[RETRACTED ARTICLE] Association between periodontal disease and subclinical atherosclerosis: the ELSA-Brasil study

[ARTIGO RETRATADO] Associação entre doença periodontal e aterosclerose subclínica: estudo ELSA-Brasil

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To the Editor: We wish to retract our article *Association Between Periodontal Disease and Subclinical Atherosclerosis: The ELSA-Brasil Study*, published in CSP in May 2012. Contrary to the article's title and methodology as described, the data did not come from the ELSA-Brasil study [Brazilian Longitudinal Study of Adult Health], but were collected independently and with different objectives. Thus, the article is not a supplementary study to the ELSA-Brasil study and should not be referred to as such. The point in common between this study and ELSA-Brasil is that the study population in both consists of employees from a public university in the State of Espírito Santo, Brazil. However the points and methodology for measuring the intima-media thickness (IMT) were different from those adopted by ELSA-Brasil. The authors apologize to the Executive Board of the ELSA-Brasil study and to the Editor and readers of *Cadernos de Saúde Pública* for this error.

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Association between periodontal disease and subclinical atherosclerosis: the ELSA-Brasil study

Associação entre doença periodontal e aterosclerose subclínica: Estudo ELSA-Brasil

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Abstract

The aim of this study was to investigate the relationship between periodontal disease and increased thickness of the carotid artery intima-media complex. A cross-sectional study was conducted with 220 adults (age ≥ 35 years) among participants in the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil). Carotid artery ultrasound and periodontal clinical examinations were conducted and included visible plaque index, gingival bleeding on probing index, probing pocket depth (PPD), and clinical attachment level (CAL). Individuals with increased carotid artery thickness showed fewer teeth and higher frequency of CAL ≥ 3mm, CAL ≥ 4mm, CAL ≥ 5mm, and CAL ≥ 6mm and PPD ≥ 4mm (p < 0.05). Despite the use of 18 definitions for periodontal disease, only one confirmed the hypothesis of an association between periodontal disease and subclinical atherosclerosis. Individuals with 10% or more sites with CAL ≥ 4mm were more likely to present carotid thickening.

Atherosclerosis; Carotid Artery Diseases; Periodontics

Introduction

Atherosclerosis is one of the leading causes of adult mortality and morbidity in Latin America [1]. Due to its different etiologies, many underlying causes remain unknown [2].

Studies have suggested that periodontal disease is associated with the early development of atherosclerotic lesions in the carotid artery [3,4,5,6]. Periodontal disease is a chronic multifactorial immune disease that occurs in response to periodontopathogenic antigens. The condition begins with inflammation of the tissues surrounding and supporting the teeth and can progress until involving the entire periodontium, including the alveolar bone, cementum, and periodontal ligament, leading to irreversible loss of the periodontium and eventually tooth loss in the more advanced stages [7].

The association between periodontal disease and atherosclerotic cardiovascular disease has received considerable attention [8,9], but these studies' findings are not consistent. Some studies report that periodontal disease, through an inflammatory process, can cause infection of the vascular endothelium and contribute to the occurrence of atherosclerosis, increasing the risk of myocardial ischemia and infarction, always preceded by thromboembolic events [10]. In addition to this hypothesis, it has been suggested that periodontal microorganisms can induce or accelerate atherosclerosis through different

mechanisms, for example: favoring the local increase in lymphocytes, macrophages, and production of tissue growth factors; local release of endotoxin (lipopolysaccharides), and molecular mimicry between microbial and human heat shock protein 60, inducing an autoimmune reaction. In addition, the systemic increase in cytokines with activation of inflammatory markers and stimulation of pro-coagulants can lead to thrombosis and acute ischemia, besides inducing changes in lipoproteins, resulting in pre-atherosclerotic conditions [11].

Mild to moderate periodontal disease affects 30-50% of the adult population, while the severe generalized form affects 5-15% of adults in the United States [12]. The multifactorial etiology of periodontal disease includes both specific subgingival bacteria and individual factors such as age, race, and gender, and systemic factors like smoking, diabetes, osteoporosis, and stress. In addition, poor diet, low socioeconomic status, and limited access to health services have been associated with its occurrence [12].

Among the risk factors presented for periodontal disease, age, smoking, and diabetes mellitus are generally considered potential confounding variables in studies on associations in periodontal disease [10].

Inflammation is a common characteristic both in atherosclerosis and periodontal disease, and thus a common mediator of these two conditions [13,14]. There is no consensus concerning the possible influence of periodontal disease on the thickness of the carotid artery intima-media complex (IMC). The majority of studies that have evaluated this association present methodological limitations, like small sample size, lack of control of confounding variables, presence of bias, and discrepancies in the case definition for periodontal disease [15,16], thus limiting the internal validity and potentially jeopardizing the conclusions.

The majority of the literature reviewed in the studies [8,17] supports a modest association between periodontal disease and atherosclerosis. However, lack of standardization of measures and definitions of periodontal disease, as well as the potential confounding factors common to both conditions, hinder interpretation of the results [18].

A better understanding of the relationship between periodontal disease and the risks of subclinical atherosclerosis motivated the current study, the objective of which was to investigate the relationship between clinical parameters of periodontal disease and thickening of the carotid IMC, used as a proxy for diagnosing subclinical vascular disease in adults.

Methods

Participants

A cross-sectional study was conducted among participants in the *Brazilian Longitudinal Study of Adult Health* (the ELSA-Brasil). The ELSA-Brasil study is a multicenter cohort study consisting of 15 thousand employees from public institutions of higher learning and research in the Northeast, South, and Southeast regions of Brazil. The purpose of the study is to investigate the incidence and risk factors for chronic diseases, in particular cardiovascular diseases and diabetes. The supplemental oral health study for ELSA-Brasil was based on data collected in the ELSA project in the State of Espírito Santo in 2009-2010, after anthropometric examination and carotid ultrasound.

This study's target population consisted of male and female active and retired employees from 35 to 74 years of age, from the ELSA project/Espírito Santo. The sample universe consisted of the 497 participants in the ELSA project that were treated and had undergone ultrasound of the common carotid artery by a single examiner. Providing for possible losses, all were invited to participate in the study. The only exclusion criterion was the use of total upper and lower dental prostheses.

The final sample consisted of 220 participants (78 with increased IMC thickness and 142 with normal IMC). This sample size allowed detecting an expected 25% (estimated) difference between the proportion of periodontal disease in the sample with normal carotid IMC and in the sample with altered carotid IMC, with a minimum power of 80% and 5% significance.

An intra-examiner clinical calibration study for the periodontal examination was conducted previously. A single examiner responsible for examination in the principal study performed the intra-examiner calibration, under the supervision of the external observer, in the same location and under the same conditions of lighting and instrumentation, with employees from the same age bracket as the study participants. Seventeen patients were examined, with 48-hour intervals between examinations. The clinical parameters considered for calibration were: probing pocket depth (PPD) and clinical attachment level (CAL) of teeth 16, 11, 27, 31, 37, and 46, with a total of 96 measurements performed (48 measurements at two moments). Reliability between measurements was tested using the intra-class correlation coefficient (ICC) and comparison of the means with the matched t test. Of 48 comparisons, 41 showed statistically significant correlations, of which 5 with ICC > 0.80 and 3 with ICC

from 0.50 to 0.80. The analysis did not include three comparisons, because there was no variation in the measurements. In the comparison of means, 47 of the 48 comparisons were statistically significant.

Periodontal clinical examination

Participants were submitted to periodontal examination by a single calibrated examiner who was blind to the carotid ultrasound data.

Periodontal clinical measurements used in the study were: plaque index (PI) [19], gingival bleeding index (GBI) [19], PPD, and CAL. The PI and GBI parameters were measured dichotomously as the presence or absence of bacterial plaque and bleeding after periodontal probing.

For PPD, CAL, GBI, and PI, six measurements were taken per tooth, corresponding to the mesiobuccal, midbuccal, distobuccal, mesiolingual, midlingual, and distolingual surfaces. All the clinical measurements were taken in all the teeth, except for the third molars.

PPD measurements were recorded in millimeters from the free gingival margin to the bottom of the gingival sulcus or periodontal pocket. In the CAL measurements, the cementum-dentin junction and gingival level were used as reference points. PPD and CAL measurements were recorded with a North Carolina model periodontal probe (Hu-Friedy, Chicago, USA), with 1-millimeter markings over a total of 15 mm and a tip with 0.35mm diameter.

When the gingival margin or cementum-dentin junction was located between two marks on the periodontal probe, the value from the deepest marking was recorded. In addition to the periodontal measurements, the number of natural teeth was also recorded. All measurements were taken in a single sitting.

Ultrasound examination

The arterial wall consists of three layers: the intima, a thin endothelial layer that borders on the blood-filled lumen; the adventitia, the external layer bordering on the surrounding tissue, and the media, a layer between these internal and external layers. Due to the easily discernible borders between the lumen and the intima and between the media and adventitia, the intima and media are generally evaluated together, which provides the measurement of the IMC thickness.

Progression of atherosclerotic disease is frequently accompanied by a visible thickening of the IMC and the presence of fibrotic or calcified plaques [20].

Measuring the carotid artery IMC thickness is a way of evaluating one of the most important indicators of cardiovascular disease in patients. Its use is based on the possibility of predicting the outcomes of future cardiovascular events with a non-invasive technique, namely ultrasound (US), providing a diagnostic gain based on the importance of IMC thickening as a risk factor for cardiovascular disease [20].

IMC thickness was measured bilaterally next to the carotid sinus at the base of the neck, using Toshiba Ultrasound Aplio XG (Model SSA, 790 A, Toshiba, Barueri, Brazil). The test was performed by a researcher who was blind to the periodontal parameters and other patient characteristics.

Comparison groups

There is still much disagreement on which IMC thickness offers the best result for methodological standardization. Standardization of a protocol to measure IMC changes would facilitate the comparison of results from studies using this technique [20].

According to the consensus statement of the American Society of Echocardiography on the use of carotid ultrasound to identify subclinical vascular disease, the sample's 75th percentile corresponds to the values adopted as possible future risk of cardiovascular disease [20].

This study used the value corresponding to the sample's 75th percentile as altered carotid IMC thickness, which varied from 0.95mm in the right common carotid artery to 0.98mm in the left common carotid artery. Thus, participants with right common carotid artery ≥ 0.95mm and left common carotid artery ≥ 0.98mm were defined as having altered carotid IMC.

Covariables

The sociodemographic characteristics were collected through a structured interview conducted by trained interviewers and included: age, gender, marital status, self-reported race/skin color, schooling, family income, smoking, and self-reported hypertension, diabetes, and insulin use. The anthropometric characteristic evaluated by the study was body mass index (BMI = kg/m^2), or weight (kg) divided by height squared (m^2). The equipment used to obtain these measurements included a stadiometer accurate to 0.1cm, electronic scales calibrated in grams (Toledo 200kg; Toledo do Brasil Indústria de Balanças Ltda., São Bernardo do Campo, Brazil), anthropometric tape measure, 150cm – Mabbis, Gulick model (CARDIOMED, Curitiba, Brazil), 20kg test weight – total 80kg, mobile footrest with height on 8cm

plane, and 1.20x0.50cm mirror. BMI was classified according to the World Health Organization (WHO) classification [21].

Periodontal clinical parameters and definition of periodontal disease

All the clinical parameters, PI, GBI, PPD, and CAL, were computed for each study subject and later for each group (normal and altered carotid IMC thickness). Clinical parameters analyzed by the study were number and frequency of sites with PPD and CAL ≥ 3mm, ≥ 4mm, ≥ 5mm, and ≥ 6mm.

Thirteen different definitions of periodontal disease were used according to the literature [12,15,22,23,24,25,26,27,28,29,30,31,32], plus five more definitions. Definition 1: 10% or more sites with PPD ≥ 4mm and CAL ≥ 4mm; definition 2: 10% or more sites with PPD ≥ 4mm and CAL ≥ 4mm and GBI ≥ 10%; definition 3: 20% or more sites with CAL ≥ 3mm; definition 4: 20% or more sites with CAL ≥ 4mm; and definition 5: 10% or more sites with CAL ≥ 4mm.

Statistical analysis

Comparisons between IMC groups were performed with the chi-square test, Fisher's exact test, Mann-Whitney test, and t test. Correlation between the periodontal clinical parameters and carotid artery IMC thickness was evaluated with the Spearman correlation coefficient. Simple logistic regression was performed to test the association between different definitions of periodontal disease and altered carotid IMC thickness through odds ratios (OR) with 95% confidence intervals (95%CI). Multivariate analyses were then used to adjust covariables. All analyses used SPSS, version 18.0 (SPSS Inc., Chicago, USA). Statistical significance was set at 0.05 ($p \leq 0.05$).

Research ethics issues

Participants were required to sign a prior informed consent form. The project was approved by the Institutional Review Board of the Federal University in Espírito Santo (Universidade Federal do Espírito Santo; protocol nº. 145/08).

Results

The sample consisted of 220 individuals among the 497 participants in the ELSA-ES project. It was not possible to contact 160 participants (32.1%).

Of the 337 individuals that were invited, 61 (18.1%) refused to participate. Of the 276 that agreed, 45 (16%) failed to appear for the examination and 11 (4.34%) were excluded because they were using total upper and lower dental prostheses (Figure 1).

There were proportionally more females among the group that agreed to participate (58.2%). 65.8% of the study sample were married. White skin color/race was the most common (45.4%), followed by brown race (*pardo*) (33.5%). Table 1 shows the participants' sociodemographic characteristics.

Table 2 shows the sociodemographic characteristics and BMI according to IMC thickness (altered versus normal). Mean age and the proportion of male individuals and those with diabetes, hypertension, and overweight/obesity were statistically higher in the group with altered IMC. Smoking did not differ statistically between groups ($p = 0.5604$).

Table 3 compares number of teeth and periodontal parameters between groups. Mean number of teeth present, number of sites with CAL ≥ 3mm, CAL ≥ 4mm, CAL ≥ 5mm, and CAL ≥ 6mm, and frequency of sites with CAL ≥ 4mm, CAL ≥ 5mm, and CAL ≥ 6mm and PPD ≥ 4mm were statistically higher in the group with altered IMC thickness as compared to the group with normal IMC. Associations were observed between periodontal clinical parameters and carotid IMC thickness, based on analyses of correlations. Right carotid artery IMC thickening was correlated with PPD ≥ 5mm and CAL ≥ 5mm and CAL ≥ 6mm ($p < 0.05$), while left carotid artery IMC thickening was associated with PPD ≥ 4mm, PPD ≥ 5mm, and CAL ≥ 5mm and CAL ≥ 6mm ($p < 0.05$) (Table 4).

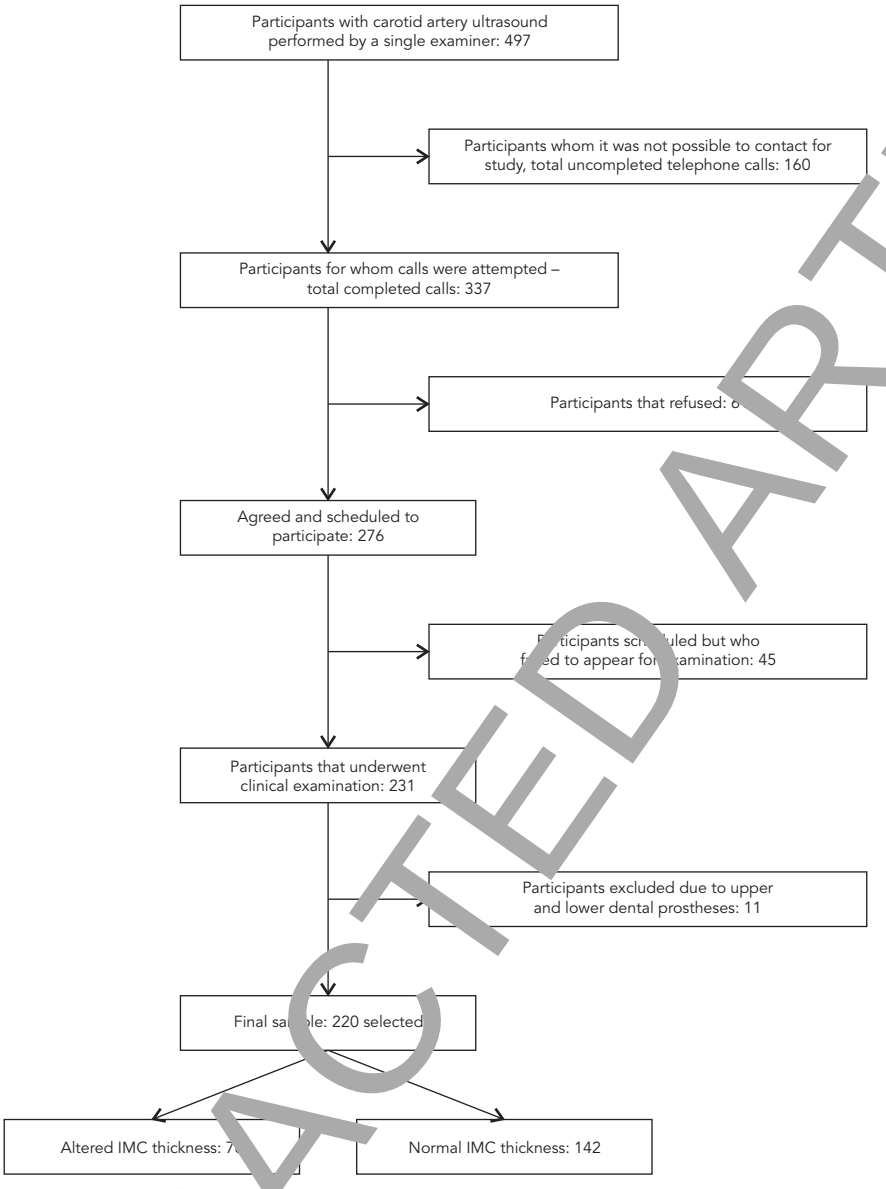
Table 5 shows the crude and adjusted associations between different definitions of periodontal disease and altered carotid IMC thickness.

Among the 18 definitions of periodontal disease, seven showed a positive unadjusted association between periodontal disease and altered carotid IMC thickness. In the multivariate analysis, which included the confounding variables, only definition 5 of periodontal disease remained associated with the outcome. The odds of detecting altered carotid IMC thickness were 2.56 times higher in those with at least 10% of sites with CAL ≥ 4mm (95%CI: 1.12-5.88).

Table 6 shows the results of multivariate analysis between the variables age, gender, hypertension, diabetes, BMI, periodontal disease, and altered carotid IMC thickness. In the final logistic regression model, in addition to periodontal disease (definition 5), only age remained associated with altered carotid IMC thickness (OR = 1.04; 95%CI: 1.01-1.08).

Figure 1

Flow chart for screening participants.



IMC: intima-media complex.

Discussion

In this study, individuals with normal carotid IMC thickness had more teeth present, and tooth loss was statistically higher in individuals with altered IMC thickness, corroborating another study [16] showing that prevalence of carotid plaques increased substantially with increased tooth loss; the largest difference was observed between individuals that lost 10 to 19 teeth compared to those that lost zero to nine teeth. According to the authors, edentulism or increased tooth loss was more likely due to sequelae of periodontal disease [16].

Various clinical parameters of periodontal disease, especially those related to CAL, were statistically correlated with bilateral carotid IMC thickness. In addition, these parameters were

Table 1

Participants' characteristics: variables and covariables of the 220 adults examined in the study.

Variable/Category	All subjects (N = 220)	
	n	%
Age *	52.7 ± 8.5	
Gender		
Female	128	58
Male	92	41.8
Marital status		
Married	144	65.8
Divorced/Separated	36	16.4
Single	27	12.3
Widowed	12	5.5
Race/Color		
White	9	45.4
Brown	73	33.5
Black	44	20.2
Asian/Indigenous	2	1.0
Schooling		
Primary	1	18.8
Secondary	60	27.5
University	43	19.7
Graduate	74	33.9
Family income (minimum wages)		
≤ 3	48	22.1
4-6	77	35.3
7-10	38	17.4
≥ 10	55	25.2

* Mean and standard deviati

more frequent in individuals with altered mean carotid IMC thickness. Although 18 definitions of periodontal disease were used, only one confirmed the hypothesis of an association between periodontal disease and subclinical atherosclerosis. Individuals with 10% or more sites with CAL ≥ 4mm showed higher odds of carotid IMC thickening.

As in the study by Demmer et al. [4], measures of severity and extent of CAL and higher tooth loss were associated with chronic markers such as altered IMC thickness, while the same was not observed with PPD.

Findings from studies on the association between periodontal disease and atherosclerosis are highly dependent on how periodontal disease is defined. There is no consensus on the standard definition for diagnosing periodontal disease in these studies. In addition, other limitations were observed, such as indirect, inadequate, or incomplete measurements of periodontal disease, as well as self-reported periodontal disease [33]. This scenario produces inconsistent findings, leading researchers to question both the magnitude and significance of the observed associations [8,17].

Although there are studies on the association between periodontal disease and cardiovascular diseases, little research has specifically addressed the possible systemic effects of the systemic dissemination of oral microorganisms in humans [4,13].

In a longitudinal study that defined bacterial exposure using immunoglobulin G (IgG) serum antibodies, the odds of carotid atherosclerosis were higher in subjects with elevated levels of oral microorganisms. This association was independent of smoking, suggesting that the latter was not a confounding or effect-modifying variable [14]. Likewise, the present study found no association between smoking and subclinical atherosclerosis.

Table 2

Risk fact ors of the 220 adults according to carotid intima-media complex (IMC) group.

Risk factors/Category	Total (N = 220)	Normal IMC		Altered IMC		%	p-val e
		%	n = 142	%	n = 78		
Age *	52.7 ± 8.5		51.1 ± 8.2		55.4 ± 8.5		0.0001 **
Gender							
Female	128	58.2	91	64.1	37	47.4	0.0166 ***
Male	92	41.8	51	35.9	41	52.6	
Smoking							
Smoker	18	8.3	12	8.5	6	7.8	0.5604 ***
Former smoker	72	33.0	43	30.5	29	37.7	
Never smoked	128	58.7	86	61.0	42	54.5	
Hypertension							
No	134	61.5	96	68.1	38	49.4	0.0066 ***
Yes	84	38.5	45	31.9	39	50.6	
Diabetes							
No	192	88.1	129	[illegible]	63	81.8	0.0352 ***
Yes	26	11.9	12	[illegible]5	14	18.2	
Insulin							
No	214	98.2	140	99.3	74	96.1	0.0938 ***
Yes	4	1.8	1	0.7	3	3.9	
BMI							
Underweight	6	2.7	[illegible]	4.2	0	0.0	0.0211 ***
Normal weight	74	33.6	[illegible]	35.9	23	29.5	
Overweight	98	44.5	62	43.7	36	46.2	
Obesity	38	17.3	[illegible]	16.2	15	19.2	
Morbid obesity	4	1.8	0	0.0	4	5.1	

BMI: body mass index.

* Mean and standard deviation;

** t test;

*** Chi-square test.

Recent studies found modest a sociations between advanced periodontal disease d toot loss and carotid IMC thicken ing in developed countries [4,6]. Other studies w re co ted in individuals with associated co liti ns such as chronic kidney disease [3] or kidney ansplant [34].

The observed as ociat n bet en severe periodontal disease and in eased carotid IMC thickness had been r orte in a previous study [15]. Severe periodo al dise e was associated with increased m n IMC thic ess (OR = 1.312; 95%CI: 1.0 1.6 but this association did not remain after the adju d analysis.

Sev e periodontal disease was also associated th subclinical atherosclerosis (IMC thickness > 0.8 mm) i systemically healthy young individ s and th age ≤ 40 years [5]. Even using nt ag ackets, both the previous study and ur study found an association, so age is an im ortant confounding variable [16]. Another difference that appeared when comparing our findings with those of previous studies relates to the cutoff between altered and normal IMC thickness [5]. It is difficult to compare studies that use the altered versus normal classification of IMC thickness, because there is no consensus on the cutoff to define the altered group, since this is done with the 75th percentile of IMC thickness for the sample. Thus, the classification of altered carotid IMC thickness depends on the distribution of measurements of IMC thickness in each study.

A limitation of the current study was its cross-sectional design, which does not allow inferences on causality. Importantly, only one of the 18 definitions of periodontal disease was associated with carotid IMC thickening after multivariate analysis, and in this measurement only CAL was considered. Although there is no clinical parameter that indicates activity of periodontal disease,

Table 3

Periodontal clinical parameters according to normal versus altered carotid intima-media complex (IMC).

Clinical parameters	Normal IMC (n = 142)		Altered IMC (n = 78)		p-value *
	Mean	SD	Mean	SD	
Number of teeth	22.9	6.7	19.9	7.9	0040
Clinical attachment level					
≥ 3mm, number of sites	55.1	27.3	55.2	31.5	0.7339
% of sites	42.7	21.2	50.6	23.7	0.0147
≥ 4mm, number of sites	23.8	25.1	29.8	29.2	0.0139
% of sites	20.2	22.2	30.7	27.5	0.0003
≥ 5mm, number of sites	10.2	14.9	14.9	1	0.0017
% of sites	9.5	15.0	18.1	23.2	0.0002
≥ 6mm, number of sites	4.7	10.1	8.4	16.4	0.0017
% of sites	4.5	9.3	10.3	18.3	0.0003
Probing pocket depth					
≥ 3mm, number of sites	33.6	23.9	33.2	24.4	0.8221
% of sites	24.8	16.7	2	18.4	0.1396
≥ 4mm, number of sites	6.1	11.1	3	12.4	0.1596
% of sites	4.8	8.7	8.	12.9	0.0431
≥ 5mm, number of sites	2.1	6.0	3.5	7.0	0.1157
% of sites	1.8	4.9	4.1	8.4	0.0785
≥ 6mm, number of sites	0.7	2.1	1.3	3.7	0.2361
% of sites	0.6	1.7	1.8	5.0	0.1722
Gingival bleeding					
Number of sites	20.7	5.6	18.8	15.9	0.2498
% of sites	16.1	12.2	17.0	14.6	0.9497
Plaque					
% of sites	30.2	7	32.0	25.4	0.596

SD: standard deviation.

* Mann-Whitney test for comparison of groups.

Table 4

Correlation matrix (Spe efficient) between periodontal clinical parameters and carotid artery intima-media complex (IMC) thi

	Carotid artery IMC	
	Right carotid	Left carotid
Pro ng pocket depth (%)		
≥ 4mm	0.090 (p = 0.183)	0.155 (p = 0.022) *
≥ m	0.143 (p = 0.034) *	0.163 (p = 0.016) *
≥ 6mm	0.119 (p = 0.078)	0.104 (p = 0.123)
Clinical attachment level (%)		
≥ 4mm	0.177 (p = 0.009)	0.195 (p = 0.004)
≥ 5mm	0.201 (p = 0.003) *	0.209 (p = 0.002) *
≥ 6mm	0.184 (p = 0.006) *	0.220 (p = 0.001) *

* $p < 0.05$.

Table 5

Crude and adjusted odds ratios (OR) and respective 95% confidence intervals (95%CI) for relationship between altered carotid intima-media comp[illegible] (IMC) and periodontal disease, age, gender, hypertension, diabetes, and body mass index (BMI).

Definition of periodontal disease	Crude OR (95%CI)	Adjus[illegible] OR ([illegible]%CI) *
Models from literature		
> 1 site with PPD ≥ 4mm and ≥ 50% GBP [22]	1.85 (0.37-9.2[illegible])	
≥ 4 sites with PPD ≥ 3.5mm [23]	1.56 (0.89-2.74)	
≥ 60% of sites with CAL ≥ 3mm [24]	1.60 (0.84-[illegible]04)	
≥ 4 sites with CAL ≥ 3mm and PPD ≥ 4mm [25]	1.5[illegible] (0.89-2.74)	
> 5% sites with PPD ≥ 5mm and > 5% sites with CAL ≥ 3mm [26]	[illegible] (0.95-4.33)	
≥ 4 teeth with ≥ 1 site with CAL ≥ 3mm and PPD ≥ 4mm in the same site [27]	1.56 ([illegible]-2.74)	
Periodontal health: absence of PPD > 3mm and no site with CAL > 2mm, mild periodontitis, and severe periodontitis ≥ 4 sites with PPD ≥ 5mm and CAL ≥ 2mm [28]	1.96 (0.98-[illegible])	
Mean PPD, plaque index, GBP > median [29]	[illegible].71 (0.95-3.08)	
No disease: PPD < 5mm, disease ≥ 1 site PPD ≥ 5mm [30]	1.[illegible] ([illegible]-2.58)	
≥ 6 sites with PPD ≥ 5mm and ≥ 1 site with CAL ≥ 2mm [31]	1.69 (0.76-3.77)	
≥ 1 site with PPD ≥ 5mm and ≥ 2 sites with CAL > 6mm and GBP > 5% [32]	**[illegible].06 (1.11-3.83)**	1.83 (0.97-3.46)
No disease: < 30% CAL ≥ 3 severe disease: ≥ 30% CAL ≥ 3mm [15]	**2.40 (1.20-4.78)**	1.79 (0.86-3.69)
Severe periodontal disease: ≥ 30% CAL ≥ 5mm [12]	**2.80 (1.18-6.61)**	1.27 (0.47-3.45)
Proposed models		
Definition 1: ≥ 10% of sites with PPD ≥ 4mm and CAL ≥ 4mm	**2.54 (1.28-5.07)**	2.02 (0.97-4.21)
Definition 2: ≥ 10% of sites with PPD ≥ 4mm and CAL ≥ 4mm and GBP ≥ 10%	**2.23 (1.11-4.50)**	1.97 (0.96-4.06)
Definition 3: ≥ 20% of sites with CAL ≥ 3mm	1.72 (0.60-4.94)	1.52 (0.51-4.52)
Definition 4: ≥ 20% of sites with CAL ≥ 4mm	**1.76 (1.01-3.08)**	1.61 (0.91-2.87)
Definition 5: ≥ 10% of sites with CAL ≥ 4mm	**3.44 (1.58-7.51)**	**2.56 (1.12-5.88)**

CAL: clinical attachment level; GBP: gingival bleeding on probing; P[illegible]D: probing pe[illegible]epth.
* Adjusted for gender, age, hypertension.

Table 6

Results of multiple logistic regression analysis, crude and adjusted o[illegible] ratios (OR) with respective 95% confidence intervals (95%CI) for relationship between altered carotid [illegible]tery intima-media complex (IMC) (dependent variable) and periodontal disease, age, gender, hypertension, diabetes, [illegible]nd body mass [illegible]dex (BMI) (independent variables) for the best observed model (definition 5).

Variable/Category	Crude OR (95%CI)	Adjusted OR
Age *	1.06 (1.03-1.10)	1.04 (1.01-1.08)
Gender		
Male	1.98 (1.13-3.47)	1.78 (0.97-3.27)
Hypertension		
Yes	2.19 (1.24-3.87)	1.85 (0.98-3.48)
Diabetes		
Yes	2.39 (1.04-5.47)	1.34 (0.55-3.25)
Periodontal [illegible]isease		
Yes	3.44 (1.58-7.51)	2.56 (1.12-5.88)
BMI		
[illegible]derwei[illegible]ht/Norm[illegible]	1.00	1.00
Ov[illegible]ght	1.44 (0.76-2.72)	1.51 (0.76-2.97)
[illegible]Obesity	2.05 (0.94-4.45)	2.05 (0.87-4.85)

* p < [illegible]05 in the adjusted analysis.
Not[illegible] definition 5: ≥ 10% of sites with clinical attachment level (CAL) ≥ 4mm.

definitions that include PPD and bleeding are considered more robust, since CAL is known to be related to history and sequelae of periodontal disease.

Another limitation of this study is that only clinical measurements of periodontal disease were evaluated. Microbiological data and inflammatory markers for periodontal disease have been proven as more specific indicators [13,14] as compared to clinical parameters. The study also failed to measure such risk parameters for cardiovascular disease as C-reactive protein, cholesterol (LDL and HDL), and triglycerides.

A recent study reported the effect of periodontal treatment on changes in the carotid. The observations indicated that changes in IMT thickness after periodontal treatment were possible in systemically healthy individuals [9]. Future intervention studies are necessary to better characterize the role of periodontal disease and its products on clinical and subclinical cardiovascular events.

Based on the current study's findings, we conclude that different measurements for the severity of periodontal disease and number of teeth were associated with carotid thickness. In addition, individuals with 10% or more sites with CAL ≥ 4mm showed higher odds of altered carotid thickness after controlling for confounding factors.

Resumo

O objetivo deste trabalho foi investigar a relação entre doença periodontal e a alteração da espessura do complexo médio-intimal da carótida. Foi conduzido um estudo transversal com 220 indivíduos (idade ≥ 35 anos) participantes do Estudo Longitudinal de Saúde do Adulto (ELSA-Brasil). Foram realizados ultrassonografia da artéria carótida e exame clínico periodontal que incluiu índice de placa visível, índice de sangramento à sondagem, profundidade de bolsa à sondagem (PBS) e nível clínico de inserção (NCI). Indivíduos com espessura da carótida com alteração tiveram menos dentes presentes, maior frequência de NCI ≥ 3mm, NCI ≥ 4mm, NCI ≥ 5mm e NCI ≥ 6mm e PBS ≥ 4mm em comparação com aqueles sem alteração (p ≤ 0,05). Apesar de usadas 17 definições para a doença periodontal, apenas uma confirmou a hipótese de associação entre a doença periodontal e a aterosclerose subclínica. Indivíduos com 10% ou mais dos sítios com NCI ≥ 4mm tiveram maior chance de apresentar espessamento de carótida.

Aterosclerose; Doença das Artérias Carótidas; Periodontia

Contributors

R. M. Batista participated in the study conceptualization and design, data collection, analysis, and interpretation, and writing of the article and was responsible for the study as a whole. E. P. Rosetti collaborated in the study conceptualization and design, data analysis and interpretation, writing of the article, critical revision of the text, and final approval of the article. E. Zandonade contributed to the study conceptualization and design, data analysis and interpretation, statistical analysis, writing of the article, critical revision of the text, and final approval. L. H. Roelke participated in the data collection and critical revision of the text. M. V. Vettore contributed to the data analysis and interpretation and critical revision of the text. A. E. Oliveira collaborated in the study conceptualization and design, writing of the article, and critical revision of the text.

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