



## Periodontitis and cardiovascular disease: A literature review

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### Review Article

#### Abstract

**BACKGROUND:** Cardiovascular diseases (CVDs) are in charge of many deaths worldwide including myocardial infarction (MI), hypertension (HTN), coronary atherosclerosis (CAS), infective endocarditis (IE), heart failure (HF), arterial fibrillation (AF), and peripheral artery disease (PAD). Besides, periodontitis is the sixth prevalent disease among humans and it seems that there are common risk factors between these diseases which are creating communication between prevalence and treatment. The purpose of this study is to assess the articles that reviewed the relationship between heart diseases and periodontitis.

**METHODS:** Three databases, including PubMed, Scopus, and Web of Science were searched until November 2020. The search terms “periodontal disease, periodontitis, oral health, cardiovascular disease, atherosclerosis, myocardial infarction, hypertension, coronary heart disease, angina pectoris, arterial fibrillation, arrhythmia, and peripheral artery disease” were used in combination to identify the publications providing data.

**RESULTS:** MI, HTN, atherosclerosis diseases for coronary artery, IE, HF, AF, and PAD were associated with periodontitis. It seems that the treatment of periodontitis may help to improve the state of mentioned heart-related diseases. However, more studies are needed to prove this relationship.

**CONCLUSION:** The prevalence of heart diseases is more common in individuals with periodontitis.

**Keywords:** Periodontitis; Periodontal Disease; Systemic Inflammation; Cardiovascular Disease; Atherosclerosis; Myocardial Infarction; Hypertension

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#### Introduction

Heart-related diseases involve a wide range of health problems (including heart muscle-related disease and the vascular system supplying the heart, such as coronary arteries with narrowing or blockage of the coronary arteries) which can result in myocardial infarction (MI), increasing blood pressure (due to atherosclerosis, arterial stiffness, or endothelial dysfunction), infective endocarditis (IE) (infection of endocarditis layer of the heart), and heart failure (HF) (disability of heart muscles in pumping blood).

Periodontitis is a chronic multifactorial inflammatory disease caused by the accumulation of bacterial biofilm and characterized by progressive destruction of the tooth-supporting apparatus. It is a major public health issue.<sup>1</sup>

Recent studies have reported that there has been an increase in the impact of oral health on

atherosclerosis and subsequent cardiovascular disease (CVD). Yet, the current evidence indicates that poor oral health is a risk factor for CVD.<sup>2</sup>

There are two hypothetical reasons for the association of CVD and periodontitis: first, increasing levels of systemic inflammation and inflammatory mediators<sup>3,4</sup> and second, entry of organisms to the blood flow due to the damaged periodontal tissues.<sup>4</sup> Systemic inflammation due to periodontitis can cause dysfunction in vessels.<sup>5</sup>

In the past two decades, various studies have indicated that periodontitis may increase the risk of CVD.<sup>6</sup>

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The association of periodontitis and CVD has been proven, but there is not enough evidence indicating that the treatment of chronic periodontitis may result in the prevention of CVD.<sup>6</sup>

Periodontitis and almost any heart-related diseases are multifactorial. These factors such as smoking, diabetes, addiction, and old age are common in both diseases, and removing any of these factors helps treatment progression of both diseases.<sup>7</sup>

Many studies claimed that there was a relationship between periodontal diseases and heart-related diseases;<sup>8-14</sup> however, there are various reports which denied this association,<sup>15,16</sup> but due to the lack of evidence, we need to study more about this link.

The purpose of this study is to investigate the effects of periodontitis on heart-related diseases. Therefore, by collecting these articles, we are trying to provide our audience with a more comprehensive association between periodontitis and heart-related diseases.

### 1. Hypertension (HTN)

HTN seems to be related to periodontitis.<sup>17-22</sup> Studies show that systolic and diastolic pressure is higher in patients who have suffered from periodontitis.<sup>22</sup> In addition, in the study conducted by the 3<sup>rd</sup> National Health and Nutrition Examination Survey (NHANES III), a positive linear relationship between systolic pressure and severe periodontitis is found in middle-aged patients.<sup>23</sup> Moreover, tooth loss is related to high blood pressure levels.<sup>24,25</sup> As we know, periodontitis is the main reason for tooth loss in adults. Mechanisms that may explain this relationship include endothelial dysfunction (due to the systemic inflammation caused by periodontitis),<sup>26,27</sup> oxidative stress,<sup>28</sup> inflammatory mediators,<sup>3,26,27,29-31</sup> and bacteremia.<sup>32,33</sup> On the other hand, it has been observed that high blood pressure can worsen the periodontal disease due to the microcirculation changes and subsequent ischemia in the periodontium, which favors periodontitis.<sup>17-19</sup> Moreover, it has been indicated that periodontal treatment has a positive effect on decreasing blood pressure.<sup>34-36</sup> However, the reliability of this evidence is still limited. A recent systematic review indicates that oral health assessment and management cannot affect the overall health and quality of life (QOL), but it can affect patients with HTN.<sup>37</sup>

### 2. Atherosclerotic cardiovascular disease (ACD)

A various systematic review based on

observational epidemiologic studies suggests that there is a relationship between periodontal disease and ACD.<sup>2,38-40</sup> In 2013, Dietrich et al. found that this association was stronger in younger compared with older patients. Besides, this relationship was more obvious in men than in women. There is limited evidence to suggest an association between chronic periodontitis and the risk of recurrent CVD in patients with atherosclerosis.<sup>39</sup> So far, no evidence has been found to reject the causative relationship between CVD and oral health.

According to several meta-analyses, patients with chronic periodontitis are at greater risk for developing coronary heart disease (CHD).<sup>12,40-42</sup> Helfand et al. explored non-traditional risk factors for CVD (excluding diabetes, blood pressure, and cholesterol levels) to explain the risk of CHD in people who were not at high risk for common risk factors. In this research, chronic periodontitis was one of the nine variables studied.<sup>43</sup> In 2014, a conducted meta-analysis indicated that periodontitis was associated with an increased risk of stroke.<sup>44</sup> In addition, in the study done by Briggs et al., the association between ACD and the progression of periodontal disease in individuals over 40 was indicated.<sup>24</sup> In this regard, the hemostatic and inflammatory factors play an important role in supporting the relationship between poor oral health and ACD.<sup>45</sup> Periodontal disease is associated with an increase in several chronic inflammatory markers which can play a significant role in this regard due to the available evidence of chronic inflammation in ACD.<sup>41,46,47</sup> According to the most recent consensus report in 2020, patients associated with periodontitis who have suffered from CVD are at a greater risk of CVD side effects. Moreover, patients with CVD should be questioned about any signs and symptoms of periodontitis. In addition, it is suggested that periodontal treatment should seriously be followed in patients with CVD.<sup>48</sup>

### 3. IE

There are studies which are supporting periodontitis as a risk factor for IE.<sup>49,50</sup> Periodontitis is a factor that can result in the transmission of bacteria from the oral cavity to the bloodstream.<sup>51</sup> The study by Dhotre et al. indicated periodontitis in 42.5% of patients with IE.<sup>52</sup> A worldwide study reported that the incidence of bacteremia after the tooth extraction was 13%-96% and indicated that bacteremia might be increased by the presence of diseases including gingivitis, periodontitis, and other odontogenic infections.<sup>53</sup> This IE has resulted from

bacteremia. Among the organisms, *Streptococcus viridans* plays the most important role which results in bacteremia.<sup>54</sup> Nakatani et al. found that periodontitis could be a predisposing factor that could result in IE.<sup>55</sup> Based on the study by Dhotre et al. in 2017, there is a positive relationship between periodontitis and IE which can be related to the common role of *Streptococcus viridans* and other organisms.<sup>50</sup> On the other hand, Ninomiya et al. study did not indicate a significant difference in the oral conditions of patients with endocarditis and healthy individuals. But the study is not reliable due to the insufficient number of samples.<sup>56</sup> It seems that more comprehensive studies are needed to investigate the effect of periodontitis on IE.

#### 4. MI

MI and periodontal disease have many common risk factors, including diabetes, smoking, and infection.<sup>57,58</sup> There are various studies in this area indicating that the periodontal disease is associated with an increased risk of MI.<sup>59-62</sup> In 1989, Mattila et al. reported that oral health in patients with MI was worse than healthy controls.<sup>63</sup> Akamatsu et al. demonstrated that periodontal pathogens induced MI in the animal model.<sup>64</sup> Nowadays, it is believed that both MI and periodontal disease are multifactorial in nature; however, epidemiologic studies failed to find a relationship between these diseases.<sup>65,66</sup> Recently, a systematic review by Sidhu concluded that no relationship between MI and periodontal diseases could have been confirmed.<sup>67</sup> As a result, there is still not enough evidence indicating that periodontal treatment would prevent and/or treat cardiac disease including MI, which is congruent with a recent report from the American Heart Association.<sup>2</sup> The researchers are still looking for stronger reasons which would support this relationship. According to consensus report, in 2020, patients with periodontitis are more likely to suffer from MI.<sup>48</sup>

#### 5. HF

HF is one of the most important causes of death worldwide.<sup>68,69</sup> There are studies indicating a possible relationship between periodontitis and HF.<sup>70-72</sup> Frohlich et al. found that patients with HF had a higher prevalence of periodontitis. However, in their study, there was no relationship between the severity of periodontitis and the severity of symptoms caused by HF etiology.<sup>71</sup> On the other hand, Wood and Johnson reported an association between these diseases and claimed that patients

with periodontitis had a faster progression in HF. In addition, tomatoes have a protective effect against HF due to their antioxidant and anti-inflammatory materials such as lycopene and carotenoids. Besides, these materials can prevent inflammatory periodontal reactions.<sup>70</sup> In addition, in 2017, Schulze-Spate et al. were able to show the connection between HF and periodontitis. Further, the patients with HF experienced greater severity of periodontitis which is related to increased turn-over markers. The local and systemic factors like inflammatory mediators and cytokines would help to prove this relationship.<sup>72</sup>

In 2014, in the study conducted by Jockel-Schneider et al., patients with periodontitis showed greater arterial stiffness.<sup>73</sup> Since the increase in arterial stiffness is associated with left ventricular hypertrophy (LVH)<sup>74,75</sup> and due to the fact that systemic inflammation has an important effect on the structure and function of the left ventricle (LV) and can cause LVH,<sup>76</sup> therefore, increased inflammatory marker level due to periodontitis may be indirectly related to HF. Related studies on the association between periodontitis and structural changes in the heart confirm this hypothesis.<sup>17-19</sup> Moreover, the increase in periodontitis level is related to LVH.<sup>17,18</sup> In the study conducted by Aoyama et al. in patients with higher antibody levels due to periodontitis, the prevalence of HF is more common than the healthy ones; therefore, pathogens related to periodontitis may result in HF.<sup>1</sup>

#### 6. Arterial fibrillation (AF)

AF is the most typical cardiac arrhythmia worldwide.<sup>77</sup> Inflammation is known to have a potential role in AF development.<sup>78</sup> About AF and periodontal disease, there are limited studies which found out this relationship. Chen et al. conducted a cohort study and concluded that there was an increased risk of AF or flutter in the periodontal disease group compared with the patients without the periodontal disease.<sup>79</sup> Chang et al. conducted another study among 161286 subjects from the National Health Insurance Service-Health Screening Cohort (NHIS-HEALS) which had no medical history of AF, HF, or cardiac valvular diseases. To assess oral hygiene, they evaluated the presence of periodontal disease, any dental visit, number of missing teeth, etc. They concluded that oral hygiene enhancement resulted in decreasing the risk of AF. They also suggested that subjects with good oral hygiene might have a reduced risk of AF.<sup>80</sup> About the other types of arrhythmia, there are not

enough studies that assess this association with periodontal disease.

### 7. Peripheral artery disease (PAD)

PAD is the abnormality of upper or lower limb arteries. The main cause is atherosclerosis, but other conditions such as thrombosis, vasculitis, etc. also can lead to this problem.<sup>81</sup> The systematic review conducted by Yang et al. indicates that there may be a possible association between periodontal diseases and PAD. They also mentioned that there was a 5-fold increase in the risk of developing PAD compared to healthy individuals.<sup>82</sup> There is another study that confirmed the previous study claiming that the prevalence of periodontitis and edentulism (tooth loss) had a higher rate in patients with PAD. This is because chronic inflammation is a common feature of both PAD and periodontal disease.<sup>83</sup>

### 8. Other CVDs

Karhunen et al. conducted a study through 300 middle-aged men who were the victims of sudden death and subjected to medico-legal autopsy and they carried out the panoramic X-ray which can indicate dental lesions. They concluded that men who suffer from sudden cardiac death in early middle age seem to present a higher rate of dental pathology. The result showed 72.1% horizontal bone loss and 30.9% vertical pockets, which are signs of periodontitis.<sup>84</sup> Due to the lack of studies in this field, further study is needed to be done to obtain more accurate conclusions. There are not enough studies on other types of CVD.

### Conclusion

From all the records that have been retrieved, it seems that the evidence is in favor of the relationship between periodontitis and CVD. However, some studies are not supporting this association, but it is crucial for physicians to not forget and consider the state of oral health when dealing with heart-related diseases; this may help the patients to treat heart-related diseases by treating the oral infections with control of inflammatory mediators.

On the other hand, treatment of some heart diseases including HTN may affect the improvement of the oral periodontal state.

In general, in today's societies, the final aim is the improvement of the patient's QOL, and it is not achievable except by control of the entire patient's problems including oral and heart-related problems.

By the way, for achieving more reasons and

pieces of evidence, we need to perform more comprehensive studies, particularly for heart diseases that are not common and there is not enough evidence to show the relationship between them and periodontitis.

We have found that CVD is directly related to periodontal disease and periodontal disease is an infectious and multifactorial disease of microbial origin, but like other infectious diseases, it is not treated with antibiotics alone. Therefore, it is better for physicians who treat patients with CVD to evaluate the patient's oral health and symptoms such as tooth mobility, bad breath, gingival bleeding during the brushing, flossing, or eating, or bad taste of mouth which relates to oral infection. If there are any suspected cases of oral tissue inflammation or periodontal disease, the physician must refer the patient to the periodontist for further evaluation and treatments such as scaling, root planning, oral health instruction, and other complementary treatments like local antibiotic therapy or antiseptic mouthwashes.

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### Conflict of Interests

Authors have no conflict of interests.

### Authors' Contribution

Both authors have made substantive contributions to this study and have reviewed the final paper prior to its submission.

AR: Conceptualization, methodology, writing original draft, reviewing, and editing

ZA: Conceptualization, methodology, writing original draft, investigation, reviewing, editing, supervision.

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