

Association between obesity and chronic periodontitis

A nationwide population-based cohort study in Taiwan

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Abstract

Previous studies have suggested that obesity might be associated with chronic periodontitis (CP); however, no clear conclusions have been reached so far. In this retrospective cohort study, we aimed to investigate the association between obesity and CP by using a large population-based dataset in Taiwan.

A population-based retrospective cohort study was conducted using the Longitudinal Health Insurance Database 2010 (LHID2010) derived from the National Health Insurance Research database in Taiwan, from 2000 to 2013. Obesity and non-obesity groups were matched with sex, age, urbanization level, socioeconomic status, and the related comorbidities by using the propensity score method at a 1:2 ratio.

An obese cohort (n = 4140) and a non-obese cohort (n = 8280) were included in this study, with an average age of 41.7 ± 13.8 years and 42.0 ± 14.0 years, respectively. The risk of CP for the patients with obesity was 1.12-fold compared with those without obesity (hazard ratio, 1.12; 95% confidence interval, 1.01–1.25). In the subgroup analysis according to age and sex, the hazard ratio of CP were 1.98 (95% confidence interval, 1.22–3.22) in the subgroup of age equal to or older than 65 years. The risk of CP showed no difference between obesity and non-obesity groups in both sex.

This population-based cohort study demonstrated that obesity was associated with the development of CP in Taiwan.

Abbreviations: BMI = body mass index, CI = confidence interval, CP = chronic periodontitis, ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification, NHIRD = National Health Insurance Register Database, NHRI = National Health Research Institute.

Keywords: chronic periodontitis, obesity, overweight

1. Introduction

Obesity is defined as excessive fat accumulation that might impair health and is diagnosed at a body mass index (BMI) $\geq 30 \text{ kg/m}^2$.^[1]

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The authors have no conflicts of interest to disclose.

The data that support the findings of this study are available from a third party, but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are available from the authors upon reasonable request and with permission of the third party.

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The fundamental cause of obesity is an energy imbalance between calorie consumption and calorie expenditure.^[2] Obesity is an epidemic issue worldwide and a major contributor to the global burden of chronic diseases. The majority of obese individuals develop type 2 diabetes, dyslipidemia, hypertension, and cardiovascular disease.^[2] In 2017, the World Obesity Federation identified ‘obesity’ as a “chronic relapsing disease process,” and encouraged addressing the concern through clinical intervention.^[1] At the population level, these complex obesity-related issues have remained one of the biggest challenge for clinicians.

Periodontal disease is an inflammatory disorder of tooth-supporting structures resulting from the interaction between pathogenic bacteria and the host immune response.^[3] Poor oral hygiene, bacterial biofilm accumulation, and possibly occlusal trauma were sufficient to initiate the disease.^[3] Clinical manifestations of chronic periodontitis (CP) include gingival inflammation — which may lead to periodontal pocket formation as a result of loss of gingival attachment — gingival recession, alveolar bone loss, tooth mobility, and tooth loss.^[4] CP is placing as the sixth most prevalent health issue among adults globally, with 11.2% of the population suffering from its severe impact worldwide.^[5,6] Prior studies demonstrated that CP links to many systemic diseases, including type 2 diabetes, peptic ulcer disease, and cardiovascular disease.^[7,8]

Within the non-communicable diseases in the world, CP and obesity are both categorized as chronic inflammatory diseases. A characteristic periodontal inflammatory infiltrate is observed in CP, as unregulated proteinases involved in the defense against

microbes have been shown to increase periodontal tissue destruction. In the case of obesity, obesity is increasingly defined as a chronic disease with low-grade inflammatory state, due to the expression of pro-inflammatory factors and diminished expression of anti-inflammatory factors.^[2,9] Moreover, results from previous studies^[10–12] demonstrated that there are positive associations between the two multifactorial chronic diseases. Despite the evidence noted, however, there is a lack of population-based studies and real-world data to explore the link between CP and obesity. Our aim is to investigate the association between obesity and CP using Taiwanese population-based data.

2. Methods

2.1. Data source and study design

The dataset used in this cohort study was derived from the National Health Insurance Register Database (NHIRD) in Taiwan, which was released by the National Health Research Institute (NHRI) and includes all the original claims data and registration files from 2000 to 2013, for one million individuals randomly sampled in 2010 nation-wide. Data from the NHIRD covers more than 99% among the Taiwanese population. The disease diagnoses were defined according to the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM). The study was performed in agreement with the Declaration of Helsinki and was approved by the Institutional Review Board of Chung Shan Medical University Hospital (CSMUH No.CS2–15017, Date: 10/04/2015).

2.2. Patients identification and measurement

We used a subset of the NHIRD (2000–2013), focusing on nearly a million random individuals from outpatient settings in 2010 (N=993,232). We identified patients meeting criteria for obesity based on the use of ICD-9-CM code 278: overweight, obesity and other hyperalimentation. To increase the validity of the subdataset, cases were selected only if they were diagnosed with obesity at least twice during two separate outpatient visits. We identified patients with CP based on the use of ICD-9-CM code 523.4: CP, chronic pericementitis. To increase the accuracy of the diagnosis, patients who met criteria for CP must be diagnosed with CP at least twice.

Patients with a diagnosis of periodontitis before the diagnosis of obesity, aged less than 20 years old, withdrew from the health insurance program, or had missing data were excluded from the study. For the non-obese cohort, we conditionally matched subjects in a 1:4 ratio by age and sex. The propensity score method was conducted by further matching age, sex, monthly income, urbanization, hypertension, hyperlipidemia, diabetes, chronic obstructive pulmonary disease, anxiety, depression, and insomnia at a 1:2 ratio. The process of selecting the dataset is shown in Figure 1.

2.3. Statistical analyses

Student *t*-test for continuous variables and the chi-squared test for categorical variables were performed for statistical analyses. The propensity score method was used for creating a cohort and a control group. Propensity score method is often used and analyzed in observational studies, which mimics particular characteristics of a randomized controlled trial.^[13] The Kaplan

Meier analysis and log-rank test were used for calculating the between-group difference of cumulative incidence rates of CP. The multivariable Cox proportional hazard model was used to estimate the hazard ratio (HR) of CP between groups. All results are presented in HRs and 95% confidence intervals (CIs). A 2-sided $P < .05$ was considered statistically significant. All analyses were conducted in SPSS version 22 (SPSS Inc., Chicago, IL).

3. Results

An obese cohort (n=4140) and a non-obese cohort (n=8280) were included in this study, with an average age of 41.7 ± 13.8 years and 42.0 ± 14.0 years, respectively. Table 1 summarizes the overall characteristics of each cohort, including age, sex, urbanization, monthly income, and the related comorbidity, which showed no significant difference between 1:2 matched cohorts ($P > .05$).

The obesity group was 12% more likely to have a diagnosis of CP, compared to the non-obesity group (HR, 1.12; 95% CI, 1.01–1.25). After adjusting for the confounding factors, those aged > 65 years had 26% less risk of having CP than those aged 20 to 39 years (HR, 0.74; 95% CI, 0.56–0.98). Furthermore, those with monthly income over NTD \$ 40,000 had a 37% higher risk for a CP diagnosis than those with monthly income less than NTD \$20,000 (HR=1.37, 95% CI, 1.19–1.56). Patients who experienced anxiety had higher risk for CP compared to those without anxiety (HR=1.49, 95% CI, 1.09–2.02). Conversely, individuals who lived in suburban settings had lower risk for CP than those who lived in urban areas (HR=0.80, 95% CI, 0.71–0.91). Figure 2 shows the higher cumulative incidence of CP in the obesity group in the 14-years follow-up period.

The subgroup analysis was shown in Table 3. In the subgroup of age equal to or older than 65 years, obese patients had almost two times higher risk for CP (HR, 1.98; 95% CI, 1.22–3.22). On the other hand, the risk for CP was similar for individuals between 40 to 65 years old, and 20 to 39 years old, regardless of whether they were considered obese. In the subgroup of sex, there were no significant differences in risk for CP between men and women.

4. Discussion

Based on this 13-year nationwide, population-based, retrospective cohort study, results suggest that there is a positive association between obesity and CP, particularly for certain subgroups. Overall, patients with obesity were 1.12 times more likely to develop CP when compared to patients who were not obese (HR, 1.12; 95% CI, 1.01–1.25). To the best of our knowledge, this is the first study to survey the association between CP and obesity using large-scale, population-based data.

Previously, small-scale, longitudinal cohort studies demonstrated similar results of a positive association between obesity and CP.^[14–16] Given that standards of obesity may vary with age, sex, genetic or cultural background, the inclusion criteria of obesity in our study was based on ICD-9 diagnostic codes in addition to having the diagnoses from at least two outpatient department visits. Obesity is not only a status with body weight that is grossly above the acceptable or desirable weight, it also means a BMI of greater than 30 kg/m^2 , usually due to accumulation of excess body fat. It is also recognized that the weight gain was directly associated with development of

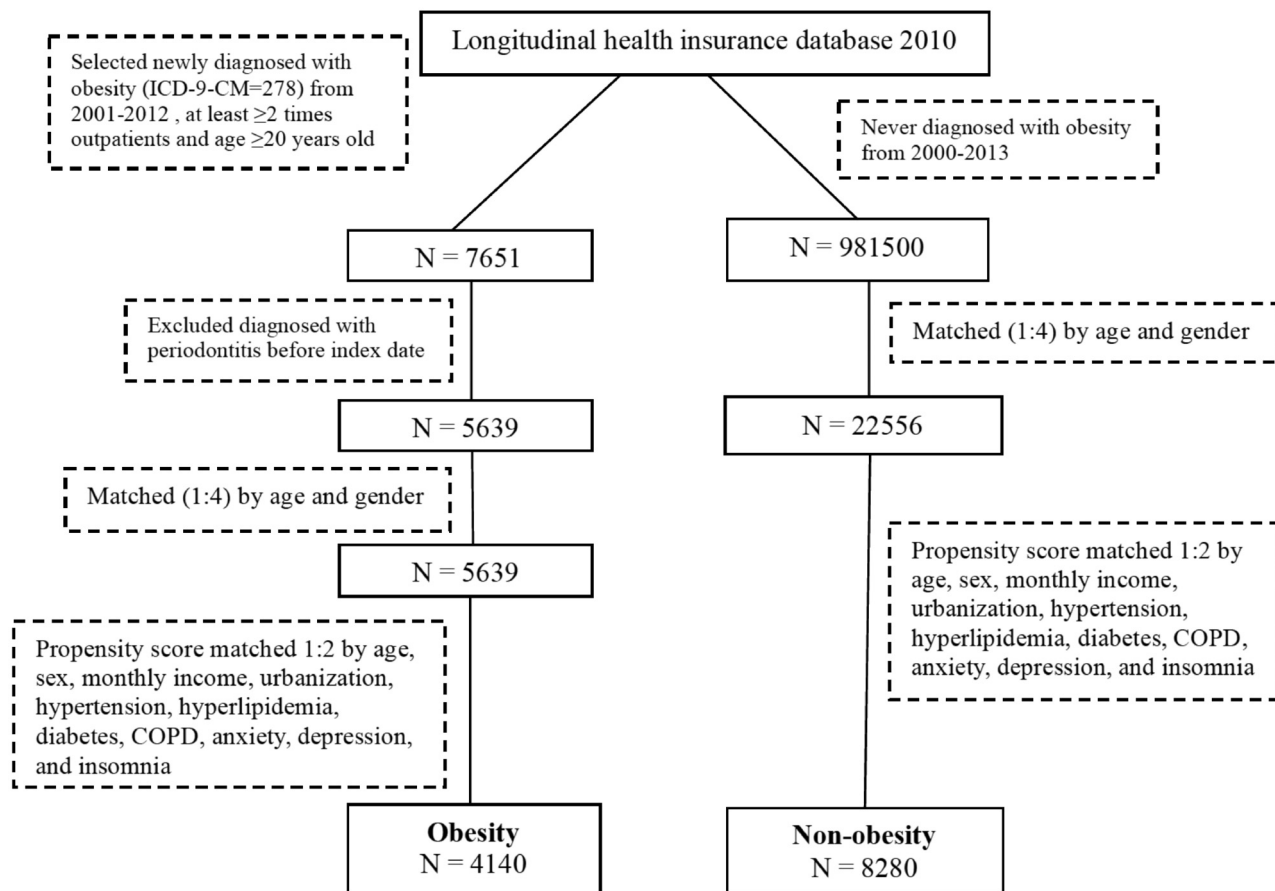


Figure 1. The flow diagram of the study participants.

Table 1
Demographic data of matched study cohorts.

	Obesity (N = 4140)	Non-obesity (N = 8280)	P-value
Age			.458
20–39	2061 (49.8%)	4098 (49.5%)	
40–64	1809 (43.7%)	3592 (43.4%)	
≥65	270 (6.5%)	590 (7.1%)	
Mean ± SD	41.7 ± 13.8	42.0 ± 14.0	.205
Sex			.518
Female	2751 (66.4%)	5550 (67.0%)	
Male	1389 (33.6%)	2730 (33.0%)	
Monthly income			.941
<NT \$20,000	1846 (44.6%)	3680 (44.4%)	
NT \$20,000–NT \$40,000	1478 (35.7%)	2946 (35.6%)	
>NT \$40,000	816 (19.7%)	1654 (20.0%)	
Urbanization			
Urban	2653 (64.1%)	5290 (63.9%)	
Suburban	1175 (28.4%)	2344 (28.3%)	
Rural	312 (7.5%)	646 (7.8%)	
Hypertension	515 (12.4%)	1121 (13.5%)	.088
Hyperlipidemia	178 (4.3%)	318 (3.8%)	.218
Diabetes	236 (5.7%)	405 (4.9%)	.055
COPD	58 (1.4%)	135 (1.6%)	.330
Anxiety	99 (2.4%)	191 (2.3%)	.769
Depression	56 (1.4%)	128 (1.5%)	.401
Insomnia	85 (2.1%)	202 (2.4%)	.177

COPD = chronic obstructive pulmonary disease.

periodontitis.^[16] Furthermore, moderate to severe weight gain tends to worsen CP symptoms and accelerated alveolar bone loss.^[17]

Obesity is generally defined through BMI with over 25 kg/m² or 30 kg/m² in the different area or population. Previous studies have reported a dose-response relationship for the association between obesity and periodontitis.^[12] However, some experts considered that other indicators were more appropriate for depicting disease progression. It is considered that central obesity, such as waist circumference and waist-to-hip ratio, are more important than BMI alone. One Finnish study used BMI, body fat percentage, and waist circumference as the obesity indicators, all of which showed a positive association with the deepened periodontal pocket.^[18] Moreover, visceral fat, but not total fat, plays the key role for obesity and other systemic diseases in recent viewpoint.^[2] A cross-sectional study demonstrated that abdominal obesity, instead of general obesity, was contributing to periodontal attachment loss and bleeding on probing.^[19] Likewise, our population-based cohort study corroborated the same positive association by using the health insurance derived database.

Data on whether men or women pose greater risk of CP has been inconsistent in previous studies. Some studies^[20,21] indicate that men are at a greater risk of developing periodontitis than women. However, other articles^[8,15] revealed that women had a higher risk of developing CP because of an increase in gingival inflammation due to hormonal fluctuations. In this study, there

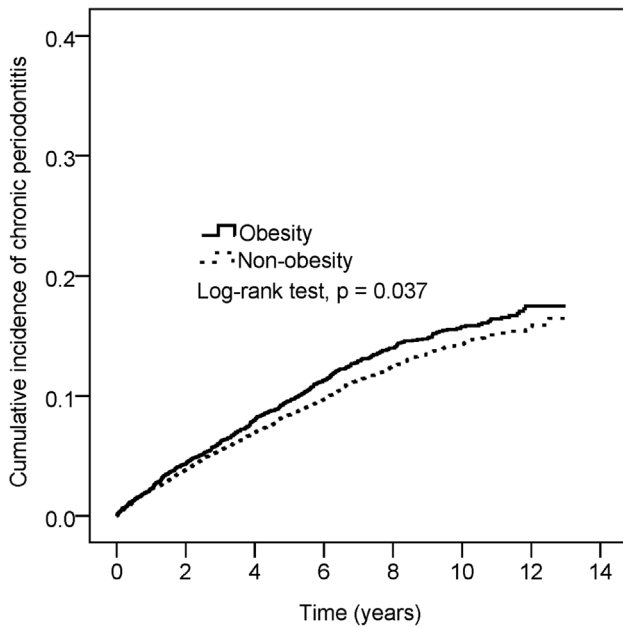


Figure 2. The Kaplan-Meier plot for the cumulative incidence of chronic periodontitis with obesity and non-obesity subjects in this cohort study.

were no significant differences in the risk for CP by sex. While the pooled estimate of CP risk is 1.12-fold in obese cohort, a stratified analysis by sex demonstrated no significant associations between CP and obesity in both sex (Table 3). This result may be inferred

from our previous study,^[22] where both men and women demonstrated a similar age-effect pattern of CP prevalence in Taiwan, a result that was echoed in a systematic review.^[23] It remains unclear whether there is a biologic basis for sexual dimorphism in periodontal diseases, or if there are other sex-specific modifications to CP, given that there is evidence that sex can be a factor that modifies the pathogenesis and progression of several health conditions.^[24,25]

Age is a risk factor for the development of CP due to the destruction of the surrounding tissue and the exposure to bacterial plaque over time.^[26] In general, our results confirmed that the impact of CP increased with age. In our subgroup analysis, higher risk of CP in the obese group was noted in those aged 65 or older. Obesity may further induce inflammation, this increasing the severity of destruction in multiple sites of the body, including gums. Thus, elderly individuals with obesity pose a higher risk of developing CP. Interestingly, our results showed that there is reduced risk of CP in patients 65 years or older compared to patients below 65 years old. This result might derive from the characteristic of NHIRD. In a previous study^[22], we noted that because of the awareness of periodontitis in Taiwan Government, the national health insurance provided dental prophylaxis twice a year to the public above 12 years old. Due to early diagnosis and intervention for periodontitis, the Taiwanese population might exhibit this unique reverse effect.

The pathophysiology underlying the association between CP and obesity has been under debate; however, based on the results of this study and previous data, the relationship between CP and obesity could be explained in several ways. Adipocytes secrete pro-inflammatory cytokines such as TNF- α and IL-6, which

Table 2
Cox proportional hazard model analysis for risk of chronic periodontitis.

	Univariate		Multivariate*	
	HR (95% CI)	P value	HR (95% CI)	P value
Group				
Non-obesity	Reference		Reference	
Obesity	1.12 (1.01–1.25)	.037	1.12 (1.01–1.25)	.038
Age				
20–39	Reference		Reference	
40–64	1.11 (1.00–1.23)	.053	1.05 (0.94–1.18)	.390
≥65	0.72 (0.56–0.92)	.010	0.74 (0.56–0.98)	.033
Sex				
Female	Reference		Reference	
Male	0.95 (0.85–1.06)	.348	0.92 (0.82–1.03)	.134
Monthly income				
<NT \$20,000	Reference		Reference	
NT \$20,000–NT \$40,000	1.03 (0.91–1.16)	.625	1.02 (0.91–1.16)	.693
>NT \$40,000	1.41 (1.24–1.61)	<.001	1.37 (1.19–1.56)	<.001
Urbanization				
Urban	Reference		Reference	
Suburban	0.77 (0.68–0.88)	<.001	0.80 (0.71–0.91)	<.001
Rural	0.82 (0.67–1.00)	.055	0.88 (0.71–1.08)	.231
Hypertension	0.95 (0.81–1.12)	.568	1.02 (0.85–1.22)	.847
Hyperlipidemia	1.16 (0.89–1.50)	.266	1.17 (0.89–1.53)	.262
Diabetes	0.94 (0.73–1.20)	.619	0.98 (0.76–1.27)	.873
COPD	1.09 (0.73–1.63)	.682	1.16 (0.77–1.75)	.464
Anxiety	1.44 (1.07–1.94)	.017	1.49 (1.09–2.02)	.011
Depression	0.92 (0.58–1.44)	.705	0.82 (0.52–1.30)	.403
Insomnia	1.00 (0.70–1.42)	.991	0.99 (0.69–1.42)	.955

CI = confidence interval, COPD = chronic obstructive pulmonary disease.

* Adjusted for age, sex, monthly income, urbanization, hypertension, hyperlipidemia, diabetes, COPD, anxiety, depression, and insomnia.

Table 3
Hazard ratios of chronic periodontitis in subgroup analysis of obesity.

	Obesity		Non-obesity		HR (95% C.I.)	P value
	N	No. of chronic periodontitis	N	No. of chronic periodontitis		
Age						
20–39	2061	242	4098	447	1.07 (0.92–1.26)	.366
40–64	1809	242	3592	433	1.10 (0.94–1.29)	.224
≥65	270	31	590	34	1.98 (1.22–3.22)	.006
p for interaction=0.063						
Sex						
Female	2751	350	5550	643	1.09 (0.96–1.24)	.194
Male	1389	165	2730	271	1.19 (0.98–1.45)	.071
p for interaction=0.438						

CI=confidence interval, N=number.

cause systemic inflammation.^[2,21] TNF- α contributes to the onset of periodontitis through the stimulation of osteoclast formation, inducing alveolar bone destruction and connective tissue degradation. TNF- α is considered to be a contributor of early stage periodontitis in the obese population.^[27] Moreover, obesity-induced chronic inflammation and oxidative stress could condition the development of insulin resistance (IR), and there is some data to suggest that IR leads to the development of type 2 DM and CP.^[28]

One major limitation of our study was the lack of anthropometric data and health-related behaviors, such as cigarette smoking and alcohol consumption. However, the NHIRD provided sufficient sample size to assess the association of diseases, and was representative of a national population. The diagnosis of obesity and CP based on ICD-9 diagnostic codes, instead of the clinical indicators, is another inherent shortcoming of the database. Nevertheless, a well-matched cohort group and control group can minimize the potential biases of sex, age, urbanization, socioeconomic status, and related comorbidities.

Our findings suggest that further research at a population level should be carried out to understand the magnitude of effect between CP and obesity. These findings might have some important clinical implications. First, obesity may increase the risk for CP. With the addition of specific guidelines guided by data, clinicians could be aware of the potential association. For example, physicians could refer obese patients to dental professionals for further periodontal interventions. Second, both obesity and CP are urgent issues for the global burden of disease. Health policy makers can place more emphasis on this topic in order to prevent and address these issues. By identifying target groups for prevention and intervention and producing various health promotion policies, administrations can reduce the risk of both issues. In this population-based level study, the results may raise a consensus on the effect of CP and obesity and support the notion of obesity is a factor contribution to CP.

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Formal analysis: Yu-Hsun Wang.

Investigation: Tai-Hsin Lin.

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Project administration: Yu-Chao Chang.

Validation: Yu-Chao Chang.

Writing – original draft: Tsung-Po Chen, Hui-Chieh Yu, Yu-Chao Chang.

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