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Effect of Periodontitis and Toothbrushing Frequency on Obesity Onset: A Cohort Study

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Background: Material/Methods:		The interplay between obesity and periodontitis has risk factor for periodontitis, the inverse relationship i whether periodontitis and toothbrushing frequency a This cohort study included 1619 employees of a busin 2006 underwent in prescribed annual health checks, b	been widely examined. While obesity was reported as a is still little explored. Therefore, we aimed to determine ffect the onset of obesity. ess enterprise headquartered in Tokyo, who in 2002 and oth general and dental-specific, and who were not obese				
Co	Results: nclusions:	tory variables were presence/absence of periodontal pockets and toothbrushing frequency in 2002; their rela- tionships were examined by multiple logistic regression analysis. Subjects with periodontal pockets \geq 4 mm showed a significantly higher odds ratio (OR) for onset of obesity at 4 years than those without periodontal pockets [OR: 1.59, 95% CI (confidence interval): 1.08–2.35, p<0.05]. Similarly, subjects who brushed their teeth \geq 3 times/day had a significantly lower obesity OR than those who brushed \leq 1 time/day (OR: 0.49, 95% CI: 0.28–0.85, p<0.01). The presence of periodontal pockets and toothbrushing frequency are significantly associated with the on-					
		set of obesity. Periodontal pockets \geq 4 mm are associated with increased risk of obesity, while frequent tooth- brushing (\geq 3 times/day) appears to reduce the risk of obesity.					
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Background

Obesity is a worldwide health problem and is not specific to developed nations [1]. In 2014, the World Health Organization (WHO) estimated the worldwide population of obese adults at roughly 600 million and forecast a further increase due to increased intake of high-calorie foods and sedentary lifestyles [2]. Obesity is a major risk factor for many diseases that markedly reduce the quality of life, such as type 2 diabetes, dyslipidemia, hypertension, arteriosclerosis, cardiovascular and cerebrovascular diseases, and sleep-disordered breathing [1]. These diseases are highly prevalent in middle-aged adults, who comprise the majority of the working population [3,4]. Therefore, prevention of obesity is also important from a socioeconomic perspective.

Periodontitis is a chronic inflammatory disease that is known to negatively affect the systemic health status. The relationship between obesity and periodontal disease has been examined in several cross-sectional studies [5–8] and was reported in their systematic reviews and meta-analyses [9–11]. In addition, several cohort studies have shown that obesity actually affects the onset of periodontal disease [12–15]. However, few epidemiological studies have determined the effects of periodontal disease on the development of obesity; the only such study on this topic followed children from childhood to adolescence [12]. However, as both periodontal disease and obesity become more prevalent with age [3,6], there is also a clear need to evaluate this impact in adults.

Toothbrushing is the most basic method to prevent periodontal disease [16]. A systematic review and meta-analyses reported that good oral hygiene as measured by the amount of plaque accumulation and good oral healthcare habits as evident by toothbrushing frequency or visits to a dental hygienist/dentist decreased the risk of periodontitis [17]. Toothbrushing practices have recently been reported to affect the onset of diabetes mellitus and dyslipidemia [18], as well as metabolic syndrome [19]. Despite the fact that obesity is the main cause of metabolic syndrome [20], very few studies have examined the possible relationship between toothbrushing practices and obesity. Apart from a cross-sectional study using the results of the Korea National Health and Nutrition Examination Survey [21], assessing the relationship between toothbrushing frequency and obesity, there have been few longitudinal studies.

We have previously reported that periodontitis increases the risk of developing metabolic syndrome in a longitudinal cohort study from which we excluded not only obese individuals, but also individuals with hypertension, hyperglycemia, or dyslipidemia [22]. Therefore, in the present study, we examined whether periodontitis and toothbrushing frequency affect the development of obesity in non-obese individuals, including those with hypertension, hyperglycemia, or dyslipidemia.



Figure 1. Flow chart for selection of the study population. BMI, body mass index: BMI ≥25, obese; BMI <25, not obese.

Material and Methods

Study population

The present study was conducted with the approval of the Nihon University School of Dentistry Institutional Review Board (approval number: 2007-7). After the study aim and protocol were fully explained, the participants provided informed consent.

Initially, the study population comprised 2373 employees of a business headquartered in Tokyo who, in 2002, underwent prescribed annual health checks, both general and dental-specific, conducted voluntarily by a health insurance association. Although 99.9% of employees underwent the general health check, only 82.8% underwent the dental health check; thus, only those were considered. The analysis set was then narrowed down to those employees who also underwent both health checks in 2006 (2078 employees), and who were not obese in 2002 [final set of 1619 employees: 1286 men and 333 women; mean age of 39.7 years (age range, 20–56 years)]. In this study, obesity was defined as body mass index (BMI) \geq 25 [20]. Figure 1 shows the flow chart for the selection of the study population.

Periodontitis examination

Periodontitis was evaluated and classified according to the World Health Organization's Community Periodontal Index (CPI) [23]. With the oversight of a dentist, a dental hygienist examined 10 index teeth in the 6 sextants; the highest CPI code attributed to that sample was recorded as the subject's CPI. Based on the results obtained in the initial examination in 2002, the subjects were divided into 2 subgroups: CPI 0–2 (absence of periodontal pockets) and CPI 3–4 (presence of periodontal pockets \geq 4 mm).

General examination

BMI was calculated from each individual's height and body weight. Blood pressure was measured in a seated position with an automated sphygmomanometer. Blood was collected from a vein in the arm, with the subjects having fasted from 9 p.m. the previous night, and the levels of triglycerides, HDL cholesterol, and fasting blood glucose were determined. Hypertension was defined as systolic blood pressure \geq 130 mmHg and/or a diastolic blood pressure \geq 85 mmHg. Dyslipidemia was defined as a triglyceride level \geq 150 mg/dL and/or an HDL cholesterol level <40 mg/dL. A fasting blood glucose \geq 110 mg/dL was defined as hyperglycemia.

Self-administered questionnaire

Toothbrushing and other aspects of lifestyle were examined with a self-administered questionnaire during annual general health checks. Toothbrushing practices were examined in terms of daily frequency (i.e., how many times the subjects brushed their teeth daily). Accordingly, the subjects were divided into subgroups of once or less daily (≤ 1 time/day), twice daily (2 times/day), or 3 or more times daily (≥ 3 times/day). Smoking habits and ability to maintain a healthy body weight were examined with the following respective questions, "Do you smoke?" and "Are you making an effort to maintain a healthy body weight?"; the subjects were then divided based on their "yes" or "no" answers.

Statistical analysis

Subjects' baseline characteristics were compared using Pearson's χ^2 test based on presence/absence of periodontal pockets and daily toothbrushing frequency. The relationships of obesity at 4 years with presence/absence of periodontal pockets and daily toothbrushing frequency at baseline and/or 4 years were analyzed using forced entry multiple logistic regression (adjusted for hypertension, dyslipidemia, hyperglycemia, smoking habits, ability to maintain a healthy body weight, age, and sex) to determine the odds ratio (OR) and the 95% confidence interval (CI). Statistical analyses were performed using JMP (ver. 13.0; SAS Institute, Tokyo, Japan) with the level of statistical significance set at <5% (p<0.05).

Results

Subjects' baseline characteristics

At baseline, in 2002, hypertension, dyslipidemia, and hyperglycemia were present in 25.3% (n=410), 16.0% (n=260), and 4.6% (n=75), respectively, of the 1619 non-obese subjects included in this study; all of the above conditions were significantly more prevalent among subjects with periodontal pockets than among those without them. A total of 36.1% (n=584) of subjects responded that they smoke and 28.5% (n=461) responded that they do not make efforts to maintain a healthy body weight. Smoking was significantly more common among subjects with periodontal pockets than among subjects without, but the presence of periodontal pockets was not significantly different between subjects who maintained a healthy body weight and those who did not (Table 1).

Daily toothbrushing frequency was once or less for 9.1% of subjects (n=147), twice for 39.2% (n=635), and 3 or more times for 51.7% (n=837). These percentages of toothbrushing frequencies significantly differed according to the presence or absence of periodontal pockets (Table 1).

Compared to subjects without periodontal pockets, the group of subjects with periodontal pockets included significantly higher percentages of men and people aged \geq 40 years (Table 1). In comparisons involving daily toothbrushing frequency, significant differences were observed for all items studied (Table 2).

Effects of periodontal pockets presence and toothbrushing frequency at baseline on obesity onset

At baseline, in 2002, none of the 1619 subjects were obese; 4 years later in 2006, 140 subjects (corresponding to 8.6%) had developed obesity (BMI \geq 25). None of the subjects had a BMI \geq 30 in 2006. The group of subjects with periodontal pockets (CPI 3–4) showed a significantly higher OR for onset of obesity at 4 years than the group of subjects without periodontal pockets (CPI 0–2) (1.59, 95% CI: 1.08–2.35, p<0.05) (Table 3).

For the group of subjects who brushed their teeth ≥ 3 times/day or who brushed 2 times/day, the ORs for onset of obesity at 4 years were 0.49 (95% CI: 0.28–0.85, p<0.01) or 0.62 (95% CI: 0.37–1.06, p=0.08), respectively, in relation to the group of subjects who brushed ≤ 1 time/day. Thus, the OR was significantly lower for subjects with toothbrushing frequency ≥ 3 times/day (Table 3).

Participants who made an effort to maintain a healthy body weight showed significantly lower OR (0.44, 95% CI: 0.30–0.62, p<0.01) for onset of obesity at 4 years than the group who did not. The ORs for onset of obesity were significantly lower in females than in males (0.48, 95% CI: 0.26–0.89, p<0.05). There was no significant difference in the OR for onset of obesity relative to hypertension, dyslipidemia, hyperglycemia, smoking, and age at baseline (Table 3).

Changes in the presence of periodontal pockets at baseline and at 4 years and its effects on obesity onset

Among the 1190 subjects without periodontal pockets at baseline, 1006 subjects (84.5%) remained without periodontal

Variables	Without (n=1,	pockets 190)	With pockets (n=429)		P value
	N	%	N	%	
Hypertension					
No	932	78.3	277	64.6	<0.001
Yes	258	21.7	152	35.4	
Dyslipidemia					
No	1,027	86.3	332	77.4	<0.001
Yes	163	13.7	97	22.6	
Hyperglycemia					
No	1,152	96.8	392	91.4	<0.001
Yes	38	3.2	37	8.6	
Smoking habit					
No	809	68.0	226	52.7	<0.001
Yes	381	32.0	203	47.3	
Making an effort to maintain a healthy body weig	ht				
No	344	28.9	117	27.3	0.520
Yes	846	71.1	312	72.7	
Age					
<40year	745	62.6	135	31.5	<0.001
≥40year	445	37.4	294	68.5	
Gender					
Male	898	75.5	388	90.4	<0.001
Female	292	24.5	41	9.6	
Toothbrushing frequency					
≤1 time/day	88	7.4	59	13.8	
2 times/day	435	36.6	200	46.6	<0.001
≥3 times/day	667	56.1	170	39.6	

Table 1. Characteristics of study population in relation to the presence of periodontal pockets at baseline.

pockets at 4 years and 184 (15.5%) developed periodontal pockets. Among the 429 subjects with periodontal pockets at baseline, 216 (50.3%) still had periodontal pockets, and 213 (49.7%) were without periodontal pockets. The group with periodontal pockets at both baseline and 4 years had a significantly higher OR for the onset of obesity at 4 years than the group without periodontal pockets at both baseline and 4 years (2.22, 95% Cl: 1.34–3.68, p<0.01) (Table 4).

Discussion

In this cohort study, we showed that periodontitis and toothbrushing frequency may have an effect on the onset of obesity. This study can increase our knowledge of the events related to development of obesity, and improve our understanding of how dental health care may influence this clinical condition.

One of the most widely used indices of obesity is BMI. While the WHO defines obesity as BMI \geq 30, in this study, as all the participants were Japanese, a BMI \geq 25 was considered obese

	The frequencies of toothbrushing						
Variables	≤1 time/day (n=147)		2 times/day (n=635)		≥3 times/day (n=837)		P value
	N	%	N	%	N	%	
Hypertension							
No	95	64.6	462	72.8	652	77.9	0.001
Yes	52	35.4	173	27.2	185	22.1	
Dyslipidemia							
No	107	72.8	511	80.5	741	88.5	<0.001
Yes	40	27.2	124	19.5	96	11.5	
Hyperglycemia							
No	129	87.8	597	94	818	97.7	<0.001
Yes	18	12.2	38	6	19	2.3	
Smoking habit							
No	68	46.3	353	55.6	614	73.4	<0.001
Yes	79	53.7	282	44.1	223	26.6	
Making an effort to maintain a healthy body weight							
No	57	38.8	187	29.5	217	25.9	0.005
Yes	90	61.2	448	70.6	620	74.1	
Age							
<40year	50	34.0	341	54.7	489	58.4	<0.001
≥40year	97	66.0	294	46.3	348	41.6	
Gender							
Male	144	98.0	574	90.4	568	67.9	<0.001
Female	3	2.0	61	9.6	269	16.6	

Table 2. Characteristics of study population in relation to the frequencies of toothbrushing at baseline.

as per the guidelines of the Japan Society for the Study of Obesity, which is based on studies that have reported that BMI \geq 25 in the Japanese population are associated with increased prevalence of glucose intolerance, dyslipidemia, and hypertension [20,24]. The incidence of obesity in 4 years of follow-up was 8.6% and there was no subject with BMI \geq 30 by the end of the study period. The mean age of the participants was 40 years and consisted mostly of men. This incidence was largely consistent with that reported in previous studies [25,26]. In fact, in the Japan Public Health Center Study, a multipurpose cohort study, the incidence of obesity (BMI \geq 25) in a 10-year follow-up period was 12.5%, 9.1%, and 7% among men aged 40–44, 50–54, and 60–64 years, respectively; the prevalence of obesity decreased with age and was slightly lower among women than among men [25]. Additionally, a large-scale study among

Japanese reported that from age 50 years onwards, the prevalence of obesity decreased among men but increased among women; consequently, from age 60 years onwards, obesity becomes more prevalent among women [26].

Previous studies have found a relationship between obesity and periodontal disease [9–11]. Li et al. [12], who studied a group of subjects aged 12–18 years, reported that obesity at age 15 years was associated with periodontal diseases at age 18 years; however, there was no significant association between periodontal diseases at age 12 or 15 years and obesity at age 15 or 18 years. Nonetheless, in previous studies that we conducted with subjects negative for all indicators of metabolic syndrome, including obesity [22,27], we observed a significant association between the cumulative duration of having

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Table 3	Relationshir	hetween	obesity in	2006 and	neriodontal	nockets and	toothbrushing	frequency	in 2002
Table 5.	Relationship	Detween	obesity in	1 2000 anu	penouonitai	pockets and	LOOLIIDIUSIIIIE	; nequency	/ 111 2002.

	Number of subjects in 2006 (n, %)				Adjusted OP	
Condition in 2002	Non-obesity (n=1,479, 91.4%)		Obesity (n=140, 8.6%)		(95%CI)	
Periodontal pockets						
Without pocket	1,103	(92.7)	87	(7.3)	1	
With pocket	376	(87.6)	53	(12.4)	1.59 (1.08–2.35)*	
Toothbrushing frequency						
≤1 time/day	123	(83.7)	24	(16.3)	1	
2 times/day	574	(90.4)	61	(9.6)	0.62 (0.37–1.06)	
≥3 times/day	782	(93.4)	55	(6.6)	0.49 (0.28–0.85)**	
Hypertension						
No	1,114	(92.1)	95	(7.9)	1	
Yes	365	(89.0)	45	(11.0)	1.18 (0.79–1.77)	
Dyslipidemia						
No	1,250	(92.0)	109	(8.0)	1	
Yes	229	(88.1)	31	(11.9)	1.22 (0.78–1.91)	
Hyperglycemia						
No	1,411	(91.4)	133	(8.6)	1	
Yes	68	(90.7)	7	(9.3)	0.75 (0.32–1.73)	
Smoking habit						
No	947	(91.5)	88	(8.5)	1	
Yes	532	(91.1)	52	(8.9)	0.76 (0.52–1.12)	
Making an effort to maintain a healthy body weight						
No	396	(85.9)	65	(14.1)	1	
Yes	1,083	(93.5)	75	(6.5)	0.44 (0.30–0.62)**	
Age						
<40year	812	(92.3)	68	(7.7)	1	
≥40year	667	(90.3)	72	(9.7)	1.01 (0.68–1.48)	
Gender						
Male	1,159	(90.1)	127	(9.9)	1	
Female	320	(96.1)	13	(3.9)	0.48 (0.26–0.89)*	

* p<0.05; ** p<0.01. Confounders: hypertension, dyslipidemia, hyperglycemia, smoking habit, making an effort to maintain a healthy body weight, age, and gender. OR – odds ratio; CI – confidence interval.

periodontal disease and obesity 9 years later [22], although a significant association between periodontal disease at baseline and onset of obesity in a 4-year follow-up period was not observed [27]. In the present study, we examined subjects who were not obese at baseline (although the baseline blood pressure, blood glucose, and lipid values exceeded the reference values in some subjects), and we observed a significant association between periodontitis (having periodontal pockets) at

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	Number of subject			
Condition in 2002 and 2006	Non-obesity	Obesity	Adjusted OR (95%Cl)	
	(n=1,479, 91.4%)	(n=140, 8.6%)		
Periodontal pockets				
Without pocket at both times	934 (92.8)	72 (7.2)	1	
With pocket only in 2006	169 (91.9)	15 (8.1)	0.95 (0.52–1.75)	
With pocket only in 2002	196 (90.7)	20 (9.3)	1.12 (0.65–1.95)	
With pocket at both times	180 (84.5)	33 (15.5)	2.22 (1.34–3.68)**	

Table 4. Relationship between obesity in 2006 and the change in periodontal pockets.

** p<0.01. Confounders: hypertension, dyslipidemia, hyperglycemia, smoking habit, making an effort to maintain a healthy body weight, toothbrushing frequency, age, and gender. OR – odds ratio; CI – confidence interval.

baseline and the onset of obesity after 4 years, when adjustments for confounders including hypertension, dyslipidemia, hyperglycemia, smoking status, ability to maintain a healthy body weight, age, and sex were made. These findings suggest that periodontitis in adulthood increases the risk of future obesity. To determine the change in the status of periodontitis after 4 years, we divided the subjects into 4 groups based on the presence of periodontal pockets at baseline and/or 4 years later, and investigated its association with the onset of obesity. The multiple logistic analysis revealed that the group of participants with periodontal pockets at both the baseline and 4 years later showed a significantly higher OR (2.22, p<0.01) for onset of obesity than in the group of subjects without periodontal pockets at both the baseline and 4 years later. These results suggest that periodontitis as a risk factor for obesity is a modifiable factor, and the risk of obesity may be elevated in people with untreated periodontitis. Still, multiple logistic regression analysis did not show an association of baseline hypertension, hyperglycemia, or dyslipidemia with the onset of obesity in the 4-year follow-up period.

In contrast, we observed an inverse relationship between toothbrushing frequency at baseline and the onset of obesity 4 years later: subjects with a high toothbrushing frequency (i.e., good toothbrushing practice) were considered to have a low risk of becoming obese. Other studies have also reported a relationship between these parameters, including a crosssectional study using the results of the Korea National Health and Nutrition Examination Survey [21]. However, to the best of our knowledge, our study is the first longitudinal study to demonstrate this. It was reported that brushing teeth as frequently as ≥ 3 times/day is associated with a low risk of developing diabetes mellitus, dyslipidemia [18], and metabolic syndrome [19]. Our findings are in agreement with these studies, as the onset of obesity underlies these metabolic abnormalities.

Toothbrushing effectively reduces the levels of oral bacteria and gingivitis [28]. Periodontitis is a chronic inflammatory disease caused by persistent infection by periodontopathic bacteria, and which often progresses without subjective symptoms. In a 4-year cohort study involving working adults, Yamazaki et al. [29] reported that subjects who brushed their teeth frequently (≥3 times/day) had a low risk of developing periodontal pockets. In contrast, patients with periodontitis are known to have elevated blood levels of inflammatory markers such as C-reactive protein (CRP) and IL-6 [30,31]. Additionally, periodontal disease is considered a chronic disease that spreads mildly, but systemically [32,33]. In an in vitro study, stimulation of adipocytes with CRP and inflammatory cytokines led to enhanced differentiation of adipocytes and elevated production of maturation-promoting proteinases such as matrix metalloproteinases [34]. Furthermore, induced experimental periodontitis in rats resulted in elevated levels of the monocyte chemotactic factor (monocyte chemoattractant protein-1) in serum and lipids in the liver [35]. Therefore, considering these epidemiological, in vitro, and animal data, our results suggest that good toothbrushing practices are effective in preventing periodontitis and, consequently, in reducing the risk of developing obesity.

Exercise and dietary habits are major determinants of obesity and can affect its onset as confounding factors [1]; however, we adjusted for lifestyle habits related to caloric intake and expenditure, which were determined by asking subjects whether they were maintaining a healthy body weight in the multiple logistic regression analysis. This analysis revealed that there is a significant association between the onset of obesity and a positive response to the question, "Are you making an effort to maintain a healthy body weight?" (Table 3). Even when dividing subjects into 4 groups based on the answer to this question at baseline and 4 years later ("yes" at both baseline and 4 years, "yes" at baseline only, "yes" at 4 years only, and "no" at both times), multiple logistic analysis still indicated that the group who answered yes at both times and the group who answered yes at 4 years only had significantly lower ORs (0.14 for yes at both times and 0.27 for yes at 4 years only, p<0.01) for the onset of obesity than the group who answered no at both times (data not shown). These findings might indicate that this item of the questionnaire reflected regular exercise habits or dietary habit, but these habits were not directly examined in this study. Moreover, these findings also indicate that the main cause of obesity is recent excess calorie intake, which is largely caused by inadequate healthy lifestyle habits.

The present study has some limitations. We used BMI, but obesity can be assessed in several other ways, such as waist and hip circumferences, and subcutaneous fat thickness [3,12]. These indicators aid in estimating central obesity, which is more closely linked to metabolic syndrome than BMI is [20]. Moreover, we evaluated periodontitis based on CPI, which only evaluates index teeth and can potentially underestimate the degree of periodontitis. The question about smoking in this study also did not clarify the duration or the frequency of smoking. These limitations were mainly because we used the results of regular medical health checkups, which are designed and conducted specifically to help working adults to

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manage their health. Therefore, further understanding of the causal relationship between periodontitis/toothbrushing frequency and the onset of obesity may require not only cohort studies, using methods that enable a greater characterization of subjects' obesity, lifestyle, and periodontitis status, but also interventional studies.

Conclusions

The presence/absence of periodontal pockets and toothbrushing frequency were found to be significantly associated with the onset of obesity. Our findings suggest that periodontal pockets \geq 4 mm might increase the risk of obesity, while frequent toothbrushing might reduce its risk.

Conflicts of interest

None.

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