STUDY ON THE ASSOCIATION BETWEEN THE SEVERITY OF CHRONIC PERIODONTITIS AND CAROTID ATHEROSCLEROSIS

Ovidiu Nicolaiciuc\(^1\), Irina Georgeta Sufaru\(^*\), Ioana Sioustis\(^2\), Liliana Pasarin\(^1\), Zenovia Surlari\(^1\), Stefan Luchian\(^2\), Delia Nicolaiciuc\(^3\), Tiberiu Tirca\(^3\), Ciprian Rezus\(^4\), Silvia Martu\(^1\)

\(^1\)“Grigore T. Popa” University of Medicine and Pharmacy, Faculty of Dental Medicine, Department of Periodontology, Iasi, Romania.
\(^2\) PhD Student “Gr. T. Popa” University of Medicine and Pharmacy, Iasi, Romania.
\(^3\) University of Medicine and Pharmacy, Faculty of Dental Medicine, Craiova, Romania.
\(^4\)“Grigore T. Popa” University of Medicine and Pharmacy, Faculty of Medicine, Department of Internal Medicine, Iasi, Romania.

Corresponding autor: Irina Georgeta Sufaru
e-mail: irina_ursarescu@yahoo.com
Ioana Sioustis
e-mail: ioanasioustis@yahoo.com

Abstract
Introduction and aim of the study: The aim of this study was to evaluate whether there is a correlation between the severity of chronic periodontitis and atherosclerosis, quantified by intima-media thickness (IMT).

Materials and method: Fifty adult patients who received consecutive duplex carotid scans in the lab were included. The study included patients diagnosed with atherosclerosis and healthy patients. The following periodontal clinical variables were evaluated: plaque index; bleeding on probing; probing depth (PD); gingival recession; the level of clinical attachment (CAL).

Results: Regarding the magnitude of PD, most sites were found in the test group: 33.9% for IMT> 1 mm without plaque and 47.1% for the atheroma group; differences were statistically significant between groups (\(p <0.05\)). The atheroma plaque group revealed 11.8% of subjects with mild periodontitis, 17.6% moderate periodontitis and 70.6% severe periodontitis. In patients with a history of stroke, more severe forms of periodontitis were associated with an increase in IMT and atheroma plaques (\(p<0.001\)).

Discussions: Approximately 70% of patients with atheroma plaques experienced severe periodontitis, 17.6% moderate periodontitis and 70.6% severe periodontitis. In patients with a history of stroke, more severe forms of periodontitis were associated with an increase in IMT and atheroma plaques (\(p<0.001\)).

Conclusions: This research has shown an association between the most severe forms of periodontitis and an increase in the intima-medium thickness. In addition, the increased severity of periodontal disease was associated with the presence of atheroma plaques in a significant number of patients, suggesting at least an association between the two pathologies.

Key words: periodontitis, atherosclerosis, intima-media thickness

INTRODUCTION
According to the World Health Organization (WHO), ischemic heart disease and stroke are responsible for more deaths (12.2% and 9.7% respectively) than all cancers. Due to the aging of the population and an increase in the prevalence of vascular risk factors, the rate of vascular death is estimated to reach...
31.7% in 2030,[1] despite all developments in prevention, diagnosis and treatment. [2,3] Vascular disease is mainly due to atherosclerosis, a condition where an arterial wall thickens due to the accumulation of fatty substances such as cholesterol associated with cellular changes and chronic inflammation in the walls of the vessels. [4] After an increase in the intima-media thickness (IMT), it may progress to the development of an atherosclerotic plaque with progressive narrowing of the lumen. Clinical consequences could be an ischemic event, either by distal embolism of a plaque fragment or by the progression of luminal stenosis to occlusion of the artery. [5] Periodontal disease is site-specific, fluctuating continuously with periods of exacerbation and remission, and its progression is facilitated by the morphological characteristics of the affected tissues. [6,7,8] The clinical consequences of this pathology, such as its progression and severity, depend on the host's inflammatory and immune response to specific bacteria that become part of oral biofilm. [9,10,11] Periodontitis requires the presence of oral bacteria and some of these have been identified in the atheroma plaques.[12] Moreover, specific antibodies, reacting to periodontal bacteria and pro-inflammatory proteins, have been isolated in patients affected by stroke. [13,14] In the literature, some theories on a possible relationship between the severity of periodontitis and the presence of atherosclerosis or asthma have been postulated, although complete information is still missing.[15,16] Therefore, the aim of this study was to evaluate whether there is a correlation between the severity of chronic periodontitis and atherosclerosis, quantified by intima-media thickness.

**MATERIALS AND METHOD**

The subjects signed the informed consent in writing after the purpose and procedures of the study were carefully explained to each patient. Fifty adult patients who received consecutive duplex carotid scans in the lab were included. Medical history, including smoking habits, pregnancy status, information on systemic pathologies and types of drugs (including anti-inflammatory drugs) has been analysed. The study included patients diagnosed with atherosclerosis and healthy patients. Pregnant patients, patients requiring prophylaxis of infectious endocarditis before periodontal examination, or any other reason that would prevent periodontal examination were excluded from the study.

Carotid evaluation was performed with a high resolution ultrasound device, the Philips HDI 5000 platform, ultrasound imaging (Philips Healthcare, Andover, MA, USA), using a linear probe (5-12 MHz frequency). All pictures were acquired by the same expert before the periodontal examination. IMT was measured along a minimum of 10 mm long distal and proximal carotid artery inner carotid artery in the longitudinal plane, perpendicular to the ultrasound beam, revealing both arterial walls near and far.

After several manual method measurements (IMT measurements were performed on sonographic screen during ultrasound and supported by a digital archiving system), the thickest point was selected to increase the reliability and reproducibility of the technique. In addition to these IMT determinations, the presence of atherosclerotic plaques was recorded in the common and / or internal carotid arteries. IMT was defined as a double-line model visualized by ecotomography on both artery walls, in a longitudinal image, consisting of two parallel lines, which are formed by the edges of leading two anatomical boundaries: lumen-media and intima-adventice. The atheroma plaque was defined as a focal structure that imparts in the arterial lumen at least 0.5 mm or 50% of the surrounding IMT value, or exhibits a thickness > 1.5 mm, measured from the adventitial media interface to the intima-lumen interface. Patients were divided into two main groups, depending on the ultrasound imaging of the carotid artery: the test group had IMT> 1 mm or the presence of any carotid atherosclerotic plaque, and the control group...
had IMT <1 mm and the absence of atherosclerotic plaques. The periodontal examination was performed at the level of all teeth (six points per teeth) with a manual periodontal probe (Hu-Friedy Manufacturing Inc, Chicago, IL, United States). The following clinical variables were evaluated: plaque index; bleeding on probing; probing depth (PD); gingival recession; the level of clinical attachment (CAL). The severity of each clinical case was determined according to CAL. CAL between 1 mm and 2 mm was classified as mild periodontitis, 3-4 mm as moderate periodontitis and CAL greater than 5 mm as severe periodontitis. Statistical analysis was performed using the SPSS® vs.17.0 statistical packet (SPSS Inc., IL, Chicago, USA), assuming a significance level of p <0.05. The Kruskal-Wallis test was used to compare central (median) trend measures in more than two groups when distribution normality and homogeneity were not observed (by the Shapiro-Wilk test). The Mann-Whitney test was used to compare the central trend measures of two independent groups. The association between categorical variables was evaluated using the chi-square test or the Fisher test.

RESULTS

The characterization of the study groups is presented in Table 1. The sample consisted of 50 subjects (25 males and 25 females), with an average age of 56.1 (± 14.8) years. Fifteen of the individuals had an IMT <1 mm (control group) and 35 had an IMT greater than 1 mm and / or atheroma plaques (test group).

The study included significantly more women (73.3%) in the control group. For the test group, gender differences were found only in patients who already had atheroma plaques (men 70.6%, p <0.05). The mean age of the control group (40.8 ± 11.9) was significantly different from the test group (62.9 ± 10.4). The overall percentage of smokers was 12%; they were more common in the test group (29.4% versus 6.7%, P <0.05), and all smokers in this group had atheroma plaques.

For previous vascular events, 4% of the sample had a previous acute myocardial infarction, 32% had a stroke (Table 2). Multidimensional analysis has shown that IMT progression has been significantly associated with an increase in patient age: every year, the probability of having an IMT greater than 1 mm increases by 1.2 times and the likelihood of having an approximately 1.3 times.

Periodontal data are presented in Table 2. For all patients (n=50), the mean percentage of sites with PD greater than 4 mm was 35.5%.

Regarding the magnitude of PD, most sites were found in the test group: 33.9% for IMT > 1 mm without plaque and 47.1% for the atheroma group (Table 2). In the control group, the corresponding value was 24.3%; differences were statistically significant between groups (p < 0.05). Percentage of PD < 4 mm was higher in the control group (p < 0.05). The plaque index was 61.4% in the control group, and 70.8% and 70.3%, respectively, with and without an atheroma plaque in the test group. There were no statistically significant differences between groups.

Table 1. Demographic and clinical characteristics of study subjects

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<th>Control group</th>
<th>Test group</th>
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<tr>
<td></td>
<td>IMT&lt;1mm</td>
<td>IMT&gt;1mm</td>
<td>Atheroma plaques</td>
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<tr>
<td></td>
<td>(n=15)</td>
<td>(n = 18)</td>
<td>(n=17)</td>
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<tr>
<td>Global</td>
<td>15 (30%)</td>
<td>18 (36%)</td>
<td>17 (34%)</td>
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<tr>
<td>Gender</td>
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<tr>
<td>Male</td>
<td>4 (26.7%)</td>
<td>9 (50%)</td>
<td>12 (70.6%)</td>
</tr>
<tr>
<td>Female</td>
<td>11 (73.3%)</td>
<td>9 (50%)</td>
<td>5 (29.4%)</td>
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<tr>
<td>Age</td>
<td>40.8 (±10.9)</td>
<td>62.9 (±10.2)</td>
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Table 2. Comparison of periodontal characteristics between study groups

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Bleeding on probing did not reveal statistically significant differences per group (p > 0.05): 35.7% in the control group; 43.4% in IMT > 1 group mm; and 31.6% in the platelet group of atheroma. All patients had periodontitis, although with varying degrees of severity. As shown in Table 2, diagnosis more frequently was severe periodontitis (40%); moderate and mild periodontitis and 13.3% had severe periodontitis. In the IMT group > 1 mm without atheroma plaque 22.2% of patients had mild periodontitis, moderate periodontitis 44.4% and severe periodontitis 33.3%.

The atheroma plaque group revealed 11.8%...
of subjects with mild periodontitis, 17.6% moderate periodontitis and 70.6% severe periodontitis. In patients with a history of stroke, more severe forms of periodontitis were associated with an increase in IMT and atheroma plaques (p <0.001).

Results from multivariate analysis showed that age was the only observed risk factor, significantly associated with moderate periodontitis (OR=1.09). On the other hand, three factors remained independent and positively associated with severe periodontitis: age, male gender and plaque index (age: OR=1.10; male gender: OR=14.3; plate index: OR=1.05, OR calculated for 1% increments).

DISCUSSIONS
The present study has demonstrated an association between the severity of the periodontitis and the carotid atherosclerotic disease. Chronic inflammation plays a fundamental role in atherogenesis and chronic infection due to several agents such as lymphotoxin-alpha has been shown to be a potential cause of this chronic inflammation.[17] In this context, several studies have appeared supporting the theory that pro-inflammatory mediators are responsible for this association.[18,19] Other explanations are related to autoimmune response to periodontal bacteria and proteins involved in atherosclerosis [13], as well as bacterial invasion, affecting platelets, endothelial cells and macrophages. [20,21,22]

Approximately 70% of patients with atheroma plaque experienced severe periodontitis, suggesting at least one association between the two pathologies. This group had the highest percentage of severe periodontitis, which means that the more severe periodontitis levels were linked to more advanced forms of atherosclerosis. Within the test group, age and gender have been shown to have a bias effect.

Throughout history, there was a belief that diseases that affect the oral cavity, such as periodontal disease, may have an effect on the rest of the body. [23,24] Epidemiological studies have involved periodontal disease as a risk factor for CVD development. Cardiovasc. The nature of the relationship between periodontal disease and CVD is unclear due to the lack of appropriate surrogate markers.

The thickening of the intima-media arterial layers may be a preliminary step in the formation of the atheroma plaque. The processes underlying chronic inflammation can increase plaque instability, with rupture and adhesion of the thrombus, leading to severe episodes in the end, such as strokes. Therefore, IMT gains importance as a marker of atherosclerosis and correlates with risk factors for stroke. The population with IMT> 1 mm and / or the atheroma plate also showed a higher vascular risk. [24]

Regarding periodontal status, this study suggested an association between the most severe forms of periodontitis and an increase in IMT. Franek et al.[25] have found an association between periodontitis and the development of atherosclerosis, although they have not made an association between the severity increases of both pathologies.

This study attempts to correlate the distinct levels of periodontal and atherosclerotic pathology, revealing a progressive increase in both pathologies. By comparing the test and control groups, we noticed statistically significant differences, not only for the severity of periodontal disease, but also for age and sex. Geismar et al.[26] noted that the association between periodontal disease and CVD was mainly dependent on age (over 60 years) but also related to diabetes and smoking habits rather than directly from the pathologies themselves. [27,28]

The bacterial plaque index, described in the literature as a risk factor for periodontal disease, has been demonstrated in our study as a factor in the presence of periodontitis but related to lighter and moderate forms of periodontitis and without any influence on the rest of variables.[14,15]

This is consistent with other studies in which the individual sensitivity of each patient was highlighted. This indicates that, although the bacterial plaque is necessary at the onset of periodontitis and
during its progression, the severity of periodontitis will depend on systemic risks and patient behaviour. [29] Due to the fact that there are only six smokers in the study, there is not enough statistical capacity to detect a difference between groups.

**CONCLUSIONS**

This research has shown an association between the most severe forms of periodontitis and an increase in the intima-medium thickness. In addition, the increased severity of periodontal disease was associated with the presence of atheroma plaques in a significant number of patients, suggesting at least an association between the two pathologies. Also, the advanced age has been shown to be a risk factor for severe periodontitis. In conclusion, the association found between the severity of periodontitis and carotid atherosclerosis, including subclinical forms, suggests that periodontal disease may be a risk factor for atherosclerotic disease.

**References**


