100
>9	71 (35.5)	129 (64.5)		26 (17.4)	123 (82.6)	
Family income						
Low	13 (29.5)	31 (70.5)	.265	5 (17.9)	23 (82.1)	.813
Average	126 (33.7)	248 (66.3)		65 (22.4)	225 (77.6)	
High	26 (43.3)	34 (56.7)		10 (20.0)	40 (80.0)	
Triglycerides	2.52 ± 2.57	2.79 ± 2.23	.231	1.933 ± 0.931	1.97 ± 1.83	.843
Lipoprotein						
High density	1.29 ± 0.31	1.35 ± 0.33	.062	1.253 ± 0.276	1.40 ± 0.39	<.001*
Low density	2.95 ± 1.07	2.86 ± 0.97	.354	2.983 ± 0.652	2.81 ± 0.92	.056
Fasting blood glucose	7.58 ± 2.66	7.13 ± 2.64	.079	5.173 ± 0.373	5.19 ± 0.41	.802
Body mass index	26.47 ± 3.39	25.85 ± 3.73	.073	26.241 ± 3.220	25.31 ± 4.09	.061
Waist:hip ratio	0.92 ± 0.064	0.91 ± 0.083	.071	0.913 ± 0.0615	0.88 ± 0.087	.004*
Hypertension						
Yes	93 (43.9)	119 (56.1)	<.001*	44 (27.8)	114 (72.2)	.014*
No	72 (27.0)	195 (73.0)		36 (17.1)	174 (82.9)	
Smoking status						
Yes	71 (45.5)	85 (54.5)	<.001*	36 (27.5)	95 (72.5)	.047*
No	94 (29.1)	229 (70.9)		44 (18.6)	193 (81.4)	
No. of lost teeth	4.72 ± 4.89	3.72 ± 4.45	.029*	4.425 ± 4.844	3.46 ± 4.22	.108
Plaque index	1.87 ± 0.52	1.70 ± 0.52	.001*	1.757 ± 0.492	1.54 ± 0.46	<.001*
Probing depth	2.90 ± 0.87	2.77 ± 0.75	.080	2.739 ± 0.807	2.67 ± 0.80	.521
Bleeding index	2.04 ± 0.54	2.06 ± 0.56	.755	1.976 ± 0.520	1.99 ± 0.56	.866
Attachment loss	3.13 ± 1.71	2.53 ± 1.57	<.001*	2.662 ± 1.739	2.30 ± 1.57	.074
3%	57.23 ± 26.99	46.52 ± 27.67	<.001*	47.97 ± 28.54	42.64 ± 28.09	.136
4%	40.07 ± 29.08	31.26 ± 26.58	.001*	32.96 ± 28.28	27.77 ± 25.85	.121
5%	28.18 ± 27.28	20.75 ± 23.27	.003*	22.38 ± 24.77	17.43 ± 21.40	.078
6%	16.38 ± 11.09	11.09 ± 17.03	.009*	12.78 ± 19.81	8.68 ± 15.82	.091
Blood pressure						
Systolic	137.97 ± 18.57	131.87 ± 16.86	<.001*	140.071 ± 16.079	130.71 ± 18.58	<.001*
Diastolic	81.13 ± 11.72	79.36 ± 10.28	.089	81.967 ± 10.926	80.56 ± 11.16	.316
Maximal cIMT	1.38 ± 0.17	0.98 ± 0.13	<.001*	1.400 ± 0.183	0.96 ± 0.14	<.001*

Values in *n* (%) or mean ± SD.
cIMT, carotid intima–media wall thickness.

diabetic or hyperglycemic patients. Increased cIMT has been found to be associated with periodontal inflammation in patients with diabetes, as reflected by increased probing depth and bleeding-on-probing scores (Franek *et al.*, 2012). Participants with diabetes and severe periodontitis are more susceptible to subclinical atherosclerosis and coronary heart disease (Southerland *et al.*, 2012), and the effect of periodontal treatment on atherosclerotic disease was most noticeable in patients with cardiovascular disease and/or diabetes (Teeuw *et al.*, 2014).

A relationship between atherosclerosis and periodontitis has been demonstrated epidemiologically (Tonetti and Van Dyke, 2013), and possible pathologic mechanisms linking the two have been studied. Poor oral hygiene not only increased the risk of severe periodontitis and chronic inflammation (Schillinger *et al.*, 2006) but also increased the number and virulence of periodontal pathogens that entered the bloodstream. Tonetti and Van Dyke (2013) have suggested a plausible biological mechanism for the 2 disorders in which, after entry of periodontal bacteria into the circulation, multiple host inflammatory and immune responses are activated that promote the formation, maturation, and exacerbation of atheroma. Other reviews have speculated that the relationship between atherosclerosis and periodontitis could be mediated by oxidative stress/mitochondrial dysfunction (Bullon *et al.*, 2014).

Although the correlations between atherosclerosis and periodontitis discussed above were not found in overall study

Table 3. Multiple Linear Regression Analysis of Maximal cIMT and Periodontal Parameters

	Unadjusted		Adjusted	
	β (95% CI)	*p*	β (95% CI)	*p*
Total sample				
No. of lost teeth	0.000 (–0.004, 0.005)	.827	0.000 (–0.004, 0.005)	.827
Mean PLI	0.087 (0.048, 0.127)	<.001*	0.068 (0.033, 0.103)	<.001*
Mean PD	–0.011 (–0.043, 0.021)	.500	–0.006 (–0.038, 0.027)	.721
Mean AL	0.014 (0.003, 0.026)	.014*	0.004 (–0.012, 0.021)	.601
Mean BI	–0.045 (–0.084, 0.006)	.025*	–0.023 (–0.055, 0.008)	.150
Hyperglycemic group				
No. of lost teeth	0.001 (–0.005, 0.007)	.770	0.000 (–0.006, 0.006)	.947
Mean PLI	0.055 (0.004, 0.106)	.033*	0.050 (–0.001, 0.101)	.053
Mean PD	–0.006 (–0.048, 0.037)	.794	–0.010 (–0.055, 0.035)	.649
Mean AL	0.023 (0.011, 0.036)	<.001*	0.018 (0.005, 0.031)	.006*
Mean BI	–0.039 (–0.090, 0.012)	.133	–0.027 (–0.080, 0.025)	.303
Euglycemic group				
No. of lost teeth	0.002 (–0.005, 0.008)	.672	0.002 (–0.005, 0.009)	.592
Mean PLI	0.133 (0.075, 0.191)	<.001*	0.066 (0.017, 0.115)	.008*
Mean PD	–0.019 (–0.067, 0.030)	.448	–0.001 (–0.049, 0.047)	.975
Mean AL	0.010 (–0.014, 0.034)	.415	–0.012 (–0.037, 0.013)	.338
Mean BI	–0.053 (–0.114, 0.008)	.090	–0.010 (–0.070, 0.050)	.746

Multiple linear regression analysis was adjusted for sex, age, educational level, family income, body mass index, waist:hip ratio, blood lipid level, hypertension, diabetes, and smoking.
cIMT, carotid intima–media wall thickness; CI, confidence interval; PLI, plaque index; PD, probing depth; AL, attachment loss; BI, bleeding index.
*$p < .05$.

Table 4. Multivariate Analysis of Maximal cIMT and AL 3% to 6% in Hyperglycemic Participants after Adjustment

	Multiple Linear Regression Analysis			Multivariate Logistic Regression Analysis		
AL	β	95% CI	*p*	OR	95% CI	*p*
3%	0.001	0.000, 0.002	.004*	1.013	1.005, 1.021	.001*
4%	0.001	0.000, 0.002	.011*	1.009	1.002, 1.016	.016*
5%	0.001	0.000, 0.002	.033*	1.008	1.000, 1.017	.047*
6%	0.000	–0.001, 0.002	.489	1.010	0.999, 1.020	.071

Multivariate analysis was adjusted for sex, age, educational level, family income, body mass index, waist:hip ratio, blood lipid level, hypertension, diabetes, and smoking.
cIMT, carotid intima–media wall thickness; AL, attachment loss; CI, confidence interval; OR, odds ratio.
*$p < .05$.

samples or in euglycemic participants, a linear and dose-dependent association between periodontal status and cIMT regardless of blood glucose was revealed in a Japanese population (Hayashida *et al.*, 2013). The risk of greater cIMT (>1 mm) increased by 43% and 25% with each 1-mm increase in mean probing depth and AL, respectively. Diabetes has long been known to relate to periodontitis, atherosclerosis (Wagenknecht *et al.*, 1997), and cardiovascular disease. The hyperglycemic state increases production of reactive oxygen species and oxidative stress, leading to an inflammatory response that in turn aggravates insulin resistance and hyperglycemia (Chistiakov *et al.*, 2012). Altered vascular pathology, endothelial dysfunction, and a widespread inflammatory reaction under such circumstances might explain the effect of hyperglycemia on atherosclerosis and periodontitis. The possible synergy of hyperglycemia and periodontitis in the pathogenesis of atherosclerosis needs further investigation (Southerland *et al.*, 2012).

There may be several reasons for the differences between our study and previous reports. The methods used for examination differ. We measured mesiobuccal and distal-lingual sites for all teeth, whereas some researchers measured mesiobuccal and midbuccal sites (Hayashida *et al.*, 2013), which might underestimate the severity of periodontitis, and others measured 6 sites per tooth in 2 randomly selected quadrants (Jung *et al.*, 2013) or all 4 quadrants (Southerland *et al.*, 2012). Factors that might affect probing accuracy have been discussed by the American Academy of Periodontology (Armitage *et al.*, 2003). The average age of the participants in our study was greater than that in

Table 5. Multivariate Logistic Regression Analysis of Maximal cIMT ≥ 1.2 mm and Periodontal Parameters

	Unadjusted		Adjusted	
	OR (95% CI)	*p*	OR (95% CI)	*p*
Total sample				
No. of lost teeth	0.997 (0.956, 1.040)	.896	0.996 (0.953, 1.042)	.876
Mean PLI	2.357 (1.606, 3.460)	<.001*	2.051 (1.410, 2.982)	<.001*
Mean PD	0.945 (0.702, 1.270)	.706	0.929 (0.662, 1.303)	.669
Mean AL	1.117 (1.004, 1.243)	.042*	1.079 (0.913, 1.275)	.372
Mean BI	0.621 (0.452, 0.853)	.003*	0.720 (0.512, 1.012)	.059
Hyperglycemic group				
No. of lost teeth	0.987 (0.936, 1.040)	.630	0.984 (0.930, 1.043)	.593
Mean PLI	1.668 (1.045, 2.661)	.032*	1.615 (0.981, 2.658)	.059
Mean PD	0.975 (0.665, 1.429)	.896	0.839 (0.538, 1.309)	.440
Mean AL	1.190 (1.037, 1.366)	.013*	1.183 (1.021, 1.371)	.025*
Mean BI	0.662 (0.447, 0.979)	.039	0.717 (0.428, 1.199)	.205
Euglycemic group				
No. of lost teeth	1.015 (0.959, 1.074)	.602	1.023 (0.951, 1.100)	.547
Mean PLI	3.747 (2.014, 6.973)	<.001*	2.122 (1.204, 3.741)	.009*
Mean PD	0.871 (0.563, 1.348)	.536	0.978 (0.546, 1.752)	.941
Mean AL	0.993 (0.773, 1.277)	.959	0.865 (0.654, 1.145)	.312
Mean BI	0.542 (0.312, 0.941)	.030*	0.787 (0.370, 1.674)	.534

Multivariate logistic regression analysis was adjusted for sex, age, educational level, family income, body mass index, waist:hip ratio, blood lipid level, hypertension, diabetes, and smoking.
cIMT, carotid intima–media wall thickness; OR, odds ratio; CI, confidence interval; PLI, plaque index; PD, probing depth; AL, attachment loss; BI, bleeding index.
*$p < .05$.

other studies, and because age is an important factor in atherosclerosis, diabetes, and periodontitis, this may have influenced our results.

No significant relationship between number of lost teeth and cIMT was found in this study, unlike that in others (Schillinger *et al.*, 2006; Jung *et al.*, 2013), probably because neither our study nor previous research recorded the cause of lost teeth. Other than severe periodontitis, reasons for tooth loss include extraction due to caries, trauma, and congenital absence. Also, we excluded participants with <10 teeth, which might have affected the results.

Despite its widespread use in clinical and scientific research, the true merits of employing cIMT for predicting future risk of cardiovascular disease remain controversial (Budoff, 2011; Mearns, 2012). Another limitation of our study is the use of old ultrasonography data; modern equipment might have been less problematic.

This was a cross-sectional study, and it could not demonstrate a cause-and-effect relationship between subclinical atherosclerosis and periodontal status. Only clinical parameters were considered; inflammatory markers of atherosclerosis and microbiologic factors were not addressed.

In conclusion, a linear and dose-dependent association between mean AL, AL 3% to 5%, and maximal cIMT and atherosclerotic plaque was identified in hyperglycemic participants. Poor oral hygiene was correlated with maximal cIMT and atherosclerotic plaque in all participants, including those with euglycemia.

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