

ATHEROSCLEROTIC CARDIOVASCULAR DISEASE AND ORAL HEALTH: PATHOPHYSIOLOGICAL LINKS AND CLINICAL IMPLICATIONS

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Abstract

Atherosclerosis is one of the leading causes of morbidity and mortality worldwide, with chronic inflammation playing a central role in its pathogenesis. Increasing evidence suggests that oral health, particularly the presence of periodontal disease, is closely linked to the progression of atherosclerosis and an increased cardiovascular risk. The underlying mechanisms include the dissemination of oral bacteria into the systemic circulation, activation of the inflammatory response, and impairment of endothelial function, which promote atherosclerotic plaque formation and acute cardiovascular events. Studies indicate that patients with periodontitis exhibit elevated levels of inflammatory proteins such as C-reactive protein and interleukin-6, highlighting systemic inflammation as a key link between these two conditions. Moreover, periodontal treatments appear to have beneficial effects on inflammatory markers and vascular health, suggesting a potential therapeutic role. In this context, a multidisciplinary approach incorporating dental screening into cardiovascular prevention and fostering collaboration between dentists and cardiologists could improve patient outcomes. Integrating oral health into current medical strategies may represent a crucial step in reducing cardiovascular risk and optimizing atherosclerosis prevention.

Keywords: atherosclerotic cardiovascular disease, oral health, systemic inflammation, periodontitis, endothelial dysfunction, atherosclerosis.

Introduction

Atherosclerotic cardiovascular disease (ASCVD) is one of the leading causes of morbidity and mortality worldwide, significantly impacting quality of life and healthcare costs. The atherosclerotic process is complex, involving chronic inflammation, endothelial dysfunction, lipid accumulation, and vascular remodeling, ultimately leading to severe complications such as myocardial infarction and stroke. On the other hand, oral health plays a crucial role in maintaining systemic balance, and inflammatory oral diseases, particularly periodontitis and advanced

dental caries, have been linked to various systemic conditions, including diabetes, respiratory diseases, and ASCVD [1-4].

In recent decades, research has highlighted a bidirectional relationship between poor oral health and cardiovascular disease, suggesting that inflammatory processes in periodontal disease may contribute to the initiation and progression of atherosclerosis. This has sparked significant interest in understanding the mechanisms by which oral bacteria and the associated immune response can influence ASCVD pathogenesis. Inflammation plays a central role in both conditions, indicating

a common pathophysiological mechanism. In periodontitis, pathogenic bacteria trigger a localized inflammatory response that, over time, can lead to systemic effects through the release of inflammatory mediators into the bloodstream. This process may exacerbate endothelial dysfunction, promote lipid deposition in arterial walls, and accelerate atherosclerotic plaque formation [2-5].

Moreover, epidemiological studies have demonstrated a significant association between periodontitis and the risk of major cardiovascular events, such as myocardial infarction and stroke. Individuals with severe periodontitis exhibit elevated levels of C-reactive protein, a key inflammatory marker linked to cardiovascular risk. Additionally, the presence of periodontal pathogens in atherosclerotic lesions has been confirmed through molecular biology techniques, suggesting a direct involvement of these bacteria in thrombogenic and inflammatory processes [2-6].

In addition to the pathophysiological aspects, shared risk factors for both ASCVD and oral diseases must be considered, including smoking, diabetes mellitus, and an unhealthy lifestyle. Smoking is a major risk factor for both periodontitis and atherosclerosis, exerting a synergistic effect in exacerbating inflammation and endothelial dysfunction. Diabetes mellitus, through chronic hyperglycemia and impaired immune response, promotes the progression of both periodontal disease and unstable atherosclerotic plaques. In this context, preventive strategies should not only focus on treating periodontal disease but also on educating patients about the importance of a healthy lifestyle (figure 1) [4-8].

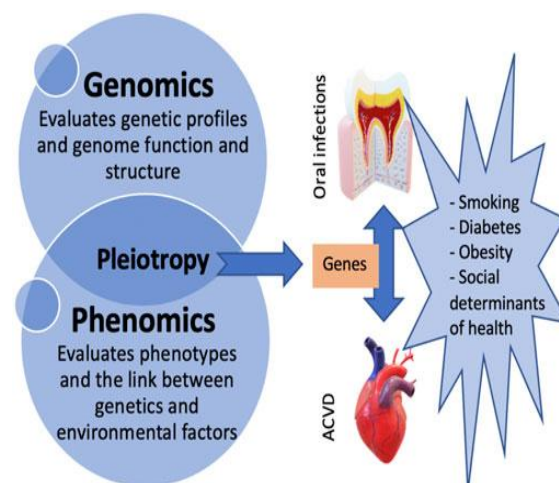


Figure 1. Diagram depicting the concept of pleiotropy and the connection between oral infections, atherosclerotic cardiovascular disease (ACVD), and associated risk factors [8].

Another potential mechanism linking oral health to ASCVD is endotoxemia induced by oral bacteria. In periodontitis, tissue destruction facilitates the entry of pathogens into the systemic circulation, triggering an exaggerated immune response and promoting a persistent pro-inflammatory state. This phenomenon contributes to increased oxidative stress and endothelial dysfunction, both of which are essential factors in atherosclerosis development. Beyond inflammatory implications, oral infections may also influence coagulation pathways, increasing the risk of thrombus formation and acute cardiovascular complications [6-8].

Common pathophysiological mechanisms

The connection between atherosclerotic cardiovascular disease and oral health is supported by multiple common pathophysiological mechanisms involving chronic inflammation, bacterial

infection, endothelial dysfunction, and alterations in the immune system. The inflammatory process plays a crucial role in both conditions, significantly impacting the progression of atherosclerosis and tissue destruction in periodontal diseases [4,7-10].

In periodontitis, pathogenic bacteria such as *Porphyromonas gingivalis*, *Tannerella forsythia*, and *Treponema denticola* trigger a strong inflammatory response by activating the innate immune

system and releasing pro-inflammatory cytokines such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF- α), and C-reactive protein (CRP). These inflammatory molecules do not remain localized but enter the systemic circulation, contributing to endothelial dysfunction, increased oxidative stress, and the acceleration of the atherosclerotic process (figure 2) [7-11].

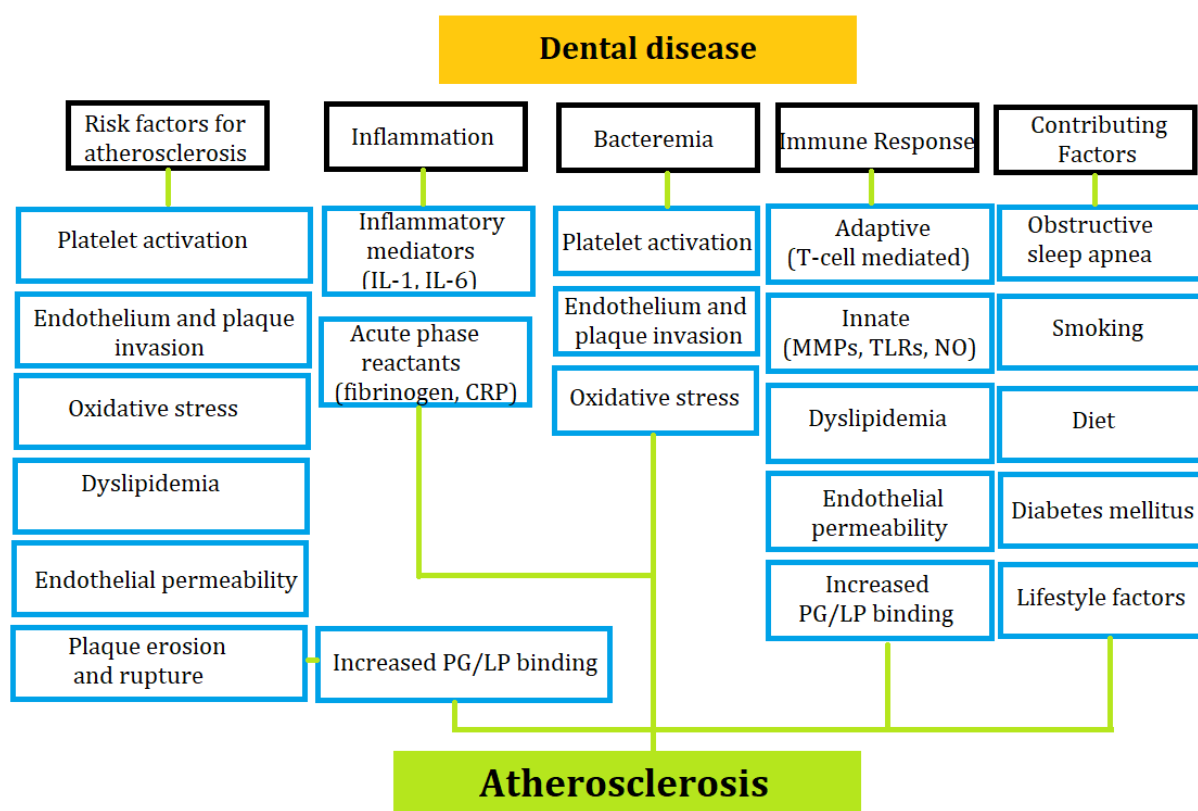


Figure 2. Hypothesized pathways connecting dental pathology and atherosclerosis. Abbreviations: IL (Interleukin); CRP (C-reactive protein); MMP (Matrix metalloproteinase); TLR (Toll-like receptor); NO (Nitric oxide); PG (Proteoglycan); LP (Lipoprotein) [11].

Another major mechanism by which periodontal diseases contribute to atherosclerosis is through the alteration of endothelial function. The endothelium plays a fundamental role in regulating blood flow and maintaining a balance between

procoagulant and anticoagulant factors. Chronic inflammation generated by oral infections leads to a decrease in the bioavailability of nitric oxide (NO), a crucial vasodilator in maintaining vascular tone and preventing platelet aggregation.

The reduction in NO synthesis and the increased production of reactive oxygen species contribute to arterial wall stiffening and the promotion of a pro-thrombotic environment. Additionally, elevated levels of fibrinogen and other systemic inflammatory markers favor hypercoagulability, increasing the risk of acute cardiovascular events such as myocardial infarction and stroke [6-11].

Alongside these inflammatory and thrombotic mechanisms, the impact on lipid metabolism must also be considered. Periodontal diseases have been correlated with dyslipidemia, characterized by increased levels of oxidized LDL cholesterol and decreased HDL cholesterol, which accelerates lipid deposition in the vascular wall. Systemic inflammation induced by oral infections stimulates macrophage activation and their transformation into foam cells, contributing to the enlargement and instability of atherosclerotic plaques. On the other hand, dyslipidemia is also a risk factor for worsening periodontal diseases, creating a vicious cycle between oral health and atherosclerotic cardiovascular disease [7-12].

In this complex interplay, the immune system plays a crucial role in modulating the relationship between oral

inflammation and atherosclerosis. In periodontitis, excessive activation of immune cells such as neutrophils and T lymphocytes leads to the release of large amounts of proteases and inflammatory cytokines, contributing to periodontal tissue destruction. This persistent immune activation has systemic effects, promoting low-grade chronic inflammation, a central mechanism in the development of atherosclerosis. Furthermore, autoimmune reactions generated by molecular mimicry between oral bacterial antigens and endothelial structures can lead to vascular autoaggression, accelerating cardiovascular disease progression [8-12].

Another important aspect is the influence of periodontal diseases on the response to cardiovascular treatments. Patients with chronic oral inflammation often show reduced sensitivity to lipid-lowering and anti-inflammatory therapies, potentially limiting the effectiveness of preventive strategies used in atherosclerotic disease. Moreover, patients undergoing cardiovascular surgical interventions, such as coronary bypass or stent implantation, are at increased risk of postoperative infections if oral health is poor, highlighting the need for an integrated approach to these two medical fields [8-12].

<i>Mechanism</i>	<i>Description</i>	<i>Impact on ASCVD</i>	<i>Supporting evidence</i>
<i>Chronic inflammation</i>	Periodontal infections induce a systemic inflammatory response characterized by increased cytokines (IL-6, TNF- α) and C-reactive protein (CRP), promoting atherosclerosis.	Promotes atherogenesis, plaque instability, and increases cardiovascular event risk.	Elevated systemic inflammatory markers in patients with periodontitis and ASCVD.
<i>Bacterial endotoxemia</i>	Oral bacteria such as *Porphyromonas gingivalis* and *Fusobacterium nucleatum* enter the bloodstream, triggering immune activation and vascular damage.	Facilitates bacterial colonization in atherosclerotic plaques, exacerbating vascular inflammation.	DNA of periodontal pathogens detected in atherosclerotic plaques.

Endothelial dysfunction	Chronic inflammation leads to reduced nitric oxide (NO) bioavailability, impairing vasodilation and increasing vascular stiffness, a key factor in ASCVD progression.	Enhances arterial rigidity and disrupts endothelial function, leading to hypertension and ischemia.	Lower nitric oxide levels and endothelial dysfunction observed in periodontitis patients.
Hypercoagulability	Inflammation-driven increases in fibrinogen and platelet aggregation enhance blood clot formation, elevating the risk of thrombotic cardiovascular events.	Increases thrombosis risk, raising the likelihood of myocardial infarction and stroke.	Increased fibrinogen and platelet aggregation in individuals with periodontal disease.
Lipid metabolism alterations	Periodontal disease is linked to increased levels of oxidized LDL cholesterol and reduced HDL cholesterol, contributing to lipid deposition in arterial walls.	Aggravates lipid accumulation in arteries, accelerating plaque development and rupture.	Positive correlation between periodontitis severity and dyslipidemia markers.
Immune system dysregulation	Prolonged immune activation results in heightened oxidative stress, macrophage infiltration into atherosclerotic plaques, and potential autoimmune vascular damage.	Triggers chronic vascular inflammation and impairs the immune response, worsening ASCVD outcomes.	Immune response abnormalities and autoantibody presence in ASCVD patients with poor oral health.

Table 1. The table presents the main pathophysiological mechanisms linking oral health to atherosclerotic cardiovascular disease (ASCVD). It highlights processes such as chronic inflammation, bacterial endotoxemia, and endothelial dysfunction, along with their impact on atherosclerosis progression. Additionally, it includes clinical evidence supporting the association between periodontitis and cardiovascular risk [5,8-13].

Clinical evidence of the association between ASCVD and oral health

The link between atherosclerotic cardiovascular disease and oral health is supported by numerous epidemiological, observational, and interventional studies demonstrating that chronic inflammation caused by periodontal diseases can contribute to the progression of atherosclerosis and increase the risk of major cardiovascular events. Research has shown that patients with moderate or severe periodontitis have a higher risk of myocardial infarction and stroke compared to individuals with optimal oral health. The pathophysiological mechanisms underlying this correlation include systemic inflammatory responses, bacterial endotoxemia, endothelial dysfunction, and thrombotic activation, all of which are involved in the progression of atherosclerotic disease. Elevated levels of

systemic inflammatory markers, such as C-reactive protein, interleukin-6, and tumor necrosis factor- α , are significantly increased in patients with periodontal diseases, indicating that oral inflammation can have widespread effects on the entire body [9-14].

The analysis of atherosclerotic lesions has revealed the presence of pathogenic oral bacteria, such as *Porphyromonas gingivalis*, *Aggregatibacter actinomycetemcomitans*, and *Fusobacterium nucleatum*, in the atherosclerotic plaques of patients with cardiovascular disease. The identification of these microorganisms through molecular biology techniques has confirmed the hypothesis that periodontal bacteria can migrate into the circulatory system and contribute to the initiation and progression of the atherosclerotic process [10-14].

Several longitudinal studies have examined the effects of periodontal treatment on cardiovascular risk, concluding that reducing oral inflammation leads to improvements in essential vascular parameters. For example, research has shown that patients who underwent intensive periodontal treatment experienced a significant reduction in C-reactive protein levels and an improvement in endothelial function, suggesting that periodontal therapy can have a beneficial impact on cardiovascular health. Moreover, some studies have reported a decrease in cardiovascular events among patients with periodontal disease who received anti-inflammatory and antimicrobial therapies, further supporting the idea that oral health can directly influence cardiovascular prognosis [8,10-14].

Supporting this theory, evidence suggests that patients with severe periodontitis are more likely to develop metabolic syndrome, a condition that includes hypertension, insulin resistance, and dyslipidemia, all of which contribute to the progression of atherosclerosis. Research has shown that chronic inflammation induced by oral infections can contribute to increased insulin resistance and worsening lipid profiles, partially explaining the close relationship between periodontal disease and cardiovascular risk. Additionally, patients with diabetes mellitus, who are predisposed to cardiovascular complications, are also at a higher risk of developing periodontitis, suggesting a reciprocal influence between these conditions [11-15].

Another important aspect is the role of smoking, a common risk factor for both periodontitis and atherosclerosis. Smoking alters immune responses, increases

oxidative stress, and impairs tissue regeneration, thereby contributing to the progression of periodontal disease and vascular damage [11-16].

Given this evidence, more specialists are recommending the integration of dental screening into the assessment of patients at high cardiovascular risk. Early identification of signs of oral inflammation and the implementation of appropriate preventive measures could reduce the risk of cardiovascular complications and improve the management of patients with atherosclerotic disease [12-16].

Clinical implications and therapeutic approaches

The connection between atherosclerotic cardiovascular disease and oral health has significant clinical implications, highlighting the need for integrated prevention and treatment strategies that address both systemic inflammation and specific risk factors associated with each condition. Given that chronic inflammation is a common mechanism in both diseases, effective management of oral health could have a positive impact on reducing cardiovascular risk. Therefore, dental screening should be included in the assessment of patients at high cardiovascular risk, and dentists and cardiologists should collaborate to optimize the care of patients with both periodontal disease and atherosclerosis [13-17].

An essential aspect of this integrated approach is educating patients about the importance of oral health in cardiovascular disease prevention. In many cases, patients with cardiovascular risk factors are unaware of the impact of periodontal disease on their overall health, leading to poor oral hygiene

and delayed treatment. Awareness campaigns should emphasize that maintaining proper oral hygiene, attending regular dental check-ups, and promptly treating gingival inflammation can help reduce cardiovascular risk. Additionally, patients with atherosclerosis or cardiovascular risk factors such as diabetes, hypertension, or dyslipidemia should be encouraged to undergo regular dental evaluations to prevent the onset or worsening of periodontal diseases [14-17].

A crucial component of the therapeutic strategy involves dental treatments aimed at reducing oral inflammation and eliminating infectious foci. Periodontal therapy, including professional scaling, subgingival curettage, and local antimicrobial treatments, has been shown to lower levels of C-reactive protein and other systemic inflammatory markers, suggesting a positive impact on cardiovascular health. In patients with severe periodontitis, surgical periodontal treatments may be necessary to control inflammation and prevent tooth loss. Additionally, systemic antibiotics combined with mechanical therapy have been found to be effective in eliminating pathogenic bacteria and reducing inflammation, although their use should be carefully managed to prevent antibiotic resistance [8,14-17].

From a cardiological perspective, patients with periodontal disease should

receive close monitoring and optimized treatment for cardiovascular risk factors. Studies have shown that therapies aimed at reducing systemic inflammation, such as statins and angiotensin-converting enzyme inhibitors, may also benefit oral health by decreasing inflammation and improving endothelial function. Furthermore, the use of antiplatelet agents and anticoagulants in cardiovascular prevention requires careful management in patients undergoing invasive dental treatments to minimize the risk of excessive bleeding. In this regard, collaboration between cardiologists and dentists is essential to adjust medication regimens and mitigate perioperative risks for dental procedures in patients with cardiovascular conditions [15-17].

Another important aspect of managing patients with both cardiovascular risk and periodontal disease is implementing lifestyle modifications that positively impact both oral and cardiovascular health. Smoking cessation, adopting a balanced diet rich in antioxidants and omega-3 fatty acids, and maintaining a healthy weight are essential measures for preventing the progression of both atherosclerosis and periodontal disease. Smoking, in particular, is a major risk factor for both periodontal bone loss and endothelial dysfunction, and quitting this habit can have long-term benefits for both conditions [15-18].

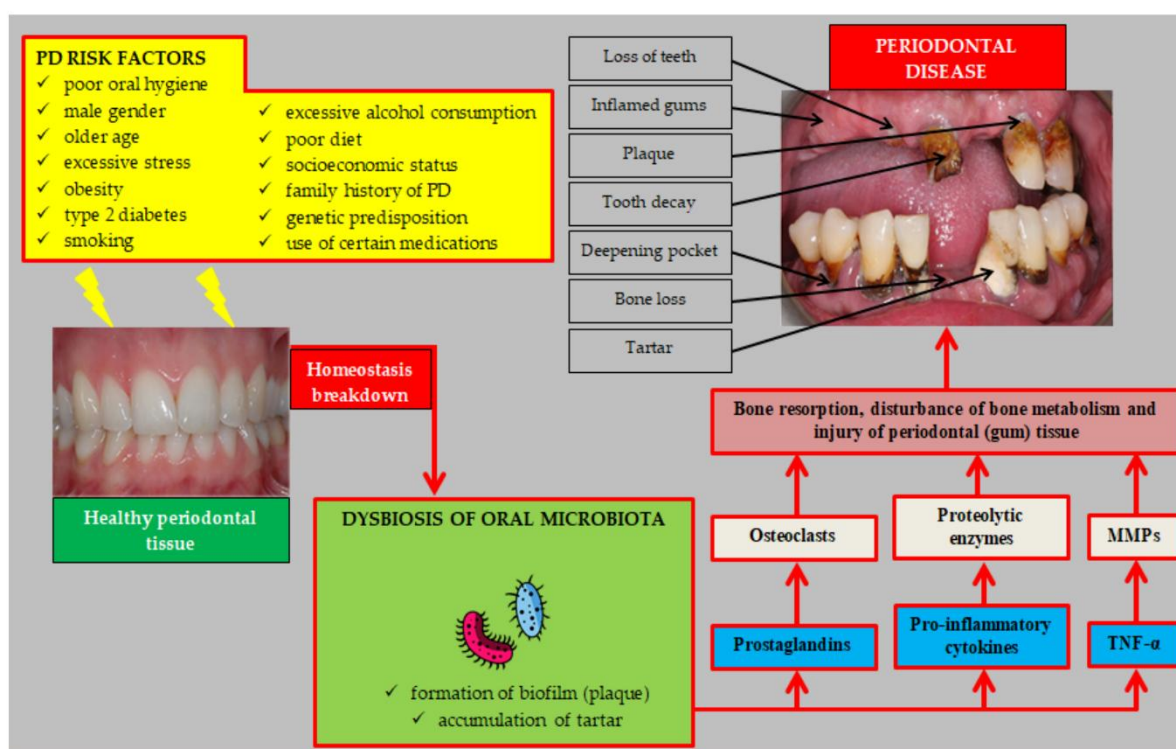


Figure 3. Pathogenesis of periodontal disease. Abbreviations: PD (periodontal disease); TNF- α (tumor necrosis factor alpha); MMPs (matrix metalloproteinases) [18].

The clinical implications of the relationship between oral health and atherosclerotic cardiovascular disease emphasize the need for a multidisciplinary approach that includes regular dental screening, patient education, and collaboration between dental and cardiology specialists. Periodontal treatments can help reduce systemic inflammation and improve endothelial function, potentially benefiting cardiovascular health. Conversely, optimizing cardiovascular risk management and adopting a healthy lifestyle can positively influence oral health, preventing the onset and progression of periodontal disease. Integrating these measures into a comprehensive prevention and treatment strategy could help reduce the incidence of cardiovascular events and improve patients' quality of life, highlighting the importance

of a holistic approach in modern medicine[14-18].

Future research directions

In the context of the relationship between atherosclerotic cardiovascular disease and oral health, future research directions need to focus on elucidating the pathophysiological mechanisms by which oral inflammation contributes to the progression of atherosclerosis and how dental interventions can influence cardiovascular risk. Although multiple studies have demonstrated the association between periodontal disease and major cardiovascular events, clear confirmation of the causal relationship through large-scale longitudinal and interventional studies remains necessary. Detailed investigation of the systemic immune response to oral infections could provide essential

information on the direct impact of chronic inflammation on endothelial dysfunction and on the activation of thrombotic processes [16-20].

Another important area of research is the evaluation of the effect of dental therapies on inflammatory markers and vascular function. Although some studies have reported decreased levels of C-reactive protein and improved endothelial function after periodontal treatments, these results need to be validated by controlled clinical trials, which follow the evolution of patients in the long term and establish the real impact of dental interventions on the prevention of cardiovascular events [16-21].

A promising research direction is investigating the use of essential oils in the management of oral inflammation and their impact on cardiovascular risk. Some essential oils, such as tea tree, cloves, peppermint, and lavender, have demonstrated antimicrobial and anti-inflammatory properties, reducing oral bacterial load and levels of pro-inflammatory cytokines. Future studies should explore the effect of these compounds on the oral microbiome, systemic inflammatory markers, and endothelial function, evaluating their potential as adjuvant therapies in the prevention of atherosclerosis by reducing chronic inflammation generated by periodontal disease [22-27].

Another relevant research direction is to investigate the impact of dental inclusion, especially of impacted wisdom teeth, on systemic inflammation and cardiovascular risk. The impacted wisdom tooth can cause chronic local inflammation, pericoronaritis and recurrent infections, contributing to increased levels of systemic

inflammatory markers such as C-reactive protein and interleukin-6. Future studies should look at whether prophylactic extraction of impacted molars can reduce systemic inflammatory load and positively influence cardiovascular health, especially in patients with atherosclerotic risk factors [28-39].

An innovative research direction is the use of biomaterials in the management of periodontal diseases and their impact on reducing systemic inflammation and cardiovascular risk. Antibacterial hydrogels, nanotechnology-based materials, and bioresorbable membranes can facilitate tissue regeneration and reduce oral microbial load, thereby limiting the systemic inflammatory response associated with atherosclerosis. Future studies should look at whether the use of these biomaterials in advanced periodontal treatments can decrease systemic inflammatory markers and improve endothelial function, thereby helping to prevent cardiovascular disease progression by controlling chronic oral inflammation [40-48].

Another key aspect is to explore the impact of environmental and lifestyle factors on the relationship between oral health and atherosclerosis. Although smoking, unbalanced diet, and chronic stress have been shown to worsen both periodontal and cardiovascular disease, future research should investigate how lifestyle changes influence common inflammatory markers and the risk of cardiovascular events. Interventional studies combining dental treatments with lifestyle changes could provide further evidence on how an integrated approach can reduce the risks associated with these conditions [49].

Conclusions

The relationship between oral health and atherosclerotic cardiovascular disease is supported by numerous clinical, epidemiological and pathophysiological evidence, demonstrating that chronic inflammation generated by periodontal diseases can have a negative impact on the cardiovascular system. Systemic inflammation induced by periodontal pathogenic bacteria contributes to endothelial dysfunction, the formation of atherosclerotic plaques and an increased risk of cardiovascular events. Studies show that patients with severe periodontitis have high levels of C-reactive protein and proinflammatory cytokines, factors recognized for their role in the progression of atherosclerosis. These data suggest that oral health is an essential factor in maintaining systemic inflammatory balance.

Clinical evaluations have shown that periodontal treatments can reduce inflammatory markers and improve endothelial function, indicating a potential benefit of these interventions on cardiovascular health. However, the variability of individual responses and the lack of conclusive longitudinal studies make it necessary to better understand the long-term effect of dental therapies on reducing cardiovascular risk.

A preventive approach focused on maintaining oral health could help reduce cardiovascular risk by controlling chronic

inflammatory processes. Educating patients about the importance of oral hygiene, regular screening, and early periodontal treatments are essential strategies in preventing cardiovascular complications. In this context, interdisciplinary collaboration between dentists and cardiologists becomes essential for the effective management of patients with high cardiovascular risk. Better integration of oral health into preventive medicine could significantly reduce the impact of cardiovascular disease on the general population.

Another important aspect is the influence of lifestyle on oral and cardiovascular health. Smoking, unhealthy diet and chronic stress are factors that favor both the development of periodontitis and atherosclerosis, by amplifying systemic inflammation and accelerating vascular degenerative processes. Quitting smoking, eating a balanced diet, and reducing stress could have beneficial effects on both conditions, highlighting the need for an integrated approach to overall health.

The integration of alternative and complementary therapies, such as the use of essential oils with an antimicrobial and anti-inflammatory effect, is another promising direction in the control of oral inflammation and, implicitly, in reducing cardiovascular risk. Future research should assess the effectiveness of these substances objectively, establishing their impact on the oral microbiome and on the systemic immune response.

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