Systematic Review and Meta-Analysis

Medicine®

OPEN

Salivary matrix metalloproteinase (MMP)-8 as a biomarker for periodontitis

A PRISMA-compliant systematic review and meta-analysis

Lin Zhang, MSc, RN[a], Xiue Li, RN[b], Hong Yan, RN[a], Lei Huang, PhD[c,*]

Abstract

Background: Salivary matrix metalloproteinase (MMP)-8 is currently considered to be one of the most promising biomarkers for early diagnosis of periodontitis, however, several recent studies showed conflicting results.

Objective: To determine the salivary matrix metalloproteinase (MMP)-8 levels between periodontitis patients and healthy individuals, and to assess its diagnostic value in periodontitis.

Methods: Literatures were searched on PubMed and Embase databases up to August 2017, for articles reporting salivary MMP-8 levels between periodontitis patients and health controls with the data of means ± standard deviation (SD). Methodological quality was assessed by the Newcastle Ottawa scale (NOS). Standard mean differences (SMDs), heterogeneity, and publication bias were assessed by Stata 13.0 software.

Results: A total of 10 studies including 485 periodontitis patients and 379 healthy controls that met the preset inclusion criteria were included, the qualities of these studies were either good (n = 7) or moderate (n = 3). Eight studies showed salivary MMP-8 levels were higher in periodontitis patients compared with healthy controls ($P < .05$), while 2 studies showed opposite results ($P > .05$). The pooled SMD was 1.195 (95% CI: 0.720–1.670), with I^2 of 89.3%, indicating high heterogeneity. Funnel plot showed publication bias existed.

Conclusion: Our meta-analysis showed that salivary MMP-8 levels were significantly higher in periodontitis patients compared with healthy controls overall. Due to the heterogeneity and publication bias of included studies, further high quality studies are still needed to verify the conclusion.

Abbreviations: IL = interleukin, MMP = matrix metalloproteinase, NOS = Newcastle Ottawa scale, PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses, SD = standard deviation, SMDs = standard mean differences, TNF-α = tumor necrosis factor-α.

Keywords: biomarker, matrix metalloproteinase (MMP)-8, meta-analysis, periodontitis, salivary

1. Introduction

Periodontitis is an inflammatory disease caused by bacterial infection, with the characteristics of periodontal damage, alveolar bone resorption, and eventually tooth loss.[1] It is generally considered to be one of the most common diseases worldwide, with a prevalence of 15% to 20%.[2] Of greater concern, periodontitis has been shown to be associated with other serious diseases, such as coronary heart disease, head and neck carcinoma, and chronic obstructive pulmonary disease.[3–5] Therefore, early detection and intervention of periodontitis is of great importance. Differentiating destructive periodontitis patients from healthy individuals is simple at professional level, which mainly rely on clinical diagnostic criteria such as probing depth, attachment level, bleeding on probing, plague index, and radiographic assessment.[6] However, the early stage of initiation and/or progression remains a challenge for dentist based on the above clinical diagnostic criteria.[7] Saliva has the advantages of being easily and noninvasively collected, thus biomarkers from saliva for early detection of periodontitis are desirable.

In the past few years, great efforts have been made to explore these biomarkers. As periodontitis is an inflammatory response, the inflammatory process will lead to increased secretion of pro-inflammatory cytokines such as interleukin (IL)-1α, IL-1β, IL-6, and tumor necrosis factor-α (TNF-α).[8] Following this, neutrophils release a variety of enzymes such as matrix metalloproteinase (MMP), and inflammatory mediators. Biomarker detections from saliva are noninvasive, easily accessible, and economically friendly, and several types of salivary biomarkers have been shown to be associated with both oral diseases and systemic diseases.[9] Salivary biomarkers such as IL-1, IL-6, and MMP-8 have been reported to be significantly elevated in periodontitis patients compared with healthy controls.[10]

MMPs are key proteases involved in periodontitis and associated with periodontal status.[11,12] Type I collagen accounts for large quantities of periondontal extracellular matrix, thus

Editor: Fateh Rahimi.

This study was supported by a grant from the National Natural Science Foundation of China to Lei Huang (Grant no. 81201338).

The authors have no conflicts of interest to disclose.

[a] Department of VIP Dental Service, [b] Department of Nursing, Peking University School and Hospital of Stomatology, [c] Department of Clinical Laboratory, Peking University First Hospital, Beijing, China.

[*] Correspondence: Lei Huang, Department of Clinical Laboratory, Peking University First Hospital, Beijing, China (e-mail: leihuang2031@bjmu.edu.cn).

Medicine (2018) 97:3(e9642)

Received: 28 September 2017 / Received in final form: 20 December 2017 / Accepted: 27 December 2017

http://dx.doi.org/10.1097/MD.0000000000009642

special attention has been paid to collagenases and gelatinase such as MMP-8, MMP-13, MMP-2, and MMP-9 in periodontitis. Because type I collagen represents the bulk component of periodontal extracellular matrix, thus special attention has been paid to collagenases.[13] Among them, MMP-8 is the main collagenase in periodontitis; moreover, 90% to 95% of collagenolytic activity in gingival crevicular fluid originated from MMP-8. Thus MMP-8 is currently considered to be one of the most promising biomarkers for periodontitis in oral fluids.[13] While some studies showed higher levels of salivary MMP-8 in periodontitis patients compared with healthy individuals,[14,15] other studies showed opposite or contradictory results.[16,17]

To the best of our knowledge, the diagnostic value of salivary MMP-8 in periodontitis has not been systematically evaluated with all currently available data yet. Therefore, we aim to do a systematic review and meta-analysis to determine its diagnostic value between periodontitis patients and healthy controls.

2. Materials and methods

2.1. Focused question

The focused question was "Do salivary MMP-8 level differ significantly between periodontitis patients and healthy controls?" If answer is "yes," we could use MMP-8 as a potential biomarker for early diagnosis of periodontitis.

2.2. Search strategy

We searched PubMed and Embase electric database (up to August 2017) for the studies reporting salivary MMP-8 level between periodontitis patients and healthy controls with the data of means ± standard deviation (SD) and sample size (number of patients included).

The following search terms were used: (1) "matrix metalloproteinase-8" OR "matrix metalloproteinase 8" OR "MMP-8" OR "MMP8"; (2) "salivary" OR "saliva"; (3) "periodontitis" OR "periodontal disease." Then the above three parts were connected by Boolean operator "AND." Articles published in other languages except English, in-vitro studies and animal studies were excluded, and no other filter was set. We also searched reference lists from original articles or reviews to include more related studies. The authors were contacted for details if needed.

2.3. Study selection

The included studies should fulfill the following criteria: (1) clinical trials, either cross-sectional or observational studies in human; (2) presence of periodontitis patients compared with healthy controls; (3) evaluated salivary MMP-8 in relation to periodontitis; (4) studies that presented with numerical values of sample size and mean ± SD of MMP-8 levels, or it could be calculated from available data of the study.

2.4. Data extraction and quality assessment

Two authors (LZ and LH) independently identified included studies and extracted the data for further analysis. The data were tabulated by the study participants, inclusion criteria for peridontitis patients and healthy controls, assay used for detecting MMP-8, regions of the study performed, salivary MMP-8 levels (mean ± SD) with sample size, and statistical significance (*P* value). Discrepancy was resolved by consensus meeting with other co-authors to arrive at consensus. The whole process of literature selection was summarized in Figure 1, according to PRISMA guidelines.[18]

Methodological quality assessment was done by 2 authors based on Newcastle Ottawa scale (NOS) grading system, the details of each item in this grading system were described previously,[19] which was used for quality evaluation of observational studies and nonrandomized studies.

2.5. Statistical analyses

Meta-analysis was conducted to the primary outcome: mean salivary MMP-8 level (mean ± SD) between periodontitis patients and healthy controls. Forest plot was produced reporting standardized mean differences (SMDs) and 95% confidence interval (CI), which were calculated for each study. SMD is the mean divided by the SD of a difference in each study between patients and controls. It can be seen as the mean difference if all data were transformed to a scale where SD within groups was equal to 1.0. Funnel plot was used for the evaluation of public bias.

Heterogeneity was assessed using Higgins I^2, Tau-square, and Chi-square tests, with $I^2 > 75\%$ indicating relevant heterogeneity.[20] When the heterogeneity test was statistically significant, random-effects model was used. Otherwise fix-effects model was used. Publication bias was assessed by funnel plot. All the above statistical analyses were performed with Stata 13.0 software (Stata Corporation, College Station, TX). A P value $< .05$ was considered to be statistically significant.

2.6. Ethical review

This study was a systematic review and meta-analysis, and did not involve patient consent. Thus ethical approval could be waived.

3. Results

3.1. Identification of studies

The searches yielded 275 relevant articles for consideration primarily. After reviewing the titles and abstracts, 251 articles were excluded because they did not fulfill the inclusion criteria. Around 25 studies were selected for full-text review, and 15 studies were excluded in this step (Fig. 1). A total of 10 studies, including 485 periodontitis patients and 379 health controls that met the preset inclusion criteria were included for meta-analysis,[6,10,14–17,21–24] the characteristics of the 10 studies were summarized in Table 1.

3.2. Quality assessment

Study quality as assessed by the NOS was summarized in Table 2, the quality varied across the studies. Among the 10 included studies, 7 studies were graded as good quality and 3 studies were graded as moderate quality. All 10 studies met the NOS criteria for case definition, and had good representativeness.

3.3. Data synthesis and meta-analysis

The salivary MMP-8 levels from each independent study of both periodontitis patients and health controls were summarized in Table 1. The study of Gursoy et al[17] enrolled patients with MMP-8 detected by 2 different methods (immunofluorometric

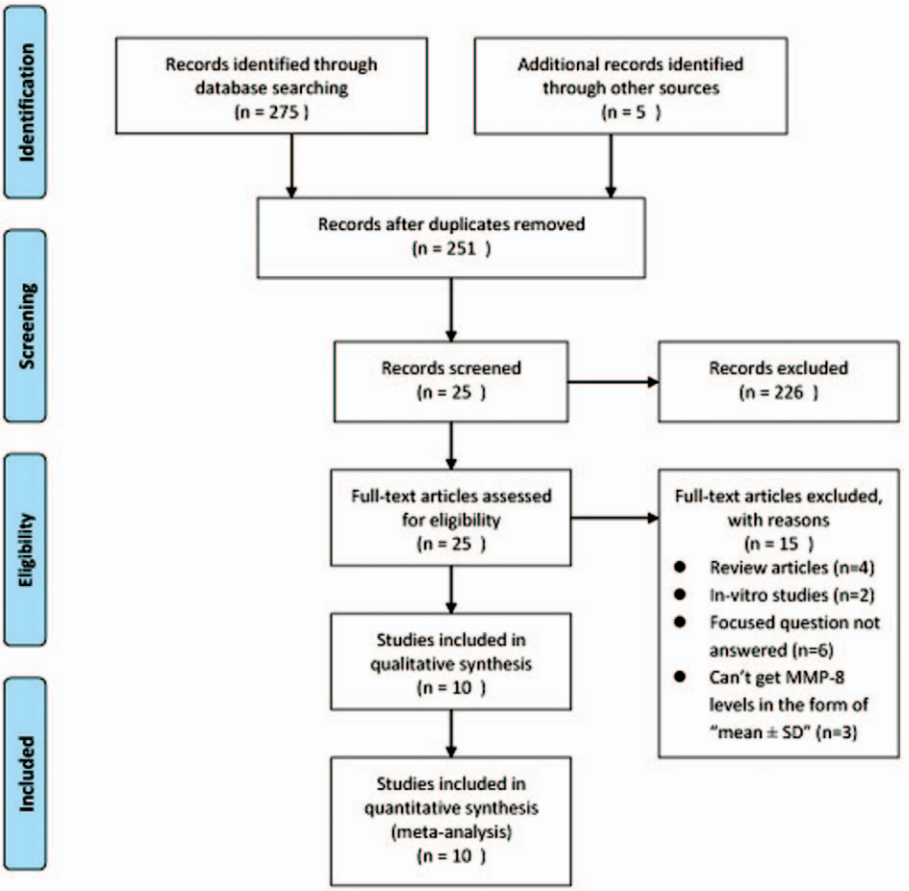

Figure 1. PRISMA flow diagram for studies retrieved through the searching and selection process. PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

assay [IFMA] and enzyme linked immunosorbent assay [ELISA]), with separate data of MMP-8 levels (mean ± SD), respectively, thus the 2 set of data were analyzed separately. The range of MMP-8 levels (mean ± SD) varied greatly among different studies, from 2.95 ± 0.66 (n=27) to 888.6 ± 990.1 (n = 84) in periodontitis patients, and from 2.51 ± 0.81 (n = 18) to 309.4 ± 183.4 (n = 81) in healthy controls.

The pooled SMD was 1.195 (95% CI: 0.720–1.670), with the forest plot drawn in Figure 2. For heterogeneity testing, Chi-square was 93.66 ($P < .05$), and I^2 (variation in SMD attributable to heterogeneity) was 89.3%. The estimate of between-study variance Tau-square was 0.5373. Test of SMD = 0, $z = 4.93$ ($P < .05$). Thus the variability in difference was significant. Funnel plot was shown in Figure 3, indicating publication bias.

4. Discussion

This meta-analysis systematically evaluated the salivary MMP-8 levels between periodontitis patients and healthy controls of 10 independent studies from different countries. In general, our results showed that MMP-8 level was significantly higher in periodontitis patients than in health controls, although the heterogeneity exists among different studies.

MMPs are proteolytic enzymes belonging to zinc protease super family involved in physiological degradation of extracellular matrix proteins and basement membranes, and they can be categorized into several groups.[13] MMP-8 belongs to collagenase group, which exhibits a unique ability to decompose type I and III collagen.[13] MMP-8 levels have been found to correlate with the levels of type I collagen degradation products, overcoming the protective shield of tissue inhibitors of MMP in disease active sites compared with inactive sites from periodontitis patients and healthy controls.[25] Therefore, it can be hypothesized that MMP-8 acts as a biomarker in periodontitis.

The salivary level of MMP-8 varied greatly between different studies and the SD was also relatively variable in some studies,[10,17,21,22] which may partly be explained by the variation in salivary flow rate, use of antimicrobial agents, and smoking habits. These factors may cause interference in salivary analysis to some extent. On the other hand, different detection methods (such as ELISA, IFMA, and Luminex) may also contribute to the variability.

SMD was calculated in order to reduce discrepancy. Our results showed that $I^2 = 89.3\%$, indicating substantial heterogeneity. Thus random-effects model was used for SMD estimation. The heterogeneity may be due to different detection methods used, such as IFMA versus ELISA, which may be explained by the different specificity of antibodies used in the 2 methods.[26] The heterogeneity may also be induced by the unstandardized diagnosis criteria for periodontitis, different enrolling criteria for healthy controls, different study population (gender, age), and different study designs. Funnel plot analysis indicated publication bias existed, which may be partially explained by 3 studies with relatively small sample size locating far away from the funnel's

Table 1

Characteristics of the 10 studies included in this study.

Study (author, year)	Salivary MMP-8 levels (mean ± SD) (ng/mL)	Criteria for periodontitis	Criteria for controls	Detection method	Origin	Periodontitis vs control *P*
Miller et al, 2006	Periodontitis: 408.6 ± 423.3 (n = 28) Control: 95.1 ± 80.1 (n = 29)	Subjects were included if at least 30% of periodontal sites demonstrated bleeding on probing, at least 20% of periodontal sites had probing depths (PD) of ≥4 mm, at least 5% of periodontal sites had interproximal clinical attachment loss (CAL) >2 mm, and radiographic bone loss was evident in posterior vertical bitewing films.	Healthy adults of similar age, race and sex who had BOP <10% of their periodontal sites, had <2% periodontal sites of PD ≥5 mm, had <1% periodontal sites of CAL >2 mm, and had no radiographic bone loss evident in posterior vertical bitewing films.	ELISA	USA	*P* = .0005
Gursoy et al, 2010 (1)	Periodontitis: 888.6 ± 990.1 (n = 84) Control: 309.4 ± 183.4 (n = 81)	Advanced periodontitis, each subject had at least 14 teeth with a probing pocket depth (PPD) ≥4 mm	Subjects with no teeth with PPD ≥4 mm	IFMA	Finland	*P* < .05
Gursoy et al, 2010 (2)	Periodontitis: 89.8 ± 53.1 (n = 84) Control: 74.1 ± 44.8 (n = 81)			ELISA	Finland	*P* > .05
Ebersole et al, 2013	Periodontitis: 283.47 ± 203.47 (n = 50) Control: 52.63 ± 40.62 (n = 30)	With the diagnosis of chronic adult periodontitis, had 5 qualifying sites in 2 quadrants with a minimum of 2 affected teeth in each quadrant with each site having PPD ≥5 mm, clinical attachment level (CAL) > 3 mm, and BOP score ≥2	In good general health and periodontal health, PPD ≥5 mm in <2% of sites, no PPD ≥6 mm, CAL of >2 mm in <1% of sites.	ELISA	USA	*P* < .0001
Meschiari et al, 2013	Periodontitis: 2.95 ± 0.66 (n = 27) Control: 2.51 ± 0.81 (n = 18)	Had at least 2 teeth with probing sites ≥5 mm, clinical attachment loss ≥6 mm, and evidence of alveolar bone loss observed in radiographs	Periodontally healthy subjects, with the following exclusion criteria: any periodontal surgery within 6 month; any chronic diseases, infectious diseases, immunological diseases, pregnancy, lactation, smoking, and use of medication.	ELISA	Brazil	*P* < .05
Kushlinskii et al, 2011	Periodontitis: 298.37 ± 234.81 (n = 82) Control: 249.0 ± 187.7 (n = 63)	Patients with chronic generalized periondontitis	Subjects with intact periodontium	Enzyme immune assay	Russia	*P* > .05
Gupta et al, 2015	Periodontitis: 348.26 ± 202.1 (n = 20) Control: 190.91 ± 143.89 (n = 20)	Patients with chronic periodontitis, which was assessed on the basis of PPD, CAL, gingival index (GI), and plaque index (PI)	Periodontally healthy subjects	ELISA	India	*P* < .05
Johnson et al, 2016	Periodontitis: 129.8 ± 891.9 (n = 31) Control: 51.9 ± 102.4 (n = 10)	Mild: ≥20% of sites with BOP, and ≥20% of sites with PPD = 4 mm; Moderate: ≥20% of sites with BOP, and >20% sites with PPD = 4 mm, ≤20% PPD = 5 mm; Advanced: ≥20% of sites with BOP and >20% PPD ≥5 mm	<10% sites with BOP, <2% sites with PPD >3 mm, and no sites with PPD ≥5 mm	Luminex	USA	*P* = .011
Rangbulla et al, 2017	Periodontitis: 672.18 ± 411.0 (n = 30) Control: 57.95 ± 31.64 (n = 20)	At least 20 teeth present; PD ≥5 mm and loss of CAL ≥4 mm in at least three teeth each in any two quadrants; Non-smokers; Individuals who have not undergone professional oral prophylaxis during the past 12 month and individuals who have not received any antibiotic, anti-inflammatory medication 6 months prior to the start of the study.	Clinically healthy periodontium. Exclusion criteria: Patients with systemic diseases; Patients undergoing or who have undergone organ transplantation; Patients on corticosteroid medications or cytotoxic drugs; Pregnant and lactating patients.	ELISA	India	*P* < .001
Noack et al, 2017	Periodontitis: 100.35 ± 15.82 (n = 20) Control: 26.11 ± 28.40 (n = 20)	Had at least 20 teeth excluding third molars. Exclusion criteria: systemic diseases and medications; Treatment with antibiotics <8 weeks before the study, pregnancy or breast feeding.	Periodontally healthy subjects	Time-resolved immune-		Fluorometric assay
Germany	*P* < .05					
Martinez et al, 2017	Periodontitis: 333 ± 66.7 (n = 29) Control: 66.7 ± 33.3 (n = 7)	With generalized moderate to severe chronic periodontitis, at least 15 own teeth with >30% of sites affected presenting AL ≥3 mm. Exclusion: any systemic disease, smokers or former smokers, use of antibiotics or nonsteroid anti-inflammatory drugs, and ongoing use of medication.	At least 20 own teeth with no interpoximal attachment loss and without clinical signs and symptoms of gingival inflammation.	ELISA	Sweden	*P* < .05

BOP = bleeding on probing, CAL = clinical attachment loss, ELISA = enzyme linked immunosorbent assay, GI = gingival index, IFMA = immunofluorometric assay, MMP = matrix metalloproteinase, PI = plaque, index, PD = probing depths, PPD = probing pocket depth.

Table 2

Quality assessment of the 10 included studies by Newcastle–Ottawa scale.

Study	Selection	Comparability	Exposure	Score	Quality
Miller et al[24]	☆☆☆	☆☆	☆☆	7	Good
Gursoy et al[17]	☆☆	☆	☆	4	Moderate
Ebersole et al[10]	☆☆☆	☆	☆☆	6	Good
Meschiari et al[21]	☆☆☆	☆☆	☆☆	7	Good
Kushlinskii et al[16]	☆☆	☆	☆	4	Moderate
Gupta et al[6]	☆☆☆	☆☆	☆	6	Good
Johnson et al[22]	☆☆☆	☆	☆☆	6	Good
Rangbulla et al[14]	☆☆☆	☆☆	☆	6	Good
Noack et al[15]	☆☆☆	☆☆	☆	6	Good
Martinez et al[23]	☆☆	☆	☆	4	Moderate

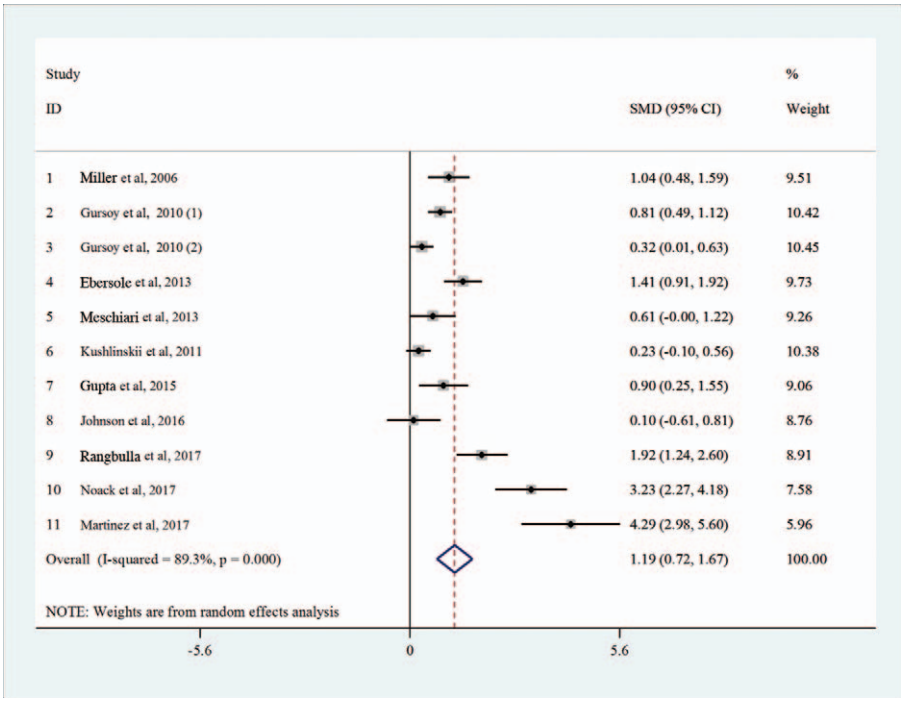

Figure 2. Forest plot presenting SMDs of salivary MMP-8 levels between periodontitis patients and healthy controls. MMP = matrix metalloproteinase, SMDs = standard mean differences.

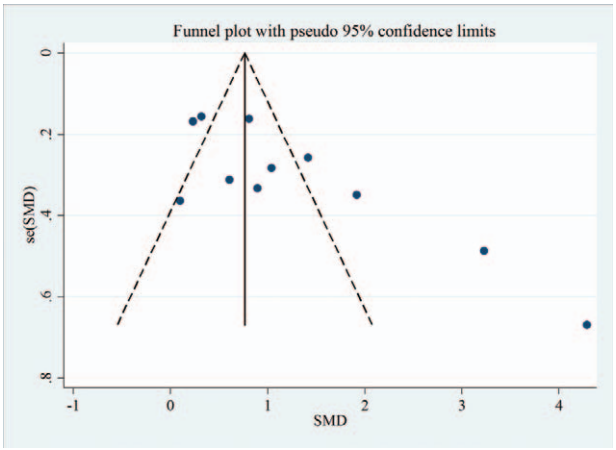

Figure 3. Funnel plot for MMP-8 levels among different studies. MMP = matrix metalloproteinase.

margin. Therefore, the findings in this meta-analysis should be analyzed with caution. Thus further high-quality studies with robust design and larger sample size are highly recommended.

In conclusion, our meta-analysis results suggested that, salivary MMP-8 levels were significantly higher in periodontitis patients than in healthy controls. Substantial heterogeneity existed among these included studies, thus prospective studies and randomized designs with larger sample size are still needed to verify our results in the future.

References

[1] Pihlstrom BL, Michalowicz BS, Johnson NW. Periodontal diseases. Lancet 2005;366:1809–20.
[2] Kassebaum NJ, Bernabe E, Dahiya M, et al. Global burden of severe periodontitis in 1990–2010: a systematic review and meta-regression. J Dent Res 2014;93:1045–53.
[3] Leng WD, Zeng XT, Kwong JS, et al. Periodontal disease and risk of coronary heart disease: an updated meta-analysis of prospective cohort studies. Int J Cardiol 2015;201:469–72.

[4] Zeng XT, Deng AP, Li C, et al. Periodontal disease and risk of head and neck cancer: a meta-analysis of observational studies. PloS One 2013;8:e79017.
[5] Zeng XT, Tu ML, Liu DY, et al. Periodontal disease and risk of chronic obstructive pulmonary disease: a meta-analysis of observational studies. PLoS One 2012;7:e46508.
[6] Gupta N, Gupta ND, Gupta A, et al. Role of salivary matrix metalloproteinase-8 (MMP-8) in chronic periodontitis diagnosis. Front Med 2015;9:72–6.
[7] Ghiabi E, Weerasinghe S. The periodontal examination profile of general dentists in Nova Scotia, Canada. J Periodontol 2011;82:33–40.
[8] Silswal N, Singh AK, Aruna B, et al. Human resistin stimulates the pro-inflammatory cytokines TNF-alpha and IL-12 in macrophages by NF-kappaB-dependent pathway. Biochem Biophys Res Commun 2005;334: 1092–101.
[9] Rathnayake N, Akerman S, Klinge B, et al. Salivary biomarkers for detection of systemic diseases. PLoS One 2013;8:e61356.
[10] Ebersole JL, Schuster JL, Stevens J, et al. Patterns of salivary analytes provide diagnostic capacity for distinguishing chronic adult periodontitis from health. J Clin Immunol 2013;33:271–9.
[11] Sorsa T, Mantyla P, Tervahartiala T, et al. MMP activation in diagnostics of periodontitis and systemic inflammation. J Clin Periodontol 2011;38:817–9.
[12] Rathnayake N, Gustafsson A, Norhammar A, et al. Salivary matrix metalloproteinase-8 and -9 and myeloperoxidase in relation to coronary heart and periodontal diseases: a subgroup report from the PAROKRANK study (periodontitis and its relation to coronary artery disease). PLoS One 2015;10:e0126370.
[13] Franco C, Patricia HR, Timo S, et al. Matrix metalloproteinases as regulators of periodontal inflammation. Int J Mol Sci 2017;18:pii: E440.
[14] Rangbulla V, Nirola A, Gupta M, et al. Salivary IgA, interleukin-1beta and MMP-8 as salivary biomarkers in chronic periodontitis patients. Chin J Dent Res 2017;20:43–51.
[15] Noack B, Kipping T, Tervahartiala T, et al. Association between serum and oral matrix metalloproteinase-8 levels and periodontal health status. J Periodontal Res 2017;52:824–31.
[16] Kushlinskii NE, Solovykh EA, Karaoglanova TB, et al. Content of matrix metalloproteinase-8 and matrix metalloproteinase-9 in oral fluid of patients with chronic generalized periodontitis. Bull Exp Biol Med 2011;152:240–4.
[17] Gursoy UK, Kononen E, Pradhan-Palikhe P, et al. Salivary MMP-8, TIMP-1, and ICTP as markers of advanced periodontitis. J Clin Periodontol 2010;37:487–93.
[18] Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Ann Int Med 2009;151: 264–269.
[19] Hartling L, Milne A, Hamm MP, et al. Testing the Newcastle Ottawa scale showed low reliability between individual reviewers. J Clin Epidemiol 2013;66:982–93.
[20] Borenstein M, Hedges LV, Higgins JP, et al. A basic introduction to fixed-effect and random-effects models for meta-analysis. Res Synth Methods 2010;1:97–111.
[21] Meschiari CA, Marcaccini AM, Santos Moura BC, et al. Salivary MMPs, TIMPs, and MPO levels in periodontal disease patients and controls. Clin Chim Acta 2013;421:140–6.
[22] Johnson N, Ebersole JL, Kryscio RJ, et al. Rapid assessment of salivary MMP-8 and periodontal disease using lateral flow immunoassay. Oral Dis 2016;22:681–7.
[23] Martinez GL, Majster M, Bjurshammar N, et al. Salivary colony stimulating factor-1 and interleukin-34 in periodontal disease. J Periodontol 2017;88:e140–9.
[24] Miller CS, King CPJr, Langub MC, et al. Salivary biomarkers of existing periodontal disease: a cross-sectional study. J Am Dent Assoc 2006; 137:322–9.
[25] Sorsa T, Gursoy UK, Nwhator S, et al. Analysis of matrix metalloproteinases, especially MMP-8, in gingival creviclular fluid, mouthrinse and saliva for monitoring periodontal diseases. Periodontology 2000 2016;70:142–63.
[26] Sorsa T, Hernandez M, Leppilahti J, et al. Detection of gingival crevicular fluid MMP-8 levels with different laboratory and chair-side methods. Oral Dis 2010;16:39–45.