

The relationship between periodontitis and metabolic syndrome among a Korean nationally representative sample of adults

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Abstract

Aims: The aim of this study was to examine whether metabolic syndrome (MS) is associated with periodontitis in a representative sample of Korean adults, who were involved in the Fourth Korea National Health and Nutrition Examination Survey (KNHANES).

Materials and Methods: A total of 7178 subjects over the age of 19 years who participated in KNHANES were examined. MS was defined as the definition proposed by the National Cholesterol Education Program Adult Treatment Panel III and the abdominal obesity cut-off line based on Korean Society for the Study of Obesity. The periodontal status was assessed by the Community Periodontal Index. Multivariate logistic regression analysis was carried out adjusting for the sociodemographics, oral health behaviours and status, and health behaviour. All analyses considered a complex sampling design, and multivariate analysis was also performed in the subgroups (age, gender, current smoking status).

Results: Multivariate logistic regression analysis revealed significant associations between MS and periodontitis. After adjusting for all covariates, the adjusted odds ratio (OR) of periodontitis (community periodontal index \geq 3) was 1.55 (1.32–1.83) for MS. In subgroup analysis, periodontitis is associated with MS in subjects over age 40 and the adjusted ORs were higher in females and in the smoker group than in males and in non-smokers.

Conclusions: MS is associated with periodontitis.

Conflict of interest and source of funding statement

The authors declare no conflicts of interest related to this study.

The study was self-supported, but the Korea Center for Disease Control and Prevention provided the data of the Fourth Korea National Health and Nutrition Examination Survey to be used in the study.

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Metabolic syndrome (MS) consists of a cluster of clinical and biological abnormalities that are affected by insulin resistance and promote cardiovascular diseases (CVD) (Benguigui et al. 2010). Several definitions for MS have been proposed by the World Health Organization (WHO) (Alberti & Zimmet 1998), International Diabetes Federation (IDF) (Alberti et al. 2006), European Group for the Study of Insulin Resistance (EGIR) (Balkau et al. 2002), and American Heart Association/National Heart, Lung, and

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Blood Institute (Grundy et al. 2004) as National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III and modified NCEP ATP III) (Expert Panel on the Detection Evaluation, and Treatment of High Blood Cholesterol in Adults 2001).

The prevalence of MS was reported to be higher in developed countries than in developing countries (Cameron et al. 2004). The prevalence of MS in United States was 21.6% in 2003–2004 (D'Aiuto et al. 2008). In Chinese adults, it was 9.8% in men and 17.8% in women (Li et al. 2009). The prevalence in Korean adults was 27.7% in 1998 and 28.1% in 2005 (Park et al. 2010). This relatively high prevalence might be due to the rapidly ageing population in Korea (Korean National Statistical Office, 2005). Prevention, early screening, and early intervention of MS are important for decreasing the morbidity and mortality associated with CVD (Isomaa et al. 2001, Sarti & Gallagher 2006, Bustos et al. 2007), which is a major cause of death globally (WHO, 2007).

Periodontitis is a chronic and longlasting low-grade inflammatory disease (Li et al. 2009) that leads to a breakdown of the connective tissue and bone that anchors the teeth to the jaws (Williams 1990). Periodontitis is one of the most common chronic diseases in the world (Albander et al. 1999). In Korea, the prevalence of periodontitis is 73.4% among adults (Korea Center for Disease Control and Prevention & Ministry of Health and Welfare 2008). Periodontitis is also related to systemic alterations, such as diabetes, rheumatoid arthritis, and osteoporosis (Genco 1996).

Both periodontitis and MS are associated with systemic inflammation and insulin resistance, and these two diseases might be linked through a common pathophysiological pathway (D'Aiuto et al. 2010). Recent studies suggested a potential association between periodontitis and MS (D'Aiuto et al. 2008, Li et al. 2009, Benguigui et al, 2010, Morita et al. 2010). Although MS has become common in Asian countries (Rakugi & Ogihara 2005, Park et al. 2008), few studies have examined the relationship between MS and periodontitis based on a comprehensive, nationwide, and representative survey in Asia.

The aim of this study was to examine whether MS is independently associated with periodontitis using a representative sample of Korean adults adjusted for socio-demographics, health and oral health behaviours, and oral health status.

Materials and Methods

Study design and subject selection

The data included a subset of the Fourth Korea National Health and Nutrition Examination Survey (KNHANES) conducted in 2008 by the Korea Center for Disease Control and Prevention (KCDC). The sampling protocol for the KNHANES was designed to involve a complex, stratified, multistage, prob-

ability-cluster survey of a representative sample of the non-institutionalized civilian population in Korea. The survey was performed by the Korean Ministry of Health. The target population of the survey was all non-institutionalized civilian Korean individuals aged 1 year or older. The survey used stratified multistage probability sampling units based on geographic area, gender, and age, which were determined based on the household registries of the 2005 National Census Registry, the most recent 5-year national census in Korea. Using the 2005 census data, 200 primary sampling units (PSU) were selected across Korea. The final sample set for KNHANES included 4600 households. A total of 7178 subjects aged over 19 participated in KNHANES, but 6520 of the subjects, who participated in a periodontal examination, were examined for MS. A detailed description of the sampling is described in the KNHANES report (KCDC 2008).

Clinical variables

MS

MS was defined based on NCEP-ATP III that was revised in 2005 and abdominal obesity determined was based on the Korean Society for the Study of Obesity guidelines. The waist circumference (WC) criteria for obesity were WC \geq 90 cm in males, and \geq 85 cm in females (Park et al. 2010) according to the IDF's suggestion that the ethnicspecific cut-off values of the WC are appropriate for a diagnosis of MS (Grundy 2006). The other components for a diagnosis of MS are as follows: plasma triglycerides $\geq 150 \text{ mg/dl}$; reduced HDL cholesterol below 40 mg/dl in males, 50 mg/dl in females; high blood pressure \geq 130/85 mmHg or antihypertensive drug treatment; elevated fasting glucose \geq 100 mg/dl or hypoglycaemic drug treatment. The subjects who satisfied at least three of the upper five criteria were assessed as having MS.

Periodontitis

The WHO community periodontal index (CPI) was used to assess periodontitis. Periodontitis was defined as a CPI greater than or equal to "code 3", which indicates that at least one site had a > 3.5 mm (code 4 > 5.5 mm) – pocket. The index tooth numbers were 11, 16, 17, 26, 27, 31, 36, 37, 46, and 47.

A CPI probe that met the WHO guidelines was used (WHO 1997). The mouth was divided into sextants. An approximately 20 g probing force was used. In 2008 KNHANES, 15 trained dentists examined the periodontal status of the subjects. The inter-examiner mean of Kappa value was 0.89 (0.55–1.00) (KCDC 2008).

Covariates

The socio-demographic variables included gender, age, household income, educational level, and childhood background. Household income was the family income adjusting for the number of family members. The educational level was assessed by highest diploma, and subjects' backgrounds were father's economic state and the parents' presence in childhood.

The oral health behaviours included use of dental floss and inter-proximal toothbrush. As health behaviours, alcohol consumption experience and current smoking status were included. According to the current smoking status, the subjects were divided to three groups (non-smokers: those who had never smoked or had smoked fewer than 100 cigarettes in their life, current smokers: those who were currently smoking and had smoked 100 cigarettes or more in their whole life, past smokers: those who had smoked in the past but they stopped smoking at that time).

The oral health status included the number of active caries teeth, number of decayed, missing, or filled permanent teeth, and the number of present permanent teeth.

Statistical analysis

The individual weighted factors were used and the complex sampling design of the survey was considered to obtain the variances. Multivariate logistic regression analyses were applied to examine the relationships between MS and its components and periodontitis. The odds ratios of periodontitis for MS were adjusted for above-mentioned covariates in the logistic model. As the interaction terms of periodontitis with age, gender, and smoking were significant, subgroup analyses were performed to gain estimates stratified according to effect modifiers. We adopted 40 years as cut off, because the prevalence of periodontitis may generally increases rapidly from the age of 40. Statistical analyses were performed using PASW version 18.0 software.

Results

Periodontitis defined as a CPI code ≥ 3 was 32.9% (code 4 was 5.9%). Tables 1, 2, and 3 list the characteristics of the study subjects categorized by the periodontal status.

Table 4 showed the significant associations between MS and periodontitis in the multivariate logistic regression models. Of the five components of MS. three components except for abdominal obesity and high blood pressure showed higher odds ratios (ORs) for periodontitis. The adjusted ORs were 1.55 (95% CI: 1.32–1.83) for MS, 1.38 (95% CI: 1.17-1.62) for elevated triglyceride, 1.34 (95% CI: 1.14-1.56) for reduced HDL-cholesterol, and 1.43 (95% CI: 1.22-1.68) for elevated blood glucose. The results of subgroup analyses were also presented in Table 4. While in the group aged less than 40 years, MS was not associated with periodontitis, in the group 40 years or more, the adjusted ORs for MS were significantly associated with periodontitis. In gender, the adjusted ORs for MS were 1.49 (95% CI: 1.18-1.88) in the male group and 1.66 (95% CI: 1.35-2.03) in the female group. In current smokers, the adjusted OR for MS was 1.69 (95% CI: 1.37-2.07), which was higher than that of the non-smoker group (adjusted ORs: 1.43; 95% CI: 1.10-1.84).

Discussion

In this study, an association was found between MS and periodontitis after adjusting for the socio-demographic variables, oral and general health behaviour, and oral health status. Subjects with high triglyceride and blood glucose and low HDL-cholesterol levels also had significantly higher ORs for periodontitis.

Several studies reported a positive correlation between MS and periodontitis through a cross-sectional survey. Although most of these studies deal with small samples, few studies assessed a nationally representative sample similar to the present study. For example, D'Aiuto et al. (2008) conducted a survey of 13,994 men and women aged 17 years or older among the US population. They found that severe periodontitis is associated with MS in middle-aged individuals. Timonen et al. (2010) performed a survey targeting 8028 people aged 30 years or over in Finland, and reported that MS had a weak association with a periodontitis. This study revealed a stronger associations between periodontitis and MS than those of Timonen's study. This disparity might be due to the differences in the confounders and ethnical backgrounds.

Some studies on MS and periodontitis were implemented over Asian countries

Table 1. Univariate comparisons of the socio-demographic characteristics in subjects with and without periodontitis

	N	o periodontitis		Periodontitis
	n	% (95% CI)*	n	% (95% CI)*
Age $(n = 7178)$	37.79 (3	7.03–38.55) [†]	55.00 (5	4.22–55.79) [†]
Gender	, i i i i i i i i i i i i i i i i i i i	,	,	,
Male	1584	46.7 (44.8-48.5)	1110	54.0 (52.2-55.8)
Female	2464	53.3 (51.5-55.2)	1670	46.0 (44.2-47.8)
Highest diploma ($n = 6803$	3)			· · · · ·
Primary school	509	8.8 (7.7-10.1)	1507	38.1 (35.5-40.7)
Middle school	326	7.6 (6.7-8.8)	444	15.3 (13.8–17.0)
High school	1584	47.2 (44.6-49.8)	728	27.9 (25.9–30.1)
≥University or College	1269	36.3 (33.5-39.2)	436	18.7 (16.5-21.2)
Household income $(n = 69)$	(28) [‡]			
< 25%	492	10.2 (8.5-12.1)	956	24.1 (21.6-26.7)
25-50%	993	25.6 (23.1-28.2)	830	28.7 (26.2-31.3)
50-75%	1165	30.1 (27.8-32.5)	644	24.7 (22.4–27.2)
>75%	1276	34.1 (30.5-37.9)	572	22.6 (19.6-25.9)
Childhood background: fat	her's econom	nic status $(n = 6678)$		
Employed	3211	90.1 (88.9-91.2)	2552	83.9 (82.4-85.4)
Unemployed	96	2.4 (1.9–3.1)	107	3.3 (2.8-4.1)
Parted [§]	314	7.4 (6.5–8.4)	398	12.7 (11.4–14.1)

*Weighted percent and 95% confidence interval.

[†]Weighted mean and 95% confidence interval.

[‡]Household income: monthly average family equivalent income (= monthly average household income/ $\sqrt{(\text{the number of household members})}$.

[§]Father's bereavement, parents' separation, or divorce.

using a non-representative sample. Kushiyama et al. (2009) revealed a positive relationship between MS and periodontitis among 1070 Japanese adults in Miyazaki city. Khader et al. (2008) also reported that patients with MS displayed more severe and extensive periodontitis than subjects without MS in Jordan. A case-control study of Li et al. (2009) in China found that patients with MS had poor periodontal conditions. Han et al. (2010) examined the significant relationship between MS and periodontitis among 1046 adults in the Shiwha-Banwol of Korea. The results of these studies are identical to the present study in terms of the significant association between MS and periodontitis, but the weight of each component in MS contributing to this link was different.

An analysis of the data from 13,710 participants in the NHANES III showed that severe periodontitis was associated with MS in participants aged older than 45 years (D'Aiuto et al. 2008). Han et al. (2010) and Morita et al. (2010) also reported that the association between MS and periodontitis was higher in older subjects, males, and smokers.

Our results showed that periodontitis was associated with MS in subject over age 40 and the association was higher in smokers, which was supported by previous results that showed a positive association. These results, however, showed that periodontitis was associated more strongly with MS in females, which is opposite to those reported elsewhere (Han et al. 2010, Morita et al. 2010). Further studies will be needed to elucidate the gender difference.

When the components of MS were examined separately, the associations of single component of MS were slightly weaker than the association for MS. Of the five components of MS, elevated fasting glucose was the strongest determinants of periodontitis. These results showed similar trends to those of Timonen et al. (2010). As reported previously, high blood glucose has an adverse effect on periodontal health and periodontal infections also have an adverse effect on glycaemic control (Taylor 2001). Recent studies have suggested that adipose tissue secretes a bioactive substance, which may injure the periodontal tissue directly (Saito & Shimazaki 2007). Therefore, the positive relationship between periodontitis and MS may be due to an aggregate of the association of these components

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Table 2. Univariate comparisons between the subjects with and without periodontitis in oral and general health status

	N	o periodontitis]	Periodontitis
	n	% (95% CI)*	n	% (95% CI)*
Active caries $(n = 6681)$	0.8	3 (0.75–0.90) [†]	0.9	01 (0.82–1.00) [†]
DMFT $(n = 6681)$	5.7	'6 (5.57–5.95) [†]	7.2	$(6.85 - 7.55)^{\dagger}$
Present permanent teeth $(n = 6834)$	28.2	$6(28.15-28.37)^{\dagger}$	21.9	$2(21.46-22.37)^{\dagger}$
MS $(n = 6520)$. ,		` ´
No	2844	81.8 (80.0-83.4)	1825	63.1 (60.9-65.2)
Yes	704	18.2 (16.6-20.0)	1147	36.9 (34.8-39.1)
Waist circumference (cm) $(n = 6759)$	79.7	6 (79.23–80.29) [†]	83.6	8 (83.14–84.22) [†]
Normal	2857	79.8 (78.0-81.5)	1995	66.9 (64.4-69.3)
Abdominal obesity [‡]	805	20.2 (18.5-22.0)	1102	33.1 (30.7-35.6)
Triglyceride (mg/dl) $(n = 6614)$	122.39) (110.14–111.53) [†]	154.11	(147.90–160.33) [†]
<150 mg/dl	2743	76.3 (74.6–77.9)	1971	63.7 (61.5-65.9)
$\geq 150 \text{mg/dl}$	862	23.7 (22.1–25.4)	1038	36.3 (34.1-38.5)
HDL-cholesterol (mg/dl) ($n = 6614$)	49.5	4 (49.04–50.04) [†]	46.4	9 (45.91–47.08) [†]
Normal	2139	63.9 (61.7-66.0)	1445	51.9 (49.6-54.3)
Low HDL-C [§]	1466	36.1 (34.0-38.3)	1564	48.1 (45.7–50.4)
High blood pressure $(n = 6836)^{\parallel}$	SBP:	110.84 (110.15-	SBP:	120.12 (119.11–
		111.53) [†]		$121.14)^{\dagger}$
	DBI	P: 73.61 (73.07–	DBI	P: 76.94 (76.29–
		74.16) [†]		$(77.58)^{\dagger}$
No	2991	81.5 (79.9-82.9)	1960	63.8 (61.4-66.1)
Yes	718	18.5 (17.1-20.1)	1167	36.2 (33.9–38.6)
Elevated fasting glucose $(n = 6594)^{\P}$	93.9	0 (93.22–94.57) [†]	102.79	(101.60–103.99) [†]
No	2859	81.3 (79.6-82.9)	1842	62.1 (60.0-64.2)
Yes	733	18.7 (17.1–20.4)	1160	37.9 (35.8-40.0)

*Weighted percent and 95% confidence interval.

[†]Weighted mean and 95% confidence interval.

[‡]Waist circumference ≥ 90 cm in men, ≥ 85 cm in women.

[§]High-density lipoprotein cholesterol (HDL-C) $\leq 40 \text{ mg/dl}$ in men, $\leq 50 \text{ mg/dl}$ in women.

^{||} SBP≥130 or DBP ≥85 mmHg or antihypertensive drug treatment.

[¶]Elevated fasting glucose $\geq 100 \text{ mg/dl}$ or hypoglycaemic drug treatment.

Table 3. Univariate comparisons of the oral and general health behaviours in subjects with and without periodontitis

	N	o periodontitis		Periodontitis
	n	% (95% CI)*	n	% (95% CI)*
Oral health behaviour	s			
Use of floss $(n = 6804)$	4)			
No	3107	84.3 (82.6-85.8)	2939	93.5 (92.2–94.6)
Yes	585	15.7 (14.2–17.4)	173	6.5 (5.4–7.8)
Use of interproximal t	tooth brush (n	= 6804)		
No	3277	89.1 (87.8-90.3)	2878	90.7 (89.4-92.0)
Yes	415	10.9 (9.7–12.2)	234	9.3 (8.0-10.6)
General health behavi	ours			
Alcohol consumption	experience in	a lifetime $(n = 6803)$		
No	380	8.2 (7.2–9.3)	615	15.7 (14.4–17.1)
Yes	3312	91.8 (90.7-92.8)	2496	84.3 (82.9-85.6)
Present smoking statu	s $(n = 6799)$			
Past smoker	130	4.2 (3.5-5.0)	60	1.9 (1.4-2.6)
Current smoker	1239	39.7 (37.9-41.5)	1418	52.2 (50.1-54.2)
Non-smoker	2322	56.2 (54.4–57.9)	1630	45.9 (44.0-47.9)

*Weighted percent and 95% confidence interval.

with periodontitis. In the present study, blood pressure was not associated with periodontitis. Shimazaki et al. (2007) also mentioned that, although many of the participants with higher pocket depth values were taking antihypertensive medications, a strong relationship between blood pressure and periodontitis would not be expected. However, Kushiyama et al. (2009) and Han et al. (2010) reported conflicting results.

Two hypotheses are suggested to explain the relationship between periodontitis and MS (Li et al. 2009). One hypothesis is a cause-effect relationship. Morita et al. (2010) examined the association between periodontitis and the changes in MS components to accumulate evidence of a causal relationship in a cohort study. A total of 1023 subjects showed that the presence of periodontal pockets was associated with a positive conversion of the MS components in a 4vear checkup. Acharya et al. (2010) reported that periodontal therapy produced significant modulation of the serum high-sensitivity C-reactive protein, total leucocytes, serum triglycerides, and HDL, and might benefit individuals affected by both MS and advanced periodontal disease. These studies suggest that preventing periodontal disease may also prevent MS, whereas Shimazaki et al. (2007) proposed that there is a bidirectional association between the components of MS and periodontal disease. Nevertheless, a longitudinal, long term, well-designed cohort study on a largesample will be needed to confirm the causal link between MS and periodontitis.

The other hypothesis was that they share common risk factors. Ohnishi et al. (2009) proposed that the generation of oxidative stress is an underlying systemic condition in both periodontitis and MS. In addition, Bullon et al. (2009) suggested oxidative stress to be a potential common link to explain the relationship between each component of MS and periodontitis.

According to the joint statement from the American Diabetes Association and the European Association for the Study of Diabetes in 2005, MS has been defined imprecisely, there is a lack of certainty regarding its pathogenesis, and there is considerable doubt regarding the substance of MS (Kahn et al. 2005). After this assertion, there has been considerable controversy over the past 5 years regarding the significance of MS. The fundamental questions are still controversial (Cheta 2006. Citrome et al. 2006, Giugliano & Esposito 2006, Psaty et al. 2006) but MS is a widely accepted concept that identifies a centrally obese patient with an increased risk of CVD and diabetes (Eckel et al. 2010). Furthermore, the criteria for diagnosis of MS have been largely harmonized in the recent update of the NCEP ATP III definition and the IDF definition, and the present study followed this definition. In this respect, it would be meaningful to study MS and its association with periodontitis.

	Total	Age g	troup	Ger	ıder	Current	smoker
		< 40 age	≥40 age	Male	Female	Yes	No
Metabolic syndrome	1.55 (1.32–1.83)	1.30 (0.91–1.86)	1.47 (1.23–1.76)	1.49 (1.18–1.88)	1.66 (1.35–2.03)	1.69 (1.37–2.07)	1.43 (1.10–1.8
Abdominal obesity*	1.19(0.99-1.41)	1.01(0.70-1.46)	1.22 (1.00–1.49)	0.93 (0.73–1.19)	1.59 (1.29–1.97)	1.53 (1.23–1.90)	0.92 (0.70–1.2
Elevated triglyceride [†]	1.38 (1.17–1.62)	1.21 (0.84–1.74)	1.31 (1.10–1.57)	1.48 (1.18–1.85)	1.27 (1.00–1.61)	1.22 (0.98–1.52)	1.51 (1.18–1.9
Reduced HDL-cholesterol [‡]	1.34 (1.14–1.56)	1.35 (1.02–1.79)	1.26 (1.06–1.51)	1.42 (1.16–1.74)	1.25 (1.02–1.54)	1.35 (1.12–1.63)	1.33 (1.08–1.0
Elevated blood pressure [§]	1.12(0.94 - 1.34)	0.82(0.49 - 1.35)	1.14(0.96 - 1.36)	1.11(0.87 - 1.41)	1.20 (0.95–1.52)	1.11(0.88 - 1.40)	1.12 (0.88–1.4
Elevated fasting glucose	1.43 (1.22–1.68)	1.18(0.82 - 1.69)	1.32 (1.12–1.57)	1.42 (1.14–1.77)	1.42 (1.12–1.78)	1.48(1.17 - 1.88)	1.35 (1.07–1.7

Waist circumference $\geq 90 \text{ cm}$ in men, $\geq 85 \text{ cm}$ in women. each modifier.

Fasting Triglycerides $\ge 150 \text{ mg/dl}.$

High-density lipoprotein cholesterol (HDL-C) $\leq 40 \text{ mg/dl}$ in men, $\leq 50 \text{ mg/dl}$ in women.

 $SBP \ge 140$ or $DBP \ge 90$ mmHg or antihypertensive drug treatment

Diabetes mellitus, serum fasting glucose ≥126 mg/dl

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> This study had several limitations. The periodontal status was assessed by the CPI. Although CPI is an easier way of evaluating the periodontal treatment needs in a community setting, it can overestimate or underestimate the prevalence of periodontitis because the use of representative teeth includes pseudo pockets (Kingman & Albandar 2002). One of the most important limitations of this study is its cross-sectional design, which makes it impossible to determine the direction of the causal relationship between MS and periodontitis.

> Nevertheless, an association was found between MS and periodontitis after adjusting for various potential confounders, including socio-demographic variables, health and oral health behavioural factors, and oral health status. Most studies did not consider as many confounders as the present study. The confounding factors are not only restricted to the present general health and socioeconomic status but also to the background of the individual subjects as well as to the oral and general health behaviours that could affect the periodontal health and metabolic dysfunction. In addition, this study was carried out comprehensively in a Korean representative population sample.

Conclusions

Periodontitis is significantly associated with MS as defined using the NCEP-ATP III criteria. The underlying biological mechanisms showing a causaleffect relationship between MS and periodontitis remain to be determined through prospective cohort studies.

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Clinical Relevance

Scientific rationale for study: Although an association between periodontitis and MS has been reported in some studies, more studies will be needed to confirm the association. In particular, few studies have examined the relationship between MS and perioGrundy, S. M. (2006) Does the metabolic syndrome exist? *Diabetes care* **29**, 1689–1692.

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dontitis based on a comprehensive, nationwide and representative survey in Asia.

Principle findings: Among a Korean nationally representative sample of adults, this study found that periodontitis is associated with MS and its components.

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Practical implications: Periodontitis is associated with MS in Koreans over age 40 and further studies are needed to determine if there is a cause and effect relationship between these two conditions. This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.