

Artificial Intelligence And The Oral Microbiome In Cardiovascular Disease: Mechanisms, Prediction Models, And Clinical Translation

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ABSTRACT

Cardiovascular disease (CVD) remains a major cause of illness and death worldwide, creating an ongoing need for better methods of early detection and risk assessment. Interest in the oral microbiome has increased because of its potential role in systemic health, while artificial intelligence (AI) has become a valuable tool for analyzing complex biological and clinical data. Together, these fields offer new opportunities to improve cardiovascular risk assessment and support personalized care. This narrative review explores the relationship between the oral microbiome and cardiovascular disease and discusses how AI can be applied to oral microbiome data for cardiovascular risk prediction. It also reviews the potential of machine learning techniques to identify microbial patterns, support risk stratification, and assist clinical decision-making. In addition, the role of explainable artificial intelligence (XAI) is discussed as an approach to improve model transparency and facilitate clinical interpretation. By bringing together current knowledge from oral microbiology, cardiovascular medicine, and AI, this review outlines the opportunities and challenges of integrating these fields into clinical practice. It also highlights future directions for AI-enabled oral microbiome analysis in supporting earlier cardiovascular risk assessment and more personalized approaches to disease prevention and patient care.

Keywords: Artificial Intelligence, Machine Learning, Oral Microbiome, Cardiovascular Disease, Periodontal Disease.

INTRODUCTION

Cardiovascular disease (CVD) remains the leading cause of global mortality, driven by complex interactions between metabolic dysfunction, systemic inflammation, and environmental factors. Increasing evidence suggests that chronic infections and microbial dysbiosis play a central role in cardiovascular pathogenesis, shifting attention toward the microbiome as a key regulator of vascular health [1].

Among microbial communities, the oral microbiome has emerged as a major contributor to systemic

inflammation and cardiovascular risk. Periodontitis, a chronic inflammatory disease of the supporting structures of the teeth, is strongly associated with increased risk of coronary artery disease and heart failure. This relationship is mediated through bacterial dissemination, endotoxemia, and persistent low-grade inflammation [2,3].

Mechanistic studies have demonstrated that periodontal pathogens and their metabolic products can enter the bloodstream, triggering immune activation and endothelial dysfunction. These processes accelerate atherosclerotic plaque formation

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and vascular remodeling, forming the basis of the oral-vascular axis [4]. This axis highlights the bidirectional relationship between periodontal inflammation and systemic cardiovascular injury [5].

Clinical evidence further supports this association. Large-scale cardiovascular guidelines recognize periodontal disease as a contributing factor to atherosclerotic cardiovascular disease, emphasizing its importance in risk stratification and prevention strategies [6]. Additionally, studies exploring causality suggest that periodontal inflammation may not only correlate with but also contribute to cardiovascular disease progression [7].

Despite these findings, translating oral microbiome research into clinically actionable cardiovascular prediction remains challenging. Traditional statistical models are often insufficient to capture the complexity of host-microbe interactions and multi-layered biological data [8].

Artificial intelligence (AI) and machine learning (ML) offer powerful solutions to this challenge by enabling integration of heterogeneous datasets, including clinical records, biomarkers, imaging, and multi-omics microbial profiles. In periodontology, AI-based models have demonstrated strong performance in early disease detection, risk prediction, and identification of systemic associations [9,10].

Similarly, in cardiovascular research, ML approaches have been successfully applied to predict coronary heart disease and heart failure risk in patients with periodontal disease, demonstrating the predictive potential of integrating dental and cardiovascular datasets [11,12]. Recent advances further show that combining oral microbiome profiles with AI-driven models improves cardiovascular risk stratification and enables discovery of microbial signatures linked to disease progression [13].

However, despite high predictive performance, many AI models remain limited by lack of interpretability, which restricts their clinical translation. Explainable artificial intelligence (XAI) has therefore emerged as a critical advancement, enabling transparent decision-making and improving clinician trust in AI-based cardiovascular risk models [14,15].

Together, these developments highlight a new precision medicine paradigm that integrates oral microbiome biology with advanced computational modeling. By combining microbial dysbiosis, immune-inflammatory pathways, and AI-driven analytics, this approach may enhance early detection and prevention of cardiovascular disease.

This narrative review aims to (1) summarize mechanistic links between oral microbiome dysbiosis and cardiovascular disease, (2) evaluate AI-based predictive models integrating periodontal and cardiovascular data, and (3) discuss the role of explainable AI in improving clinical translation.

METHODS:

A narrative literature review was conducted to identify relevant publications on the relationship between the oral microbiome, cardiovascular disease, and artificial intelligence (AI). Electronic searches were performed using PubMed/MEDLINE and Google Scholar from database inception through June 2026. Search terms included "oral microbiome," "periodontal disease," "cardiovascular disease," "artificial intelligence," "machine learning," "explainable artificial intelligence," "oral dysbiosis," and "cardiovascular risk."

Only English-language, peer-reviewed articles with freely available full-text access were considered. Original research articles, review articles, and relevant clinical guidelines were selected based on their relevance to the objectives of this narrative review. Reference lists of selected articles were also screened to identify additional relevant publications. A total of 21 references were included in the final manuscript.

RESULT:

• The Oral Microbiome and Cardiovascular Disease Mechanisms

Composition of the Oral Microbiome:

The oral microbiome represents one of the most complex microbial ecosystems in the human body, consisting of diverse bacterial communities that exist in a finely balanced symbiosis with the host. In health, this ecosystem contributes to oral homeostasis; however, perturbations in microbial diversity and

abundance can result in dysbiosis, which has been increasingly implicated in systemic inflammatory diseases, including cardiovascular disease [1,14].

The oral cavity harbors more than 700 bacterial species that colonize distinct ecological niches, including the tongue dorsum, buccal mucosa, saliva, supragingival and subgingival dental plaque, and gingival crevices. These microbial communities are dominated by commensal genera such as *Streptococcus*, *Actinomyces*, *Veillonella*, *Neisseria*, and *Haemophilus*, which contribute to maintenance of microbial homeostasis by limiting colonization by pathogenic organisms and supporting normal immune function. The composition of the oral microbiome is influenced by multiple host and environmental factors, including oral hygiene, dietary habits, smoking, aging, systemic diseases such as diabetes mellitus, antibiotic exposure, and salivary composition. Disruption of this balanced microbial ecosystem can alter both the diversity and functional activity of oral microorganisms, promoting dysbiosis and creating a microenvironment that favors chronic inflammation and disease progression [1,14,15].

Emerging evidence suggests that the oral microbiome functions not only as a local ecosystem but also as a systemic regulator of immune and inflammatory pathways. Microbial metabolites and bacterial components can enter the bloodstream, influencing distant organs and contributing to vascular dysfunction [15]. This positions the oral cavity as a potential microbial reservoir linking local infection to systemic disease processes [1,15].

Oral Microbial Dysbiosis and Periodontitis:

Periodontitis is a prototypical dysbiosis-driven inflammatory disease characterized by disruption of microbial homeostasis and overgrowth of pathogenic species. This imbalance leads to a chronic host inflammatory response, resulting in destruction of periodontal tissues and formation of periodontal pockets that serve as a continuous source of microbial and inflammatory burden [14,16].

Periodontal dysbiosis is characterized by a shift from a predominantly commensal microbial community to one enriched with pathogenic species, particularly the so-called "red complex" bacteria, including *Porphyromonas gingivalis*, *Treponema denticola*, and

Tannerella forsythia. Other organisms such as *Fusobacterium nucleatum* and *Aggregatibacter actinomycetemcomitans* also contribute to disease progression through synergistic interactions within the subgingival biofilm. These microorganisms express a variety of virulence factors, including lipopolysaccharides (LPS), proteolytic enzymes, fimbriae, and adhesins, which facilitate bacterial colonization, tissue invasion, immune evasion, and persistent inflammation. The resulting disruption of host-microbe homeostasis promotes progressive destruction of the periodontal ligament and alveolar bone, ultimately leading to tooth-supporting tissue loss if left untreated [14-16].

Beyond local tissue injury, periodontal pathogens activate both innate and adaptive immune responses. Recognition of bacterial components by pattern recognition receptors, including Toll-like receptors, stimulates intracellular signaling pathways that promote the release of pro-inflammatory cytokines such as interleukin (IL)-1 β , IL-6, and tumor necrosis factor- α (TNF- α). Sustained production of these inflammatory mediators amplifies oxidative stress, promotes recruitment of neutrophils and macrophages, and contributes to chronic systemic inflammation. Repeated episodes of transient bacteremia during routine activities such as tooth brushing or chewing may further facilitate dissemination of oral microorganisms and their inflammatory products into the systemic circulation, providing a biological basis for the association between periodontal disease and cardiovascular pathology [15-18].

The inflammatory cascade triggered by periodontal dysbiosis is not limited to the oral cavity. Pro-inflammatory cytokines, bacterial endotoxins, and immune mediators can enter the systemic circulation, contributing to a sustained low-grade inflammatory state. This systemic inflammation is a key mechanism linking periodontal disease with endothelial dysfunction and vascular injury [15,16].

The concept of the oral-vascular axis provides a mechanistic framework for this interaction. It describes how periodontal inflammation influences vascular biology through immune activation, microbial translocation, and endothelial response dysregulation. This axis highlights a bidirectional

relationship in which vascular inflammation may also exacerbate periodontal disease progression [16].

Evidence Linking Oral Microbiome and Cardiovascular Disease:

A substantial body of evidence supports the association between oral microbiome dysbiosis and cardiovascular disease. Mechanistic studies demonstrate that oral pathogens and their metabolites can contribute to endothelial dysfunction, oxidative stress, and atherosclerotic plaque formation, thereby accelerating cardiovascular pathology [15].

Clinical and epidemiological data further reinforce this association. The American Heart Association recognizes periodontal disease as a contributor to atherosclerotic cardiovascular disease, emphasizing its importance in cardiovascular risk assessment and prevention strategies [17]. In addition, causal inference studies suggest that periodontal inflammation may play a contributory role in cardiovascular disease development rather than being a mere associative marker [18,19].

Recent integrative studies have expanded this paradigm by demonstrating that microbial signatures may be used for cardiovascular risk prediction. These studies show that oral microbiome profiles, when combined with computational approaches, can enhance disease stratification and improve predictive accuracy for cardiovascular outcomes [12,13].

Overall, these findings support a strong biological and clinical link between oral microbial dysbiosis and cardiovascular disease, mediated through systemic inflammation, immune activation, and vascular endothelial injury [14-16,18].

• Artificial Intelligence in Periodontology and Microbiome Research

Evolution of AI in Periodontology:

Artificial intelligence (AI) and machine learning (ML) have rapidly transformed periodontology by enabling data-driven approaches for disease detection, risk prediction, and treatment planning. Traditional periodontal diagnosis relies on clinical indices and radiographic assessment, which are often limited by subjectivity and inter-examiner variability. AI-based systems overcome these limitations by

integrating large-scale datasets and identifying complex nonlinear patterns associated with disease progression [9,10].

Recent scoping evidence highlights that AI applications in periodontology have expanded from simple diagnostic support systems to advanced predictive frameworks capable of integrating clinical, demographic, and molecular data [9]. These developments suggest a shift toward precision dentistry, where computational models assist clinicians in early detection and personalized disease management [10].

Machine Learning for Periodontal and Systemic Risk Prediction:

Machine learning approaches have demonstrated significant potential in predicting periodontal disease severity and its systemic associations. Predictive models using blood biomarkers, demographic factors, and clinical variables have shown promising accuracy in identifying individuals at high risk of periodontitis [17]. Similarly, large-scale electronic health record-based models have been developed to improve early identification of periodontal disease and its systemic complications [18].

Beyond local periodontal outcomes, AI models have also been applied to assess systemic disease risk in periodontal patients. Studies have demonstrated that machine learning algorithms can successfully predict cardiovascular outcomes, including coronary heart disease and heart failure, in individuals with periodontal disease [11,12]. These findings reinforce the concept that periodontal status may serve as a valuable predictor of systemic vascular risk when analyzed using advanced computational techniques.

Integrative multi-omics approaches have further enhanced AI-based periodontal research by identifying molecular biomarkers associated with disease progression. For example, machine learning analysis of multi-omics datasets has identified key regulatory proteins linked to periodontal inflammation, highlighting the potential of AI to uncover novel biological mechanisms [19].

AI in Oral Microbiome and Multi-Omics Integration:

The application of AI in microbiome research has enabled deeper understanding of the complex interactions between microbial communities and host physiology. Oral microbiome data, characterized by high dimensionality and heterogeneity, is particularly well-suited for machine learning-based analysis. AI algorithms can identify microbial signatures associated with disease states, enabling improved classification and risk stratification [20].

Recent studies have demonstrated that integration of oral microbiome profiles with AI-driven models can significantly improve cardiovascular disease prediction accuracy. These models incorporate microbial composition data alongside clinical and imaging features to enhance predictive performance and identify disease-associated microbial patterns [13].

Furthermore, emerging computational frameworks aim to integrate microbiome data with broader systemic datasets, including radiomics and electronic health records, to develop comprehensive predictive ecosystems for cardiovascular disease [8]. Such integrative approaches reflect a shift from single-domain analysis to systems-level modeling in biomedical research.

Explainable AI and Clinical Translation:

Despite strong predictive performance, many AI models in periodontology and microbiome research function as “black-box” systems, limiting their interpretability and clinical adoption. This has led to increasing emphasis on explainable artificial intelligence (XAI), which provides transparency in model decision-making and enhances clinician trust [14].

Explainable AI methods allow identification of key features driving predictions, enabling clinicians to understand how periodontal and microbiome-related variables contribute to systemic disease risk. In cardiovascular applications, XAI frameworks have been shown to improve model interpretability while maintaining high predictive accuracy [15].

The integration of explainability into periodontal AI systems is particularly important for clinical translation, as it supports evidence-based decision-making and facilitates adoption in real-world healthcare settings. By bridging the gap between computational performance and clinical

interpretability, XAI represents a critical step toward the implementation of precision dentistry and precision cardiovascular medicine [14,15]

• Clinical Implications and Future Directions

Clinical Implications for Dentistry and Cardiology:

The growing body of evidence linking the oral microbiome with cardiovascular disease has important clinical implications for both dentistry and cardiology. Periodontal disease should no longer be viewed as an isolated oral condition but rather as a component of systemic inflammatory burden with potential cardiovascular consequences [5,6]. Recognition of this

oral-systemic connection supports the integration of periodontal assessment into cardiovascular risk evaluation, particularly in patients with established risk factors such as diabetes, hypertension, and metabolic syndrome.

From a cardiology perspective, incorporating oral health status into cardiovascular risk stratification may improve early identification of high-risk individuals. The American Heart Association has already acknowledged periodontal disease as a potential contributor to atherosclerotic cardiovascular disease, emphasizing the need for interdisciplinary collaboration between dental and medical professionals [6]. This shift supports a more holistic model of patient care in which oral inflammation is considered alongside traditional cardiovascular risk markers.

In addition, emerging machine learning models demonstrate that periodontal and oral microbiome data can enhance prediction of cardiovascular outcomes such as coronary artery disease and heart failure [11,12,20]. These findings suggest that dental records and microbiome profiles may eventually serve as auxiliary diagnostic tools in cardiovascular risk prediction systems.

Role of Artificial Intelligence in Clinical Translation:

Artificial intelligence is playing an increasingly important role in translating complex, oral-systemic interactions into clinically usable tools. Machine learning algorithms have been successfully applied to predict periodontal disease, metabolic syndrome, and cardiovascular outcomes using clinical, biomarker, and electronic health record data [16-18]. These models demonstrate the potential of AI to integrate heterogeneous datasets and support early intervention strategies.

In cardiovascular applications, AI-based systems have shown promise in identifying patients with increased risk of coronary heart disease and heart failure among individuals with periodontal disease [11,12]. Furthermore, multimodal approaches combining imaging, radiomics, and clinical data have improved the identification of vascular changes such as carotid stenosis in periodontal patients [21]. These developments highlight the expanding scope of AI beyond prediction toward multimodal disease characterization.

However, despite these advances, most current models remain in early translational stages and are not yet widely implemented in routine clinical practice. Issues such as dataset heterogeneity, lack of external validation, and limited integration into healthcare systems continue to restrict real-world adoption.

Importance of Explainable Artificial Intelligence:

One of the key barriers to clinical implementation of AI in healthcare is the “black-box” nature of many machine learning models. Clinicians require interpretability to trust and act on AI-generated predictions. Explainable artificial intelligence (XAI) addresses this limitation by providing transparency in model decision-making and identifying the most influential predictive features [14].

In cardiovascular medicine, XAI frameworks have been proposed to improve risk prediction accuracy while maintaining interpretability, enabling clinicians to better understand how different clinical and biological variables contribute to disease outcomes [15]. In the context of periodontal-cardiovascular interactions, XAI could help identify which microbial

or inflammatory signatures are most strongly associated with systemic disease progression.

Thus, integrating explainable AI into periodontal and microbiome-based predictive models is essential for bridging the gap between computational performance and clinical usability.

Future Directions:

Future research should focus on developing integrated multi-omics and AI-driven platforms that combine oral microbiome data, clinical periodontal parameters, imaging features, and systemic biomarkers. Such integrative frameworks could enable more accurate prediction of cardiovascular risk and facilitate personalized prevention strategies [8,20].

Longitudinal cohort studies are needed to establish causal relationships between oral dysbiosis and cardiovascular outcomes, as most current evidence remains cross-sectional or associative in nature [5,7]. In addition, large-scale external validation studies are required to ensure the generalizability of AI-based predictive models across diverse populations.

Another important direction involves the development of standardized datasets and interoperable digital health systems that allow seamless integration of dental and medical records. This would enhance the applicability of AI models in real-world clinical settings and support interdisciplinary care pathways.

Finally, combining explainable AI with microbiome research represents a promising frontier for precision medicine. By improving transparency and biological interpretability, future models may not only predict disease risk but also uncover novel therapeutic targets linking oral health with cardiovascular disease [14,15].

DISCUSSION:

This narrative review synthesizes current evidence linking the oral microbiome, periodontal disease, cardiovascular pathology, and artificial intelligence (AI)-driven predictive modeling. The findings highlight a converging framework in which oral dysbiosis is not merely a localized infection but a biologically active contributor to systemic vascular inflammation and atherosclerotic disease progression

[2,5,6]. At the same time, advances in AI and multi-omics analytics are reshaping how these complex interactions are studied, modeled, and potentially translated into clinical practice [8,11,12].

A central theme emerging from the literature is the mechanistic continuity between periodontal inflammation and cardiovascular disease. Dysbiosis of the oral microbiome leads to persistent immune activation, endothelial dysfunction, and systemic inflammatory burden through microbial translocation and circulating inflammatory mediators [3,4]. These processes provide a plausible biological explanation for the observed epidemiological association between periodontitis and cardiovascular disease, which has been increasingly recognized by major cardiovascular authorities [6]. However, despite strong associative and mechanistic evidence, causality remains incompletely established, and heterogeneity in study design continues to limit definitive conclusions [7].

From a translational perspective, AI-based methodologies have introduced a paradigm shift in periodontal and cardiovascular research. Machine learning models have demonstrated the ability to integrate clinical, biomarker, and electronic health record data to predict periodontal disease and its systemic consequences with increasing accuracy [16-18]. Importantly, recent studies have extended these models to cardiovascular endpoints, including coronary heart disease and heart failure in patients with periodontitis [11,12]. These findings suggest that periodontal health data may function as a clinically relevant predictor of systemic vascular risk when analyzed through computational frameworks.

Furthermore, multimodal AI approaches integrating imaging, radiomics, and clinical features have demonstrated additional value in identifying subclinical vascular pathology, such as carotid stenosis in periodontal populations [21]. This expands the role of AI from simple risk prediction toward integrated phenotyping of oral-systemic disease interactions. Similarly,

microbiome-based predictive models are emerging as promising tools for cardiovascular risk stratification, highlighting the diagnostic potential of microbial signatures beyond traditional clinical markers [20].

Despite these advances, several critical challenges remain. Most AI models in this field are still in early developmental stages, often limited by small sample sizes, single-center datasets, and lack of external validation. This raises concerns regarding reproducibility and generalizability across diverse populations. In addition, many models function as “black-box” systems, limiting clinical interpretability and hindering adoption in routine practice.

Explainable artificial intelligence (XAI) has therefore emerged as a crucial component for clinical translation. By improving model transparency and identifying key predictive features, XAI enhances clinician trust and facilitates integration into decision-making pathways [14,15]. In the context of periodontal-cardiovascular interactions, explainability is particularly important because biological plausibility must align with computational outputs to ensure clinical acceptance.

Another important limitation in the current literature is the predominance of cross-sectional and associative studies. While mechanistic pathways linking oral dysbiosis to vascular inflammation are well described, longitudinal studies are still needed to establish temporal and causal relationships [5,7]. Additionally, variability in microbiome sequencing methods, AI architectures, and clinical endpoints introduces significant heterogeneity, complicating direct comparison across studies.

Looking forward, the integration of multi-omics datasets, longitudinal cohort data, and real-world electronic health records offers a promising avenue for advancing this field. The development of standardized datasets and interoperable AI systems could significantly enhance model robustness and clinical applicability. Moreover, combining microbial signatures with imaging and systemic biomarkers may enable the development of highly accurate, personalized cardiovascular risk prediction models.

In conclusion, the intersection of oral microbiome research and artificial intelligence represents a rapidly evolving frontier in precision medicine. While current evidence strongly supports a biological and computational link between periodontal disease and cardiovascular outcomes, further methodological standardization, validation, and explainability are essential before these tools can be fully integrated into

clinical practice. The future of this field lies in the convergence of dentistry, cardiology, microbiology, and data science to develop integrated predictive frameworks that improve both oral and systemic health outcomes.

CONCLUSION

This narrative review highlights the emerging role of the oral microbiome and artificial intelligence (AI) in advancing cardiovascular risk assessment. Integrating oral microbiome research with AI-driven analytical approaches offers new opportunities to improve disease prediction, support personalized care, and strengthen the connection between oral and cardiovascular health.

Although several challenges remain before these approaches can be widely implemented in clinical practice, continued advances in microbiome research, AI technologies, and interdisciplinary collaboration are expected to accelerate progress toward precision cardiovascular medicine.

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