Community Dent Oral Epidemiol 2011; 39: 393–397

COMMUNITY DENTISTRY AND ORAL EPIDEMIOLOGY

Association between tooth extraction due to infection and myocardial infarction

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Håheim LL, Olsen I, Rønningen KS. Association between tooth extraction due to infection and myocardial infarction. Community Dent Oral Epidemiol 2011; 39: 393–397. © 2011 John Wiley & Sons A/S

Abstract – *Objective:* To explore whether the association between tooth extraction and nonfatal myocardial infarction (MI) varies by reason for extraction. *Methods:* Men of the Oslo study of 1972/73 took part in the health survey in 2000 (n = 6530) then aged 48–77 years. The present analysis is a nested case–control study of the men with a self-reported history of MI as cases (n = 548) and randomly drawn controls (n = 625). Reasons for extraction (self-reported) were recorded as periodontal infections (marginal periodontitis) or apical infection of a single tooth, and these were grouped as infection due to extractions. Extractions due to trauma or other causes were grouped as noninfection extractions. *Results:* More men with a history of MI had extracted teeth than controls (92.7% versus 88.6%; P = 0.020). The prospective logistic regression analysis predicting nonfatal MI showed strength of association between infection extraction, no extraction, or noninfection extractions combined [odds ratio (OR) = 1.64; 95% confidence interval (CI): 1.24, 2.16] in adjusted analysis and crude analysis (OR = 1.73; 95% CI: 1.34, 2.23). Adjustment was made for known risk factors for MI and periodontitis in 1972/73, such as systolic blood pressure, smoking, total cholesterol, BMI, and education recorded in the 2000 screening. *Conclusions:* Extractions due to dental infections were associated with nonfatal MI in elderly men.

Key words: infection; myocardial infarction; tooth extraction

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Submitted 26 May 2010;
accepted 25 March 2011

Tooth extractions cause bacteraemia (1), but the degree of bacteraemia is associated with the individual's immuno-inflammatory response and the bacteriological status. Bacteraemia following extractions is of a transient nature in otherwise healthy individuals. Extractions in children treated under general anaesthesia showed the duration of the bacteraemia to be <15 min after extraction (2). In surgical removal of third molars, an initially high level of bacteraemia has been observed independent of the oral health status (3). Positive bacterial blood cultures persisted for at least 15 min following extraction of 3–4 teeth. Among men with clinical cardiovascular disease, tooth loss and periodontitis were associated with approximately 10% higher carotid plaque prevalence and intima-media thickness of the carotid arteries (4); this was not seen in women. Chlorhexidine mouthwash administered 30 s before any tooth extraction reduced the level of bacteraemia to 2% within 1 h after extraction under general anaesthesia (5). These studies did not differentiate between causes of extractions. There has been a range of studies approaching the issue of association of oral infections and CVD using varying study design (6).

Most tooth extractions are attributed to infection but are also performed in cases of trauma and as part of an orthodontic treatment plan. This study explores whether the reason for extraction is associated with myocardial infarction (MI).

Materials and methods

The Oslo study cohort of men was first studied in 1972/73 (7). The main objective was to study

doi: 10.1111/j.1600-0528.2011.00616.x

prevention and epidemiology of cardiovascular diseases. The participants were aged 20–49 years in 1972. The second health examination named Oslo II was carried out from January to June 2000 by the former National Screening Service, now part of the Norwegian Institute of Public Health, Oslo (8). The 1972/73 survey data were used in a prospective analysis. In all, 12 764 men were invited in 2000. The men were aged 48–77 years, but the majority was 69–77 years. On the basis of this repeat examination, we performed a nested case–control study of men who attended both surveys, consisting of the men with a self-reported history of MI as cases (n = 548) and controls (n = 625) who were selected randomly by 5-year strata to match the age distribution of cases. Cases among the age-groups 48–67 years were few, and four controls per case were selected versus one control per case for the older age-groups. In short, at the screening in 2000, the men had a blood sample taken to estimate total serum cholesterol level, HDL, triglycerides, and glucose levels. The height, weight, waist, and hip circumference were measured in addition to blood pressure. Self-reported information was obtained from two questionnaires and included questions on medical as well as social issues, diet, drinking, smoking, tooth extractions and oral infections, sickness in the family, memory, mental health, muscular or skeletal pain, family and friends, physical activity, slimming, education, physical functioning and feeling of safety, use of health services, pattern of habitation, medication, and satisfaction with life in general. Men with tooth extractions were recorded as those ever having had teeth extracted. This was further subgrouped into periodontal disease (marginal periodontitis), apical infection of a single tooth, trauma, and other causes. Other causes include mainly extractions attributed to orthodontic treatment, but could be treatment for cancer, supernumary teeth, and other rare conditions.

The IgG antibody analyses to four oral bacteria in serum sampled in Oslo II were carried out at the Norwegian Institute of Public Health. Serum was stored frozen and later analyzed for antibodies to the periodontopathogenic bacteria *Porphyromonas gingivalis* (PG), *Aggregatibacter actinomycetemcomitans* (AA), *Tannerella forsythia* (TF), and *Treponema denticola* (TD) by the ELISA method (9). C-reactive protein (CRP) was measured at Ullevål University Hospital, Oslo. CRP analyses were carried out using the Tina-quant CRP (latex) high-sensitivity assay from Roche (Basel, Switzerland) adapted to the Hitachi 917 autoanalyzer.

The extractions were categorized into four groups: no history of extractions, noninfection, infections, and both. Analyses showed no significant differences in logistic analysis between noninfection extractions and no extractions. These groups were combined to improve power. Likewise, the infection and combined infection and noninfection extraction groups were combined. The statistical analyses included descriptive statistics and logistic regression. A multivariate analysis adjusted for known major risk factors for MI is presented. The study was performed in accordance with the Helsinki Declaration, and all participants gave their informed consent. The analyses were performed using SPSS version 16.0 (10).

Results

A major observation in 2000 was that a higher proportion of men with a history of MI had ever had teeth extracted than the age-matched controls (92.7% versus 88.6%, P = 0.020 (Table 1). There was a significant difference in distribution of reasons for extractions between cases and controls ($P < 0.001$) (Table 1). Analyses of the known risk factors in 2000 such as daily smoker, total cholesterol, systolic blood pressure, and BMI confirmed significant differences between cases and controls. However, a higher number of cases than controls took antihypertensive medication (59.5% versus 28.4%) and cholesterol-lowering drugs/statins (63.8% versus 12.7%). The large differential use of cholesterol medications between cases and controls is a likely explanation for the low total cholesterol recorded for the cases. The same pattern was observed for daily smokers, where it is likely that smokers quit smoking post-MI. The differences between cases and controls were evident in the 1972/73 baseline measurements (11). Significant changes could be observed in 2000 and in particular for daily smokers. Systolic blood pressure and BMI had increased, but total cholesterol was reduced with the coincidental high level of cholesterol-lowering drugs among cases in particular. More controls than cases reported current periodontal infection (8.4% versus 4.6%). Antibody levels to the four known periodontal pathogens (*A. actinomycetemcomitans*, *T. forsythia*, *T. denticola*, and *P. gingivalis*) did not differ significantly

Table 1. Baseline characteristics of cases of myocardial infarction and age-matched controls at the screening of the Oslo study in 1972/73 and the Oslo II-study in 2000[a]

Risk factors	Cases n = 548	Controls n = 625	P-value
Screening data 1972/73			
Age	28.5	29.9	<0.000
Age category in 2000			
48–57	53.6 ± 1.1	54.3 ± 2.3	0.463
58–67	64.5 ± 2.8	63.1 ± 2.7	0.391
68–77	72.0 ± 2.8	72.0 ± 2.7	0.858
Systolic blood pressure (mm Hg)	136.8 ± 16.6	131.6 ± 13.4	<0.001
Body mass index (kg/cm^2)	24.9 ± 2.8	24.3 ± 2.5	<0.001
Total serum cholesterol (mmol/l)	7.1 ± 1.4	6.5 ± 1.1	<0.001
Daily smokers (% yes)	52.0	39.7	<0.001
Antihypertensive medication (% yes)	3.1	1.6	0.117
Screening data 2000			
Systolic blood pressure (mm Hg)	141.3 ± 21.5	144.3 ± 19.2	0.012
Body mass index (kg/cm^2)	27.1 ± 3.5	26.3 ± 3.3	<0.001
Total serum cholesterol (mmol/l)	5.3 ± 1.1	6.0 ± 1.0	<0.001
Daily smokers (% yes, missing = 6)	15.8	19.6	0.001
Cholesterol reducing drugs (% yes)	60.6%	12.3%	<0.001
Antihypertensive medication (% yes, missing = 34)	59.5%	28.4%	<0.001
Tooth extraction history			
Ever extracted teeth, n (% yes)[b]	492 (92.7%)	536 (88.6%)	0.020
Number of men no extractions or providing a reason for extraction[c]: (missing = 105)			
No extractions, n (%)	32 (6.3)	60 (10.7)	
Extractions; noninfection (because of trauma or other cause), n (%)	110 (21.8)	167 (29.7)	
Extractions; infections (periodontal disease, apical infection), n (%)	272 (53.9)	257 (48.6)	
Extractions due to both infection and noninfection, n (%)	19 (18.0)	79 (14.1)	
Sum extractions	433 (100%)	563 (100%)	<0.001
Current oral infection			
Periodontal infection (periodontitis)	24 (4.6)	50 (8.4)	0.011
Pain in single teeth, n (%)	27 (5.3)	31 (5.3)	ns
Other nondental infection or disease, n (%)	18 (3.6)	10 (1.8)	ns
Antibody (IgG) levels[d]			
Aggregatibacter actinomycetemcomitans	72.06 ± 98.13	92.56 ± 92.79	0.216
Tannerella forsythia	76.87 ± 69.93	91.71 ± 121.88	0.315
Treponema denticola	54.34 ± 40.91	81.68 ± 152.63	0.304
Porphyromonas gingivalis	279.51 ± 797.56	146.50 ± 200.57	0.211
Hs-CRP (mg/l)	3.30 ± 4.04	5.39 ± 17.15	0.000

[a]Plus minus values are mean ± SD; chi-square test for categorical variables and Student's t-test for independent samples for continuous variables, ns denotes nonsignificance.
[b]Computations for each row exclude several men with missing data, for example, 17 cases and 20 controls did not respond to the question about tooth extraction and are not included in the row 'ever extracted teeth'.
[c]Pearson chi-square.
[d]Mean (SD) of optical density (OD)-reading (significance test of log-transformed data), ELISA analyses.

between the cases and controls consistent with large standard deviations. CRP was higher in cases than in controls.

A prospective logistic regression analysis was performed to assess the association between reason for extraction and MI in crude and adjusted analysis adjusting for known risk factors for MI using 1972/73 data and 2000 data on education (Table 2). Extractions attributed to infections were significant predictors in the prospective analysis using risk factors of 1972/73: crude analysis; OR = 1.73; 95% CI: 1.34, 2.23, adjusted analysis; OR = 1.64; 95% CI: 1.24, 2.16. A sensitivity analysis adjusting for 2000 covariates gave the same risk pattern but slightly higher risk estimates (results not shown).

Table 2. Multivariable logistic regression analysis of risk for incident myocardial infarction by dental extraction status at the screening in 1972/73 of the Oslo study

	Prospective cohort analysis Total = 1028, missing 145			Crude analysis Total = 1068, missing 105		
Extraction status	OR	95% CI	*P*-value	OR	95% CI	*P*-value
None and noninfection reference category	1.00	–	–	1.00	–	–
Infection and combined infection and noninfection	1.64	1.24–2.16	0.001	1.73	1.34–2.23	<0.001

OR, odds ratio; CI, confidence interval.
Adjusted in 1972/73 analysis for daily smoker, systolic blood pressure, total cholesterol, body mass index, and years of education (recorded in 2000).

The stratified effect modification analysis of daily smokers versus nonsmokers per 1972/73 on the categories of reason for extraction was carried out to study the effect of smoking as a confounder for periodontal infection and MI (Table 3) (12). Infection extraction was a significant predictor in both smoking categories although the OR was higher among daily smokers (daily smokers: OR = 1.86; 95% CI: 1.22, 2.82; nondaily smokers: OR = 1.50; 95% CI: 1.03, 2.18). The interaction term was nonsignificant ($P = 0.803$).

Discussion

The study showed a significant association between a history of MI and a history of extractions because of infections, while there was no apparent association between a history of MI and tooth extractions because of trauma or other causes. This result remained significant after adjusting for known risk factors for MI and upper quartile level of antibodies to periodontal pathogens. These observations support the research that indicates an association between oral infections and MI (6). The observation of a difference in strength of association between infection and noninfection extractions and MI in our study indicates that the underlying infection is the factor of importance and not extractions per se. The comparative analyses of a prospective analysis with adjustment of 1972/73 baseline data and the cross-sectional analysis of the case–control study gave the same risk pattern by extraction history yielding only somewhat lower risk estimates.

In elderly men, it is expected that there is a certain baseline level of antibodies to bacteria in their blood because of prior or current infections. Antibodies to the four common periodontal pathogens studied were present in all individuals (9). Other studies examined the bacterial products and their proatherogenic potential (13–15). These studies sought to explain how chronic infections in particular may be involved in atherosclerosis and may increase the risk of cardiovascular diseases. Tooth extraction increases the risk of a bacteriaemia that activates the immune system.

A limitation of this study is that it included men only. We do not know whether the periodontal disease or the MI came first, although even knowing the timing of the clinical dental and coronary events would not completely sort out temporality, since both conditions develop over years. Furthermore, as individuals have teeth extracted for different causes through life, a certain degree of misclassification of this risk factor cannot be ignored. The disease history of MI and extractions was self-reported, but

Table 3. Analyses for effect modification of smoking status in 1972/73 with extraction status on cases during follow-up on prediction of incident myocardial infarction in the Oslo study

	Daily smoker $n = 463$, missing = 70			Nondaily smoker $n = 565$, missing = 75		
Extraction status	OR	95% CI	*P*-value	OR	95% CI	*P*-value
None and noninfection; reference category	1.00	–	–	1.00	–	–
Infection and combined infection and noninfection	1.86	1.22, 2.82	0.004	1.50	1.03, 2.18	0.033

OR, odds ratio; CI, confidence interval.
Interaction analysis: extraction by daily smoker: *P*-value = 0.803 (missing = 105).
Adjusted in 1972/73 analysis for body mass index, systolic blood pressure, total cholesterol, and years of education (recorded in 2000).

both tooth extraction and MI were significant events for the person involved, and the patients will probably remember them although they are different in nature. The event rate of MI is higher in elderly than in younger persons giving sufficient power in this study to identify significant relations between cause and event. It is feasible that we are observing a combination of a common underlying trait of MI and oral infections. Chronic marginal periodontitis (6) and pulpal inflammation have been found to be associated with coronary heart disease (16). However, increased risk of oral infections post-MI is not likely to increase to such a large extent indicating a situation of reverse causality. Conditions like diabetes and obesity/metabolic syndrome, which are known to have high levels of inflammatory markers, are also associated with increased risk of MI. Oral health status shares common risk factors for MI as both are known to be linked to a person's socioeconomic status. Another common predictor is smoking known to increase the severity of marginal periodontitis. Adjustment for age, daily smokers, systolic blood pressure, BMI, years of education, common risk factors for MI confirmed the finding of difference between infection and noninfection extractions. This association is slightly modified by the reported higher prevalence of current periodontal infections among controls.

In conclusion, the results indicate a relationship between oral health and heart disease. The increased association between MI and causes of tooth extractions because of infections supports the theory of oral infection being associated with MI. The study indicates that maintaining good oral health may be a necessary element in the prevention of MI.

Acknowledgements

Lars Lundby, Norwegian Institute of Public Health (NIPH), is thanked for his great contribution in analyzing the serum samples and Hans Jørgen Dahlmann, NIPH, for his technical advice on these analyses.

Conflict of interest and source of funding

The authors declare that they have no conflict of interest. The study was supported financially by funding from Research Health & Rehabilitation through the applicant organization National Organization for Heart and Lung Disease in Norway. The National Organization for Heart and Lung Disease is also thanked for additional financial support from their research fund.

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