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Research Article

The Periodontal-Cardiovascular Axis: Mechanisms, Clinical Implications, and Integrated Management Strategies

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Abstract

A growing body of evidence underscores a significant bidirectional relationship between periodontal disease (PD) and cardiovascular diseases (CVD), particularly atherosclerotic cardiovascular disease (ASCVD) and its interventions. This review synthesizes current knowledge on the pathophysiological mechanisms linking oral dysbiosis and chronic periodontal inflammation to endothelial dysfunction, plaque instability, and adverse cardiovascular events. We examine epidemiological data establishing PD as an independent risk factor for CVD, explore shared inflammatory pathways, and critically evaluate clinical evidence regarding the impact of periodontal treatment on cardiovascular surrogate markers and hard outcomes. Furthermore, we discuss the implications for interdisciplinary care models integrating dentistry and clinical cardiology. A comprehensive literature search of PubMed, Embase, and Cochrane Library databases was conducted, encompassing observational studies, randomized controlled trials (RCTs), systematic reviews, and mechanistic investigations. The evidence strongly supports PD as a contributor to cardiovascular risk via systemic inflammation, bacteremia, and immune dysregulation. While periodontal therapy improves endothelial function and reduces systemic inflammation, large-scale RCTs on hard cardiovascular endpoints are ongoing. Collaborative management strategies between dental and cardiovascular health professionals are crucial for optimizing patient outcomes and warrant broader implementation.

Keywords: periodontal disease; cardiovascular diseases; atherosclerosis; inflammation; endothelial dysfunction; periodontal therapy; cardiovascular risk factors; interdisciplinary communication; porphyromonas gingivalis; c-reactive protein

Introduction

Periodontal disease (PD), a chronic inflammatory condition initiated by dysbiotic oral biofilms and characterized by destruction of the tooth-supporting apparatus, affects nearly half of adults globally [1]. Concurrently, cardiovascular diseases (CVD), particularly atherosclerotic cardiovascular disease (ASCVD), remain the leading cause of mortality worldwide [2]. Historically viewed as separate entities, compelling epidemiological, microbiological, and immunological evidence now reveals a significant association between PD and CVD, independent of traditional risk factors [3,4]. This association extends beyond correlation, implicating PD as a potential modifiable risk factor influencing cardiovascular risk stratification, interventions, and outcomes [5]. This article explores the intricate biological mechanisms underpinning the periodontal-cardiovascular axis, reviews the clinical evidence linking PD to ASCVD and cardiovascular interventions, and advocates for integrated patient management paradigms.

Pathophysiological Mechanisms:

Bridging the Oral-Systemic Divide

The biological plausibility of the PD-CVD link rests on several interconnected pathways: Bacteremia and Direct Microbial Effects: Routine mastication, dental procedures, or even oral hygiene can transiently introduce periodontal pathogens (e.g., Porphyromonas gingivalis, Aggregatibacter actinomycetemcomitans, Tannerella forsythia) into the bloodstream [6]. These pathogens, their virulence factors (e.g., gingipains), and bacterial DNA have been detected within atherosclerotic plaques retrieved during carotid endarterectomy or coronary artery bypass grafting [7,8]. P. gingivalis, in particular, can invade endothelial cells, promote foam cell formation, and exacerbate plaque inflammation and instability through mechanisms involving Toll-like receptor (TLR) activation (especially TLR2/4) and manipulation of host cell signaling [9,10].

Systemic Inflammation: PD represents a significant reservoir of chronic low-grade inflammation. Pro-inflammatory cytokines (e.g., interleukin-1β [IL-1β], IL-6, tumor necrosis factor-alpha [TNF-α]) and acute-phase proteins (notably C-reactive protein [CRP]) produced locally in the gingiva readily enter the systemic circulation [11]. Elevated systemic

levels of CRP, IL-6, and fibrinogen are established risk markers and mediators of endothelial dysfunction, atherogenesis, and plaque vulnerability [12,13]. Periodontal treatment significantly reduces these systemic inflammatory markers [14]. Endothelial Dysfunction: A critical early event in atherosclerosis. Circulating inflammatory mediators from PD, along with direct effects of periodontal pathogens, impair endothelial nitric oxide (NO) bioavailability, promote vasoconstriction, increase vascular permeability, and enhance expression of adhesion molecules (e.g., VCAM-1, ICAM-1), facilitating monocyte recruitment into the arterial intima [15]. Studies using flow-mediated dilation (FMD) consistently show impaired endothelial function in PD patients, which improves following periodontal therapy [16].

Autoimmunity and Molecular Mimicry: Molecular similarity between bacterial heat shock proteins (HSPs) (e.g., GroEL from *P. gingivalis*) and human HSP60 can trigger cross-reactive autoimmune responses. Antibodies generated against bacterial HSPs may target human endothelial HSPs, contributing to endothelial damage and atheroma formation [17,18]. Platelet Activation and Hypercoagulability: Periodontal pathogens and systemic inflammation can activate platelets and upregulate pro-coagulant factors (e.g., fibrinogen, von Willebrand factor), potentially increasing thrombotic risk, a crucial factor in acute coronary syndromes (ACS) and complications post-stent implantation or other cardiovascular interventions [19].

Epidemiological and Clinical Evidence: Association and Intervention

Numerous large-scale epidemiological studies substantiate PD as an independent risk factor for CVD:

- Meta-analyses of prospective cohort studies report a significantly increased risk of coronary heart disease (CHD) (Hazard Ratio [HR] ranging 1.14-1.49), stroke (HR 1.63), and peripheral arterial disease in individuals with PD, even after adjusting for smoking, diabetes, and socioeconomic status [3,20,21].
- The severity and extent of PD correlate positively with CVD risk. Tooth loss, a surrogate for historical severe PD, is also independently associated with incident CVD and CVD mortality [22].
- PD is linked to worse outcomes in patients undergoing cardiovascular interventions. Patients with PD undergoing coronary artery bypass grafting (CABG) have higher rates of postoperative complications, including infections and cardiovascular events [23]. Similarly, PD is associated with an increased risk of myocardial infarction (MI) and stent thrombosis post-percutaneous coronary intervention (PCI) [24].

Impact of Periodontal Therapy on Cardiovascular Parameters:

While large-scale RCTs powered for hard endpoints (MI, stroke, death) are complex and ongoing, evidence on surrogate markers is promising:

Endothelial Function: RCTs demonstrate that non-surgical periodontal therapy (scaling and root planing, SRP) significantly improves FMD within weeks to months, indicating enhanced endothelial function [16,25].

Systemic Inflammation: Periodontal therapy consistently reduces serum levels of CRP, IL-6, and other inflammatory markers [14,26]. This reduction is comparable to the effect of statins in some studies.

Metabolic Parameters: Improvements in glycemic control (HbA1c) in diabetic patients post-periodontal therapy are well-documented, indirectly benefiting cardiovascular risk [27].

Cardiovascular Events: The INVEST trial, though underpowered for its primary composite endpoint, suggested a potential benefit of periodontal therapy in reducing cardiovascular events in high-risk populations [28]. Other smaller RCTs and observational studies hint at reduced hospitalization rates and mortality in CVD patients receiving periodontal care [29]. The ongoing IMPROVE trial aims to provide definitive evidence on hard endpoints [30].

Implications for Clinical Cardiology and Cardiovascular Interventions

The evidence necessitates a paradigm shift towards integrated care:

Cardiologist's Role:

Screening & Inquiry: Routinely inquire about oral health symptoms (bleeding gums, loose teeth), history of PD diagnosis/treatment, and frequency of dental visits during cardiovascular risk assessment and in patients with established CVD, especially pre-operatively (CABG, valve surgery, PCI) [31].

Risk Stratification: Recognize severe PD as a potential modifier of overall cardiovascular risk, particularly in intermediate-risk patients.

Referral: Actively refer patients with signs or symptoms of PD, or those lacking regular dental care, for comprehensive periodontal evaluation and treatment [5].

Patient Education: Emphasize the importance of optimal oral hygiene and regular dental care as part of holistic cardiovascular health management.

Dentist's/Periodontist's Role:

CVD Risk Awareness: Be cognizant of the patient's CVD status and risk factors (hypertension, dyslipidemia, diabetes, smoking history). Screen for undiagnosed hypertension [32].

Medical History: Obtain detailed and updated cardiovascular history (diagnoses, medications - especially anticoagulants/antiplatelets, interventions, recent events).

Risk Assessment & Communication: Identify patients with severe PD as potentially having increased cardiovascular risk. Communicate findings and treatment plans to the patient's cardiologist/primary care physician, especially regarding planned invasive procedures [31].

Management Optimization: Provide thorough periodontal therapy (SRP, adjunctive antimicrobials if indicated, maintenance) to reduce the oral inflammatory burden. Coordinate timing of invasive dental procedures (e.g., complex extractions, extensive surgery) with the cardiology team for patients on antithrombotics or with unstable cardiac conditions.

Antibiotic Prophylaxis: Adhere strictly to current guidelines (e.g., AHA/ACC) regarding antibiotic prophylaxis for infective endocarditis only in the highest-risk cardiac conditions [33].

Future Directions

Key research priorities include: Large, well-designed RCTs (like IMPROVE) evaluating the effect of intensive periodontal treatment on hard cardiovascular endpoints (MACE) [30]. Mechanistic studies elucidating the specific contributions of individual pathogens and virulence factors. Investigating the impact of periodontal treatment on outcomes post-specific cardiovascular interventions (PCI, CABG, TAVI). Development and validation of integrated risk prediction models incorporating PD status. Exploring novel anti-inflammatory therapies targeting pathways shared by PD and ASCVD. Assessing the cost-effectiveness of integrated dental-cardiac care models.

Conclusion

The link between periodontal disease and cardiovascular disease, particularly atherosclerotic cardiovascular disease and its interventions, is firmly established by robust biological mechanisms and substantial epidemiological evidence. Chronic oral inflammation contributes to systemic inflammation, endothelial dysfunction, and potentially

accelerates atherosclerosis and increases thrombotic risk. Periodontal therapy demonstrably improves surrogate cardiovascular markers like endothelial function and systemic inflammation. While definitive proof of causality regarding hard endpoints awaits large RCT results, the current evidence strongly supports the integration of oral health into cardiovascular risk assessment and management. Collaborative care models, involving proactive screening, communication, and co-management between dentists, periodontists, cardiologists, and primary care physicians, are essential for optimizing both oral and cardiovascular health outcomes. Recognizing and addressing the periodontal-cardiovascular axis represents a crucial step towards more comprehensive and effective patient care.

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