

CHRONIC ORAL INFLAMMATION AND CARDIOVASCULAR RISK

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Abstract

Chronic inflammatory diseases of the oral cavity, especially periodontal disease, are highly prevalent pathologies characterized by persistent inflammation of the supporting tissues of the teeth, mainly caused by bacterial colonization and local immune response. A growing body of evidence suggests a pathogenic link between periodontal disease and cardiovascular disease (CVD), which is responsible for most global mortality. This review explores the pathophysiological, immunological, and epidemiological connections between chronic oral inflammation and cardiovascular risk. Proposed mechanisms include transient bacteremia caused by dental manipulations or spontaneous gingival bleeding, dissemination of bacterial products (e.g., lipopolysaccharides), and systemic activation of the inflammatory response. These processes can lead to endothelial dysfunction, acceleration of atherogenesis, and instability of atherosclerotic plaques. Systemic inflammatory markers, such as C-reactive protein (CRP), interleukins, and TNF- α , are often elevated in patients with severe periodontitis, correlating with an increased cardiovascular risk. Epidemiological data support the association between periodontitis and pathologies such as acute myocardial infarction, stroke, and ischemic coronary artery disease. Although the direct causal relationship remains partially elucidated, the importance of evaluating and treating chronic oral inflammation in the context of cardiovascular prevention is becoming increasingly evident. Integrating dentistry into cardiovascular risk assessment could be an important step in preventive medicine, and future research should aim at developing common biomarkers and interdisciplinary therapeutic strategies.

Keywords: oral health; chronic periodontitis; cardiovascular diseases; systemic inflammation; inflammatory markers

Introduction

Cardiovascular disease (CVD) is currently the leading cause of morbidity and mortality worldwide, contributing significantly to the global burden of disease and the costs of public health systems. Despite considerable progress in recent decades in the field of early diagnosis, pharmacological and interventional therapies, the incidence and prevalence of cardiovascular diseases continue to increase, reflecting the persistent influence of traditional risk factors and modern lifestyles [1,2].

In parallel, inflammatory diseases of the oral cavity – especially chronic periodontal disease – are widespread conditions, affecting

a significant percentage of the adult population globally. They are classified as chronic non-communicable inflammatory diseases, having the ability to induce systemic effects that go beyond the strictly dental sphere. Chronic periodontitis is characterized by long-lasting inflammation of the periodontal tissues, i.e., the structures that support the teeth (gum, periodontal ligament, cementum, and alveolar bone). The inflammatory process is triggered and perpetuated by the accumulation of subgingival bacterial biofilm, which causes the activation of the local immune response and, over time, leads to the progressive destruction of dental supporting tissues, with the potential for tooth loss [1-3].

In the context of the expansion of the medical perspective on chronic diseases, in recent years, the relationship between oral pathology and systemic diseases has become an increasingly approached research topic, with a focus on the potential interconnection between chronic periodontitis and CVD. It is assumed that there is a bidirectional link between these two pathological conditions, supported by common pathophysiological mechanisms and, above all, by the central role of chronic inflammation in both entities. This association is supported by a growing body of experimental, clinical, and epidemiological evidence [2,3].

The mechanisms by which oral inflammation can influence cardiovascular pathology include the release into the systemic circulation of inflammatory mediators (such as interleukins, TNF- α , and C-reactive protein), which contribute to the development of endothelial dysfunction, the initiation of the atherosclerotic process, and the progression of cardiovascular disease. In addition, the presence of gingival lesions facilitates the penetration of oral pathogenic bacteria and their metabolic products (e.g., lipopolysaccharides) into the bloodstream, which causes an amplified systemic immune response, potentially harmful to vascular health [1,3].

In light of these complex and interrelated interactions between oral health and the cardiovascular system, the main objective of this review is to analyze in an integrated way the latest scientific evidence on the association between chronic oral inflammation and increased risk of cardiovascular events. It also aims to highlight the main pathophysiological mechanisms involved, as well as to discuss the clinical and therapeutic implications of these findings, with emphasis on the need for an interdisciplinary

approach in the prevention and management of chronic diseases [1-3].

This paper is structured as a narrative review, aiming to integrate the most recent evidence on the relationship between chronic oral inflammation and cardiovascular risk. The novelty of this work lies in its multidimensional approach to the connection between oral dysbiosis, systemic inflammatory response, and cardiovascular disease pathogenesis, providing an updated perspective on shared mechanisms. From a practical standpoint, the article underscores the importance of interdisciplinary collaboration between dental and cardiovascular specialists and highlights the role of periodontal assessment in the prevention and management of cardiovascular risk.

By integrating inflammatory, microbiological, and clinical perspectives, this article provides an original contribution by emphasizing how chronic oral inflammation can act as both a trigger and amplifier of systemic atherosclerotic processes. The paper synthesizes recent international findings (2021–2025), offering an updated view on the role of the oral microbiome and systemic immune response in the development of cardiovascular complications.

From a clinical standpoint, the article highlights the importance of periodontal assessment in cardiovascular disease prevention and the need for interdisciplinary collaboration between dental and cardiac specialists to ensure a comprehensive, patient-centered preventive approach.

General aspects of chronic oral inflammation

Chronic oral inflammation is mainly represented by periodontal diseases, which constitute a heterogeneous group of inflammatory diseases characterized by

multifactorial etiology and a progressive evolution. These conditions affect the supporting structures of dental units, including the gum, periodontal ligament, root cement, and alveolar bone. Basically, persistent inflammation in these areas causes a series of local structural and functional changes, with important consequences both on oral health and on the general condition of the patient [2,3].

The updated international classifications have refined the delimitation of the clinical forms of periodontal disease, defining two major entities: gingivitis and periodontitis, each with subtypes and varying degrees of severity. Gingivitis is considered an early and reversible form of the disease, characterized by localized inflammation of the gum tissues without bone damage, often triggered by the accumulation of plaque. In contrast, periodontitis involves deeper and more extensive inflammation, accompanied by irreversible tissue destruction, loss of epithelial attachment and bone resorption, which leads, in the absence of treatment, to tooth mobility and tooth loss [2,3].

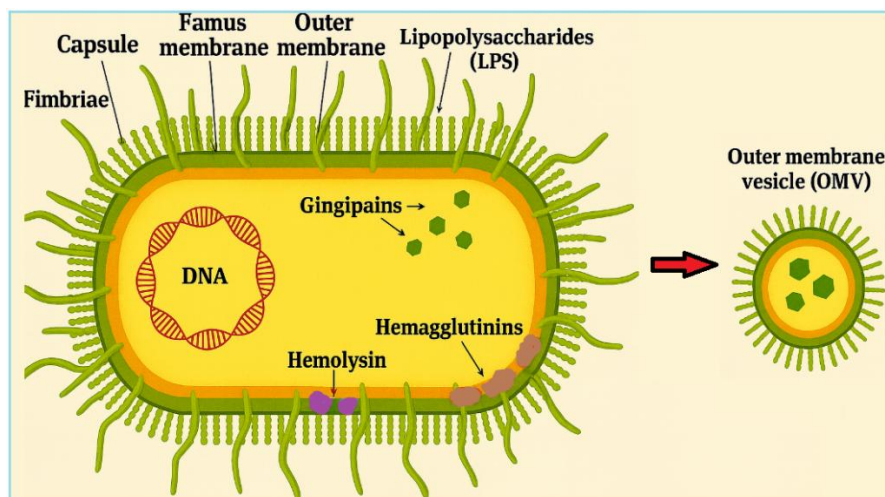
Within periodontitis, several clinical forms are distinguished, the most common being chronic periodontitis and aggressive periodontitis. They are differentiated according to the age of onset, the rate of progression, the distribution of lesions, and, last but not least, according to the characteristics of the host's immune response. Chronic periodontitis has a slow evolution and is more prevalent in adults, while the aggressive form begins earlier and is characterized by rapid destruction, often disproportionate to the amount of plaque present [2,3].

Gingivitis, although often ignored by patients due to minimal symptoms, is an

important condition because it represents a precursor stage in the evolution towards more severe forms of periodontal disease. It is completely reversible through proper oral hygiene and early professional intervention. In contrast, periodontitis involves deep chronic inflammatory processes, with irreversible damage to the dental support apparatus, and is increasingly recognized as having a potential systemic impact, contributing to low-grade systemic inflammation and being associated with various chronic diseases, including cardiovascular disease [3,4].

The etiopathogenesis of periodontitis is complex and involves a dynamic interaction between pathogenic microbial agents and the host's immune system. At the center of the etiological process is the accumulation of subgingival bacterial biofilm, populated mainly by anaerobic Gram-negative bacterial species. Among the most important species identified are *Porphyromonas gingivalis*, *Tannerella forsythia*, and *Treponema denticola*, bacteria considered part of the "red complex" associated with severe forms of periodontal disease [3–5].

These bacteria do not act in isolation, but within a dynamic microbial ecosystem, capable of evading the host's defense mechanisms and inducing a persistent and destructive immune response. The initial inflammatory response, designed to control the infection, turns over time into a chronic pathological process, characterized by the release of pro-inflammatory cytokines, the recruitment of immune cells, and the activation of tissue degradation mechanisms. Thus, the result is a paradoxical destructiveness generated by the body's own defense mechanisms, which contributes not only to tooth loss but also to systemic inflammatory responses with distant impact [3–5].



Imagine 1. Structura *Porphyromonas gingivalis* [5]

Oral dysbiosis, i.e., the imbalance between the resident microbiota and the host's defense mechanisms, plays a central role in initiating and maintaining chronic local inflammation. The local inflammatory response triggers the production of proinflammatory cytokines such as interleukin-1 β (IL-1 β), interleukin-6 (IL-6), and tumor necrosis factor alpha (TNF- α), which contribute to tissue destruction and amplification of the inflammatory process [3,5].

In addition to local effects, these mediators can enter the systemic circulation, causing increased levels of C-reactive protein (CRP) – a recognized marker of systemic inflammation and cardiovascular risk. Thus, chronic oral inflammation cannot be considered an isolated phenomenon, but a

potential source of systemic inflammation with multisystemic implications [3-5].

The link between chronic systemic inflammation and cardiovascular pathology

Chronic oral inflammation, especially in the context of periodontal disease, does not remain a process limited to the oral cavity, but can have significant systemic reverberations by generating a persistent state of low-grade inflammation [3,5].

Subgingival plaque, in association with oral dysbiosis, favors the penetration into the systemic circulation of pathogenic bacteria and their antigenic products, such as lipopolysaccharides (LPS), causing episodes of transient bacteremia. These repeated events stimulate the activation of circulating immune cells, triggering a sustained systemic inflammatory response [4,5].

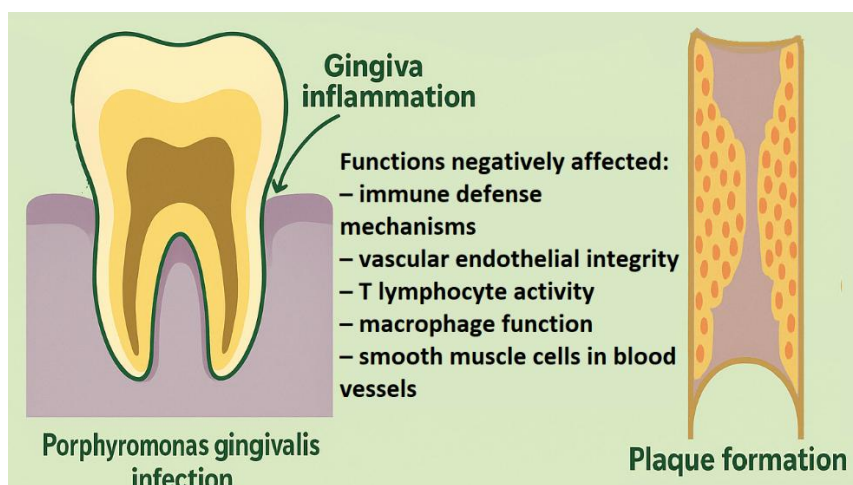


Image 2. Interaction between chronic oral infection with *Porphyromonas gingivalis* and atherosclerotic cardiovascular risk [5].

The persistent immune response, induced by chronic oral inflammation, contributes to endothelial dysfunction, an early event in the atherogenic cascade. Under the action of proinflammatory cytokines – such as interleukin-1 β (IL-1 β), interleukin-6 (IL-6), and tumor necrosis factor alpha (TNF- α) – endothelial cells undergo phenotypic changes, losing vasodilator and antithrombotic properties, and acquiring a pro-inflammatory and pro-atherogenic profile. This phenomenon facilitates the adhesion of monocytes, the formation of foam cells, and the development of atheroma plaques [3-5].

A central role in this interaction is attributed to C-reactive protein (CRP), a serum marker of acute and chronic inflammation, the concentration of which increases significantly in patients with severe periodontitis. Increased CRP levels were directly correlated with the severity of vascular damage and the risk of major cardiovascular events, being included in coronary risk prediction models. Thus, chronic oral inflammation, by maintaining a systemic inflammatory state and affecting the vasculature, can represent an important pathogenic link in the initiation and progression of cardiovascular diseases [5,6].

Pathophysiological mechanisms

The link between chronic oral inflammation and cardiovascular pathology is supported by a number of proposed pathophysiological mechanisms, which explain how local events at the periodontal level can contribute to the initiation and progression of vascular lesions [5-7].

One of the most discussed mechanisms involves the appearance of transient bacteremia, caused by daily activities such as brushing or chewing, in patients with active periodontal disease. This bacteremia allows access to oral pathogens, such as *Porphyromonas gingivalis*, *Aggregatibacter actinomycetemcomitans*, and *Fusobacterium nucleatum*, into the systemic circulation, with the potential to colonize the vascular endothelium [5,6].

Vascular colonization by these pathogens favors the activation of endothelial cells, stimulating the expression of adhesion molecules (VCAM-1, ICAM-1, selectins), facilitating the adhesion of leukocytes and their migration into the vascular wall. This process contributes to the initiation of the formation of atherosclerotic plaque, in which

monocytes differentiate into macrophages, lipid phagocytes, and the formation of foam cells participates. In addition, bacterial components, such as *P. gingivalis* LPS, can induce the expression of Toll-like receptors (TLRs), amplifying the local inflammatory response. Another central mechanism involves chronic low-grade inflammation, fueled by the systemic activation of proinflammatory cytokines, especially IL-1 β , IL-6, and TNF- α , with direct effects on the vasculature. These cytokines contribute to oxidative stress, reduced bioavailability of nitrogen oxides (NO), and maladaptive vascular remodeling [6,7].

Over time, this sustained inflammatory environment leads to the progression of atherosclerotic lesions, plaque instability, and an increased risk of acute cardiovascular events. Thus, the interaction between periodontal pathogens and the vascular system

can be considered a key element in the common pathogenesis of oral inflammation and cardiovascular disease [6-8].

The role of the oral microbiome in cardiovascular pathology

The oral microbiome plays an essential role in maintaining oral and systemic health. The composition of this microbiome is influenced by factors such as oral hygiene, diet, immune status, and the presence of pathological conditions. Normally, the oral microbiome is balanced, with a predominance of beneficial bacteria, but dysbiosis, i.e., an imbalance in its structure, can favor colonization with pathogenic species that contribute to the development of chronic inflammation and systemic damage to the body, including the cardiovascular system [8,10].

Table 1. Key mechanisms linking the oral microbiome to cardiovascular disease

Element	Description
<i>Involved Bacteria</i>	Porphyromonas gingivalis, Fusobacterium nucleatum, Aggregatibacter actinomycetemcomitans
<i>Associated Conditions</i>	Periodontal disease, atherosclerosis, and cardiovascular diseases
<i>Mechanism of Systemic Entry</i>	Transient bacteremia through gingival bleeding or dental procedures
<i>Bacterial Virulence Factors</i>	Toxins, proteases, lipopolysaccharides (LPS)
<i>Immune Activation</i>	Activation of proinflammatory cytokines: IL-1 β , IL-6, TNF- α
<i>Systemic Effects</i>	Chronic inflammation, endothelial dysfunction, and endothelial cell activation
<i>Metabolic Influence</i>	Interference with lipid metabolism, an increase in LDL, and oxidized LDL
<i>Oxidative Stress</i>	Production of reactive oxygen species (ROS)
<i>Cardiovascular Consequences</i>	Formation and instability of atherosclerotic plaques, increased risk of myocardial infarction and stroke

Table 1 shows the main oral bacteria involved in cardiovascular pathology, the mechanisms by which they enter the systemic circulation, the virulent factors produced, and the biological effects induced. The links between chronic inflammation, endothelial dysfunction, and the increased risk of atherosclerosis and acute cardiovascular events are highlighted.

One of the best-documented associations is the link between the dysbiotic oral microbiome and cardiovascular disease, especially atherosclerosis. Pathogenic bacterial species, such as *Porphyromonas gingivalis*, *Fusobacterium nucleatum*, and *Aggregatibacter actinomycetemcomitans*, are frequently involved in the development of periodontal disease and, through transient bacteremia, can reach the systemic circulation [8-10].

These bacteria produce a number of toxins and virulent factors that interact with the immune system and promote a systemic inflammatory response. In particular, *P. gingivalis* is able to invade and colonize the vascular endothelium, activating endothelial cells and triggering an inflammatory reaction that favors the development of atheroma plaques. The mechanisms by which the oral microbiome influences cardiovascular pathology are complex and involve multiple pathways. Oral bacteria can activate pro-inflammatory cytokines, such as IL-1 β , IL-6, and TNF- α , which circulate in the body and contribute to endothelial dysfunction, a crucial step in the formation of atherosclerotic plaque. Also, oral bacteria can interfere with lipid metabolism and contribute to increased levels of low-density lipoprotein (LDL) and oxidized lipoprotein, factors that promote atherosclerosis [8,9].

The dysbiotic oral microbiome also plays a role in generating an environment

favorable to oxidative stress by producing reactive oxygen species (ROS), which induce endothelial damage and aggravate the atherosclerotic process. Furthermore, chronic inflammation generated by oral bacteria and their long-term activity can contribute to atherosclerotic plaque instability, increasing the risk of acute cardiovascular events such as myocardial infarction and stroke [8-10].

Treating periodontal disease and improving oral hygiene can have a beneficial effect on reducing cardiovascular risk. Various studies have shown that periodontal interventions, such as subgingival scaling, can significantly decrease systemic inflammatory markers, such as C-reactive protein (CRP) and interleukin-6 (IL-6), which are involved in the pathogenesis of atherosclerosis. These interventions can improve endothelial function and reduce blood pressure, having a protective effect on the cardiovascular system [8-10].

Thus, the oral microbiome is not only an indicator of oral health but also an important factor in systemic health, and interventions to maintain a balanced microbiome can have significant benefits not only for the prevention of oral conditions but also for reducing cardiovascular risk [12-14].

It highlights the importance of integrating oral health into the assessment of the patient's overall risk, especially in the case of those with cardiovascular risk factors, and the need for a multidisciplinary approach that includes both dentists and cardiologists [14,15].

Clinical and therapeutic implications

The recognition of the connection between chronic oral inflammation and cardiovascular pathology causes a paradigm shift in the assessment of the patient's overall risk, emphasizing the importance of

integrating oral health into the cardiovascular prevention strategy [15,16].

The assessment of periodontal status should be included in the extended anamnesis of patients at cardiovascular risk, especially in the presence of multiple risk factors such as diabetes, smoking, or dyslipidemia. The presence of active periodontal disease could be an indirect clinical marker of a persistent systemic inflammatory status. In this context, the effective therapeutic approach requires the collaboration of a multidisciplinary team that includes the cardiologist, the dentist (especially the periodontology specialist), and the family doctor. Effective communication between these specialists allows for an integrative approach to the patient, in which oral health management becomes an active part of cardiovascular risk control [15-17].

The clinical and therapeutic implications in dental practice involve not only the correct management of post-extraction complications and oropharyngeal conditions, but also the use of modern materials and techniques, from ceramic orthodontic devices and bioresorbable scaffolding, to biocompatible biomaterials for pre-implant bone reconstruction and the evaluation of behavioral factors involved in dentin sensitivity [19-24]

Data from recent literature suggest that active treatment of periodontal disease, including subgingival scaling, mechanical curettage, and rigorous oral hygiene, is associated with a significant reduction in serum levels of systemic inflammatory markers, such as CRP and IL-6. Some studies have reported an improvement in endothelial function and a decrease in arterial stiffness after periodontal therapy. These findings support the hypothesis that effective treatment of chronic oral inflammation not only has local benefits but can actively contribute to the

reduction of cardiovascular risk, representing a promising direction in personalized and preventive medicine [16-18].

Conclusions

Oral dysbiosis, defined as an imbalance between beneficial and pathogenic microorganisms in the oral cavity, has a significant impact on cardiovascular health, especially through its contribution to the development and progression of atherosclerosis and coronary artery disease. The presence of bacteria such as *Porphyromonas gingivalis*, *Fusobacterium nucleatum*, and *Aggregatibacter actinomycetemcomitans* has been associated with the formation of atherosclerotic plaques, which act through complex inflammatory and immunological mechanisms. Severe periodontal infections can induce transient bacteremia, facilitating the access of pathogens into the systemic circulation, where they interact with the vascular endothelium and promote the appearance of endothelial dysfunction, a key factor in the pathogenesis of cardiovascular diseases.

Oral bacterial colonization stimulates the production of proinflammatory cytokines such as IL-1 β , IL-6, and TNF- α , which maintain systemic inflammation and accelerate the atherosclerotic process. Oral dysbiosis also influences lipid metabolism, causing increased levels of oxidized LDL and lipoproteins, both of which are involved in the initiation and worsening of vascular damage. Clinical studies have shown that the treatment of periodontal disease, by improving oral hygiene and performing subgingival scaling, reduces the levels of systemic inflammatory markers and improves endothelial function, suggesting an indirect cardiovascular benefit. In this context, it is essential to adopt a multidisciplinary approach in which the collaboration between

dentists and cardiologists contributes to the early identification and integrated management of patients with high

cardiovascular risk, especially those with periodontal diseases and associated risk factors.

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