Does Dental Disease Hurt Your Heart?

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Abstract

Recent research has yielded conflicting data regarding the relationship between dental disease, particularly periodontitis, and cardiovascular disease. A causative relationship would have major ramifications for health care. There is a plausible theoretical basis for such a link, as increased levels of inflammatory mediators may increase the risk of atherosclerotic plaque formation. Nevertheless, a clinical confirmation of a causative relationship has been difficult, in part because cardiovascular disease and periodontal disease share common risk factors such as increasing age and tobacco use, and because cardiovascular medications may increase the risk of periodontitis. Patients should be encouraged to control documented risk factors for cardiovascular disease and to maintain oral health for its well-known health benefits.

MeSH Key Words: *coronary disease/epidemiology; focal infection, dental/complications; periodontitis/epidemiology; risk factors*

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What can a clinician say to patients who may be contemplating radical measures to eliminate dental disease as a means of controlling their risk of heart disease? Can dentists advertise control of oral disease as "good for your heart"? Can dental professionals take partial credit for the contemporary decline in the prevalence of and mortality caused by cardiovascular disease (CVD)? The jaw bone–hip bone connection has been the subject of intense research, discussion and controversy for the last decade or so. We review here the literature about this topic and discuss current answers to these questions through a critical evaluation of the available evidence.

Dental diseases are the most common infectious diseases in the world.[1] A number of studies in recent years have attempted to examine the potential relationship between dental diseases and CVD. These studies have been the subject of controversy, yet they have received considerable publicity in both the lay and medical press. For example, the American Heart Association states that "While there are conflicting data regarding this hypothesis, no substantial evidence has been presented that oral microorganisms are etiologic for cardiovascular disease, nor that they cause or exacerbate acute cardiovascular events such as myocardial infarction, stroke, unstable angina or death."[2] Nevertheless, the American Dental Association published a special supplement in June 2002 entitled "Oral Health, Heart Health."

The implications of a direct link between oral infections and CVD are numerous, and may have a significant effect on public health in North America. If such a connection is indeed accepted, we may change the way we prevent or treat CVD, which is still the leading cause of mortality on the continent. We may also radically change the way we perceive dental care, and this in turn may have major implications for the relationship between dentistry and medicine, as well as between dental insurance and medical insurance.

What Is the Postulated Link?

It is biologically plausible that oral, in particular periodontal, disease may increase the risk of CVD. Beck and others[3] hypothesized that periodontal disease, through its mostly gram-negative pathogens, provides a biological burden of endotoxin (lipopolysaccharide [LPS]) and inflammatory cytokines, which may initiate and exacerbate atherogenesis or thromboembolic events. Similarly, in 1998 Page[4] suggested that LPS and gram-negative oral bacteria

may enter the bloodstream and increase susceptibility to systemic diseases. He emphasized the possible role of inflammatory cytokines produced in response to chronic periodontal infection in systemic events like platelet aggregation, thrombosis and formation of atheroma. Herzberg and Weyer[5] agreed, and in an animal model, determined that plaque bacteria may induce platelet aggregation. Lowe[6] pointed out that hemostatic and rheological variables are associated with both prevalent and incident CVD, and may be mechanisms through which risk factors such as smoking, hyperlipidemia and infections, including oral infections, promote vascular events. Kinane[7] proposed that the 2 main processes linking periodontitis and atherosclerosis are LPS-related responses and the hyperresponsive-monocyte phenomenon. However, they concluded that the evidence was insufficient at present and that more study was needed.

Oral pathogens are not the only bacteria that have a postulated link to the development of atherosclerosis. *Chlamydia pneumoniae* and *Helicobacter pylori* are also suspected infectious agents in atherogenesis. However, evidence linking *C. pneumoniae* to CVD is contradictory.[8,9] Whincup and others[10] found only a weak association between infection with *H. pylori* and CVD in a study that controlled for tobacco use.

Additional studies to connect oral disease and CVD have been done with surrogate markers for the latter. Danesh and others[11] reviewed inflammatory markers that have been associated with coronary heart disease and concluded that fibrinogen, C-reactive protein (CRP), albumin levels and leukocyte counts are associated with risk of coronary heart disease. This was further substantiated by Ridker and others.[12] Fredriksson and others[13] found that CRP levels were higher for patients with periodontal disease and that periodontal lesions may induce hyperreactivity in neutrophils. Noack and others[14] also found a positive correlation between CRP levels and periodontal disease. Although these findings do not prove a cause–effect relationship, they do contribute to the circumstantial evidence of a connection between oral and cardiovascular diseases, and point to possible mechanisms of interinfluence.

Other comorbid conditions were also studied. Anemia increases the risk of a cardiovascular event. Hutter and others[15] suggested that patients with periodontitis had lower hematocrit and hemoglobin levels after adjustment for confounders. However, analysis of the data of this study by Merchant[16] suggested that differences in risk factors for anemia had not been completely adjusted for.

Hypercholesterolemia is another cardiovascular risk factor.[17] Katz and others[18] demonstrated that patients with this condition have more severe periodontal disease, although the same association was not seen between high triglyceride levels and periodontitis.

Upper body obesity, another risk factor for CVD, was associated with periodontitis in 643 healthy dentate Japanese subjects by Saito and others,[19] who earlier reported an association between periodontitis and body mass index. Abdominal obesity has been linked with increased CRP and inflammatory cytokine levels, as well as other risk factors for CVD. In an analysis of this study, Ritchie[20] stated that "their study shows that failure to measure and adjust for this variable in periodontitis-systemic disease relationships could potentially distort the true association."

What Have Clinical Studies Shown?

Mattila and others[21] first reported an association between poor dental health and heart attack in a case-control study comparing 100 patients with acute myocardial infarct and 102 community members. DeStefano and others[22] found that patients with periodontitis had a 25% increased risk of coronary heart disease, and that men under 50 who developed periodontal disease had a relative risk of 1.72 for coronary heart disease. They also suggested that the risk of total mortality was associated with the severity of periodontal disease. Mendez and others[23] found a 2.27 increment in the risk of peripheral vascular disease among U.S. veterans with clinically significant periodontal disease. Loesche and others[24] found that the rate of cerebrovascular accident (stroke) was associated with many indicators of dental disease such as plaque index, oral neglect and oral hygiene, and was inversely associated with salivary flow. Arbes and others[25] examined data from the National Health and Nutrition Examination Survey (NHANES) for 5,564 adults and found that the adjusted odds ratio for self-reported heart attacks was 3.8 among patients who had loss of periodontal attachment greater than 3 mm at 67% or more of the sites. Wu and others[26] examined NHANES data for 9,962 adults and suggested a relative risk of 2.11 for cerebrovascular disease among patients with periodontitis and 1.41 among edentulous patients. Buhlin and others[27] found that CVD and hypertension were associated with gingival bleeding, and CVD was associated with wearing dentures, after adjustment for potential confounders.

The debate about whether periodontal disease is a risk factor for cardiovascular disease is still unresolved.

A recent study by Meurman and others[28] found poorer oral health in 256 patients with severe heart disease than in 250 controls without coronary heart disease. They found that the levels of inflammatory markers were consistently higher among patients with coronary heart disease. The difference in CRP and fibrinogen values between the group with coronary heart disease and the group with

noncoronary heart disease was significant, but the difference in white blood cell counts was not. Serum *H. pylori* and *C. pneumoniae* antibodies were also significantly higher for patients with coronary heart disease. The authors suggested that acute soft-tissue inflammation, such as gingivitis, pericoronitis or remaining root tips, may contribute more to the levels of inflammatory cytokines than to a single chronic pathologic process, such as periodontitis, which is often subclinical. They also noted that patients with coronary heart disease were more likely to be hypertensive and that many hypertension medications cause xerostomia, which in turn promotes oral disease. This study did not, however, adjust for the effects of smoking on oral health, in particular on periodontitis.

Conversely, Joshipura and others[29] found no significant association between periodontal disease and coronary heart disease in a study of 44,119 adult U.S. males. Hujoel and others[30] looked at NHANES data for 636 patients with CVD and found no relation between CVD and the presence of periodontitis or gingivitis. In 2002 Joshipura and Douglass[31] reviewed cohort studies of periodontal disease and tooth loss in relation to coronary heart disease or stroke, and found that the adjusted relative risk ratios were low (range 1.01–1.37).

Perhaps more revealing, a prospective longitudinal study[32] with 12 years of follow-up that used univariate analyses to examine data for over 6,500 subjects showed that oral diseases were associated with CVD. However, adjustment for well-known risk factors, such as smoking, obesity, hypertension and age, reduced all the associations to statistical insignificance.

Finally, a meta-analysis of data about the relationship between periodontal disease and CVD showed only a modest increase in the risk ratio.[33] However, this study used highly restrictive inclusion of data, leaving out all cross-sectional trials and those that had fewer than 100 patients.

So What Does It All Mean?

The debate about whether periodontal disease is a risk factor for CVD is interesting, but still unresolved.

Although some studies have demonstrated that the relative risk for CVD is increased among patients with periodontitis, some analyses have been potentially confounded by the fact that smoking and diabetes seem to have a causal relationship with both CVD and periodontitis. Additionally, many cardiovascular medications cause hyposalivation, which is associated with an increased risk of dental disease.

All in all, it is plausible that oral inflammatory cytokines and immune activation directly affect the vasculature located only a few centimetres away. It is also conceivable that frequent bacteremia (caused, for example, by chewing and tooth brushing) could induce hypercoagulable states. However, as long as the mechanism of CVD remains obscure, it will be difficult to determine the real relationship between oral and cardiovascular disease.

Even though definitive proof is currently elusive, patients should be strongly encouraged to prevent and treat all oral diseases, including periodontal disease. One of the most important steps a patient can take to prevent CVD is to abstain from smoking — smoking is an acknowledged risk factor in the development of oral disease.[34]

Conclusions

The relationship between oral disease and CVD remains controversial. Based on current evidence, periodontal and other oral disease may have at best a modest correlation with the development of CVD and resulting mortality. The biological mechanism for such a correlation has not been elucidated. Patients should be encouraged to concentrate on controlling well-known risk factors for CVD and to seek the well-documented benefits of treating dental disease: freedom from pain and infection, improved chewing ability, improved esthetics and control of halitosis. ◆

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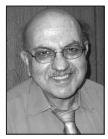

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