REVIEW

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Oral Health and Cardiovascular Disease

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ABSTRACT

Several studies have examined a potential relationship between periodontal disease and cardiovascular disease. This article aims to update the evidence for a potential association by summarizing the evidence for causality between periodontitis and comorbidities linked to cardiovascular disease, including hypertension, atrial fibrillation, coronary artery disease, diabetes mellitus, and hyperlipidemia. We additionally discuss the evidence for periodontal therapy as a means to improved management of these comorbidities, with the larger goal of examining the value of periodontal therapy on reduction of cardiovascular disease risk.

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KEYWORDS: Cardiovascular disease; Oral health; Oral hygiene; Periodontal disease

INTRODUCTION

Periodontitis is a bacterially induced inflammatory disease that destroys the connective tissue and bone that support the teeth.[1] It is estimated that roughly half of all adults in the United States have mild to moderate forms of the disease.[2] Mounting evidence suggests that chronic inflammation increases the risk of cardiovascular disease.[3] This has led to speculation that periodontitis may be a modifiable risk factor contributing to the development of cardiovascular disease.[4,5] Diabetes mellitus, hypertension, hyperlipidemia, coronary artery disease, and atrial fibrillation have all been shown to be risk factors for, or sequelae of, cardiovascular disease. In this review, we will discuss the evidence about the association between these pathologies and periodontitis.

PATHOPHYSIOLOGY

Several mechanisms have been proposed to explain the association between periodontal and cardiovascular disease. Platelet activation by oral bacteria, specifically *Streptococcus mutans* and *Streptococcus sanguinis*, can lead to localized thrombus formation, and secretion of pro-inflammatory cytokines from the platelets themselves, which contributes to inflammation, atherogenesis, and thrombogenesis.[6,7] Systemic inflammation has additionally been theorized to underscore the observed association between cardiovascular disease and periodontitis. Strong evidence exists that increased cardiovascular disease risk is associated with elevated levels of pro-inflammatory cytokines, such as interleukin (IL)-1, IL-6, and tumor necrosis factor (TNF)-α, and acute phase proteins such as C-reactive protein (CRP).[8,9]

HYPERTENSION

Epidemiological studies have suggested the existence of a positive relationship between oral health disorders and

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hypertension.[10,11] Periodontitis has been linked to systemic inflammatory mediators such as CRP and IL-6, both of which are known to affect endothelial function.[4] It has further been posited that immune cells are primed in the chronically inflamed periodontium, making them predisposed to chemotactic recruitment to perivascular tissues, a step that leads to development of outright hypertension and atherosclerotic disease.[12,13]

The prevalence of hypertension in adults with concurrent periodontitis was summarized in a meta-analysis by Muñoz Aguilera et al[14] using 30 prospective and retrospective studies between 2003 and 2018. In 25 of the 30 analyzed studies, the prevalence of hypertension was higher in adults with a diagnosis of periodontitis (range 7%-77%) compared with those not suffering from the disease (range 4%-70%).[14] Periodontitis was found to be greater in individuals with hypertension in the reviewed studies (29%-61%) compared with those without hypertension (17%-39%).[14] The evidence of a causal relationship between periodontal disease and hypertension is further supported by prospect cohort studies demonstrating improvement in blood pressure following periodontal therapy.[15,16]

CLINICAL SIGNIFICANCE

- Periodontitis could lead to deteriorating cardiovascular health due to chronic systemic inflammatory disease.
- There is no strong evidence on the effects of periodontitis on hard cardiovascular disease end points (myocardial infarction, stroke, cardiovascular death).
- Periodontal therapy may contribute to improved outcomes in cardiovascular health due to decreased systemic inflammation.

ATRIAL FIBRILLATION

Systemic inflammation has been shown to be a significant factor in the development of atrial remodeling in animal and human studies.[17] Chen et al[18] revealed that patients with periodontitis had a 31% higher risk of developing atrial fibrillation than patients without periodontal disease, an increased risk that remained statistically significant after adjusting for common comorbidities. Further research has demonstrated an association between prevalent atrial fibrillation and increased dental plaque levels, bleeding on probing, and periodontal inflamed surface area.[19,20]

The atria of atrial fibrillation patients are infiltrated by inflammatory cells, underlying the theory that systemic inflammation can drive the development of arrythmia. Other studies have demonstrated that patients with atrial fibrillation have increased levels of inflammatory markers, including CRP, TNF-α, and plasma IL-6.[21] CRP downregulates nitric oxide, promoting endothelial cell apoptosis.[22] TNF has also been shown to contribute to the pathogenesis of atrial fibrillation via augmenting pulmonary vein arrhythmogenicity and inducing abnormal calcium homeostasis.[23] Several studies have confirmed increases of these systemic biomarkers in patients with periodontitis.[24,25]

CORONARY ARTERY DISEASE

Coronary artery disease and periodontitis have been associated since a landmark study in 1989 by Mattila et al[26] revealed significantly worse dental health in patients with acute myocardial infarction after adjusting for other risk factors. Mattila et al[27] provided further evidence of this linkage in 1993, with a study demonstrating that coronary atherosclerosis on diagnostic coronary angiography was associated with dental infections in males after adjusting for risk factors. These findings were echoed in a publication by Buhlin et al,[28] which found metrics of periodontitis to be associated with angiographically verified coronary artery narrowing in patients with stable coronary artery disease. A similar study by Costa et al[29] quantified the association by demonstrating a 2.79-times higher risk of developing coronary artery disease in patients with pre-existing periodontitis.

There is increasing evidence that periodontitis contributes to atherosclerosis. An immunohistological study by Ford et al[30] found that periodontopathic bacteria species were found more frequently in atherosclerotic lesions. A follow-up study by Ford et al[31] found oral bacteria in 75% of atherosclerotic plaque specimens analyzed. Analysis of cardiovascular specimens containing thrombus tissues demonstrated that *S. mutans*, a common pathogen in periodontitis, was the most prevalent bacteria (78%).[32] Cytokines, which are elevated in patients with periodontitis, have been implicated in endothelial dysfunction and initiation of atherosclerosis.[33] Tonetti et al[34] found improved endothelial function in the form of increased flow-mediated dilation 6 months following periodontal treatment in patients with coronary artery disease.

DIABETES MELLITUS

The causal relationship between periodontitis and type 2 diabetes mellitus is well established.[35] Several studies suggest that the association between diabetes mellitus and periodontitis is bidirectional.[36] Individuals with diabetes mellitus are more likely to develop periodontitis, and diabetic patients with periodontitis have worse glycemic control.[37,38] Several randomized controlled trials have found that treatment of chronic periodontitis improves glycemic control in patients with diabetes mellitus, chiefly through reduction of hemoglobin (Hb)A1c.[39,40]

Oxidative stress appears to be a major link, as it can activate proinflammatory pathways common to both disease processes.[41] Allen et al[42] observed that diabetes mellitus patients with periodontitis had compromised glycemic

control and increased oxidative stress markers. Chen et al[43] presented data suggesting that increased CRP in the setting of periodontitis was associated with increased levels of HbA1c. A prospective cohort study of 126,805 patients with diabetes and periodontal disease by Merchant et al[44] revealed an association between periodontal therapy and reduced HbA1c while controlling for confounding lifestyle factors such as smoking and BMI, demonstrating a potential rationale for periodontal treatment as a means for enhanced glycemic control.

HYPERLIPIDEMIA

Several studies show a bidirectional relationship between hyperlipidemia and periodontal disease.[45] Patients with mild or moderate hyperlipidemia manifested higher values of periodontal parameters compared with normolipidemic individuals.[46,47] In parallel, Cutler et al[48] and Moeintaghavi et al[49] demonstrated that periodontitis patients have 12% and 52% higher mean total cholesterol and triglycerides, respectively, as compared with patients without periodontal disease. Buhlin et al[50] demonstrated an association between high cholesterol and periodontitis, while Morita et al[51] found that serum triglyceride level might be a potential indicator for the presence of periodontal disease.

Hyperlipidemia has a deregulatory effect on the immune system, resulting in increased susceptibility to periodontitis and other infections.[52] His mechanism may be partly explained by hyperlipidemia-induced white blood cell hyperactivity, subsequently leading to increased oxygen radicals, which, in turn, are associated with progression of periodontitis in adults.[53,54] Concomitantly, increased cytokines in the setting of periodontitis stimulate the hypothalamic-pituitary-adrenal axis, leading to increased serum cortisol and glucagon.[55,56] D'Aiuto et al[57] investigated the impact of intensive periodontal therapy on hyperlipidemia, revealing a decrease in total and low-density lipoprotein cholesterol following 2 months of periodontal treatment.

MANAGEMENT

To date, no well-powered studies of the effects of periodontal treatment on hard cardiovascular disease end points (myocardial infarction, stroke, cardiovascular death) have been conducted.[58] However, the aforementioned studies of an association between periodontal therapy and cardiovascular disease suggest that treatment of periodontitis may improve the cardiovascular disease risk profile. This hypothesis is underscored by a population-based study conducted in 2015 in Taiwan by Chou et al,[59] which suggested that a dose−response relationship exists between periodontitis severity and cardiovascular disease risk. A similar study by Park et al[60] found that ≥1 tooth brushing per day or ≥1 regular dental visit for professional cleaning per year reduced cardiovascular risk by 9% and 14%, respectively. These findings suggest that adherence to daily oral hygiene may be an effective way to reduce the risk of cardiovascular disease.

CONCLUSION

Available data strongly suggest that periodontitis may have overall health consequences, specifically pertaining to cardiovascular disease and associated diagnoses. Significant evidence exists that periodontal therapy may contribute to improved outcomes in these pathologies. Prospective studies are warranted to confirm these findings and guide clinical practice for the management of periodontitis with regard to cardiovascular disease risk and outcomes.

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