Influence of the Periodontium on Cardiovascular Disease

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ABSTRACT

The results of several recent cross-sectional and longitudinal human epidemiologic studies have demonstrated a statistical link between the occurrence of destructive periodontal disease in the oral cavity and an increased risk of cardiovascular disease. Several theories have been advanced to explain the association of the two diseases. However, it is not presently known if periodontitis plays an etiologic role in the pathogenesis of cardiovascular disease or whether the relationship is merely a statistical correlate for an undetermined risk factor common to both diseases. The strength and limitations of the available data from major studies are discussed, along with potential clinical implications for dental practitioners.

INTRODUCTION

Until recently, the most widely recognized link between the status of the periodontium in the oral cavity and cardiovascular disease was related to the key role played by inflamed gingival tissues in the pathogenesis of subacute infective endocarditis. Chewing, oral hygiene procedures, trauma, and various dental therapies have an increased potential in the presence of gingival inflammation to seed viridans streptococci and periodontal pathogens (i.e., Actinobacillus actinomycetemcomitans) from subgingival dental plaque biofilms into the bloodstream and increase the risk of subacute infective endocarditis in individuals with pre-existing valvular heart conditions.[1] Subactute infective endocarditis thus represents a type of "dental focal infection" where systemic dissemination of certain pathogenic oral microorganisms via transient bacteremias leads to clinical disease at a non-oral body site.[2]

More recently, emerging research data has implicated destructive periodontal disease as a risk factor in other types of heart conditions, most notably, acute myocardial infarction and coronary heart disease. This paper will provide a critical review of major studies reported to date on this issue and their possible implications for dental practitioners.

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Finland Studies

Mattila et al.[3] in Finland in 1989 first suggested a relationship between oral health status and acute myocardial infarction ("heart attack"). Using a case-control study design, 100 consecutive persons admitted for hospitalization for acute myocardial infarction were compared to age, gender, and place-of-residence matched control subjects randomly selected from the Helsinki, Finland community. Oral health status was evaluated using a newly created "total dental index", which provided a cumulative score ranging from a minimum of zero (good oral health status) to a maximum of ten (poor oral health status) based on the number of dental caries (scored on a 0-3 scale), the number of 4-5 mm and ≥ 6 mm probing depths, or presence of suppuration (scored on a 0-3 scale), the number of radiographic periapical lesions and/or vertical bone defects (scored on a 0-3 scale), and presence of pericoronitis (scored as 1 if present). Other conventional cardiovascular risk factors evaluated on the patient groups included serum total cholesterol concentrations, serum triglyceride concentrations, serum high density lipoprotein cholesterol concentrations, serum C peptide concentrations, history of infections, smoking habits, hypertension, diabetes, age, and socioeconomic status. Patients with acute myocardial infarction yielded significantly higher total dental index scores than the community control subjects. Multiple stepwise logistic regression analysis using conventional risk factors and the total dental index as independent variables confirmed the association between the total dental index and acute myocardial infarction to be statistically significant (P = 0.004), even when age, total cholesterol, tryglycerides, hypertension, diabetes and smoking were taken into account. Hence, the authors concluded that "dental caries or periodontal disease, or both, is more common among patients with acute myocardial infarction than among controls matched for age and sex".[3]

A second cross-sectional investigation by Mattila et al.[4] used a "pantomography index", which scored the total number of radiographic periapical lesions, caries, vertical bony defects, and furcation involvements. Pantomography index scores, age, and serum triglyceride levels were significantly correlated in multivariate analysis with the degree of coronary atherosclerosis in 88 males examined with diagnostic coronary angiography, even after controlling for total cholesterol, HDL cholesterol, smoking, hypertension, body mass and socioeconomic status. These findings again implicated the oral health status as a possible determinant for cardiovascular pathology.

A third study involving the total dental index was a 7-year follow-up longitudinal investigation of 182 males and 32 females with a previous history of myocardial infarction.[5] Baseline total dental index scores were found to be a significant predictor of new coronary events over the subsequent 7-year time period. This study provided a time sequence relationship further implicating oral health status as a risk factor for subsequent heart disease.

However, inherent shortcomings in the total dental index and the pantomography index as surrogate measures of oral health status severely limits interpretation of all of the above study findings. Since the various types of oral pathology (i.e., caries, periodontitis, periapical lesions) found on clinical or radiographic examination are not differentiated by either index, it is not clear what the relative contribution of periodontal disease vs. dental caries (or periapical lesions and/or pericoronitis) is in relationship to the assessed cardiovascular conditions. Thus, studies using total dental index or pantomography index scores do not specifically implicate periodontal disease as a risk factor in acute myocardial infarction or coronary heart disease. An overall ill-defined poor oral health status is instead reflected in high total dental index and high pantomography index scores rather than specific dental diseases. Additionally, the arbitrary 0-10 scale used in the total dental index has not been biologically validated to date or shown to be reproducible in calibration studies. Thus, by using the total dental index or the pantomography index, the fundamental assessment techniques used in the above studies to evaluate the periodontal status of study subjects is open to question and unresolved relative to their validity.

Another critical weakness of the Mattila et al. studies was the failure to collect subject data on diet and exercise habits, which are important independent known risk factors for myocardial infarction. Since dietary habits are likely to be highly correlated to total dental index scores (i.e., high caries rates are associated with high dietary sucrose), this may account for the statistical association of total dental index scores with acute myocardial infarction. Thus, the association of total dental index scores with acute myocardial infarction may be a spurious association confounded by dietary factors, rather than a true causal relationship.

NHANES-I Follow-up Study

The National Health and Nutrition Examination Survey I (NHANES-I) and its epidemiological follow-up study over the following 14 years involved a population-based evaluation of the systemic and oral health of a representative sample of American adults aged 25-74 years at baseline. DeStefano et al.[6] related baseline dental examination data for 9,760 subjects with their subsequent median 14-year incidence of death or hospitalization due to coronary heart disease, and total mortality. Persons identified with periodontitis at the baseline oral examinations were found to exhibit a 25% excess risk for developing coronary heart disease over the following 14 year period as compared to individuals with minimal periodontal disease, even after statistical adjustments were made for potentially confounding risk factors such as age, gender, race, education, marital status, systolic blood pressure, total cholesterol levels, body mass, diabetes, physical activity, alcohol consumption, poverty and smoking. The effect of oral status on subsequent cardiovascular outcome was most pronounced in males younger than 50 years of age at baseline, where periodontitis-affected younger males had a 72% excess risk of subsequent coronary heart disease as compared to younger

males with periodontal health and gingivitis.[6]

The large subject sample size representative of USA adults, the standardized oral and medical evaluations, the longitudinal study design, and the statistical analysis carried out by DeStefano et al.[6] are strengths of the investigation. However, the periodontal classification of subjects was only broadly made into the categories of "no disease", "gingivitis", "periodontitis" (which was determined solely on probing depth values), and "no teeth". No measurements of periodontal attachment loss were recorded in the oral examinations, no differentiation was made between early, moderate and advanced forms of periodontitis, and no assessments of furcation involvements were carried out. Thus, the clinical methodology used in the DeStefano et al. analysis provided periodontal data that is incomplete and subject to misclassification and misinterpretation. Interestingly, the excess risk of coronary heart disease associated with periodontitis was of a similar magnitude as that associated with subjects with no teeth at baseline, where no ongoing periodontal infection was possible. This would indicate that either edentulous subjects possess increased risk of coronary heart disease due to residual effects of previous periodontitis when teeth were present, or that other unrelated and to date unidentified risk factors exist.

VA Normative Aging Study

Another longitudinal database examined for periodontal-cardiovascular relationships was from the combined outcomes of the VA Normative Aging Study and Dental Longitudinal Study.[7] Incidence data over an 18-year period for coronary heart disease and fatal heart attack for 1,147 males with no history of coronary heart disease at baseline was related to baseline periodontal status, which was assessed by mean whole-mouth interproximal alveolar bone height measured with a 5-point Schei ruler and worst clinical probing depth values. When comparing persons classified with "Hi" amounts of bone loss (> 20% mean bone loss score) vs. those classified with "Lo" bone

loss (≤ 20 mean bone loss score), the multivariate incidence odds ratios adjusted for age and other recognized risk factors for cardiovascular disease were 1.5 for the relationship between "Hi" alveolar bone loss at baseline and subsequent total coronary heart disease, and 1.9 between "Hi" alveolar bone loss and fatal coronary heart disease. This indicates an approximate two times greater risk for a fatal coronary heart event over an 18-year period in persons with pre-exisiting marked alveolar bone loss vs. persons with minimal periodontal disease or periodontal health. Analysis of clinical probing data showed that persons with all of their teeth demonstrating a worst probing depth > 3 mm at baseline experienced a 3.6 times greater odds of developing coronary heart disease over the following 18-year period as compared to subjects with all probing depths ≤ 3 mm.[7]

The strength of the study are the standardized medical evaluations, the entry criteria of systemically-healthy study subjects followed longitudinally for disease incidence, and the magnitude of the odds ratios (3.6) demonstrating a relationship between probing data and development of coronary heart disease. Bone loss measurements were taken from non-standardized radiographs using visual assessments of broad gradations (20% increments) of bone loss, which are more difficult to calibrate. Unfortunately, no clinical periodontal attachment loss assessments, which are a "gold standard" for identification of periodontal breakdown, were made with clinical probing measurements carried out in the study.

Elderly US Veterans Study

A cross-sectional study of 320 males > 60 years of age assessed history of coronary heart disease relative to periodontal status, which included measurement of clinical periodontal attachment loss.[8] Coronary heart disease was found to be 2.9 times more prevalent in older dentate persons with only 1-14 teeth vs. those with 15-28 teeth. Interestingly, the 1-14 tooth subject group with coronary heart disease exhibited a significantly higher proportion (81% vs. 59-62%) of teeth with clinical periodontal attachment

loss of > 4 mm than individuals with 15-28 teeth. Elevated BANA test scores from interproximal plaque samples, which screen for typsin-like enzyme activity most likely to be derived from the periodontal bacterial pathogens Porphyromonas gingivalis, Bacteroides forsythus or Treponema denticola, were two times more likely to be found in subjects affected by coronary heart disease.

Possible Biologic Mechanisms of Action

Despite the limitations of the major studies detailed above, there appears to be a statistical link established between the status of periodontal tissues and heart disease by them and additional reports.[9] This association needs to be clarified by additional studies which more accurately classify persons with periodontitis and better capture the degree and extent of periodontal disease breakdown in study subjects relative to their cardiovascular status. However, a plausible biologic mechanism explaining the apparent statistical association of the two disease conditions has not been established, and is essential to determine if any type of causal inference is to be made between the periodontal disease and heart disease. At present, three basic theories have been advanced. First, it has been proposed that transient bacteremias from inflamed gingival tissues introduce pathogenic microorganisms from subgingival dental plaque biofilms into the bloodstream, where they induce pathologic damage to blood vessels and promote clot formation.[10] Supporting this dental focal infection hypothesis are the intriguing findings that the major bacterial pathogen in adult periodontitis, Porphyromonas gingivalis, possesses a platelet-aggregation capability unique among subgingival plaque microorganisms[11, 12], and is a common inhabitant of atheromatous plaques removed from carotid arteries[13], and thus possibly also in coronary arteries. In this model, microbial infection associated with periodontitis lesions would contribute to coronary heart disease and act as an adjunctive etiologic factor to other established risk factors after the metastatic

spread of the plaque organisms into the bloodstream via transient bacteremias.

The second theory suggests that persons jointly affected by periodontitis and coronary heart disease exhibit a genetically-determined hyperinflammatory immune response to bacterial challenge.[7,9] Abnormally elevated secretion of pro-inflammatory and tissue damaging mediators such as prostaglandin E_2 and interleukin 1β from peripheral blood monocytes in hyperinflammatory phenotype-positive individuals are proposed to account for the increased risk for both periodontitis and coronary heart disease.[7,9] Thus, a host susceptibility trait common to both periodontitis and heart disease would be operational.

In the third theory, an infectious etiologic agent common to both periodontitis and coronary heart disease has been proposed. Slots[14] has pointed out that certain herpesviruses, particularly cytomegalovirus and Epstein-Barr virus, may be recovered from both periodontitis lesions in the oral cavity and diseased coronary arteries. It is suggested that perhaps herpesviruses may independently give rise to both periodontal disease and cardiovascular disease. Thus, no cause-effect relationship between periodontal disease and heart disease would exist if both conditions are etiologically associated with a common infectious agent.

Conclusions and Implications for Dental Professionals

The weight of evidence from large-scale epidemiologic studies supports the notion that persons with periodontitis also appear to possess a greater risk of developing coronary heart disease. This association presently exists only at a statistical level, with no firm explanations established which account for the joint disease relationship. Thus, a causal relationship whereby periodontal disease contributes to the etiology of coronary heart disease has not been scientifically documented to date.

Dental practitioners should be aware of these findings to more intelligently interact with inquiring patients. However, present data do not support the premise that periodontal therapy or any other oral intervention has any impact on reducing the risk of coronary heart disease. Rather, patients with periodontitis should be urged to maintain medical surveillance of their cardiovascular status, and work on controlling or reducing all known risk factors associated with coronary heart disease, including periodontal infections.

Author	Type of Study	No. of Study Subjects	Major Findings
Mattila et al. [3]	Case-control	100 consecutive myocardial infarction cases	Total dental index index significantly associated with acute myocardial infarction.
Mattila et al. [4]	Case-control	88 male	Pantomography index significantly associated with degree of coronary atherosclerosis.
Mattila et al. [5]	Longitudinal 7 year	214 previous myocardial infarction cases	Total dental index index at baseline significantly associated with new coronary events after 7 years.
DeStefano et al. [6]	Longitudinal 14 year	9760	25% greater risk of coronary heart disease after 14 years in patients with periodontitis at baseline. 72% greater risk of coronary heart disease in males younger than 50 years with periodontitis.
Beck et al. [7]	Longitudinal 18 year	1147	1.5 greater risk for total coronary events after 18 years in patients with > 20% mean alveolar bone loss at baseline. 1.9 greater odds of coronary heart disease in all males at baseline exhibit > 3 mm mean probing depths.
Loesche et al. [8]	Case-control	320 male	2.5% male coronary heart disease in older dentate patients with only 1-14 teeth and 61% of teeth with > 4 mm periodontal attachment loss. Coronary heart disease subjects 2.5 more likely to yield beta-hemolytic dental plaque.

Table. Summary of Selected Studies on Oral Health Status and Heart Disease.

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