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Original Article

# Relationship between Metabolic Syndrome Components and Periodontal Disease in a Japanese General Population: the Suita Study

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***Aim*: A positive association between metabolic syndrome (MetS) and periodontal status has recently been noted. However, no study has evaluated the relationship by sex and in a general urban population using the uniform definition proposed in the 2009 Joint Interim Statement. The aim of this study was to clarify the relationship between MetS and periodontal status using the uniform definition in a general urban Japanese population.**

***Methods*: A total of 1,856 Japanese men and women (mean age: 66.4 years) were studied using data from the Suita study. Periodontal status was evaluated by the Community Periodontal Index (CPI). MetS was defined using the 2009 Joint Interim Statement. The associations of the MetS and its components with periodontal disease were investigated using multiple logistic regression analysis adjusting for age, drinking, and smoking.**

***Results*: Among the components of the MetS, low HDL cholesterol level was significantly associated with periodontal disease in men and women [odds ratios (OR)=2.39 and 1.53; 95% confidence intervals=1.36−4.19 and 1.06−2.19]. Furthermore, the risk of periodontal disease showed 1.43-, 1.42-, and 1.89-fold increases in those with 2, 3, and ≥4 components, respectively, compared with those having no components ($P_{trend}<0.001$). For the analysis by sex, the risk of periodontal disease was increased 2.27- and 1.76-fold in those with ≥4 components in men and women, respectively (both $P_{trend}=0.001$).**

***Conclusion*: These findings suggest that MetS and lower HDL cholesterol are associated with periodontal disease. Subjects with two or more MetS components had a significantly higher prevalence of periodontal disease.**

**Key words:** Metabolic syndrome, Periodontal disease, Low HDL cholesterol, Cross-sectional study, Suita study



## Introduction

Metabolic syndrome is a complex medical disorder characterized by abdominal obesity, elevated blood pressure, high fasting plasma glucose, and hyperlipidemia[1]. It is becoming common worldwide[2], including Japan[3]. Preventing metabolic syndrome is of great importance to prevent cardiovascular disease[4-7].

Recently, there has been interest in the effects of oral health on prevention of systemic disease. Previous studies have reported an association between periodontal disease and the metabolic syndrome[8-11] or its components[12-19]. However, these previous studies targeted a specific sex and used a local definition of metabolic syndrome. Some studies have recently evaluated the relationship between the new standardized definition of metabolic syndrome[20] and periodontal status

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in a specific sex and in a rural area[19, 21] and evaluated the relationship with severe periodontal disease[10] using the new diagnostic criteria in Japan, but there is no evidence for the association by sex in an urban population. The purpose of the present study was, therefore, to investigate the association between the new international standardized definition of metabolic syndrome and periodontal status. In this study, the hypothesis that the metabolic syndrome and a higher number of its components are positively associated with periodontal status was tested in a general urban Japanese population.

## Methods

### Study Participants

The Suita study is a population-based cohort study of cardiovascular disease; the details of the study design have been described elsewhere[22]. During the biannual follow-up survey of the Suita study, 2,083 subjects were recruited to both medical check-ups and dental examinations between June 2008 and September 2013. Of these, 227 individuals were excluded due to non-fasting blood collection ($n=109$) and incomplete periodontal data ($n=118$). Finally, 1,856 subjects (1,084 women and 772 men, mean age 66.4 ± 7.8 years) were included in the study. The study protocol was approved by the Ethics Committee of the National Cerebral and Cardiovascular Center (M19-62). Written, informed consent was obtained from all participants.

### Periodontal Tissue Examination

Periodontal status was assessed using the Community Periodontal Index (CPI)[23] by means of partial 10 index teeth recording. Ten teeth were examined, comprising eight designated molars (first and second molars) and two incisors (upper right and left central incisors), and if this test could not be performed because of loss of one or both of the central incisors concerned, the same tooth on the opposite side was examined. No evaluation was performed if all relevant teeth were missing. Periodontal status was examined using a CPI probe (YDM, Tokyo, Japan) to evaluate each tooth with respect to six periodontal pockets according to the following criteria, and the highest-value code was recorded. The CPI codes were as follows: no sign of inflammation of the gingiva (Code 0); evident bleeding after probing (Code 1); dental calculus deposits (including those detected by probing $<4$ mm beneath the gingival margin, Code 2); periodontal pocket depth $\geq 4$ mm and $<6$ mm (Code 3); periodontal pocket depth $\geq 6$ mm (Code 4). This examination was performed by five dentists who had undergone calibration in advance. Cohen's $\kappa$ value for the consistency of the periodontal tissue examinations among the five dentists was 0.78. In this study, periodontitis was defined as CPI Code $\geq 3$.

### Medical Examination

Well-trained nurses measured blood pressure twice in a seated position with an automated sphygmomanometer (Colin BP-I03ill; Omron, Kyoto, Japan) and an appropriately sized cuff according to a standard protocol after at least 5 minutes of rest prior to the initial blood pressure reading. Systolic (SBP) and diastolic blood pressure (DBP) values were taken as the average of two measurements recorded $>1$ minute apart[22].

At the baseline examination, routine blood tests were performed, including triglycerides, high-density lipoprotein (HDL) cholesterol, and fasting blood glucose. The metabolic syndrome was defined using the uniform definition proposed in the 2009 Joint Interim Statement[20]. Each component of the metabolic syndrome is as follows: high blood pressure (SBP $\geq 130$ mmHg and/or DBP $\geq 85$ mmHg, and/or taking antihypertensive medication), low serum HDL cholesterol ($<40$ mg/dL in men and $<50$ mg/dL in women), hypertriglyceridemia (triglycerides $\geq 150$ mg/dL, and/or taking antihyperlipidemia medication), high plasma glucose (fasting blood glucose $\geq 100$ mg/dL, and/or on diabetic therapy), and abdominal obesity measured by waist circumference (waist circumference $\geq 90$ cm in men and $\geq 80$ cm in women) according to the Asian diagnostic criteria. The presence of any three of the five risk factors constitutes a diagnosis of metabolic syndrome.

### Lifestyle Variables

Information on lifestyle, including drinking and smoking habits, was collected with normalized questionnaires by well-trained nurses through interviews. Drinking and smoking were divided into never drinker/smoker, former drinker/smoker, or current drinker/smoker.

### Statistical Analysis

The subjects were divided into two groups in each sex according to the presence/absence of periodontal disease. Odds ratios (ORs) and 95% confidence intervals (95% CI) for the risk of each component with respect to periodontal diseases were calculated by logistic regression analyses adjusted for age and smoking and drinking status, with components of metabolic syndrome as covariates in the multivariate analysis. In addition, the association between the presence of periodontal disease and the number of compo-

**Table 1.** Characteristics of the study subjects

| Characteristic | Men ($n$=772) | | Women ($n$=1084) | |
|---|---|---|---|---|
| | CPI=0,1,2 | CPI=3,4 | CPI=0,1,2 | CPI=3,4 |
| Number | 326 | 446 | 596 | 488 |
| Age, years | 66.5±8.4 | 67.3±7.3 | 65.7±8.0 | 66.4±7.6 |
| Waist circumference, cm | 85.1±7.8 | 86.5±7.7 | 81.3±9.6 | 82.5±9.0 |
| Blood pressure | | | | |
| Systolic blood pressure, mmHg | 130.0±10.9 | 131.0±17.5 | 125.6±20.0 | 128.4±20.9 |
| Diastolic blood pressure, mmHg | 80.0±10.9 | 80.9±10.5 | 75.2±10.9 | 76.8±11.2 |
| Fasting blood glucose, mg/dL | 107.9±19.4 | 110.0±24.7 | 100.4±14.1 | 101.4±14.5 |
| HDL cholesterol, mg/dL | 58.8±14.7 | 55.5±15.8 | 67.0±15.0 | 63.9±15.2 |
| Triglycerides, mg/dL | 108.7±64.3 | 117.6±72.1 | 96.5±78.2 | 100.9±48.6 |
| Smoking status, % | | | | |
| Current | 16.3 | 19.7 | 4.2 | 3.3 |
| Quitting | 56.7 | 56.5 | 6.5 | 5.1 |
| Never | 27.0 | 23.8 | 89.3 | 91.6 |
| Drinking status, % | | | | |
| Current | 68.4 | 70.2 | 26.5 | 29.3 |
| Quitting | 5.8 | 5.8 | 2.2 | 2.0 |
| Never | 25.8 | 24.0 | 71.3 | 68.6 |
| CPI code, % | | | | |
| 0 | 30.6 | | 39.5 | |
| 1 | 1.3 | | 1.8 | |
| 2 | 10.4 | | 13.7 | |
| 3 | 36.4 | | 32.1 | |
| 4 | 21.4 | | 12.9 | |

nents of metabolic syndrome, age-adjusted and multivariate-adjusted for age, smoking status, and drinking status, was evaluated. A $P$ value $<0.05$ was considered significant for all comparisons. All analyses were performed with IBM SPSS Statistics 21 (SPSS Inc., IBM, Tokyo, Japan).

## Results

The baseline characteristics of the study subjects by sex according to periodontal status are shown in **Table 1**. The subjects with periodontal disease were older and had higher SBP and DBP, triglycerides, and fasting blood glucose and greater waist circumference than those without periodontal disease (**Table 1**).

**Table 2** shows the relationship between each component of metabolic syndrome and periodontal disease. Of the five components of the metabolic syndrome in the multivariate-adjusted analysis, low HDL cholesterol level was associated with periodontal disease in men and women (ORs=2.39 and 1.53; 95% CIs=1.36−4.19 and 1.06−2.19, respectively). In addition, the metabolic syndrome was associated with periodontal disease in men and women (ORs=1.40 and 1.42; 95% CIs=1.03−1.90 and 1.10−1.83, respectively).

**Table 3** shows the relationship between the number of components of metabolic syndrome and periodontal disease. The subjects with two, three, and four or five components of metabolic syndrome had a higher prevalence of periodontal disease than the subjects without the components in multivariate-adjusted analysis. On stratified analysis by sex, subjects with four or five components of metabolic syndrome had a higher prevalence than subjects with no components in both men and women (ORs=2.27 and 1.76; 95% CIs: 1.20−4.28 and 1.11−2.78, respectively). Furthermore, with the addition of one more component, the risk of periodontal disease showed 1.23- and 1.17-fold increases in men and women, respectively.

## Discussion

This is, to the best of our knowledge, the first study to show the relationship between the components of metabolic syndrome and periodontal status by sex in a general urban population using the criteria of the 2009 Joint Interim Statement. Periodontal dis-

**Table 2.** Relationships between components of the metabolic syndrome and periodontal status

| | Men ($n$ = 772) Periodontal status, n | | Women ($n$ = 1084) Periodontal status, n | |
|---|---|---|---|---|
| | − | + | − | + |
| Participants, n | 326 | 446 | 596 | 488 |
| Abdominal obesity | | | | |
| Cases, n | 82 | 136 | 317 | 297 |
| Age-adjusted ORs | 1 (Ref) | 1.31 (0.95-1.80) | 1 (Ref) | 1.34 (1.04-1.71) |
| Multivariable-adjusted ORs | 1 (Ref) | 1.23 (0.88-1.72) | 1 (Ref) | 1.23 (0.95-1.60) |
| High blood pressure | | | | |
| Cases, n | 206 | 302 | 303 | 280 |
| Age-adjusted ORs | 1 (Ref) | 1.16 (0.85-1.58) | 1 (Ref) | 1.12 (0.88-1.44) |
| Multivariable-adjusted ORs | 1 (Ref) | 1.10 (0.79-1.52) | 1 (Ref) | 1.15 (0.89-1.50) |
| High fasting plasma glucose | | | | |
| Cases, n | 216 | 307 | 252 | 225 |
| Age-adjusted ORs | 1 (Ref) | 1.14 (0.84-1.54) | 1 (Ref) | 1.16 (0.91-1.47) |
| Multivariable-adjusted ORs | 1 (Ref) | 1.03 (0.75-1.41) | 1 (Ref) | 1.06 (0.82-1.36) |
| Low HDL cholesterol | | | | |
| Cases, n | 18 | 57 | 68 | 83 |
| Age-adjusted ORs | 1 (Ref) | 2.48 (1.42-4.28) | 1 (Ref) | 1.57 (1.11-2.22) |
| Multivariable-adjusted ORs | 1 (Ref) | 2.39 (1.36-4.19) | 1 (Ref) | 1.53 (1.06-2.19) |
| High triglycerides | | | | |
| Cases, n | 95 | 165 | 177 | 166 |
| Age-adjusted ORs | 1 (Ref) | 1.42 (1.05-1.93) | 1 (Ref) | 1.19 (0.92-1.54) |
| Multivariable-adjusted ORs | 1 (Ref) | 1.32 (0.96-1.81) | 1 (Ref) | 1.07 (0.81-1.41) |
| Metabolic syndrome | | | | |
| Cases, n | 102 | 172 | 199 | 203 |
| Age-adjusted ORs | 1 (Ref) | 1.36 (1.00-1.84) | 1 (Ref) | 1.39 (1.08-1.79) |
| Multivariable-adjusted ORs | 1 (Ref) | 1.40 (1.03-1.90) | 1 (Ref) | 1.42 (1.10-1.83) |

- Periodontal disease: CPI code 0 to 2: −, CPI code 3 to 4: +
- Multivariable-adjusted for age, smoking status, drinking status, and metabolic syndrome components except a component entered as an objective variable
- Abdominal obesity: Men < 90 cm, Women < 80 cm: −, Men ≥ 90 cm, Women ≥ 80 cm: +
- High blood pressure: systolic < 130 and diastolic < 85 mmHg: −, systolic ≥ 130 and/or diastolic ≥ 85 mmHg: +
- High fasting plasma glucose: < 100 mg/dl: −, ≥ 100 mg/dl: +
- Low HDL cholesterol: Men ≥ 40 mg/dl, Women ≥ 50 mg/dl: −, Men < 40 mg/dl, Women < 50 mg/dl: +
- High triglycerides: < 150 mg/dl: −, ≥ 150 mg/dl: +
- Metabolic syndrome adjusted for age, smoking status, and drinking status

ease was correlated with low HDL cholesterol and metabolic syndrome in men and women. In addition, the risk of periodontal disease increased according to the number of components.

In this study, subjects with low HDL cholesterol levels had a higher risk for periodontal disease. This result was reasonable in the light of the previous studies, which reported that periodontal disease was associated with metabolic syndrome[8] and changes in HDL subclass ratio comprise a useful marker for metabolic syndrome[24]. Similar to our results, several studies reported a significant relationship between dyslipidemia and periodontal disease. Katz *et al*. reported that a low HDL cholesterol level was significantly associated with a high CPI score (Code 4)[15], and Morita *et al*. showed an association between periodontal pockets (CPI score ≥ 3) and a low HDL cholesterol level[18]. Based on these reports, HDL cholesterol has an anti-atherogenic action, and subjects with a low HDL cholesterol level had a higher risk for periodontal disease. Furthermore, Pussinen *et al*. reported that the serum HDL cholesterol concentration increased after periodontal treatment[25], meaning that the abnormal lipid metabolism was related to chronic inflammation caused by periodontal disease. The association between periodontal disease and metabolic syndrome with and without lower HDL cholesterol was evaluated. Metabolic syndrome without lower HDL choles-

**Table 3.** Risk for periodontal status by number of components of metabolic syndrome

| | Number of components of metabolic syndrome | | | | | | |
|---|---|---|---|---|---|---|---|
| | 0 | 1 | 2 | 3 | 4 | ORs* | trend P |
| Men and Women | | | | | | | |
| Periodontal status, n | | | | | | | |
| − | 141 | 246 | 234 | 203 | 98 | | |
| + | 107 | 178 | 274 | 231 | 144 | | |
| Sex, age-adjusted OR | 1 | 0.90 (0.65-1.23) | 1.39 (1.01-1.89) | 1.37 (0.99-1.89) | 1.83 (1.27-2.64) | 1.18 (1.09-1.27) | <0.001 |
| Multivariable-adjusted OR | 1 | 0.90 (0.65-1.24) | 1.43 (1.05-1.96) | 1.42 (1.03-1.96) | 1.89 (1.31-2.73) | 1.18 (1.10-1.27) | <0.001 |
| Men | | | | | | | |
| Periodontal status, n | | | | | | | |
| − | 40 | 86 | 98 | 74 | 28 | | |
| + | 48 | 89 | 147 | 112 | 60 | | |
| Age-adjusted OR | 1 | 1.08 (0.64-1.85) | 1.55 (0.93-2.60) | 1.56 (0.91-2.66) | 2.19 (1.16-4.13) | 1.22 (1.07-1.38) | 0.002 |
| Multivariable-adjusted OR | 1 | 1.08 (0.63-1.84) | 1.55 (0.93-2.59) | 1.59 (0.93-2.72) | 2.27 (1.20-4.28) | 1.23 (1.08-1.39) | 0.001 |
| Women | | | | | | | |
| Periodontal status, n | | | | | | | |
| − | 101 | 160 | 136 | 129 | 70 | | |
| + | 69 | 89 | 127 | 119 | 84 | | |
| Age-adjusted OR | 1 | 0.80 (0.54-1.20) | 1.33 (0.90-1.99) | 1.31 (0.87-1.97) | 1.70 (1.08-2.68) | 1.16 (1.06-1.27) | 0.002 |
| Multivariable-adjusted OR | 1 | 0.80 (0.54-1.21) | 1.35 (0.91-2.20) | 1.34 (0.89-2.02) | 1.76 (1.11-2.68) | 1.17 (1.06-1.29) | 0.001 |

• Adjusted for age, smoking status, and drinking status
• ORs*: odds ratios for increasing by one component

terol was not significantly associated with periodontal disease in men and women (odds ratio, OR=1.21 and 1.25; 95% confidence intervals=0.87−1.67 and 0.94−1.67). These data are shown in **Supplemental Table 1**. However, the detailed mechanism was not determined in this study.

Each of abdominal obesity[12], hypertension[16], high fasting plasma glucose[17], and high triglycerides[13] had a significant relationship with periodontal disease in independent analyses. However, in this study, these components of metabolic syndrome did not have a significant relationship with periodontitis. The discrepancy may be due to differences in the obesity, blood glucose level, and periodontal status cut-offs or indices used in other studies.

Previous reports about the relationship between metabolic syndrome and periodontal disease[8] were searched; and there were 21 cross-sectional studies, but 14 of them focused on population research[10, 11, 19, 26-37]. Their results are shown in **Supplemental Table 2**. In Japan, a previous study[22] of men and women over 40 years showed that subjects with more metabolic syndrome components had a significantly higher prevalence of periodontitis. In addition, in the sex-specific analysis[27], mean pocket depth (PD) ≥3 mm or 3.5 mm was associated with metabolic syndrome in women, but not in men. These previous reports suggested that there were sex differences in the association between metabolic syndrome and periodontal disease, but it was considered that this association was a consequence of smoking habits. In the results adjusting for smoking status, there was no sex difference.

Some studies of the association between periodontal disease and metabolic syndrome used the Japanese definition of metabolic syndrome[38], where abdominal obesity is essential for the definition of metabolic syndrome[9, 18, 39, 40] (**Supplemental Table 3**). Yamamoto *et al*. showed no association between periodontal disease and metabolic syndrome, simply because of a small sample size[9]. On the other hand, Morita *et al*. showed a close association in workers[18], which is compatible with the present study. In the present study, metabolic syndrome was associated with periodontal disease only in men (**Supplemental Table 4**).

In the present study, both men and women with two or more components and men or women with four or more components of the metabolic syndrome had a higher prevalence of periodontal disease than those with no components. When considering the relationship between the combination of any two components and periodontal disease, subjects with the com-

bination of high fasting plasma glucose and high triglycerides had a higher prevalence of periodontal disease. Furthermore, when considering the combination of any three components, subjects with two combinations had a higher prevalence: the combination of high blood pressure, low HDL cholesterol, and (1) high fasting plasma glucose or (2) abdominal obesity (data not shown). However, one cannot reach any conclusions from the results of each combination analysis due to the small sample sizes.

Recent studies of the relationship between metabolic syndrome and periodontal disease focus on the physiologically active substances produced by adipose cells. In this research, the mechanism for metabolic syndrome as a possible risk factor for periodontal disease has been suggested[14, 41, 42]. Tumor necrosis factor-$\alpha$ (TNF$\alpha$), one of the physiologically active substances, causes alveolar bone resorption and aggravates periodontal status[43, 44]. Furthermore, TNF$\alpha$ produced by adipose cells raises insulin resistance and results in diabetes[41], suggesting the possibility that TNF$\alpha$ indirectly increases the risk of periodontal disease[42]. On the other hand, it has been suggested that not only does metabolic syndrome have an impact on periodontal disease, but also conversely, periodontal disease is likely to be involved in the pathogenesis of metabolic syndrome[42, 45-47]. It has been suggested that inflammatory cytokines caused by periodontal pathogenic bacteria, such as interleukin-1$\beta$ or TNF$\alpha$, may raise triglyceride or LDL cholesterol levels and induce abnormal lipid metabolism[46, 47]. Moreover, it has been suggested that TNF$\alpha$ produced by periodontal disease may increase insulin resistance and induce or aggravate diabetes[42]. As mentioned above, many mechanisms may be involved in the relationship between metabolic syndrome and periodontal disease.

The present study has several limitations. The primary limitation is a dilution bias. This study was based on a single-day measurement of metabolic syndrome components, which may lead to a misclassification of the components. Such inaccuracy in exposure measurement may lead to underestimation, but there was a positive association between metabolic syndrome and periodontal disease. Second, due to the cross-sectional study design, causality cannot be inferred from the present study. However, it could be speculated that the physiologically active substances produced by the adipose cells aggravate periodontal status, but some studies showed that inflammatory cytokines caused by periodontal pathogenic bacteria induce components of metabolic syndrome[43, 47].

Third, in this study, waist circumference was measured at the umbilical level of participants in the standing position. The joint statement[20] recommends waist circumference should be measured in a horizontal plane, midway between the inferior margin of the ribs and the superior border of the iliac crest. Albert[20] reported that if the higher waist circumference cut points were used to diagnose the metabolic syndrome, fewer individuals with metabolic syndrome should be identified than if the lower cut points were used. However, when the NHLBI/AHA definition is used for the United States with the higher or lower cut points, the difference in metabolic syndrome prevalence is relatively small, because abdominal obesity is highly correlated with the other 4 components of the syndrome and because the prevalence of obesity is so high. In addition, a previous study reported that even if the cutoff value of waist circumference was changed, the risk of cardiovascular disease was almost the same[48]. Therefore, measurement difference is not likely to have contributed to the outcome. Fourth, the sample size for examining the combinations of metabolic syndrome components was still insufficient. However, this is the first study of the association between metabolic syndrome and periodontal disease involving a general population.

In conclusion, low HDL cholesterol and metabolic syndrome were positively associated with periodontal disease. Subjects with two or more components of metabolic syndrome had a significantly higher prevalence of periodontal disease. Given the results of this study, a person who has periodontal disease may wish to have themselves checked for metabolic syndrome, and a person with metabolic syndrome may also wish to be checked for periodontal disease.

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## Disclosures

The authors declare that they have no conflict of interests.

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**Supplemental Table 1.**
Relationships between metabolic syndrome with or without low HDL cholesterol as a factor and periodontal status

| | MetS (−) | MetS (+)<br>Low HDLC (+) | MetS (+)<br>Low HDLC (−) |
|---|---|---|---|
| Men | | | |
| Periodontitis (−), n | 224 | 13 | 89 |
| Periodontitis (+), n | 274 | 43 | 129 |
| Adjusted OR (95%CI) | 1 (Ref) | 2.68 (1.40-5.14) | 1.21 (0.87-1.67) |
| Women | | | |
| Periodontitis (−), n | 397 | 54 | 145 |
| Periodontitis (+), n | 285 | 70 | 133 |
| Adjusted OR (95%CI) | 1 (Ref) | 1.84 (1.24-2.72) | 1.25 (0.94-1.67) |

MetS, metabolic syndrome; HDLC, HDL cholesterol; OR, odds ratio; 95%CI, 95% confidence interval
Adjusted for age, smoking status, and drinking status

**Supplemental Table 2.** Periodontal disease and Metabolic Syndrome

| Race | Number of subjects | Age range (years) | Criteria for periodontitis | Criteria for MetS | Odds ratio | Comments and modifying factors | Literature |
|---|---|---|---|---|---|---|---|
| Asia | | | | | | | |
| Japanese | 584 all females | 40-79, mean 55.7 ± 8.8 | Subjects divided into 2 groups; (1) mean pocket depth (PD) < 2 mm and ≥ 2 mm, (2) mean clinical attachment loss < 3 mm and ≥ 3 mm. | NCEP ATP III | 3.3 (1.2-8.8), $p < 0.05$ | The more components of MetS, the higher the OR of having greater PD and CAD. Modifying factors: large waist circumference. Low HDL, high fasting glucose level enhances the strength of the association. | Shimazaki *et al.* (2007)[18] |
| Japanese | 1070 | 40-70, mean 60 | Subjects divided into 2 groups based on CPI: low (code ≤ 3) and high (code 4) | NCEP ATP III | 3 positive components, 2.13 (1.22-3.70) ($p = 0.008$), 4-5 positive components, 2.34 (1.08-5.08) ($p = 0.032$) | Modifying factor: hypertension and low HDL | Kushiyama *et al.* (2009)[9] |
| Japanese | 6421 (4944 males, 1477 females) | 34-77 | PD and CAL measured at MB sites; none/mild if ≤ 3 mm, moderate if 4-5 mm, severe if ≥ 6 mm | NCEP ATP III excluding waist circumferences (used BMI ≥ 25 kg/m$^2$) | Severe periodontitis associated with MetS. 1.35 (1.03-1.77), $p < 0.05$ PD > 4 mm associated with MetS. 1.44 (1.22-1.70), $p < 0.001$ | Sever PD and severe CAL or moderate PD and moderate CAL had significantly higher ORs for MetS. Severe CAL without severe PD was not significantly associated with MetS. Modifying factors: age, alcohol consumption, BMI, tooth brushing | Fukui *et al.* (2012)[26] |
| Japanese | 2370 (1040 males, 1330 females) | 40-79 | PD, CAL | Joint classification (waist circumferences ≥ 90 cm in male, ≥ 80 cm in females | Mean PD ≥ 3 mm or 3.5 mm associated with MetS in females, but not in males | Modifying factor: sex | Furuta *et al.* (2013)[24] |
| Korean | 1046 (457 males, 589 females) | 18-84, mean 42.3 ± 12.2 | CPI | Joint classification (waist circumferences ≥ 90cm in males, ≥ 85cm in females), FGL > 110 mg/dL | CPI (3-4) associated with ≥ 3 positive components of MetS. OR 1.7 (1.22-2.37), $p = 0.002$ | If 3 positive components, OR of having periodontitis 1.53 (1.05-2.23), if 4 or 5 positive components, OR 2.20 (1.28-3.78). Modifying factors: age, sex, smoking, high glucose and hypertension | Han *et al.* (2010)[27] |

(Cont Supplemental Table 2)

| Race | Number of subjects | Age range (years) | Criteria for periodontitis | Criteria for MetS | Odds ratio | Comments and modifying factors | Literature |
|---|---|---|---|---|---|---|---|
| Asia | | | | | | | |
| Korean | 6520 | ≥19 | CPI code ≥3 | NCEP ATP III except abdominal obesity ≥90 cm in males, ≥85 cm in females | OR 1.55 (1.32-1.83) | If <40 years, 1.3 (0.91-1.86), MetS did not associated with periodontitis. If >40 years, significantly associated 1.47 (1.23-1.76). No difference in sex. Modifying factors: age | Kwon *et al.* (2011)[28] |
| Korean | 399 | ≥60, mean 72.3 | CPI code ≥3 | Combination of different classifications: BMI ≥25 b kg/m$^2$, BP ≥140/90 mmHg, FGL ≥126 mg/dL, HG ≥240 mg/dL | If 2 or more MetS components, more likely to have periodontal disease ($p<0.05$) | Subjects with a greater number of MetS components, more likely to have periodontal disease. | Lee *et al.* (2013)[29] |
| Taiwan | 33740 | Control: 50.55±12.93 in male, 49.96±12.43 in females, gingivitis: 47.06±11.78 in male, 48.47±11.48 in female, periodontitis: 53.22±11.15 in male, 54.15±11.08 in female | Periodontal disease defined as combination of the following: tooth mobility, gingival inflammation, periodontal pocketing | NCEP ATP III except waist circumference was modified for cutoff values for Asians (≥90 cm in males, ≥80 cm in females) or BMI ≥27 kg/m$^2$ | MetS associated with periodontitis in females: OR 1.52 (1.41-1.63) $p<0.001$, in males: OR 1.04 (0.96-1.12) $p=0.317$ nonsignificant | Females but not males showed weak associated between MetS and periodontitis. Modifying factor: sex | Tu *et al.* (2013)[30] |
| Europe and the United States | | | | | | | |
| America | 13994 | ≥17 | Moderate periodontitis: two sites, not on the same tooth, with CAL ≥4 mm, or one site with PD >4 mm. Severe periodontitis: if two sites, not on the same tooth, had CAL ≥6 mm and at least one site had PD ≥4 mm | NCEP ATP III | Severe periodontitis and MetS associated. OR 1.74 (1.10-2.76), $p<0.05$ if age >44 years | After adjusting age, if ≥45 years with periodontitis, 2.31× greater chance to have MetS (1.13-4.73). Modifying factor: age | D'Aiuto *et al.* (2008)[10] |
| America | 456 | ≥25 | Severe periodontitis: history of S/R or loose teeth; mild/moderate periodontitis: self-evaluation of own gum condition; no periodontal disease: self-evaluation of having excellent or good gums | AHA/NHLBI | 1.5× more likely to have MetS if severe periodontitis is present | Subjects with severe periodontal disease were 1.5× more likely to have MetS compared with subjects without periodontal disease. Modifying factor: age | Bensley *et al.* (2011)[31] |

(Cont Supplemental Table 2)

| Race | Number of subjects | Age range (years) | Criteria for periodontitis | Criteria for MetS | Odds ratio | Comments and modifying factors | Literature |
|---|---|---|---|---|---|---|---|
| Europe and the United States | | | | | | | |
| America | 200 | Mean 56.8 ± 12.7 | Distance between CEJ and cleft of alveolar bone measured on panoramic radiograph. None or slight bone loss: 1-2 mm, moderate: 3-4 mm, or severe ≥ 5 mm | Modification of NCEP ATP III: 2 or more rather than 3 or more of the criteria outlined in NCEP ATP III | Moderate to severe bone loss association 2.61 (1.1-6.1), $p < 0.05$ | Moderate to severe bone loss significantly more associated with MetS | Nesbitt *et al.* (2010)[32] |
| Sweden | 1016 | 70 | Number of remaining teeth were self-reported | NCEP ATP III | Number of teeth self-reported is less in those with MetS compared with those without MetS ($p = 0.0001$) | Number of teeth is less in those with MetS compared with those without MetS, and in proportion to number of MetS components. Modifying factor: smoking, inflammation | Holmlund *et al.* (2007)[33] |
| France | 255 | 35-74, mean 58 | Moderate periodontitis: two sites, not on the same tooth, with CAL ≥4mm, or one site with PD >4 mm. Severe periodontitis: if two sites, not on the same tooth, had CAL ≥6 mm and at least one site had PD ≥4 mm | NCEP ATP III plus HOMA-IR | $p = 0.05$ | After adjusting confounders, only HOMA index remain associated with severe periodontitis. Modifying factor: increase in % of periodontal pockets and gingival bleeding | Benguigui *et al.* (2010)[34] |
| Australia | 7431 | ≥20 | Periodontitis: mean PD <2.5 mm. Moderate severe periodontitis: mean PD ≥2.5 mm | NCEP ATP III | 4.7 (2.0-11.2), $p < 0.001$, only in females | In females, if 2 or more MetS, the higher OR of having periodontal disease. Modifying factors: abdominal obesity was highest contributing factor for associated between MetS and periodontal disease in both males and females | Andriankaja *et al.* (2010)[35] |

**Supplemental Table 3.** Periodontal disease and metabolic syndrome using domestic criteria

| Number of subjects | Age range (years) | Criteria for periodontitis | Odds ratio | Comments and Modifying factors | Literature |
|---|---|---|---|---|---|
| 246 | 30-64 | CPI code ≥ 3 | 2.1 (1.0-4.5), $p < 0.05$ | Subjects with a fasting blood glucose level ≥ 110 mg/dl were at increased risk of having periodontitis. Modifying factors: sex, age | Yamamoto *et al.* (2007)[8] |
| 2478 (2028 men and 450 women) | 24-60, mean age 43.3 years | CPI code ≥ 3 | If 2 or more MetS components, more likely to have periodontal disease ($p < 0.05$) | If 2 positive components, OR of having periodontitis 1.8 (1.4-2.3), if 3 or 4 positive components, OR 2.4 (1.7-2.7). Modifying factors: sex, smoking habits | Morita *et al.* (2009)[17] |
| 488 (190 men and 298 women) | 40-74 | Saliva occult blood test. Subjects were divided into two groups, screen-positive and screen-negative | 2.49 (1.34-4.63) | Using the screen-negative group as a referent group, metabolic syndrome of the screen-positive group was calculated to be 2.49 (1.34-4.63). Modifying factors: sex, smoking habits | Iwasaki *et al.* (2011)[37] |
| 234 | 80 years old | Subjects divided into 3 groups. 1: severe periodontitis: having 6 or more interproximal sites with clinical attachment level (CAL) ≥ 6 mm and 3 or more interproximal sites with probing depth (PPD) ≥ 5 mm; 2: moderate periodontitis: having 6 more interproximal site with CAL ≥ 4 mm or 6 or more interproximal sites with PPD ≥ 5 mm; 3: no or mild periodontitis: neither moderate nor severe periodontitis | 2.24 (1.14-4.41) | MetS was associated with the presence and severity of periodontitis: OR 2.24 (1.14-4.41). There were no significant associations of each MetS components with periodontitis. Modifying factors: sex | Minagawa *et al.* (2015)[38] |

**Supplemental Table 4.** Relationships between metabolic syndrome using domestic criteria and periodontal status

| Periodontitis | Men | | Women | | Men and Women | |
|---|---|---|---|---|---|---|
| | − | + | − | + | − | + |
| Participants, n | 326 | 446 | 596 | 488 | 922 | 934 |
| Metabolic syndrome Cases, n | 80 | 158 | 58 | 53 | 138 | 211 |
| Adjusted ORs (95%Cis) | 1 (Ref) | 1.72 (1.25-2.37) | 1 (Ref) | 1.12 (0.75-1.09) | 1 (Ref) | 1.43 (1.12-1.84) |

• Adjusted for age, smoking status, and drinking status