Original Research Article

Correlation between Pulpal Inflammation (Using RCT as a Surrogate) and Coronary Heart Disease (CHD) Cases

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ABSTRACT

Background: Coronary artery disease (CAD) has been recorded as the leading cause of morbidity and mortality worldwide. Primarily caused by coronary caries, pulpal inflammation contributes to root canal therapy (RCT). Chronic inflammation has been related to a variety of cardiovascular diseases. This research assesses the correlation between pulpal inflammation (using RCT as a surrogate) and coronary heart disease (CHD) cases.

Material and method: The present follow up study was conducted in the department of dentistry. The study population comprised of Health Professionals' (HP's). Of the 12,289 participants who replied to the questionnaire, we had 11,158 participants who answered questions from the RCT and from caries. We recorded 382 CHD cases among eligible men who were CVD-free at baseline in 2001, when the research started. The relation between RCT and the resulting CHD accident was measured.

Results: When we evaluated RCT as a risk factor for subsequent CHD, the association was not significant in the analysis adjusting for age, smoking, and family history of MI (RR=1.41), and remained insignificant in the multivariate analyses too (RR=1.34). The association between RCT and incident CHD was limited to dentists.

Conclusion: Dental caries was not associated with CHD. The results suggest a possible modest association between pulpal inflammation and CHD.

INTRODUCTION

Coronary artery disease (CAD) is a leading cause of morbidity and mortality globally[1]. Studies showed a link between CAD and oral infections as early as the 1980s and this subject has recently generated renewed interest within the field in cardiac and dental science[2]. Several scholars have suggested a causal relationship, while others have been more wary[3,4]. Ylöstalo and colleagues[5] have documented linkages between a range of dental conditions (self-reported gingivitis, dental caries, and tooth loss) and angina pectoris. However, they suggested the associations could have been caused by confounding factors.

Antecedent dental caries and endodontic inflammation may theoretically also lead to the connections. While some studies have found correlations between a cumulative oral health factor (including dental caries, periapical lesions, missing teeth, and periodontal disease) and cardiovascular disease, very few studies have independently examined advanced dental caries or pulpal/root canal therapy (RCT)[6].

Inflammation of the pulpal is mainly caused by coronal caries. Pulpitis refers to a periapical inflammatory response which

may result in a systemic inflammatory response which may increase the risk of CHD. RCT attempts to biomechanically or with intracanal antimicrobial agents to eradicate the microorganisms within the root canal.RCT is an elective procedure for teeth with an acute non-reversible pulpitis (pulpal inflammation) to prolong the teeth's life; extraction is the alternative treatment. We assume that RCT is mostly a direct result of pulpal inflammation, and therefore an appropriate surrogate measure[7].

In this study, we assess the correlation of dental caries and pulpal inflammation using RCT as a predictor within a large cohort sample of health professionals with incident CHD. We wanted to test the hypothesis that pulpal inflammation would result in increased CHD risk.

MATERIAL AND METHOD

The present follow up study was conducted in the department of dentistry. Ethical permission was taken from the institute and written informed consent from the study participants. The study population comprised of Health Professionals' (HP's). Health Professionals' includes dentists, veterinarians, pharmacists, optometrists, osteopaths, and podiatrists having age of 40 to 75 year old. The research omitted HPs that refused to provide the informed consent. Of the 12,289 participants who replied to the questionnaire, we had 11,158 participants who answered questions from the RCT and from caries. Before the follow-up, we omitted participants who recorded myocardial infarction, stroke, re-vascularization procedures or diabetes and participants who did not provide RCT details on time periods from the analyses. Our overall survey contained 11,158 participants in the research.

Data was collected through the creation of a questionnaire (either by face-to-face consultation or by mailing the questionnaire) comprising of information on medical history, fitness habits and cardiovascular incidence & other outcomes.

Questions concerning RCT and dental caries were also applied to the questionnaires that were sent to the entire HP group. The specific questions asked were:

1. How many of your permanent teeth ever had root canal therapy? Responses were: 0, 1, 2-4, 5-9, and 10+

2. Questions were also asked replacing root canal therapy with a cavity.

Participants filled questionnaire every 2 years. The exposure predictor for RCT was time-dependent, and over time people would adjust their RCT status. For example, to estimate the risk of developing CHD in 2011 through 2014, someone who had no RCT between 2001 and 2010 would have been allocated to the unexposed category. In 2011-2014, he would have been allocated to the exposed category to estimate the likelihood of CHD in 2015-2019 if he had RCT in 2011-2014.For the primary study, between 2001 and 2014 we classified RCT as none, or one or more root canals. Because most people have 10 or more carious lesions we classified caries with caries past as 10 + or < 10 teeth. Also participants who reported at least one post 2001 carious lesion were considered positive for caries.

The primary endpoint for this analysis was event CHD comprising reported non-fatal myocardial infarction with related etiologies. They tracked 11,158 eligible men and measured CHD occurrence from 2000 through 2019. For all participants who recorded accident CHD we checked the medical records. Physicians who were ignorant of the participants ' backgrounds were checked Myocardial infarction was verified using guidelines from the World Health Organization: signs with any physiological shifts in the electrocardiography or elevated cardiac enzymes[8]. Infarctions that involved hospital admission, and for which confirmatory information was obtained by interview or letter but for which no medical records were available, were classified as probable. Our case description omitted the percentage of self-reported cardiovascular events that

were eventually not verified by medical records or experience.

Statistical analysis: Data so collected was tabulated in an excel sheet, under the guidance of statistician. Data was analyzed using IBM SPSS. Statistics Windows, Version 22.0. (Armonk, NY: IBMCorp) for the generation of descriptive and inferential statistics. We recorded 382 CHD cases among eligible men who were CVD-free at baseline in 2001, when the research started. The relation between RCT and the resulting CHD accident was measured. To determine the duration of activation, we have performed analyzes restricted to current or remote RCTs. For the study we used Cox proportional hazard models to measure relative risks (RR, incident rate ratios) and confidence intervals of 95 percent. Caries is measured as a quantitative metric that compared those with 10 or more teeth with caries past to less than 10 carious teeth. We also evaluated a composite measure combining people with one or more RCT or 10 or more carious teeth compared to those with no RCT and less than 10 carious teeth.

Analysis restricted to confirmed cases produced similar results to analyze covering verified and suspected cases, albeit with less precision. Analyzes were controlled for age, smoking, alcohol, myocardial infarction family history (MI), body mass index, physical activity, use of multivitamin supplements, use of vitamin E, use of aspirin, recorded hypertension and hypercholesterolemia. For each follow-up cycle, such variables have been revised. We monitored the average number of teeth and event tooth loss in addition to external analyzes. During follow-up, we carried out subgroup analyzes by age group, smoking status, baseline number of teeth and incidental loss of the tooth. We have separately assessed the relationship among dentists and non-dentists.

RESULTS

Table 1 shows the characteristics of the study population. Men with RCT have slightly less favorable CVD risk profiles and they are older. Only 9.16% of the subjects were current smokers.

Table 2 shows the relation between RCT, caries, and CHD. When we evaluated RCT as a risk factor for subsequent CHD, the association was not significant in the analysis adjusting for age, smoking, and family history of MI (RR=1.41), and remained insignificant in the multivariate analyses (RR=1.34). The association became slightly stronger when we excluded men with only one RCT, hence, comparing men with two or more RCT to men with 0 RCT (multivariate RR=1.39). The combination of one or more RCT or 10 or more carious teeth compared to 0 RCT and less than 10 carious teeth also did not show any association (RR=1.27).

Table 3 shows the association among different subgroups for one or more RCT. The association between RCT and incident CHD was limited to dentists. Among dentists there was a significant association between baseline RCT and incidence of CHD in the analysis adjusted for age, smoking, and family history for MI, (RR=1.46).

Table 1: Characteristics of the study population

Characteristics	N=382
Age (year), Mean±SD	48.19±8.13
Current smokers, N (%)	35 (9.16%)
Family History of Myocardial Infarction, N (%)	22 (5.76%)
Body Mass Index (Kg/m^2)	24.13±4.18
Hypertension, N (%)	56 (14.17%)
High Cholesterol, N (%)	38 (9.95%)
Supplement Use (Multivitamin), N (%)	87 (22.78%)
Sugar Intake (teaspoon/day), Mean±SD	1.40±2.34

Table 2: Association between RCT and dental caries with incidence of CHD

Number of RCT or Carious Teeth	CHD Cases	Relative Risk (95% CI)	
		Adjusted for Age, Smoking, Family History of MI	Multivariate[a]
0 vs ≥1 RCT	382	1.41 (1.04-1.67)	1.34 (1.06-1.64)
0 vs ≥2 RCT	337	1.48 (1.08-1.76)	1.39 (1.05-1.73)
≥10 vs <10 Caries	138	1.13 (0.91-1.40)	1.19 (0.93-1.45)
≥1 RCT or ≥10 Caries	132	1.18 (0.93-1.45)	1.27 (0.95-1.48)

a: Models adjusted for age (5-yr categories); smoking (never, former, current: 1-14, 15-24, >25 cigarettes/day); alcohol (7 categories); family history of myocardial infarction (MI, before age 60); body mass index (quintiles); physical activity (quintiles); multivitamin supplement use; vitamin E use; aspirin use; reported hypertension and hypercholesterolemia.

Table 3: Sub-group analysis of the association between one or more root canal treated teeth and CHD

Variables	Multivariate Relative Risk[a] (95% CI)		
	Overall	Dentists	Non-dentists
Overall	1.35 (1.04-1.68)	1.46 (1.09-1.63)	1.25 (1.05-1.55)
≤24 Teeth	1.22 (1.01-1.62)	1.49 (1.05-1.81)	1.01 (0.88-1.61)
>24 Teeth	1.49 (1.08-1.70)	1.41 (1.11-1.74)	1.11 (0.94-1.49)
Age≤50	1.32 (0.96-1.91)	1.44 (1.15-1.79)	1.20 (0.86-1.79)
Age >50	1.48 (1.04-1.99)	1.58 (1.07-2.14)	1.47 (1.08-1.92)
Current smokers	1.39 (0.94-1.96)	1.51 (1.16-2.53)	1.27 (0.97-1.61)

a: Models adjusted for age (5-yr categories); current smoking (25≥cigarettes/d); alcohol (7 categories); family history of myocardial infarction (before age 60); body mass index (quintiles); physical activity (quintiles); multivitamin supplement use; reported hypertension and hypercholesterolemia.

DISCUSSION

The present study found a significant association between history of RCT and incidence of CHD. Cardio-vascular diseases and infections of endodontic origin share similar inflammatory mediators in the initiation and progression of the process[9,10]. Berlin-Broneretal[11]&Khalighinejad et al[12] suggest an association between cardio-vascular diseases and existing periapical lesions.

The association was further restricted to the dentists. For the greater correlation between dentists, one explanation is that RCT may be a more valid measure of pulpal and periapal inflammation among dentists than among nondentists. That is, certain root canals are done on teeth that have no pulpitis, e.g. therapeutic endodontics in specific instances of prosthodontics prior to crown installation. The RCT would not be a sign of pulpal or periapical inflammation when the RCT is performed for the preparation of crowns. When there has been no pulpal irritation, dentists may be less inclined to expose themselves to the root canal treatment. For the nondentist participants in this analysis, our a priori conclusion that an RCT is directly related to pulpal inflammation may less often be the case. Consequently, the interaction between RCT and pulpal inflammation and, thus, between RCT and CHD event may be greater among dentists than among nondentists in this study population, resulting in a stronger correlation with CHD occurrence.

Consistent with some previous studies[6,13], we did not find an association between dental caries and incident CHD in multivariate analyses. Number of carious teeth was not associated with CHD. Possible reasons could be that there is no biologic relationship. The fact that the association was present among the dentists, rather than the nondentists, increases the biological plausibility as discussed above. The dose response for number of RCT, the persistence of the association with in all subgroups among the dentists, and the lack of association with caries also makes the association between RCT and incidence of CHD among dentists, less likely to be a result of chance. Previous study[14] showed associations between RCT and/or periapical lesions and CVD, but the associations were not significant in multivariate analyses. These studies had lower power and only the composite measures were significant in multivariate analyses, hence, it is hard to know whether there was a real association between RCT and CHD. Kyosti Oikarinen et al[15] also revealed a significant association between radiographically diagnosed periodontal diseases and CAD. Pratyaksha S. Panwar et al[3] in 2019 reported that coronary artery disease participants have a high chance of being affected with pulp stones.

It is possible that CHD could influence whether a person undergoes RCT. However, our study design is prospective and excludes participants with pre-existing CHD. Hence, the association observed is not because of CHD affecting the likelihood of RCT.

The limitation of the present study was that our measure of pulpal inflammation is based on self-reported RCT obtained from questionnaires. RCT could have been performed in response to a chronic or acute pulpal inflammation (which

cannot be differentiated in our RCT measure). Also we could not distinguish between acute and chronic inflammation. The strength of present study is its sample size and follow up of patients.

CONCLUSION

It can be concluded from the results of the present study that RCT was associated with a small increased risk of incident CHD among men. The collaboration was restricted to dentists where pulpal inflammation is more likely to be demonstrated by the RCT than by nondental health professionals. More research is needed to corroborate the relationship in other communities between pulpal inflammation and CHD, to determine whether the correlation is causal, and to examine mechanisms for this interaction.

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