Comparison of Frequency and Duration of Periodontal Disease With Progression of Coronary Artery Calcium in Patients With and Without Type 1 Diabetes Mellitus

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People with type 1 diabetes mellitus manifest a greater burden of both periodontal disease and coronary artery disease (CAD); however, little is known about their interrelation. Coronary artery calcium (CAC) measures subclinical atherosclerosis and predicts major adverse coronary events. The relation between periodontal disease and CAC progression in individuals with type 1 diabetes has not been previously described. We determined the prevalence and progression of CAC in relation to self-reported periodontal disease. Multivariate logistic and tobit regression models were used to examine the relation between periodontal disease duration and CAC progression and whether this relation differs by diabetes status after controlling for age, gender, total and high-density lipoprotein cholesterol, hypertension, smoking, body mass index (BMI), duration of diabetes, and baseline CAC. A total of 473 patients with type 1 diabetes and 548 without diabetes were followed for a mean of 6.1 years. At baseline, the prevalence and duration of periodontal disease did not differ between subjects with and without diabetes (14.5% vs 13.4%, p = 0.60; 6 vs 9 years, p = 0.18). Duration of periodontal disease was not significantly associated with baseline CAC prevalence. In patients with type 1 diabetes, periodontal disease duration was significantly related to CAC progression (p = 0.004) but not in subjects without diabetes (p = 0.63). In conclusion, this study suggests that periodontal disease is an independent predictor of long-term progression of CAC in patients with type 1 diabetes. **(Am J Cardiol 2015;■:■−■)**

Coronary artery calcium (CAC) is an established marker of atherosclerotic plaque burden that is increased in patients with type 1 diabetes.[1,2] To date, the influence of periodontal disease on CAC progression in patients with type 1 diabetes has not been established. The Coronary Artery Calcification in Type 1 Diabetes (CACTI) Study was used to examine the relation between periodontal disease and CAC progression over prolonged follow-up. We hypothesized that periodontal disease would be increased in type 1 diabetic individuals compared with non-diabetic individuals, and that the presence and duration of periodontal disease would predict CAC progression.

Methods

Subjects were identified from the CACTI Study. CACTI is a prospective cohort study examining the prevalence of CAC in patients with type 1 diabetes and a comparable group of controls with no history of atherosclerotic cardiovascular disease. Detailed descriptions of the study design have previously been published.[2] Participants in this study included those who had completed the 6-year (range 4.1 to 8.5 years) follow-up visit and had complete data for all covariates (n = 1,021). Informed consent was provided by all study participants, and the protocol was reviewed and approved by the Colorado Multiple Institutional Review Board.

Physical examination measurements included height, weight, waist and hip circumference, and systolic and diastolic blood pressure. Hypertension was defined as systolic blood pressure ≥140 mm Hg, diastolic blood pressure ≥90 mm Hg, or treatment with antihypertensive medication. A fasting blood sample was collected and stored at −80°C until assayed for measurement of total cholesterol, high-density lipoprotein, and triglyceride levels. Low-density lipoprotein (LDL) cholesterol was calculated using the Friedewald equation.[3] All subjects were given standardized questionnaires to obtain demographics, medical history, medication use, and current and past smoking status. Subjects were asked if they had ever been told by a dentist or dental hygienist that they have gum disease. If yes, then they were asked the age of diagnosis. Self-reported periodontal disease has been evaluated in other studies and demonstrated to be reasonably accurate.[4,5]

Two sets of images for CAC scoring were obtained between March 2000 and May 2002 using an ultrafast Imatron C-150XLP electron beam computed tomography scanner

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See page 5 for disclosure information.

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Table 1
Participant characteristics at baseline

Variable	Overall (n=1021)	Diabetes (n=473)	No Diabetes (n=548)	p-value
Age (years)*	39 (±9)	37 (±9)	41 (±9)	<0.001
Sex (male)†	496 (48.6%)	217 (45.9%)	279 (50.9%)	0.11
Race (white)†	911 (89.6%)	448 (95.1%)	463 (84.8%)	<0.001
Hispanic†	67 (6.6%)	16 (3.4%)	51 (9.4%)	<0.001
Past smoking†‡	214 (21.3%)	94 (20.3%)	120 (22.2%)	0.46
Current smoking†‡	94 (9.4%)	50 (10.8%)	44 (8.2%)	0.15
Hypertension†	273 (26.8%)	190 (40.3%)	83 (15.2%)	<0.001
Antihypertensive drugs†	203 (19.9%)	163 (34.5%)	40 (7.3%)	<0.001
Lipid lowering drugs†	112 (11.0%)	77 (16.3%)	35 (6.4%)	<0.001
Hemoglobin A_{1c} (%)*	6.6 (±1.5)	7.9 (±1.2)	5.5 (±0.4)	<0.001
Systolic blood pressure (mm Hg)*	115.4 (±12.8)	116.7 (±13.3)	114.3 (±12.3)	0.004
Diastolic blood pressure (mm Hg)*	78.1 (±8.5)	77.1 (±8.6)	79.0 (±8.4)	<0.001
Total cholesterol (mg/dL)*	184 (±37)	173 (±33)	193 (±37)	<0.001
High-density lipoprotein cholesterol (mg/dL)*	53 (±16)	56 (±17)	51 (±15)	<0.001
Low-density lipoprotein cholesterol (mg/dL)*	108 (±32)	99 (±28)	116 (±33)	<0.001
Triglycerides (mg/dL)§	90 (67-129)	76 (60-105)	104 (77-155)	<0.001
Body mass index (kg/m^2)*	26.2 (±4.5)	26.1 (±4.2)	26.2 (±4.8)	0.74
C-reactive protein (mg/l)§	1.2 (0.89-2.0)	1.2 (0.89-2.1)	1.2 (0.88-1.9)	0.49
Self-reported periodontal disease at baseline†	141 (13.9%)	68 (14.5%)	73 (13.4%)	0.60
Self-reported periodontal disease at follow-up†	185 (18.2%)	103 (21.9%)	82 (15.0%)	0.005
Duration of periodontal disease (years)§	9 (3-13)	6 (2-11)	9 (4-15)	0.18
Duration of diabetes (years)*	N/A	23 (±9)	N/A	N/A
Coronary artery calcification prevalence (>0) at baseline†	317 (31.1%)	169 (35.7%)	148 (27.0%)	0.003
Coronary artery calcification prevalence (>0) at follow-up†	534 (52.9%)	278 (59.5%)	256 (47.2%)	<0.001
Coronary artery calcification score of positives at baseline§	8.2 (1.4-72.4)	14.6 (1.4-98.9)	4.7 (1.1-31.8)	0.011
Coronary artery calcification score of positives at follow-up§	13.7 (2.2-100.4)	30.9 (3.3-201.7)	8.0 (1.5-51.2)	<0.001
Coronary artery calcification progression prevalence¶	359 (35.2%)	201 (42.5%)	158 (28.8%)	<0.001
Coronary artery calcification progression ≥2.5§‖	5.7 (3.9-9.5)	6.5 (4.2-10.9)	5.0 (3.6-7.6)	<0.001

* Data presented as mean ± SD, p-value from t-test.
† Data presented as number (%), p-value from chi-square or Fisher's exact.
‡ Referent category never smoking.
§ Data presented as median (interquartile range), p-value from Wilcoxon rank sum test.
‖ Difference in square-root transformed volume scores between baseline and follow-up for those with positive progression (≥2.5) only.
¶ Data presented as number (%) of those with progression of CAC (≥2.5 square-root transformed units difference in volume scores between baseline and follow-up).

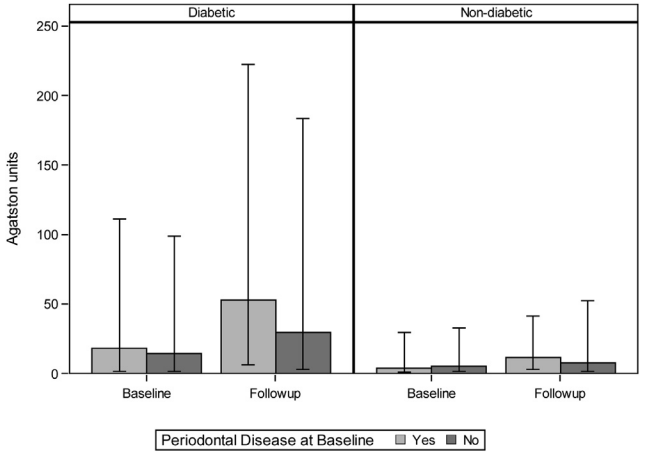

Figure 1. Median (IQR) CAC score by diabetes status at baseline and follow-up. CAC measured in Agatston units and interquartile range (IQR). *Light bars* represent self-reported periodontal disease at baseline. *Dark bars* represent no periodontal disease at baseline.

(Imatron, San Francisco, California). The estimated radiation dose for each examination was 2.25 mSv. The CAC score was assessed using the Agatston method, and the total volume score using the volumetric method was calculated from the images, as described previously.[6] Follow-up scans were performed approximately 6 years after the baseline visit between February 2006 and March 2009. Prevalence of CAC was defined as a CAC score >0. Progression of CAC was defined as the change in the square-root−transformed volume score between the follow-up visit and the baseline visit. We used the difference in the square-root−transformed volume for all analysis.

Differences in characteristics at baseline and follow-up were compared by diabetes status. Parametric continuous data are presented as means and standard deviation. Nonparametric data are presented as the median and interquartile range with the exception of the CAC scores. CAC scores were presented as the prevalence of positive CAC (>0) and as the median and interquartile range of only the positive values. Categorical data were tabulated as the number of subjects and the percent. Statistical testing to detect differences between groups included the *t* test for parametric continuous data, the Wilcoxon rank-sum test for nonparametric data, and the chi-square test for categorical data.

Logistic and tobit regression were used to determine the independent effect of periodontal disease presence at