

Heart Diseases

Association between cardiovascular diseases and periodontal disease - what do we know?

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There has been a growing body of research on periodontal disease carried out over the past five decades, and three distinctive phases of this research, namely the aetiopathologic phase, the risk factor phase and the periodontal disease–systemic health phase, have been identified¹. More recently the focus has been on the third phase, where the influence of periodontal disease on systemic diseases has been considerably explored. Consequently, the emerging evidence may point to a significant association between periodontal disease and certain systemic diseases and conditions including cardiovascular diseases^{2,3}, respiratory diseases⁴, diabetes and complications of diabetes^{5,6} and adverse pregnancy outcomes⁷. Of these, cardiovascular diseases are regarded as the leading cause of mortality in Australians, accounting for not only over 16% of all deaths but also 16% of the total disease burden in 2007⁸. The aim of this information sheet is to update dental professionals on the cardiovascular–periodontal disease relationship.

Background

Oral sepsis had been cited as a cause for systemic illness as far back as 1880 when an American dentist named Miller postulated the focal infection theory where microbes in the oral cavity were implicated in systemic diseases⁹. This was followed by a remarkable increase in tooth extractions relative to restorative treatments in dentistry until the late 1940s—all periodontally and endodontically involved teeth were pulled out to avoid possible foci of infection^{9,10}. However, with the development of biomedical research and emerging evidence against the focal infection theory, this era came to an end by the mid 20th century. Consequently, little was discussed about the relationship between oral health and systemic diseases until 1989. The finding that oral health was significantly worse in patients with a history of acute myocardial infarction compared with control subjects, as revealed by Mattila and colleagues², has

inspired researchers to revisit the relationship between oral health and general health. This, in turn, led to a series of research activities exploring the influence of periodontal disease on cardiovascular health to such an extent that publications on this theme have appeared in nearly 200 different journals over the past two decades¹¹. A new term—'periodontal medicine'—also evolved by the end of the 20th century, acknowledging the significance of periodontal–systemic relationships¹². Notwithstanding this growing body of evidence, there may be a lack of congruity among researchers with regard to comprehensive understanding of periodontal–cardiovascular relationships, which further substantiates the need for this kind of information sheet.

Risk Factors

The aetiology for both cardiovascular diseases (CVD) and periodontal disease (PD) is multifactorial in nature¹¹. Modifiable risk factors for CVD include dyslipidemia, smoking, diabetes mellitus, hypertension, physical inactivity and obesity, while non-modifiable risk factors associated with CVD are age, ethnicity, sex and family history of cardiovascular diseases^{11,12}. It has been established that these factors play a prominent role in atherosclerosis, and that timely intervention in modifiable risk factors, in particular, is crucial in halting the atherosclerotic process as well as the clinical manifestations associated with it.

Local colonisation of dental plaque-forming bacteria, systemic conditions including diabetes mellitus, osteoporosis, rheumatoid arthritis and respiratory diseases are associated with the aetiology of PD, whereas age, ethnicity, sex, smoking, stress and poor coping behaviour, and obesity have a key role in the development of the disease^{1,11,13–16}. In fact, smoking has been implicated as a cause of PD in the US Surgeon General's report¹⁷.

Interestingly, PD and CVD share many risk factors such as smoking, diabetes mellitus, age, ethnicity, sex, socioeconomic status, stress and obesity, which would possibly result in confounding any association between them^{11,13}. For instance, smoking, which is strongly linked with both PD and CVD, may hamper understanding PD–CVD relationships. Nonetheless, some studies have shown that cardiovascular events may occur among non-smoking patients with PD, even after controlling for other confounding variables, and hence PD may be related to CVD regardless of the confounding effects of smoking^{14,15}.

Further information

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Pathophysiological pathways

Various pathogenic mechanisms have been proposed to explain the association between PD and CVD. These mechanisms may individually or jointly contribute to a plausible association.

1. Effects of periodontal bacteria on platelets:

Porphyromonas gingivalis and *Streptococcus sanguis* have been shown to stimulate platelet aggregation and thrombosis¹⁶.

2. Autoimmune reactions / molecular mimicry:

Cross-reacting antibodies to periodontal bacteria and human heat shock proteins (HSPs) including HSP60 on endothelial cells have been recognised. These autoimmune responses could provoke endothelial damage and atherosclerosis¹⁸.

3. Invasion and/or uptake of periodontal bacteria in endothelial cells and phagocytes:

Specific periodontal pathogens and their components have been identified in human atheromatous tissues. For instance, *P. gingivalis* and *A. actinomycetemcomitans* were present in atheromatous plaque of 79% and 67% patients, respectively¹⁹.

4. Systemic inflammation:

Both PD and CVD have been associated with increased systemic inflammatory markers such as C-reactive protein (CRP), which has also been indicated as an independent predictor of future CVD²⁰.

Evidence for an association between PD and CVD

A vast number of studies carried out to explore the relationship between CVD and PD have been reported in the literature. Lockhart and colleagues¹¹, for example, in a comprehensive review on this topic, identified well over 500 peer-reviewed English publications, a majority of which appeared in periodontal and dental-related journals during the past six decades. These studies comprise animal experiments as well as human observational and intervention studies including investigations into endothelial function and systemic inflammation.

- **Animal experiments:** Studies using both mice and pig models have demonstrated that periodontopathic bacteria such as *P. gingivalis* could induce atherosclerosis in these animals, and DNA components of *P. gingivalis* could be isolated from atheromatous lesions in them^{21,22}.

- **Human observational studies:** Epidemiological studies have been conducted where PD was used as exposure for various CVD outcomes such as cerebral vascular

accident (stroke), acute myocardial infarction and acute coronary syndrome. In these studies PD has been assessed by self-reporting²³, clinical or radiographic measurements²⁴, bacterial colonisation²⁵ and serological evaluation²⁶, while odds ratios, relative risks or hazard ratios have been reported in the analyses as measures of association. Despite a few cohort studies that have not been able to detect any significant role played by PD on the aetiology of CVD^{13,27}, the majority of other studies have pointed to an association between PD and CVD, primarily based on the fact that they share common aetiological pathways²⁸.

- **Human intervention studies:** It has not yet been conclusively determined in human intervention trials whether surgical or non-surgical periodontal therapy has any beneficial effects in modifying the risk for CVD or the complications of CVD^{1,11,28}. There has been some evidence, however, for improvement in endothelial function and substantial reduction of inflammatory markers in periodontal patients who have been managed with non-surgical periodontal treatment, corroborating the view that cardiovascular effects from PD could partly be explained through endothelial dysfunction and associated systemic inflammation²⁹. Paraskevas and colleagues³⁰, in a systematic review exploring the periodontal treatment – serum CRP relationship, suggested that evidence for the periodontal therapy-related decline in serum CRP levels was mediocre. The Periodontitis and Vascular Events (PAVE) study—a multicentre pilot study investigating the effects of periodontal therapy on the secondary prevention of cardiac events—has revealed that any effect of periodontal treatment in reducing high-sensitivity CRP levels may be neutralised by obesity and, consequently, inflated among non-obese subjects³¹. The authors highlighted not only the importance of considering the role of other cardiovascular risk factors including obesity in PD–CVD relationships but also the necessity of maintaining sustainable periodontal care in future studies.

Budoff and colleagues³² have stated that the level of evidence in evidence-based research can be categorised into three levels, namely A (supporting data emanating from multiple randomised clinical trials), B (supporting data derived from single randomised trials or non-randomised trials) and C (consensus opinion of experts). A recent scientific statement from the American Heart Association indicates that, while evidence for both periodontal–cardiovascular disease relationships and the beneficial effects of periodontal therapy in reducing local periodontal

inflammation is corroborated by level of evidence A, neither the causative role played by PD in CVD nor the effect of periodontal therapy in decreasing systemic inflammation is supported by levels of evidence A or B¹¹.

Role of oral healthcare professionals in the prevention and control of CVD

Given that both PD and CVD share common modifiable risk factors including tobacco smoking, diabetes mellitus, stress and obesity, medical and dental professionals in particular, and all healthcare practitioners in general, can adopt a standardised approach to educate patients about such risk factors, as well as associated lifestyle changes for the successful prevention and control of both these conditions³³. This includes encouraging patients to:

- reduce their total calorie intake and consumption of foods high in cholesterol, saturated- and trans-fatty acids, and salt.
- increase their consumption of foods with low saturated fat and high fibre.
- control their weight via increased daily physical activity and reduced total calorie intake.
- discontinue smoking.

It has also been recommended that sugar intake be reduced, alongside other lifestyle changes, to curtail the cardiovascular risk³⁴. Accordingly, dental professionals who have been routinely involved in advising their patients to cut down on sugar can effectively convey this message in view of reducing the risk for both dental caries and cardiovascular disease.

Management of PD in CVD patients

The standard treatment for PD in CVD patients has been shown to be effective without undesirable cardiovascular consequences, and there has been no evidence to suggest that PD in CVD patients should be managed differently^{31,33,35}. Although there has been no strong evidence to support a cause and effect relationship between PD and CVD, or to suggest any substantial beneficial effect of periodontal therapy on CVD outcomes, currently available evidence may be adequate to advocate comprehensive interprofessional coordination among medical and dental professionals in the co-management of PD in CVD patients³³. The following basic recommendations, some of which have recently been concurrently published by two prominent cardiology and periodontology journals, would be useful in guiding medical and dental healthcare professionals who deal with

patients already afflicted with, or at risk of developing, PD and CVD^{33,35}.

- Patients with moderate to severe PD should be advised that they may have a higher risk of developing CVD than periodontally healthy people, and PD patients with one or more risk factors for CVD should seek medical evaluation if they have not done so in the past 12 months.
- Cardiovascular risk factors such as hyperlipidaemia, hypertension, smoking and metabolic syndrome in PD patients should be controlled and co-managed by dental and medical professionals.
- Medical and dental professionals should work together to control common risk factors for PD and CVD in patients with both these conditions.
- Standard treatment including plaque and gingivitis control, and oral hygiene instructions including the use of anti-plaque toothpaste as well as mouthrinse and interproximal cleaning, should be provided to manage PD in patients with CVD.

Conclusion

There has been some evidence, emanating mainly from observational studies, to suggest that PD may be associated with CVD irrespective of the effects of known confounding factors including tobacco smoking. Testimony for a causal relationship between PD and CVD or for the beneficial effects of periodontal treatment on CVD outcomes, however, is neither substantial nor convincing. Further research with well-designed intervention trials that incorporate standardised case-definitions as well as consistent treatment protocols for PD, and that control for effect-modifiers and confounders of the PD–CVD relationship, would be of paramount importance to address such concerns. Nonetheless, the currently available evidence may be strong enough to support an inter-professional multifaceted approach by dental and medical professionals to modify common risk factors for PD and CVD and subsequently manage these conditions. Accordingly, dental professionals may have a pivotal role to play in improving both the periodontal and cardiovascular health of their patients.