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Severe and moderate periodontitis are associated with acute myocardial infarction

Isaac S. Gomes-Filho¹ D | Julita Maria F. Coelho¹ | Samilly S. Miranda¹ | Simone S. Cruz^{1,2} | Soraya C. Trindade¹ | Eneida M.M. Cerqueira¹ | Johelle S. Passos-Soares^{1,3} | Maria da Conceição N. Costa⁴ | Maria Isabel P. Vianna³ | Ana Cláudia M.G. Figueiredo^{1,2} D | Alexandre Marcelo Hintz¹ | Amanda F. Coelho¹ | Luiz Carlos S. Passos⁵ | Maurício L. Barreto⁴ | Frank Scannapieco⁶ D

¹Department of Health, Feira de Santana State University, Feira de Santana, Bahia, Brazil

²Department of Epidemiology, Federal University of Recôncavo of Bahia, Santo Antônio de Jesus, Bahia, Brazil

³Department of Preventive Dentistry, Federal University of Bahia, Salvador, Bahia, Brazil

⁴Department of Epidemiology, Collective Health InstituteFederal University of Bahia, Salvador, Bahia, Brazil

⁵Department of Medicine, Federal University of Bahia, Salvador, Bahia, Brazil

⁶Department of Oral Biology, University of Buffalo, Buffalo, New York

Correspondence

Prof. Isaac Suzart Gomes-Filho – Avenida Getúlio Vargas, 379, Centro, Feira de Santana, Zip Code: 44025-010, Bahia, Brazil. Email: isuzart@gmail.com

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Abstract

Background: An association between periodontitis and cardiovascular disease is now well documented; however, the effect of periodontitis severity levels on this outcome, specifically on acute myocardial infarction (AMI), remains unexplored. This study investigated the association between levels of periodontitis severity (exposure) and AMI (outcome).

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Methods: This case-control study, matched by sex and age, was conducted with 621 participants, with 207 individuals treated in the emergency department of Santa Izabel and Ana Nery Hospitals in Salvador, Bahia, Brazil, diagnosed with a first AMI event, and compared to 414 individuals without a diagnosis of AMI. Levels of periodontitis severity followed two criteria: (1) Center for Disease Prevention and Control and American Academy of Periodontology; (2) Gomes-Filho et al. (2018) using criteria that also evaluated bleeding upon probing. Conditional logistic regression analysis was performed and odds ratios (ORs) and their 95% confidence intervals (CIs) were obtained.

Results: The adjusted association measurements showed a positive association between both severe ($OR_{adjusted}$ ranged from 2.21 to 3.92; 95% CI ranged from 1.03 to 10.05) and moderate periodontitis ($OR_{adjusted}$ ranged from 1.96 to 2.51; 95% CI ranged from 1.02 to 6.19), and AMI, for both periodontitis diagnostic criteria. It demonstrated that among those with moderate and severe periodontitis, the chance of

Check for updates having AMI was approximately two to four times greater than among those without periodontitis.

Conclusion: The findings demonstrate that there is an association between the severity of the periodontal condition and AMI, suggesting a possible relationship among the levels of periodontitis severity and the cardiovascular condition.

KEYWORDS

cardiovascular diseases, epidemiology, periodontal medicine; periodontitis

1 | INTRODUCTION

Previous studies have suggested an association between periodontal disease and coronary heart disease,¹⁻³ as well as investigating the biological mechanisms that connect these diseases.⁴ However, the studies are still inconclusive concerning the effect of periodontitis severity levels on cardiac outcomes, specifically acute myocardial infarction (AMI). Existing studies are few,⁵⁻¹⁰ mostly employing different definitions of the exposure severity, thus contributing to the lack of a consensus on this relationship.

Both periodontitis and myocardial infarction are important public health problems. Over the past decade, cardiovascular diseases have become one of the leading causes of mortality worldwide, accounting for about 31% of all global deaths in 2016, especially those resulting from heart attack and stroke,¹¹ Ischemic heart disease accounted for more than 9 million deaths during this same period.¹² More than threequarters of all deaths from cardiovascular diseases occur in low- and middle-income countries.¹¹ In Brazil,¹³ cardiovascular diseases remain the leading cause of mortality, accounting for about 27% of all deaths in 2017. Of these deaths, about 26% were attributed to AMI.¹³

Regarding periodontitis, the global burden of this disease remains high and trends to increase because of aging population, improved tooth retention and exposure to risk factors. Consequently, increasing the risk to associated morbidity, such as systemic diseases.¹⁴

Although a new classification for the diagnosis of periodontal diseases has been recently published,¹⁵ its use in previous studies on the topic has not yet been observed. The Center for Disease Prevention and Control and American Academy of Periodontology (CDC-AAP)^{16,17} recommend a classification of severity levels, based on clinical attachment level and probing depth, widely utilized. However, this criterion does not include the evaluation of the gingival inflammation, relevant clinical parameter relative to assessment of disease risk.¹⁴

Therefore, the goal of this study was to investigate if levels of periodontitis severity are associated with AMI, using previously widely employed periodontitis severity cases definitions (CDC-AAP).^{16,17} Additionally, to give more validity to the findings, alternative criteria were used to define periodontitis that included bleeding on probing to the clinical parameters of the aforementioned periodontitis severity case definition.¹⁸

2 | MATERIALS AND METHODS

2.1 | Study sample

A matched case-control study was conducted in individuals assisted in the emergency department of Santa Izabel Hospital and Ana Nery Hospital that provide general health care, in Salvador, Bahia, Brazil, between September 2008 and April 2009. Those who agreed to participate in the study signed an informed consent form. This study was approved by the human subjects Ethics Committee of Feira de Santana State University and was conducted in accordance with the Helsinki Declaration of 1975, as revised in 2013.

The case and control groups were defined as follows: the case group consisted of individuals diagnosed with a first event AMI in the hospital emergency department. After the individual accepted the invitation to participate in the study, an oral examination was performed in the intensive care unit. As the case group was formed, the control group were also formed, with individuals without a report of AMI matched by sex and age during the same period, with the same sex of the cases, and with age in a range 5 years above or below the case's age.

The control group consisted of individuals admitted to these hospitals over the same time period, for treatment of other diseases, such as orthopedic diseases, viral infections, among others. In addition, control subjects also included companions or neighbors of the case individuals that had no prior history of infarction that were selected following house-tohouse visits starting from the household of the case until a match was found. If more than one match was found in the household, selection was based on a draw. Blood relatives of the cases were not selected as controls. To prevent the inclusion of false positives in the control group, the Rose Chest Pain Questionnaire¹⁹ was applied to the participants of this group, with the purpose of identifying possible past history of angina, and an electrocardiogram was performed, to confirm the absence of Q wave.

Inclusion criteria required individuals to have at least four teeth to ensure the validity of periodontal status measurements, to not be pregnant, have no diagnosis of cancer or HIV-AIDS, to have not used anti- inflammatory medication in the last 2 months and to have not experienced periodontal treatment in the 6 months prior to the study. Exclusion criteria included individuals with anterior infarction, percutaneous coronary revascularization history within 6 months, or surgical revascularization in the 2 months prior to the study.

2.2 | Data collection procedures

During the period of data collection, all participants answered a questionnaire, through interview, to obtain information related to socioeconomic and demographic characteristics, general and oral health conditions, habits and lifestyle, medical and dental history and access to oral health care. Blood samples collected from cases and controls after 12 hours fasting period were used to obtain a full blood count, blood glucose, triglyceride, total cholesterol, urea, creatinine, and C-reactive protein levels. Plasma levels of glucose, triglycerides, total cholesterol, HDL-C and, LDL-C fractions were determined. Blood pressure was measured, and body mass index (BMI) and waist-hip ratio (WHR) were calculated after weighing each participant.

Up to 7 days after the interview, control individuals underwent a complete periodontal examination by a single examiner (JMSFC) at the home of the participant or in the hospital. In the case group, it was performed up to 7 days after the infarction event at the hospital. The following periodontal clinical parameters were evaluated: gingival pocket probing depth, gingival recession measurement, clinical attachment level, bleeding on probing, visible plaque index, and number of present teeth. All participants were assessed at six sites per tooth except the third molars, such as, mesiobuccal, midbuccal, distobuccal, mesiolingual/palatal, midlingual/palatal and distolingual/palatal regions, using a Williams periodontal probe.^{*} The visible plaque index was evaluated in four regions per tooth (mesial, distal, buccal, palatal/lingual).

The probing depth was measured as the distance from the gingival margin to the deepest region of probe penetration.²⁰ The gingival recession, as the distance between the cementum-enamel junction and the gingival margin. And, the clinical attachment level by adding the probing depth to the gingival recession values of each site.²¹ The bleeding index was obtained by observing its occurrence up to 10 seconds after the examination of probing depth. The visible plaque index was evaluated using the same probe JOURNAL OF Periodontology

to confirm the presence of biofilm deposits on the tooth surface. $^{\rm 22}$

Examiner training was conducted previously to the clinical examination. Reproducibility was assessed through replication of the periodontal measurements. This was performed using an experienced periodontist (I.S.G.F.) as a reference, on about 10% of the sample. The intra-examiner k index (± 1 mm) for probing depth and recession measurements were, respectively, 0.84 and 0.89. The inter-examiner k index (± 1 mm) showed agreement rates of 0.81 and 0.86 for these measurements, respectively.

During the periodontal examination, the examiner was blind to the cardiac condition of the individuals. For the case group, the complete records of the AMI diagnosis, lipid profile data, and BMI were obtained from the medical records of study participants.

2.3 | Sample size

To calculate the minimum sample size, the following estimates were used. A prevalence of 2.7% for severe periodontitis among individuals without a diagnosis of AMI—the control group—and a prevalence of 12.1% of severe periodontitis among those with a diagnosis of AMI—case group.⁵ A study power of 90%, 95% confidence level, and the 1:2 ratio between cases and controls were also employed. The minimum estimated sample size was 390 individuals, taking into consideration the most severe periodontal condition.

2.4 | Diagnosis of periodontitis severity—exposure

The individuals were classified and grouped into three different levels of periodontitis severity: mild, moderate, and severe periodontitis, according to two definitions: 1) Center for Disease Prevention and Control and American Academy of Periodontology (CDC-AAP)^{16,17}; 2) Gomes-Filho et al. (2018).¹⁸ The choice of a second criterion was because of the need to include the clinical parameter of bleeding on probing, very relevant to evaluate periodontal inflammation. The remaining individuals were considered to be without periodontitis (Table 1).

2.5 | Diagnosis of acute myocardial infarction—outcome

The individuals were divided into groups with and without AMI according to the diagnosis made by the cardiologist responsible for the cardiology service of the hospitals during the data collection period. Individuals diagnosed with a first myocardial infarction were selected as cases if they showed: (1) angina or anginous pain, or the ischemic equivalent (intense sweating, a feeling of impending death or

^{*} Hu-Friedy, Chicago, IL.



Severity level	Severe periodontitis	Moderate periodontitis	Mild periodontitis	No periodontitis			
Centers for Disease Control and Prevention and the American Academy of Periodontology (2007, 2012) ^{16,17}							
Clinical attachment level (CAL)	≥2 interproximal sites with CAL ≥ 6 millimeters (not in the same tooth)	≥2 interproximal sites with CAL ≥ 4 millimeters (not in the same tooth)	≥2 interproximal sites with CAL ≥ 3 millimeters (not in the same tooth)	No evidence of mild, moderate or severe periodontitis			
	AND	OR	AND				
Probing depth (PD)	≥1 interproximal site with PD ≥5 mm	≥2 interproximal site with PD ≥5 mm (not in the same tooth)	≥2 interproximal sites with PD ≥ 4 mm (not in the same tooth) or 1 site with PD ≥ 5 mm				
Gomes-Filho et al. (2018) ¹⁸							
Probing depth (PD)	\geq 4 teeth with \geq 1 site with PD \geq 5 mm	\geq 4 teeth with \geq 1 site with PD \geq 4 mm	\geq 4 teeth with \geq 1 site with PD \geq 4 mm	Individuals who were not included in the previous groups			
	AND	AND	AND				
Clinical attachment level (CAL)	$CAL \ge 5 \text{ mm on the}$ same site	$CAL \ge 3 \text{ mm on the}$ same site	$CAL \ge 1 \text{ mm on the}$ same site				
	AND	AND	AND				
Bleeding upon probing	Bleeding upon stimulus (on the same site)	Bleeding upon stimulus (on the same site)	Bleeding upon stimulus (on the same site)				

TABLE 1 Diagnostic criteria used for periodontitis case definitions

syncope), (2) changes in heart electrical conduction during the electrocardiogram examination (ECG) and, (3) elevation and rapid rising of myocardial cell necrosis markers: Creatine Kinase-MB (CK-MB) > 4.45 ng/mL in two successive assays or in only one assay, if the value was more than twice the reference value, and troponin T in serum > 0.1 µg/mL, at least once during the first 24 hours.²³⁻²⁵ The enzyme assays were performed using the chemiluminescence technique.

2.6 | Covariables investigated

The following covariables were investigated: age (in years), sex (male or female), race/skin color (white or not white), marital status (married, single, divorced, or widowed), schooling level (in years of study), family income (in minimum salary), homeowner (yes or no), and household density (number of persons in the household). Current smoking habit (yes or no, in the last 6 months), alcoholic beverage consumption (yes or no, at least three times a week), physical activity (active or not, walking, weight training, among others, at least three times a week), consultation with dentist (yes or no, at least once a year), participant received oral health guidance (yes or no, at least once in a lifetime), tooth brushing (yes or no and frequency of brushing), dental floss usage (yes or no, at least once a day). Presence or absence of the following diseases or conditions pulmonary disease, renal disease, hypercholesterolemia, and BMI (kg/m²). They were categorized according to their distribution in the sample, or with previous studies on the topic.

2.7 | Data analysis

Descriptive analysis was performed on the exposure variables (mild, moderate, and severe periodontitis), outcome variable (AMI) and all covariables. To assess the degree of homogeneity between the case and control groups, the chi-square test of Pearson was used for categorical variables, because of the distribution of the covariables, with a significance level of 5%.

The selection of modifier and confounding covariables was based on a presumed causality relationship between periodontitis severity levels and AMI. Thereby, a theoretical conceptual framework was employed and the following covariables were selected as confounders: schooling level, current smoking habit, hypercholesterolemia, and BMI. Additionally, the presence of effect-modifying covariables was investigated using the maximum likelihood ratio test (P < 0.05). For those covariables in which the presence of effect modification was not identified, the presence of confounders was tested using the backward strategy, a covariable being considered confounding when producing a change of at least 10% in the association measurement.

Association measurements between periodontitis severity levels and AMI were performed by conditional logistic regression analysis. Thus, measurements were estimated using statistical models constructed as follows: mild periodontitis versus no periodontitis, moderate periodontitis versus no periodontitis, severe periodontitis versus no periodontitis. Odds ratios (ORs) and their 95% confidence intervals (CIs), both crude and adjusted, were obtained from all possible statistical models.

To validate the analysis models employed, the Hosmer-Lemeshow test was used to verify the goodness of fit of the conditional logistic regression models. Data analysis was performed using SPSS—Statistical Package for the Social Sciences, version 17.0^* and STATA version 10.0.

3 | RESULTS

The initial sample of the present study included 633 individuals that were invited and accepted; however, 12 of them (six women in the case group and six men belonging to the control group) withdrew from participation during the examination period, constituting a loss rate of 1.9%. A total of 621 participants, 300 women and 321 men were enrolled in this study, with a mean age for the case group of 59.66 \pm 10.97 (\pm SD), median of 58 years and a range of 41 to 91 years and for the control group of 59.29 \pm 10.87 (\pm SD), median of 59 years and a range of 40 to 89 years.

Table 2 shows the socioeconomic-demographic characteristics, related to life habits and general health status of the case group and the control group, with no statistically significant difference among the groups for the majority of the evaluated covariables. Covariables with few observations were not included in Table 2.

Regarding the characteristics related to general health and severity of periodontitis, statistically significant differences were observed among the comparison groups for the following covariables: hypercholesterolemia (P = 0.03) and levels of moderate (P = 0.02 and P = 0.02) and severe periodontitis (P = 0.04 and P < 0.01) for the two definition criteria used. Individuals diagnosed with AMI when compared to controls had a higher occurrence of hypercholesterolemia.

The distribution of periodontitis levels varied considerably depending on the type of severity definition criteria employed (Table 2). Mild periodontitis frequency was very low in both groups, making it impossible to estimate the association measurement for this level. For moderate periodontitis, the occurrence was approximately three to five times greater using the CDC-AAP (2007, 2012)^{16,17} criterion when compared to that of Gomes-Filho et al. (2018),¹⁸ also for both comparison groups. Severe periodontitis frequency was approximately four to six times higher using CDC-AAP (2007, 2012)^{16,17} criterion when compared to that of Gomes-Filho et al. (2018),¹⁸ in both cases and controls. Furthermore, using the CDC-AAP (2007, 2012)^{16,17} criterion, the occurrence of individuals without periodontitis was less than 10%,

* SPSS Inc., Chicago, IL.

both in the case group and in the control. The frequency of moderate and severe periodontitis severity levels was compared, showing a statistically significant difference among the groups.

All crude measurements showed an association between moderate and severe periodontitis and AMI, with statistical significance (Table 3). The magnitude of the association was lower than the other definition when the criterion of Gomes-Filho et al. $(2018)^{18}$ was used to define the level of periodontitis severity: moderate and severe ($OR_{crude} = 1.73, 95\%$ CI: [1.10 to 2.73], and $OR_{crude} = 2.19, 95\%$ CI: [1.03 to 4.65], respectively). The magnitude of the association according to the CDC-AAP definition (2007; 2012)^{16,17} for moderate and severe periodontitis was $OR_{crude} = 2.82, 95\%$ CI: [1.16 to 6.85], and $OR_{crude} = 4.18, 95\%$ CI: [1.66 to 10.51], respectively.

In the final model of the conditional logistic regression analysis, modifier factors were not identified. Four covariables were selected as confounders: schooling level, current smoking habit, hypercholesterolemia, and BMI. However, for the association between severe periodontitis and AMI, when using the Gomes-Filho et al. (2018)¹⁸ criterion, because of the number of available cases, only three confounders were selected.

After adjustments (Table 3), the association was confirmed. When the Gomes-Filho et al. criterion for periodontitis was employed (2018),¹⁸ the adjusted measurements showed a slight increase compared to the crude measurements ($OR_{adjusted} = 1.96$, 95% CI: [1.21 to 3.17] and $OR_{adjusted} = 2.21,95\%$ CI: [1.03 to 4.73], moderate and severe periodontitis, respectively). In contrast, for the CDC-AAP criteria (2007, 2012),^{16,17} the adjusted measurements showed a slight decrease ($OR_{adjusted} = 2.51, 95\%$ CI: [1.02 to 6.19], and OR_{adjusted} = 3.92, 95% CI: [1.53 to 10.05], moderate and severe periodontitis, respectively). Adjusted measurements for the association between periodontitis (moderate and severe) and AMI showed that among those participants with moderate and severe periodontitis, the chance of having AMI was approximately two to four times higher than among those without periodontitis. However, the chance of having AMI was higher among those individuals with severe periodontitis than those with moderate periodontitis, for both definition criteria of periodontitis severity used in this study, demonstrating a possible relationship among the levels of periodontitis severity on AMI.

The Hosmer-Lemeshow statistical test was applied to verify the goodness of fit of the regression models employed. P values ranged from 0.07 to 0.22 and the null hypothesis was rejected, indicating the good quality of the regression models used. 6

TABLE 2 Number (N) and percentage (%) of characteristics related to socioeconomic, demographic, life habits and oral health status, general health conditions and severity of periodontitis between case (individuals with a diagnosis of acute myocardial infarction) and control (individuals with no history of acute myocardial infarction) groups

	Case group		Control group		
Characteristics	<i>N</i> = 207		N = 414		
Age (in years)	Ν	%	Ν	%	$P^{^{\mathrm{a}}}$
≥59	103	49.8	211	51.0	0.77
Sex					
Male	109	52.7	212	51.2	0.73
Race/skin color					
Not white	173	83.6	328	79.2	0.20
Marital status					
Single/divorced/widowed	84	40.8	173	42.0	0.77
Schooling level (years of study)					
≤4 years	163	78.7	321	77.5	0.73
Family income ^b					
≤1 minimum salary	109	53.7	222	54.9	0.77
Homeowner					
No	25	12.6	50	12.3	0.93
Household density					
>3 persons	88	42.9	185	45.2	0.59
Current smoking habit					
Yes (in the last 6 months)	34	16.4	52	12.6	0.19
Alcoholic beverage consumption					
Yes (at least three times a week)	101	49.0	180	43.6	0.20
Physical activity					
No	129	65.8	260	65.2	0.87
Consultation with dentist					
No	72	34.8	152	36.7	0.64
Participant received guidance on oral health					
No	105	50.7	205	49.6	0.80
Frequency of tooth brushing					
Insufficient—less than three times per day	115	56.6	240	58.8	0.61
Dental floss usage					
No	165	82.1	338	84.1	0.54
Pulmonary disease					
Yes	07	3.4	17	4.1	0.66
Renal disease					
Yes	21	10.3	39	9.5	0.74
Hypercholesterolemia					
Yes	23	11.1	25	6.0	0.03
Body mass index (kg/m ²)					
≥25	128	69.9	239	63.4	0.13
Severity of periodontitis (Gomes-Filho et al. 2018) ¹⁸					
Severe periodontitis	15	7.2	15	3.6	0.04
Moderate periodontitis	43	20.8	57	13.8	0.02
Mild periodontitis	0	-	03	0.7	-
No periodontitis	149	72.0	339	81.9	

(Continues)

TABLE 2 (Continued)

	Case group)	Control g	roup	
Characteristics	<i>N</i> = 207		N = 414		
Severity of periodontitis (CDC-AAP 2007, 2012) ^{16,17}					
Severe periodontitis	64	30.9	91	22.0	< 0.01
Moderate periodontitis	134	64.7	285	68.8	0.02
Mild periodontitis	02	1.0	0	-	-
No periodontitis	07	3.4	38	9.2	

^a*P* value: significance level ≤ 0.05 .

^bMinimum salary value at the time of data collection: R\$465,00 (US\$ 273.22/monthly).

TABLE 3 Crude and adjusted odds ratio (OR) for the association between periodontitis severity level and acute myocardial infarction (AMI)

Periodontitis severity level and AMI	OR _{crude}	95% CI	P^{a}	OR _{adjusted}	95% CI	$\boldsymbol{P}^{\mathrm{a}}$
Gomes-Filho et al. (2018) ¹⁸ criterion						
Moderate periodontitis	1.73	1.10-2.73	0.02	1.96 ^b	1.21-3.17	< 0.01
Severe periodontitis	2.19	1.03-4.65	0.04	2.21 ^b	1.03-4.73	0.04
CDC-AAP (2007, 2012) ^{16,17} criterion						
Moderate periodontitis	2.82	1.16-6.85	0.02	2.51 [°]	1.02-6.19	0.05
Severe periodontitis	4.18	1.66-10.51	< 0.01	3.92°	1.53-10.05	< 0.01

^a*P* value: significance level ≤ 0.05 .

^bAdjusted for schooling level, current smoking habit, and hypercholesterolemia.

^cAdjusted for schooling level, current smoking habit, hypercholesterolemia, and body mass index.

4 | DISCUSSION

The main findings of this study showed that there is an association between moderate and severe periodontitis severity levels and AMI, for the two sets of criteria used, after adjustment of the association measurement for the following confounders: schooling level, current smoking habit, hypercholesterolemia, and BMI. These findings are in agreement with the few previous studies on the topic.^{5,9} The more recent study found association between severe periodontitis and myocardial infarction only in females.¹⁰

The magnitude of the observed association between periodontitis severity levels and AMI varied widely in previous studies (OR = 1.08 to 14.01)⁵⁻¹⁰ in comparison with the association measurements of this study (OR = 1.96 to 3.92). One of the factors that may have influenced on these results is that most previous studies used small sample sizes, reflecting on the accuracy of the association measurements. Another factor is the multiple periodontitis severity levels definitions employed. A recent investigation⁹ used one of the criteria employed in the present study^{16,17}; however, the participants were divided only in two groups: (1) with severe periodontitis, and (2) without severe periodontitis, that included moderate and mild periodontitis and no periodontitis in the same stratum.

In this study, one of the criteria employed to stratify periodontitis, according to its three severity levels, is endorsed by the CDC-AAP of the United States of America.^{16,17} The second set of criteria combine three clinical parameters: probing depth, clinical attachment level, and bleeding on probing to define disease severity levels, for at least four teeth with one or more compromised sites.¹⁸ Bleeding on probing added the evaluation of gingival inflammation. In addition to adding another clinical parameter, this second set of criteria also uses a greater number of sites compromised by the disease for diagnosis when compared to the CDC-AAP criterion.^{16,17} The magnitude of the association measurements, both for moderate periodontitis and AMI and for severe periodontitis and myocardial infarction, was higher when using the second set of criteria^{16,17} than for the first set of criteria.¹⁸

The difference in the occurrence of periodontitis severity levels among the criteria is because of the fact that the CDC-AAP criterion^{16,17} is used for periodontitis screening in population-based studies, whereas the Gomes-Filho et al. criterion¹⁸ has higher specificity, which avoids false-positive diagnosis of periodontitis among participants.²⁶

Another finding of this study is that the association measurements between severe periodontitis and myocardial infarction were higher than those of moderate periodontitis and the outcome. It suggested a possible relationship among the levels of periodontitis severity on the infarction. However, in relation to the lower level of severity, the number of individuals classified with mild periodontitis was too small for the present sample, probably because of the high average age of the studied group, which was around 60 years. Thus, it was not possible to estimate the association measurement

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for the mentioned stratum. It therefore cannot be stated from the present study findings that there is a dose-response relationship between periodontitis severity levels and myocardial infarction.

Moreover, periodontitis can predispose to myocardial infarction as a result of a number of possible biological mechanisms that, together, may be responsible for the increased inflammatory response in atheromatous lesions because of periodontal infection.⁴ These mechanisms include increased systemic levels of inflammatory mediators stimulated by bacteria or their products in distant sites of the oral cavity. Besides that, high hemostatic and thrombotic markers that promote a prothrombotic and inflammation status; cross-reactive systemic antibodies that promote inflammation and interact with the atheroma; dyslipidemia promotion with a consequent increase in proinflammatory lipid classes and subclasses; and common genetic susceptibility factors present in both diseases leading to increased inflammatory responses.²⁷⁻³¹

With the aim of strengthening the results, during the sample selection the cases and controls were matched for sex and age, as well as the adjustments performed in the analysis to neutralize these confounders, given that they can influence both the exposure and the outcome.

The conceptual framework for this study was based on the knowledge that both the frequency of periodontitis and infarction increases with age.^{7,32-34} Moreover, it has higher frequency in men,^{6,7,33} in smokers,^{7,8,33,35} in overweight or obese individuals,^{7,33,36,37} and in those with hypercholesterolemia.^{6,7,33} Furthermore, among those with the lowest socioeconomic status, represented in this study by schooling level, the frequency of these two diseases is also higher.^{5,38,39} Considering the limit of confounders able to be included in the adjusted analysis model, as well as preventing overadjustment, only one covariable was selected to represent the general health condition: hypercholesterolemia.³⁹

It is known that other factors could be associated with periodontitis and myocardial infarction characterizing a limitation of the study. Genetic factors, for example, likely play a role in this association.¹ Moreover, one cannot exclude the possibility of a spurious association between the two diseases because of residual confounding represented by factors that were not measured in this study. Another limitation is the observational, case-control design, which is not the most suitable design to infer a causal link between the two studied conditions.

5 | CONCLUSION

These research results suggest that the more severe the periodontal condition is, the greater the relationship with myocardial infarction, that is, severe periodontitis has a higher strength of association than moderate periodontitis in relation to myocardial infarction. The results argue for provision of dental care for individuals with more severe levels of periodontitis, as these conditions may be related to myocardial infarction.

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ORCID

Isaac S. Gomes-Filho https://orcid.org/0000-0002-4270-8491 Ana Cláudia M.G. Figueiredo https://orcid.org/0000-0003-2842-9848 Frank Scannapieco https://orcid.org/0000-0002-8804-6593

REFERENCES

- Tonetti MS, Van Dyke TE; Working Group 1 of the Joint EFP/AAP Workshop. Periodontitis and atherosclerotic cardiovascular disease: consensus report of the Joint EFP/AAP Workshop on Periodontitis and Systemic Diseases. J Periodontol. 2013;84(4 Suppl):S24-S29.
- Gupta M, Chaturvedi R, Jain A. Role of cardiovascular disease markers in periodontal infection: understanding the risk. *Indian J Dent Res.* 2015;26(3):231-236.
- Andriankaja OM, Genco RJ, Dorn J, et al. The use of different measurements and definitions of periodontal disease in the study of the association between periodontal disease and risk of myocardial infarction. *J Periodontol*. 2006;77(6):1067-1073.
- Schenkein HA, Loos BG. Inflammatory mechanisms linking periodontal diseases to cardiovascular diseases. J Clin Periodontol. 2013;14:S51-69.
- Persson RG, Ohlsson O, Pettersson T, Renvert S. Chronic periodontitis: a significant relationship with acute myocardial infarction. *Eur Heart J.* 2003;24(23):2108-2115.
- 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 Periodontal Res.* 2005;40(1):36-42.
- Stein JM, Kuch B, Conrads G, et al. Clinical periodontal and microbiologic parameters in patients with acute myocardial infarction. *J Periodontol*. 2009;80(10):1581-1589.
- Marfil-Álvarez R, Mesa F, Arrebola-Moreno A, et al. Acute myocardial infarct size is related to periodontitis extent and severity. *J Dent Res.* 2014;93(10):993-998.
- Górski B, Nargiełło E, Grabowska E, Opolski G, Górska R. The association between dental status and risk of acute myocardial infarction among poles: case-control study. *Adv Clin Exp Med*. 2016;25(5):861-870.

- Organization W-WH. Cardiovascular diseases. 2017. https://www. who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(CV DS). Accessed December 5, 2019.
- Organization W-WH. The top 10 causes of death. 2018. https:// www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-de ath. Accessed December 5, 2019.
- DATASUS. Information systems in health—vital statistics (in Portuguese). 2018. http://tabnet.datasus.gov.br/cgi/deftohtm.exe?sim/ cnv/obt10uf.def. Accessed 28 April, 2018.
- Tonetti MS, Jepsen S, Jin L, Otomo-Corgel J. Impact of the global burden of periodontal diseases on health, nutrition and wellbeing of mankind: a call for global action. *J Clin Periodontol*. 2017;44(5):456-462.
- Caton JG, Armitage G, Berglundh T, et al. A new classification scheme for periodontal and peri-implant diseases and conditions introduction and key changes from the 1999 classification. *J Clin Periodontol.* 2018;89(suppl 1):S1-S8.
- Page RC, Eke PI. Case definitions for use in population-based surveillance of periodontitis. *J Periodontol*. 2007;78(7):1387-1399.
- Eke PI, Page RC, Wei L, Thornton-Evans G, Genco RJ. Update of the case definitions for population-based surveillance of periodontitis. *J Periodontol*. 2012;83(12):1449-1454.
- Gomes-Filho IS, Trindade SC, Passos-Soares JS, et al. Clinical diagnosis criteria for periodontal disease: an update. *J Dent Health Oral Disord Ther*. 2018;9(5):354-356. https://doi.org/10.15406/jdhodt.2018.09.00408
- Rose G, McCartney P, Reid DD. Self-administration of a questionnaire on chest pain and intermittent claudication. *Br J Prev Soc Med.* 1977;31(1):42-48.
- Pihlstrom BL, Ortiz-Campos C, Mchugh RB. A randomized fouryears study of periodontal therapy. *J Periodontol*. 1981;52(5):227-242.
- 21. Ramfjord SP. Indices for prevalence and incidence of periodontal disease. *J Periodontol*. 1959;30(1):51-59.
- Ainamo J, Bay I. Periodontal indexes for and in practice. *Tandlaege-bladet*. 1976;80(5):149-152.
- Cannon CP, Weintraub WS, Demopoulos LA, et al. Comparison of early invasive and conservative strategies in patients with unstable coronary syndromes treated with the glycoprotein IIb/IIIa inhibitor tirofiban. N Engl J Med. 2001;344(25):1879-1887.
- 24. Kumar A, Cannon CP. Acute coronary syndromes: diagnosis and management, part I. *Mayo Clin Proc.* 2009;84(10):917-938.
- (SBC) BSoC. Guidelines of the Brazilian Cardiology Society on unstable angina and acute myocardial infarction without ST segment elevation (IInd ed., 2007). 2014. http://publicacoes.cardiol.br/ consenso/2007/diretriz_SIMI.asp. Accessed February 14, 2016.
- Gomes-Filho IS, Cruz SS, Rezende EJ, et al. Exposure measurement in the association between periodontal disease and prematurity/low birth weight. *J Clin Periodontol*. 2007;34(11):957-963.

 Preshaw PM, Taylor JJ. How has research into cytokine interactions and their role in driving immune responses impacted our understanding of periodontitis. *J Clin Periodontol*. 2011;11(38 suppl):60-84.

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- Gibson FC, Genco CA. Porphyromonas gingivalis mediated periodontal disease and atherosclerosis: disparate diseases with commonalities in pathogenesis through TLRs. *Curr Pharm Des*. 2007;13(36):3665-3675.
- Gibson FC, Yumoto H, Takahashi Y, Chou HH, Genco CA. Innate immune signaling and Porphyromonas gingivalis-accelerated atherosclerosis. *J Dent Res.* 2006;85(2):106-121.
- Hayashi C, Gudino CV, Gibson FC, Genco CA. Review: pathogeninduced inflammation at sites distant from oral infection: bacterial persistence and induction of cell-specific innate immune inflammatory pathways. *Mol Oral Microbiol.* 2010;25(5):305-316.
- Teles R, Wang CY. Mechanisms involved in the association between periodontal diseases and cardiovascular disease. *Oral Dis.* 2011;17(5):450-461.
- de Macêdo TC, Costa Mda C, Gomes-Filho IS, Vianna MI, Santos CT. Factors related to periodontal disease in a rural population. *Braz Oral Res.* 2006;20(3):257-262. https://doi.org/10.1590/S1806-83242006000300014.
- Dregan A, Charlton J, Chowienczyk P, Gulliford MC. Chronic inflammatory disorders and risk of type 2 diabetes mellitus, coronary heart disease, and stroke: a population-based cohort study. *Circulation*. 2014;130(10):837-844.
- D'Aiuto F, Sabbah W, Netuveli G, et al. Association of the metabolic syndrome with severe periodontitis in a large U.S. population-based survey. *J Clin Endocrinol Metab.* 2008;93(10): 3989-3994.
- Susin C, Oppermann RV, Haugejorden O, Albandar JM. Periodontal attachment loss attributable to cigarette smoking in an urban Brazilian population. *J Clin Periodontol*. 2004;31(11):951-958.
- Jagannathachary S, Kamaraj D. Obesity and periodontal disease. J Indian Soc Periodontol. 2010;14(2):96-100.
- Dahiya P, Kamal R, Gupta R. Obesity, periodontal and general health: relationship and management. *Indian J Endocrinol Metab.* 2012;16(1):88-93.
- Rothman KJ, Greeland S, Lash TL. Modern Epidemiology. Porto Alegre: Artmed; 2011:405-445. https://shop.lww.com/ Modern-Epidemiology/p/9781451190052
- Rashid S, Simms A, Batin P, Kurian J, Gale CP. Inequalities in care in patients with acute myocardial infarction. *World J Cardiol.* 2015;7(12):895-901.

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