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Relation of body mass index, periodontitis and *Tannerella forsythia*

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Abstract

Objective: To determine if there were differences in periodontal status and the composition of the subgingival microbiota in individuals who exhibited different body mass indices (BMI).

Material and Methods: One hundred and twenty-one periodontally healthy/gingivitis and 574 chronic periodontitis subjects had height and weight determined and were measured for probing pocket depth, clinical attachment level, bleeding on probing, gingival redness and presence of visible plaque. Subgingival plaque samples taken from each tooth were individually analysed for their content of 40 bacterial species using checkerboard DNA–DNA hybridization.

Results: Crude odds ratios (ORs) [95% confidence interval (CI)] of overweight and obese individuals exhibiting periodontitis were 3.1 (1.9–4.8) and 5.3 (2.8–9.5), respectively, when compared with subjects with normal BMI. Logistic regression analysis indicated an OR (95% CI) of 2.3 (1.2–4.5) for an obese subject to exhibit periodontitis after adjusting for age, gender and smoking status. Individuals <46.8 years (median age) were responsible for this association. Only *Tannerella forsythia* differed significantly in proportions among BMI groups and was significantly higher in obese periodontally healthy/gingivitis individuals.

Conclusion: The data suggest that an overgrowth of *T. forsythia* occurs in the subgingival biofilms of periodontally healthy, overweight and obese individuals that might put them at risk for initiation and progression of periodontitis.

Key words: BMI; periodontal; subgingival plaque; *Tannerella forsythia*

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Over the past few decades, obesity has become a significant world-wide health problem. In the United States, it was reported that in 2003–2004, 17% of children and adolescents aged 2–19 years of age were overweight and 32.2% of adults were obese (Ogden et al. 2006). According to the Center for Disease Control and Prevention (CDC), in 2005–2006, 34% of US adults over 20 years of age were obese. Obesity has been associated with many serious, life-threatening medical conditions including cardiovascular disease (Wilson et al. 2008), various cancers (Calle et al. 2003) and diabetes (Steppan et al. 2001, Mokdad et al. 2003) as well as endocrine (van der Steeg et al. 2008), musculoskeletal (Tukker et al. 2008), respiratory (Poulain et al. 2006) and psychological disorders (Simon et al. 2006, Scott et al. 2008). Central obesity is a risk factor for metabolic syndrome, a group of conditions or risk factors that increase a subject's risk for cardiovascular disease (Grundy 2004).

Conflict of interest and source of funding statement

No conflict of interests.

Being overweight or obese also has been associated with an increased risk for periodontal disease. Studies have described an association between either obesity, increased body weight or increased body mass index (BMI) and periodontal diseases in humans (Saito et al. 2001, 2005, Al-Zahrani et al. 2003, Wood et al. 2003, Alabdulkarim et al. 2005; Dalla Vecchia et al. 2005, Genco et al. 2005, Nishida et al. 2005, Borges-Yanez et al. 2006, Reeves et al. 2006, Linden et al. 2007, Ylostalo et al. 2008). In addition, Shimazaki et al. (2007) reported that metabolic syndrome increased the risk for periodontitis, while increased levels of serum Resistin, an adipokine secreted from adipose tissues, was significantly associated with having periodontitis in a population of Japanese women (Saito et al. 2008).

The relationship between obesity and pathogenic subgingival species has received little attention. In an animal study, mice with diet-induced obesity infected orally and systemically with *Porphyromonas gingivalis*, had significantly increased alveolar bone loss compared with lean, infected controls (Amar et al. 2007). The authors suggested that obesity interfered with the ability of the immune system to cope with *P. gingivalis* infection. Obesity in humans might enhance the risk of an individual exhibiting periodontitis, by increasing the numbers or proportions of pathogenic subgingival species. The composition of the subgingival microbiota is affected by local factors such as the periodontal status of the subject and the individual site (Socransky & Haffajee 2005). Different ''host-level'' characteristics have been shown to alter the composition of the subgingival microbiota. These include current cigarette smoking (Haffajee & Socransky 2001), a genetic polymorphism in the interleukin-1 (IL-1) gene cluster (Socransky et al. 2000), Sjogren's syndrome (Socransky & Haffajee 2005) and even geographic location for subjects with similar clinical periodontal status (Haffajee et al. 2004, 2005). The notion in the present investigation was that another host-level factor, being overweight or obese, might influence the composition of the subgingival microbiota and affect the local host response to periodontal pathogens. Thus, two hypotheses were tested in this investigation. The first was whether being overweight or obese was associated with an increased risk of having periodontitis after adjusting for factors such as age, gender and smoking status. The second was whether there was a shift in the subgingival microbiota in obese subjects that might account for an increased risk of periodontitis.

Material and Methods

Subject population, clinical monitoring and microbiological assessment

Seven hundred and forty-four sequential subjects who were enrolled in 15 different longitudinal clinical studies in the Department of Periodontology at The Forsyth Institute between 2000 and 2008 were selected for study. The subjects ranged in age from 18 to 86 years and were considered to be periodontally healthy or exhibiting gingivitis ($N = 151$) or with periodontitis; i.e. with evidence of prior attachment loss ($N = 593$). The studies in which the subjects were participating were approved by The Forsyth Institute Institutional Review Board and conformed to the guidelines of the Declaration of Helsinki. All subjects provided signed informed consent. In this cross-sectional study, only baseline clinical measurements were used and included: plaque accumulation (0/1), gingival redness (0/1), bleeding on probing (BOP) (0/1), probing pocket depth (PD) and clinical attachment level (CAL) measured at six sites per tooth (mesiobuccal, buccal, distobuccal, distolingual, lingual and mesiolingual) at all teeth excluding third molars. PD and CAL measurements were repeated and the mean of the pair of measurements computed for each site.

Exclusion criteria for all subjects included: periodontal or antibiotic therapy in the previous 6 months; any systemic condition which might have influenced the course of periodontal disease or treatment (e.g. diabetes and AIDS); any systemic condition which required antibiotic coverage for routine periodontal procedures (e.g. certain heart conditions and joint replacements). Since different clinical inclusion and exclusion criteria were used for recruitment of subjects in the different studies, the proportion of sites with PD $\geqslant$4 mm and CAL $\geqslant$4 mm in the subjects initially classified as healthy/gingivitis or periodontitis was determined (Fig. 1). Forty-nine subjects were eliminated who had PD or CAL values in the region of overlap of the two distributions presented in Fig. 1. Thus, periodontally healthy/gingivitis subjects ($N = 121$) had at least 24 teeth and $<2\%$ of sites with PD$\geqslant$4 mm and $<2\%$ of sites with CAL$\geqslant$4 mm. Periodontitis subjects ($N = 574$) had at least 20 teeth and $>5\%$ of sites with PD$\geqslant$4 mm and/or $>5\%$ of sites with CAL$\geqslant$4 mm. The periodontal and other features of the two subject groups are presented in Table 1.

In addition to clinical measurements, subjects were measured for height, weight and total body fat (Tanita Body Composition Analyzer BF 350; Tanita Corporation, Tokyo, Japan). BMI was computed as weight (kg)/height in m^2. Systolic and diastolic blood pressure were measured using an ADC wrist monitor (American Diagnostic Corporation, Hauppauge, NY, USA). Smoking history was recorded by means of a questionnaire and the answers confirmed with the subject by the examining clinician. Age was computed as the time from the date of birth to the clinical monitoring visit.

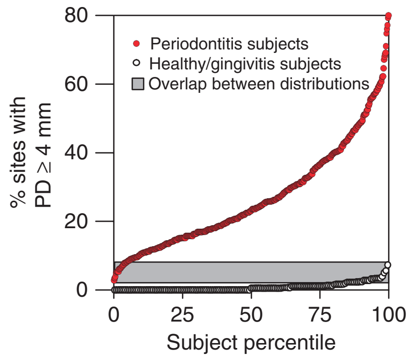

Fig. 1. Percent of sites with PD$\geqslant$4 mm in 151 subjects initially characterized as periodontally healthy or with gingivitis (white circles) and 593 subjects initially characterized as exhibiting periodontitis (red circles). The grey zone indicates subjects who overlapped in the % of sites with PD$\geqslant$4 mm. Subjects below this zone were designated as periodontally healthy/gingivitis and those above the zone were designated as periodontitis. Forty-nine subjects in the grey zone were not included in subsequent analyses. PD, pocket depth.

Six hundred and twenty-four of the 695 subjects had subgingival plaque samples taken as part of the protocol of their studies. Subgingival biofilm samples were taken from the mesial surface of each tooth (excluding third molars) using individual sterile Gracey curettes and analysed for their content of 40 bacterial species using checkerboard DNA–DNA hybridization (Socransky et al. 1994, 2004). A total of 15,858 subgingival biofilm samples were evaluated (an average of 25.4 samples per subject).

Data analysis

Seven hundred and forty-four sequential subjects were enrolled in this study. After eliminating 49 subjects whose periodontal status in terms of PD and CAL overlapped, data from 121 healthy/gingivitis and 574 periodontitis subjects were available for analysis. Initially, the odds ratios (ORs) and 95% confidence intervals (CIs) of an individual exhibiting periodontitis were determined for subjects subset into three BMI categories: normal $<$24.9; overweight 25–29.9; obese $\geqslant$30. The proportions of individuals who were normal, overweight or obese were compared in the periodontal health/gingivitis and periodontitis groups. Significance of differences in proportions was determined by χ^2-analysis. Similar analyses were performed with subjects subset according

Table 1. Mean (±SD) clinical periodontal, physical and demographic features of the subjects

	Health	Periodontitis
N	121	574
Mean pocket depth (PD) (mm)	1.97 ± 0.29	3.13 ± 0.64
Mean attachment level (AL) (mm)	1.35 ± 0.42	3.36 ± 1.02
% of sites with		
Visible plaque	43.9 ± 62.7	72.7 ± 63.9
Gingival redness	22.6 ± 27.7	64.6 ± 48.1
Bleeding on probing	4.7 ± 6.1	26.4 ± 22.8
Suppuration	0.0 ± 0.0	0.8 ± 2.5
PD > 6 mm	0 ± 0	4 ± 7
PD 4–6 mm	1 ± 1	24 ± 13
AL > 6 mm	0 ± 0	8 ± 11
AL 4–6 mm	0 ± 0	27 ± 15
Age (years)	33.7 ± 9.6	49.6 ± 12.4
% males	31	55
Number of missing teeth	0.7 ± 1.7	2.9 ± 2.9
Systolic blood pressure	118.3 ± 13.6	129.3 ± 16.4
Diastolic blood pressure	72.3 ± 9.1	78.3 ± 11.4
% current smokers	2	20
Body mass index	24.69 ± 5.63	27.91 ± 5.74
% obese	11	29
% overweight or obese	35	67
% body fat	25.0 ± 10.2	29.5 ± 10.2

Differences between health and periodontitis were significantly different for all parameters at $p<0.001$ using either the Mann Whitney test or X^2 analysis. X^2 analysis was used for % males, % current smokers, % obese and % overweight or obese subjects.

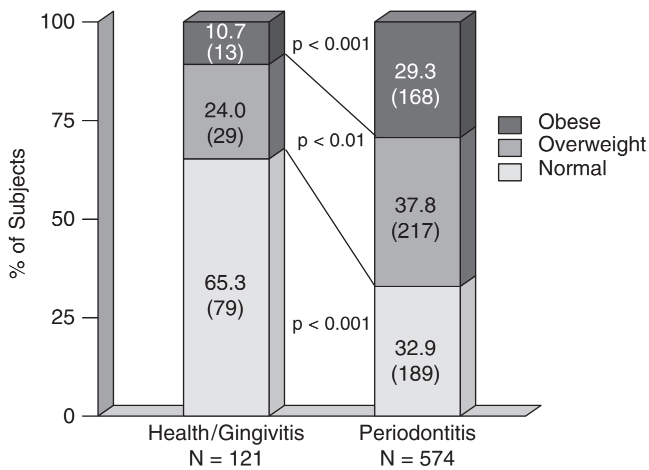

Fig. 2. Percentage of periodontally healthy/gingivitis ($N = 121$) or periodontitis subjects ($N = 574$) who had BMIs <25 (normal), from 25 to 29.9 (overweight) or ⩾30 (obese). Numbers in parentheses indicate the number of subjects in each disease/BMI category. The overall association between BMI category and periodontal status was significant at $p<0.001$ using χ^2-analysis ($\chi^2 = 45.7$). BMI, body mass index.

to gender and the median age for the subject population (46.8 years). Logistic regression analysis was used to examine the association between obesity (*versus* normal and overweight) and periodontal status after adjusting for age, gender and smoking status. The analysis was repeated using non-smokers only.

The mean clinical parameters were compared in subjects subset according to BMI categories and age groups subset at the 25th, 50th and 75th percentiles. Significance of differences in mean clinical values among BMI groups was determined using the Kruskal–Wallis test. Mean clinical parameters were compared in subjects subset into eight categories based on the median age of 46.8 years for the subject population, gender and not obese *versus* obese. Overall significance of differences among the eight groups for each clinical parameter was determined using ANOVA and significance of difference between obese and non-obese categories in each age/gender group was determined using protected least significant difference (LSD).

Counts and proportions of each bacterial species were determined for each sample site, averaged within each subject and then averaged across subjects in the three BMI groups. Significance of differences among BMI groups for each species was determined using the Kruskal–Wallis test and adjusted for multiple comparisons (Socransky et al. 1991) with an experiment-wise Type 1 error rate of $p<0.05$. The counts and proportions were determined for each species at sites subset according to probing PD ranges of <4, 4–6 and >6 mm, averaged within each subject for each PD range separately and then averaged in each range across subjects in the three BMI categories. Significance of differences for each species among BMI categories in each probing PD range was determined using the Kruskal–Wallis test and adjusted for multiple comparisons (Socransky et al. 1991). Differences in mean proportions of each species were also sought among BMI categories in healthy/gingivitis and periodontitis subjects using ANOVA and differences among BMI categories in the healthy/gingivitis and periodontitis groups separately using protected LSD. Scatter plots were prepared and regression analysis used to examine the relationship between BMI and mean proportions of individual species in periodontally healthy/gingivitis and periodontitis subjects separately. Mean species proportions were compared in subjects subset into eight categories based on the median age of 46.8 years for the subject population, gender and not obese *versus* obese subjects. Overall significance for each species among the eight groups was determined using ANOVA and significance of difference between obese and non-obese categories in each age/gender group was determined using LSD.

Results

Relation of periodontal status to obesity

Figure 2 presents the crude distribution of subjects who had a normal BMI or were overweight or obese and exhibited either periodontal health/gingivitis or periodontitis. There were far greater proportions of overweight and obese individuals in the subjects with periodontitis compared with periodontally healthy/gingivitis individuals. Indeed, almost two-thirds of the healthy/gingivitis subjects had a normal BMI whereas only about one-third of periodontitis subjects had a BMI <25. Individuals who were overweight or obese were 3.07 (95% CI, 1.91–4.84) and 5.31 (95% CI, 2.79–9.50) times more likely to have periodontitis respectively than subjects with a normal BMI.

Because periodontal status is known to be related to age, cigarette smoking and gender, the analysis was repeated using logistic regression to adjust for these potentially confounding variables (Table 2). The analysis indicated that BMI was significantly associated with periodontal status even after adjusting for age, smoking status and gender. The next question was whether this association was true for all subjects in the investigated group or was confined to subsets of subjects divided by age, gender and smoking status. To investigate the last factor, current smokers were eliminated from the database and the logistic regression analysis repeated. Essentially the same ORs and significance values were obtained suggesting that the association held in non-smokers. There were too few smokers in the periodontally healthy/gingivitis group to permit analysis of current smokers only.

There was a difference in the association of BMI groups with periodontal status between males and females (Fig. 3). Periodontally healthy/gingivitis females exhibited a larger percentage of subjects in the normal range of BMI than female periodontitis subjects and also a much greater proportion than periodontally healthy/gingivitis males. The proportion of overweight and obese female subjects was much greater in periodontitis subjects than in periodontally healthy/gingivitis subjects, but lower than the corresponding proportions in periodontally healthy/gingivitis and periodontally diseased males. The potential confounding variables of age and smoking status were not significantly different between males and females using the Mann-Whitney test.

Because age was strongly related to periodontal status, the subjects were subset into two groups according to the median age of 46.8 years of the entire subject population. There was a strong association between BMI group and periodontal status in the subjects younger than 46.8 years (Fig. 3). There was no significant association between these parameters in the older subjects. However, it must be pointed out that there were only 11 subjects in the periodontally healthy/gingivitis group above the median age in the present study.

The above findings, summarized in Table 3, suggested that obesity and periodontal status were associated in the overall population and strongly associated in younger and female subjects. We further subset the data into four categories based on gender and the age categories described above (Table 3). Younger, female subjects exhibited the strongest relationship between obesity and periodontal status. The OR for an individual in this group who was obese to exhibit periodontitis was 5.56 ($p<0.001$). This is in contrast to older females and both younger and older males where the ORs for exhibiting periodontitis in an obese individual were not statistically significant, although, as mentioned above, there were only 10 older females and one older male in the healthy/gingivitis group.

Clinical periodontal parameters were compared in subjects subset according to BMI and age. Only the subjects who

Table 2. Logistic regression analysis of demographic factors in periodontally healthy/gingivitis and periodontitis subjects

Variable	β	Odds ratio	Lower 95% CI	Upper 95% CI	p
Intercept	− 3.96				
Male gender	1.01	2.74	1.68	4.46	0.0000
Age	0.11	1.12	1.09	1.15	0.0000
Obese *versus* overweight and normal	0.84	2.31	1.19	4.49	0.0086
Current smoker	2.00	7.42	2.46	22.39	0.0000

$\text{Log}_e\,(p/1-p) = -3.96 + 1.01$ male gender $+0.11$ age $+0.84$ obese *versus* overweight and normal $+2.00$ current smoker.
$\chi^2 = 216.72$ with 4DF, $p<0.0001$.

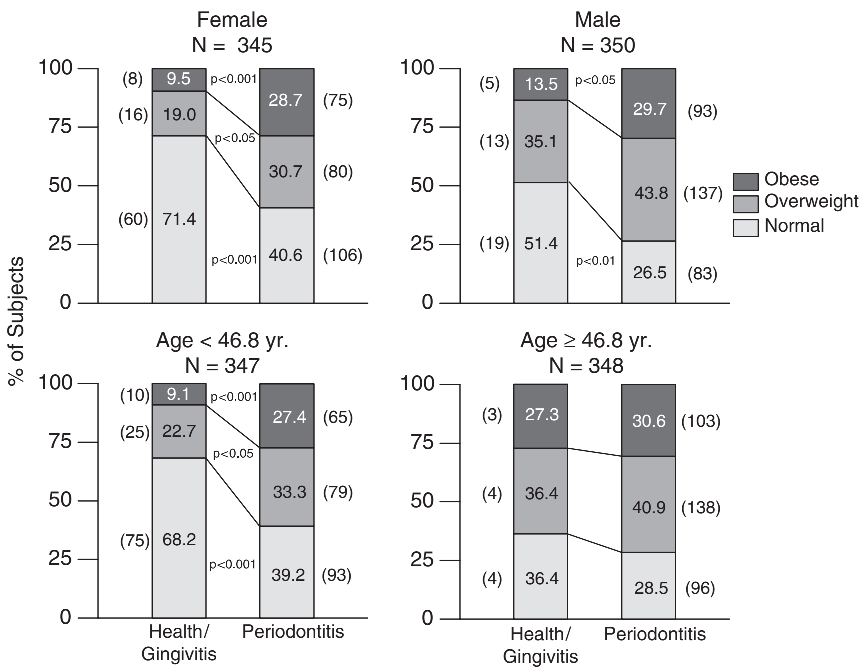

Fig. 3. Distribution of periodontally healthy/gingivitis or periodontitis subjects who had BMIs <25 (normal), from 25 to 29.9 (overweight) or ≥30 (obese) subset according to gender (top two panels) and age (bottom two panels) cut at the median of the subject population (46.8 years). Numbers in parentheses beside the bars indicate the number of subjects in each disease/BMI category. The overall association between BMI category and periodontal status was significant in females ($\chi^2 = 25.4$, $p<0.001$) and males ($\chi^2 = 10.7$, $p<0.01$) using χ^2-analysis. The overall association between BMI category and periodontal status in younger individuals was significant at $p<0.001$ ($\chi^2 = 27.5$), but was not significant in older individuals. BMI, body mass index.

Table 3. Odds ratios (ORs) of exhibiting periodontitis in obese individuals (*versus* overweight and normal), overall and subset according to gender and median age for the population

Group	Not obese and health	Not obese and disease	Obese and health	Obese and disease	χ^2	p	OR
Overall	108	406	13	168	17.80	<0.001	3.44
Non-smokers	105	318	13	137	17.68	<0.001	3.48
Females	76	186	8	75	12.84	<0.001	3.83
Males	32	220	5	93	4.31	<0.05	2.71
Age <46.8 years	100	172	10	65	14.91	<0.001	3.78
Age ⩾46.8 years	8	234	3	103	0.05	NS	1.17
Female <46.8 years	69	72	5	29	13.15	<0.001	5.56
Female ⩾46.8 years	7	114	3	46	0.01	NS	0.94
Male <46.8 years	31	100	5	36	2.48	NS	2.23
Male ⩾46.8 years	1	120	0	57	0.47	NS	–

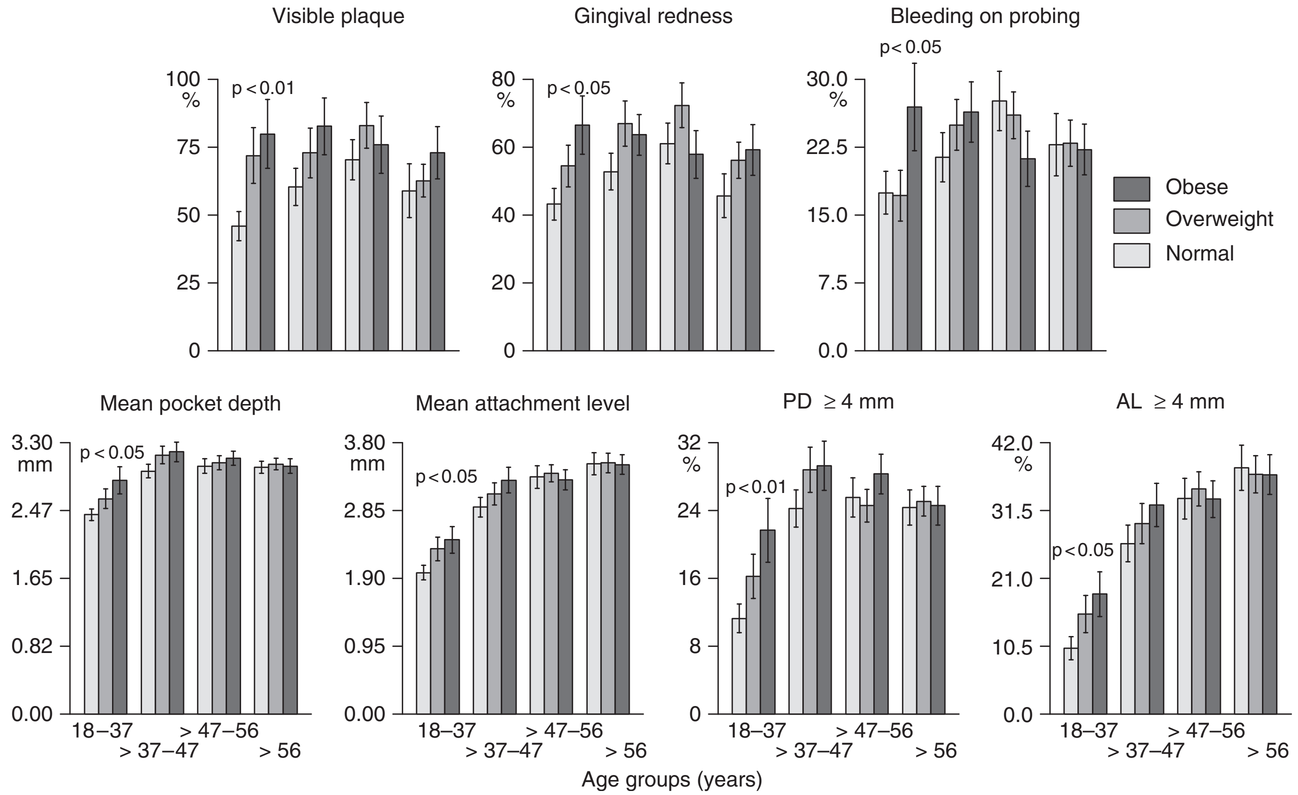

Fig. 4. Mean (± SEM) clinical periodontal parameters in subjects subset according to BMI categories and age. The subjects were subset into three BMI categories; normal (<25), overweight (25–29.9) and obese (⩾30) and four age groups based on the 25th, 50th and 75th percentiles of the subject population distribution which were 36.7, 46.8 and 56.2 years, respectively. Significance of differences among BMI categories in each age group was determined using the Kruskal–Wallis test. BMI, body mass index.

were in the youngest age group exhibited significant differences in clinical parameters among BMI categories. These included the % of sites with visible plaque, gingival redness and BOP as well as mean PD, mean CAL and percentage of sites with PD and CAL ⩾4 mm (Fig. 4).

The remarkable differences in periodontal status observed in Table 3 when subjects were subset according to age, gender and obesity were further examined by comparing mean clinical parameters in the eight age/gender/obesity groups (Fig. 5). The major differences in gingival redness and BOP between obese and non-obese subjects occurred in younger females and for PD and CAL parameters in younger females and males.

Relation of subgingival microbial composition and obesity

Six hundred and twenty-four of the subjects had received full-mouth subgingival sampling as part of the protocol for their respective studies. The mean counts and prevalence (% of sites colonized) of all 40 test species did not differ significantly among BMI groups after adjusting for 40 comparisons (data not shown). However, the proportions of *Tannerella forsythia* differed significantly in subjects subset into the normal, overweight and obese BMI groups ($p<0.01$, after adjusting for multiple comparisons; Fig. 6, left and upper right panel). These differences were further enhanced if subjects were subset into

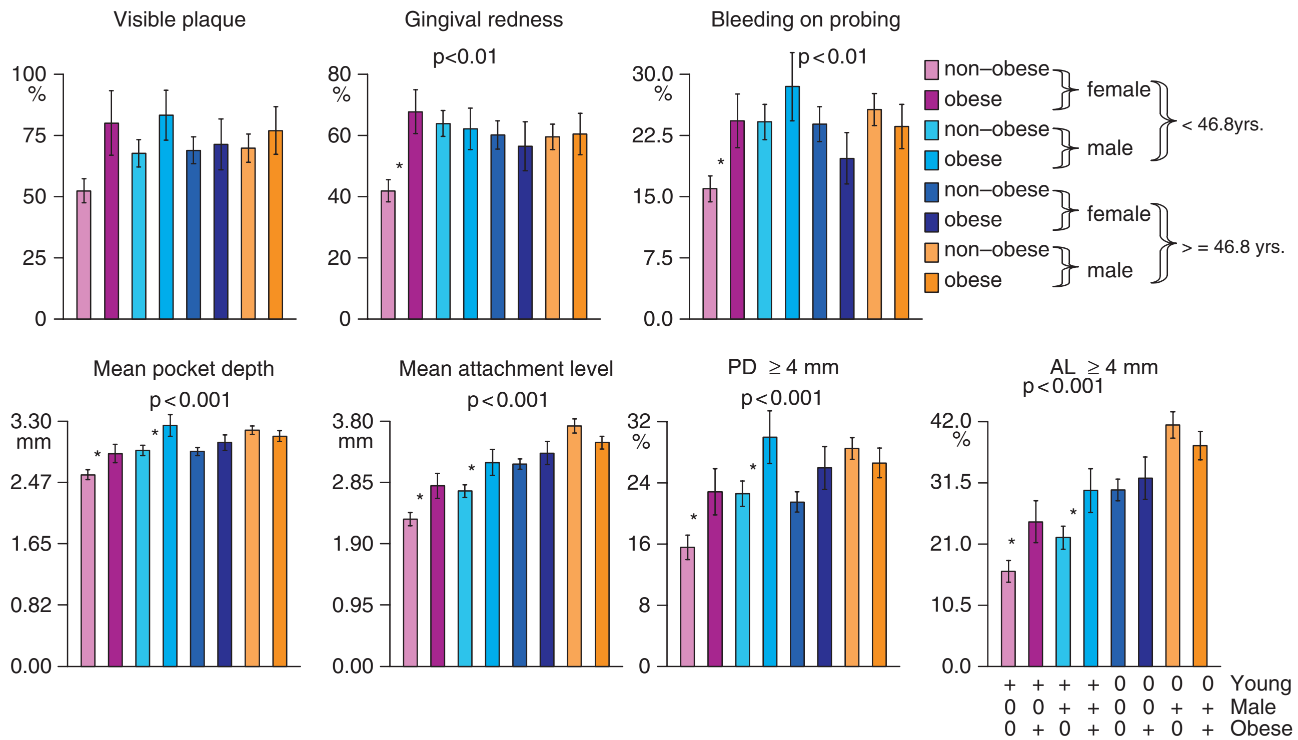

Fig. 5. Mean (± SEM) clinical periodontal parameters in subjects subset according age, gender and BMI category. The subjects were subset into two age categories based on the median age of the subjects (46.8 years), males and females, and not obese (BMI < 30) or obese (BMI ⩾ 30). Overall significance was determined using ANOVA and significance of difference between BMI categories in each age/gender group was determined using protected LSD and indicated in the figure as an asterisk. BMI, body mass index; LSD, least significant difference.

four BMI groups to include class 2 obese subjects (BMI ⩾ 35; Fig. 6 lower right panel). The increased proportions of *T. forsythia* were due to a significant increase at periodontal sites < 4 and 4–6 mm in obese individuals (Fig. 7). Differences among BMI groups were not significant for pockets with probing depth > 6 mm.

When subjects were subset into periodontally healthy/gingivitis and periodontitis groups, differences in the proportions of *T. forsythia* among BMI categories were most striking in periodontally healthy/gingivitis individuals (Fig. 8). The proportion of *T. forsythia* was least in the normal BMI group and most in the obese group in the periodontally healthy/gingivitis subjects while there was little difference among BMI groups in the periodontitis subjects. Other species of the red complex, *P. gingivalis* and *Treponema denticola*, as well as the other test species, did not demonstrate this relationship. The relationship between BMI and the proportions of the three red complex species are shown in Fig. 9 which demonstrates the strong relationship of BMI to *T. forsythia* in the periodontally healthy/gingivitis subjects ($r = 0.43$, $p < 0.001$ after adjusting for 40 comparisons).

In Fig. 5 it was observed that younger individuals, of both genders, exhibited more severe disease in obese individuals compared with normal BMI subjects. There was little difference between obese and non-obese males or females who were ⩾ the median age of 46.8 years. This analysis was emulated using the proportions of *T. forsythia* as the outcome variable (Fig. 10). There was a significant difference in mean proportions of *T. forsythia* between both obese and non-obese males and females who were younger than 46.8 years, but there was no difference between these groups in the older individuals. Indeed the highest mean proportions of *T. forsythia* were observed in the obese, younger subjects.

Discussion

In this study, obesity, as measured by BMI, related to periodontal status, particularly in younger individuals. This was in accord with a number of studies (Alabdulkarim et al. 2005, Dalla Vecchia et al. 2005, Nishida et al. 2005, Saito et al. 2005, Borges-Yanez et al. 2006, Linden et al. 2007, Ylostalo et al. 2008) including those that evaluated data from National Surveys (Al-Zahrani et al. 2003, Wood et al. 2003, Reeves et al. 2006). In the current study, obesity related to periodontal status in terms of health/gingivitis *versus* periodontitis after adjusting for age, gender and smoking status. The relationship was very strong in individuals younger than the median age (46.8 years) for the subject group. Clinical parameters including presence or absence of visible plaque, gingival redness, BOP, mean PD and mean CAL also related to BMI status, but primarily in the youngest age quartile (18–37 years, Fig. 4). When subjects were subset according to age, gender and obesity (Fig. 5), the major differences between obesity status for the clinical parameters occurred in subjects who were younger and most strikingly in young females.

Studies that attempt to relate periodontal disease to the systemic status of an individual are often confronted with the issue that periodontal disease increases with age and most of the

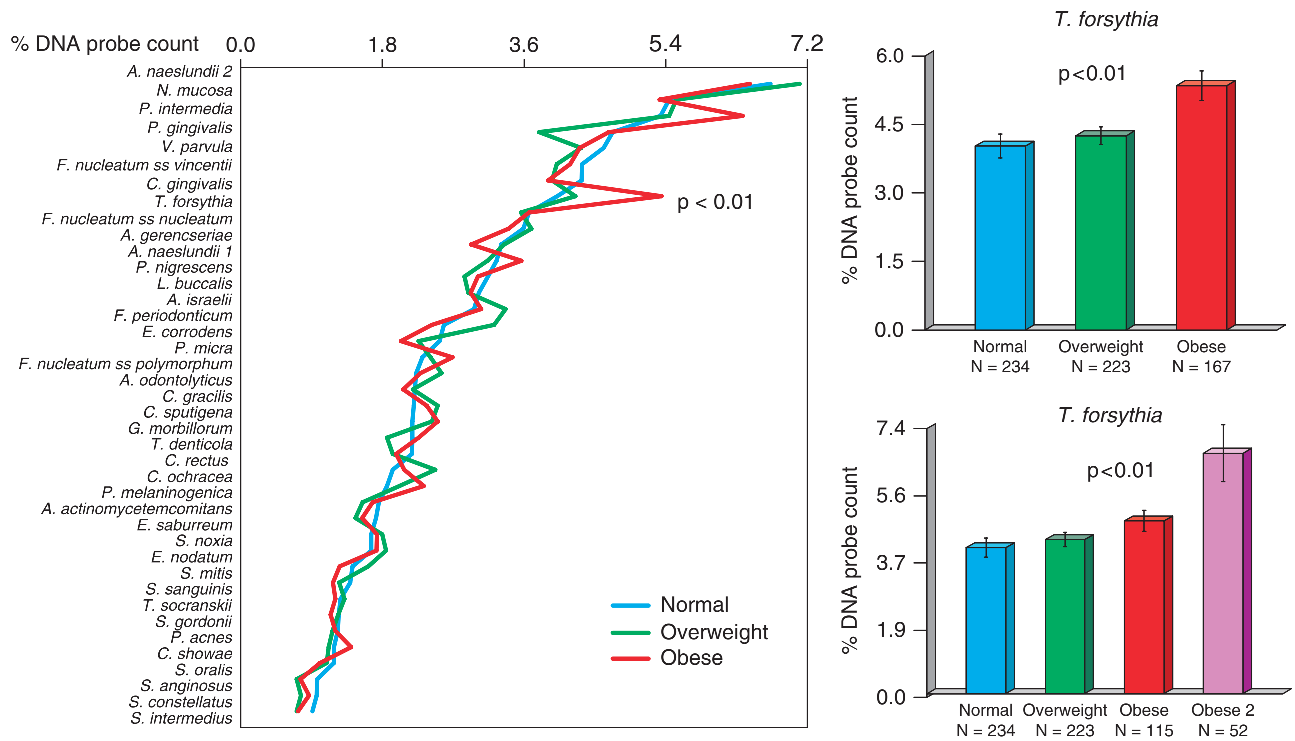

Fig. 6. Mean proportions of the 40 test species in subjects subset into normal, overweight and obese BMI categories (left panel). The proportion that each species comprised of each sample was computed, averaged within a subject for up to 28 sites and then averaged across subjects in the three BMI groups separately. Significance of differences among groups was determined using the Kruskal–Wallis test and adjusted for multiple comparisons (Socransky et al. 1991). The species were ordered in descending order according to the proportions in the normal group. The right panels present the mean proportions (± SEM) of *Tannerella forsythia* in the three BMI groups (top panel) and for subjects subset into four BMI groups, the three described above and class 2 obese subjects with a BMI ⩾ 35 (bottom panel). Significance of difference among BMI groups was determined using the Kruskal–Wallis test and adjusted for multiple comparisons. BMI, body mass index.

systemic conditions of interest such as diabetes, heart disease, stroke and obesity also increase in prevalence with age. Thus, the investigator ''adjusts'' statistically for age, and other confounding variables or examines the subjects in ''strata''. Subjects can be subset into more homogeneous groups in terms of age, smoking status or other factors. Both of these approaches were used in this study. After adjusting for age, gender and smoking status using a logistic regression model, BMI was still significantly associated with periodontal status. Diabetes was not taken into consideration since all the subjects, as far as we or the subjects knew, did not have diabetes, a standard exclusion criterion for our studies. Other investigators have also found that the association between obesity and periodontal status persisted after adjusting for potential confounding variables (Al-Zahrani et al. 2003, Alabdulkarim et al. 2005, Reeves et al. 2006, Linden et al. 2007).

Examining the relationship between obesity and periodontal status of subjects in different ''strata'' was very revealing. The association between obesity and periodontal status differed for different age ranges. In the current investigation, the odds of an obese, younger subject <46.8 years having periodontitis was almost four times as great as the odds for non-obese subjects in the same age group (Table 3). However, firm conclusions could not be drawn concerning the older subjects because there were only 11 subjects in the periodontally healthy/gingivitis group who were greater than the median age. These data are in accord with the findings from the National Health and Nutrition Examination Survey (NHANES III) study (Al-Zahrani et al. 2003). Subjects aged 18–34 years showed a significant association between obesity and periodontal disease with an adjusted OR of 1.76, (95% CI, 1.19–2.61) and between high waist circumference and periodontal disease (adjusted OR 2.27, 95% CI, 1.48–3.49). Subjects in the older age ranges of 35–59 and 60–90 years did not show a significant association between either obesity or increased waist circumference and periodontitis. Similar findings relating age and obesity to alveolar bone loss were reported in a study that evaluated 400 subjects ⩾ 18 years (Alabdulkarim et al. 2005). The OR for obese subjects <40 years exhibiting alveolar bone loss was 2.67 (95% CI, 1.09–6.58), while in subjects ⩾ 40 years the value was 1.06 (95% CI, 0.57–1.95).

Other studies have examined subjects in specific, but limited age ranges. Linden et al. (2007) examined 60–70-year-old males in the United Kingdom and reported that obese subjects showed a significant adjusted OR of 1.77 of demonstrating ''low threshold periodontitis'', as defined by at least two teeth with ⩾ 6 mm clinical attachment loss and at least one site with PD ⩾ 5 mm. Reeves et al. (2006) evaluated data from the NHANES III study. They examined the association between total body weight and waist circumference with chronic periodontitis in 2452 subjects aged 13–21 years who were non-smokers. They found that both total body weight and waist circumference were associated with an increased risk for periodontitis in the older subjects of their study (17–21 years), but not in the younger subjects (13–16 years).

Gender also had an impact on the relationship between obesity and periodontal status. In the current investigation, there were significantly higher proportions of normal BMI subjects in both healthy and periodontally diseased females compared with male subjects in the same clinical groups, although the proportions of obese males and females in the periodontitis group were similar (Fig. 3). Obese females exhibited slightly higher odds of having periodontal disease than obese males with significant ORs of 3.83 and 2.71, respectively (Table 3). Other studies have reported the effect of gender on the relationship between obesity and periodontitis. In accordance with the current investigation, Alabdulkarim et al. (2005) found a significant association between obesity and periodontitis in both males and females, although the OR for exhibiting periodontal disease was higher in obese females (OR = 3.14, 95% CI, 1.64–6.05) than obese males (OR = 1.95, 95% CI, 1.09–3.49). Dalla Vecchia et al. (2005) using multivariate analyses found that obese females were significantly more likely to have periodontitis than normal weight females (OR = 2.1), while there was no significant difference in the prevalence of periodontitis among BMI groups in males.

In the present investigation, obese non-smokers exhibited similar ORs and significance levels of exhibiting periodontitis as the overall study population. However, since there were only three current smokers in the healthy/gingivitis group and none of these were obese the association between obesity and periodontal status in smokers could not be determined. However, it has been shown in other studies that both current and non-smokers showed a significant association between obesity and alveolar bone loss (Alabdulkarim et al. 2005). A study in Japanese subjects indicated that both smoking (pack years) and obesity were independent risk factors for periodontitis, exhibiting a clear dose–response relationship (Nishida et al. 2005). Dalla Vecchia et al. (2005) demonstrated that while there was a significant relationship between BMI and periodontitis in female non-smokers, this association was not significant in smokers of both genders and in male non-smokers. They suggested that smoking may attenuate the association between periodontitis and obesity.

This investigation and most of the other cited studies suggest that periodontal disease status is associated with obesity that the relationship is strongest in younger adults and may be enhanced in females. The question is why this relationship exists. The data of the present investigation suggest the possibility that a periodontal pathogen, *T. forsythia*, overgrows in shallow sulci/pockets of periodontally healthy or gingivitis subjects who are obese or overweight. The higher levels and proportions of this species in the subgingival biofilms of these individuals may put them at increased risk for periodontal disease initiation and progression and thus, a higher proportion of overweight and obese individuals eventually could exhibit periodontitis.

The question then arises: Why do the differences in the association between periodontal status and obesity appear to diminish in older subjects? The accurate answer is that we do not know. However, it is known that the prevalence, extent and severity of periodontitis increases in subject cohorts of increas-

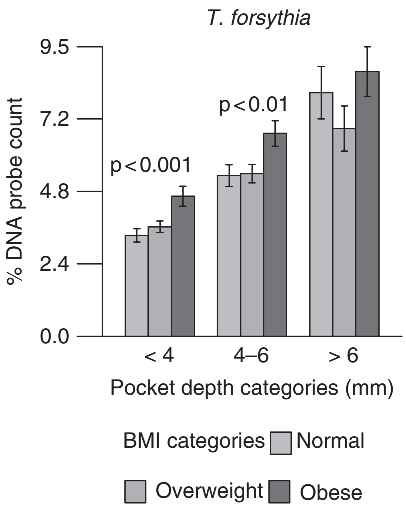

Fig. 7. Mean proportions (± SEM) of *Tannerella forsythia* at sites with probing pocket depths <4, 4–6 and >6 mm in subjects subset into normal, overweight and obese BMI categories. The proportion that *T. forsythia* comprised of each sample was computed, averaged within a subject in each probing pocket depth category and then averaged across subjects in the pocket depth/BMI groups separately. Significance of differences among BMI groups for each pocket depth category was determined using the Kruskal–Wallis test and adjusted for multiple comparisons (Socransky et al. 1991). BMI, body mass index.

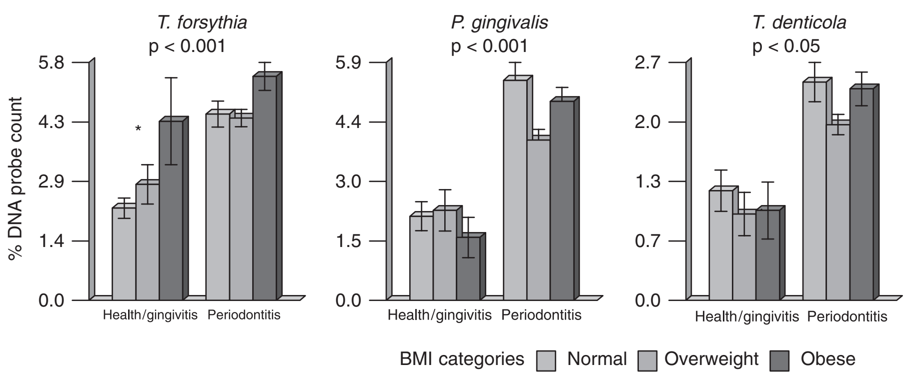

Fig. 8. Mean proportions (± SEM) of *Tannerella forsythia*, *Porphyromonas gingivalis* and *Treponema denticola* in the three BMI categories in health/gingivitis or periodontitis subjects. The proportion that each species comprised of each sample was computed, averaged within a subject and then averaged across subjects in BMI/periodontal status groups separately. Proportions differed significantly among the six groups for each species using ANOVA and adjusting for multiple comparisons. The only significant difference between BMI groups within health/gingivitis or periodontitis categories was for *T. forsythia* in the health/gingivitis category as evaluated using protected LSD and indicated in the figure as an asterisk. BMI, body mass index; LSD, least significant difference.

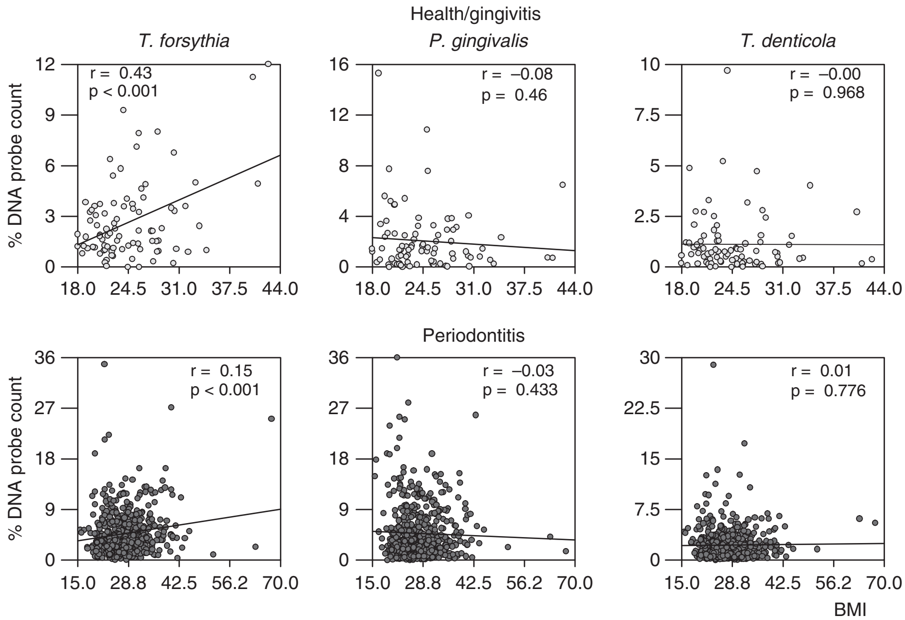

Fig. 9. Scatter plots of BMI (*x*-axis) and mean proportions of the red complex species (*Tannerella forsythia*, *Porphyromonas gingivalis*, *Treponema denticola*; *y*-axis) in subjects subset according to health/gingivitis (top three panels, $N = 88$) and periodontitis (bottom three panels, $N = 536$). Each circle represents the mean proportion of the species averaged across up to 28 sites in an individual subject. The Pearson correlation coefficient (*r*) was employed to evaluate the association between BMI and species proportions. The *p*-values in the figure represent unadjusted values. However, the correlation between BMI and proportions of *T. forsythia* were significant at $p < 0.01$ and $p < 0.05$ in healthy/gingivitis and periodontitis subjects, respectively, after adjusting for 40 comparisons. BMI, body mass index.

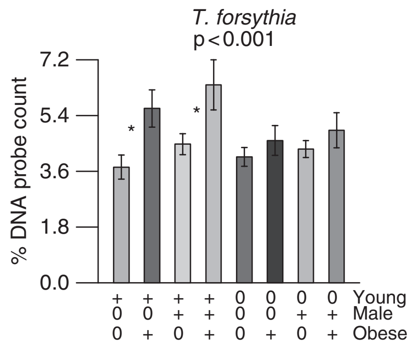

Fig. 10. Mean (± SEM) proportions of *Tannerella forsythia* in subjects subset according age, gender and BMI categories. The subjects were subset into two age categories based on the median subject age (46.8 years), males and females, and not obese (BMI < 30) or obese (BMI ≥ 30). Overall significance of differences was determined using ANOVA and significance of difference between BMI categories in each age/gender group was determined using protected LSD and indicated in the figure as an asterisk. BMI, body mass index; LSD, least significant difference.

ing age, even in subjects who are considered to be systemically healthy. The reason for this increase in disease is not known, but it might be speculated that prolonged, continuous exposure to periodontal pathogens might eventually lead to disease initiation at some periodontal sites. Further, it is possible that there may be periods of diminished host resistance during an individual's life that allow the pathogens to briefly ''gain the upper hand'' and initiate disease. Given enough time, the effect of prolonged pathogen exposure and/or lapses in host defense in aging individuals may diminish the difference in periodontal status between obese and non-obese groups. Further, once disease has been initiated and deeper periodontal pockets have been formed, it is likely that the altered local environment may be more important in controlling pathogen levels than the state of being obese or not. To be more specific, one might speculate that a deep periodontal pocket, e.g. > 6 mm, and increased local inflammation may have a greater effect on subgingival microbial composition than being obese or not. This is substantiated in Fig. 7 where it may be observed that deep periodontal pockets in obese subjects with periodontitis have a similar *T. forsythia* level to deep periodontal pockets in non-obese individuals with periodontitis. It is not clear why *T. forsythia* overgrows in younger, obese or overweight periodontally healthy/gingivitis individuals. Conceivably, a growth factor may be supplied to *T. forsythia* or a supporting subgingival species. Alternatively some host mechanism controlling levels of this species might be compromised. In either event, the increased levels of this species provide a threat to the adjacent tissues that might warrant greater preventive procedures in such individuals to deter initiation of periodontitis and maintain periodontal health. Other explanations of the association between obesity and periodontal status have been suggested. These include the host's ability to cope with infection (Perlstein and Bissada 1977, Amar et al. 2007), serum CRP levels (Slade et al. 2003), blood glucose levels (Katz et al. 2000), nutritional status (Marcenes et al. 2003, Sahyoun et al. 2003), cytokine levels, specifically tumour necrosis factor α (TNF-α) in gingival crevicular fluid samples (Lundin et al. 2004), as well as psychological stress (da Silva et al. 1995).

There were limitations to the present study that included subject selection, age structure of the clinical groups, classification of subjects into those with periodontal health or periodontitis and the cross-sectional nature of the data. The subjects were participants in a series of different randomized clinical studies and were not selected specifically to examine the relationship between periodontal disease status and BMI categories. However, all subjects were sequentially enrolled who fit the entry criteria of the various studies and all consented to determination of their BMI. Because of the nature of recruitment, the age distribution of subjects differed between the periodontally healthy/gingivitis group (median age 31.9 years) and the periodontitis group (median age 49.9 years). Thus, when subjects were subset into the different groups based on age, periodontal status and obesity, only 11 subjects were categorized as ''older'' subjects in the healthy/gingivitis group, limiting conclusions that could be drawn regarding the ''older'' subject group. There was difficulty in categorizing subjects into periodontal health/gingivitis and periodontitis. This was due, in large part, to the different inclusion and exclusion criteria of the studies from which the subjects were drawn. The distinction of periodontal health/gingivitis from periodontitis is not a problem unique to this investigation in that subjects present with a spectrum of clinical characteristics. Some subjects would be ''obviously'' periodontally healthy while others would be ''obviously'' periodontally diseased. Between these categories exists a subset of subjects who are not clearly one or the other. We eliminated this indeterminate group by removing subjects who had overlapping levels of PD and CAL when originally categorized into healthy/gingivitis or periodontitis categories. However, inclusion of these 49 subjects in their original health or periodontitis groupings and re-analysing the data did not alter the conclusions of this investigation (data not shown). The cross-sectional nature of the study was also a limitation in that we did not know how long a subject had been overweight or obese or when periodontitis became established. Studies comparing the chronology of these events would be quite informative.

The results of the present investigation provided answers to the two hypotheses proposed in the Introduction. First, subjects, particularly younger females who were overweight or obese, were at greater risk for periodontitis than subjects with a normal BMI after adjusting for age, gender and smoking status. Second, the periodontal pathogen, *T. forsythia*, was in greater proportions in gingival sulci in periodontally healthy/gingivitis subjects who were obese, potentially increasing their risk of developing periodontitis. Assuming that randomized follow-up studies confirm the association of obesity with periodontal status and the levels and proportions of certain subgingival microbial species, the meaning of such an association is not clear. The most likely explanation would be that a change in periodontal tissue status that is due to metabolic changes associated with obesity might in some fashion affect subgingival microbial colonization patterns or compromise periodontal tissue host defenses, altering the extent and progression of periodontal disease. While this conjecture is certainly possible, other explanations are equally plausible. Differences between obese and non-obese individuals in dietary patterns, lifestyle, home-care procedures, oral habits and genetic background might be the ''direct'' reason for their apparently greater levels of periodontal disease. Nonetheless, the recognition of an association among obesity, periodontal status and increased colonization by the periodontal pathogen, *T. forsythia*, may be the first step in attempting to unravel the biologic mechanism(s) underlying this association.

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Clinical Relevance

Scientific rationale for the study: An association between obesity and periodontitis has been suggested. However, no studies have examined the relationship of obesity with the composition of the subgingival microbiota and whether microbial shifts in obese individuals might be associated with an increased risk of periodontitis.

Principal findings: Subjects, particularly younger females who were overweight or obese, were at greater risk for periodontitis than subjects with a normal BMI after adjusting for age, gender and smoking status. The periodontal pathogen, *T. forsythia*, was in greater proportions in gingival sulci in periodontally healthy/gingivitis subjects who were obese, potentially increasing their risk of developing periodontitis.

Practical implications: Given the increased risk for developing periodontal disease in younger, obese individuals, particularly females, these individuals should be monitored and provided with aggressive preventive measures and/or treatment to prevent initiation or progression of periodontitis.