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The Association Between Dental Status and Risk of Acute Myocardial Infarction Among Poles: Case-control Study

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A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article; E – critical revision of the article; F – final approval of article

Abstract

Background. Results of scientific research on the effects of periodontitis on the incidence of myocardial infarction (MI) are ambiguous.

Objectives. The aim of this study was to investigate the association of the severity and extent of periodontitis with acute MI in Poles.

Material and Methods. This case-control study included 134 cases hospitalized with acute MI under the age of 70 years and 155 controls drawn from the general population with no MI history. Sociodemographic, cardiologic and periodontal variables were assessed. Three periodontal indicators were evaluated: (1) the severity of periodontitis classified in accordance with Page and Eke definition, (2) the extent of periodontitis determined on the basis of the percentage of sites with CAL $\geq$ 3 mm (Arbes Index) and (3) tooth loss ($>$ 10 teeth). In a logistic regression model, the association of periodontal parameters with MI occurrence was evaluated after adjusting for well-known cardiovascular risk factors.

Results. The extent of periodontitis was significantly associated with the risk of acute MI even after adjusting for age, sex, tobacco smoking, hypertension, diabetes, BMI, education and income (odds ratio [OR] = 2.4; 95% confidence interval [CI] = 1.1 to 5.2; p = 0.0203). However, the severity of periodontitis was associated with MI after adjusting for age and sex (OR = 2.0; 95% CI = 1.2–3.5; p = 0.0109), but not after adjusting for the other above-mentioned risk factors. The association between the number of lost teeth and acute MI was significant after adjusting for age, sex, tobacco smoking, arterial hypertension and diabetes mellitus (OR = 2.1; 95% CI = 1.2–5.9; p = 0.0151).

Conclusions. This study proves the positive association between periodontitis and acute MI in Poles. This association seems to be stronger with regard to the extent rather than to the severity of periodontitis (Adv Clin Exp Med 2016, 25, 5, 861–870).

Key words: periodontitis, acute myocardial infarction, risk factor.

Cardiovascular diseases (CVD) constitute the most frequent cause of death worldwide. According to the National Institute of Public Health, in Poland in 2010, 456 individuals per 100,000 died of CVD, which accounted for 46.0% of all deaths [1]. MI was the cause of 17,800 deaths, which represented 10.0% of deaths from cardiovascular causes. Etiopathogenesis of CVD as social diseases is multifactorial, but the coexistence of traditional CVD risk factors does not fully explain the overall cardiovascular risk in all patients. Due to the fatal

consequences of CVD, all attempts to identify other modifiable risk factors are extremely important, as they would contribute to more effective prevention of CVD.

The amount of evidence confirming the role of chronic inflammatory processes in initiation and progression of CVD continues to increase [2]. However, it is not conclusively clarified whether local inflammation in the periodontium is sufficient to trigger a systemic inflammatory cascade and initiate atherosclerosis [3]. In view of conflict-

ing results of studies, two meta-analyses on the association between periodontitis and CVD were conducted [4, 5]. Both demonstrated that periodontitis independently increases the risk of coronary heart disease (CHD). Most recently, a comprehensive review performed by the American Heart Association (AHA) working group, as well as a report by the Joint Workshop of European Federation of Periodontology and the American Academy of Periodontology (EFP/AAP) highlighted that periodontitis is associated with CVD independently of known confounders, but there is no evidence for a causal link [3, 6]. What is more, the Fifth Joint Task Force of the European Society of Cardiology (ESC) and Other Societies on Cardiovascular Disease Prevention in Clinical Practice stated that “periodontitis can be considered a risk indicator for a generally decreased cardiovascular health status” [7]. However, all of the statements concluded that more studies are needed to draw further conclusions.

This is of great importance due to the widespread occurrence of periodontal disease in the Polish population. Among Poles periodontitis occurred in 57.2% of those aged 35–44 years and even more frequently among older people in contrast to 37.2% of adults between the age of 35–44 years in the United States [8, 9].

To date, few studies have assessed the association between periodontitis and MI, but the results of conducted research are inconclusive. Some of them demonstrated that periodontitis constitutes an independent MI risk factor [10–17], whereas other studies did not confirm these relationships [18–20]. Therefore, the aim of this study was to answer the question whether the periodontitis severity and extent is an independent and significant risk factor for acute MI in adult Poles under the age of 70 years.

Material and Methods

Study Sample

This study was conducted in the Department of Oral Medicine and Periodontal Diseases, Medical University of Warsaw (MUW) and in the First Clinic and Department of Cardiology, Faculty of Medicine, MUW, in 2011–2013 in accordance with the STROBE guidelines. All participants were Polish Caucasians.

The study group included 134 patients (29 women, 105 men) hospitalized in the First Clinic and Department of Cardiology due to acute MI on the second or third day of hospitalization. The mean age of this group was 54.3 years (± 8.1).

The inclusion criteria were: 1) MI history and 2) age under 70 years. MI (STEMI and NSTEMI) was diagnosed in accordance with the criteria of Guidelines of ESC. The exclusion criteria included: 1) edentulousness; 2) cancer; 3) rheumatic disease; 4) autoimmune disease; 5) chronic liver disease; 6) chronic renal disease stage 4 and 5; 7) stroke history. Recruitment and inclusion of patients in the study group was conducted by a single cardiologist (EN).

The control group consisted of people selected by the Ministry of the Interior and Administration from the general population of adult Poles who reported to Department of Oral Medicine and Periodontal Diseases. These individuals had to meet the following criteria: 1) age under 70 years; 2) present natural teeth; 3) no cancer history; 4) no rheumatic disease history; 5) no autoimmune disease history; 6) no chronic liver disease; 7) no chronic renal disease; 8) no stroke history, and 9) no MI history. The control group included 155 individuals (94 women, 61 men). The average age of this group was 54.9 (± 10.0) years.

Social and medical history of the participants was taken. Physical examinations were performed by a single cardiologist (EN). Similarly, a single dentist (BG) conducted dental and periodontal examinations. The study was carried out taking into account the ethical standards resulting from the Declaration of Helsinki of 1975, as revised in 2000. The research was approved by the Bioethics Committee, MUW (approval number KB-145/2011). All individuals involved in the study declared a conscious approval to participate in the project by signing the informed consent form.

Data Collection

Sociodemographic and general medical history of the participants were taken using a tailor-made questionnaire. Information about education, income, and nicotine use was obtained from interviews. Education was defined as primary, secondary and higher. Income was determined on the basis of income per family member per month: < €200, €200–350, > €350. The participants were classified as current smokers if they declared smoking 10 or more cigarettes a day continually for at least five years, past smokers and never smokers.

Arterial hypertension was defined as systolic blood pressure ≥ 140 mm Hg or diastolic blood pressure ≥ 90 mm Hg (mean of three consecutive measurements taken at five-minute intervals using a certified sphygmomanometer), or as previous use of antihypertensive drugs.

The patient was considered diabetic if fasting blood glucose level exceeded 126 mg/dL in two

consecutive tests, random blood sugar was over 200 mg/dL or if the patient was taking drugs due to diagnosed diabetes.

Measurements of height and weight were performed using the physician scale with height rod. Measurements of body height in the standing position were made with 1 cm accuracy and body weight was assessed in the standing position with 0.1 kg accuracy. Waist circumference (in cm) and hip circumference (in cm) were determined using a body measuring tape. Body mass index (BMI) was calculated by dividing body weight (kg) by height (in m²). Overweight was diagnosed in case of BMI 25–29.9 kg/m², and obesity when BMI ≥ 30 kg/m². Waist-hip ratio (WHR) was calculated by dividing waist circumference by hip circumference.

Dental Examination and Periodontal Measurement

Dental and periodontal examinations were performed by one examiner (BG). A calibration exercise was carried out on 10 patients probed twice before conducting a periodontal examination to reach intraexaminer reproducibility. Calibration was accepted if $\geq 90\%$ of the recordings (pocket depth, clinical attachment level) could be reproduced within a difference of 1.0 mm.

Dental and periodontal examinations were performed in artificial light, using a dental mirror and a periodontal probe with 1 mm scale (HU-FRIEDY PCPUNC 15). The examinations did not include third molars.

Dichotomous plaque index (PI) by O'Leary was established on four surfaces of all teeth (mesial, distal, lingual and buccal). The index was evaluated as the ratio of the surfaces with plaque to all tested surfaces. Bleeding on probing index (BoP) by Ainamo and Bay was evaluated at 4 points around all teeth: mesial-buccal (MB), buccal (B), distal buccal (DB) and lingual (L). BoP was calculated by dividing the sum of bleeding points by the sum of all the test points. Pocket depth (PD) and clinical attachment level (CAL) were evaluated at four sites per tooth: MB, B, DB, L. PD was defined as the distance from the gingival margin to the bottom of the pocket established by probing (in mm). CAL was defined as the distance between the bottom of the pocket determined by probing and the cemento-enamel junction (in mm). Measurements were rounded down to the nearest mm.

Clinical diagnosis of periodontitis and its severity was made in accordance with the case definitions for surveillance of periodontitis proposed by the Centers for Disease Control and AAP (Page and Eke definition) as follows:

- mild periodontitis as ≥ 2 interproximal sites with CAL ≥ 3 mm and ≥ 2 interproximal sites with PD ≥ 4 mm (not on the same tooth),
- moderate periodontitis as ≥ 2 interproximal sites with CAL ≥ 4 mm or ≥ 2 interproximal sites with PD ≥ 5 mm (not on the same tooth),
- severe periodontitis as ≥ 2 interproximal sites with CAL ≥ 6 mm (not on the same tooth) and ≥ 1 interproximal site with PD ≥ 5 mm [21].

The extent of periodontitis was classified by the percentage of sites with CAL ≥ 3 mm in line with Arbes Index: 0% = absent; $> 0 - \leq 33\%$ = mild; $> 33 - \leq 67\%$ = moderate; and $> 67\%$ = extensive periodontitis [10].

Data Analyses

Statistical analysis of the collected data was performed using the PQStat v. 1.4.4 software. Data was analyzed using the χ^2 test for categorical variables and Mann-Whitney U test for continuous variables. The threshold for statistical significance was assumed at $p = 0.05$, odds ratio (OR) of MI or severe periodontitis was determined with 95% confidence interval (95% CI).

Because a correlation between CVD risk factors and the occurrence of MI, as well as periodontitis was confirmed, some models were constructed taking into account the CVD risk factors and periodontal parameters as potential independent variables while the case status was a dependent variable.

Multivariate analysis was performed by forward selection. The first two parameters included in the model were non-modifiable factors associated with CVD and periodontitis: age and gender of the patients. The next step was adding classical CVD risk factors to the models: smoking, arterial hypertension, diabetes mellitus and BMI. The last considered group included the parameters determining the socio-economic status: education and income. Subsequently, the severity of periodontitis, the extent of periodontitis and the number of lost teeth were included in the multivariate models one at a time. These parameters were converted into dichotomous forms, where the risk factors were: diagnosis of severe periodontitis according to Page and Eke definitions, diagnosis of extensive periodontitis in line with Arbes Index, and over 10 extracted teeth, respectively.

Results

Table 1 shows the relationship between the occurrence of classical CVD risk factors and MI. A higher risk of MI was observed in: individuals over the age of 50 years, men, those with lower

Table 1. Bivariate association between acute myocardial infarction, socio-economic variables and risk factors of acute myocardial infarction

Parameter		Case group (n = 134)	Control group (n = 155)	OR (unadjusted)	p-value
Age, mean $\pm$ SD		54.3 $\pm$ 8.1	54.9 $\pm$ 10.0	–	0.3952*
Age, n (%)	< 50	32 (23.9)	65 (42.2)	1.00	0.0016†
	$\geq$ 50	102 (76.1)	89 (57.8)	2.3 (1.4–3.9)	
Sex, n (%)	female	29 (21.6)	94 (60.6)	1.00	< 0.0001†
	male	105 (78.4)	61 (39.4)	5.6 (3.3–9.4)	
Education, n (%)	university	27 (20.2)	82 (52.9)	1.00	< 0.0001†
	secondary	61 (45.5)	63 (40.6)	2.9 (1.7–5.1)	
	primary	46 (34.3)	10 (6.4)	14.0 (6.2–31.4)	
Income, n (%)	< €200	45 (33.6)	96 (61.9)	1.00	< 0.0001†
	€200–350	50 (37.3)	41 (26.4)	2.6 (1.5–4.5)	
	> €350	39 (29.1)	18 (11.6)	4.6 (2.4–9.0)	
Smoking, n (%)	never	27 (20.2)	93 (60.0)	1.00	< 0.0001†
	past	23 (17.2)	36 (23.2)	2.2 (1.1–4.3)	
	current	84 (62.7)	26 (26.8)	11.1 (6.0–20.6)	
Smoking, pack-years, mean $\pm$ SD		22.3 $\pm$ 19.4	7.3 $\pm$ 12.1	–	< 0.0001*
Hypertension, n (%)	no	32 (24.1)	105 (67.7)	1.00	< 0.0001†
	yes	101 (75.9)	50 (32.3)	6.6 (3.9–11.2)	
Systolic blood pressure, mean $\pm$ SD		136.7 $\pm$ 20.9	124.7 $\pm$ 9.9	–	0.0001*
Diastolic blood pressure, mean $\pm$ SD		80.1 $\pm$ 11.6	82.4 $\pm$ 6.8	–	0.1221*
Diabetes, n (%)	no	106 (79.1)	145 (93.6)	1.00	0.0006†
	yes	28 (20.9)	10 (6.5)	3.8 (1.8–8.2)	
BMI, mean $\pm$ SD		28.7 $\pm$ 5.0	26.0 $\pm$ 4.1	–	< 0.0001*
Body weight, n (%)	normal weight	28 (21.4)	60 (39.2)	1.00	0.0018†
	overweight	57 (43.5)	61 (39.9)	2.0 (1.1–3.6)	
	obesity	46 (35.1)	32 (20.9)	3.1 (1.6–5.8)	
WHR, mean $\pm$ SD		0.98 $\pm$ 0.09	0.87 $\pm$ 0.10	–	< 0.0001*

SD – standard deviation; * Mann-Whitney U test; † χ^2 test.

education and income, current smokers and – to a lesser extent – former smokers, patients with diagnosed hypertension or diabetes, overweight or obese individuals.

There were statistically significant differences in the periodontal status and all periodontal parameters between cases and controls (Table 2). Patients in the study group had worse periodontal indices and a higher number of lost teeth.

In the subsequent analyzes the three chosen periodontal indicators were used in dichotomous forms, dividing patients according to the presence of severe periodontitis, extensive periodontitis and more than 10 lost teeth. A relationship (Table 3) was observed between the severity and the extent of periodontitis and age above 50 years, male gender, education, level of income, tobacco smok-

ing and hypertension. However, only the presence of severe periodontitis was associated with body weight.

We observed increased unadjusted ORs of MI for the severity of periodontitis, the extent of periodontitis and the high number of lost teeth (Table 4). After adjusting for non-modifiable CVD risk factors, i.e., age and gender, these values slightly decreased, but a strong and statistically significant relationship between all evaluated parameters and the occurrence of MI still remained. Adjustment for further variables in the multivariate models gradually reduced the significance of periodontal parameters, but even after including all the variables (age, sex, smoking, hypertension, diabetes, BMI, education, income), an independent association between the extent of periodon-

Table 2. Bivariate association between acute myocardial infarction and oral health variables

Parameter		Case group (n = 134)	Control group (n = 155)	OR (unadjusted)	p-value
Plaque index (%), mean $\pm$ SD		85.7 $\pm$ 20.0	65.1 $\pm$ 24.8	–	< 0.0001*
Bleeding on probing index (%), mean $\pm$ SD		49.9 $\pm$ 29.9	39.5 $\pm$ 26.0	–	0.0033*
Pocket depth (mm), mean $\pm$ SD		2.9 $\pm$ 1.1	2.2 $\pm$ 0.8	–	< 0.0001*
Clinical attachment loss (mm), mean $\pm$ SD		4.2 $\pm$ 2.0	2.5 $\pm$ 1.5	–	< 0.0001*
Severity of periodontitis, n (%)‡	no periodontitis	7 (5.2)	38 (24.5)	1.00	< 0.0001†
	mild	7 (5.2)	9 (5.8)	4.2 (1.2–15.1)	
	moderate	45 (33.6)	64 (41.3)	3.8 (1.6–9.3)	
	severe	75 (56.0)	44 (28.4)	9.3 (3.8–22.5)	
Extent of periodontitis, n (%)§	> 0 – $\leq$ 33%	8 (6.0)	45 (29.0)	1.00	< 0.0001†
	> 33 – $\leq$ 67%	30 (22.4)	54 (34.8)	3.1 (1.3–7.5)	
	> 67%	96 (71.6)	56 (36.1)	9.6 (4.2–21.9)	
Number of teeth lost, median (Q1–Q3)		10 (6–17)	4 (2–8)	–	< 0.0001*

SD – standard deviation; * Mann-Whitney U test; † χ^2 test; ‡ severity of periodontitis defined in accordance with Page and Eke definition [20, 21]; § extent of periodontitis defined in accordance with Arbes Index [10].

titis, expressed as a percentage of sites with CAL $\geq$ 3 mm and the risk of MI still remained significant (OR = 2.4; 95% CI 1.1–5.2).

Discussion

The obtained results demonstrate that the severity and extent of periodontitis is positively associated with acute MI, but this relationship is stronger with the extent of the disease than its severity. Although many previous studies indicate that periodontitis increases the risk of CVD, this association requires verification.

Periodontitis and CVD share several common risk factors with well-documented impact, such as age, low socio-economic status and cigarette smoking [3, 6, 7]. The most important variable in the assessment of a causal relationship between periodontitis and CVD is smoking, because it represents both a confounder, as well as a modifying agent [6]. Statistical analysis adjusted for smoking does not rule out residual confounding, but recent research suggests that the relationship between periodontitis and CVD can be independent of smoking [14]. In the present study, the impact of smoking as a confounder was closely monitored. Similarly to other reports, smoking was determined by dividing the subjects into smokers at the time of the study, in the past, and never smokers [11, 12].

Among the periodontal parameters related to systemic diseases, CAL seems to be the most important, because it is a measure of cumulative life-

time experience of periodontitis. However, periodontitis cannot be verified by measurements of single variable and the evaluation of disease presence requires measurement of PD and BoP. Previous studies assessing the relationship between periodontitis and MI indicate a clear discrepancy of applied periodontal parameters and definitions of periodontitis, which makes comparisons of data obtained by different researchers harder. Some studies evaluated the alveolar bone loss on radiographs, BoP and root furcation involvement [22], alveolar bone loss on radiographs and PD [14], CAL [10, 15], PD and CAL on selected teeth [12, 16], and PD and CAL for all teeth excluding third molars [11, 13].

The utility of periodontal classification systems remains “burdened with ambiguity and limitations” [21]. In the present study, the severity of periodontitis was classified in accordance with Page and Eke definition, whilst the extent of periodontitis was determined on the basis of the percentage of sites with CAL $\geq$ 3 mm (Arbes Index). Similarly, both the severity and the extent of periodontitis were significantly associated with MI in a bivariate analysis. After adjusting for age, gender, smoking, hypertension, diabetes, BMI, education and income, the influence of periodontitis on MI risk was less pronounced but still statistically significant in the case of the extent of disease (adjusted OR = 2.4, 95% CI 1.1–5.2), but not for its severity. Andriankaja et al. [13] reported a slightly lesser effect of CAL on MI, obtaining OR 1.34 (95% CI = 1.15–1.57) for men and

Table 3. Association between the extent (Arbes Index) and severity (Page and Eke definition) of periodontitis and well-known risk factors of acute myocardial infarction

Parameter		Extent of periodontitis			Severity of periodontitis		
		extensive periodontitis (n = 152)	no extensive periodontitis (n = 137)	p-value	severe periodontitis (n = 119)	no severe periodontitis (n = 170)	p-value
Age, n (%)	< 50	32 (21.2)	65 (47.4)	< 0.0001*	23 (19.3)	74 (43.8)	< 0.0001*
	≥ 50	119 (78.8)	72 (52.5)		96 (80.7)	95 (56.2)	
Sex, n (%)	female	53 (34.9)	70 (51.1)	0.0053*	33 (27.7)	90 (52.9)	< 0.0001*
	male	99 (65.1)	67 (48.9)		86 (72.3)	80 (47.1)	
Education, n (%)	university	38 (25.0)	71 (51.8)	< 0.0001*	26 (21.8)	83 (48.8)	< 0.0001*
	secondary	68 (44.7)	56 (40.9)		56 (47.1)	68 (40.0)	
	primary	46 (30.3)	10 (7.3)		37 (31.1)	19 (11.2)	
Income, n (%)	< €200	56 (36.8)	85 (62.0)	< 0.0001*	44 (37.0)	97 (57.1)	0.0013*
	€200–€350	54 (35.5)	37 (27.0)		42 (35.3)	49 (28.8)	
	> €350	42 (27.6)	15 (11.0)		33 (27.7)	24 (14.1)	
Smoking habits, n (%)	never	48 (31.6)	72 (52.6)	0.0003*	37 (31.1)	83 (48.8)	0.0010*
	past	31 (20.4)	28 (20.4)		22 (18.5)	37 (21.8)	
	current	73 (48.0)	37 (27.0)		60 (50.4)	50 (29.4)	
Smoking, pack-years, mean ± SD		19.3 ± 19.3	8.6 ± 13.4	< 0.0001†	19.3 ± 22.7	10.7 ± 15.7	< 0.0001†
Hypertension, n (%)	no	61 (40.4)	76 (55.5)	0.0105*	43 (36.4)	94 (55.3)	0.0016*
	yes	90 (59.6)	61 (44.5)		75 (63.6)	76 (44.7)	
Systolic blood pressure, mean ± SD		135.8 ± 19.8	129.4 ± 17.7	0.0125†	137.8 ± 19.1	129.0 ± 18.4	0.0016†
Diastolic blood pressure, mean ± SD		80.5 ± 10.5	81.0 ± 10.7	0.8577†	80.8 ± 10.4	80.6 ± 10.9	0.7265†
Diabetes, n (%)	no	127 (83.6)	124 (90.5)	0.0805*	98 (82.4)	153 (90.0)	0.0583*
	yes	25 (16.4)	13 (9.5)		21 (17.6)	17 (10.0)	
BMI, mean ± SD		27.8 ± 4.9	26.7 ± 4.4	0.1115†	28.0 ± 4.7	26.8 ± 4.6	0.0781†
Body weight, n (%)	normal weight	40 (26.7)	48 (35.8)	0.2184*	27 (23.1)	61 (36.5)	0.0384*
	overweight	68 (45.3)	50 (37.3)		57 (48.7)	61 (36.5)	
	obesity	42 (28.0)	36 (26.9)		33 (28.2)	45 (27.0)	
WHR, mean ± SD		0.95 ± 0.09	0.92 ± 0.13	0.0264†	0.96 ± 0.11	0.92 ± 0.10	0.0093†

SD – standard deviation; * χ^2 test; † U Mann-Whitney test.

OR 2.08 (95% CI = 1.47–2.94) for women after adjustment for age, BMI, physical activity, diabetes and smoking. Likewise, López et al. [11] received crude OR 3.78 (95% CI = 1.60–8.92) and adjusted OR 3.17 (1.31–7.63) after adjusting for diabetes, systolic blood pressure and smoking. This can partly be explained by the fact that the study by López et al. [11] included a younger age group of 30–50 years, where lower CAL values can be expected. On the other hand, Cueto et al. [12] observed a stronger association between periodonti-

tis and MI with OR = 4.42 (95% CI = 2.22–8.82). After adjusting for other risk factors in a multivariate analysis (sex, age, smoking, hypertension, diabetes, hypercholesterolemia, regular physical activity), OR reached the value of 3.31 (95% CI = 1.42–7.71). Arbes et al. [10] showed that periodontitis increases the risk of MI on a sample from the NHANES III study. Unadjusted OR for CAL ≥ 3 mm in 0–33% of tested sites was 2.2 (95% CI = 1.3–3.8), and in 33–67% of tested sites it equaled 5.5 (95% CI = 3.4–9.1) and

Table 4. Crude and adjusted OR estimates (with 95% CI) for the association between case status and the periodontal parameters: Severity of periodontitis in accordance with Page and Eke definition, extent of periodontitis in accordance with Arbes Index and number of lost teeth

	Unadjusted		Model I *		Model II †		Model III ‡	
	OR (95% CI)	p-value (χ^2 test)	OR (95% CI)	Wald p-value	OR (95% CI)	Wald p-value	OR (95% CI)	Wald p-value
Severity of periodontitis §	3.2 (2.0–5.2)	< 0.0001	2.0 (1.2–3.5)	0.0109	1.2 (0.6–2.4)	0.6057	0.9 (0.4–1.9)	0.7852
Extent of periodontitis #	4.5 (2.7–7.4)	< 0.0001	3.7 (2.1–6.4)	< 0.0001	3.2 (1.6–6.6)	0.0011	2.4 (1.1–5.2)	0.0203
Number of lost teeth ¶	4.2 (2.5–7.2)	< 0.0001	4.9 (2.6–9.4)	< 0.0001	2.7 (1.2–5.9)	0.0151	2.1 (0.9–4.9)	0.0758

SD – standard deviation; * model adjusted for age and sex; † model adjusted for age, sex, smoking, arterial hypertension, diabetes mellitus and BMI; ‡ model adjusted for age, sex, smoking, arterial hypertension, diabetes mellitus, BMI, education and income; § severe periodontitis defined in accordance with Page and Eke definition [21]; # extensive periodontitis defined in accordance with Arbes Index (> 67% of sites with CAL $\geq$ 3 mm) [10], ¶ > 10 teeth lost.

in > 67% of tested sites 9.8 (95% CI = 4.5–21.0). After adjusting for age, sex, race, wealth, smoking, diabetes, high blood pressure, BMI, and blood cholesterol, the authors obtained OR of 1.4 (95% CI = 0.8–2.5), 2.3 (95% CI = 1.2–4.4) and 3.8 (95% CI = 1.5–9.7), respectively. In a recent study, the extent and severity of periodontitis were significantly associated with acute MI size as measured by troponin I and myoglobin levels [15]. However, only the extent index accounted for serum levels of myoglobin, total leukocytes and neutrophils.

The biological model of the association between periodontitis and MI takes into account several potential mechanisms [2]. They include the direct impact of microorganisms on the vascular endothelium, the influence of cytokines and proinflammatory mediators, cross-reactivity leading to autoimmune reactions, and genetically determined common susceptibility to periodontitis and atherosclerosis. The greater is the extent of periodontitis, the bigger is the chronic dissemination of bacteria, toxins and inflammatory mediators into the bloodstream, which may explain the results of our study. Immunologically competent cells stimulated by bacterial lipopolysaccharides secrete excessive amounts of pro-inflammatory mediators (IL-1, IL-6, TNF- α , PGE2), which stimulate the liver to produce acute phase proteins (CRP), intensify platelet aggregation processes and increase plasma viscosity [2]. The presence of inflammation affects the various stages of atherosclerotic plaque development – from initiating the formation of plaque to its rupture [6, 7].

Recent studies provided new information on the association between periodontitis and MI. Lund

Häheim et al. [23] proved a positive correlation between the high titer of serum antibodies against specific periopathogens and the risk of MI. Another study confirmed a positive association between the total burden of periodontal pathogens – primarily the number of *Porphyromonas gingivalis* and MI [24]. On the other hand, in the most recent research, plasma antibodies against periodontal pathogens were inversely associated with coronary heart remodeling, but not with the extent of coronary atherosclerosis [25].

However, not all scientific studies confirm a relationship between periodontitis and MI [18–20]. Physicians' Health Study [18] and the National Survey Questionnaire Sweden [19], which included more than 5,000 people, showed no impact of periodontitis on MI. In the two quoted studies though, the results were based solely on self-reported periodontal and oral status. This methodology might be the cause of the erroneous classification, which, in turn, could have translated into the obtained results.

Our research showed a relationship between the number of lost teeth and MI, similarly to the studies by other authors [14, 22, 26, 27]. Most recently, a linear relationship between tooth loss and the degree of arterial stiffness that differed depending on sex was suggested [28]. In our study, OR of MI in patients with a large number of extracted teeth (> 10) was calculated at 4.2 (95% CI = 2.5–7.2) and remains significant after adjusting for age, sex, smoking, hypertension and diabetes (OR = 2.7; 95% CI = 1.2–5.9). After completing the model with education and income, an independent correlation between the number of lost teeth and the risk of MI was no longer observed. Periodontitis

is the main cause of tooth loss in the middle-aged and elderly [29]. However, in this study tooth loss has been registered in a cross-sectional design and thus might have not been entirely due to periodontal disease. A relationship between tooth loss and MI can result from many other factors, including dental caries and its complications, bacteremia associated with teeth extraction and the presence of confounders, such as socio-economic status and various behavioral factors. Nevertheless, most researchers did not confirm a relationship between the number of teeth and the risk of MI [11, 19, 30]. Still, all the quoted studies have some limitations; namely, the study by Buhlin et al. [19] was a survey which did not include clinical verification, the study by López et al. [11] included individuals aged 30–50 years, and the study by Syrjälä et al. [30] involved elderly people above 75 years of age.

This research has several constraints that need attention when interpreting the presented data. The study group included patients during hospitalization, and a periodontal examination was performed two or three days after MI episode, thus CVD could have negatively affected the oral health. Nonetheless, due to the chronic nature of periodontitis, the impact of hospitalization on the results seems to be doubtful. Plaque indices were not analyzed, as probably the period of hospitalization could have negatively impacted the scores in this area. In addition, CAL and PD measurements were made at four, rather than six, sites, which could have led to an underestimation of the occurrence of periodontitis. In the authors' opinion, however, a more comprehensive periodontal examination was contraindicated in patients after MI due to their general condition. Patients who died of MI after admission to the hospital were not included in the study; therefore, a cause-effect relationship between periodontitis and MI could be underestimated, which is more probable than an overestimation of these associations.

Also, the use of blind experiment methodology on the examiner would be preferable but imprac-

tical due to the hospitalization of all the patients in the study group in the cardiology ward. Nonetheless, the researcher evaluating the state of periodontal tissues was calibrated.

Particular attention should be paid to errors associated with the impact of confounders and modifying factors. There are no studies evaluating the associations between periodontitis and MI, which would also permit us to control all potential confounding variables. In our study potential confounding variables were assessed and an attempt was made to construct statistical models in logistic regression analysis, controlling the most important of these variables.

To sum up, according to the authors' knowledge, this study is the first one that assessed the effects of both the severity (Page and Eke definition) and the extent of periodontitis (Arbes Index) on the incidence of MI and the largest case-control study of this kind that was conducted in Central Europe and in Poland [31]. It is also one of the few works that have assessed the relationship between the number of teeth and MI [11, 17, 22, 26, 27, 30]. The authors demonstrated a strong positive association between the extent of periodontitis and MI, independent of classical CVD risk factors, including tobacco smoking. Still, further and more methodologically perfected studies on larger samples are needed in order to assess the strength of the relationship between periodontitis and MI. The most important factor seems to be protection against errors associated with the influence of confounders and modifying factors, and the use of uniform diagnostic standards of periodontitis. The demonstration of a causal relationship between periodontitis and MI could have significant clinical implications, because it would mean that periodontal treatment may be an element of primary and/or secondary prevention of MI. If such a relationship is not causal, then the fact that both periodontitis and MI are diseases of high morbidity and they largely relate to the same population is still important from a public health perspective.

References

- [1] **Wojtyniak B, Goryński P, Moskalewicz B:** The health situation of Poles and its determinants. National Institute of Public Health – National Institute of Hygiene, Warszawa 2012, ISBN 83-89379-63-9, 59–74.
- [2] **Schenkein HA, Loos BG:** Inflammatory mechanisms linking periodontal diseases to cardiovascular diseases. *J Periodontol* 2013, 84, Suppl 4, 51–69.
- [3] **Tonetti MS, Van Dyke TE:** Periodontitis and atherosclerotic cardiovascular disease: Consensus report of the joint EFP/AAP workshop on periodontitis and systemic diseases. *J Periodontol* 2013, 84 Suppl 4, 24–29.
- [4] **Bahekar AA, Singh S, Saha S, Molnar J, Arora R:** The prevalence and incidence of coronary heart disease is significantly increased in periodontitis: A meta-analysis. *Am Heart J* 2007, 154, 830–837.
- [5] **Humphrey LL, Fu R, Buckley DI, Freeman M, Helfand M:** Periodontal disease and coronary heart disease incidence: A systematic review and meta-analysis. *J Gen Intern Med* 2008, 23, 2079–2086.

- [6] Lockhart PB, Bolger AF, Papapanou PN, Osinbowale O, Trevisan M, Levison ME, Tauber KA, Newburegr JW, Gornik HL, Gewitz MH, Wilson WR, Smith SC, Baddour LM: Periodontal disease and atherosclerotic vascular disease: Does the evidence support an independent association? A scientific statement from the American Heart Association. *Circulation* 2012, 125, 2520–2544.
- [7] Perk J, De Backer G, Gohlke H, Graham I, Reiner Z, Verschuren M, Albus C, Benlian P, Boysen G, Cifkova R, Deaton C, Ebrahim S, Fisher M, Germano G, Hobbs R, Hoes A, Karadeniz S, Mezzani A, Prescott E, Ryden L, Scherer M, Syväne M, Scholte op Reimer WJ, Vrints C, Wood D, Zamorano JL, Zannad F: European guidelines on cardiovascular disease prevention in clinical practice (v. 2012). The fifth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Risk Prevention in Clinical Practice (constituted by representatives of nine societies and by invited experts). *Eur Heart J* 2012, 33, 1635–1701.
- [8] Górski R, Pietruska M, Dembowska E, Wysokińska-Miszczuk J, Włosowicz M, Konopka T: Prevalence of periodontal diseases in 35–44 year-olds in the large urban agglomeration. *Dent Med Probl* 2012, 49, 19–27.
- [9] Eke PI, Dye BA, Wei L, Slade GD, Thornton-Evans GO, Borgnakke WS, Taylor GW, Page RC, Beck JD, Genco RJ: Update on prevalence of periodontitis in the United States: NHANES 2009 to 2012. *J Periodontol* 2015, 86, 611–622.
- [10] Arbes SJ, Slade GD, Beck JD: Association between extent of periodontal attachment loss and self-reported history of heart attack: An analysis of NHANES III data. *J Dent Res* 1999, 78, 1777–1782.
- [11] López R, Oyarzún M, Naranjo C, Cumsille F, Ortiz M, Baelum V: Coronary heart disease and periodontitis – a case control study in Chilean adults. *J Clin Periodontol* 2002, 29, 468–473.
- [12] Cueto A, Mesa F, Bravo M, Ocaña-Riola R: Periodontitis as risk factor for acute myocardial infarction. A case control study of Spanish adults. *J Periodont Res* 2005, 40, 36–42.
- [13] Andriankaja OM, Genco RJ, Dorn J, Dmochowski J, Hovey K, Falkner KL, Trevisan M: Periodontal disease and risk of myocardial infarction: The role of gender and smoking. *Eur J Epidemiol* 2007, 22, 699–705.
- [14] Dietrich T, Jimenez M, Krall Kaye EA, Vokonas PS, Garcia RI: Age-dependent associations between chronic periodontitis/edentulism and risk of coronary heart disease. *Circulation* 2008, 117, 1668–1674.
- [15] Marfil-Álvarez R, Mesa F, Arrebola-Moreno A, Ramirez-Hernández JA, Magán-Fernández A, O'Valle F, Galindo-Moreno P, Catena A: Acute myocardial infarct size is related to periodontitis extent and severity. *J Dent Res* 2014, 93, 993–998.
- [16] Parkar SM, Modi GN, Jani J: Periodontitis as risk factor for acute myocardial infarction: A case control study. *Heart Views* 2013, 14, 5–11.
- [17] Noguchi S, Toyokawa S, Miyoshi Y, Suyama Y, Inoue K, Kobayashi Y: Five-year follow-up study of the association between periodontal disease and myocardial infarction among Japanese male workers: MY Health Up Study. *J Public Health (Oxf)* 2015, 37, 605–611.
- [18] Howell TH, Ridker PM, Ajani UA, Hennekens CH, Christen WG: Periodontal disease and risk of subsequent cardiovascular disease in U.S. male physicians. *J Am Coll Cardiol* 2001, 37, 445–501.
- [19] Buhlin K, Gustafsson A, Håkansson J, Klinge B: Oral health and cardiovascular disease in Sweden. Results of a national questionnaires study. *J Clin Periodontol* 2002, 29, 254–259.
- [20] Johansson SC, Ravald N, Pagonis C, Richter A: Periodontitis in patients with coronary artery disease: An 8-year follow-up. *J Periodontol* 2014, 85, 417–425.
- [21] Slots J: Periodontology: Past, present, perspectives. *Periodontology* 2000 2013, 62, 7–19.
- [22] Holmlund A, Holm G, Lind L: Severity of periodontal disease and number of remaining teeth are related to the prevalence of myocardial infarction and hypertension in a study based on 4,254 subjects. *J Periodontol* 2006, 77, 1173–1178.
- [23] Lund Häheim L, Olsen I, Nafstad P, Schwarze P, Rønningen KS: Antibody levels to single bacteria or in combination against myocardial infarction. *J Clin Periodontol* 2008, 35, 473–478.
- [24] Paspuleti MK, Nagireddy RR, Dinahalli R, Anumala D, Kishore Kumar A, Chavan V: Microbiological tests to identify a link between periodontitis and acute myocardial infarction – an original research. *Iran J Microbiol* 2013, 5, 391–395.
- [25] de Boer SP, Cheng JM, Rangé H, Garcia-Garcia HM, Heo JH, Akkerhuis KM, Meilhac O, Cosler G, Pussinen PJ, van Geuns RJ, Serruys PW, Boersma E, Kardys I: Antibodies to periodontal pathogens are associated with coronary plaque remodeling but not with vulnerability or burden. *Atherosclerosis* 2014, 237, 84–91.
- [26] Spivakovsky S: Myocardial infarction and tooth extraction associated. *Evid Based Dent* 2012, 13, 110. DOI: 10.1038/sj.ebd.6400894.
- [27] Liljeström JM, Havulinna AS, Paju S, Männistö S, Salomaa V, Pussinen PJ: Missing teeth predict incident cardiovascular events, diabetes, and death. *J Dent Res* 2015, May, 19. pii: 0022034515586352. [Epub ahead of print].
- [28] Asai K, Yamori M, Yamazaki T, Yamaguchi A, Takahashi K, Sekine A, Kosugi S, Matsuda F, Nakayama T, Bessho K: Tooth loss and atherosclerosis: The Nagahama study. *J Dent Res* 2015, 94, Suppl 3, 52–58.
- [29] Seirafi AH, Ebrahimi R, Golkari A, Khosropanah H, Soolari A: Tooth loss assessment during periodontal maintenance in erratic vs. complete compliance in a periodontal private practice in Shiraz, Iran: A 10-year retrospective study. *J Int Acad Periodontol* 2014, 16, 43–49.
- [30] Syrjälä AMH, Ylöstalo P, Hartikainen S, Sulkava R, Knuuttila ML: Number of teeth and myocardial infarction and stroke among elderly never smokers. *J Negat Results Biomed* 2009, 8, 6. DOI: 10.1186/1477-5751-8-6.
- [31] Woźakowska-Kapłon B, Włosowicz M, Gorczyca-Michta I, Górski R: Oral health status and the occurrence and clinical course of myocardial infarction in hospital phase: A case-control study. *Cardiol J* 2013, 20, 370–377.

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