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Association of periodontitis with carotid artery intima–media thickness and arterial stiffness in community-dwelling people in Japan: The Nagasaki Islands study

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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 1053 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 mean periodontal pocket depth corresponded to a 0.02-mm increase in maximal cIMT ($\beta = 0.018$; $P = 0.049$) and also to a 0.1 increase in mean CAVI ($\beta = 0.133$; $P = 0.040$). In addition, each 1-mm increase in the mean periodontal attachment loss corresponded to a 0.01-mm increase in maximal cIMT ($\beta = 0.013$; $P = 0.040$). 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 >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.

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

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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 2029 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 1053 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 −20 °C for <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:

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

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 mesio-buccal 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