

THE INTERRELATIONSHIP BETWEEN ORAL HEALTH AND CARDIOVASCULAR DISEASE

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Abstract

Oral health is a fundamental component of overall health and directly contributes to an individual's physical, psychological, and social well-being. Epidemiological data suggest a potential association between periodontal disease and cardiovascular disease (CVD). Nonetheless, a clear consensus on a direct link between these pathologies has not been established, largely due to the substantial overlap in shared risk factors and comorbidities that characterize both conditions. This review seeks to re-examine and update the available evidence supporting this association by synthesizing data relevant to causality between periodontitis and CVD-related comorbidities, including endocarditis, hypertension (HTN), atrial fibrillation (AF), and coronary artery disease (CAD). Oral health is integrated into overall health because disorders of the oral cavity—particularly complicated dental caries and periodontal diseases—can act as persistent sources of infection and chronic inflammation, with the potential to induce transient bacteremia and a systemic inflammatory response. Consequently, maintaining optimal oral health has implications that extend beyond the local level and may contribute to the prevention and management of systemic conditions; however, establishing a direct causal relationship is often limited by the presence of comorbidities and the influence of confounding factors. The article also examines how periodontal therapy may support improved control of CVD-related comorbidities by reducing periodontal inflammation and the associated systemic inflammation. In this context, periodontal care is considered a potential adjunctive strategy within multidisciplinary management of patients with overlapping oral and systemic disease.

Key words: oral health, cardiovascular disease (CVD), systemic inflammation.

1. INTRODUCTION

Developed by the Vision 2020 Think Tank through broad stakeholder consultation, this initiative marks the beginning of a process to establish tools and indicators for measuring oral health. The definition states:

"Oral health is multifaceted and includes the ability to speak, smile, smell, taste, touch, chew, swallow, and convey a range of emotions through facial expressions with confidence and

without pain, discomfort, and disease of the craniofacial complex". Further attributes of oral health are as follows:

- It is a fundamental component of health and physical and mental wellbeing. It exists along a continuum influenced by the values and attitudes of people and communities.
- It reflects the physiological, social, and psychological

attributes that are essential to the quality of life.

- It is influenced by the person's changing experiences, perceptions, expectations, and ability to adapt to circumstances." [1]

The relationship between oral diseases and overall health is multifactorial and complex. Systemic conditions can affect oral health through direct pathophysiological mechanisms or indirectly via behavioural changes related to the disease itself or its treatment. Conversely, alterations in oral health may also influence systemic health outcomes.

Tooth loss has been strongly associated with increased all-cause mortality, cardiovascular disease-related mortality [2,3], and diminished quality of life [4].

Periodontitis is a bacterially induced, chronic inflammatory disease characterized by progressive destruction of the connective tissue and alveolar bone supporting the teeth [5]. It is estimated that approximately half of adults in the United States present with mild to moderate disease, while severe periodontitis affects up to 15% of U.S. adults [6]. Worldwide severe periodontitis is estimated to affect 19% of the adult population, accounting for more than 1 billion cases [7].

Growing evidence indicates that chronic inflammation is associated with an increased risk of cardiovascular disease (CVD) [8].

Accordingly, periodontitis has been proposed as a potentially modifiable risk factor in CVD pathogenesis, a hypothesis supported by epidemiological data demonstrating an association between CVD and periodontitis [9,10]. CVD and its sequelae—coronary artery disease (CAD), acute myocardial infarction, stroke, and peripheral arterial disease—remain major contributors to global morbidity and mortality [11]. Endocarditis, diabetes mellitus (DM), hypertension (HTN), hyperlipidemia (HLD), CAD, and atrial fibrillation (AF) have all been identified as risk factors for, or sequelae of, CVD.

Diabetes mellitus (DM), hypertension (HTN), hyperlipidemia (HLD), atrial fibrillation (AF), coronary artery disease (CAD), and endocarditis have each been demonstrated to function as either risk factors for CVD or as sequelae of CVD.[12]

This review examines the evidence on the association and pathophysiological links between periodontitis and CVD. We synthesize data supporting causality between periodontitis and major CVD comorbidities and evaluate whether periodontal therapy may improve comorbidity control and thereby reduce CVD risk.

2. PATHOPHYSIOLOGY

Periodontitis and CVD are worldwide noncommunicable diseases with shared risk factors. The interplay between the two clinical entities arises from two complementary pathways: a direct pathway, underpinned by

systemic inflammatory response, cytokine spillover, and endothelial invasion by oral pathogens; and an indirect pathway, driven by shared risk factors and potential confounders. [13]. A growing body of research indicates that periodontitis may play a role in CVD development, although the precise causal relationship between the two conditions has yet to be clearly defined.

Multiple mechanisms have been proposed to account for the observed association between periodontal disease and cardiovascular disease.

Evidence indicates that oral bacterial species can translocate into the bloodstream and induce bacteremia. This phenomenon has been documented after routine daily activities (toothbrushing, flossing, chewing, or biting an apple), though it has been more extensively investigated following dental procedures (tooth polishing, scaling, tooth extraction, surgical extraction of third molars, and periodontal probing). A systematic review has linked bacteremia risk to periodontal health status, indicating a higher likelihood of bacteremia in gingival inflammation [14]. Bacteria that enter the circulation from periodontal plaque have been reported to trigger platelet activation, aggregation, and thrombosis. In particular, platelet activation by oral bacteria such as *Streptococcus mutans* and *S. sanguinis* may promote localized thrombus formation and stimulate platelets to release pro-inflammatory cytokines, thereby

contributing to inflammation, atherogenesis, and thrombogenesis [15,16]. In addition, *Porphyromonas gingivalis* has been implicated in CVD through activation of factor X, prothrombin, and protein C, fostering a prothrombotic state and facilitating intravascular clot formation [17].

Via hematogenous and lymphatic dissemination, as well as inhalation of bacterial pathogens, periodontal infections may exert systemic effects. These effects may occur directly through transmigration of microorganisms, microbial components, inflammatory mediators, and activated immune cells from periodontal lesions, or indirectly through inflammatory or dysregulated responses in distant organs to these disseminated mediators and microbial products [18].

Accordingly, periodontitis may be regarded as a condition with systemic relevance, given its capacity to induce a pro-inflammatory milieu, promote a prothrombotic tendency, and modulate immune function, with downstream effects on multiple organ systems. Fibrinogen and C-reactive protein (CRP) are acute-phase reactants produced in response to infection and inflammation. Their synthesis occurs predominantly in hepatocytes, largely under the influence of pro-inflammatory cytokines—particularly IL-6—as well as bacterial components. Clinically, CRP is widely used as a biomarker for the detection of infectious and inflammatory processes, to inform treatment

decisions in acute and chronic conditions, and to monitor disease course in disorders including cardiovascular disease, metabolic syndrome, diabetes mellitus, obesity, and cancer [19]. Historically, the systemic effects of bacterial infections have been assessed using CRP and fibrinogen as key biomarkers [20].

In a recent single-center cross-sectional study, Beukers et al. assessed the prevalence of comorbidity and multimorbidity patterns among individuals with and without periodontal disease. Their findings showed a higher burden of comorbidities and multimorbidities in participants with periodontal disease compared with those without comorbidity (46.3% vs. 30.9%, respectively; adjOR 1.36, CI 1.30–1.43). The identification of distinct comorbidity clusters points to heterogeneous pathophysiological overlap between periodontitis and specific systemic diseases. In this context, periodontal disease may be viewed as a component of multimorbidity, co-occurring with other systemic conditions within defined patient subgroups [21]. Additional studies have reported reductions in high-sensitivity C-reactive protein following periodontal therapy, with the decrease being statistically significant among individuals with cardiovascular disease as a comorbid condition [22,23].

Evidence also indicates a positive association between elevated CRP

levels and periodontitis severity, with more advanced periodontal destruction and higher inflammatory burden tending to coincide with higher systemic CRP concentrations.[24,25]

Systemic inflammation has also been proposed as a key mechanism underlying the reported association between cardiovascular disease (CVD) and periodontitis. Substantial evidence indicates that increased CVD risk correlates with elevated circulating levels of pro-inflammatory cytokines, including IL-1, IL-6, and tumor necrosis factor- α (TNF- α), as well as acute-phase proteins such as C-reactive protein (CRP) [26,27].

Periodontitis-associated systemic inflammation may facilitate molecular mimicry and the development of autoreactive antibodies directed against heat shock proteins (HSP). It has been proposed that bacterial dissemination and the ensuing inflammatory response enhance HSP expression in endothelial cells [28]. Because HSPs are highly conserved across species, antibodies elicited against oral bacterial HSPs may cross-react with HSPs upregulated in stressed endothelial tissue, thereby promoting endothelial injury [29].

Cardiovascular disease is accompanied by endothelial activation, reflected by increased expression of the stress protein HSP60 and upregulation of adhesion molecules. This phenotype promotes leukocyte tethering, adhesion, and transmigration into the arterial intima, thereby amplifying local inflammation and accelerating

the transition from early, potentially reversible fatty streaks to established, irreversible atherosclerotic lesions characterized by persistent inflammatory cell infiltration and progressive plaque development [30].

Collectively, inflammatory processes within periodontal tissues exert systemic effects, including stimulation of hepatic acute-phase responses that increase circulating levels of C-reactive protein (CRP) and fibrinogen. These findings support the concept that periodontitis extends beyond a localized oral condition and may be regarded as a disease with systemic implications.

Despite plausible biological mechanisms and consistent epidemiologic associations, establishing a causal link between periodontitis and cardiovascular disease (CVD) remains challenging. This is largely due to shared risk factors (e.g., smoking, diabetes, obesity, age, socioeconomic status) and variability in disease definitions and outcomes across studies. Moreover, although periodontal therapy may improve inflammatory biomarkers and some surrogate vascular measures, definitive evidence for reduced major cardiovascular events is still limited.

3.HYPERTENSION

In Europe, cardiovascular disease (CVD) accounts for approximately 3.9 million deaths annually (about 45% of all deaths), with ischemic heart disease, stroke, and hypertension—

often progressing to heart failure—among the principal contributors to CVD-related mortality. Periodontitis is likewise a chronic non-communicable disease (NCD) with high prevalence; severe periodontitis affects an estimated 11.2% of the global population, ranking as the sixth most common human disease [31].

Cardiovascular disease (CVD) remains the most prevalent cause of premature death worldwide. It had been suspected for decades that increased activity of the sympathetic nervous system (SNS) might play a pathogenetic role in the development and progression of hypertension, heart failure (HF) and CVD [32].

Hypertension, defined by the International Society of Hypertension as persistently elevated systolic blood pressure (SBP) >140 mmHg and/or diastolic blood pressure (DBP) ≥90 mmHg, affects more than 1.5 billion individuals worldwide [33].

Hypertension is a cardiovascular disease that develops gradually and is often sustained by chronic systemic inflammation.

Periodontitis has been implicated as a potential driver of the persistent low-grade systemic inflammation thought to underlie cardiovascular disease (CVD) and hypertension (HTN) [34].

Periodontitis is associated with increased systemic levels of inflammatory mediators, including C-reactive protein (CRP) and interleukin-6 (IL-6). These biomarkers

are not only indicators of heightened inflammatory burden but also exert direct effects on vascular biology by promoting endothelial activation and dysfunction, thereby impairing normal endothelial regulation of vascular tone and inflammatory cell recruitment [8]. In brief, these mediators impair endothelial function, increasing vascular resistance and, consequently, blood pressure.

A research group synthesized evidence on hypertension (HTN) prevalence among adults with concomitant periodontitis in a meta-analysis of 30 prospective and retrospective studies published between 2003 and 2018 [35]. In 25 of the 30 included studies, HTN prevalence was higher in individuals diagnosed with periodontitis (7–77%) than in those without periodontitis (4–70%) [10].

In a separate analysis of approximately 12,000 participants from the Third National Health and Nutrition Examination Survey (NHANES III), individuals with moderate to severe periodontitis exhibited higher systolic blood pressure than those with mild periodontal disease.

This study examined the association between multiple indicators of periodontal inflammation and periodontal disease and arterial blood pressure among U.S. adults aged 17 years and older. They analyzed data from the Third National Health and Nutrition Examination Survey (NHANES III), including 6,617 men and 7,377 women who underwent a periodontal examination. Blood

pressure was evaluated both as a continuous measure and as a binary outcome using a standard hypertension definition. Periodontal measures—extent of gingival bleeding, probing pocket depth, clinical attachment loss, and a periodontitis case definition—were tested for associations with blood pressure using a series of regression models with stepwise adjustment for potential confounders, including demographic factors, inflammatory markers, chronic conditions, smoking, BMI, and socioeconomic status. [36]

Evidence supporting a causal link between periodontal disease and hypertension is further strengthened by prospective cohort studies showing that blood pressure improves after periodontal treatment.[37-39]

Periodontal treatment led to significant reductions in CRP, IL-6, and fibrinogen, as well as decreases in blood pressure, left ventricular mass (LVM), and arterial stiffness, thereby reducing cardiovascular risk in patients with refractory hypertension.[39]

4. ENDOCARDITIS

The association between oral health and endocarditis has been recognized since the early 1900s [40]. In 1955, this evidence prompted the American Heart Association to recommend antibiotic use to reduce the risk of endocarditis in patients with underlying heart disease [41]. Infective endocarditis (IE) is an inflammatory condition most often caused by bacteria that enter the

bloodstream and subsequently colonize the endocardium, heart valves, or vascular structures. Despite advances in antimicrobial therapy and cardiac surgery, IE still carries considerable morbidity and mortality, making primary prevention and earlier, more accurate diagnosis key strategies in reducing its burden. Notably, for more than 50 years the oral microbiota has been recognized as an important risk factor for IE. Accordingly, although guidance differs between the American Heart Association and the European Society of Cardiology, both emphasize maintaining good oral hygiene and using antibiotic prophylaxis for high-risk patients undergoing certain dental procedures. [42]. An association between poor oral hygiene and endocarditis-related bacteremia, showing an almost eightfold increase in bacteremia risk when bleeding was triggered by routine toothbrushing [43].

Several microbial species have been identified as leading causes of endocarditis. Approximately 90% of the bacteria implicated are transient or resident members of the oral microbiome, including *Streptococcus viridans*, *Streptococcus bovis*, *Enterococcus faecalis*, and *Staphylococcus aureus* [44].

The European Society of Cardiology (ESC) [45-47], together with several national and multinational professional societies, has issued guidelines and periodic updates on infective endocarditis prevention, offering differing recommendations on

when antibiotic prophylaxis is indicated before dental procedures. However particularly for patients with congenital heart disease (CHD), there remains no consensus on whether these preventive recommendations can be fully and consistently applied [48,49].

The administration of antibiotics prior to dental interventions in order to prevent this mechanism was initially recommended almost seventy years ago and has been the subject of research and intensive discussion ever since [50].

5. ATRIAL FIBRILLATION

Systemic inflammation has been identified as a significant contributor to the development of atrial remodeling in both animal and human studies [51,52].

Patients with periodontitis had a 31% higher risk of developing AF compared with those without periodontal disease, and this association remained statistically significant after adjustment for common comorbidities. A dose–response relationship has also been observed between more frequent daily tooth brushing and AF risk: individuals who brush at least three times per day have a significantly lower risk of AF than those who brush only once or twice [53].

In a case–control study, a research group assessed the prevalence of periodontal disease (PD) among patients with atrial fibrillation (AF), finding that 47 of 227 AF patients (20.7%) had PD [54]. AF patients with and without PD were followed for a

mean of ~18 months; arrhythmia events were significantly more frequent in those with PD than in those without PD (93.6% vs. 17.4%, $P < 0.001$). Multivariate analysis indicated that PD was an independent predictor of arrhythmia and major adverse cardiac events during follow-up in AF patients.

In this review, only one prospective cohort study and one cross-sectional study examined the association between severe periodontal disease (PD) and atrial fibrillation. However, given that severe PD affects about 10% of the global population [55] and that approximately 16.3% of severe PD cases are associated with atrial fibrillation [56], greater attention should be paid to the risk of atrial fibrillation in individuals with severe PD.

The atria of patients with AF show infiltration by inflammatory cells, supporting the concept that systemic inflammation can promote arrhythmia development [57]. Other studies have found elevated inflammatory markers in AF patients, including CRP, TNF- α , and plasma IL-6 [58]. Better oral health appears to help prevent AF and may reduce the risk of recurrence. Regular, moderate oral care—including brushing two to three times daily—can improve oral health and may lower AF risk. Oral health promotion and prevention of oral disease should therefore be integrated into strategies to prevent new-onset atrial fibrillation, and future AF-related education should place greater

emphasis on oral health awareness. [59]

6. CORONARY ARTERY DISEASE

In most developed countries, coronary artery disease (CAD)—largely driven by atherosclerotic narrowing of the coronary arteries—remains a leading cause of death. Between the 1990s and the 2000s, mortality from acute myocardial infarction fell by as much as 50%. CAD incidence is influenced by factors such as age, sex, and socioeconomic conditions. Atherosclerosis involves multiple interrelated processes, including dyslipidemia, thrombosis, inflammation, vascular smooth muscle cell activation and remodeling, platelet activation, endothelial dysfunction, oxidative stress, altered extracellular matrix metabolism, and genetic susceptibility [60].

Coronary artery disease (CAD) and periodontitis have been linked since a research group found significantly poorer dental health in patients with acute myocardial infarction even after adjustment for other risk factors [61].

Porphyromonas gingivalis and *Porphyromonas nigrescens* were associated with higher odds of carotid artery atherosclerosis confirmed by ultrasound, a condition linked to CAD [62,63]. Angina—a common manifestation of CAD—was more frequent in individuals with high dental calculus scores [64].

Growing evidence suggests that periodontitis may contribute to atherosclerosis and, ultimately,

coronary artery disease (CAD). One proposed mechanism is the invasion of vascular endothelium by periodontal pathogens. In an immunohistologic study, periodontopathic bacterial species were detected more frequently in atherosclerotic lesions than other commonly implicated pathogens [65].

Analysis of cardiovascular specimens containing thrombotic tissue showed that *Streptococcus mutans*—a bacterium commonly associated with periodontitis—was the most frequently detected organism (78%) [66]. In addition, other periodontal pathogens, including *Porphyromonas gingivalis*, *Prevotella intermedia*, and *Tannerella forsythia*, have also been identified in atherosclerotic lesions of the coronary arteries [67]. Patients with coronary artery disease, periodontal therapy was followed by improved endothelial function, demonstrated by increased flow-mediated dilation six months after treatment. [68]

The number of missing teeth is associated with the degree of coronary atherosclerosis, especially in young patients and short-duration diabetic patients. Limitations of the study are the size of the study and the use of Coronary Artery Calcium score as the primary outcome measure; a causal relationship could not be identified due to a lack of information on the time sequence of events [69].

According to the latest 2020 consensus report, individuals with periodontitis who have a history of cardiovascular disease (CVD) are at increased risk of CVD-related complications. The

report also recommends that patients with CVD be routinely asked about signs and symptoms of periodontitis. Furthermore, it emphasizes that periodontal care should be strongly encouraged and closely maintained in patients with CVD. [31]

7.CONCLUSIONS

The available evidence supports a consistent association between periodontitis and cardiovascular disease, particularly atherosclerosis and coronary artery disease. Proposed pathways include sustained systemic inflammation, endothelial dysfunction, and prothrombotic effects, supported by the frequent detection of periodontal pathogens in atherosclerotic and thrombotic cardiovascular specimens and by observed vascular functional improvements after periodontal therapy in selected studies. From a clinical perspective, cardiovascular risk assessment should consider periodontal status, and patients with established cardiovascular disease should be screened for signs of periodontitis and referred for appropriate periodontal care. Further adequately powered, long-term interventional studies are required to determine whether periodontal treatment translates into a reduction in major adverse cardiovascular events. Consistent adherence to daily oral hygiene practices may support periodontal disease control and may thereby contribute to a reduction in cardiovascular disease risk.

Effective management of the oral–cardiovascular link requires coordinated collaboration between dental and medical professionals. Routine communication between dentists, periodontists, cardiologists, and primary care clinicians can facilitate earlier identification of periodontitis in patients with cardiovascular disease and, conversely, timely cardiovascular risk assessment in patients with advanced periodontal disease. Integrating periodontal status into medical history-taking and cardiovascular risk stratification supports more comprehensive risk modification, including targeted counseling on

smoking cessation, diabetes control, diet, and hygiene behaviors.

In addition, structured referral pathways and shared follow-up can improve continuity of care, treatment adherence, and monitoring of inflammatory burden and vascular risk over time. Such multidisciplinary models may ultimately improve patient outcomes by addressing common risk factors and reducing the impact of chronic inflammation on systemic health.

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