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Salivary Lysozyme and Prevalent Coronary Heart Disease:

Possible Effects of Oral Health on Endothelial Dysfunction

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To the Editor:

Total leukocyte count in the peripheral blood has been reported to be a significant predictor of future cardiac events and mortality.[1] Leukocyte-derived salivary lysozyme has been associated with oral infection,[2] and serum lysozyme has been implicated in impaired glucose metabolism,[3] a contributory factor for endothelial dysfunction.[4] We postulated that salivary lysozyme, therefore, would be associated with coronary heart disease (CHD).

This study was approved by the joint ethical committee of the Kuopio University Hospital and the University of Kuopio. We investigated the relationship between the CHD and lysozyme levels in a case-control study of 250 angiographically confirmed CHD patients and 250 sex- and age-matched controls, adjusting for age, sex, smoking, body mass index (BMI), diabetes mellitus, total cholesterol/high-density lipoprotein (HDL) cholesterol, hypertension, and serum C-reactive protein (CRP) levels ≥10 mg/L or ≥3 mg/L using logistic regression analyses. To assess the specific contribution of oral health through impaired glucose metabolism, we controlled for the Asymptotic Dental Score (ADS), an estimate of oral infection burden, comprising 5 major oral pathologies, namely pericoronitis, gingivitis, dental caries, root remnants, and the edentulous state.[5]

The basic characteristics of the cohort (Table I, available online at http://atvb.ahajournals.org) and cross-tabulation of lysozyme levels and other vascular risk factors are presented online (Table II, available online at http://atvb.ahajournals.org). After adjustment for established cardiac risk factors including age, sex, smoking, total cholesterol/HDL cholesterol, diabetes, hypertension, BMI, and CRP, odds ratios (ORs) with 95% CIs for the association between salivary lysozyme and CHD increased from 1.00 (the reference group) to 1.16 (0.51 to 2.63), 1.82 (0.83 to 4.01), and 3.62 (1.60 to 8.16) from the lowest to highest quartiles of salivary lysozyme (*P* value for linear trend <0.0001; Figure; Table III, available online at http://atvb. ahajournals.org). Models using log-transformed lysozyme or omitting the intermediate variables such as diabetes or hypertension generated similar results. When we adjusted for the ADS, the ORs (CI) decreased slightly to 1.00, 1.12 (0.48 to 2.62), 1.92 (0.85 to 4.34), and 3.45 (1.50 to7.93). When we adjusted for CRP using a threshold of 3 mg/L, the OR for the fourth quartile of lysozyme decreased to 2.73 (1.53 to 4.87) compared with the other 3 quartiles combined and the C-statistic also decreased, suggesting a reduced explanatory ability of CRP at 3 mg/L.

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Salivary lysozyme conferred a much stronger association with CHD than the ADS oral infection score. We hypothesize that this additional risk increase might be attributable to impaired glucose metabolism and subsequent accumulation of advanced glycation end products (AGE) as depicted in the conceptual model (Figure I, available online at http://atvb.ahajournals.org). However, this hypothesis calls for further prospective studies.

Lysozyme is secreted locally, and there is no significant correlation between serum and salivary lysozyme.[6] Salivary lysozyme may underscore dual pathways by which poor oral health may contribute to CHD pathogenesis.[5] Poor dentition is a limiting factor for adequate intake of beneficial nutrients to prevent CHD (ie, fiber,[7] antioxidants,[8,9] and fruits and vegetables[10]). Moreover, edentulism encourages high fat and carbohydrate intake,[11,12] thus, it may contribute to a higher level of AGE and subsequent CHD.[13-15]

The conclusion of our meta-analysis,[16] that persons with periodontal disease might be at a higher risk of developing cardiovascular disease, has been corroborated by several recent trials reporting that periodontal treatment decreased the level of systemic CRP[17-19] and further by other immunologic studies that linked the periodontal pathogen *Porphyromonas gingivalis* to atherosclerosis.[20-22]

Leukocytes may play a role in cardiopathogenesis, as Kowolik et al[23] and Margolis et al[24] concurred. Salivary lysozyme may be a marker for the dual contribution of oral leukocytes to cardiopathogenesis, via infection and elevated AGE deriving from an unhealthy diet.

In conclusion, increased quartiles of salivary lysozyme, which may be a consequence of oral infection or impaired glucose metabolism, were associated with increasing ORs (1.00, 1.16, 1.82, and 3.62, respectively, P for trend <0.0001) for CHD after controlling for traditional CHD risk factors.

Further prospective investigations are warranted to establish whether this is a causal relationship.

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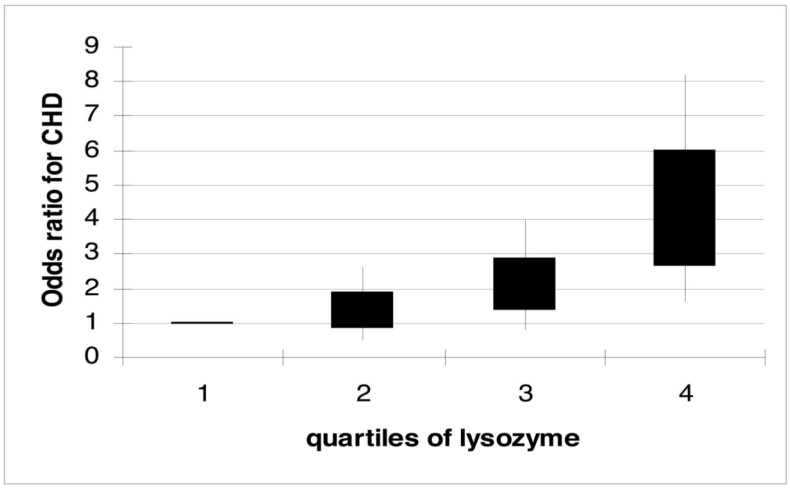

Black boxes : mid points of Upper and lower confidence limits
Vertical lines: 95% confidence limits

1. .
OR for CHD according to the quartiles of lysosyme levels.