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Cardiovascular Disease as an Associated Driver of Periodontal Deterioration - A Narrative Review

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Abstract

The reverse relationship between cardiovascular disease and periodontal disease, how cardiovascular disease contributes to periodontal deterioration, remains unexplored despite extensive studies on the conventional relationship. This narrative review explores emerging evidence supporting four key mechanisms by which cardiovascular disease and its management can contribute to periodontal deterioration. Amlodipine and nifedipine are some of the common calcium channel blockers, causing drug-induced gingival overgrowth by creating pseudopockets. Medications used for treating heart failure cause hyposalivation and inflammatory mediators like interleukins and tumor necrosis factor accelerate alveolar bone loss through osteoclast activation matrix metalloproteinase upregulation, due to chronic inflammation. Somatic mutations in the DNMT3A gene, which is associated with clonal hematopoiesis promote cardiovascular pathology and inflammatory periodontal bone loss through a shared molecular mechanism. These four pathways collectively suggest that cardiovascular disease is a plausible associated contributor to periodontal deterioration, despite the absence of prospective causal evidence. Future prospective studies are needed to confirm causal direction and validate these pathways in human cohorts.

Keywords: Cardiovascular Disease, Periodontitis, Systemic Inflammation, Gingival Overgrowth, Hyposalivation, Clonal Hematopoiesis, DNMT3A, Alveolar Bone Loss, Calcium Channel Blockers.

Introduction

For over three decades, the relationship between periodontal disease and cardiovascular disease has occupied a prominent position in oral medicine and cardiology research. However, most of the research has revolved around a single direction, how chronic periodontal inflammation contributes to the onset and progression of cardiovascular conditions. There is reliable research on this relationship, from large reviews to genetic studies by major health organizations like the American Heart Association and European Federation of Periodontology. Periodontal disease can thus be linked to

oral health as well as higher risk of coronary heart disease, stroke, atrial fibrillation, hypertension, and heart failure. While this reviews associative evidence, it does not establish a proven causal pathway from CVD to periodontitis but builds the evidence base for future prospective studies.

Yet in this well-recognized landscape, a critical direction remains unexplored, the reverse pathway. The real question is how does cardiovascular disease, through its systemic inflammatory milieu, its required pharmacological treatments, its physiological consequences, and its associated genetic mechanisms, drive the deterioration of periodontal health? Given that an estimated 17.9 million people die annually from cardiovascular disease and a large proportion of these patients are on long term pharmacotherapy. The scale of this potential reverse direction is clinically significant and systematically unaddressed.

Adding to this, the role of clonal hematopoiesis driven by DMT3A mutations show a shared mechanism which simultaneously drives both cardiovascular pathology and periodontal bone loss. This review's primary objective is to synthesize and clinically frame the reverse direction of the PD-CVD bidirectional relationship, wherein CVD acts as an associated contributor to periodontal destruction. This finding, published in Cell in 2024, marks this as a critical mechanism that has not yet been incorporated into clinical practice guidelines. By doing so, it will provide the evidence base needed for clinical guidelines, interdisciplinary treatment protocols, and future research priorities focused on this clinically significant pathway.

Multiple reports such as the 2025 American Heart Association statement, have renewed focus on the link between periodontal health and CVD, including a 2023 European consensus report, and a 2024 study has shown that intensive gum treatment can improve a marker of artery health. However, most of this research looks at how periodontal health affects cardiovascular disease, not the other way around. We still don't clearly understand how having cardiovascular disease, being treated for it, or carrying genetic risk might influence a person's periodontal health over time. Closing this gap is important, because the people most affected by cardiovascular disease are often the same ones at higher risk for poor periodontal health, making this two-way relationship critical for better care and prevention. yet been synthesized into clinical literature.

Methods

A review of the published literature was conducted to examine the influence of cardiovascular disease on periodontal health through pharmacological, physiological, genetic, and inflammatory mechanisms. PubMed, MEDLINE and the Cochrane Library were searched from database inception through March 2025. Search terms included combinations of: ("cardiovascular disease" OR "heart failure" OR "coronary heart disease" OR "hypertension" OR "atherosclerosis") AND ("periodontal disease" OR "periodontitis" OR "gingival overgrowth" OR "DIGO") AND ("drug-induced" OR "calcium channel blocker" OR "clonal hematopoiesis" OR "DNMT3A" OR "trained immunity" OR "hyposalivation" OR "systemic inflammation").

Results

Drug-Induced Gingival Overgrowth from Cardiovascular Medications

Calcium channel blockers are used to control hypertension, angina, and arrhythmias apart from ACE inhibitors, beta-blockers and statins. First generation dihydropyridines such as nifedipine and amlodipine are the most common drugs causing drug-induced gingival

overgrowth, showing a direct, pharmacological pathway by which cardiovascular disease treatment causes periodontal tissue pathology.

The prevalence of drug-induced gingival overgrowth in patients taking nifedipine ranges from 20% to 50% across different studies, with clinically significant overgrowth reported at 6.3% in a large periodontal screening study involving 17,991 subjects. [16] The case-control study from Oral Biobank diagnosed 22% of 91 patients on calcium channel blockers for at least 12 months. [5] The Frontiers in Oral Health study revealed a direct association between systemic CVD medication intake and the severity and progression rate of periodontitis at the population level. [6]

The molecular mechanism involves inhibition of L-type calcium channels in gingival fibroblasts, disrupting the collagen degradation by reducing matrix metalloproteinase activity and leading to accumulation of extracellular collagen matrix. At the same time, Calcium channel blockers block aldosterone synthesis, triggering adrenal androgen excess that promotes gingival fibroblast proliferation through dihydrotestosterone receptor pathways. A critical co-factor in this process is dental plaque as patients with poor oral hygiene on Calcium channel blockers develop significantly more severe DIGO. Drug-induced gingival overgrowth creates pseudopockets that harbor anaerobic bacteria, promote dysbiosis, and can progress to true periodontal pockets with alveolar bone loss.

Heart Failure and Hyposalivation

Loop diuretics and thiazide diuretics are common groups of drugs used for management of heart failure which reduce the salivary flow as a systemic side effect. Saliva plays a critical role in periodontal disease, providing mechanical lavage, delivering antimicrobial peptides, maintaining neutral oral pH and inhibiting periodontal biofilm formation. When diuretics cause hyposalivation and reduce salivary flow, each of these protective functions is compromised.

Patients with advanced heart failure often experience dyspnea, which makes them rely more on mouth-breathing, which further desiccates oral mucosal surfaces and disrupts the oral microbiome. Beta blockers which are commonly prescribed in heart failure also cause reduced salivary flow. Symptoms of Heart failure such as physical deconditioning, dyspnea, and fatigue reduce the patient's ability to maintain adequate oral hygiene. Periodontitis is significantly associated with heart failure, with mechanisms including both the shared inflammatory burden and the direct oral health consequences of cardiac dysfunction, according to the NHANES III population data. [7,8]

Clonal Hematopoiesis and Shared Inflammatory Mechanism

Clonal hematopoiesis refers to the age-related accumulation of somatic mutations in hematopoietic stem cells. DNMT3A mutations are associated with a 1.9-fold increased risk of coronary heart disease and 4-fold increased risk of heart failure. Recent evidence from a 2024 cell study shows direct evidence that DNMT3a mutant clonal hematopoiesis also promotes inflammatory alveolar bone loss, key indicator of periodontitis. 1 This finding suggests that clonal hematopoiesis acts as a shared molecular driver of both cardiovascular pathology and periodontal bone loss, meaning both disease progress through the same genetic-inflammatory mechanism in patients carrying DNMT3A mutations.

Similar to this, a 2022 cell study showed that maladaptive innate immune training of myelopoiesis links inflammatory comorbidities, providing a cellular mechanism by which cardiovascular inflammation creates systemic immune memory that increases

destructive responses in the periodontium. A patient whose monocytes have been reprogrammed by cardiovascular inflammation will show a significantly heightened tissue destructive response in the periodontium, thereby accelerating the periodontal attachment loss independent of local bacterial burden. Current evidence also suggests that trained immunity of myeloid cells may be a conserved feature of chronic inflammatory diseases including atherosclerosis, raising the hypothesis that cardiovascular inflammation may epigenetically prime myeloid cells toward exaggerated periodontal tissue destruction. However, there is a requirement for prospective clinical studies to validate this.

Sustained Systemic Inflammation

Patients with cardiovascular disease maintain elevated levels of C-reactive protein (CRP), interleukin-6 (IL-6), tumor necrosis factor-alpha, and fibrinogen. The atherosclerosis in cardiovascular diseases is driven by macrophage foam cell accumulation, oxidized LDL, and pro-inflammatory cytokine signaling. This sustained inflammatory state may have a direct effect on periodontal tissues.

Chronic elevation of pro-inflammatory cytokines, particularly IL-6 and tumor necrosis factor- alpha directly activate osteoclast differentiation through the RANK signaling pathways and stimulate matrix metalloproteinase production in periodontal tissues. Due to the lowered

threshold for systemic inflammation, there is accelerated periodontal tissue destruction. A key finding that IL-1β blockade with canakinumab significantly reduced recurrent cardiovascular events suggest that the shared inflammatory pathway involving IL-6 and CRP signaling may also exert a protective effect on periodontal tissues. [9]

Discussion

This review is one of the first synthesis of bidirectional periodontal-cardiovascular associations. By shifting the focus from the conventional PD-CVD pathway to the reverse direction, four diverse evidence-based mechanisms are identified through which cardiovascular disease may contribute to periodontal deterioration, each with clinical implications.

The neglect of this direction can be attributed to research framing. Clinical disciplines such as periodontology and cardiology operate separately while the original hypothesis linking oral health to systemic disease goes from the bacteria in the mouth to the heart. There is a clear evidence-to-practice gap because calcium channel blockers are among the most prescribed medications for cardiovascular disease, yet cardiologists do not routinely assess periodontal status before initiating the treatment. Similarly, the DNMT3A mutation aspect has not yet entered the periodontal or the cardiovascular clinical guidelines.

These four pathways create a self-reinforcing cycle, in which cardiovascular disease and its treatment worsen periodontal health through, genetic, pharmacological, physiological, and inflammatory mechanisms. This results in periodontitis which further increase bacterial load, elevates systemic inflammatory markers, and accelerates cardiovascular pathology.

Several limitations of the current evidence base need to be acknowledged. Although each proposed biological pathway is plausible and supported by associative data, none of the cited studies were designed to clearly determine the causal direction between cardiovascular disease and periodontal disease. Most of the evidence regarding DNMT3A-related clonal hematopoiesis comes from animal models. To draw stronger conclusions, prospective longitudinal studies are needed in human

CVD populations. Compare those with and without DNMT3A mutations to track periodontal outcomes over time. Additionally, Embase and Scopus were not included in the electronic search strategy and their exclusion may have introduced selection bias toward studies indexed in PubMed, MEDLINE and the Cochrane Library alone. The substantial variation in study designs and outcome definitions prevented quantitative synthesis of the results.

Confounding variables may partly reflect overlapping risk factors rather than a true causal effect from CVD to PD as they independently affect the severity of CVD and periodontal health. This should be kept in mind when interpreting the strength and direction of the reported relationships.

Conclusion

Cardiovascular disease is an outcome of poor periodontal health as well as an associated contributor to periodontal deterioration through four distinct pathways backed by evidence. This review is focused on contributing to the periodontal-cardiovascular literature by synthesizing the reverse direction, which is rarely addressed by existing umbrella review, or meta-analyses.

Future research studies should look at comparing clinical attachment loss, probing depth, and plaque index in hypertensive patients treated with calcium channel blockers versus ACE inhibitors controlling for baseline oral hygiene, smoking status, and age with randomized controlled trials of heart failure patients undergoing periodontal therapy, using salivary flow rate and gingival index as primary periodontal outcomes alongside systemic inflammatory markers.

Additionally, a randomized controlled trial of intensive periodontal therapy in patients with heart failure using salivary flow rate and gingival index as primary periodontal outcomes alongside systemic inflammatory markers would help validate whether periodontal intervention can reduce oral and systemic inflammation.

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