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Periodontal disease and metabolic syndrome: A qualitative critical review of their association

Keiko Watanabe [a,*], *Yale D. Cho* [b]

[a] *Department of Periodontics, College of Dentistry, University of Illinois at Chicago, IL, USA*
[b] *Undergraduate Program, College of Dentistry, University of Illinois at Chicago, IL, USA*

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ABSTRACT

Background: Metabolic syndrome (MetS) is a conglomerate of several physical conditions/diseases that, as a group, increases the risk of mortality resulting from development of T2DM and cardiovascular diseases (CVD). These conditions/diseases include glucose intolerance/insulin resistance, hypertension, obesity, and dyslipidemia. The results from epidemiological studies suggest that there is an association between metabolic syndrome (MetS) and periodontitis, it is therefore important to understand the current status of the association and a possible contribution of periodontitis to MetS.

Objective: This review will qualitatively analyze published papers on the association of MetS and periodontitis/periodontal disease to clarify the current status of the association and suggest future directions for studies which may unravel the causal relationship between them.

Results: Of 309 papers related to MetS and periodontitis, 26 are original research papers that investigated the relationship/association between periodontal disease and MetS. Criteria used to assess periodontitis and MetS as well as overall study designs and patient recruitment criteria varied greatly among these studies.

Conclusion: All these studies demonstrated a positive association between periodontal disease and MetS. However, due to the heterogeneity of criteria to assess periodontitis and MetS and also paucity of longitudinal studies, it is difficult to determine the relative contribution of periodontitis to MetS. Age and the number of positive components of MetS appear to strengthen the relationship, however, incidence of each disease entity increases with ageing. Thus, mechanistic studies are also necessary to unravel the inter-relationship between periodontitis and MetS. In this regard, a use of animal models will be helpful as they are more uniform in regards to genetic background and have minimum confounding factors. Finally, development of accurate, quantitative assessment of gingival inflammation are necessary in order to determine the influence of periodontal disease on the development of MetS and its components.

* *Corresponding author at*: Department of Periodontics, College of Dentistry, University of Illinois at Chicago, 801 South Paulina Street, Chicago, IL, USA. Tel.: +1 312 996 0636; fax: +1 312 996 0943.
E-mail address: keiko@uic.edu (K. Watanabe).

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1. Introduction

Metabolic syndrome (MetS) is a combination of derangements including obesity, insulin resistance or glucose intolerance, hypertension, and dyslipidemia which collectively increase the risk of development of T2DM and cardiovascular diseases. The consequences in terms of T2DM alone are severe as evidenced by the 2–4 fold increase in mortality in T2DM patients relative to non-diabetic individuals.[1,2] Furthermore, subjects with cardiovascular disease have the highest mortality rate in the US.[3] Thus, subjects with MetS have a high risk of having or developing T2DM and cardiovascular diseases,[4,5] and thus may increase mortality rates.[6] The results from cross-sectional studies indicate that there is an association between MetS and periodontitis although the defining criteria for MetS and the means of assessing periodontitis have varied over time. However, the extent to which the association is bidirectional as well as underlying mechanisms for this association are not well understood.

PubMed, SCOPUS, and Cochrane Library searches were performed using the combination of keywords: periodontal disease; periodontitis; pocket depth; periodontal pocket; periodontal pocketing; attachment loss; clinical attachment loss; Metabolic syndrome and syndrome X. All publications pertaining to this topic written in English up to December 2013 were selected. Two hundred and twenty four papers out of 250 results from SCOPUS search and 31 papers out of 57 results from PubMed search were manually excluded as these either did not focus on association/interrelation between MetS and periodontal diseases; or were review papers,[7–10] or were studies/reviews focused on cytokines and other biomarkers.[10–16] Two papers from the Cochrane Library search matched with those from the SCOPUS search (Appendix 2). In addition a number of studies reported on the association between periodontal disease and one or two components of MetS.[17–24]

Although most studies indicate that the association between periodontitis and MetS exists, there is variation in the reported degree of association between periodontitis and MetS. This variation may be due to the fact that many variables were involved in assessing the association between periodontitis and MetS. These variables include different methodology/criteria used to assess periodontitis, definitions of MetS, and criteria used for subject recruitment. In addition, there are several different approaches to determine the association between these two diseases/conditions: determining co-morbidity, odds ratios for subjects with MetS who have periodontitis and vice versa, case-control studies, and longitudinal studies. These differences further complicate the comparison of these studies.

In this review, we will discuss the variables involved in determining the association between periodontal disease and MetS and suggest future studies that will unravel the causal nature of the relationship and its underlying mechanisms.

2. Critical factors involved in assessing the association between periodontitis and MetS.

2.1. Criteria used to assess periodontal disease

The terms ''periodontal disease'' and ''periodontitis'' are frequently used interchangeably in the literature, however these terms are not synonymous as ''periodontal disease'' refers to periodontitis or gingivitis or both. Thus, a necessary consideration is to clarify if a study reports on the association between periodontitis and MetS or gingivitis and MetS or the combination of the two.

Criteria for assessing periodontitis, gingivitis, and oral hygiene status are all relevant and should be carefully considered. Measurements and indices used to determine the periodontal condition in the studies reviewed varied greatly. These include probing or pocket depths (PD) with different cutoff values for periodontitis[11,25–30] clinical attachment loss (CAL) with different cutoff values,[11,25,27,28,31,32] Community Periodontal Index (CPI),[33–39] and bone loss between the CEJ and the crest of alveolar bone using panoramic radiographs[40] or bite wing radiographs.[41] Some studies used Plaque Index[42] and Gingival Index[43] for clinical evaluation, and some used Ramfjord's Periodontal Disease Index.[31,32,44] Other variations include the number of teeth and sites on teeth examined.[25–32,39,44–47] A few studies used self-evaluation of the periodontal condition[48,49] or tooth mobility and a non-specified index of gingival inflammation[50] (Tables 1 and 2).

2.1.1. Pocket/probing depth

Among the studies that used PD to determine the presence of periodontitis, one study used a mean PD greater than 2 mm[25] to define periodontitis and a PD greater than 2.5 mm[26] to define moderate–severe periodontitis. Other studies used a PD of 4–5 mm (or CPI 3) and PD $\geq$ 6 mm (CPI 4) to define periodontitis,[33–36,38,51] or two or more inter-proximal sites with PD $\geq$ 5 mm, not on the same tooth[52] to define periodontitis. Subjects with a mean PD of $\geq$ 2 mm could potentially have no attachment loss and no gingival inflammation and therefore have healthy gingiva or alternatively gingivitis using this criterion. A PD of 4 mm may also be due to gingivitis.

2.1.2. Clinical attachment level or attachment loss (CAL)

Studies that used clinical attachment loss for assessing periodontitis also varied greatly in terms of cutoff values. For example, mean CAL $\geq$ 3 mm[11,30,32] or a CAL of $\geq$4 mm in 2 or more sites, but not on the same tooth have been used in diagnosing periodontitis.[27,28] In some studies, moderate periodontitis was diagnosed as two sites, not on the same tooth, with a CAL $\geq$ 4 mm or one site with PD (defined as ''gingival probing depth'' by the investigators) $>$ 4 mm, and severe periodontitis was diagnosed by combining CAL and PD assessment, i.e., if two sites, not on the same tooth, with a CAL $\geq$ 6 mm and at least one site with a PD $\geq$ 4 mm.[27]

In one study healthy gingiva was defined as no CAL or bleeding on probing (BOP), early periodontitis as CAL $\geq$ 1 mm