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Association between periodontal disease and ischemic heart disease among Swedish women. A cross-sectional study

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Abstract

Objective. The aim of this cross-sectional study was to analyze the relationship between chronic periodontitis and ischemic heart disease (IHD). ***Material and Methods.*** A cross-section of women aged 38 to 84 years were examined in 1992–93 (analysis based on $n = 1056$). Medical and dental examinations were included in the analysis specifically with regard to IHD and periodontitis. Other well-known risk factors for IHD were used as covariates in multivariable statistical analysis. ***Results.*** Among the dentate women in this study ($n = 847$), 74 had IHD and 773 did not. There was no statistically significant difference between numbers of pathological gingival pockets between these groups (58.1% had one or more pathological pockets in the IHD group compared to 57.6% in the non-IHD group). Bivariate analysis of dentate individuals showed significant associations between IHD and number of missing teeth, age, body mass index, waist/hip ratio, life satisfaction, hypertension, and levels of cholesterol and triglycerides. However, in the final multivariable logistic regression model, with the exception of age, only number of teeth (<17 teeth) OR = 2.13 (CI 1.20; 3.77) was found to be significantly associated with IHD. Moreover, edentulous women had an OR of 1.94 (CI 1.05; 3.60) in relation to IHD (age-adjusted model). ***Conclusions.*** In the present study, periodontitis did not seem to have a statistically significant relationship with IHD. The number of missing teeth showed a strong association with IHD, and this may act as a proxy variable tapping an array of different risk factors and behaviors.

Key Words: *Epidemiology, ischemic heart disease, periodontitis, population study, women*

Introduction

Over the past few decades, oral diseases, particularly periodontitis, have been discussed as possible risk factors for ischemic heart disease (IHD) [1–3]. The prevalence of moderate periodontitis or gingivitis in the Swedish population is about 60%, and between 10% and 15% suffer from severe periodontitis leading to loss of teeth if untreated [4]. In the Western industrialized world, IHD is one of the leading causes of death [5]. Since the prevalences of these two chronic inflammatory diseases are high, any possible association between them would concern many people.

Well-known risk factors in common for the two diseases include smoking, diabetes, and low socioeconomic status. Some studies suggest that these risk factors have not been fully taken into account and that therefore the association between periodontitis and IHD has been overestimated [6].

On the other hand, some authors explain the connection between periodontitis and IHD as the result of an invasion of periodontal pathogens into the endothelial and smooth muscle cells of the arteries that in turn stimulate platelet aggregation [7,8]. This may lead to a systemic inflammatory response favoring an atherosclerotic process.

A correlation between oral infectious lesions, as found on radiographs, and coronary atheromatosis has been shown by Mattila et al. [9] in a predominantly male population. This association was not found among the females participating in the same study, but there were only 12 compared to 88 men in

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the study [10]. The gender difference is of particular interest since some authors have suggested that women have fewer risk factors for heart disease than men [11]. The Prospective Population Study of Women in Gothenburg has also indicated a different pattern of risk factors in women compared to men. Increased waist/hip ratio (WHR) and high triglycerides have been considered to be more important risk factors for women compared to men [12,13]. Estradiol has been suggested to have a protective effect against IHD [14], which could explain why women usually get IHD later in life than men [15]. However, middle-aged women who do contract myocardial infarction usually have a worse prognosis than men, due to higher risk factor burden (diabetes, hyperlipidemia) [16].

Most studies on the association between periodontal disease and IHD have been carried out in male populations, but Buhlin et al. carried out a study in a solely female population consisting of middle-aged and elderly women in Sweden [17]. Consecutively selected women with diagnosed IHD ($n=143$) underwent a thorough dental examination and were compared to 50 women without IHD. The study indicated that women with IHD had worse oral health than women with no history of IHD.

In the literature, differing results concerning an association between periodontitis in females and IHD have called for further investigations in a larger, randomized female population. Previously, mostly epidemiological studies have been published and very few, if any, randomized clinical trials. The aim of this cross-sectional study was to explore a possible association between IHD and periodontitis in middle-aged and elderly women participating in the Prospective Population Study of Women in Gothenburg.

Material and methods

The Prospective Population Study of Women in Gothenburg, Sweden, was initiated in 1968. Gothenburg has a population of approximately 450,000 inhabitants. Randomly selected by date of birth, 1622 women (ages 38, 46, 50, 54 and 60 years) were sampled for a combined medical, psychiatric and dental examination; 1462 took part, corresponding to a participation rate of 90.1% [18]. The same women were re-examined in 1980–81 [19] and in 1992–93 [20].

At the 1992–93 examination, new probands, also randomly selected and representative of the age groups, born 1942 and 1954 were added. Moreover, a few women born in 1922 and 1930, and who had moved to Gothenburg after 1968, were also randomly selected and included in the study. Thus, for this cross-sectional study from 1992–93, which this article is based on, information was provided for 1056 women regarding IHD (Table I).

Table I. Number of women with and without IHD in the different age groups in the Population Study of Women in Gothenburg 1992–93.

Age	IHD	Non-IHD	Total
38	0	61	61
50	0	92	92
62	18	260	278
70	36	267	303
74	35	188	223
78	13	67	80
84	4	15	19
Total	106	950	1056

The dental examination was conducted by dentists and included a panoramic radiography, a clinical inspection of the teeth, gums and oral mucosa, color photography of the dentition, and a questionnaire.

Subjects diagnosed with angina pectoris and/or a history of myocardial infarction ($n=106$, Table I) constituted the outcome variable. Myocardial infarction was diagnosed if at least two of the following criteria were present: 1) central chest pain >30 min, 2) transient rise of transaminase activities, and 3) typical ECG changes of recent onset [21]. Angina pectoris was diagnosed using the questionnaire by Rose [22]. The independent variables were obtained as follows: numbers of teeth were registered from the panoramic radiograph, and numbers of periodontally deepened gingival pockets were measured by probing at mesiobuccal and distobuccal sites of all teeth with a millimetre-graded probe. Pockets of 6 mm or more were registered as evidence of active periodontitis. In the analysis, periodontitis was considered as the presence of one or more pathological pocket. The other independent variables were obtained from the medical part of the study (Table II) and constituted other well-known risk factors of IHD.

Age was used as a continuous variable in the analysis. Hypertension and diabetes were dichotomized (yes/no), where hypertension was answered with "yes" if the proband had systolic blood pressure of 160 or more and/or diastolic blood pressure of 95 or more and/or was treated pharmacologically for hypertension. A subject was defined as having diabetes if on anti-diabetes therapy (insulin and/or tablets) or if two fasting blood samples showed glucose concentrations according to the current World Health Organization definition of diabetes (blood glucose concentration of ≥ 7.0 mmol/l). Body mass index (BMI) was calculated. WHR was calculated by dividing waist circumference by hip circumference. Cholesterol, triglycerides, and serum high-density lipoprotein (HDL) concentrations were obtained from blood samples collected in the fasting state and measured as mmol/l. Smoking was assessed as never, former, or current, and wine consumption as never, weekly, or daily. For marital status, the

Table II. Frequencies, or mean values, and standard deviations of the independent variables in women with and without IHD, respectively, in the 847 dentate women.

	IHD ($n=74$)		Non-IHD ($n=773$)	
No. of teeth*				
≥17	45.9%		74.0%	
<17	54.1%		26.0%	
Probing depth (≥6 mm)				
No pathological pockets	41.9%		42.4%	
One or more pockets	58.1%		57.6%	
Life situation*				
Satisfied	77.0%		86.2%	
Not satisfied	23.0%		13.8%	
Marital status				
Married	53.4%		57.3%	
Widow	30.1%		20.0%	
Divorced/unmarried	16.4%		22.7%	
Smoking				
Non-smoker	62.2%		56.9%	
Ex-smoker	23.0%		22.7%	
Current smoker	14.9%		20.4%	
Wine consumtion				
Never	27.0%		21.0%	
Once a week or less	66.2%		71.4%	
Daily	6.8%		7.6%	
Diabetes				
Non-diabetic	90.5%		95.6%	
Diabetic	9.5%		4.4%	
Hypertension*				
No hypertension	45.9%		61.5%	
Hypertension	54.1%		38.5%	
Body mass index*	Mean	SD	Mean	SD
	27.0	4.6	25.7	4.1
Waist-hip-ratio*	Mean	SD	Mean	SD
	0.84	0.06	0.82	0.06
Serum cholesterol*	Mean	SD	Mean	SD
	6.5	1.3	6.2	1.1
Serum triglycerides*	Mean	SD	Mean	SD
	1.6	0.9	1.4	0.7
Serum HDL	Mean	SD	Mean	SD
	1.5	0.5	1.6	0.4

*$p < 0.05$.

women were categorized as married, widow, or unmarried/divorced. The participants evaluated their life situation after being asked in the questionnaire "Are you satisfied with your life situation?" on a Likert scale from 1 to 7, anchored by 1 = couldn't be better and 7 = couldn't be worse. The variable was then divided into "acceptable" (1–4) and "poor" (5–7) as a crude measure of general well-being.

Statistical analysis

Statistical analysis was carried out using the computer program SPSS and included the chi-square test, *t*-test, and bivariate and multivariate logistic regression including all the above variables. Differences were considered statistically significant for values of $p < 0.05$. The number of individuals included in the analyses varied because of missing values in the different variables.

Results

The first analysis was based on the number of dentate individuals ($n = 847$). In this group, 74 women (8.7%) were diagnosed with IHD. Among the independent risk variables, bivariate analysis showed that having fewer remaining teeth, being older, being less satisfied with life situation, having hypertension, and higher mean values of BMI, WHR, cholesterol, and triglycerides were statistically significantly associated with having IHD (Table II).

However, in the multivariate logistic regression analysis, including all significant variables in the bivariate analyses, only two statistically significant variables related to IHD remained, i.e having fewer remaining teeth and an ageing effect (Table III).

Periodontitis was detected by probing the gingival pocket at two sites of each tooth and 58% of the women had one or more pathological pocket (i.e. a pocket depth of 6 mm or more) (Table II). For

Table III. Associations between IHD (outcome variable) and the independent variables (multiple logistic regression; dentate women). Odds ratios, 95% confidence intervals and *p*-values.

	OR	95% CI	*p*-value
No. of teeth			0.01
≥17	1.00 (reference)		
<17	2.13	1.20; 3.77	
Age	1.08	1.03; 1.13	0.002
Probing depth (≥ 6mm)			0.58
No pathological pockets	1.00 (reference)		
One or more pockets	0.86	0.50;1.50	
Life situation			0.35
Satisfied	1.00 (reference)		
Not satisfied	1.40	0.70;2.80	
Marital status			0.41
Married	1.00 (reference)		
Widow	0.88	0.46;1.64	0.66
Divorced/unmarried	0.60	0.28;1.28	0.18
Smoking			0.91
Non-smoker	1.00 (reference)		
Ex-smoker	1.15	0.57;2.30	0.70
Current smoker	0.96	0.44-2.11	0.92
Wine consumption			0.95
Never	1.00 (reference)		
Once a week or less	0.96	0.51–1.79	0.90
Daily	1.15	0.33–3.98	0.83
Diabetes			0.59
Non-diabetic	1.00 (reference)		
Diabetic	1.33	0.47–3.81	
Hypertension			0.68
No hypertension	1.00 (reference)		
Hypertension	1.12	0.65–1.95	
Body mass index	1.07	0.99–1.14	0.067
Waist/hip ratio	0.39	0.002–62.52	0.72
Serum cholesterol	1.17	0.90–1.52	0.25
Serum triglycerides	1.04	0.64–1.70	0.88
Serum HDL	0.77	0.34–1.73	0.53

further analysis, this variable was also trichotomized into no pathological pockets, 1–5 pathological pockets, and 5 or more pathological pockets. Logistic regression analysis using IHD as the outcome variable showed no significant differences between the groups. However, women with more than five gingival pockets showed an OR of 1.18, i.e. 18% non-significant, higher risk of reported IHD than women with fewer gingival pockets.

Among the edentulous women ($n=125$), 20 suffered from IHD. When adjusted for age, edentulous women showed an OR of 1.94, and women with 1–16 teeth an OR of 2.33 compared to the reference category, women with ≥17 remaining teeth (Table IV).

Discussion

The objective of this cross-sectional study was to explore the association between IHD and periodontitis in middle-aged and elderly women in Gothenburg, Sweden. We could not find that pathological gingival pockets, measuring the level of periodontitis, were associated with IHD. However, tooth loss was predictive of IHD.

Since 1989, when Mattila et al. [9] showed that dental infections were associated with an increased risk of myocardial infarction, there have been several other cohort and cross-sectional studies suggesting a positive association between dental infections/periodontitis and IHD. Beck et al. [1], on comparing

Table IV. Association between prevalence of IHD and number of teeth, including edentulous women (logistic regression analysis)

	Edentulous	1–16 teeth	17–28 teeth
Non-IHD	105 (84%)	201 (83%)	572 (94%)
IHD	20 (16%)	40 (17%)	34 (6%)
OR (95% CI) ($p<0.001$)	3.20 (1.77;5.78)	3.34 (2.06;5.44)	1.0 (ref)
*OR (95% CI) ($p=0.003$)	1.94 (1.05;3.60)	2.33 (1.41;3.86)	1.0 (ref)

*Age adjusted.

subjects with "high" and "low" bone loss, found a significant OR of 1.5 for cardiovascular disease (CVD). For subjects in the same study whose teeth all had at least one site with probing depth exceeding 3 mm, OR was as high as 3.6. Beck thus found a dose–response relationship between severity of periodontal disease and risk of CVD. The OR was adjusted for age and other well-known risk factors. An increased risk of IHD associated with periodontitis and poor oral hygiene (RR = 1.25) was found by DeStefano et al. [23]. For subjects 50 years and younger, the relative risk (RR) was even more pronounced (RR = 1.72). In another study by Mattila et al. [24], an association between dental diseases and CVD was most characteristic for subjects who were 50 years old or younger. In our study, no subjects in the younger age groups were diagnosed with IHD, but since those age groups were few in number in our sample, the results concerning these age groups are inconclusive.

As mentioned earlier, Hujoel et al. [6] found a non-significant risk of IHD for gingivitis (hazard ratio (HR) = 1.05) and periodontitis (HR = 1.14), i.e. comparable to the findings in this study.

The association between peridontitis and IHD is not fully explained and several causal connections have been discussed. One explanation could be the release of bacteria, bacterial products, or proinflammatory cytokines. There have been indications that *Porphyromonas gingivalis* has the ability to cause thrombosis by platelet aggregation. Buhlin et al. [25] showed that patients with chronic infections such as periodontitis have higher concentrations of c-reactive protein (CRP) and interleukin-6 (IL-6) compared to a matched control group. Elevated CRP and IL-6 concentrations influence the atherosclerotic process by their effect on the coagulation process.

Furthermore, another explanation for the connection between the two diseases periodontitis and IHD could be that chronic inflammation in the oral cavity leads to a release of tumor necrosis factor alpha (TNFα) and interleukin 1 beta (IL-1b), both of which have the capacity to influence the lipid metabolism. Buhlin et al. [25] also showed that patients with periodontitis had a lower blood concentration of HDL compared to a periodontally healthy control group. The lipid profile (the ratio between total cholesterol and HDL) was thus elevated in patients with peridontitis. An elevated lipid profile is known to be a risk factor for IHD.

Tooth loss has been significantly associated with IHD; for example, studies by Paunio et al. [26] and Loesche et al. [27]. Joshipura et al. [28] showed a positive association, with a relative risk (RR) of 1.7 for tooth loss, but only in subjects with pre-existing periodontitis. In our study, there was a strong association with IHD for women with less than 17 teeth when controlled for other well-known risk factors. It is possible that number of teeth acts as a proxy variable tapping an array of different risk factors and behaviors that are hard to determine in this type of study. Tooth loss is a robust and important risk factor and health indicator demonstrated in the multivariable analysis, where known risk factors such as hypertension, obesity, abdominal obesity and hyperlipidemia, all associated with poor health and accordingly tooth loss, in this cross-sectional study did not show the same strong, independent association as tooth loss [29]. One explanation could be that tooth loss captures more variation in relation to IHD compared to, for example, smoking, hypertension, and obesity. In addition, it may be speculated that health-related behaviors and oral health behavior are associated with tooth loss. Thus, dietary habits, physical activity, and self-preventive measures might possibly covary with number of teeth. Moreover, in a majority of studies from the medical field of research, no dental variables have been included among the measured variables of risk indicators.

This cross-sectional study is not valid for establishing a cause–effect relationship. We cannot therefore conclude that the association between tooth loss and IHD is causal. Both IHD and periodontitis are chronic diseases with, in most cases, slow progress of the disease. It is therefore very difficult to determine when the disease actually started and whether or not the two diseases (IHD and periodontits) have developed in parallel. Thus, the temporal relationship between the exposure and outcome variables may not be possible to determine with this cross-sectional design. However, the association between the variables is still very important to assess.

Some authors have emphasized socio-economic factors as crucial confounders when studying possible risk factors for IHD. We partly adjusted the statistical model with regard to socio-economic factors in this study. We controlled for marital status, satisfaction with life situation, and alcohol, and smoking habits. In 2005, in another study based on the Prospective Population Study of Women in Gothenburg, Cabrera et al. [30] showed that morbidity from stroke and myocardial infarction significantly increased with tooth loss independently of socio-economic status and other covariates.

Ischemic heart disease was diagnosed as having a history of either myocardial infarction or angina pectoris, defined as typical chest pain during exertion, relieved by rest or nitroglycerine. The diagnosis of angina pectoris could be regarded as less well defined compared to myocardial infarction, but the Rose questionnaire algorithm for angina pectoris is accepted and often used to verify coronary artery disease in population studies. Although there was no possibility of further verifying the diagnosis of significant coronary artery disease, and it thus being possible that some false-positive cases of angina

pectoris were included, this fact would only be crucial if our results had been the opposite, i.e. a significant association between periodontal disease and IHD.

Although this study was carried out on a randomized selected group of women, the question always has to be asked whether the women studied really were representative of the total group of women in Gothenburg. In 1997, Bengtsson et al. [20] published a 24-year follow-up study with special reference to participation, representativeness, and mortality in the Population Study of Women in Gothenburg. Participation rate was high throughout the study period; participants were mainly characteristic of women of the same ages in the general population even after 24 years; mortality after 24 years was higher in non-participants than in participants; while there was no difference in survival between women who were invited and women who were not invited to the study. Hence, we dare say that the results from our study are representative of the female population in Gothenburg in the age groups studied.

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