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The Association between Periodontal Disease and Cardiovascular Disease Risk: A Systematic Review

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ABSTRACT

Objectives: To ritically evaluate and synthesize the existing evidence on the association between periodontal disease (PD) and cardiovascular disease (CVD) risk. Methods: A total of 1332 pertinent publications were found after a comprehensive search across four databases. 67 full-text publications were examined after duplicates were eliminated using Rayyan QCRI and relevance was checked; twelve studies finally satisfied the requirements for inclusion. Results: We included twelve studies with a total of 1,288,208 participants, and 658,052 (51%) were males. The prevalence of CVD in patients with PD ranged from 1.9% of HF to 57.5% of ACVD. Studies on hypertension suggest that severe periodontitis correlates with an elevated risk, especially in younger individuals, and that even moderate gingivitis could independently contribute to high blood pressure. For atherosclerotic cardiovascular disease (ACVD), evidence is mixed, with some studies finding no significant impact, while others report a substantial increase in carotid plaques and arterial thickness associated with severe periodontitis. The risk of general CVD appears consistently elevated in individuals with advanced periodontitis, even after adjusting for confounders like smoking. Additionally, moderate to severe periodontitis is linked to a higher likelihood of heart failure. Conclusion: This review reinforces the evidence that PD is linked to a higher risk of cardiovascular conditions, including hypertension, ACVD, CVD, and heart failure. While PD may contribute to cardiovascular risk, further research is needed to confirm causation and understand mechanisms. Clinicians are encouraged to consider oral health's role in systemic health and incorporate periodontal care into cardiovascular risk management, potentially reducing cardiovascular risks and enhancing overall health outcomes.

KEYWORDS: Periodontal disease; Periodontitis; Cardiovascular disease; Coronary artery disease; Systematic review.

1. Introduction

Both CVD and PD are quite common worldwide and have a significant impact on healthcare [1]. PD is independently linked to subclinical and clinical CVD in a variety of populations, according to numerous epidemiologic and observational studies [1]. Inflammation plays a significant part in the pathophysiology of both illnesses, which are complex and share numerous risk factors. Periodontitis is linked to a higher risk of coronary artery disease (CAD) and all-cause mortality, according to recent data from large cohort studies. This association also extended to preclinical CVD and stable CAD [2]. Furthermore, genetic research has revealed a common susceptibility gene implicated in the pathophysiology of both CVD and PD [3].

A wide spectrum of chronic inflammatory diseases that impact the gingiva, bone, and periodontal ligaments that maintain the structure of teeth are included in PD; in fact, chronic inflammatory PD affects roughly 20–50% of people worldwide, posing a significant burden [4]. Significantly, it was discovered that, even in the absence of conventional cardiovascular risk factors like obesity and hypertension, people with periodontitis had an increased and accelerated risk of CVD, including CAD, stroke, myocardial infarction (MI), and atherosclerosis [5].

It's interesting to note that, in addition to conventional cardiovascular risk factors, the bacterial burden of these species in subgingival plaque samples has been linked to subclinical carotid intima media thickness [6]. The oral cavity's high vascularization and the sulcular epithelium's relative thinness and friability are two of the many elements that aid in the bacteria's translocation [5].

Despite the observed association, the relationship between PD and CVD remains complex, with numerous factors influencing both conditions. Given the high prevalence and significant impact of these diseases on public health, it is essential to systematically evaluate current literature to determine the strength and nature of this association. This review aims to provide a comprehensive understanding of the potential link between PD and CVD, as this may have implications for preventive strategies and patient management.

The primary objective of this systematic review is to critically evaluate and synthesize the existing evidence on the association between PD and CVD risk. By systematically reviewing and analyzing observational and interventional studies, this review seeks to clarify whether PD is an independent risk factor for CVD or if the association can be attributed to shared risk factors and confounding variables.

2. Methods

Search strategy

The PRISMA and GATHER criteria were adhered to in the systematic review. To locate pertinent research on the association between PD and CVD risk, a comprehensive search was carried out. Four electronic databases were searched by the reviewers: SCOPUS, Web of Science, Cochrane, and PubMed. Included were studies between 2022-2024. We eliminated any duplicates and uploaded all of the abstracts and titles that we could find using electronic searches into Rayyan. After

that, all of the study texts that met the requirements for inclusion based on the abstract or title were gathered for a thorough examination. Two reviewers independently assessed the extracted papers' suitability and discussed any discrepancies.

Study population—selection

The PICO (Population, Intervention, Comparison, and Outcome) factors were implemented as inclusion criteria for our review: (i) Population: Patients with PD, (ii) Intervention: Risk of CVD, (iii) Comparator: Participants without PD or CVD incidence, (iv) Outcome: PD as a risk factor for CVD incidence.

Data extraction

Data from studies that satisfied the inclusion requirements were extracted by two objective reviewers using a predetermined and uniform methodology. The following information was retrieved and recorded: (i) First author (ii) Year of publication, (iii) Study design, (iv) Participants' number, (v) Age, (vi) Gender, (vii) CVD type, (viii) Prevalence of CVD, (ix) Main outcomes.

Quality review

Since bias resulting from omitted factors is frequent in studies in this field, we used the ROBINS-I technique to assess the likelihood of bias since it enables a thorough examination of confounding. The ROBINS-I tool can be used for cohort designs where individuals exposed to different staffing levels are tracked over time and is designed to assess non-randomized studies. Each paper's risk of bias was evaluated independently by two reviewers, and any differences were settled by group discussion [7].

3. Results

The specified search strategy yielded 1332 publications (Figure 1). After removing duplicates (n =764), 568 trials were evaluated based on title and abstract. Of these, 498 failed to satisfy eligibility criteria, leaving just 67 full-text articles for comprehensive review. A total of 12 satisfied the requirements for eligibility with evidence synthesis for analysis.

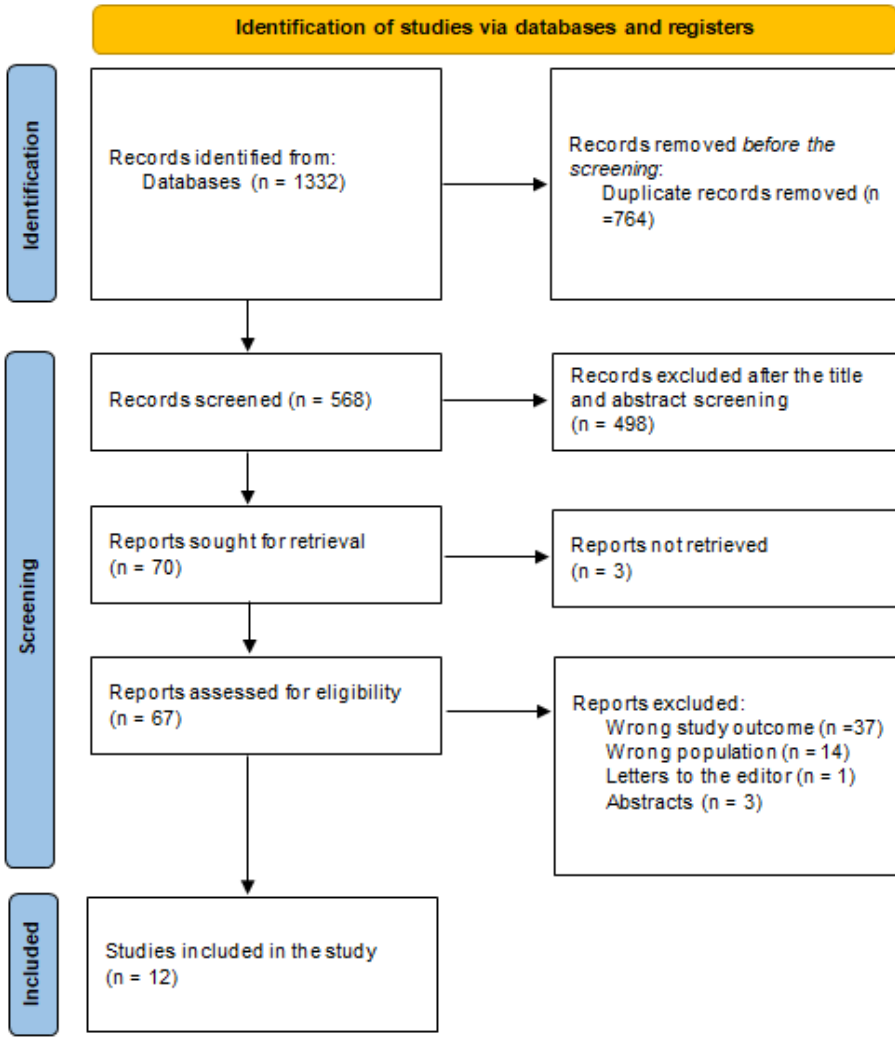

Figure (1): PRISMA flowchart [8].

Sociodemographic and clinical outcomes

We included twelve studies with a total of 1,288,208 participants and 658,052 (51%) were males. Regarding study designs, eight studies were cross-sectional [11, 14-16, 18-20], three were retrospective cohorts [9, 12, 17],and one was a case-control study [10]. Four studies were implemented in China [12, 14, 15, 19], one in The Netherlands [9], one in Italy [10], one in the USA [11], one in Rwanda [13], one Nigeria [16], one in Korea [17], one in Germany [18], and one in Norway [20].

The prevalence of CVD in patients with PD ranged from 1.9% of HF [19] to 57.5% of ACVD [10]. In studies linking PD to general CVD risk, periodontitis has consistently emerged as a risk factor. The findings indicate that the severity of PD

correlates with an increased risk of CVD, with a recommendation for periodontal assessments to enhance CVD risk prediction accuracy [11]. This association remains significant even after accounting for common confounding factors, such as smoking [15]. For example, one study noted that individuals with advanced periodontitis were more likely to exhibit higher levels of carotid intima-media thickness and carotid plaque prevalence [20]. There was a strong correlation between periodontitis and the risk of aortic calcification, especially in men and those under 65 [12]. Individuals with moderate to severe periodontitis were shown to have an elevated likelihood of developing heart failure [19].

Hypertension

Findings indicate that periodontitis is associated with an increased likelihood of developing hypertension. This association appears to be particularly pronounced in younger individuals, where severe periodontitis correlates with a higher prevalence of hypertension [13, 14]. In one study, it was observed that while moderate periodontitis was linked to hypertension, moderate gingivitis itself could independently serve as a risk factor for elevated blood pressure [16]. Another study highlighted the potential benefits of addressing oral inflammation as a preventive measure, suggesting that reducing oral inflammation might have a positive effect on blood pressure regulation [17].

ACVD

One study concluded that PD might not significantly contribute to the risk of nonfatal ACVD events, suggesting that its role in ACVD development may be negligible [9]. However, another investigation showed a robust connection between severe apical periodontitis and heightened ACVD risk, citing a fivefold increase in carotid plaque formation and a substantial increase in carotid intima-media thickness [10]. Therefore, while the evidence is varied, it leans towards a potentially meaningful association between advanced PD and atherosclerosis risk [18].

Table (1): Outcome measures of the included studies

Study ID	**Study design**	**Country**	**Sociodemographic**	**Population type**	**1. 2. tress diagnostic tool**	**3. 4. Main outcomes**
5. Beukers et al., 2023 [9]	6. Retrospective cohort	7. he Netherlands	8. N= 1,224,457 Males: 573,270 (46.8%)	9. A CVD	10. 1268 (7.5%)	11. It is difficult to consider PD a risk factor for nonfatal ACVD. The suggested function of PD in the development of ACVD incidents should be reexamined because the elevated risk is negligible.
12. Malvicini et al., 2024 [10]	13. Case-control	14. taly	15. N= 65 16. Mean age: 56.5 17. Males: 23 (35.4%)	18. A CVD	19. 7 (57.5%)	20. Given that apical periodontitis is linked to a 5-fold greater chance of carotid plaques and a 15-fold increased risk of having noticeable carotid intima-media thickenings, it may be

						considered a risk factor for ASCVD.
21. Ngamdu et al., 2022 [11]	22. Cross-sectional	23. SA	24. N= 2830 25. Mean age: 51.5 26. Males: 1416 (50.1%)	27. CVD	28. 00 (5%)	29. The severity of PD is linked to the risk of CVD. A more accurate indicator of PD-CVD correlations is periodontal exams.
30. Yu et al., 2023 [12]	31. Retrospective cohort	32. hina	33. N= 6059 34. Mean age: 47.7 35. Males: 4159 (68.6%)	36. Aortic calcification	37. A	38. Aortic calcification risk was positively correlated with periodontitis, particularly in men and people under 65.
39. Gatarayiha et al., 2024 [13]	40. Cross-sectional	41. wanda	42. N= 420 43. Age range: 22 to >55 44. Males: 195 (46.4%)	45. Hypertension	46. A	47. People who have PD, as evidenced by symptoms such as gingival recession, dental attachment loss, bleeding on probing, and periodontal pocket depths, are far more likely to develop hypertension.
48. Zhan et al., 2023 [14]	49. Cross-sectional	50. hina	51. N= 13195 52. Mean age: 56.4 53. Males: 6575 (49.8%)	54. Hypertension	55. 423 (41.1%)	56. Hypertension is linked to periodontitis. The severity of periodontitis was positively correlated with the prevalence of hypertension, especially in younger subjects.
57. Qu & Zhang, 2024 [15]	58. Cross-sectional	59. hina	60. N= 8649 61. Mean age: 51.8 62. Males: 4299 (49.7%)	63. CVD	64. A	65. This study shows a negative correlation between the probabilities of periodontitis and CVH, as determined by LE8.
66. Umeizudike et al., 2022 [16]	67. Cross-sectional	68. igeria	69. N= 150 70. Mean age: 58.1 71. Males: 55 (36.7%)	72. Hypertension	73. A	74. While moderate periodontitis manifested as shallow pockets is linked to hypertension, moderate gingivitis is an independent risk factor for hypertension.
75. Hwang et al., 2022 [17]	76. Retrospective cohort	77. orea	78. N= 10,349 79. Mean age: 51.1 80. Males: 5702 (55.1%)	81. Hypertension	82. A	83. Attempts to lessen oral inflammation should be promoted since it may be a factor in the occurrence of hypertension.
84. Lamprecht et al., 2022 [18]	85. Cross-sectional	86. ermany	87. N= 6209 88. Mean age: 62.1 89. Males: 3057 (49.2%)	90. CVD	91. A	92. After controlling for common risk variables, severe chronic periodontitis was linked to higher prevalence of carotid plaques and increased carotid intima-media

						thickness.
93. Yan et al., 2022 [19]	94. Cross-sectional	95. China	96. N= 13,202 97. Mean age: 43 98. Males: 6234 (47.2%)	99. HF	100. 63 (1.9%)	101. Heart failure is more likely to occur in persons with moderate to severe periodontitis.
102. Petrenya et al., 2022 [20]	103. Cross-sectional	104. Norway	105. N= 2623 106. Mean age: 57.8 107. Males: 1230 (46.9%)	108. CVD	109. A	110. In participants aged 65–74, periodontitis Grade B/C was linked to an overall increased risk of CVD, and smoking-related confounding did not account for this connection.

Table (2): Risk of bias assessment using ROBINS-I

Study ID	Bias due to confounding	Bias in the selection of participants into	Bias in the classification of	Bias due to deviations from the intended	Bias due to missing data	Bias in the measurement of	Bias in the selection of reported result	Overall bias
Beukers et al., 2023 [9]	Mod	Mod	Low	Low	Low	Low	Low	Low
Malvicini et al., 2024 [10]	Low	Low	Low	Low	Low	Mod	Low	Low
Ngamdu et al., 2022 [11]	Low	Mod	Low	Low	Low	Low	Low	Low
Yu et al., 2023 [12]	Low	Low	Low	Low	Low	Mod	Low	Low
Gatarayiha et al., 2024 [13]	Mod	Low	Mod	Mod	Low	Low	Low	Moderate
Zhan et al., 2023 [14]	Mod	Mod	Low	Low	Low	Mod	Mod	Moderate
Qu & Zhang, 2024 [15]	Mod	Mod	Low	Low	Low	Mod	Low	Moderate
Umeizudike et al., 2022 [16]	Low	Mod	Mod	Mod	Low	Mod	Low	Moderate
Hwang et al., 2022 [17]	Low	Mod	Mod	Mod	Low	Mod	Low	

								Moderate
Lamprecht et al., 2022 [18]	Mod	Mod	Low	Low	Low	Low	Mod	Moderate
Yan et al., 2022 [19]	Mod	Mod	Low	Low	Low	Low	Mod	Moderate
Petrenya et al., 2022 [20]	Crit	Crit	Low	Low	Mod	Low	Low	Critical

4. Discussion

This systematic review highlights a consistent association between PDand an increased risk of various cardiovascular conditions, including hypertension, ACVD, CVD, and heart failure. The findings support the hypothesis that the chronic inflammatory response characteristic of PD may contribute to systemic vascular changes, thereby increasing cardiovascular risk. The association appears stronger in severe cases of periodontitis, where the burden of inflammation and microbial spread is likely to be greater. Beck & Offenbacher reported that all of the earlier research lacked adequate, thorough, and sensitive indicators of PD as a systemic exposure. It is time to move on to the next stage of study by carrying out molecular epidemiology studies that are suitably structured to evaluate our current understanding of the molecular and cellular pathways involved, as the potential health care implications of this link may be considerable [21].

Priyamvara et al. also found that with inflammation acting as a key mediator, there seems to be a positive correlation between PD and CVD. Only a small number of prior studies have examined subclinical surrogate markers of CVD, whereas the majority have evaluated severe events including MI, heart failure, stroke, or CV-related death [22]. This suggests that the systemic inflammatory response associated with PD may play a role in cardiac function, potentially contributing to heart failure risk.

We found that periodontitis is linked to a higher risk of hypertension, especially in younger individuals with severe cases. Moderate periodontitis is also associated with hypertension, and even moderate gingivitis may independently increase blood pressure risk. Reducing oral inflammation could potentially help regulate blood pressure, highlighting the importance of oral health in hypertension prevention [13, 14, 16, 17]. Martin-Cabezas et al. also reported that A increased risk of hypertension is linked to periodontal problems, particularly severe periodontitis. However, because of the limited number of prospective studies that are now available and the unanswered issues about the underlying biological pathways, no conclusions could be drawn about the causative involvement of PD [23]. Munoz Aguilera et al. found that A favorable correlation between periodontitis and hypertension is supported by the findings of this comprehensive review.Additionally, this comprehensive analysis

verified that patients with hypertension (classified as SBP ≥140 and DBP ≥90 mmHg) had a higher prevalence of periodontitis [24]. Clinical and experimental data indicate that this association's direction may be mediated by hypertension, which alters the gingival tissue's microcirculation and causes ischaemia, inflammation, and/or the microbial makeup of the dental biofilm [25, 26].

There are several tenable explanations for why periodontitis was identified as a potential risk factor for hypertension. First of all, systemic inflammation is linked to periodontitis, and its mediators, such as TNF-α, IL-6, and CRP, can all impact endothelial function. According to clinical data, systemic endothelial function is impacted by periodontitis, which may have an effect on hypertension. In individuals with and without concomitant comorbidities such as diabetes, treatment of severe periodontitis reduces systemic inflammation, improving endothelial function [27]. Second, several data raise the possibility that bacteremia linked to the oral microbiota may also directly contribute to vascular dysfunction. There is growing experimental animal evidence suggesting an immune response to Porphyromonas gingivalis (Pg), a common periodontal infection, causes endothelial dysfunction, vascular inflammation, and blood pressure increase [28]. It's also possible that cells primed in an inflamed periodontium, such as T cells, B cells, and monocyte/macrophages, are more likely to be recruited chemotactically to perivascular adipose tissue and adventitia. This process has been demonstrated to occur before the development of vascular dysfunction, hypertension, and atherosclerosis [29]. As a result, this review poses a significant query about whether periodontitis and hypertension are causally related.

The evidence on PD and ACVD risk is mixed. One study suggests PD has a negligible role in nonfatal ACVD events, while another shows a strong association between severe apical periodontitis and increased ACVD risk, including higher carotid plaque formation and artery thickness. Overall, the findings suggest a potentially significant link between advanced PD and atherosclerosis risk [9, 10, 18]. This suggests that, particularly in cases of severe periodontitis, the structural and inflammatory changes associated with PD could exacerbate atherosclerosis. Zhao et al. similary concluded that periodontal health should be included as an extra risk factor in the current cardiovascular risk profiles since it may raise the risk for ASCVD through inflammation, tooth loss, or oral microbes [30].

The association between PD and cardiovascular health has important implications for clinical practice. Dental professionals could play a critical role in cardiovascular risk management by identifying patients with advanced periodontitis who may be at elevated risk for cardiovascular conditions. Routine periodontal assessments, particularly in patients with known cardiovascular risk factors, could help flag at-risk individuals. Additionally, interdisciplinary collaboration between dental and medical professionals might enhance preventive care, with periodontal treatment as a potential strategy to reduce systemic inflammation and cardiovascular risk. For clinicians, understanding this link underscores the value of comprehensive patient care that integrates oral health with overall health management.

Strengths and limitations

The strength of this review lies in its systematic approach to examining a diverse

range of studies across various cardiovascular conditions, which offers a comprehensive understanding of the association between PD and cardiovascular risk. By including both observational and interventional studies, the review provides a balanced view of the evidence, highlighting both well-established findings and areas that require further investigation. Additionally, the review draws from a variety of population settings, increasing the generalizability of the findings.

Despite its strengths, this review has limitations. First, the heterogeneity among studies in terms of study design, population characteristics, and definitions of PD and cardiovascular outcomes makes it challenging to draw definitive conclusions. Additionally, most studies included in this review were observational, which limits the ability to infer causation. Confounding factors, such as smoking, socioeconomic status, and access to healthcare, also pose challenges, as they may influence both periodontal and cardiovascular health independently. Lastly, variations in diagnostic criteria for both PD and cardiovascular outcomes across studies contribute to inconsistencies in findings.

5. Conclusion

In conclusion, this review supports the growing body of evidence linking PD with an increased risk of cardiovascular conditions, including hypertension, ACVD, CVD, and heart failure. While the findings suggest that PD could be a potential contributor to cardiovascular risk, further research is needed to establish causation and identify the underlying mechanisms. Clinicians should consider the implications of oral health on systemic health and the value of integrating periodontal care into cardiovascular risk management strategies. Addressing PD may offer a promising avenue for reducing cardiovascular risks and improving overall health outcomes.

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