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**Relationship between past myocardial infarction, periodontal disease
and *Porphyromonas gingivalis* serum antibodies: A case-control study**

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Introduction

When was the work published?

The research article “Relationship between past myocardial infarction, periodontal disease and *Porphyromonas gingivalis* serum antibodies: A case-control study” was published in the Cardiology Journal in 2016.

Does the work meet the standards to be considered an appropriate/academic/scholarly source? Justify your choice.

This work meets the standards to be considered an appropriate academic scholarly source because it was published in the Cardiology Journal, which is one of the well known, academic journals in the US, representing the most current source of information like all academic journals. In addition, this publication is peer reviewed and it was supported by the Faculty of Medicine, Jagiellonian University Medical College, Leading National Research Center (KNOW) 2012-2017, making the source reliable.

Are the qualifications of the author(s) appropriate for an academic article? Briefly describe the authors' qualifications

Qualifications of the authors are appropriate for an academic article. The authors of this research article are Radoslav P. Lysek, with 7 publications, K. Szafraniec at the Department of Epidemiology and Population Studies, Institute of Public Health, Jagiellonian University

Medical College, Krakow, Poland., K. Szafraniec with 58 research works with 527 citations and 4038 reads, Piotr Jankowski from the 1st Department of Cardiology, Electrophysiology and Hypertension, Jagiellonian University Medical College, Krakow, Poland with 100 publications with 1179 reads. Et.al.

What is the author's central purpose? Is it clearly stated?

In this research article, the authors' central purpose is clearly stated. According to the article, the relationship between chronic periodontitis (CP) and increased risk for cardiovascular disease (CVD) is known but quantitative assessments and mechanisms are not fully understood and further research is needed. The purpose of this study was specifically to assess the relationship between past myocardial infarction (MI), the severity of CP, and the level of serum antibody titer against the bacteria *Porphyromonas gingivalis*.

Write a 150- 200 word summary of the article that accurately conveys the content of the article.

Based on this article, even after controlling for possible confounders (unidentified factors that could influence the results), CP has been postulated to be a CVD risk factor, which is independent of well-known risk factors, such as smoking, hypertension, obesity, diabetes and hypercholesterolemia (1,2). CP is an inflammatory disease of tooth-supporting tissues and it is very common among the middle-aged and the elderly in the general population (3). CP is

induced by a pathogenic and etiologic bacteria called *Porphyromonas gingivalis* which causes gingipains (GP's) — virulence factors with multi-directional adverse impacts on the immune system. This information has led scientists to hypotheses on two mechanisms relating CP to coronary heart disease (CHD). The first is the general inflammatory host response in CP, supported by the findings that suggest elevated inflammatory markers (C-reactive protein) in CP patients decrease after successful treatment of periodontitis and that *P. gingivalis* may increase overall inflammatory response through its virulence factor, especially GPs. The second mechanism they postulated involves direct invasion of arteries and endothelial cells by periodontal pathogens, especially *P.gingivalis*. This is supported by the findings on the association between endothelial dysfunction (which plays a key role in the development of arteriosclerotic plaques) and CP. Furthermore, antibodies against *P. gingivalis* have been found in human arteriosclerotic plaques, and other findings have suggested that defects in endothelial cells and arteriosclerotic plaques caused by CP may be a background for myocardial infarction (MI). This case-control study approached the association between past MI and the clinical parameters of CP in the context of the level of serum antibody titer against *P. gingivalis* gingipains (4, 5, 6, 7).

Methods

Is the experimental design clearly described? Describe the design in your own words.

The experimental design is clearly described. In this research, a frequency-matched case-control study was performed, which is considered as a non-experimental retrospective investigation. The goal of this research was to identify factors which are associated with past myocardial infarction that are related to the periodontium health status. The study sample consisted of 97 patients after MI and 113 high-risk controls with no history of coronary heart disease (CHD). These groups were matched with age, sex, and place of residence (urban vs. rural). Data on the history of CHD and the presence of risk factors were collected. Periodontal status was determined by using the Community Periodontal index (CPI), clinical attachment loss (CAL), bleeding on probing (BOP) and pocket depth. Information (data) was converted with a quantitative method and the use of numerical tables. Immunoglobulin G antibody titers against *P. gingivalis* GPs were determined using the enzyme-linked immunosorbent assay (ELISA), in all samples using the method described by Zdzalik et al. Antibody titers are given in ELISA units. Moreover, The perfect reliability between cases and controls (1:1 matching) was also performed. The frequency-matched case-control analysis included 92 pairs of observations, but five cases were excluded due to lack of appropriately matched controls within the gender. Furthermore, results are presented as odds ratios (OR) with 95% confidence intervals. An analysis was performed using SPSS Software (IBM, Armonk, NY, USA). Statistical significance was accepted at the level of $\alpha=0.05$. In this research, all participants were informed about the study

protocol and gave their informed consent. The study was approved by the Bioethics Committee of the Jagiellonian University.

Is the investigation of sufficient duration? Evaluate, and explain your reasoning.

Unfortunately, in this article, the duration of the study is not clearly stated. However, it is more likely to be cross-sectional because samples of the population were assessed at one time.

Have the possible influences on the findings been identified and controls instituted?

Describe and evaluate the use of controls and possible influences.

A possible influence on the findings might be that of the 113 controls, 91 (80.5%) were comprised of men and 22 (19.5%) women, i.e 5 women less than in previous MI group. Those 5 women were excluded because they had less than 6 teeth. Another factor that could be influential is that even though dental clinical examination was carried out according to World Health Organization recommendations and participants were examined by one qualified dentist, INTRA-examiner reliability could be difficult to achieve. Therefore, the ability of an examiner to rate the probing depth in the same way over time is questionable. The accuracy of the results regarding the relation between BOP and past MI could have also been lowered because BOP could have been caused by antiplatelet agents that almost all participants were taking. Moreover, in both groups, the exclusion criteria were: use of antibiotics during the 2 weeks prior to the examination, and immunosuppressive therapy or chemotherapy. Participants were considered smokers if they declared they had smoked at least one cigarette during one month

prior to the interview or had >10 ppm carbon monoxide in their exhaled air. Hypertension was defined as blood pressure >140/90 mmHg etc. These criteria might be also possible influence factors.

Has the sample been appropriately selected (if applicable)? Describe the sample used in the study, and evaluate its appropriateness.

In this study, the sample has been appropriately selected. The size of the sample was large enough to accommodate the expected loss of subjects and to demonstrate differences between groups by statistical logic. Participants after MI were recruited from five cardiology departments, serving the city of Krakow and the surrounding rural area. Patients aged >18 years and <80 years, with a definite clinical diagnosis of MI, were identified from medical records. Controls were persons with no diagnosis of MI or CHD. They were selected randomly from three general practices: two in city Krakow and one outside of Krakow. Inclusion criteria were: high CVD risk identified by attempted treatment for hypertension, hypercholesterolemia or diabetes mellitus. Information on treatment was collected from medical records using a standardized data collection form. Then, controls were matched according to their age (5-year groups), sex and place of residence (rural vs. urban) and were asked to undergo dental examination.

Is the experimental therapy compared appropriately to the control therapy? Describe and evaluate the use of the control group.

In this study, cases and controls were highly comparable with 1:1 reliability. Patients after MI were selected from 5 clinical cardiology wards serving a defined geographical area. The controls were sex, age, and the place of residence. There was a random sampling of healthy persons registered in selected primary practices serving the same residential area, and restricting the control group to persons at high risk limited confounding by CVD risk factors, which was controlled further by adjustment for these in multivariate analyses.

Results and Discussion

Have the research questions or hypothesis been answered? Restate the research questions and/or hypotheses in your own words, and describe if or how they are answered.

In this study, the hypothesis that there is a relation between chronic periodontal disease and past MI independent of classical CVD risk factors was confirmed. This hypothesis was corroborated by the association between past MI and immunological reactions against *P. gingivalis* gingipains.

Results showed that generally, patients after MI were slightly less educated than controls, had a lower mean number of teeth, and were more frequently affected by periodontal disease than controls. Moreover, experimental cases had more periodontal pockets of 6 mm or more than the control group and were more likely to have a higher percentage of BOP, more calculus deposits, or more dental plaque. The statistical analysis showed that after “adjustment for age, sex, years of education, smoking, hypertension, hypercholesterolemia, body mass index, diabetes mellitus, and the number of teeth, those patients with BOP 20–50% and BOP \geq 50% had a more

than 4 times higher odds of past MI.” Patients with CPI 4 code had 3 times higher odds of past MI and those with CAL \geq 6 mm had a 1.28 odds of past MI. Also, analysis confirmed that patients with moderate antibody titer levels had almost 3 times higher odds of past MI.

Review the results in light of the stated objectives. Does the study reveal what the researcher intended?

Because of the several findings and successes of the study, the researchers were able to find the majority of what was intended. Firstly, the use of antibody titer was a less problematic and criticized decision, while also being a better marker of immunological response for periodontal bacteria. Secondly, the study made it possible for the cases and controls to be more comparable because the restriction of the control group to persons at high risk allowed the researchers to limit confounding by CVD risk factors. However, there were some setbacks to the goals that the researchers intended to achieve. For example, the case-control design did not give them firm conclusions on causality, and the study sample had limited statistical power despite its success in indicating a strong association. Also, the relation between BOP and MI was flawed. Since nearly all MI participants were taking antiplatelet agents and they could not adjust for this effect, it made another factor possibly responsible for the results in the study, therefore not allowing solely one explanation. Another factor that may have interrupted the accuracy of the results was that some patients after MI could have just not paid attention on their oral health, developing more severe CP. In addition, although antibody levels for periodontopathic bacteria are considered to be stable over time, it remained unclear whether antibody level is an indicator

of disease history or active infection. Another limitation of the study was that it assessed only antibodies for one periodontopathogenic bacteria. It is possible that if the presence of antibodies against other periodontitis-associated bacterial species were included in the analysis the relationships could have been stronger and could reveal more about what the researchers intended.

Do you agree or disagree with the article and findings? Explain why?

In my opinion, the study showed sufficient evidence that there is a possibility of an association between periodontopathogenic bacteria and cardiovascular disease. Based on the article, there was another study that confirmed findings in which males aged 45 to 75 years who were seropositive for *P. gingivalis* had more frequent CHD than those who were seronegative for *P. Gingivalis* (8). However, some cross-sectional studies have shown no association between antibodies against *P. gingivalis* and CHD, after adjustment for classic CVD risk factors (9,10). Therefore, more studies are needed for this to be proven and clinically applied in the future.

What would you change in the article? Why? Think outside of the box. What would you add or delete?

Case-control studies are usually not sufficient for proving casualties, and neither was this study. To make the research results more accurate and effective, I would perform a longitudinal study. This would involve the same samples of individuals who are assessed at several different time points, ultimately providing better information on the growth or change in each individual.

References

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