Focused Perspective

Dental Disease, Coronary Heart Disease and Stroke, and Inflammatory Markers

What Are the Associations, and What Do They Mean?

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In addition to “classical” risk factors for coronary heart disease (CHD) and stroke, “emerging” risk predictors (which may also play roles in pathogenesis) include measures of chronic infections and of chronic, low-grade activation of inflammation and of hemostasis. As all dental healthcare professionals know (but probably fewer medical practitioners and their patients), the oral cavity is a major site of chronic infection and inflammation, particularly periodontal disease. In recent years there has been increasing interest in the “periodontal-systemic connection” between dental health parameters and the risks of cardiovascular disease, respiratory disease, diabetes mellitus, osteoporosis, and adverse pregnancy outcomes. Given that poor oral health, coronary heart disease, and stroke are major worldwide health problems, their associations are potentially important. In particular, two practical questions are of mutual interest to dental and medical healthcare practitioners and their patients. First, should dental health scores be used (in addition to classical risk factors) to predict an individual’s risk of CHD and stroke? Second, does treatment of poor dental health reduce such risk?

A further confounder of the association between dental health parameters, CHD, and stroke is their mutual association with markers of inflammation. After the initial publication of Mattila et al., a case-control study observed that patients with periodontal infections had significant elevations of plasma fibrinogen and white blood cell count, leading to the hypothesis that periodontal disease might increase risk of CHD in part by inducing a systemic proinflammatory, prothrombotic state. A subsequent cross-sectional study observed that total tooth loss (of which the two commonest causes were periodontal disease and dental caries) was also associated with some markers of activated inflammation and hemostasis (including C-reactive protein in men). Because total tooth loss abolishes periodontitis, such data suggested two alternative hypotheses. First, total tooth loss may reflect a constitutional (perhaps genetic) predisposition to severe inflammatory reactions following an inflammatory stress (such as smoking and/or periodontal infection). The association between tooth loss, CHD, and stroke might therefore reflect a common influence of “proinflammatory” constitutional states both on the need for tooth extraction after periodontitis and on the likelihood of clinical events after arterial plaque inflammation (induced by agents including smoking, lipids, and plaque infections—including infection with periodontal pathogens). Second, total tooth loss resulted in altered nutritional status, such as reduced intake of citrus fruit and vitamin C, which might increase risks of both inflammation and cardiovascular disease. A third hypothesis, that edentulous persons wearing dentures at night might develop a systemic proinflammatory, prothrombotic state as a result of chronic Candida albicans infection, was not supported by the data.

Prospective longitudinal studies are less susceptible to bias than case-control and cross-sectional studies. Over the last 10 years, nine such studies of the association of dental health parameters (including measures of periodontal disease and of tooth loss) with risk of CHD and/or stroke have been reported. A recent meta-analysis showed modest, but statistically significant, increases in cardiovascular risk associated with dental health parameters. It has been noted that many of these studies have been secondary analyses of studies that were not designed to test the association of dental health parameters and risks of CHD and stroke, and that several of these reports used questionnaires to define dental disease, leading to misclassification and dilution of the estimates of association.

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other hand, no prospective study report has performed multivariate analysis including both measures of dental disease, and measures of activated inflammation and hemostasis in the assessment of risk of CHD and stroke. This is a limitation not only in assessing the associations of dental health parameters with risk of cardiovascular disease but also in assessing the associations of markers of inflammation and hemostasis with risk of cardiovascular disease.\(^2\)

In this issue, Janket et al\(^1\) report a study that advances this field in three ways. First, they compared a recently developed dental health score (the Asymptotic Dental Score [ADS], which used asymptotic weights to increase precision) with the original Total Dental Index (TDI, which used an arbitrary weighting scheme), used by Mattila et al.\(^4\) The authors observed a significantly stronger association of the ADS (compared with the TDI) with angiographically confirmed CHD in a case-control study. This finding supports an emerging consensus\(^14\)–\(^16\) that the more precise the dental health score, the stronger are its associations with CHD and stroke in epidemiological studies, and hence the likelihood of a true biological relationship.

Second, Janket et al\(^1\) report that the more precise ADS also showed stronger associations in general with markers of activated inflammation and hemostasis, triglyceride, and total cholesterol/HDL ratio than the TDI. This finding supports an increasing body of data that poor dental health is associated with both “classical” and “emerging” risk predictors for CHD and stroke.

Third, the report of Janket et al\(^1\) compares the associations of their dental score (ADS) with the traditional Framingham Heart Score in discrimination of CHD cases and controls. A prediction model including the ADS, C-reactive protein, HDL cholesterol, and fibrinogen offered similar predictive value to the Framingham Heart Score. When the ADS was removed from the model, its predictive ability fell, suggesting that the dental score contributed to CHD prediction in addition to known biochemical predictors.

Although Janket et al\(^1\) conclude that their new dental score may be useful in screening persons without overt CHD to detect increased risk of CHD and stroke, caution is required in extrapolating from their case-control study of persons with overt CHD to the general population. Current national and international guidelines rightly emphasize the importance of using classical risk predictors (age, sex, smoking habit, diabetes, blood pressure, total cholesterol/HDL ratio) for prediction of CHD and stroke, and also provide evidence-based recommendations for lifestyle advice, reductions in blood pressure and cholesterol, and control of diabetes to reduce cardiovascular risk.\(^1\) Further studies are required to evaluate the additive predictive value of emerging risk predictors including dental health scores and markers of activated inflammation and hemostasis (and also to evaluate their potential additive roles in pathogenesis as potential causal risk factors).\(^1\)\(^,\)\(^2\) Practical limitations of comprehensive dental scores in risk prediction include the time and cost of a skilled dental healthcare professional to perform them and the reluctance of many in the general population to undergo such a procedure (which involves some time and discomfort) as part of a health screen. Nevertheless, dental healthcare professionals and investigators will doubtless promote their interests in this field, as will laboratory scientists and investigators with interests in blood tests\(^2\) and other laboratory measures for prediction of CHD and stroke. Further evaluation of all such “emerging” risk predictors for cardiovascular disease could usefully follow the example of the Fibrinogen Studies Collaboration,\(^18\) which pools and analyzes all available individual data from prospective studies.

In conclusion, the answer to the first question (Should dental health scores be used in addition to classical risk factors to predict an individual’s risk of CHD and stroke?) is “We don’t know.” The paper by Janket et al\(^1\) points us in the direction of using more sensitive dental scores in future epidemiological studies, where time and resources permit. On the other hand, these time and resource constraints will severely limit the use of such scores in screening of healthy persons for cardiovascular risk. For the second question (Does treatment of poor dental health reduce such risk?), the answer is also “We don’t know.” Further studies should include the following: the effect of treatment of periodontitis on markers of activated inflammation and hemostasis; the associations of proinflammatory genetic polymorphisms\(^19\) with dental disease, as well as with CHD and stroke; and, if possible (given the impracticality of randomized studies), prolonged observational studies of dental status (preferably defined with sensitive scores), inflammatory and hemostatic markers and risks of CHD and stroke. Meanwhile, periodontal disease obviously merits prevention and treatment as a health problem in itself, and it is also prudent to ensure adequate nutrition in edentulous persons.\(^10\)\(^,\)\(^20\)

References


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