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Decreased frequency and duration of tooth brushing is a risk factor for endothelial dysfunction

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ABSTRACT

Background: Periodontal disease is associated with endothelial dysfunction, leading to cardiovascular disease. The effect of detailed tooth brushing behavior, not only frequency but also duration of tooth brushing, on endothelial function is unclear. The purpose of this study was to evaluate the relationships of detailed methods of tooth brushing with vascular function.

Methods: We evaluated flow-mediated vasodilation (FMD), nitroglycerine-induced vasodilation, and frequency and duration of tooth brushing in 896 subjects. We divided the subjects into three groups according to the frequency and duration of tooth brushing: low frequency and short duration group (<twice/day and <2 min/procedure), low frequency or short duration group (<twice/day or <2 min/procedure), non-low frequency and non-short duration group (≥twice/day and ≥2 min/procedure).

Results: FMD in the low frequency and short duration group was significantly lower than FMD in the low frequency or short duration group and FMD in the non-low frequency and non-short duration group [3.1 (2.7)% vs. 4.2 (3.1)% and 4.7 (3.1)%, $P = 0.001$ and <0.001, respectively]. Nitroglycerine-induced vasodilation was similar in the three groups. Using the non-low frequency and non-short duration group as the reference, the low frequency and short duration of tooth brushing group was significantly associated with an increased odds ratio of a low FMD tertile after adjustment for conventional risk factors (OR: 2.25, 95% CI: 1.39–3.59; $P < 0.001$).

Conclusions: These findings suggest that low frequency and short duration of tooth brushing are associated with endothelial dysfunction.

Clinical trial registration information: URL for clinical trial: http://UMIN; registration number for clinical trial: UMIN000003409.

1. Introduction

Several lines of evidence have shown that periodontal disease increases the future risk of cardiovascular and cerebrovascular diseases [1–4]. It is thought that local and systemic inflammation initiated by bacteria associated with periodontitis promotes atherogenesis [5,6]. Poor oral health, including decreased tooth brushing behavior, plays a critical role in the pathogenesis, development, and maintenance of atherosclerosis [7].

Endothelial dysfunction is recognized as an initial step of atherosclerosis, leading to cardiovascular events [8,9]. Measurement of flow-mediated vasodilation (FMD) as an index of endothelium-dependent vasodilation and measurement of nitroglycerine-induced vasodilation as an index of endothelium-independent vasodilation in the brachial artery using high-resolution ultrasound are reliable methods for assessing vascular function [10–14]. Endothelial function assessed by FMD can serve as an independent predictor of cardiovascular events [15–19]. Periodontal disease is associated with endothelial dysfunction [20–25]. Several interventions, such as pharmacological therapy,

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supplementation therapy, and life style modifications, improve endothelial function, suggesting endothelial dysfunction is reversible [26–31]. It has been shown that treatment for periodontitis improves endothelial function [20–25].

Tooth brushing is a simple and low cost care for oral health. It is expected that tooth brushing per se improves vascular function and vascular structure, resulting in the prevention of periodontal disease. Previously, we reported that decreasing frequency of tooth brushing is independently associated with endothelial dysfunction [32]. However, the effect of more detailed tooth brushing behavior, not only frequency but also duration of tooth brushing, on endothelial function is unclear. The purpose of this study was to evaluate the relationships of detailed methods of tooth brushing with vascular function.

2. Methods

2.1. Subjects

A total of 896 subjects [560 men and 336 women, mean age of 61 (17) years] were recruited between October 2007 and October 2016. We divided the subjects into three groups according to frequency and duration of tooth brushing: low frequency and short duration group, either low frequency or short duration group, and non-low frequency and non-short duration group. Low frequency of tooth brushing was defined as <twice/day according to a previous study [32]. Short duration of tooth brushing was defined as <2 min/procedure. Hypertension was defined as systolic blood pressure >140 mm Hg or diastolic blood pressure >90 mm Hg, in a sitting position, on at least 3 different occasions. Patients with secondary forms of hypertension were excluded in all patients with hypertension on the basis of complete history; physical examination; radiological and ultrasound examinations; urinalysis; plasma rennin activity; plasma aldosterone and norepinephrine concentrations; serum creatinine, potassium, calcium, and free throxine concentrations; and 24-hour urinary excretion of 17-hydroxycorticosteroids, 17-ketogenic steroids, and vanillymandelic acid. Diabetes mellitus was defined according to the American Diabetes Association [33]. Dyslipidemia was defined according to the third report of the National Cholesterol Education Program [34]. In this study, hyperuricemia was defined as serum uric acid ≥7.0 mg/dL or antihyperuricemic drug use. Smokers was defined as those who had ever smoked. One pack-year was equivalent to 20 cigarettes per day for 1 year. Coronary heart disease included angina pectoris, myocardial infarction, and unstable angina. Unstable angina was designated when a history of prolonged ischemic chest pain (>15 min in duration) was accompanied by transient ischemic ST segment and T-wave abnormality in the electrocardiographic tracing but not accompanied by development of Q-wave abnormality or by serum enzyme changes characteristic of myocardial necrosis. Cerebrovascular disease included ischemic stroke, hemorrhagic stroke, and transient ischemic attack. Healthy subjects had no history of cardiovascular and cerebrovascular diseases, liver diseases, renal diseases, autoimmune diseases, or malignant diseases and had no coronary risk factors, including hypertension, dyslipidemia, diabetes mellitus, and smoking. The ethical committees of our institutes approved the study protocol. Written informed consent for participation in the study was obtained from all of the subjects.

2.2. Study protocol

All subjects were assessed for vascular function and structure using measurement of FMD and nitroglycerine-induced vasodilation in the brachial artery. The subjects completed a questionnaire about their oral health and tooth brushing behavior, including frequency and duration of tooth brushing. The subjects fasted overnight for at least 12 h and the study began at 08:30 h, and remained supine in a quiet, dark, air-conditioned room (constant temperature of 22 °C to 25 °C) throughout the study. A 23-gauge polyethylene catheter was inserted into the left deep antecubital vein to obtain blood samples. At 30 min of maintaining a supine position, FMD and nitroglycerin-induced vasodilation were measured. The observers were blind to the form of examination.

2.3. Measurement of FMD and nitroglycerine-induced vasodilation

Vascular response to reactive hyperemia in the brachial artery was used for assessment of endothelium-dependent FMD. A high-resolution linear artery transducer was coupled to computer-assisted analysis software (UNEXEF18G, UNEX Co., Nagoya, Japan) that used an automated edge detection system for measurement of brachial artery diameter [13,14]. A blood pressure cuff was placed around the forearm. The brachial artery was scanned longitudinally 5–10 cm above the elbow. When the clearest B-mode image of the anterior and posterior intimal interfaces between the lumen and vessel wall was obtained, the transducer was held at the same point throughout the scan by a special probe holder (UNEX Co.) to ensure consistency of the image. Depth and gain setting were set to optimize the images of the arterial lumen wall interface. When the tracking gate was placed on the intima, the artery diameter was automatically tracked, and the waveform of diameter changes over the cardiac cycle was displayed in real time using the FMD mode of the tracking system. This allowed the ultrasound images to be optimized at the start of the scan and the transducer position to be adjusted immediately for optimal tracking performance throughout the scan. Pulsed Doppler flow was assessed at baseline and during peak hyperemic flow, which was confirmed to occur within 15 s after cuff deflation. Blood flow velocity was calculated from the color Doppler data and was displayed as a waveform in real time. The baseline longitudinal image of the artery was acquired for 30 s, and then the blood pressure cuff was inflated to 50 mm Hg above systolic pressure for 5 min. The

Table 1
Clinical characteristics of the subjects according to tooth brushing behavior.

Variables	Total (n = 896)	Non-low frequency and non-short duration (n = 483)	Low frequency or short duration (n = 310)	Low frequency and short duration (n = 103)	P value
Age, year	61 ± 17	59 ± 17	62 ± 16	68 ± 12	<0.001
Gender, men/women	560/336	270/213	202/108	89/14	<0.001
Body mass index, kg/m^2	24.1 ± 3.9	23.9 ± 3.8	24.1 ± 3.9	24.5 ± 4.4	0.45
Systolic blood pressure, mm Hg	129.9 ± 18.8	128.4 ± 18.0	130.8 ± 19.7	133.5 ± 19.2	0.03
Diastolic blood pressure, mm Hg	76.4 ± 12.2	76.1 ± 12.0	76.4 ± 11.9	78.1 ± 13.2	0.32
Heart rate, beats/min	69.2 ± 12.3	69.3 ± 12.4	68.6 ± 11.9	70.1 ± 13.0	0.56
Creatinine, mg/dL	0.95 ± 0.88	0.90 ± 0.82	0.98 ± 0.97	0.95 ± 0.37	0.56
Uric acid, mg/dL	5.9 ± 1.4	5.9 ± 1.4	5.8 ± 1.5	6.2 ± 1.6	0.16
Total cholesterol, mg/dL	189.5 ± 39.7	190.0 ± 39.6	191.3 ± 40.6	183.3 ± 38.0	0.25
Triglycerides, mg/dL	134.2 ± 85.7	135.3 ± 80.0	137.5 ± 100.1	122.2 ± 63.4	0.32
High-density lipoprotein cholesterol, mg/dL	57.6 ± 15.8	58.4 ± 16.1	57.6 ± 15.8	54.8 ± 14.5	0.14
Low-density lipoprotein cholesterol, mg/dL	111.4 ± 36.2	110.5 ± 35.9	113.5 ± 36.6	109.4 ± 36.0	0.53
Glucose, mg/dL	115.2 ± 40.2	114.7 ± 42.5	114.8 ± 34.1	118.0 ± 45.4	0.77
Hemoglobin A1c, %	5.7 ± 0.8	5.6 ± 0.7	5.7 ± 0.8	5.8 ± 0.8	0.38
High-sensitivity C-reactive protein, mg/dL	0.10 ± 0.17	0.08 ± 0.11	0.11 ± 0.21	0.16 ± 0.20	0.003
Medical history, n (%)					
Hypertension	625 (69.8)	309 (64.0)	237 (76.5)	79 (76.7)	<0.001
Dyslipidemia	545 (60.8)	292 (60.5)	189 (61.0)	64 (62.1)	0.99
Diabetes mellitus	254 (28.3)	118 (24.4)	92 (29.7)	44 (42.7)	0.001
Hyperuricemia	216 (24.1)	106 (22.0)	73 (23.6)	37 (35.9)	0.01
Peripheral artery disease	86 (9.8)	41 (8.6)	30 (9.9)	15 (14.6)	0.17
Coronary artery disease	172 (19.4)	83 (17.2)	64 (20.7)	25 (24.3)	0.18
Stroke	75 (8.4)	32 (6.6)	33 (10.7)	10 (9.7)	0.12
Smoker, n (%)	447 (50.6)	212 (44.3)	158 (52.2)	77 (74.8)	<0.001
Smoking, pack-years	18.3 ± 26.9	14.1 ± 23.8	18.2 ± 26.5	35.2 ± 32.8	<0.001
Tooth extraction	516 (66.7)	264 (64.4)	170 (65.1)	82 (79.6)	0.01

All results are presented as means ± SD.

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