Evidence of the association between endodontic infections and heart diseases: a systematic review

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DOI: https://doi.org/10.54448/mdnt22S320
Received: 02-15-2022; Revised: 04-28-2022; Accepted: 05-20-2022; Published: 05-31-2022; MedNEXT-id: e22S320

Abstract

Introduction: In the scenario of heart diseases, especially cardiovascular diseases (CVD), there are several predictors of these diseases, including diseases related to oral health. Objective: It was to analyze through clinical studies the association of diseases of the oral cavity with cardiovascular diseases, to point out the main causes and treatments for future clinical studies. Methods: The rules of the Systematic Review-PRISMA Platform were followed. The research was carried out from January 2022 to April 2022 and developed based on Scopus, PubMed, Science Direct, Scielo, and Google Scholar. The quality of the studies was based on the GRADE instrument and the risk of bias was analyzed according to the Cochrane instrument. Results and Conclusion: In line with the objective proposed in the present study, the results concluded that the association between chronic endodontic infection and CVD cannot be disregarded, although it is of limited quality evidence at the moment. Thus, clinical studies observed that the risk of diagnosing CVD in patients with chronic endodontic infection was 1.38 times those without infection. Furthermore, early childhood caries showed that the microbiome profile composed of Fusobacterium, Prevotella, Capnocytophaga, and Oribacterium were more abundant in the group with congenital heart disease than in the group without congenital heart disease. Also, the greater number of missing teeth was associated with an increased risk of a first acute myocardial infarction, and endodontic inflammatory disease may contribute as an independent risk factor for cardiovascular diseases.

clinical entities reported is root canal infection and subsequent inflammation of the periapical tissues after pulp necrosis described under the term “apical periodontitis” [13-17]. In this regard, the world literature is still lacking in scientific evidence from robust randomized studies that demonstrate the evaluation and synthesis of epidemiological data on endodontic infections and their association with CVD [18].

Therefore, the present systematic review study aimed to analyze through clinical studies the association of diseases of the oral cavity with cardiovascular diseases, to point out the main causes and treatments for future clinical studies.

Methods
Study Design

The rules of the Systematic Review-PRISMA Platform (Transparent reporting of systematic reviews and meta-analysis-HTTP://www.prisma-statement.org/) were followed.

Data sources and research strategy

The search strategies for this systematic review were based on the keywords (MeSH Terms): “Oral disease. Endodontic infection. Periodontal infection. Oral microbiome. Heart diseases. Cardiovascular diseases”. The research was carried out in January 2022 to April 2022 and developed based on Scopus, PubMed, Science Direct, Scielo, and Google Scholar. Also, a combination of the keywords with the booleans "OR", “AND", and the operator "NOT" were used to target the scientific articles of interest.

Study Quality and Bias Risk

The quality of the studies was based on the GRADE instrument and the risk of bias was analyzed according to the Cochrane instrument.

Results and Discussion

A total of 114 articles were found. Initially, duplication of articles was excluded. After this process, the abstracts were evaluated and a new exclusion was performed, removing the articles that did not address the theme of this article. In total, 72 articles were fully evaluated and 29 were included and evaluated in this study (Figure 1).

Figure 2 presents the results of the risk of bias in the studies using the Funnel Plot, through the calculation of the Effect Size (Cohen's Test). The sample size was determined indirectly by the inverse of the standard error. The number of clinical studies evaluated was n=29. The graph showed asymmetric behavior, suggesting a significant risk of bias in studies with small sample sizes, which are shown at the bottom of the graph.

This presence of risk of bias is justified by the deficiency in the number of clinical studies with a significant sample size and with methodologies developed as randomized controlled studies.

Results and Discussion

In an attempt to analyze the association of diseases of the oral cavity with cardiovascular diseases,
important studies were found. Thus, one study systematically evaluated the existing evidence on the possible association between chronic endodontic infections and CVD. As a result, it was observed that the risk of CVD diagnosis in patients with chronic endodontic infection was 1.38 times those without infection. Therefore, there are indications for an identified association between chronic endodontic infection and CVD [19].

In this regard, efforts have been underway over the past 15 years to clarify regional endodontic infections and their impact on general health. This observation may have been pointed out by more recent estimates of the increase in the prevalence of CVD in the coming years by approximately 10% [20]. Furthermore, the WHO estimates that about 24 million patients will die from CVD by 2030 [3]. In this context, the identification of common pathogenic mechanisms and triggering factors for CVD is imperative for dentists to deeply analyze the effects of chronic infections of endodontic origin (such as pulp necrosis/root canal infection) [14,15,18,19].

In this sense, acute inflammation of the dental pulp, due to caries or traumatic injury, can result in pulp necrosis and subsequent tissue infection, having increased dynamics to induce the formation of apical periodontitis in the vicinity of infected internal dental structures [21]. Furthermore, a failed endodontic treatment can also serve as a substitute for the onset of apical periodontitis. Such lesions of endodontic origin arise as a result of the transmission of bacterial and microbial pathogens from the infected pulp space to the periapical region of the tooth [22]. Thus, biomarkers such as neutrophils in the initial and more acute phase, followed by the recruitment and infiltration of mast cells and macrophages as a second-line response, are allied to the chronicity of the infection. In addition, the prostaglandins, cytokines, and chemokines produced are associated with leukocyte recruitment [22-24].

In this scenario, the advent of CVD may be related, since bacteria originating from infected tissues, together with by-products of the inflammatory process and the formation of granulomas, can interact and enter the systemic circulation with an impact on blood circulation [25]. Furthermore, research has been directed towards the discovery of shared genetic antecedents and risk loci of the two entities [26].

In this sense, oral bacteria have been associated with several systemic diseases. Furthermore, the abundance of caries-associated bacteria was observed to be higher in patients with congenital heart disease (CHD) than in healthy control groups (without CHD). Thus, one study evaluated the dental microbiota in children with CHD compared to healthy control. A total of 20 children with CC and healthy control aged between two and six years. All of them were affected by early childhood caries. The microbiome profile indicated that Fusobacterium, Prevotella, Capnocytophaga, and Orribacterium were more abundant in the CC group, while Lactobacillus and Rothia were predominant in the healthy control [27].

Despite this evidence, a recent systematic review study evaluated the evidence on the relationship between chronic endodontic infections and CVD. A total of 14 studies with 960,652 human subjects were included in this review. No association was observed between endodontic infections and cardiovascular disease among individuals with heart disease. Most studies showed a moderate overall risk of bias of 57.14% (n=8). There is weak evidence on the association between cardiovascular disease and chronic endodontic infections [28].

Also, despite this, a major controlled clinical trial from 2022 looked at the association between inflammatory endodontic disease and a first myocardial infarction (AMI). A total of 805 patients with recent experience of a first AMI, gender, age, and geographically matched with a control. Panoramic radiographs were available for 797 patients and 796 controls. Patients who had a first AMI had a higher sum of decayed, missing, and filled teeth (mean 22.5 vs. 21.9) and more missing teeth (mean 7.5 vs. 6.3) than healthy controls. The number of missing teeth was associated with an increased risk of a first AMI. Furthermore, teeth without caries and filled were associated with reduced risk. Age-based analysis revealed the following variables associated with an increased risk of a first AMI: number of decayed teeth (in patients <60 years), any primary periapical lesion (in patients <65 years), and proportion of filled teeth (in patients ≥65 years). Therefore, the greater number of missing teeth was associated with an increased risk of a first AMI. In addition, the endodontic inflammatory disease may contribute as an independent risk factor for CVD [29].

**Conclusion**

Following the objective proposed in the present study, the results concluded that the association between chronic endodontic infection and CVD cannot be disregarded, although it is of limited quality evidence at the moment. Thus, clinical studies observed that the risk of diagnosing CVD in patients with chronic
endodontic infection was 1.38 times those without infection. Furthermore, early childhood caries showed that the microbiome profile composed of Fusobacterium, Prevotella, Capnocytophaga, and Orbibacterium were more abundant in the group with congenital heart disease than in the group without congenital heart disease. Also, the greater number of missing teeth was associated with an increased risk of a first acute myocardial infarction, and endodontic inflammatory disease may contribute as an independent risk factor for cardiovascular diseases.

Acknowledgement
Not applicable.

Funding
Not applicable.

Ethics approval
Not applicable.

Informed consent
Not applicable.

Data sharing statement
No additional data are available.

Conflict of interest
The authors declare no conflict of interest.

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