between obesity and periodontal disease in the United States population (7, 8). In addition, type 2 diabetes is a well-documented risk factor for periodontal disease (9–12). Since both type 2 diabetes and periodontal disease take a long time to develop and to manifest in middle-aged people, impaired glucose tolerance as a pre-diabetic condition, caused by obesity, may be a true risk factor for periodontal disease. This implies that obesity and impaired glucose condition are confounding factors associated with periodontal disease. However, no increased risk of periodontal disease with impaired glucose tolerance as a pre-diabetic condition has been reported. A fasting 75-g oral glucose tolerance test is used to diagnose diabetes, as it constitutes the definitive method for assessing a patient's glucose tolerance (13). Although previous reports have considered the role of diabetes in the relationship between obesity and periodontal disease, such studies did not use the oral glucose tolerance test to diagnose diabetic condition. The aforementioned studies used glycosylated hemoglobin A1c, the fasting plasma glucose, or a simple questionnaire about the history of diabetes; therefore, their assessment of diabetes was insufficient. The purpose of this study was to clarify the association between obesity and periodontal disease, with a precise assessment of glucose tolerance status using oral glucose tolerance test, in community-dwelling Japanese women.

Material and methods

From July to September 1998, a total of 982 Hisayama residents aged 40–79 years (21.6% of the total population in that age group) underwent a comprehensive health examination that included both a periodontal examination and a fasting 75-g oral glucose tolerance test (14). In this study, we analyzed 584 women with at least 10 teeth (15, 16).

Following the method of NHANES III (17), a periodontal examination was performed on two randomly selected quadrants, one maxillary and one mandibular, by four trained dentists, using a normal dental chair. Mean probing pocket depth and attachment loss were analyzed. The subjects were divided into quintiles with respect to each of the two periodontal measurements: mean pocket depth and mean attachment loss. Oral hygiene status was evaluated using the plaque index (18).

Blood samples were collected from the antecubital vein the morning after an overnight fast and analyzed using previously described methods (14). The World Health Organization criteria for the diagnosis of diabetes were applied (13). These are as follows: normal glucose tolerance (NGT; fasting plasma glucose level < 110 mg/dl and 2-h post-challenge glucose < 140 mg/dl), diabetes (fasting ≥ 126 mg/dl or 2-h post-challenge ≥ 200 mg/dl), and impaired glucose tolerance (other than the above, including impaired fasting glucose).

Trained nurses measured the subjects' weight, height, and waist and hip circumferences. The waist circumference was measured at the level of the umbilicus. All measurements were taken after the subjects exhaled. The hip circumference was measured around the buttocks 4 cm below the anterior superior iliac spine. As a measure of obesity, three indexes were used. Body mass index (the weight in kilograms divided by the square of the height in meters) and waist–hip ratio were calculated and the body fat of the subjects was measured by the bio-impedance method using a Body Fat Analyzer (TBF-202, TANITA Co., Japan). Each subject completed a self-administered questionnaire in advance, which was checked by trained nurses. Smoking history was estimated from the number of cigarettes smoked per day, multiplied by the number of years smoked; 4.3% of the subjects were current smokers and 2.2% of the subjects were former smokers. Social class was defined from the subjects' occupations as follows: (i) managerial position, (ii) office worker, (iii) primary industry, (iv) factory worker, and (v) homemaker or unemployed.

The differences between the mean values were evaluated using Student's *t*-test and the differences in the percentages were evaluated using the chi-squared test. Logistic regression analyses were used to determine the effect of each variable on the highest quintile of each periodontal parameter (≥ 1.9 mm for mean probing depth; ≥ 2.42 mm for mean attachment loss), and the odds ratio (OR) and 95% confidence interval (CI) were calculated. In bivariate analyses, one of the obesity indexes and the oral glucose tolerance test result were analyzed as independent variables. In the multivariate analysis, age, plaque index, smoking history, and social class were added as independent variables, as known risk factors of periodontal disease (9, 10). SPSS version 11.0 (SPSS Japan Inc., Tokyo, Japan) was used for the analyses. The design of the study and procedures for obtaining informed consent were approved by the Ethics Committee of Kyushu University Faculty of Dental Science and the Department of Health and Welfare of Hisayama town.

Results

The characteristics of the subjects were compared between subjects with the highest quintile of each periodontal parameter (≥ 1.9 mm for mean probing depth; ≥ 2.42 mm for mean attachment loss) and subjects with the four lower quintiles (Table 1). The mean body mass index, body fat, waist–hip ratio, and fasting and 2-h plasma glucose, and the proportion of social class categories differed significantly between subjects with deep and shallow pockets. In comparing the subjects with severe and non-severe attachment loss, the mean fasting and 2-h plasma glucose, hemoglobin A1c, and the proportion of social class categories differed significantly (Table 1). There were fewer teeth and the plaque index was higher in the more aggravated periodontal conditions.

Figure 1 shows the proportion of subjects with each quintile of mean probing pocket depth, according to the quartiles of body mass index, body fat, and waist–hip ratio. The proportion of subjects with the highest quintile of mean probing pocket depth increased significantly in a linear fashion with the quartiles of body mass index ($p < 0.0001$), body fat ($p = 0.0003$), and waist–hip ratio ($p = 0.007$). Figure 2

Table 1. Characteristics of subjects in each periodontal condition in Japanese women

Characteristics	Mean PD			Mean AL		
	< 1.9 mm $n = 469$	≥ 1.9 mm $n = 114$	p*	< 2.42 mm $n = 467$	≥ 2.42 mm $n = 116$	p*
	Mean (SD)			Mean (SD)		
Age (years)	55.5 (8.9)	56.8 (8.3)	0.14	54.8 (8.6)	59.4 (8.3)	< 0.0001
Number of teeth	25.4 (3.6)	23.5 (4.3)	< 0.0001	25.5 (3.6)	22.8 (4.0)	< 0.0001
Mean PD (mm)	1.4 (0.3)	2.3 (0.4)	< 0.0001	1.4 (0.4)	2.1 (0.5)	< 0.0001
Mean AL (mm)	1.7 (0.5)	2.7 (0.6)	< 0.0001	1.6 (0.5)	2.9 (0.5)	< 0.0001
Plaque index	0.9 (0.5)	1.4 (0.6)	< 0.0001	0.9 (0.5)	1.3 (0.6)	< 0.0001
Body mass index (kg m^2)	22.9 (3.5)	24.1 (2.9)	0.0004	23.0 (3.5)	23.6 (3.1)	0.09
Body fat (%)	28.0 (6.1)	30.4 (5.7)	0.0002	28.3 (6.1)	29.1 (6.1)	0.26
Waist–hip ratio	0.93 (0.06)	0.94 (0.05)	0.027	0.93 (0.06)	0.94 (0.06)	0.057
Fasting blood glucose (mg/dl)	97 (13)	103 (19)	0.0002	97 (13)	102 (19)	0.003
2-h blood glucose (mg/dl)	122 (42)	132 (52)	0.033	120 (40)	138 (57)	0.0001
Hemoglobin A1c (%)	5.2 (0.4)	5.3 (0.6)	0.053	5.2 (0.4)	5.3 (0.6)	0.005
	Number of subjects			Number of subjects		
Smoking (packyear)						
0	440	105	0.82	436	109	0.95
1–19	17	6		19	4	
20–39	11	3		11	3	
≥ 40	1	0		1	0	
Social class						
Managerial position	20	5	0.002	21	4	0.02
Office worker	101	19		103	17	
Primary industry	23	18		26	15	
Factory worker	9	3		8	4	
Homemaker or unemployed	316	69		309	76	

*Student's t-tests for mean values and chi-squared tests for the number of subjects were performed. $n = 583$.
PD, probing pocket depth; AL, attachment loss.

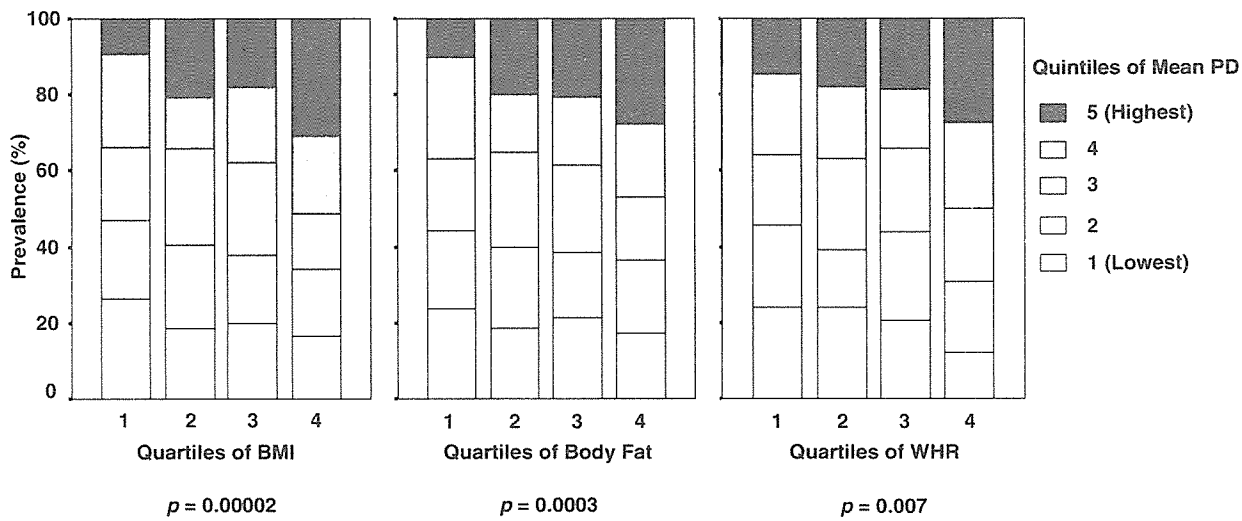

Fig. 1. Proportion of subjects with each quintile of mean probing pocket depth according to quartiles of each obesity index in Japanese women. Mantel–Haenszel chi-squared tests were performed in comparison between the highest quintile of mean probing pocket depth and the combination of lower 4 quintiles. PD, probing pocket depth; BMI, body mass index; WHR, waist–hip ratio.

shows the proportion of subjects with each quintile of mean attachment loss according to each quartile of the three obesity indexes. It is similar to Fig. 1; the highest quintile of mean attachment loss increased significantly with the quartiles of body mass index ($p = 0.02$), whereas it did not reach statistical significance when compared with the quartiles of body fat and waist–hip ratio (Fig. 2). There was a close association between every obesity

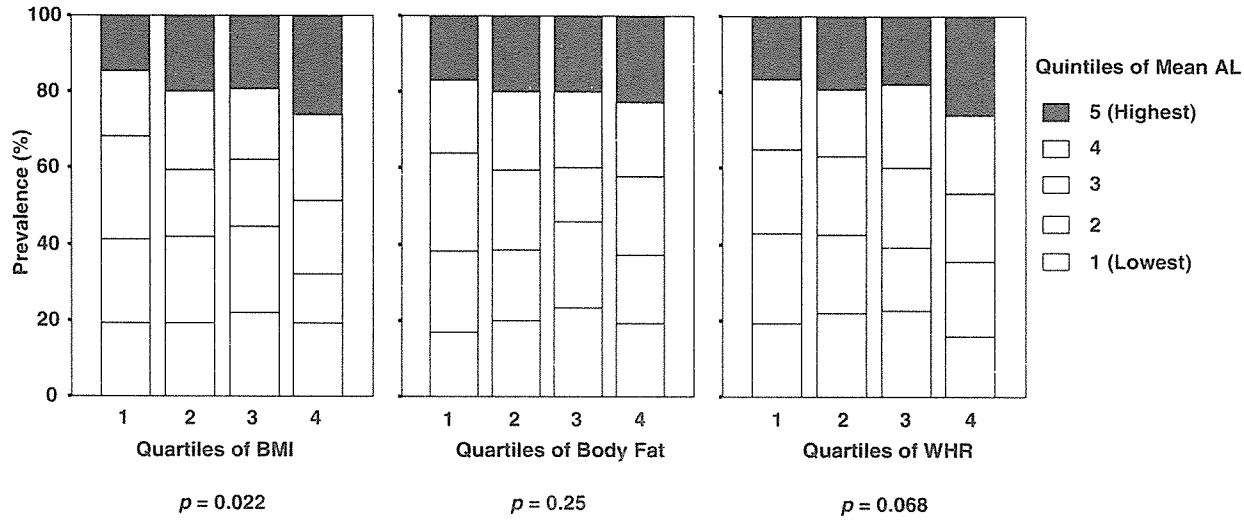

Fig. 2. Proportion of subjects with each quintile of mean attachment loss according to quartiles of each obesity index in Japanese women. Mantel–Haenszel chi-squared tests were performed in comparison between the highest quintile of mean attachment loss and the combination of lower 4 quintiles. AL, attachment loss; BMI, body mass index; WHR, waist–hip ratio.

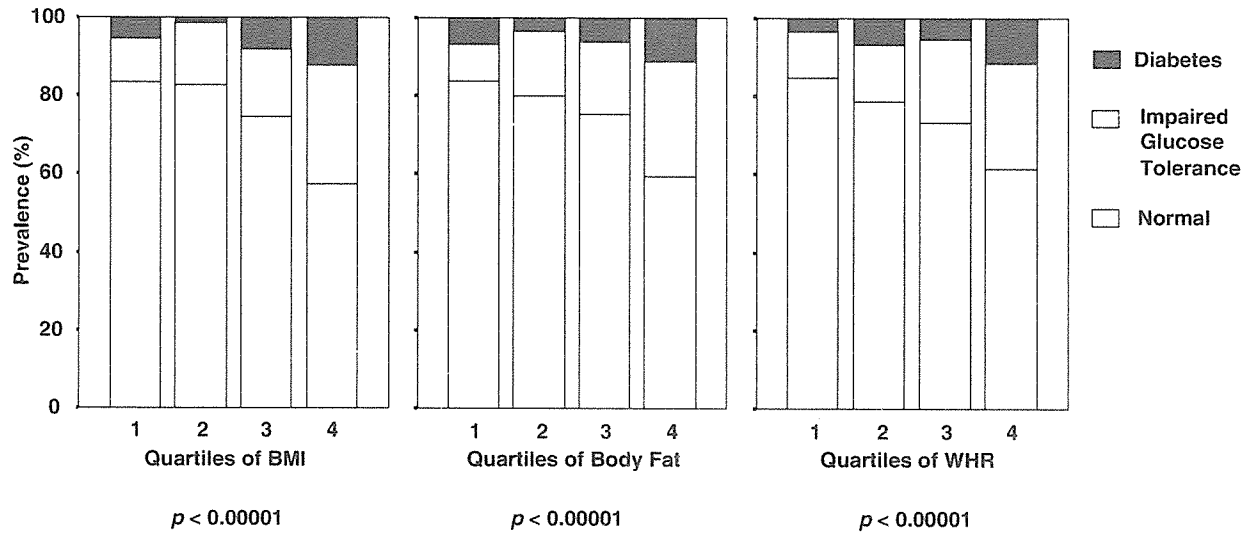

Fig. 3. Proportion of subjects with normal glucose tolerance, impaired glucose tolerance and diabetes according to quartiles of each obesity index in Japanese women. Mantel–Haenszel chi-squared tests were performed in comparison between normal glucose tolerance and the combination of impaired glucose tolerance and diabetes. BMI, body mass index; WHR, waist–hip ratio.

index and the prevalence of impaired glucose tolerance and diabetes; this was to be expected, as this association is well known (Fig. 3, $p < 0.0001$). Figure 4 shows the proportion of subjects with each quintile of the mean probing pocket depth and with each quintile of the mean attachment loss, in the subjects at each glucose tolerance status. The poorer the glucose tolerance status, the greater was the proportion of subjects with the highest quintile of mean probing pocket depth ($p = 0.008$) and mean attachment loss ($p < 0.001$) (Fig. 4). Both obesity and the oral glucose tolerance test results were significantly associated with periodontal disease in these simple comparisons.

To compare the effect of obese condition and glucose tolerance condition on periodontal disease, both variables were subject to a logistic regression analysis as independent variables, simultaneously (Tables 2A–C and Tables 3A–C). A higher body mass index was significantly associated with deep pockets, adjusted for the oral glucose tolerance test results and the other risk factors of periodontal disease (Table 2A). In the multivariate analysis, subjects with the highest quartile of body mass index had a significantly

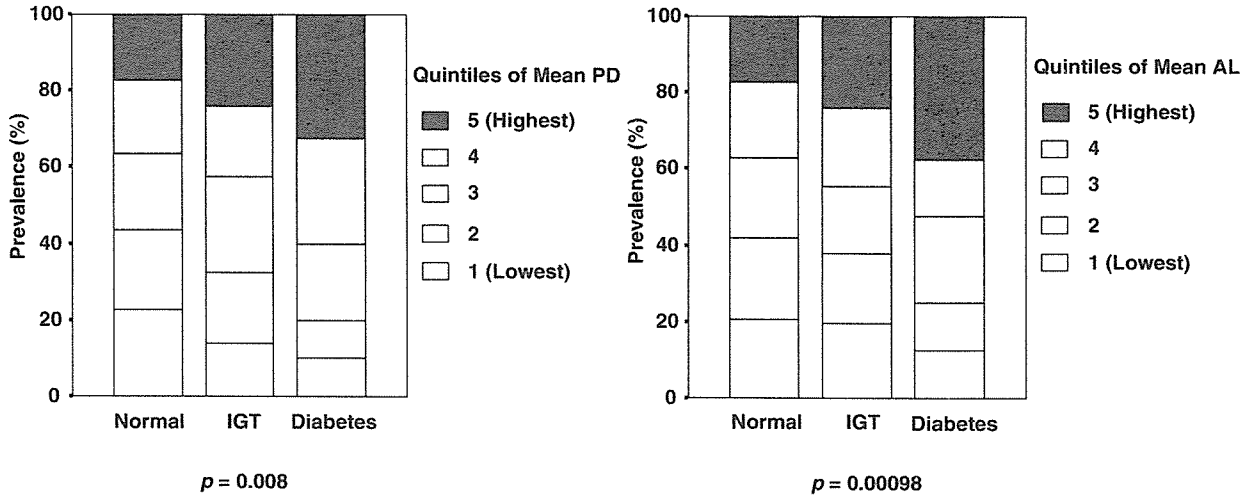

Fig. 4. Proportion of subjects with each quintile of mean probing pocket depth and with each quintile of mean attachment loss according to results of oral glucose tolerance test in Japanese women. Mantel–Haenszel chi-squared tests were performed in comparison between the highest quintile of each periodontal parameter and the combination of lower 4 quintiles. PD, probing pocket depth; AL, attachment loss; IGT, impaired glucose tolerance.

higher OR for the highest quintile of mean probing pocket depth (OR, 4.3; 95% CI, 2.1–8.9; $p < 0.001$), whereas neither impaired glucose tolerance nor diabetes were significant. In all the univariate, bivariate, and multivariate logistic regression models (Tables 2A–C), higher body mass index and body fat (highest for waist–hip ratio) were significantly associated with the highest quintile of mean probing pocket depth, even when adjusted for the oral glucose tolerance test results. The relationship between the oral glucose tolerance test results and mean probing pocket depth did not reach statistical significance when adjusted for every obesity index. Similar analyses were completed using the mean attachment loss as a dependent variable in Tables 3A–C. The results were similar to those in Tables 2A–C, although the OR of each obesity index was smaller, and was not significant, except for the crude analysis of body mass index. In the bivariate models, diabetes was significantly associated with severe attachment loss, whereas the obesity indexes were not. This differed from the results of the analysis using the mean probing pocket depth in Tables 2A–C.

Table 2A. Odds ratio for the highest quintile of mean probing pocket depth according to each quartile of body mass index and results of oral glucose tolerance test in Japanese women

	Mean PD (mm)		Odds ratio (95% CI)		
Variable	< 1.9	≥ 1.9	Univariate	Bivariate	Multivariate
BMI quartiles (kg/m^2)					
1 (15.5–20.8)	132	13	1	1	1
2 (20.8–22.7)	116	30	2.6 (1.3–5.3)†	2.7 (1.3–5.4)†	3.0 (1.4–6.3)†
3 (22.7–24.9)	120	26	2.2 (1.1–4.5)*	2.1 (1.0–4.3)*	2.3 (1.1–5.0)*
4 (25.0–46.7)	101	45	4.5 (2.3–8.8)‡	4.2 (2.1–8.2)‡	4.3 (2.1–8.9)‡
OGTT					
Normal	360	75	1	1	1
IGT	82	26	1.5 (0.9–2.5)	1.2 (0.7–2.1)	0.9 (0.5–1.7)
Diabetes	27	13	2.3 (1.1–4.7)*	2.0 (1.0–4.2)	1.4 (0.6–3.2)

Bivariate included BMI and OGTT as independent variables.
Multivariate included BMI, OGTT, age, plaque index, smoking history, and occupation as independent variables. *$p < 0.05$, †$p < 0.01$, ‡$p < 0.001$.
PD, probing pocket depth; CI, confidence interval; BMI, body mass index, OGTT, oral glucose tolerance test; IGT, impaired glucose tolerance.

Discussion

The relationship between obesity and deep pockets was observed after adjusting for the glucose tolerance status determined using the oral glucose tolerance test, which is used for the definitive diagnosis of diabetes (13). These results suggest that obesity is associated with deep pockets, independently of the glucose tolerance status, whereas obesity and glucose tolerance status are closely associated (Fig. 3). This suggests that the mechanism linking obesity and periodontal tissue differs from the reported mechanism operative in the effects of diabetes on the periodontium (10–12). Recent studies indicate that adipose tissue is an important organ that secretes several bioactive substances known as adipocytokines, which include tumor necrosis factor-α (19). These appear to be directly related to periodontal disease, as we discussed in a previous study (6). Although diabetes was significantly associated with both deep pockets and severe attachment loss in the crude analyses, the significant relationship between diabetes and deep pockets disappeared after adjusting for the obesity

Table 2B. Odds ratio for the highest quintile of mean probing pocket depth of each quartile of body fat and results of oral glucose tolerance test in Japanese women

	Mean PD (mm)		Odds ratio (95% CI)		
Variable	< 1.9	≥ 1.9	Univariate	Bivariate	Multivariate
Body fat quartiles (%)					
1 (7.9–24.1)	132	15	1	1	1
2 (24.2–27.9)	116	29	2.2 (1.1–4.3)*	2.2 (1.1–4.4)*	2.6 (1.2–5.3)*
3 (28.0–32.5)	116	30	2.3 (1.2–4.4)*	2.2 (1.1–4.4)*	2.8 (1.3–5.7)†
4 (32.6–52.5)	105	40	3.4 (1.8–6.4)‡	3.1 (1.6–6.0)‡	3.3 (1.6–6.8)†
OGTT					
Normal	360	75	1	1	1
IGT	82	26	1.5 (0.9–2.5)	1.3 (0.8–2.2)	1.0 (0.5–1.8)
Diabetes	27	13	2.3 (1.1–4.7)*	2.1 (1.0–4.4)	1.5 (0.7–3.5)

Bivariate included body fat and OGTT as independent variables.
Multivariate included Body Fat, OGTT, age, plaque index, smoking history, and occupation as independent variables. *$p < 0.05$, †$p < 0.01$, ‡$p < 0.001$.
PD, probing pocket depth; CI, confidence interval; OGTT, oral glucose tolerance test; IGT, impaired glucose tolerance.

Table 2C. Odds ratio for the highest quintile of mean probing pocket depth of each quartile of waist–hip ratio and results of oral glucose tolerance test in Japanese women

	Mean PD (mm)		Odds ratio (95% CI)		
Variable	< 1.9	≥ 1.9	Univariate	Bivariate	Multivariate
WHR quartiles					
1 (0.75–0.89)	124	21	1	1	1
2 (0.89–0.94)	120	26	1.3 (0.7–2.4)	1.2 (0.7–2.3)	1.4 (0.7–2.8)
3 (0.94–0.97)	119	27	1.3 (0.7–2.5)	1.3 (0.7–2.4)	1.2 (0.6–2.4)
4 (0.97–1.12)	106	40	2.2 (1.2–4.0)†	2.0 (1.1–3.6)*	2.1 (1.1–4.1)*
OGTT					
Normal	360	75	1	1	1
IGT	82	26	1.5 (0.9–2.5)	1.4 (0.8–2.3)	1.1 (0.6–1.9)
Diabetes	27	13	2.3 (1.1–4.7)*	2.0 (1.0–4.2)	1.5 (0.7–3.4)

Bivariate included WHR and OGTT as independent variables.
Multivariate included WHR, OGTT, age, plaque index, smoking history, and occupation as independent variables. *$p < 0.05$, †$p < 0.01$.
PD, probing pocket depth; CI, confidence interval; WHR, waist–hip ratio; OGTT, oral glucose tolerance test; IGT, impaired glucose tolerance.

Table 3A. Odds ratio for the highest quintile of mean attachment loss of each quartile of body mass index and results of oral glucose tolerance test in Japanese women

	Mean AL (mm)		Odds ratio (95% CI)		
Variable	< 2.42	≥ 2.42	Univariate	Bivariate	Multivariate
BMI quartiles (kg/m^2)					
1 (15.5–20.8)	124	21	1	1	1
2 (20.8–22.7)	117	29	1.5 (0.8–2.7)	1.5 (0.8–2.8)	1.6 (0.8–3.1)
3 (22.7–24.9)	118	28	1.4 (0.8–2.6)	1.3 (0.7–2.5)	1.3 (0.7–2.6)
4 (25.0–46.7)	108	38	2.1 (1.1–3.8)*	1.8 (1.0–3.3)	1.8 (0.9–3.4)
OGTT					
Normal	360	75	1	1	1
IGT	82	26	1.5 (0.9–2.5)	1.4 (0.8–2.3)	1.1 (0.6–1.9)
Diabetes	25	15	2.9 (1.4–5.7)*	2.7 (1.3–5.5)†	1.5 (0.7–3.2)

Bivariate included BMI and OGTT as independent variables.
Multivariate included BMI, OGTT, age, plaque index, smoking history, and occupation as independent variables. *$p < 0.05$, †$p < 0.01$.
AL, attachment loss; CI, confidence interval; BMI, body mass index; OGTT, oral glucose tolerance test; IGT, impaired glucose tolerance.

indexes (Tables 2A–C). Nevertheless, the significant relationship between diabetes and severe attachment loss remained after adjusting for the obesity indexes in the bivariate models (Tables 3A–C). In the multivariate models, the increased ORs between diabetes and both periodontal parameters did not reach statistical significance, which may be due simply to the small number of subjects, since there were only 40 diabetic subjects in this study. The oral glucose tolerance test results show the subjects' metabolic control status on that day, whereas the duration of their diabetic condition is important when studying the effects of diabetes on complications (12). Given this and the low number of subjects, this study cannot clarify the association between diabetes and periodontal disease. By contrast, impaired glucose tolerance seemed to have no association with either deep pockets or severe attachment loss in any multivariate model, despite the greater number of subjects ($n = 108$), as compared with diabetes ($n = 40$). Impaired glucose tolerance, which is an intermediate glucose condition between diabetes and normal glucose tolerance, may not have any effect on periodontal disease. This concurs with our recent report, in which deep pockets were more closely associated with the development of glucose intolerance from a normal glucose condition than with the past glucose tolerance condition itself, suggesting that deep pockets are a cause of impaired glucose tolerance (16).

In the analyses using attachment loss as a dependent variable, even the highest quartile of obesity indexes had no significant association with severe attachment loss, although the tendency was similar to the analyses using pocket depth. Although both pocket depth and attachment loss are important parameters of periodontal disease, they have slightly different meanings. A deep pocket usually means existing periodontal inflammation, whereas severe attachment loss usually represents a history of periodontal destruction, which does not always mean periodontal inflammation. Of course, the mean pocket depth and mean attachment loss are closely related ($r = 0.79$,

Table 3B. Odds ratio for the highest quintile of mean attachment loss of each quartile of body fat and results of oral glucose tolerance test in Japanese women

	Mean AL (mm)		Odds ratio (95% CI)		
Variable	< 2.42	≥ 2.42	Univariate	Bivariate	Multivariate
Body fat quartiles (%)					
1 (7.9–24.1)	122	25	1	1	1
2 (24.2–27.9)	116	29	1.2 (0.7–2.2)	1.2 (0.7–2.3)	1.3 (0.7–2.5)
3(28.0–32.5)	117	29	1.2 (0.7–2.2)	1.2 (0.6–2.1)	1.3 (0.7–2.5)
4 (32.6–52.5)	112	33	1.4 (0.8–2.6)	1.3 (0.7–2.3)	1.2 (0.6–2.3)
OGTT					
Normal	360	75	1	1	1
IGT	82	26	1.5 (0.9–2.5)	1.5 (0.9–2.5)	1.1 (0.6–2.0)
Diabetes	25	15	2.9 (1.4–5.7)*	2.8 (1.4–5.7)†	1.6 (0.7–3.4)

Bivariate included body fat and OGTT as independent variables.
Multivariate included body fat, OGTT, age, plaque index, smoking history, and occupation as independent variables. *$p < 0.05$, †$p < 0.01$.
AL, attachment loss; CI, confidence interval; OGTT, oral glucose tolerance test; IGT, impaired glucose tolerance.

Table 3C. Odds ratio for the highest quintile of mean attachment loss of each quartile of waist–hip ratio and results of oral glucose tolerance test in Japanese women

	Mean AL (mm)		Odds ratio (95% CI)		
Variable	< 2.42	≥ 2.42	Univariate	Bivariate	Multivariate
WHR quartiles					
1 (0.75–0.89)	121	24	1	1	1
2 (0.89–0.94)	118	28	1.2 (0.7–2.2)	1.1 (0.6–2.1)	1.2 (0.6–2.4)
3 (0.94–0.97)	120	26	1.1 (0.6–2.0)	1.0 (0.6–1.9)	1.0 (0.5–1.9)
4 (0.97–1.12)	108	38	1.8 (1.0–3.1)	1.5 (0.9–2.8)	1.3 (0.7–2.5)
OGTT					
Normal	360	75	1	1	1
IGT	82	26	1.5 (0.9–2.5)	1.4 (0.9–2.4)	1.1 (0.6–2.0)
Diabetes	25	15	2.9 (1.4–5.7)*	2.6 (1.3–5.3)†	1.5 (0.7–3.2)

Bivariate included WHR and OGTT as independent variables.
Multivariate included WHR, OGTT, age, plaque index, smoking history, and occupation as independent variables. *$p < 0.05$, †$p < 0.01$.
AL, attachment loss; CI, confidence interval; WHR, waist–hip ratio; OGTT, oral glucose tolerance test; IGT, impaired glucose tolerance.

$p < 0.0001$). Therefore, the tendencies in Tables 2A-C and 3A-C were similar and, given sufficient subjects, the relationship might reach statistical significance. Nevertheless, the weak or non-significant association between obesity and attachment loss found in this study suggests that the relationship between obesity and periodontal disease is limited to a relationship between obesity and the primary stage of periodontal disease. Since periodontal destruction, such as alveolar bone loss, is a result of inflammation, with the mechanism of the destruction arising as a consequence of inflammation (10), obesity may be related to the primary stage of periodontal disease and may not be related to the subsequent stage of periodontal destruction.

The NHANES III study found a relationship between obesity and periodontal disease in young adults only, using a combination of deep pockets and attachment loss as criteria of periodontal disease (7). As elderly people lose their teeth as a result of periodontal disease, the relationship between obesity and periodontal disease in the elderly could disappear. Since we limited the subjects of our study to those with ≥ 10 teeth, a relationship between obesity and deep pockets should be more easily detected in our study, as compared to the NHANES III study, which included subjects with fewer than 10 teeth. Although we could not analyze each age group separately, due to the small number of subjects, a relationship between obesity and deep pockets might be detected in the elderly if the subjects were to be limited to those with many teeth. Tobacco smoking is a well-documented risk factor for periodontal disease (9, 10). In this study, however, smoking history was not associated with either deep pockets or severe attachment loss, probably because there was a very low proportion of smokers among our female subjects. The prevalence of obesity is very low among Japanese as compared to the US population, whereas the prevalence of diabetes is about the same (1, 3, 12). As the effect of obesity on health is thought to differ among races, Japanese women may show different relationships between obesity, diabetes, and periodontal disease compared to other races. Since our study and other reports on the relationship between obesity and periodontal disease were cross-sectional studies, a prospective cohort study with different age groups and sexes is required.

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Relationship Between Drinking and Periodontitis: The Hisayama Study

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Background: Although recent studies suggest a relationship between alcohol consumption and periodontal disease, the dose-response relationship between drinking and the severity of periodontitis is unclear.

Methods: Alcohol consumption was evaluated using the frequency of drinking and the daily alcohol intake for 961 individuals aged 40 to 79 years. Periodontal status was evaluated using probing depth (PD) and clinical attachment loss (CAL).

Results: Alcohol consumption was linearly associated with the extent of PD and CAL in univariate analyses ($P<0.001$). In multivariate logistic regression analyses, the subjects drinking 15 to 29.9 g alcohol per day (odds ratio [OR] = 2.7; 95% confidence interval [CI] = 1.1 to 6.6) or more than 30 g per day (OR = 2.5; 95% CI = 1.1 to 5.7) had a significantly higher risk of having more than 35% of their teeth with PD ≥4 mm than non-drinkers, independent of other confounding variables. No significant relationship between drinking and CAL was observed in the multivariate analysis.

Conclusion: These results suggest that the effect of drinking on periodontal condition is limited to subjects with deep periodontal pockets associated with more than one-third of their teeth. *J Periodontol 2005;76:1534-1541.*

KEY WORDS

Alcoholic beverages/adverse effects; periodontitis/epidemiology; risk factors.

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Both smoking and drinking are lifestyle factors that cause health problems. Numerous studies have shown a relationship between smoking and periodontitis,[1-3] while there is very limited information about the relationship between drinking and periodontitis.[4-7] Previous studies examined the relationship between drinking and probing depth (PD)[4] or clinical attachment loss (CAL).[5] Pitiphat et al. reported a longitudinal relationship between drinking and self-reported periodontitis.[6] Recently, Nishida et al. reported that alcohol consumption is a risk indicator in subjects with the aldehyde dehydrogenase-2 ($ALDH_2$) *1/*2 genotype, but not in subjects with $ALDH_2$ *1/*1 genotype.[7] However, these studies did not find a dose-response relationship between drinking and the severity of periodontitis or conclude whether drinking has a greater effect on PD or CAL.

Drinking also affects several systemic diseases in adults, and many studies have reported J- or U-shaped associations, in which light or moderate alcohol consumption lowers the risk of hypertension,[8,9] coronary heart disease,[10,11] systemic markers of inflammation,[12] and mortality.[13] However, there are no reports on the effect of a low alcohol intake on periodontal disease. In this study, we examined the dose-response relationship between drinking and various stages of periodontal condition and examined how alcohol intake is related to periodontal condition using the results of a health examination conducted in Hisayama.

MATERIALS AND METHODS

Study Population

The Hisayama Study began in 1961 and is an ongoing population based prospective cohort study of cardiovascular diseases. The town population, based on data from national census, was shown to be representative of Japan as a whole.[14] As a part of the study, from July to September 1998, 982 Hisayama residents aged 40 to 79 years (21.6% of the total population in that age group) underwent a comprehensive health examination, including a dental examination. We excluded 21 subjects who had less than 10 teeth or lacked data for the variables studied; consequently we analyzed 961 subjects (378 male, 583 female) in this study. The Ethics Committee of Kyushu University Faculty of Dental Science and the Department of General Affairs and Health and Welfare of Hisayama approved the study design, data collection methods, and procedure for obtaining informed consent.

Oral Examination

The periodontal examination followed the method of the Third National Health and Nutrition Examination Survey (NHANES III).[15] As periodontal parameters, PD and CAL were measured at mesio-buccal and mid-buccal sites for all of the teeth present in two randomly selected quadrants: one maxillary and one mandibular. We divided the subjects into four categories according to the proportion of teeth with PD ≥4 mm. None: no teeth with PD ≥4 mm; low: 0.1% to 19.9% teeth with PD ≥4 mm; mid: 20% to 34.9% teeth with PD ≥4 mm (the second highest 10th percentile); and high: ≥35% teeth with PD ≥4 mm (the highest 10th percentile). Similarly, the proportion of teeth with CAL ≥5 mm was categorized into four categories. None: no teeth with CAL ≥5 mm; low: 0.1% to 9.9% teeth with CAL ≥5 mm; mid: 10% to 21.9% teeth with CAL ≥5 mm (the second highest 10th percentile); and high: ≥22% teeth with CAL ≥5 mm (the highest 10th percentile). Oral hygiene status was evaluated using the plaque index[16] and we used the mean score of each subject in the analyses.

General Examination

A self-administered questionnaire was completed in advance and checked by trained nurses. Participants answered items concerning their frequency of alcohol intake over the previous year and the kinds and amounts of alcoholic beverages habitually consumed. The alcohol intake per drink was converted into the weight of 100% ethanol in grams. The estimated alcohol content was 21.5 g for a cup of Japanese sake (180 ml), 22.6 g for a bottle of beer (633 ml), 35.7 g for a cup of distilled spirits (180 ml), and 31.8 g for a glass of whiskey (100 ml). The daily amount of drinking was estimated by multiplying the frequency of consuming each drink per week by the weight of ethanol in each drink and dividing the sum by seven (g/day). The daily amount of drinking was divided into four categories: non-drinker (0 g/day), light drinker (0.1 to 14.9 g/day), moderate drinker (15 to 29.9 g/day), and heavy drinker (≥30 g/day). As the number of former drinkers was very low (N = 27; 2.8%), we included past drinkers with non-drinkers. The amount of smoking, including past smoking, was given as the number of cigarettes smoked per day multiplied by the total years of smoking. The amount of smoking was divided into four categories: never smoked, light smoker (1 to 399), moderate smoker (400 to 799), and heavy smoker (≥800). Blood samples were collected from an antecubital vein after an overnight fast. Laboratory analyses of the blood samples followed previously described methods.[17] A 75 g oral glucose tolerance test was performed between 8:00 a.m. and 10:30 a.m. Before and 120 minutes after ingesting the 75 g glucose solution, blood samples were obtained for laboratory measurements. The glucose tolerance was categorized into three groups: normal (fasting and 2-hour post-challenge plasma glucose levels <110 and <140 mg/dl, respectively), diabetes (levels ≥126 or ≥200 mg/dl, respectively), and impaired (other than normal or diabetes).

Statistical Analysis

The differences in percentages were evaluated using Pearson's chi square test and its linearity was evaluated using the Mantel-Haenszel chi square test. The differences in the mean values were evaluated using Student *t* test. To protect against spurious significance with multiple inference, we used Bonferroni's correction to interpret the significance of *P* value. We performed univariate and multivariate logistic regression analyses to determine the effect of alcohol consumption on periodontal parameters, and calculated the odds ratio (OR) and 95% confidence interval (CI). As both PD and CAL were classified into four categories, we performed three logistic regression models using none versus each of the other three categories (low, mid, and high) as the dependent variable. Multivariate models were adjusted for amount of smoking, glucose tolerance, age, sex, number of teeth, and mean plaque index. The statistical analysis was performed using a software program.†

RESULTS

Tables 1 and 2 show the characteristics of the subjects according to the proportion of teeth with PD ≥4 mm and with CAL ≥5 mm, respectively. The more alcohol the subjects consumed, the greater the proportion of their teeth with PD ≥4 mm and CAL ≥5 mm,

† Version 11.0, SPSS Japan, Tokyo, Japan.

Table 1.

Study Population Variables According to Periodontal Status (PD)

Variable	Teeth With PD ≥4 mm: None 549 (57.1%)	Low 220 (22.9%)	Mid 102 (10.6%)	High 90 (9.4%)	P Value
	N (%)				
Alcohol consumption					
None (0 g/day)	355 (60.1)	126 (21.3)	67 (11.3)	43 (7.3)	<0.001*
Light (0.1-14.9 g/day	91 (59.1)	41 (26.6)	14 (9.1)	8 (5.2)	<0.001†
Moderate (15-29.9 g/day)	46 (50.0)	24 (26.1)	7 (7.6)	15 (16.3)	
Heavy (≥30 g/day)	57 (46.0)	29 (23.4)	14 (11.3)	24 (19.4)	
Smoking					
Never (0)	400 (62.3)	137 (21.3)	59 (9.2)	46 (7.2)	<0.001*
Light (1-399)	47 (52.8)	27 (30.3)	8 (9.0)	7 (7.9)	<0.001†
Moderate (400-799)	63 (51.6)	31 (25.4)	12 (9.8)	16 (13.1)	
Heavy (≥800)	39 (36.1)	25 (23.1)	23 (21.3)	21 (19.4)	
Glucose tolerance					
Normal	404 (60.3)	145 (21.6)	67 (10.0)	54 (8.1)	0.065*
Impaired	97 (50.8)	51 (26.7)	20 (10.5)	23 (12.0)	0.002†
Diabetes	48 (48.0)	24 (24.0)	15 (15.0)	13 (13.0)	
Gender					
Male	189 (50.0)	94 (24.9)	46 (12.2)	49 (13.0)	0.001*
Female	360 (61.7)	126 (21.6)	56 (9.6)	41 (7.0)	<0.001†
	Mean ± SD				
Age	55.6 ± 8.7	57.3 ± 8.5	59.0 ± 8.5§	55.6 ± 8.7	
Number teeth	25.6 ± 3.7	25.0 ± 3.5	23.7 ± 4.9§	23.7 ± 4.6§	
Mean plaque index	1.0 ± 0.5	1.1 ± 0.6‡	1.4 ± 0.7§‖	1.6 ± 0.7§‖	

* Non-linear component calculated using Pearson's chi square test.
† Linear component calculated using Mantel-Haenszel chi square test.
‡ $P<0.05$ compared with none; Student t test applied with Bonferroni's correction of P value for type 1 errors in multiple comparisons.
§ $P<0.01$ compared with none; Student t test applied with Bonferroni's correction of P value for type 1 errors in multiple comparisons.
‖ $P<0.01$ compared with low; Student t test applied with Bonferroni's correction of P value for type 1 errors in multiple comparisons.

which was the same as when the subjects consumed more cigarettes. The subjects with poor diabetic conditions had more teeth with PD ≥4 mm and CAL ≥5 mm. The variables age, gender, number of teeth, and mean plaque index were each significantly associated with the proportion of teeth with PD ≥4 mm and CAL ≥5 mm in the univariate analyses (Tables 1 and 2).

Table 3 shows the univariate and multivariate logistic regression analyses for each of the three different PD conditions. Alcohol consumption did not show any significant influence for having the low or mid PD condition. However, moderate and heavy drinkers had a significantly high OR for having a high proportion of teeth with PD ≥4 mm in the univariate and multivariate analysis adjusting for confounding variables. In the analysis, heavy smoking and a higher plaque index also had a significantly increased OR for having the high PD condition. Table 4 (pages 1540 and 1541) shows the univariate and multivariate ORs for each of the three CAL conditions. Although moderate and heavy drinking had a significantly increased OR for having a high proportion of CAL ≥5 mm in the univariate analysis, the relationship disappeared after multivariate adjustment. Moderate and heavy smoking were associated with significantly increased OR for high CAL, and heavy smoking had a significantly increased OR for low CAL.

DISCUSSION

This study showed that subjects who drank more than 15 g alcohol per day had a significantly increased risk for widespread periodontal disease; i.e., more than one third of teeth with PD ≥4 mm, as compared to non-drinkers. Conversely, drinking did not indicate an increased risk for having less than 35% of the teeth with PD ≥4 mm. It was reported that the subjects with $ALDH_2$ *1/*2 genotype who consumed ≥33 g alcohol per day had a significantly greater percentage of PD ≥3.5 mm than those whose daily consumption was lower, while there was no significant difference in periodontal status associated with alcohol consumption in $ALDH_2$ *1/*1 subjects.[7] The subjects with $ALDH_2$ genotypes *1/*2 or *2/*2 lack $ALDH_2$ activity and become flushed after alcohol intake owing to the marked elevation in the blood acetaldehyde concentration.[18] Therefore, it is thought that drinking raises the risk of periodontitis when drinking causes an accumulation of acetaldehyde. As about half of all Japanese lack $ALDH_2$ activity,[19,20] many subjects with $ALDH_2$ *1/*2 genotype might have been included in the subjects with many teeth with PD ≥4 mm in our study.

Periodontitis is a chronic inflammatory disease of the soft and hard periodontal tissues and recent studies have suggested a relationship between periodontitis and circulatory diseases.[21-23] Inflammation plays an important role in both the initiation and pro-

Table 2.

Study Population According to Periodontal Status (CAL)

Variable	Teeth With CAL ≥5 mm: None 624 (64.9%)	Low 146 (15.2%)	Mid 95 (9.9%)	High 96 (10.0%)	*P* Value
	N (%)				
Alcohol consumption					
None (0 g/day)	394 (66.7)	85 (14.4)	65 (11.0)	47 (8.0)	0.002*
Light (0.1-14.9 g/day)	106 (68.8)	26 (16.9)	12 (7.8)	10 (6.5)	<0.001†
Moderate (15-29.9 g/day)	57 (62.0)	12 (13.0)	8 (8.7)	15 (16.3)	
Heavy (≥30 g/day)	67 (54.0)	23 (18.5)	10 (8.1)	24 (19.4)	
Smoking					
Never (0)	458 (71.3)	84 (13.1)	62 (9.7)	38 (5.9)	<0.001*
Light (1-399)	53 (59.6)	18 (20.2)	10 (11.2)	8 (9.0)	<0.001†
Moderate (400-799)	70 (57.4)	20 (16.4)	14 (11.5)	18 (14.8)	
Heavy (≥800)	43 (39.8)	24 (22.2)	9 (8.3)	32 (29.6)	
Glucose tolerance					
Normal	461 (68.8)	90 (13.4)	59 (8.8)	60 (9.0)	<0.001*
Impaired	114 (59.7)	36 (18.8)	27 (14.1)	14 (7.3)	<0.001†
Diabetes	49 (49.0)	20 (20.0)	9 (9.0)	22 (22.0)	
Gender					
Male	206 (54.5)	69 (18.3)	42 (11.1)	61 (16.1)	<0.001*
Female	418 (71.7)	77 (13.2)	53 (9.1)	35 (6.0)	<0.001†
	Mean ± SD				
Age	55.0 ± 8.6	57.7 ± 8.3‡	59.7 ± 8.2‡	59.9 ± 9.1‡	
Number of teeth	25.7 ± 3.8	25.9 ± 2.7	23.5 ± 4.4‡§	22.0 ± 4.7‡§	
Mean plaque index	1.0 ± 0.6	1.1 ± 0.6	1.2 ± 0.6‡	1.6 ± 0.6‡§‖	

* Non-linear component calculated using Pearson's chi square test.
† Linear component calculated using Mantel-Haenszel chi square test.
‡ $P<0.01$ compared with none; Student *t* test applied with Bonferroni's correction of *P* value for type 1 errors in multiple comparisons.
§ $P<0.01$ compared with low; Student *t* test applied with Bonferroni's correction of *P* value for type 1 errors in multiple comparisons.
‖ $P<0.01$ compared with mid; Student *t* test applied with Bonferroni's correction of *P* value for type 1 errors in multiple comparisons.

gression of atherosclerosis,[24] and the systemic inflammatory marker such as C-reactive protein (CRP) is a predictor of cardiovascular events.[25] The subjects with periodontitis had a higher CRP level than the subjects with healthy periodontal tissue.[26,27] Periodontal disease was significantly associated with a higher CRP level in a longitudinal study[28] and recent studies reported that control of periodontal health decreased the serum CRP level.[29,30] Although CRP level is unknown in this study, as our results showed that moderate to heavy drinking was associated with a significant risk of having many teeth with deep PD, increased periodontal inflammation with alcohol consumption may increase the risk of coronary heart disease, in addition to the direct effect of alcohol on the circulatory system.

Tezal et al. reported a significant relationship between the frequency of drinking and CAL.[5] We did not find a significant relationship between drinking and CAL. It may be owing to small sample size, especially the low number of drinkers in this study. Alcohol is considered an important risk factor for various bone-related disorders, such as reduced bone mass and fractures, and chronic alcohol abuse is a major risk factor for osteoporosis.[31,32] A 2001 study found a relationship between osteoporosis and periodontitis in menopausal women.[33] If drinking exacerbates alveolar bone resorption, the observed effect of drinking on increasing periodontal pocket depth may lead to extensive periodontal destruction.

Some studies have reported J- or U-shaped relationship in which light drinkers had a lower risk of hypertension, coronary heart disease, systemic markers of inflammation, and mortality of all causes than did non-drinkers or heavy drinkers.[8-13] Previous studies of the relationship between drinking and periodontitis failed to find a significant association between light drinking and periodintitis, although two studies showed that light drinkers tended to have better periodontal health than non-drinkers.[5,7] In our study, although light drinkers had a relatively low risk for having many teeth with deep PD, the relationship was not significant statistically. It is thought that a large number of study subjects is needed to clarify the effect of light drinking on periodontitis.

Smoking is an important lifestyle-related risk factor for periodontitis, and this study suggests that heavy drinking is also a risk factor for periodontitis. Smoking cessation should be strongly recommended for patients with periodontitis. As our results were based on a cross-sectional investigation, we could not clarify causal relationship between drinking and periodontitis. Therefore, at this stage, we may advise heavy drinkers with periodontitis to reduce the amount they drink to improve both their systemic and oral health. In order to establish the

Table 3.

Risk for Low, Mid, and High Proportion of Teeth With PD ≥4 mm According to Alcohol Consumption and Other Variables

Independent Variable	Model 1				Model 2			
	Teeth With PD ≥4 mm		Univariate OR (95% CI)	Multivariate OR (95% CI)	Teeth With PD ≥4 mm		Univariate OR (95% CI)	Multivariate OR (95% CI)
	None	Low			None	Mid		
Alcohol consumption								
None (0 g/day)	355	126	1	1	355	67	1	1
Light (0.1-14.9 g/day)	91	41	1.3 (0.8-1.9)	1.3 (0.8-2.0)	91	14	0.8 (0.4-1.5)	0.7 (0.4-1.5)
Moderate (15-29.9 g/day)	46	24	1.5 (0.9-2.5)	1.3 (0.7-2.4)	46	7	0.8 (0.3-1.9)	0.8 (0.3-2.0)
Heavy (≥30 g/day)	57	29	1.4 (0.9-2.4)	1.1 (0.6-2.0)	57	14	1.3 (0.7-2.5)	0.7 (0.3-1.7)
Smoking								
Never (0)	400	137	1	1	400	59	1	1
Light (1-399)	47	27	1.7 (1.0-2.8)*	1.7 (0.9-3.1)	47	8	1.2 (0.5-2.6)	1.4 (0.6-3.7)
Moderate (400-799)	63	31	1.4 (0.9-2.3)	1.4 (0.7-2.5)	63	12	1.3 (0.7-2.5)	1.4 (0.6-3.5)
Heavy (≥800)	39	25	1.9 (1.1-3.2)*	1.6 (0.8-3.2)	39	23	4.0 (2.2-7.2)‡	3.5 (1.4-8.7)†
Glucose tolerance								
Normal	404	145	1	1	404	67	1	1
Impaired	97	51	1.5 (1.0-2.2)	1.4 (0.9-2.0)	97	20	1.2 (0.7-2.1)	1.0 (0.6-1.8)
Diabetes	48	24	1.4 (0.8-2.4)	1.1 (0.7-2.0)	48	15	1.9 (1.0-3.6)	1.5 (0.7-3.0)
Gender								
Male	189	94	1	1	189	46	1	1
Female	360	126	0.7 (0.5-1.0)*	1.1 (0.6-1.8)	360	56	0.6 (0.4-1.0)*	1.2 (0.6-2.7)
Age (years)			1.0 (1.0-1.0)*	1.0 (1.0-1.0)			1.0 (1.0-1.1)‡	1.0 (1.0-1.0)
Number of teeth			1.0 (0.9-1.0)*	1.0 (0.9-1.0)			0.9 (0.9-0.9)‡	1.0 (0.9-1.0)
Mean plaque index			1.5 (1.1-2.0)†	1.3 (1.0-1.7)			3.6 (2.5-5.2)‡	3.0 (2.0-4.4)‡

* $P<0.05$.
† $P<0.01$.
‡ $P<0.001$.

effect of drinking as a risk factor for periodontitis, larger-scale epidemiological and interventional studies, for example examining the effect of temperance and abstinence from drinking in heavy drinkers with periodontitis, are needed to confirm the causal relationship between drinking and periodontitis, as well as supportive experimental studies to clarify the mechanisms for the relationship between drinking and periodontitis.

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Table 3. (continued)

Risk for Low, Mid, and High Proportion of Teeth With PD ≥4 mm According to Alcohol Consumption and Other Variables

Model 3			
Teeth With PD ≥4 mm		Univariate	Multivariate
None	High	OR (95% CI)	OR (95% CI)
355	43	1	1
91	8	0.7 (0.3-1.6)	0.6 (0.3-1.6)
46	15	2.7 (1.4-5.2)†	2.7 (1.1-6.6)*
57	24	3.5 (2.0-6.2)‡	2.5 (1.1-5.7)*
400	46	1	1
47	7	1.3 (0.6-3.0)	1.2 (0.4-3.2)
63	16	2.2 (1.2-4.1)*	1.7 (0.7-4.2)
39	21	4.7 (2.5-8.6)‡	2.8 (1.1-7.3)*
404	54	1	1
97	23	1.8 (1.0-3.0)*	1.2 (0.7-2.3)
48	13	2.0 (1.0-4.0)*	1.3 (0.6-3.0)
189	49	1	1
360	41	0.4 (0.3-0.7)‡	1.7 (0.7-3.9)
		1.0 (1.0-1.0)	1.0 (0.9-1.0)
		0.9 (0.9-0.9)‡	0.9 (0.9-1.0)
		5.4 (3.6-8.0)‡	4.6 (3.0-7.0)‡

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Table 4.

Risk for Low, Mid, and High Proportion of Teeth With CAL ≥5 mm According to Alcohol Consumption and Other Variables

	Model 1				Model 2			
Independent Variable	Teeth With CAL ≥5 mm		Univariate OR (95% CI)	Multivariate OR (95% CI)	Teeth With CAL ≥5 mm		Univariate OR (95% CI)	Multivariate OR (95% CI)
	None	Low			None	Mid		
Alcohol consumption								
None (0 g/day)	394	85	1	1	394	65	1	1
Light (0.1-14.9 g/day)	106	26	1.1 (0.7-1.9)	1.0 (0.6-1.7)	106	12	0.7 (0.4-1.3)	0.6 (0.3-1.3)
Moderate (15-29.9 g/day)	57	12	1.0 (0.5-1.9)	0.7 (0.3-1.5)	57	8	0.9 (0.4-1.9)	0.6 (0.2-1.4)
Heavy (≥30 g/day)	67	23	1.6 (0.9-2.7)	0.9 (0.5-1.8)	67	10	0.9 (0.4-1.8)	0.5 (0.2-1.1)
Smoking								
Never (0)	458	84	1	1	458	62	1	1
Light (1-399)	53	18	1.9 (1.0-3.3)*	2.0 (1.0-3.9)	53	10	1.4 (0.7-2.9)	1.5 (0.6-3.5)
Moderate (400-799)	70	20	1.6 (0.9-2.7)	1.5 (0.8-3.1)	70	14	1.5 (0.8-2.8)	1.1 (0.5-2.6)
Heavy (≥800)	43	24	3.0 (1.8-5.3)‡	2.6 (1.3-5.4)*	43	9	1.5 (0.7-3.3)	0.9 (0.3-2.3)
Glucose tolerance								
Normal	461	90	1	1	461	59	1	1
Impaired	114	36	1.6 (1.0-2.5)*	1.5 (0.9-2.3)	114	27	1.9 (1.1-3.0)*	1.7 (1.0-2.9)*
Diabetes	49	20	2.1 (1.2-3.7)*	1.7 (0.9-3.1)	49	9	1.4 (0.7-3.1)	0.9 (0.4-2.0)
Gender								
Male	206	69	1	1	206	42	1	1
Female	418	77	0.6 (0.4-0.8)†	1.0 (0.5-1.7)	418	53	0.6 (0.4-1.0)†	0.5 (0.2-0.9)*
Age (years)			1.0 (1.0-1.1)†	1.0 (1.0-1.1)†			1.1 (1.0-1.1)‡	1.0 (1.0-1.1)†
Number teeth			1.0 (1.0-1.1)	1.1 (1.0-1.1)*			0.9 (0.8-0.9)‡	0.9 (0.9-1.0)†
Mean plaque index			1.4 (1.0-1.9)*	1.3 (0.9-1.7)			1.8 (1.3-2.6)‡	1.3 (0.8-1.8)

* $P<0.05$.
† $P<0.01$.
‡ $P<0.001$.

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Table 4. (continued)

Risk for Low, Mid, and High Proportion of Teeth With CAL ≥5 mm According to Alcohol Consumption and Other Variables

Model 3			
Teeth With CAL ≥5 mm		Univariate	Multivariate
None	High	OR (95% CI)	OR (95% CI)
394	47	1	1
106	10	0.8 (0.4-1.6)	0.6 (0.3-1.4)
57	15	2.2 (1.2-4.2)†	1.4 (0.6-3.3)
67	24	3.0 (1.7-5.2)‡	1.2 (0.5-2.6)
458	38	1	1
53	8	1.8 (0.8-4.1)	1.9 (0.7-5.1)
70	18	3.1 (1.7-5.7)‡	2.8 (1.2-6.8)*
43	32	9.0 (5.1-15.8)‡	4.9 (1.9-12.2)†
461	60	1	1
114	14	0.9 (0.5-1.7)	0.6 (0.3-1.1)
49	22	3.5 (2.0-6.1)‡	2.0 (1.0-3.9)*
206	61	1	1
418	35	0.3 (0.2-0.4)‡	1.0 (0.4-2.3)
		1.1 (1.0-1.1)‡	1.0 (1.0-1.1)
		0.8 (0.8-0.9)‡	0.9 (0.8-1.0)†
		4.3 (3.0-6.2)‡	2.9 (1.9-4.4)‡

Ⅳ. 資　料

文献レビュー（コホート共同研究班内）について

エビデンステーブルの説明

以下のエビデンステーブルは、厚生労働科学研究健康科学総合研究事業「疾病予防サービスに係わるエビデンス構築のための大規模コホート共同研究班」の分担研究者、研究協力者が係わった研究のうち公表済み文献をレビューしたものである。

本研究班は、国内の代表的なコホート研究を集めてデータ統合を行い、わが国における健康管理、疾病発症予測に関するエビデンスを構築することを目的としている。今年度、統合データに基づいて一般検査項目、飲酒、喫煙についてのデータ統合と解析を行ったが、それと並行して参加コホートを中心に既に公表されている論文について文献レビューを行うことが9月のワークショップで決まった。下記の条件で分担研究者、研究協力者に文献を提出してもらい滋賀医大のほうで取りまとめた。

（条件）

1. 独立変数（予測要因）は、基本的には一般的な検査項目（基本健康診査や定期健康診断等）や問診で聴取されたものに限る（特殊な検査や健診で実施困難なものは除外した）。ただし簡便に実施可能なものは含めた（したがって安静時心拍数や家庭血圧は含め、糖負荷検査は除外した）。
2. エンドポイントは糖尿病や高血圧、循環器疾患の発症や死亡、総死亡、医療費のいずれかとした。悪性新生物のみをエンドポイントとした研究は除外した。
3. 分担研究者、研究協力者が関与した国内のコホート研究で論文公表されているものとし、基本的にPubMedで検索可能なものとした（厚生の指標は例外的に含めた）。

これらの文献は、その検査項目や問診で将来の死亡や循環器疾患の発症を予測できるかという疑問に対する回答を示しており、その後の健康管理（保健指導、健康教育、早期治療）が必要な対象者をスクリーニングする手段を示唆していると考えられる。

＜テーブル記載事項について＞

資料は文献一覧と文献整理表の2つのシートに分けている。

文献一覧

1) No.　　：整理番号。文献整理表と共通。
2) コホート名　：研究成果の元になったコホート研究名。
3) 筆頭著者　　：論文の先頭の著者名。
4) 論文名　　：論文のタイトル。
5) 雑誌名　　：雑誌名（PubMed形式で省略）。
6) 発表年　　：論文が公表された年（西暦）。

7) 巻・ページ　：収載論文の巻（volume)、ページ。

文献整理表

1) No.　　：整理番号。文献一覧と共通。

2) コホート名　：研究成果の元になったコホート研究名。

3) 健診項目または問診項目：

その研究で独立変数（疾病発症を予測する要因、または疾病の発症要因）として設定されている健診または問診項目を記載（主要な仮説設定に用いられている項目)。

4) 対象者（年齢と人数)：

対象者の人数（その研究で実際に追跡された人数、男女別)、年齢（○歳～○歳、○歳以上、平均年齢など）を記載（論文に記載されている内容)。

5) 追跡期間：

追跡期間（平均追跡期間、記載がない場合は追跡開始初年度から最終年度までの期間)。

6) エンドポイント：

健診項目または問診項目と有意な関連が見られたエンドポイントを記載。

例）総死亡、循環器疾患死亡、脳梗塞発症、心筋梗塞発症、総医療費等。

7) 結果の要約（一覧用)：

箇条書きで主要な健診項目または問診項目とエンドポイントの関連を記載(有意差あるものを記載するが、有意差がないことが主要な結果である場合も記載)。

結果が男女別か男女計かも記載。

健診項目（問診項目）→エンドポイントで記載し、正の関連性あり ○、負の関連性あり ●、関連性なし ×、で結果を示している。例えば、「総コレステロールの高値」は冠動脈性心疾患の死亡の上昇と関連し、「HDL コレステロールの高値」は冠動脈性心疾患の死亡の低下と関連する。したがってこの場合、

総コレステロールの高値→冠動脈性心疾患死亡 ○

HDL コレステロールの高値→冠動脈性心疾患死亡 ●　となる。

8) 結果の要約（詳細)：より詳細な結果の要約。

NO.	コホート名	筆頭著者	論文名	雑誌名	発表年	巻・頁
1	The JACC Study	Hiroyasu Iso	Smoking Cessation and Mortality from Cardiovascular disease among Japanese Men and Women: the JACC Study	Am J Epidemiol	2005	161:170-179
2	The JACC Study	YINGSONG LIN	Alcohol Consumption and Mortality among Middle-aged and Elderly Japanese Men and	Ann Epidemiol.	2005	15:590-597
3	The JACC Study	Renzhe Cui	Body mass index and Mortality Form Cardiovascular Disease among Japanese Men and Women: the JACC study	Stroke	2005	36:1377-1382
4	The JACC Study	Hiroyuki Noda	Walking and Sports participation and Mortality From Coronary Heart Disease and Stroke	J Am Coll Cardiol	2005	in press
5	The JACC Study	Hiroyasu Iso	Perceived Mental Stress and Mortality from Cardiovascular Disease Among Japanese Men and Women: the Japan Collaborative Cohort Study for Evaluation of Cancer Risk Sponsored by Monbusho (JACC Study)	Circulation	2002	106:1229-1236
6	The JACC Study	Ai Ikeda	The relationships between interest for and participation in health screening and risk of mortality: The Japan Oollaborative Cohort Study	Prev Med	2005	41:767-771
7	The JACC Study	Shigeki Yamada	Risk factors for Fatal Subarachnoid Hemorrhage: The Japan Collaborative Cohort Study	Stroke	2003	34:2781-2787
8	The JACC Study	Yoshihisa Fujino	A nationwide cohort study of educational background and major causes of death among the elderly population in Japan	Prev Med	2005	40:444-451
9	The JACC Study	Akiko Tamakoshi	Self-Reported Sleep Duration as a Predictor of All-Cause Mortality: Results from the JACC Study, Japan	Sleep	2004	27:51-54
10	茨城県民コホート	入江 ふじこ	健康管理への活用を目的とした基本健康診査成績による生命予後の検討	日本公衛誌	2001	48:95-108
11	その他関連コホート	Hiroyasu Iso	Serum total cholesterol and mortality in a Japanese population	J Cli Epidemiol	1994	47:961-969
12	その他関連コホート	Akihiko Kitamura	High-Density Lipoprotein Cholesterol and Premature Coronary Heart Disease in Urban Japanese Men	Circulation	1994	89:2533-2539
13	その他関連コホート	Hiroyasu Iso	Serum Triglyccndes and Risk of Coronary Heart Disease among Japanese Men and Women	Am J Epidemiol	2001	5:490-499
14	その他関連コホート	H.Iso	Type 2 diabetes and risk of non-embolic ischaemic stroke in Japanese men and	Diabetologia	2004	47:2137-2144
15	その他関連コホート	Tetsuya Ohira	Prospective Sudy of Major and mMnor ST-T Abnormality and Risk of Stroke Among	Stroke	2003	34:e250-e253
16	その他関連コホート	Kazumasa YAMAGISHI	Smoking raises the risk of total and ischemic strokes in hypertensive men	Hypertens Res	2003	26:209-217
17	その他関連コホート	Toshifumi Mannami	Cigarette Smoking and Risk of Stroke and its Subtypes Among Middle Aged Japanese Men and Women: the JPHC Study Cohort I	Stroke	2004	35:1248-1253
18	その他関連コホート	Hiroyasu Iso	Alcohol Consumption and risk of Stroke Among Middle-aged Men: The JPHC Study Cohort	Stroke	2004	35:1124-1129
19	その他関連コホート	Tomoko Sankai	Prospectivc Study on Alcohol Intake and Risk of Subarachnoid Hemorrhage Among Japanese Men and Women	Alcohol Clin Experimentl Res	2004	24:386-389
20	その他関連コホート	Akihiko Kitamura	Alcohol intake and Premature Coronary Heart Disease in Urban Japanese Men	Am J Epidemiol	1998	147:59-65
21	その他関連コホート	Hiroyasu Iso	Alcohol Intake and the Risk of Cardiovascular Disease in Middle-Aged Japanese Men	Stroke	1995	26:767-773
22	その他関連コホート	Hiroyasu Iso	Fat and Protein Intakes and Risk of Intraparenchymal Hemorrhage among Middle-aged	Am J Epidemiol	2003	157:32-39
23	その他関連コホート	Tetsuya Ohira	Prospective Study of Depressive Symptoms and Risk of Stroke Among Japanese	Stroke	2001	32:903-908
24	その他関連コホート	山海 知子	CT所見を中心とした脳卒中の疫学的研究-コホート内症例対照研究による脳出血ならびに脳梗塞の病型別発生要因の検討	日本公衛誌	1992	39:410-420
25	茨城県コホート	Toshimi Sairenchi	Cigarette Smoking and Risk of Type 2 Diabetes Mellitus among Middle-aged and Elderly Japanese Men and Women	American Journal of Epidemiology	2004	160:158-162
26	大迫町コホート	Takayoshi Ohkubo	Prediction of ischaemic and haemorrhagic stroke by self-measured blood pressure at home: the Ohasama study	Blood Pressure Monitoring	2004	9(6):315-320
27	大迫町コホート	Atsushi Hozawa	Prognostic Value of Home Heart Rate for Cardiovascular Mortality in the General Population The Ohasama Study	Am J Hypertension	2004	17:105-1010
28	大迫町コホート	Kei Asayama	Prediction of Stroke by Self-Measurement of Blood Pressure at Home Versus Casual Screening Blood Pressure Measurement in Relation to the Joint National Committee 7 Classification The Ohasama Study	Stroke	2004	35:2356-2361
29	NIPPON DATAコホート	Tanihara S	Proteinuria is a Prognostic Marker for Cardiovascular Mortality: NIPPON DATA 80, 1980-	Journal of	2005	15(4):146-153
30	NIPPON DATAコホート	Okamura T	The inverse relationship between serum high-density lipoprotein cholesterol level and all-cause mortality in a 9.6-year follow-up study in the Japanese general population.	Atherosclerosis	2006	184(1):143-150

NO.	コホート名	筆頭著者	論文名	雑誌名	発表年	巻・頁
31	NIPPON DATAコホート	Horibe H	A Nineteen-Year Cohort Study on the Relationship of Electrocardiographic Findings to All Cause Mortality Among Subjects in The National Survey on Circulatory Disorders, NIPPON DATA80 Research Group (Appendix I) and for the Working Group to Electrocardiographic Coding for the National Survey of Circulatory Disorders, 1980 (Appendix Ⅱ)	Journal of Epidemiology	2005	15(4):125-134
32	NIPPON DATAコホート	Miyamatsu N	Different effects of blood pressure on mortality from stroke subtypes depending on BMI levels: a 19-year cohort study in the Japanese general population—NIPPON DATA80	Journal of Human Hypertension	2005	19(4):285-291
33	NIPPON DATAコホート	Nakamura Y	Association between fish consumption and all-cause and cause-specific mortality in Japan: NIPPON DATA80, 1980-99	American Journal of Medicine	2005	118:239-245
34	NIPPON DATAコホート	Ueshima H	Cigarette Smoking as a Risk Factor for Stroke Death in Japan: NIPPON DATA80	Stroke	2004	35(8):1836-41
35	NIPPON DATAコホート	Okamura T	A combination of serum low albumin and above-average cholesterol level is associated with excess mortality.	Journal of Clinical Epidemiology	2004	57:1188-1195
36	NIPPON DATAコホート	Nakamura Y	Egg Consumption, Serum Cholesterol, and Cause-Specific and All-Cause Mortality: NIPPON DATA80, 1980-94.	American Journal of Clinical Nutrition	2004	80:58-63
37	NIPPON DATAコホート	Okamura T	Resting heart rate and cause-specific death in a 16.5-year cohort study of the Japanese general population.	American Heart Journal	2004	147:1024-1032
38	NIPPON DATAコホート	小野田敏行	耐糖能異常が病型別脳卒中死亡に及ぼす影響-日本人の代表的集団NIPPON DATA80の19年間の追跡結果より-	厚生の指標	2004	51(2):10-16
39	NIPPON DATAコホート	Okamura T	What cause of mortality can we predict by cholesterol screening in the Japanese general population?	Journal of Internal Medicine	2003	253:169-180
40	NIPPON DATAコホート	NIPPON DATA Research Group (Okayama A. et	Impact of elevated blood pressure on mortality from all causes, cardiovascular diseases, heart disease and stroke among Japanese:14year follow-up of randomly selected population from Japanese - Nippon data 80	Journal of Human Hypertension	2003	17:851-857
41	NIPPON DATAコホート	Sakata K	Absence of an association between serum uric acid and mortality from cardiovascular disease: NIPPON DATA 80, 1980-1994.	European Journal of Epidemiology	2001	17:461-468
42	滋賀国保コホート	Nakamura K	Impact of hypertension on medical economics: a 10-year follow-up study of National Health Insurance in Shiga, Japan.	Hypertens Res	2005	28(11):859-864
43	滋賀国保コホート	Nakamura K	The value of combining serum alanine aminotransferase levels and body mass index to predict mortality and medical costs: a 10-year follow-up study of National Health Insurance in Shiga, Japan.	J Epidemiol	2006	16(1)15-20
44	久山町コホート	Kiyohara Y	Smoking and cardiovascular disease in the general population in Japan.	J. Hypertens.	1990	8(suppl 5): S9-S15
45	久山町コホート	Kiyohara Y	The impact of alcohol and hypertension on stroke incidence in a general Japanese population: the Hisayama Study	Stroke	1995	26: 368-372
46	久山町コホート	Tanizaki Y	Incidence and risk factors for subtypes of cerebral infarction in a general population: the Hisayama Study	Stroke	2000	31: 2616-2622
47	久山町コホート	Ohmori S	Alcohol intake and future incidence of hypertension in a general Japanese population: the Hisayama Study	Alcoholism (NY)	2002	26: 1010-1016
48	久山町コホート	Arima H	Validity of the JNC Ⅵ recommendations for the management of hypertension in a general population of Japanese elderly - the Hisayama study -	Arch. Intern. Med.	2003	163: 361-366
49	久山町コホート	Kubo M	Risk factors for renal glomerular and vascular changes in an autopsy-based population survey: the Hisayama Study	Kidney Int.	2003	63: 1508-1515
50	久山町コホート	Kiyohara Y	Dietary factors and development of impaired glucose tolerance and diabetes in a general Japanese population: the Hisayama Study	J. Epidemiol.	2003	13: 251-258
51	久山町コホート	Ninomiya T	Chronic kidney disease and cardiovascular disease in a general Japanese population: the Hisayama Study	Kidney Int	2005	68: 228-236
52	放射線影響研究所 成人健康調査コホート	Shuhei Nakanishi	Relationship between HbA_1c and mortality in a Japanese population	Diabetologia	2005	48:230-234