Association of periodontitis with carotid artery intima-media thickness and arterial stiffness in community-dwelling people in Japan

Subtitle: Periodontitis and early stage atherosclerosis

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Abstract

Objective:

Recent studies have suggested an association between periodontitis and atherosclerosis; however, the relationship between periodontal status and arterial alterations should be clarified. The purpose of this study was to examine associations between periodontal status and carotid intima-media thickness (cIMT) and arterial stiffness using the cardio-ankle vascular index (CAVI) in community dwellers.

Methods:

A community-based cross-sectional study of 1,053 subjects ≥ 40 years with 10 teeth or more was conducted in Goto, Japan from 2008 to 2010.

Results:

In a multiple linear regression analysis adjusted for age, sex, number of present teeth, and other confounders, each 1-mm increase in the mean periodontal pocket depth corresponded to a 0.02-mm increase in the maximal cIMT (β = 0.018; P= 0.049) and also to a 0.1 increase in mean CAVI (β = 0.133; P= 0.040). In addition,

each 1-mm increase in the mean periodontal attachment loss corresponded to a 0.01-mm increase in the maximal cIMT (β = 0.013; *P* = 0.040). A multiple logistic regression analysis revealed that each 1-mm increase in mean periodontal pocket depth was associated with an increased risk of a maximal cIMT > 1 mm (adjusted odds ratio [OR], 1.430; 95% confidence interval [CI], 1.067-1.918; *P* = 0.017) and mean CAVI of ≥ 8 (OR, 1.323; 95% CI, 1.003--1.743; *P* = 0.047). Furthermore, each 1-mm increase in mean periodontal attachment loss was associated with an increased risk of a maximal cIMT ~~of~~ >1 mm (OR, 1.251; 95% CI, 1.032-1.516; *P* = 0.022).

Conclusion:

A linear, dose-dependent relationship was found between periodontal pocket depth, cIMT, and arterial stiffness.

Keywords: Periodontitis; Carotid intima-media thickness; Cardio-ankle vascular index; Epidemiology

1. Introduction

Since 1989, many studies have suggested an association between periodontal disease and cardiovascular or cerebrovascular diseases [1-3]. However, the mechanism of this association has not been sufficiently clarified [4]. Atherosclerosis is a well known leading cause of vascular diseases and is considered to be an inflammatory disorder of the arteries. Periodontal disease is a chronic inflammatory disease characterized by the destruction of supportive connective tissues surrounding the roots of teeth in response to subgingival infection with various periodontal pathogens, mainly Gram-negative anaerobes. Recent evidence has shown that low-grade inflammation such as that occurring in periodontal disease may play a role in atherosclerosis [5].

Several recent studies have suggested an association between periodontal disease and markers of subclinical atherosclerosis used to assess morphological abnormalities, such as carotid intima-media thickness (cIMT) and carotid plaque, as well as functional abnormalities such as pulse-wave velocity (PWV) and flow-mediated vasodilation (FMD) of the brachial artery induced by reactive

hyperemia [6-15]. Thus, the relationship between periodontal disease and atherosclerosis is well known, but it has been little demonstrated epidemiologically in Japan. The cardio-ankle vascular index (CAVI) has recently been developed as a new tool to assess arterial stiffness of the aorta, femoral artery, and tibial artery [16] and is an appropriate atherosclerosis screening tool [17]. However, no studies have investigated the relationship between the CAVI and periodontal status. The purpose of this study was to clarify whether periodontal status was associated with two subclinical markers of early- stage atherosclerosis, namely cIMT and arterial stiffness using the CAVI, in community-dwelling Japanese adults.

2. Methods

2.1 Study population

We enrolled 2,029 subjects (766 men and 1263 women) aged ≥ 40 years who attended a “Specific Health Check-up and Guidance in Japan” between 2008

and 2010 with an oral assessment conducted in Goto City, which is comprised of > 60 islands located about 100 km off the west coast of Nagasaki Prefecture, Japan. The “Specific Health Check-up and Guidance in Japan” is an annual health check-up program conducted by the local government and directed by the Ministry of Health, Labor, and Welfare in Japan; people ≥ 40 years of age and covered by national health insurance are invited to participate in the program free of charge. All subjects gave written informed consent to participate in this study. Basic inclusion criteria were: subjects with all values for measures of subclinical atherosclerosis, laboratory data, and questionnaires; subjects without coronary heart disease (CHD) or cerebrovascular disease, and subjects with at least 10 remaining teeth who underwent a periodontal examination. The following subjects were excluded: one subject without a record of body mass index (BMI), three subjects without a blood pressure (BP) record, 399 subjects whose fasting blood samples were not collected, 16 subjects without a record of smoking status, 189 subjects taking current medication for CHD and/or with a history of CHD, 30 subjects with a history of cerebrovascular disease, 13 subjects who did

not undergo the CAVI measurement, 323 subjects with < 10 remaining teeth, and two subjects who did not undergo a periodontal examination. A total of 1,053 subjects (394 men and 659 women) were ultimately included in the analysis.

This study was approved by the Ethics Committee of Nagasaki University Graduate School of Biomedical Sciences (project registration numbers 0501120073 and 090528160) and was performed in accordance with the Declaration of Helsinki.

2.2 Data collection and laboratory measurements

Each subject's height and weight were measured, and BMI (kg/m^2) was calculated as an index of obesity. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were recorded at rest. Blood samples were collected from each participant after an overnight fast. Serum was separated and stored at −20ºC < 3 days until assay. Levels of total cholesterol (TC) and triglycerides (TG) were measured by enzymatic methods (coefficient of variations [CVs], 1.31% and 1.79%, respectively) [18, 19] and high-density lipoprotein cholesterol (HDL-C) was

measured by a direct method (CV, 1.77%)[20]; low-density lipoprotein cholesterol (LDL-C) levels were calculated by the Friedewald equation[21]. Fasting plasma glucose and hemoglobin A1c (HbA1c) levels were measured by the hexokinase UV method (CV, 0.45%) and by the latex agglutination reaction (CV, 4.29%), respectively [22, 23]. Staff members completed questionnaires that included information about each participant's smoking status and habitual drinking. Subjects who drank alcohol less than once per week, and those who drank at least once per week were defined as not habitual and habitual drinkers, respectively.

2.3 Assessment of subclinical atherosclerosis

We used two methods to assess early stage atherosclerosis. Four medical doctors measured cIMT by ultrasonography of the right and left carotid arteries using a LOGIC Book XP with a 10-MHz linear array transducer (GE Medical Systems, Milwaukee, WI, USA) [24]. The far wall of the carotid artery was displayed on a longitudinal two-dimensional ultrasonographic image as two bright white lines separated by a hypoechoic space. The distance from the leading edge of the first bright line (lumen–intima interface) to the leading edge of the

second bright line (media–adventitia interface) was identified as the cIMT. Images were stored on the hard disk of the ultrasound system, and the parts of the common carotid artery without plaque were analyzed using Intima Scope software (Media Cross, Tokyo, Japan). The maximum right and left cIMTs were used for analysis. Intra- and inter-observer variations in cIMT were 0.91 ($P<$ 0.01) and 0.78 ($P<$ 0.01), respectively. cIMT values exceeding the normal range by > 1 mm were defined as higher cIMTs, based on a previous study [25].

The CAVI was recorded with subjects in the supine position using a VaSera VS-1000 vascular screening system (Fukuda Denshi, Tokyo, Japan) by several trained clinicians. Measuring the CAVI using VaSera is very simple and performed automatically, and has good reproducibility [26]. The principles underlying the CAVI have been described by Yambe et al.[27]. Electrocardiographic electrodes were placed on both wrists, a microphone to detect heart sounds was placed on the sternum, and cuffs were wrapped around both arms and ankles to obtain automatic measurements.

The formula for measuring this index is:

$$CAVI = a\{(2\rho/\Delta P) \times \ln(Ps/Pd)\ PWV^2\} + b$$

where, Ps and Pd are systolic and diastolic BPs respectively, ΔP is Ps − Pd, ρ is blood density, and a and b are constants [26]. This equation was derived from the Bramwell-Hill equation, and the stiffness parameter β. The data were then analyzed using VSS-10 software (Fukuda Denshi), and mean values for the right and left CAVI were used. A CAVI exceeding the normal range by ≥ 8 was defined as a higher CAVI, which was reported recently to be the optimal cutoff point for arteriosclerosis [28].

2.4 Oral examination

A periodontal examination was performed using the method modified from the Third National Health and Nutrition Examination Survey [29] by one of four trained dentists, as described previously [30]. Probing pocket depth and clinical attachment loss (distance from the cementoenamel junction to the bottom of the pocket) were measured using a periodontal probe at the mesiobuccal and mid-buccal sites for all present teeth excluding the third molars. Prior to the start

of this study, all examiners were trained and calibrated using a chart, periodontal models, and volunteers at the Nagasaki University Hospital.

2.5 Statistical analysis

Results are expressed as means ± standard deviations for continuous variables. The results of categorical variables, such as the prevalence of higher cIMT (> 1.0 mm), higher CAVI (≥ 8), smoking status, and habitual drinking, results are expressed as percentages. Differences in means were assessed by Student's t-test and the Bonferroni correction after analysis of variance, as appropriate. Differences in prevalence were assessed by the chi-squared test. Pearson's correlation and partial correlation analyses were conducted between two continuous variables. Because the distribution of TG values was skewed, the values were logarithmically transformed for the regression analyses. We evaluated the associations between periodontal status parameters such as mean probing pocket depth and mean clinical attachment loss, and markers of subclinical atherosclerosis such as maximal cIMT and mean CAVI using simple

and multivariate linear regression analyses. Because of their high collinearity, we used SBP but not DBP, LDL-C and HDL-C but not TC levels, and HbA1c levels but not fasting plasma glucose, in the adjusted analyses. Furthermore, we evaluated the associations between periodontal status parameters and higher cIMT (>1 mm) and higher CAVI (≥8) using simple and multiple logistic regression analyses. The SPSS software ver. 15.0J (SPSS Japan, Tokyo, Japan) was used for statistical analyses. Values of $P < 0.05$ were considered significant.

3. Results

The characteristics of the study participants are shown in Table 1. Men were slightly older than women. The mean number of teeth present, mean probing pocket depth, and mean clinical attachment loss were significantly higher in men than those in women. BMI, HDL-C and LDL-C levels, SBP, DBP, fasting plasma glucose levels, maximal cIMT, the prevalence of cIMT > 1 mm, mean CAVI, prevalence of CAVI ≥ 8, smoking status, and habitual drinking differed significantly between men and women. All of these parameters, with the exception of LDL-C levels, were worse in men than those in women.

Maximal cIMT and mean CAVI increased significantly with age and were significantly correlated with each other ($P < 0.001$, Supplementary Fig. 1). The relationships and distributions among maximal cIMT, mean CAVI, and periodontal status are shown in Fig. 1. Maximal cIMT and mean CAVI were significantly correlated with mean probing pocket depth and mean clinical attachment loss ($P < 0.001$, Fig. 1). Correlation analyses among maximal cIMT, mean CAVI, and other variables are shown in Table 2. In simple correlation

analyses, maximal cIMT was significantly correlated with all variables except TG, TC, and LDL-C. Mean CAVI was significantly correlated with all variables except BMI and TG. The correlation coefficients suggested that age was a major contributor to maximal cIMT and mean CAVI. The results of partial correlation analyses were similar to those of simple correlation analyses. In the partial correlation analysis adjusted by for sex and age, maximal cIMT was significantly correlated with mean probing pocket depth. A partial correlation between maximal cIMT and mean clinical attachment loss was marginally significant (P= 0.053). In addition, the partial correlation between mean CAVI and mean probing pocket depth was also marginally significant (P= 0.059). Both cIMT and the CAVI of former smokers were significantly higher than those of never smokers (data not shown). Habitual drinking was not associated with cIMT or CAVI. Smoking status was associated with the prevalence of higher cIMT and CAVI, whereas habitual drinking was not (data not shown).

The results of the multiple linear regression models for maximal cIMT and mean CAVI are shown in Table 3 and Supplementary Table 1. The multiple

linear regression analysis adjusted for age and sex revealed that maximal cIMT was significantly correlated with mean probing pocket depth. A multiple linear regression analysis adjusted for age, sex, number of teeth present, BMI, log-transformed TG levels, HDL-C and LDL-C levels, HbA1c level, SBP, smoking status, and habitual drinking revealed that maximal cIMT was significantly correlated with mean probing pocket depth (P = 0.049) and mean clinical attachment loss (P = 0.040). Each 1-mm increase in mean probing pocket depth and mean clinical attachment loss corresponded to a 0.02-mm and 0.01-mm increase in cIMT after adjustment, respectively. The mean CAVI was significantly correlated with mean probing pocket depth (P = 0.040) but not with mean clinical attachment loss after adjusting for the above-mentioned covariates.

The results of the multiple logistic regression models for higher cIMT (>1 mm) and higher CAVI (≥8) are shown in Table 4 and Supplementary Table 2. The multiple logistic regression analysis adjusted for age and sex showed that the prevalence of higher cIMT (>1 mm) was significantly correlated with a 1-mm increase in mean probing pocket depth and mean clinical attachment loss.

Further adjustment for the number of teeth present , BMI, TG level, HDL-C and LDL-C levels, HbA1c level, SBP, smoking status, and habitual drinking revealed that the prevalence of higher cIMT (>1 mm) was significantly correlated with each 1-mm increase in mean probing pocket depth (adjusted odds ratio [OR], 1.430; 95% confidence interval [CI], 1.067-1.918; P=0.017), and with each 1-mm increment of mean clinical attachment loss (adjusted OR, 1.251; 95%CI, 1.032-1.516: P= 0.022). Similarly, the prevalence of higher CAVI (≥ 8) was significantly correlated with each 1-mm increase in mean probing pocket depth (adjusted OR, 1.323; 95% CI, 1.003-1.743: P= 0.047) but not with each 1-mm increase in mean clinical attachment loss after adjusting for the above-mentioned covariates. When we conducted the same multivariate analyses stratified by sex, the similar tendencies were observed but did not reach statistical significance (data not shown).

4. Discussion

We found that periodontal status was linearly and dose-dependently associated with markers of atherosclerosis, such as cIMT and CAVI, after adjusting for known risk factors of atherosclerosis. Each 1-mm increase in the mean probing pocket depth and mean clinical attachment loss corresponded to a 0.02- and 0.01-mm increase in maximal cIMT after adjustment, respectively. Moreover, the prevalence of higher cIMT (>1 mm) increased by 43% with each 1-mm increase in mean probing pocket depth and increased by 25% with each 1-mm increase in mean clinical attachment loss after adjustment, respectively. Measurements of cIMT with B-mode ultrasonography have been used as a marker of subclinical atherosclerosis. Two recent epidemiological studies showed an association between oral status and atherosclerosis using cIMT [6, 8]. Beck *et al.* [6] reported that severe periodontitis with extensive clinical attachment loss is associated with increased cIMT. Desvarieux *et al.* [8] reported that tooth loss, probably due to previous periodontal disease, is associated with cIMT and carotid artery plaque only in men. Thereafter, researchers reported that periodontal

pathogens in subgingival dental plaque were associated with increased cIMT [9] and that levels of serum immunoglobulin G antibodies to various periodontal bacteria were associated with increased cIMT [7]. The present results regarding the association between periodontal status and cIMT are consistent with these studies.

Besides cIMT, several noninvasive subclinical methods, such as FMD and PWV, have been used to assess vascular dysfunction and arterial stiffness, respectively [31]. Several previous studies of the effect of periodontal therapy on vascular endothelial function using FMD have reported that periodontal therapy results in improved endothelial function [13-15]. In contrast, the association between periodontitis and arterial stiffness remains unclear. PWV is a non-invasive clinical index of aortic stiffness [32] that enables the prediction of cardiovascular events and all-cause mortality in patients with hypertension and the general population [33, 34]. A study of the relationship between periodontal status and brachial-ankle PWV in healthy Japanese male workers reported that periodontal status is not related to baPWV after adjusting for confounding factors

[35]. The baPWV is influenced by changes in BP during examination and by the autonomic nervous system [27, 36]. The CAVI, which was recently developed by measuring PWV from the starting point of the aorta in the heart to the ankle, is similar to but more reliable than baPWV [16]. The CAVI, which reflects the stiffness of the aorta, femoral artery, and tibial artery, adjusts for BP based on the stiffness parameter ß [26, 27]. Thus, the CAVI is minimally influenced by BP at the time of measurement and has higher reproducibility than does the PWV. CAVI is an appropriate screening tool for atherosclerosis [17]. Our study is the first study to demonstrate a relationship between periodontal status and arterial stiffness using the CAVI. After adjusting for known risk factors of atherosclerosis, multivariate linear and logistic regression analyses revealed that the probing pocket depth was significantly correlated with the mean CAVI and the prevalence of higher CAVI (≥8), respectively. Each 1-mm increase in mean probing pocket depth corresponded to a 0.1 increase in mean CAVI. In addition, the prevalence of higher CAVI (≥ 8) increased by 32% with each 1-mm increase in mean probing pocket depth after adjustment. In contrast, the clinical attachment loss was not

correlated with mean CAVI or prevalence of higher CAVI (≥8). Arterial stiffness is associated with impaired endothelial function [37], and it has been proposed that periodontal pathogens or their products may directly affect endothelial function [15]. In general, probing pocket depth is a better marker of current periodontal inflammatory exposure than clinical attachment loss, which indicates a history of past periodontal destruction. Clinical attachment loss increases simply by gingival recession with heavy tooth brushing, abnormal alignment of teeth, and periodontal treatment, all of which are non-inflammatory factors. Moreover, treatment of periodontal infection could improve endothelial dysfunction within several months [14, 15]. Thus, it is feasible that clinical attachment loss less affects arterial stiffness, because deep periodontal pockets do not always exist in subjects with attachment loss. Our results indicate the relationship between periodontal status and arterial change more clearly than do previous studies [6, 8, 10].

Our study had several limitations. First, no causal relationship between periodontal disease and markers of atherosclerosis could be determined because

of the cross-sectional design of this study. We have initiated a cohort study using the same subjects. Second, subjects participated in this study on a voluntary basis and might not be representative of the Japanese population ; therefore, the results of this study may not be able to be generalized to a non-Japanese population. Third, data related to diet and physical activity were not available for this study.

In conclusion, a linear and dose-dependent association between periodontal status and markers of subclinical atherosclerosis was revealed. Periodontal status is likely to be associated both with alterations in arterial wall thickness and arterial wall stiffness during the initial change changes of atherosclerosis. Further study of how periodontal status impacts the structural and qualitative aspects of subclinical atherosclerosis is needed.

Conflicts of interest

None.

Acknowledgements

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2 932-943.
3
4
5

Figure legends

Figure 1.

Simple correlation and distribution among maximal carotid intima-media thickness (cIMT), mean cardio-ankle vascular index (CAVI), mean probing pocket depth, and mean clinical attachment loss. (Panel A) maximal cIMT and mean probing pocket depth, (Panel B) maximal cIMT and mean clinical attachment loss, (Panel C) mean CAVI and mean probing pocket depth, and (Panel D) mean CAVI and mean clinical attachment loss.

Figure 1

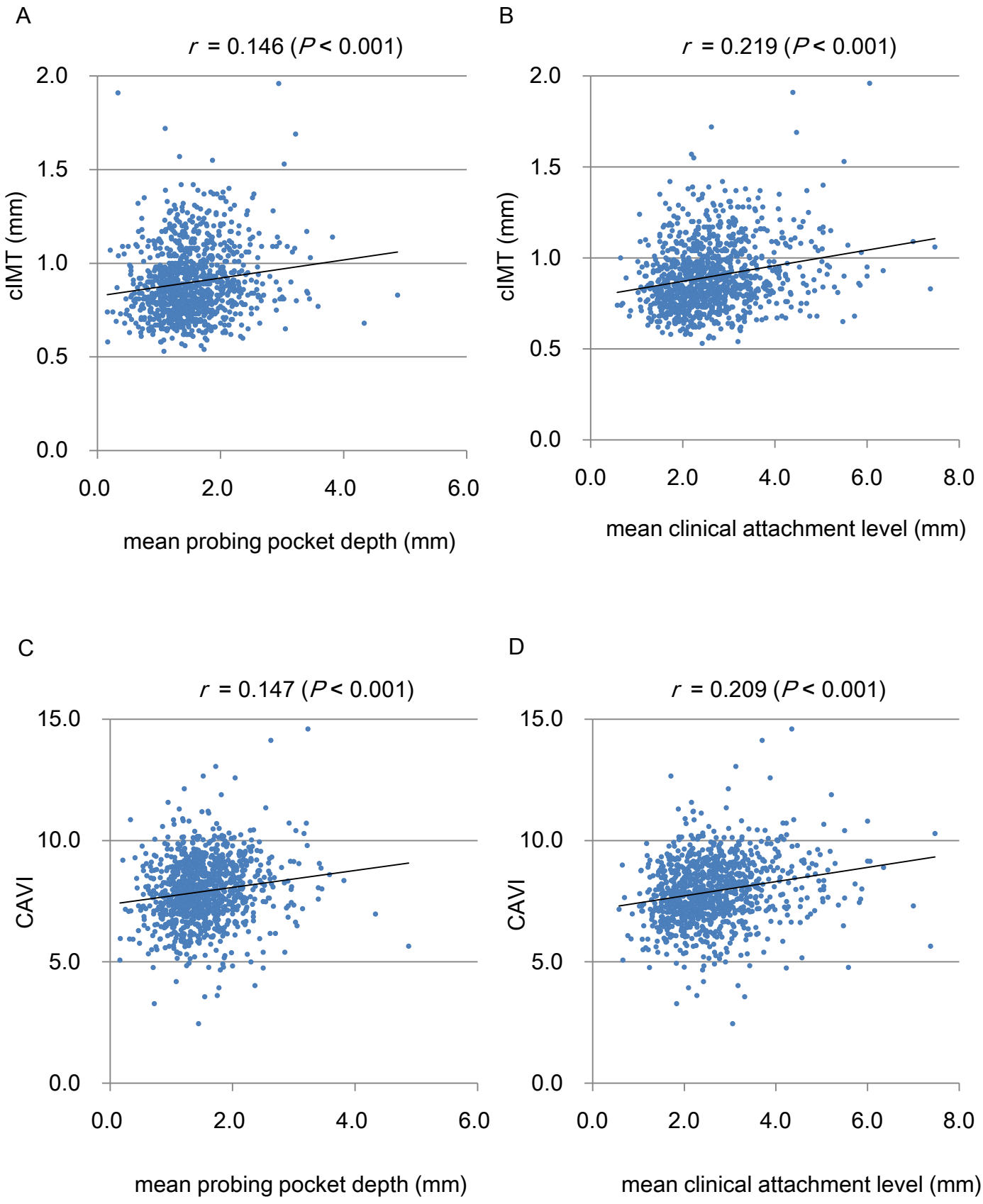
A
r = 0.146 (P < 0.001)
cIMT (mm)
2.0
1.5
1.0
0.5
0.0
0.0
2.0
4.0
6.0
mean probing pocket depth (mm)
B
r = 0.219 (P < 0.001)
cIMT (mm)
2.0
1.5
1.0
0.5
0.0
0.0
2.0
4.0
6.0
8.0
mean clinical attachment level (mm)
C
r = 0.147 (P < 0.001)
CAVI
15.0
10.0
5.0
0.0
0.0
2.0
4.0
6.0
mean probing pocket depth (mm)
D
r = 0.209 (P < 0.001)
CAVI
15.0
10.0
5.0
0.0
0.0
2.0
4.0
6.0
8.0
mean clinical attachment level (mm)

Table 1. Characteristics of the Study Subjects

	men (n=394)	women (n=659)		total (n=1053)
number of present teeth	23.3 ± 5.5	22.5 ± 5.4	†	22.8 ± 5.4
mean probing pocket depth, mm	1.64 ± 0.60	1.45 ± 0.51	**	1.52 ± 0.56
mean clinical attachment loss, mm	2.87 ± 1.07	2.46 ± 0.81	**	2.61 ± 0.94
age, y	64.7 ± 10.5	62.8 ± 9.7	†	63.5 ± 10.0
body mass index, kg/m^2	23.7 ± 2.9	22.7 ± 3.2	**	23.1 ± 3.2
triglycerides, mg/dL	109.6 ± 87.3	100.1 ± 64.0		103.7 ± 73.7
log-transformed triglycerides	1.96 ± 0.24	1.94 ± 0.22		1.95 ± 0.23
total cholesterol, mg/dL	192.8 ± 34.3	210.9 ± 33.9		204.1 ± 35.1
HDL-cholesterol, mg/dL	56.6 ± 14.3	63.7 ± 14.4	**	61.0 ± 14.8
LDL-cholesterol, mg/dL	114.2 ± 29.4	127.2 ± 30.1	**	122.3 ± 30.1
systolic blood pressure, mmHg	143.0 ± 20.5	136.4 ± 20.4	**	138.9 ± 20.7
diastolic blood pressure, mmHg	84.9 ± 11.0	81.1 ± 9.7	**	82.6 ± 10.4
fasting plasma glucose, mg/dL	102.2 ± 31.8	96.4 ± 19.2	†	98.6 ± 24.8
hemoglobin A1c	5.3 ± 0.6	5.3 ± 0.5		5.3 ± 0.5
maximal cIMT, mm	0.94 ± 0.19	0.87 ± 0.18	**	0.90 ± 0.18
prevalence of maximal cIMT > 1mm (%)	32.2	18.2	**	23.5
mean CAVI	8.22 ± 1.41	7.71 ± 1.22	**	7.90 ± 1.32
prevalence of CAVI >= 8 (%)	53.6	39.6	**	44.8
smoking status (%)				
never	43.4	95.8	**	76.1
former	37.6	2.1		15.4
current	19.0	2.1		8.5
habitual drinking (yes) (%)	42.6	6.5	**	20.0

Student's t-tests for continuous variables and chi-squared tests for categorical variables were conducted. † $P < 0.05$, ** $p < 0.001$

Table 2. Correlation between maximal cIMT, mean CAVI and other variables

	maximal cIMT						mean CAVI					
correlation coefficient	r[a]		partial[b]		partial[c]		r[a]		partial[b]		partial[c]	
number of present teeth	-0.22	**	-0.23	**	-0.27		-0.22	**	-0.24	**	0.02	
mean probing pocket depth	0.15	**	0.12	**	0.07	†	0.15	**	0.12	**	0.06	
mean clinical attachment loss	0.22	**	0.19	**	0.06		0.21	**	0.18	**	0.01	
age	0.45	**	0.45	**	-		0.54	**	0.53	**	-	
BMI	0.12	**	0.10	†	0.10	†	0.03		0.00		-0.02	†
triglycerides	0.02		0.00		0.05		0.01		-0.01		0.05	
log-transformed triglycerides	0.04		0.04		0.07	†	0.02		0.01		0.06	
total cholesterol	-0.26		0.02		0.08	†	-0.14	**	-0.10	†	-0.04	
HDL-cholesterol	-0.18	**	-0.15	**	-0.09	†	-0.18	**	-0.14	**	-0.06	†
LDL-cholesterol	0.05		0.09	†	0.11	**	-0.08	†	-0.04		-0.04	
systolic blood pressure	0.30	**	0.28	**	0.14	**	0.28	**	0.26	**	0.08	†
diastolic blood pressure	0.14	**	0.11	**	0.08	†	0.12	**	0.09	†	0.05	
fasting plasma glucose	0.22	**	0.20	**	0.18	**	0.15	**	0.13	**	0.10	†
hemoglobin A1c	0.22	**	0.23	**	0.20	**	0.12	**	0.13	**	0.08	†

[a] Pearson's correlation coefficient

[b] Partial correlation coefficient adjusted for sex

[c] Partial correlation coefficient adjusted for sex and age

† $P < 0.05$, ** $p < 0.001$

Table 3. Multiple Linear Regression Analyses for maximal cIMT and mean CAVI according to Periodontal Variables

			maximal cIMT						mean CAVI			
			β	95% CI	R^2	*P* value			β	95% CI	R^2	*P* value
mean probing pocket depth	model	1	0.048	0.029, 0.068	0.020	<0.001	model	1	0.123	0.069, 0.177	0.018	<0.001
(per 1mm greater)		2	0.021	0.003, 0.039	0.224	0.023		2	0.118	-0.004, 0.24	0.312	0.059
		3	0.018	0.000, 0.037	0.271	0.049		3	0.133	0.006, 0.259	0.323	0.040
mean clinical attachment loss	model	1	0.043	0.031, 0.054	0.047	<0.001	model	1	0.103	0.071, 0.134	0.037	<0.001
(per 1mm greater)		2	0.011	0.000, 0.022	0.223	0.053		2	0.016	-0.060, 0.092	0.309	0.687
		3	0.013	0.001, 0.025	0.271	0.040		3	0.026	-0.059, 0.111	0.320	0.548

β: partial regression coefficient

model 1 unadjusted

2 adjusted for age and sex

3 adjusted for age, sex, number of present teeth, BMI, log-transformed triglycerides, HDL-cholesterol, LDL-cholesterol, hemoglobin A1c, SBP, smoking status, and habitual drinking

Table 4. Multiple Logistic Regression Analyses for maximal cIMT > 1mm and mean CAVI >= 8 according to Periodontal Variables

			maximal cIMT > 1mm					mean CAVI >= 8		
			Odds ratio	95% CI	*P* value			Odds ratio	95% CI	*P* value
mean probing pocket depth	model	1	1.767	1.376-2.269	<0.001	model	1	1.663	1.325-2.086	<0.001
(per 1mm greater)		2	1.401	1.069-1.837	0.015		2	1.306	1.007-1.693	0.044
		3	1.430	1.067-1.918	0.017		3	1.323	1.003-1.743	0.047
mean clinical attachment loss	model	1	1.557	1.344-1.804	<0.001	model	1	1.545	1.343-1.776	<0.001
(per 1mm greater)		2	1.178	1.000-1.387	0.050		2	1.058	0.904-1.239	0.482
		3	1.251	1.032-1.516	0.022		3	1.066	0.889-1.278	0.492

model 1 unadjusted

2 adjusted for age and sex

3 adjusted for age, sex, number of present teeth, BMI, log-transformed triglycerides, HDL-cholesterol, LDL-cholesterol, hemoglobin A1c, SBP, smoking status, and habitual drinking