Association between metabolic syndrome and periodontitis: a systematic review and meta-analysis

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Abstract: The aim of the present study was to evaluate the association between metabolic syndrome (MS) and periodontitis (PD), through a systematic review and meta-analysis. Original observational studies assessing the association between MS and PD in adults, published before May 11th (2017), were identified through electronic searches of MEDLINE, EMBASE and Cochrane Library databases. The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guideline was used. For studies to be included, they had to mention the criteria used to diagnose MS and to have used at least one clinical measure to diagnose PD. There was no language restriction. Three reviewers independently identified eligible studies for possible inclusion in the systematic review and meta-analysis. The quality of the studies was evaluated by the Newcastle-Ottawa scale for observational studies. A random model meta-analysis was conducted. The strategies used to investigate heterogeneity were sequential analysis, subgroup analysis, univariate meta-regression and sensitivity analysis. Thirty-three studies met the inclusion criteria for the systematic review, and 26 had enough information to be included in the meta-analysis, totaling 52,504 patients. MS and PD were associated with an odds ratio of 1.38 (95%CI 1.26–1.51; I2 = 92.7%; $p < 0.001$). Subgroup analysis showed that complete periodontal examination (I2 = 70.6%; $p < 0.001$) partially explained the variability between studies. The present findings suggest an association between MS and PD. Individuals with MS are 38% more likely to present PD than individuals without this condition. Prospective studies should be conducted to establish cause and effect relations between MS and PD.

Keywords: Metabolic Syndrome; Periodontal Diseases; Periodontal Attachment Loss; Insulin Resistance; Review Literature as Topic.

Introduction

Periodontitis (PD) is a bacteria-induced chronic inflammatory disease, which destroys the bone and connective tissue that support the teeth. It is estimated that approximately 20 to 60% of the world's population may have some degree of destructive periodontal disease,[1,2,3,4] and that 7.4%, representing 538 million individuals, have more severe forms.[5] The condition is generally diagnosed by a clinical dental examination, since such signs and symptoms as dental mobility, halitosis, altered tooth positioning and

frequent abscesses tend to be noticed by patients only in the final stages of the disease. Patients presenting moderate and severe PD have been found to produce higher systemic levels of inflammatory and immune markers, such as C-reactive protein, interleukin-6, interleukin 1β and tumoral necrosis factor (TNF).[6,7] PD treatment is able to reduce these markers.[8]

The low-grade inflammatory status induced by untreated PD creates a systemic inflammatory phenotype that has been associated with several other systemic diseases/disorders, including cardiovascular diseases,[9] obesity,[10] insulin resistance[11] and metabolic syndrome (MS).[12,13,14,15,16] MS consists of a group of metabolic abnormalities associated with the greater likelihood of developing type 2 diabetes and cardiovascular disease.[17] According to the most recent guidelines issued in 2009 by the International Diabetes Federation (IDF) and the American Heart Association/ National Heart, Lung and Blood Institute (AHA/NHLBI), MS is defined as the combination of the following conditions: increased plasma glucose, hypertension, hypertriglyceridemia, low HDL cholesterol and/or elevated abdominal circumference.[18] Patients must have at least three of these abnormalities to be diagnosed with MS. Its prevalence varies according to the population studied and the criteria used for diagnosis; however, it is estimated that a quarter of the world population has MS. The risk of developing this condition is thought to increase proportionally with age.[19]

The association between MS and PD has become an important topic of research in the scientific literature. The presence of continuous low-grade inflammatory status could lead to the development of insulin resistance and upset the balance of interactions between cytokines and the periodontium.[17,19] PD may also influence one's general health status by affecting the host's susceptibility to systemic diseases resulting from the accumulation of gram-negative bacteria and inflammatory mediators in the bloodstream, both of which lead to inflammation.[11] These features also characterize MS.[17,19,20]

The results of the studies that evaluated the relation between PD and MS are widely discrepant.[12,13,14,15,16,21,22,23] Considering that this relationship is characterized differently by conflicting findings, there is still no consensus on the magnitude of the association between MS and PD. Since systematic reviews are important tools to reconcile these seemingly divergent findings, the aim of the present study was to assess the association between MS and PD through a systematic review and meta-analysis of observational studies.

Methodology

Focused question

Is there an association between metabolic syndrome and periodontal disease demonstrated in observational studies? The PECO strategy for the research question was: in patients diagnosed with periodontal disease and/or metabolic syndrome, the exposure was the presence of PD and/or MS, compared with patients with no PD and/or no MS. The outcome was any measure of prevalence of PD and MS.

Search strategy

The authors undertook a systematic review to locate original studies on the association between PD and MS. The study protocol was approved by the Research Committee of UFRGS (Study 22842). Observational studies were identified, focusing on participants diagnosed with PD and MS. The outcome was PD and/or MS, since cross-sectional studies have no temporal component, and do not allow both directions of the association to be investigated. The present systematic review was conducted based on guidelines established for meta-analyses of observational studies [24] and is presented according to the PRISMA Statement.

Electronic databases were systematically searched for scientific articles published before May 11th, 2017, which evaluated the association between MS and PD. The search was conducted in MEDLINE (accessed via PubMed), EMBASE and the Cochrane Library, and used the following keywords and MeSH terms (*): periodontal attachment loss* *OR* periodontics* *OR* gingivitis* *OR* periodontal diseases* *OR* gingival bleeding *OR* periodontitis* *AND* metabolic syndrome x* *OR* metabolic syndrome *OR* syndrome x *OR* plurimetabolic. There was no language restriction. Articles in Chinese, Polish and Persian were translated with online translation software.

Relevant unpublished studies were located by reviewing abstracts in the annals of main scientific events in the field since 2006. The proceedings of

the following conferences were searched: EuroPerio, promoted by the European Federation of Periodontology; IADR *General Session*, promoted by the International Association for Dental Research; AAP *Annual Meeting*, promoted by the American Academy of Periodontology; AHA *Scientific Sessions*, promoted by the American Heart Association; the ADA *Scientific Session*, promoted by the American Diabetes Association; and the EASD *Annual Meeting*, promoted by the European Association for the Study of Diabetes. The reference lists of the studies included in the review were also searched.

Two reviewers (MLM and MM) independently identified eligible studies for possible inclusion in the systematic review and meta-analysis, based on their titles and abstracts. The articles whose abstracts were selected were retrieved for full text evaluation. The studies selected for detailed analysis by these two investigators (MLM and MM) had a kappa agreement of 0.95. Disagreements were settled by a third investigator (RVO).

Studies were considered eligible when meeting the following criteria: original epidemiological study, observational, cross-sectional, case-control, or cohort design, adult sample, use of at least one clinical diagnostic criterion for PD that was clearly defined to warrant reproducibility, and clearly defined criteria for the diagnosis of MS. The studies excluded from the analysis, and the reasons for their exclusion, are reported in Figure 1.

Data extraction

The data were extracted independently by two investigators (MLM and PW), and included the participants' age, gender and smoking status, nature of the experimental design, the diagnostic criteria used for PD and MS, total number of participants, number of participants with PD and MS, and study outcomes.

Quality assessment

The quality of the studies was evaluated using the Newcastle-Ottawa scale[25] for observational studies. The scale assigns a score of zero to nine stars to each article, whereby a greater number of stars indicate a higher quality study.

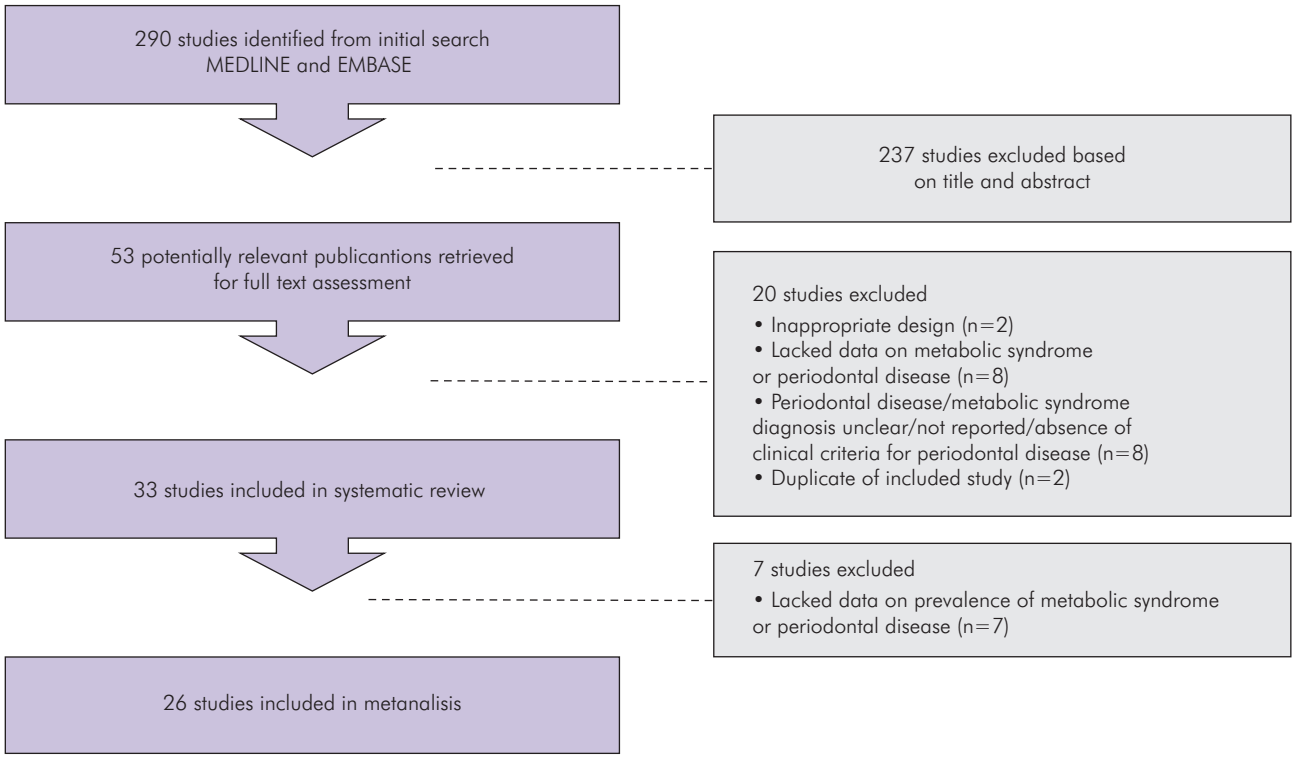

Figure 1. Flowchart of the search for studies, their selection and inclusion.

Statistical analysis

The general effect size was calculated using the reported PD and MS prevalence rates. Baseline values were used for cohort and case-control studies. When these data were not available, the authors were contacted by email. Random effect models were used in the analyses to account for between-study variability. Four strategies were used to investigate heterogeneity, considered high whenever I^2 was greater than 50%.[26] The first strategy involved univariate meta-regression, performed to assess the effect of age, gender and smoking status on estimates of heterogeneity. The second step involved successive removal of each study, so that its impact on I^2 values could be observed. In the third step, a subgroup analysis took into account the periodontal examination and the MS diagnosis criteria. The fourth and last step of the heterogeneity analysis involved the sensitivity analyses, which included only those studies that received scores of eight or nine stars on the Newcastle-Ottawa scale.[27] The possibility of publication bias was evaluated using a funnel plot of the effect size plotted against the standard error of each trial. Begg's and Egger's tests were used to evaluate funnel plot asymmetry, with significant publication bias defined as a p-value < 0.1. The analyses were performed using *STATA* software (version 12; Stata Corp, College Station, USA).

Results

The electronic search retrieved 290 articles from PubMed and EMBASE. No additional articles were found in the Cochrane Library or in any other database searched. Two hundred and thirty-seven studies were excluded based on titles and abstracts, resulting in 53 articles for full-text evaluation. A total of 33 studies met the eligibility criteria (29 cross-sectional, two case-control and two cohort studies, totalizing 52,504 participants; Figure 1) and were included in the systematic review, and 26 were included in the meta-analysis. Seven studies were not included in the meta-analysis, because there was no prevalence data for PD and/or MS.[28,29,30,31,32,33,34]

Table 1 describes the studies included in the review. The articles were published between 2007 and 2017, and most were conducted in Asian countries. PD was diagnosed by a complete periodontal examination in seventeen studies,[12,23,28,31,32,33,35,36,37,38,39,40,41,42,43,44,45] and by a partial periodontal examination in sixteen studies.[13,14,15,16,22,29,30,34,46,47,48,49,50,51,52,53] Concerning the definition criteria for PD, eleven studies[12,14,15,22,29,30,34,49,50,51,52] used the Community Periodontal Index (CPI),[54] and seven studies[23,37,40,42,43,45,47] used the classification system proposed by Page and Eke.[55] The remaining fifteen studies established other diagnostic criteria for PD.[13,16,28,31,32,33,35,36,38,39,41,44,46,48,49] Thirteen studies diagnosed MS using the National Cholesterol Education Program - Adult Treatment Panel III (NCEP ATP III) criteria,[12,13,15,16,22,23,28,32,33,37,46,49,51] ten used the 2005 IDF criteria,[29,30,35,38,39,40,41,42,47,48] four used both the IDF 2009 and AHA/NHBLI 2009 criteria,[14,36,50,52] three used the IDF 2009 criteria [44,45,53] and three studies used other classification criteria.[31,34,43] Table 2 shows the quality assessment of the included studies. Fifteen studies scored seven or more stars, indicating that 45.5% of the studies had very good quality. All the studies controlled the confounding variables. The most commonly controlled factors were age, gender and smoking habits. No article presented poor quality according to the Newcastle-Ottawa scale.

The estimated PD prevalence ranged from 5.77% to 92.89%, whereas the MS prevalence ranged from 5.22% to 83.21%. The meta-analysis revealed a positive association between MS and PD, with an odds ratio (OR) of 1.38 (95%CI 1.26–1.51; I^2 = 92.7%; p heterogeneity < 0.001) (Figure 2). Meta-regression showed that age explained 22% of the heterogeneity of the results (p = 0.01), whereas gender (p = 0.09) and smoking status (p = 0.40) failed to explain heterogeneity. In addition, none of the studies in itself could explain the heterogeneity when rerunning the meta-analysis by excluding one study at a time. Subgroup analyses were conducted by dividing the studies according to periodontal examination (complete or partial) or by the criteria used to define MS. When PD was diagnosed by a complete dentition examination, an OR of 1.16 (95%CI 1.08 –1.25; I^2 = 70.6%) was obtained (Figure 3). Studies that used a partial periodontal examination showed an OR of 1.58 (95%CI 1.38–1.82; I^2 = 90.8%). The magnitude of association between the two conditions, according to the MS criteria used, was 1.38 (95%CI

Table 1. Descriptive data of the studies included in the systematic review

Author, Year Country of Origin	Study Design	Sample (n)	Mean Age (years)	Male (%)	Current Smokers (%)	Periodontal Examination Protocol	Criteria for Metabolic Syndrome	Outcome	Measures of Association* OR or RR (95%CI)
Borges 2007 Brazil	Cross-sectional	318	57	46.2	64.3	Partial	NCEP ATP III	MS	Association between PD† and MS‡ OR 1.11 (0.67-1.83)
Shimazaki 2007 Japan	Cross-sectional	584	55.7	zero	6.7%	Partial	NCEP ATP III	PD	Women with mean PPD ≥ 2mm: OR 4.7 (2.4- 9.7) Women with mean CAL≥ 3mm: 3.3 (1.2- 8.8)
D´Aiuto 2008 USA	Cross-sectional	13,677	40.7	62.0	30.6	Partial	IDF 2005	MS	Association between PD and MS: Moderate PD: OR 1.07 (0.84-1.36) Patients aged >44 years OR 1.06 (0.83-1.34); for non-smokers OR 0.91 (0.56-1.48) Severe PD: OR 1.45 (0.91-2.33) Patients aged >44 years OR 1.74 (1.10-1.76); for non-smokers OR 2.31 (1.13-1.73)
Khader 2008 Jordan	Cross-sectional	156	47.2	35.9	41.0	Complete	NCEP ATP III	PD	Association between MS and PD: PPD and CAL were 2.2mm and 0.9m, respectively, greater in Individuals with MS as opposed to those without the condition.
Kowalski 2009 Poland	Cross-sectional	380	42.0	67.9	Not determined	Partial	IDF 2005	MS	Direct association between MS and PD was not described.
Kushiyama 2009 Japan	Cross-sectional	1,070	63.3	26.7	9.2	Complete	NCEP ATPIII	PD	Association between MS and PD: OR 2.13 (1.22-3.70)
Li 2009 China	Case-control	208	60.9	56.7	20.2	Complete	IDF 2005	MS	Association between MS and PD: OR for % CAL ≥3 and MS tertiles: 0-33 OR 6.91 (1.07-44.77) 33-67 OR 9.89 (1.50-65.24) 67-100 OR 15.60 (2.20-110.43)
Morita 2009 Japan	Cross-sectional	2,478	43.3	81.8	32.1	Partial	Modified (Japanese) IDF 2005¶	MS	Association between MS and PD: OR of 2.40 (1.70-2.70)
Andriankaja 2010 USA	Cross-sectional	7,431	40.45	47.32	26.77	Partial	NCPEP-ATPIII	PD	Association between MS and PD: OR 2.10 (1.20 -3.70) In men, OR 1.00 (0.60 -1.70) In women OR 4.70 (2.00 -11.20).
Benguigui 2010 France	Cross-sectional	255	57.9	54.9	19.2	Complete	NCEP ATPIII	PD	Association between MS and PD: Moderate: OR 1.54 (0.59-4.01) Severe: OR 1.97 (0.74-5.23)

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Han 2010 South Korea	Cross-sectional	1,046	42.3	43.7	26.5	Partial	AHA/NHBLI and IDF 2009	PD	Association between MS and PD: OR 1.70 (1.22-2.37)
Morita 2010 Japan	Retrospective Cohort	1,023	37.1	71.0	31.3	Partial	Modified (Japanese) IDF 2005 **	MS	Association between PD and MS: OR 1.60 (1.10- 2.20); individuals with PD presented with at least one symptom of MS after 4 years of follow-up.
Timonen 2010 Finland	Cross-sectional	2,050	46.0	39.2	Zero	Complete	WHO	PD	Association between MS and PD: RR of 1.19 (1.01- 1.42) for PPD ≥ 4 RR of 1.5 (0.96- 2.36) for PPD ≥ 6
Bracho 2011 Venezuela	Cross-sectional	292	48.3 % 30-49 years old	42.4	Not reported	Partial	AHA/NHBLI and IDF 2009	MS	Descriptive analysis, association not reported.
Chen 2011 Taiwan	Cross-sectional	253	58.8	46.2	29.6	Partial	NCEP ATP III	MS	Association between PD and MS: OR 2.73 (1.29-5.79)
Li 2011 China	Cross-sectional	59	57.8	42.4	6.8	Complete	IDF 2005	atherosclerosis	Primary outcome was atherosclerosis; direct association between MS and PD was not described.
Kwon 2011 Korea	Cross-sectional	7,178	45.6	37.5	37.0	Partial	NCEP ATP III	PD	Association between PD and MS: OR 1.55 (1.32-1.83)
Fukui 2012 Japan	Cross-sectional	6,421	43.4	76.9	25.1	Partial	NCEP ATP III	MS	Association between PD and MS: Moderate OR 1.25 (1.05-1.49) Severe OR 1.32 (1.01-1.71)
Yu 2012 China	Cross-sectional	903	62.6	50.5	20.2	Complete	IDF 2005	PD	Association between PD severity and MS: OR 1.524 (1.066-2.328)
Sora 2013 USA	Cross-sectional	283	55.3	24.0	42.0	Complete	NCEP ATP III	PD	Association between MS and PD: Sites with PPD ≥5mm: RR 2.18 (0.98 – 4.87) Sites with CAL ≥ 6mm : RR 2.77 (1.11 – 6.93)
Furuta 2013 Japan	Cross-sectional	2,370	59.5	43.9	Not described	Complete	NCEP ATP III	PD	MS and PPD >3.0mm Women: OR 3.06 (1.42-6.59) Men: OR 1.32 (0.75–2.34) MS and PPD >3.5mm Women: OR 3.60 (1.30–12.61) Men: OR 1.21 (0.59–2.49)
Thanakun 2014 Taiwan	Cross-sectional	125	47	42.4	8.8	Complete	AHA/NHBLI and IDF 2009	PD	Association between MS and PD: CAL>4mm: OR 3.60 (1.34-9.65) PPD> 4mm+ BOP> 10% sites: OR 6.94 (1.62-29.80)
LaMonte 2014 USA	Cross-sectional	653	65.5	zero	2.1	Complete	NCEP ATP III	MS	MS was associated with supragingival plaque OR 1.47 (1.00-2.16) MS and PD (criteria 1) Severe: OR 1.02 (0.62, 1.68) MS and PD (criteria 2) Severe: OR 1.11 (0.71, 1.75)

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Alhabashneh 2015 Jordan	Cross-sectional	280	53.8	50.7	21.8	Complete	IDF 2005	PD	Association between MS and PD: OR 3.28 (1.30-8.30)
Gomes-Filho 2015 Brazil	Cross-sectional	419	59	38.2	29.8	Complete	IDF 2005	MS	Association between PD and MS: Diagnosis of periodontitis: 0.98 (0.62 - 1.53) Severe periodontitis: 2.11 (1.01 - 4.40)
Kim 2015 Korea	Cross-sectional	6,620	60.7 63.0	47.4	16.6	Partial	AHA/NHBLI	PD	Descriptive analysis, association not reported.
Minagawa 2015 Japan	Cross-sectional	234	80	47.4	5.5	Complete	Modified (Japanese) IDF 2005¶	PD	Association between MS and severity of PD: OR 2.10 (1.03-4.28)
Safavi 2015 Iran	Cross-sectional	834	15-75	Not described	Not described	Partial	NCEP ATP III	PD	Association between PD and MS: OR 1.58 (1.1-2.2)
Chen 2016 China	Cross-sectional	303	34.9	100	31	Partial	IDF 2009	MS	Descriptive analysis, association not reported.
Jaramillo 2016 Colombia	Case-control	651	27-84	36.1	20.1	Complete	AACE 2003	PD	Association between PD and MS: OR 2.72 (1.09–6.79)
Kaye 2016 USA	Cohort	760	61	100	3.0	Complete	IDF 2009 NCEP ATP III	MS	Association between MS and PD: PPD ≥5 mm: OR 1.37 (1.14 to 1.65) CAL ≥5 mm: OR 1.19 (1.00 to 1.41)
Musskopf 2016 Brazil	Cross-sectional	363	18-81	36.1	44.1	Complete	IDF 2009	MS	Association between MS and Severe PD: PR 1.62 (1.13–2.34)
Kikui 2017 Japan	Cross-sectional	1,856	66.4	41.6	9.8	Partial	AHA/NHBLI and IDF 2009	PD	Association between PD and MS components: Three components: OR 1.42 (1.03-1.96) Four components: OR 1.89 (1.31-2.73)

*Adjusted for confounding factors; †PD: periodontitis; ‡ MS: metabolic syndrome; §CAL: clinical attachment loss; ‖PPD: periodontal pocket depth; ¶IDF 2005 criteria modified for Japanese patients: 2005 IDF criteria, considering abdominal circumference values of ≥90 cm for women and ≥ 85 for men (MATSUZAWA, 2005).

Table 2. Newcastle-Ottawa quality assessment scale adapted to observational studies.

Study	Selection	Comparability	Outcome
Borges, 2007	*	*	**
Shimazaki, 2007	**	**	**
D'Aiuto, 2008	****	**	**
Kahder, 2008	***	*	**
Kowalski, 2009	**	*	*
Kushiyama, 2009	*	**	**
Li, 2009	**	*	**
Morita, 2009	**	*	**
Adriankaja, 2010	***	**	**
Benguigui, 2010	****	**	**
Han, 2010	***	**	**
Morita, 2010	**	**	**
Timonen, 2010	***	*	*
Bracho, 2011	**	*	*
Chen, 2011	**	**	*
Li, 2011	**	*	*
Kwon, 2011	**	**	**
Fukui, 2012	***	**	***
Yu, 2012	**	**	**
Sora, 2013	***	**	***
Furuta, 2013	****	*	**
Thanakun, 2014	**	*	*
La Monte, 2014	****	**	**
Alhabashneh, 2015	***	**	***
Gomes-Filho, 2015	***	**	***
Kim, 2015	***	*	**
Minagawa, 2015	***	**	**
Safavi, 2015	***	*	**
Chen, 2016	***	*	**
Jaramillo, 2016	***	**	**
Kaye, 2016	***	**	**
Musskopf, 2016	***	**	**
Kikui, 2017	***	**	**

Scale ranges between zero and nine stars. Highest quality studies awarded maximum of four stars for selection, three stars for outcome and two stars for comparability.

1.19–1.61; I^2 = 91.3%) for NCEP ATP III, 1.28 (95%CI 1.07–1.53; I^2 = 85.9%) for IDF 2005, and 1.49 (95%CI 1.22–1.82; I^2 = 93.7%) for the IDF 2009 criteria (Figure 4). The authors also evaluated if study quality could be responsible for the heterogeneity observed. The evaluation of six studies with higher scores in the Newcastle-Ottawa quality assessment scale[16,23,37,41,42,47] did not decrease the heterogeneity (I^2 = 81.4 %; $p < 0.001$).

There was evidence of publication bias, as demonstrated by the funnel plot, Egger's regression test ($p = 0.03$) and Begg's test ($p = 0.005$; Figure 5).

Discussion

The present findings suggest that individuals with MS are 38% more likely to have PD than individuals without this condition. This meta-analysis was associated with significant heterogeneity, which may be attributed to variability across the studies, in regard to PD diagnosis (complete *vs.* partial dental examination). Our results corroborate those of the single meta-analysis, which also assessed the association between MS and PD, and which reported an OR of 1.90 (95%CI 1.54–2.34).[21] The main limitation of this meta-analysis was the inclusion of studies with PD diagnosed by both clinical and radiographic methods. Considering that low-grade inflammatory status accounts for the biological plausibility of the relationship between MS and PD, the clinical examination should be preferred in this scenario, since the presence of inflammation in periodontal tissues cannot be assessed by radiologic methods. Four studies included in the previous systematic review[21] were not included in the present study, because they used radiographic methods for PD diagnosis,[56,57] or lacked information regarding PD or MS diagnosis criteria.[58,59] The authors considered this limitation and performed a subgroup analysis, dividing the studies into two categories: those with secure PD diagnosis, defined by the presence of severe PD defined both clinically and radiographically, and those with insecure PD diagnosis, and less severe or not well-defined cases in the original study.

Several studies in the literature have investigated the relationship between MS and PD. However,

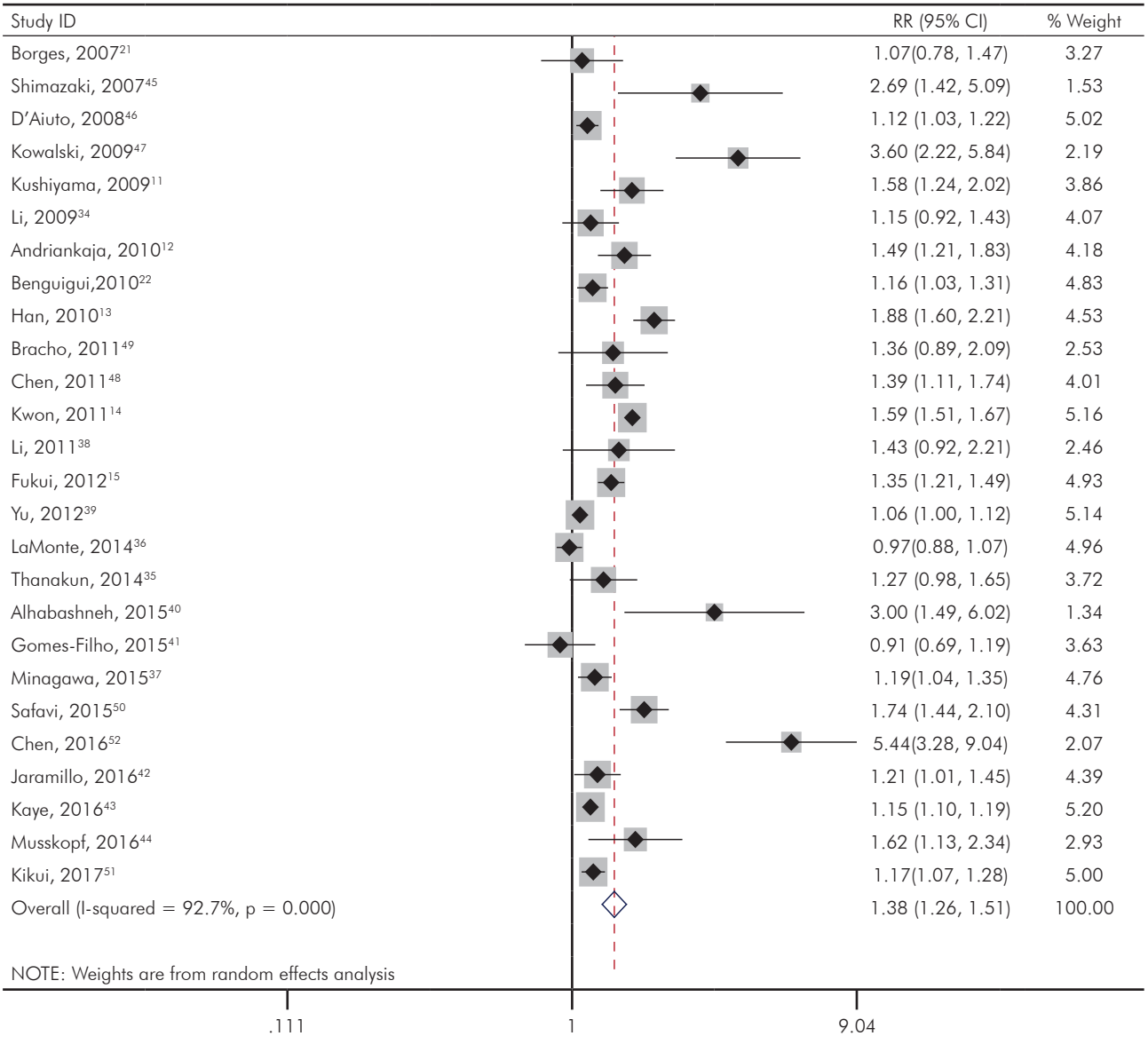

Figure 2. Meta-analyses of the association between periodontal diseases and metabolic syndrome.

the results of these studies have been widely discrepant. Whereas a number of them have reported positive associations between these two conditions,[12,13,14,15,16,21] other investigations have found no relationship between them[22,23]. Reasons for the variability in results include differences in diagnostic criteria for PD and MS, the involvement of untrained examiners in diagnosing PD, the improper control of confounding factors and the presence of selection bias.

Our meta-analysis showed significant heterogeneity, which was explored by several methods. A decrease in heterogeneity was observed when only studies using complete dental examination were considered (I^2 for all studies: 92.7% and for complete dental examination: 70.6%), indicating that studies using complete periodontal examination presented more reliable estimates. The higher variability found in studies using partial dental examination (I^2 = 90.8%) may be attributed to erroneous diagnosis of these individuals. The extension and severity of PD should be assessed by a full six-site examination, considered the gold standard for PD.[60] Half of the studies conducted partial examinations, which are known

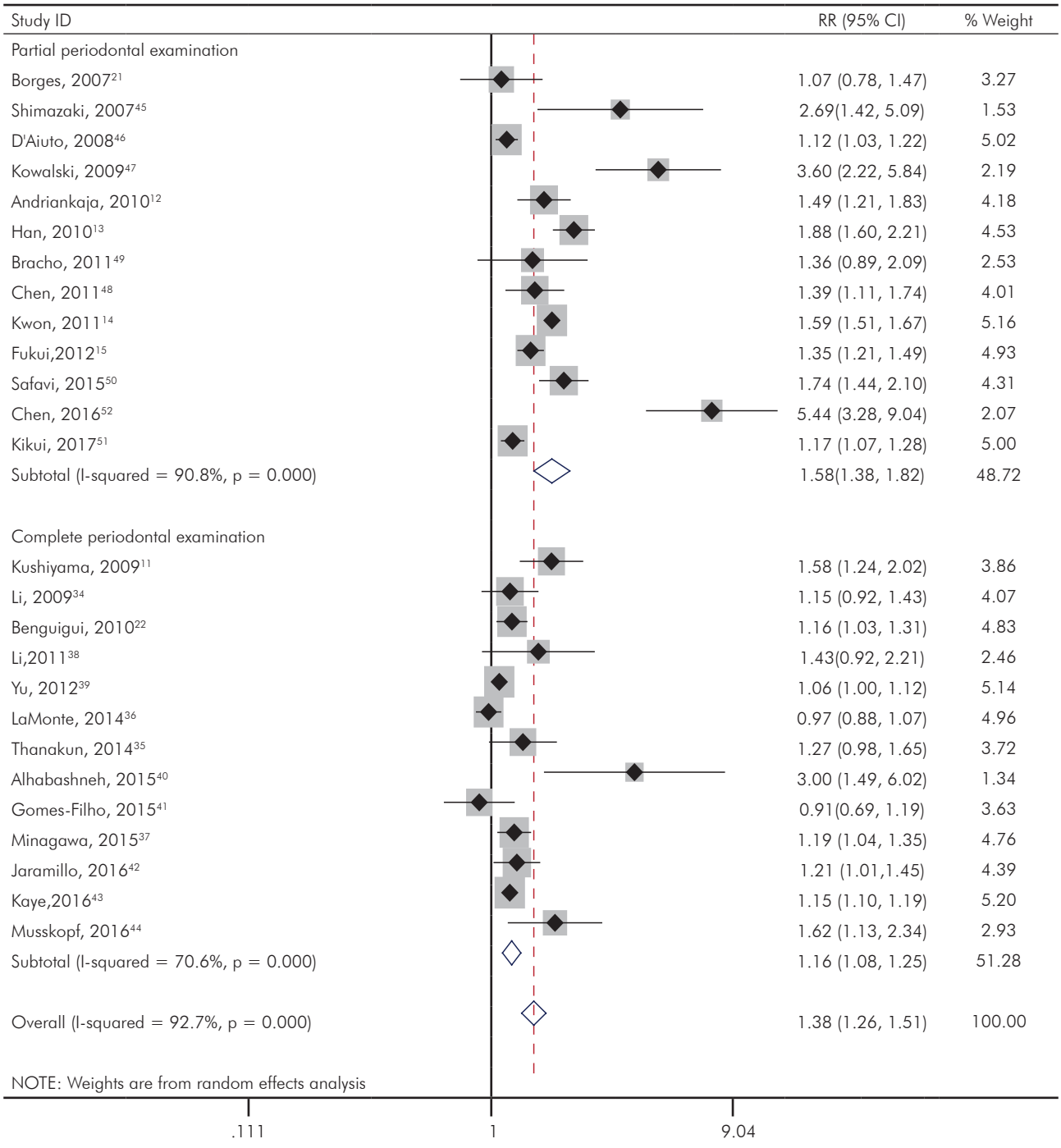

Figure 3. Subgroup analyses with complete and partial periodontal examination.

to underestimate the prevalence of PD.[60] In addition to variability in the examination protocol used to diagnose PD, the criteria used to detect this condition differed across the studies. Eleven studies used CPI criteria to diagnose the disorder. The Community Periodontal Index of Treatment Needs (CPITN)[54] was initially developed to assess the treatment needs of patients with PD, and requires ten teeth to be checked for gingival bleeding, supra- and subgingival calculus and periodontal pockets (classified according to size, namely those measuring between 4 and 5 mm and those measuring 6mm or more). WHO recommendations were

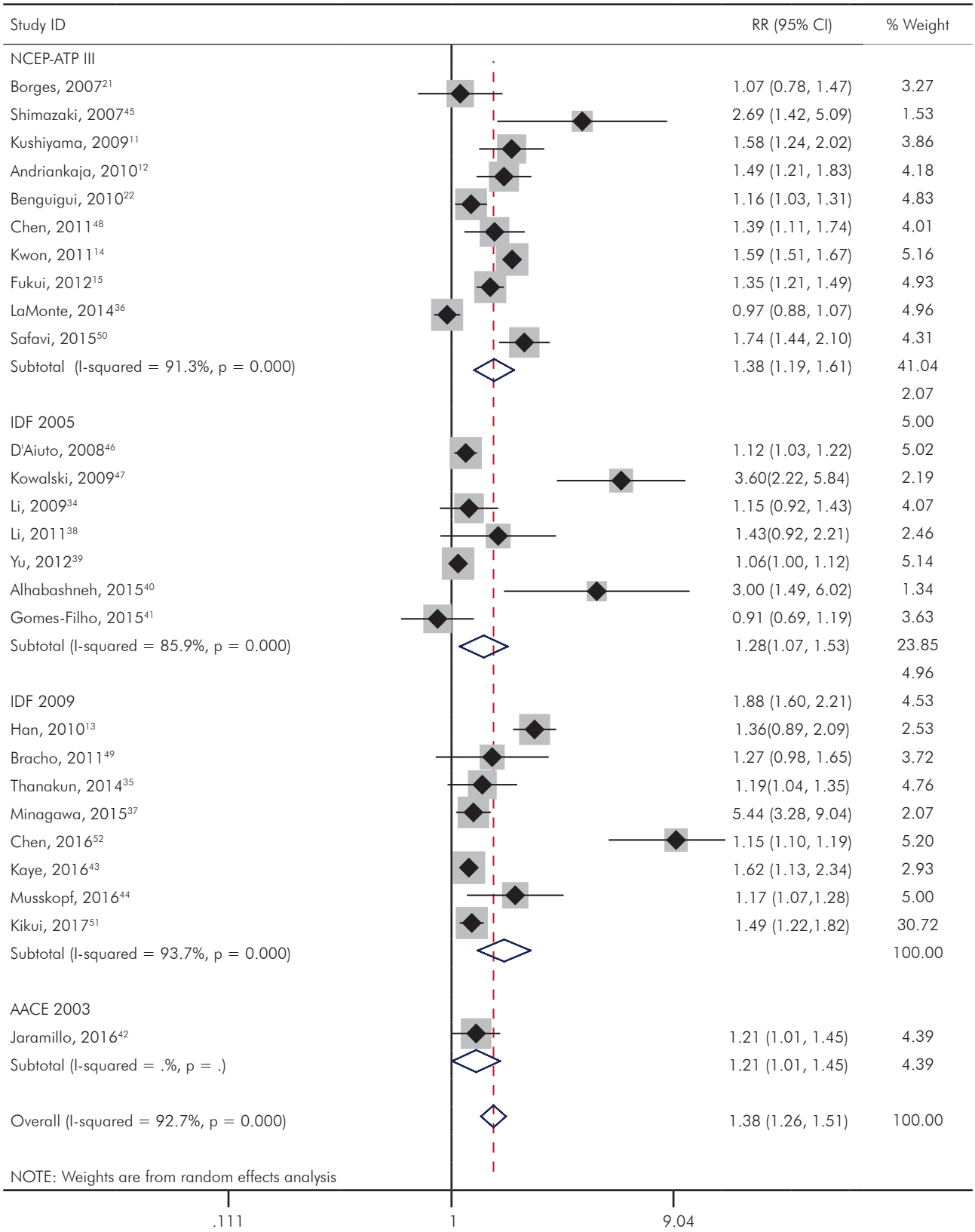

Figure 4. Subgroup analyses with criteria used for metabolic syndrome diagnosis.

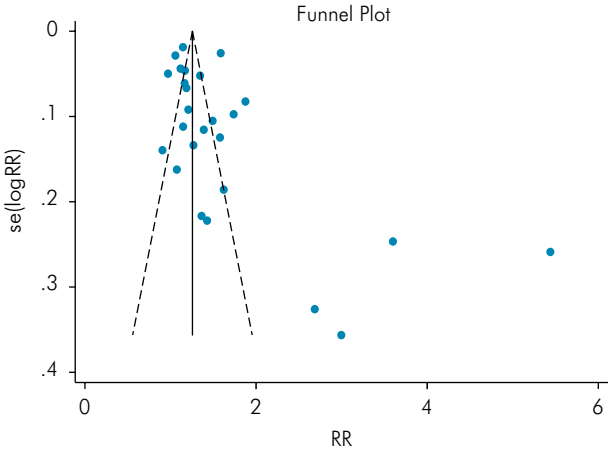

Figure 5. Funnel plot to investigate publication bias.

later amended to include the required measurement of periodontal attachment loss, leading to the renaming of the diagnostic index as CPI (Community Periodontal Index). Although the CPI was not initially designed for use in epidemiological studies, it is widely used in this type of research, although it has proved deficient in assessing the periodontal conditions of several populations reliably.[61] This low reliability may be attributed to its nature as a partial exam, and of investigating symptoms in a hierarchical sequence.

It is reasonable to think that different MS diagnostic criteria could account for the variability in the studies. For example, although the NCEP ATP III criteria are used by a number of studies, they do not account for population differences in body composition when defining abdominal circumference cut points. The existence of documented differences between the body composition of individuals of different ethnicities[62] requires population-specific visceral fat cut-offs to be established, as suggested by the IDF and AHA/NHBLI in 2005.[63] In fact, the 2009 guidelines set in consensus by these institutions established population-specific abdominal circumference cut points.[18,19] NCEP ATP III criteria may underestimate the prevalence of MS in some populations, as has been found in some studies of Asian individuals[12,15,16,49] for whom specific cut points were later recommended.[63,64] However, the variability among studies was not explained by the different MS diagnostic criteria used in the present study.

In addition to investigating the association between PD and MS, some authors also studied the association between PD and specific features of MS. When analyzing the factors separately, the results ranged from the absence of an association to an adjusted OR up to 1.8 (95%CI 1.2–2.8) for elevated abdominal circumference,[46] 2.20 (95%CI 1.40- 3.60) for low HDL cholesterol,[46] 1.59 (95%CI 1.20–2.11) for hypertension,[12] 2.20 (95%CI 1.3–3.9) for alterations in glucose homeostasis,[46] and a raw OR of 1.38 (95%CI 1.17–1.62) for hypertriglyceridemia.[15] Since these results are similar to those found for MS by these and other authors,[21] the discussion regarding the relevance of the syndrome persists. The issue of whether MS is more than a combination of its individual components remains controversial.[65] Nevertheless, treatment for one of these individual conditions could have an effect on the other, thus enhancing the treatment benefits and optimizing the effects of the intervention on the patient's health.

The nature of the present review, with the inclusion of mainly cross-sectional studies, may be considered a limitation of this meta-analysis, since no cause and effect relations could be established between the two conditions. It should also be acknowledged that unpublished studies and individual studies with quality limitations may still be relevant, despite the best efforts to conduct a broad search, and despite the lack of statistical evidence of bias.

Conclusion

In conclusion, considering its limitations, this systematic review with meta-analysis suggests an association between MS and PD. Further research in this field could include prospective studies conducted to establish cause and effect relations between these two conditions, and whether specific treatments could influence the development of both conditions.

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