

Taking oral health to heart

An overview

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Several authors have suggested that periodontal disease increases the risk of myocardial infarct, stroke and other systemic conditions.¹⁻⁵ The ADA symposium “Taking Oral Health to Heart” (held July 26-27, 2001, in Chicago) focused on the relationship between oral and cardiovascular disease, and presented the basis on which this relationship can be evaluated.

Serving as an overview, this introduction highlights some of the terminology, databases and epidemiologic studies that were discussed at the symposium.

TERMINOLOGY

It is important to understand the various terms associated with the potential relationships between oral and cardiovascular disease. Risk factors are defined as something that increases the likelihood of an event or a disease occurring, such as increasing age as a risk factor for death.

Modifiable risk factors are risk factors that can be changed, thereby—we hope—decreasing the chance that a disease will occur. A good example is smoking, a modifiable risk factor for certain forms of cancer.

Hierarchy of studies. *Case reports.*

Risk factors can be identified by analyzing a hierarchy of studies.⁶ The weakest studies are anecdotes, case histories and case reports; they are helpful because they provide the basis for generating hypotheses.

Case-control studies. The next

strongest form of evidence is provided by case-control studies, which often can identify risk indicators, but are not often able to assess the role of important confounding factors. (In case-control studies, researchers match case

Background. This article is an introduction to the 2001 ADA symposium, “Taking Oral Health to Heart,” which focused on the relationship between periodontal disease and cardiovascular disease. This overview describes the databases and terminology used in discussions of epidemiologic studies on this topic.

Conclusions. In determining if a certain disease, medication or condition is a risk factor for another entity, one must carefully evaluate and analyze the data, weigh the various other contributing risk factors and then determine the mechanism of interaction if an association is established.

Clinical Implications. This symposium provided practitioners with various concepts regarding the role of periodontal disease as a risk factor for cardiovascular disease, and the data presented represent the state of the art.

reports of a disease or disorder to the same number of cases without the condition; these cases are randomly selected from a community and matched for age and sex and then compared.)

Cross-sectional studies. Cross-sectional population-based studies often are more powerful than case-control studies because they describe large populations and allow a more rigorous assessment of confounders or corisk factors via multivariate statistical analyses. Cross-sectional studies can lead to identification of risk indicators (for example, blood pressure is an indicator of an increased risk of stroke), which are reasonable or plausible correlates of disease.

Longitudinal studies. Longitudinal studies generally are useful in providing strong evidence that a risk indicator is indeed present. Risk indicators are sometimes—but not always—confirmed as risk factors in longitudinal studies. Longitudinal studies may help resolve important questions regarding which risk indicators identified in lower-level studies are true risk factors.

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BOX**CARDIOVASCULAR DISEASE RISK FACTORS.**

- Age
- Race
- Sex
- Alcohol Use
- Hypertension
- Cholesterol Level
- Smoking
- Education
- Diabetes
- Height and Weight
- Marital Status
- Physical Activity
- History of Cardiovascular Disease
- Diet
- Poverty Level
- Infection

Intervention studies. The strongest evidence of the benefit of reducing or eliminating a risk factor is found in intervention studies. These studies use a random, controlled, masked design and evaluate the effect of therapy on the outcome or outcomes being measured. Intervention studies are in their early stages and, when completed, should provide convincing evidence for or against the existence of a relationship between periodontal disease and cardiovascular disease.

The highest form of data obtained to date regarding an association between periodontal disease and cardiovascular disease has been from longitudinal studies. In these studies, researchers have evaluated epidemiologic data that have been collected over several years.

Odds ratios. In epidemiologic studies, the measures of association have been presented as odds ratios. An odds ratio greater than 1 indicates a positive association; less than 1 indicates a negative association. An odds ratio equal to 1 indicates no association. Some investigators have questioned the meaning of an odds ratio between 1 and 2 in regard to the importance of the association being evaluated.⁷

To demonstrate the use of an odds ratio, let us

examine the data regarding the relationship of smoking to oral cancer. If the incidence of oral cancer in a smoking population is 0.002, and in a nonsmoking population it is 0.0004, then the odds ratio is calculated as follows:

$$0.002/0.0004 = 2/0.4 = 5$$

From this calculation, we can conclude that the odds of developing oral cancer among smokers is five times as high as that among nonsmokers. Also, one can calculate the increase in the odds ratio by subtracting the ratio for “no association” (that is, 1) from 5, which equals 4, and multiplying the result by 100 percent. This equals 400 percent; therefore, the odds of developing oral cancer among smokers increased by 400 percent.

BASIS FOR LONGITUDINAL STUDIES

The data for a number of the longitudinal studies discussed in this supplement were obtained from the National Health and Nutrition Epidemiological Survey I, or NHANES I, which studied 31,973 men and women from 1971 through 1975.⁸ This study was followed by the NHANES Epidemiological Follow-up Study carried out from 1982 through 1984, which studied 11,348 people who had participated in NHANES I.⁸ In 1984, a subset of these subjects (3,980) who were 55 through 74 years of age at baseline in 1971 through 1975 were re-evaluated.⁸ Researchers re-evaluated all subjects in 1987 and again in 1992.⁸ Evaluations included various measures of general health, history of cardiovascular diseases and evaluation of periodontal status.

Russell’s Periodontal Index. The NHANES researchers used Russell’s Periodontal Index,⁹ as described below, to determine the periodontal status of all subjects:

- 0 = normal;
- 1 = mild gingivitis;
- 6 = gingivitis with pocket formation, tooth firm;
- 8 = advanced destruction of periodontium with mobility.

Using this index, researchers sum all scores and calculate the mean. The disadvantages of this system are that it gives heavy weight to the destructive stages of periodontal disease and has no provision for distinguishing between slight and extreme pocketing. In addition, a periodontal probe is not used to determine pocketing.

Risk factors. The box lists the cardiovascular disease risk factors that must be evaluated in these studies. Smoking is the single largest con-

founder in evaluating the data. Smoking factors to be considered include not only smoking frequency, but also the time at smoking onset and the time at cessation for subjects who stopped smoking before entering the study or during the study.

Below are some questions that researchers need to ask:

- Is the relationship between periodontal disease and cardiovascular disease spurious?
- If there is a causal relationship between periodontal disease and cardiovascular disease, is it reversible?
- Does periodontal therapy reduce the risk of cardiovascular disease?
- What is the incidence of cardiovascular disease in edentulous patients?
- If the relationship is shown to exist, what is the mechanism of the interaction?

RISK FACTOR EVALUATION

In determining if a certain disease, medication or condition is a risk factor for another entity, one must carefully evaluate and analyze the data, weigh the various other contributing risk factors and determine the mechanism of action. For example, a recent study published in the *Journal of the American Medical Association* reported that tetracyclines or quinolones may reduce the incidence of a first myocardial infarct.¹⁰ This finding was based on an evaluation of data from a longitudinal study that gave an odds ratio of less than 1 for the incidence of myocardial infarct in patients who had a history of being medicated with tetracyclines or quinolones. However, when another statistician ruled out confounding risk factors not considered in the original analysis, an association was found only for tetracycline and not for quinolones.¹¹

Subsequently, Golub and colleagues¹² offered an explanation of the mechanism of this interaction; they suggested that tetracycline may have been effective, not because of its antibacterial effect, but because of its ability to suppress vascular inflammation owing to its inhibition of matrix metalloproteinases, or MMPs, such as collagenase and elastase. Their suggestion was supported by an earlier study¹³ that showed that doxycycline and chemically modified tetracycline inhibit the development of aortic aneurysm in a rat model via suppression of MMPs.

When evaluating longitudinal studies,

researchers and clinicians must consider a variety of factors in determining odds ratios, which, in turn, provide information relevant to the strength of a relationship between one condition and another.

CONCLUSION

The information presented above describes the databases and terminology used in discussions of epidemiologic topics presented in this supplement and published in the literature. In determining if a particular disease, condition or medication is a risk factor for another entity, one must carefully evaluate and analyze the data, weigh the various other contributing risk factors and then determine the mechanism of the relationship, if any, with the condition in question.

Because this evaluation can be done in a variety of ways, different authors may obtain different results from the same database. The ultimate solution to determining if a causal relationship exists between periodontal disease and cardiovascular disease will depend on the outcome of intervention studies now under way. ■

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