Periodontal Disease as a Potential Risk Factor for Acute Coronary Syndromes

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Objective: To investigate whether there is a relationship between active periodontal disease (PD) and acute coronary syndromes (ACS).

Methods: Three hundred and sixty-one patients (57.3% male), ages ranging from 27 to 89 (mean ± DP = 60.5 ± 12.2), were admitted to the Intensive Care Unit of a Teaching Hospital with symptoms and complementary examinations consistent with acute coronary syndrome. All the patients had a complete periodontal examination in the ICU setting, and 325 (90.9%) underwent coronary angiography for diagnostic confirmation and/or treatment planning. Periodontal examination included evaluation of all the teeth in the oral cavity and the following parameters: probing depth, clinical attachment level, plaque index, and gingival index.

Results: Of the 325 patients, 91 (28%) had coronary arteries free of obstruction or with mild obstructions (≤ 50% diameter stenosis), and the remaining 72% had severe obstructions. Fisher’s exact text yielded a p value of 0.0245 with an odds ratio of 2.571 (95% CI 1.192 to 5.547), meaning that the group with ACS and significant obstructive coronary artery disease was 2.5-fold more likely to have active PD.

Conclusion: A significant association was found between active periodontal disease and severe obstructive coronary artery in patients with acute coronary syndrome, underscoring the importance of prevention and adequate treatment of periodontal disease, which should be considered as a potential risk factor in the etiology and instability of the atherosclerotic plaque.

Key words: Periodontal disease, acute coronary syndrome, obstructive coronary artery disease, coronary atherosclerosis, inflammation, risk factor.
that S. sanguis and P. gingivalis cause thrombus formation and platelet aggregation, in addition to ST-segment changes on ECG, which is a dose-dependent response, suggesting that they may trigger cardiac ischemic episodes.60-62

Considering this, the present study was designed to assess the possible association between active periodontal disease and the degree of obstruction in patients with acute coronary syndrome (ACS).

**Methods**

Three hundred and sixty-one patients with acute coronary syndrome, that is, unstable angina or acute myocardial infarction (with or without ST-segment elevation) admitted to the Intensive Care Unit of a Teaching Hospital in the interior of São Paulo were evaluated. This diagnosis was based on patients clinical condition and complementary examinations (electrocardiogram and enzyme measurement). Patients whose clinical condition precluded adequate oral examination, such as those with coagulopathies and those with history of or greater risk for infective endocarditis, were excluded. All the others agreed to participate in the study and signed an informed consent. The study received Institutional Ethics Committee approval (File No. 5124/2001; Opinion No. 083/2001). Patients underwent specific odontological anamnesis and intraoral clinical examination by a single periodontist in the ICU during admission, in order to further clarify the condition suggestive of acute coronary failure.

The following parameters were used for PD classification:

- Clinical probing depth or pocket depth (CPD)34.
- Clinical attachment level (CAL)33.
- Bleeding index (BI)34.
- Plaque index (PI)35.

CAL and CPD were assessed using a standard manual probe calibrated in millimeters, in both arches, examining all the teeth on their surfaces: mesial buccal, buccal, distal buccal, mesial lingual, distal lingual, and lingual. Periodontal probing was performed moving the probe through these regions parallel to the long axis of the tooth at its free surfaces. All probing measurements were rounded to the nearest whole millimeter.

Periodontal disease was classified according to the following criteria: at least six teeth for assessment and more than 30% of sites whose CPD or CAL exceeded 5 mm or more than 30% of sites with CPD or CAL between 0 and 4 mm, but with ≥ 50% of bleeding on probing (BOP) at six sites per tooth: mesial buccal, mid-buccal, distal buccal, mesial lingual, mid-lingual, and distal lingual.

Of the patients with ACS, 207 (57.3%) were male. Ages ranged from 27 to 89, with mean ± standard deviation and median of age 60.5 ± 12.2 years and age 60, respectively. As for the number of teeth, 194 (53.7%) were edentulous (< 6 teeth) and 167 (46.3%) had between 6 and 28 teeth. A total of 2269 teeth were assessed, corresponding to 13,524 surfaces.

Statistical analysis was performed with Graph Pad Instat 3.00 Software using Fisher’s exact test and odds ratio (OR), with 95% confidence interval (95% CI). Alpha error was set at 0.05, and p values ≤ 0.05 were considered significant.

**Results**

Of the 167 patients who had at least six teeth for assessment, 154 (92.2%) underwent cardiac catheterization with coronary angiography during admission, so that the diagnostic of coronary event or risk stratification could be elucidated. In this group, the association between active periodontal disease and severe obstructive coronary disease was evaluated. Of these 154 patients, 49 failed to meet the diagnostic criteria for periodontal disease as established by the Method, but 105 patients did.

Among the 194 edentulous patients, 171 (88.1%) underwent cardiac catheterization during admission. Obviously, this group did not experience periodontal disease, simply because they had no teeth.

Table 1 shows the distribution of patients in each group.

The significant number of edentulous patients (53.7%) may be justified by the fact the hospital where data were collected receives subjects from several regions in the interior of São Paulo state, and many of them belong to lower socioeconomic classes; hence, they are more likely to have poorer oral conditions.

On the other hand, for this very reason, these edentulous patients would be “protected” against active periodontal disease, and according the hypothesis of the study, were expected to have an intermediate behavior between both groups. Thus, among the 49 patients free of periodontal disease and who underwent cardiac catheterization, 28 (57.1%) had severe obstructive coronary disease. Among the 171 edentulous patients who underwent cardiac catheterization, the rate of severe obstructive coronary disease was 73.7% (126 cases), while among the 105 with active periodontal disease, this rate was 76.2% (80 cases). Taking into account the existence of obstructive coronary disease of any degree, these values were 63.3%, 76.0%, and 80.9%, respectively.

Statistical analysis using Fisher’s test yielded a p value of 0.0989 and odds ratio of 0.6311, with a 95% CI ranging from 0.3834 and 1.039 for absence of periodontal disease or edentulism when comparing groups with any degree of coronary disease versus absence of coronary disease (Tab. 2).

Also regarding the presence of active periodontal disease or edentulism, no significant difference was found when groups with coronary disease of any degree versus absence of coronary disease were compared, and Fisher’s test showed a p value of 0.3726 with an odds ratio of 1.340 and a 95% CI from 0.735 to 2.444 (Tab. 3).

Statistical analysis using Fisher’s exact test indicated a p value of 0.0245 (significant) and an odds ratio of 2.571 with a 95% CI ranging from 0.004541 and 0.0547 for the presence or absence of periodontal disease, when groups of patients with severe obstructive coronary disease (≥ 50%) versus no coronary artery disease were compared (Tab. 4). According to these data, patients with severe obstructive coronary disease are 2.5 times more likely to have periodontal disease than...
those with normal coronaries. The inclusion of the subgroup with mild obstructive coronary disease (less than 50% of luminal stenosis) does not change the results, now with a p value of 0.0265 and an odds ratio of 2.468 with a 95% CI ranging from 1.156 to 5.267 for the presence or absence of periodontal disease when comparing groups of patients with any degree of coronary disease versus normal coronaries. The approximate 2.5-fold likelihood (odds) of concurrent active periodontal disease and any degree of coronary disease was maintained, compared with normal coronaries (Tab. 5).

Discussion

One of the great difficulties in comparing different studies about this subject is the lack of a consistent and consensual classification for periodontal disease. Based on published data, it is difficult to reach a conclusion whether there is or not an association between PD and CVD.

We made a point of evaluating all teeth to prevent any bias in data collection. Additionally, our classification sought to aggregate all periodontal parameters simultaneously, namely, bleeding as clinical evidence of gingival inflammation; plaque index as an indicator of infective burden; probing depth, since periodontal pockets are a reservoir for microorganisms with direct access to the connective tissue and circulatory system; and clinical attachment level, because periodontal recession is the record of past history of PD and its remissions.

In this study, the presence of obstructive coronary artery disease in ACS patients was significantly associated with active periodontal disease. The most promising hypothesis to explain this association may lie in the analysis of inflammatory markers characteristic or predictive of cardiac ischemic events. Analyzing these studies, in which inflammatory markers decrease when the subject receives periodontal treatment, or even comparing these markers in different groups of subjects with and without PD, one may consider periodontal interventions as adjuvant for preventing cardiac events19-29.

Our findings suggest that the ability of periodontopathogenic bacteria to invade periodontal tissues may offer a basis for such association. Another explanation that would validate the interrelationship between PD and CVD are gene polymorphisms, including frequency of different interleukin-1 (IL-1) and interleukin-6 (IL-6) genotypes, both of which are present in both the progression of PD and CVD. Accordingly, the patient would be hyper-responsive to harmful stimuli in the periodontal tissues and vascular endothelium. It is interesting to note that, despite the polymorphism, after periodontal treatment these patients show a significant decrease in serum C-reactive protein levels36.

In the present study, inflammatory markers were not measured. Czerniuk et al37 studied 50 consecutive patients with chronic periodontitis (41 males) admitted to the Coronary Care Unit with clinical diagnosis of ACS who underwent serial laboratory measurements, in some cases up to six months after the acute event. Although no significant differences were detected in serum tumor necrosis factor (TNFα) or IL-1 in ACS patients with advanced periodontal disease, as compared with those with a less advanced stage of the disease, the first tended to be characterized by higher mean levels of IL-1 in early and later phases of ACS, in addition to higher mean

| Table 1 - Distribution of cases without coronary artery disease, with mild obstructive coronary disease (<50%), with severe obstructive coronary disease (<50%), and that did not undergo catheterization relative to the presence or not of periodontal disease or edentulous condition |
|-----------------|-----------------|-----------------|
|                  | No periodontal disease | Periodontal disease | Edentulous |
| No periodontal disease | 18 (5.0%) | 20 (5.5%) | 41 (11.3%) |
| At least one coronary obstruction, always < 50% | 3 (0.8%) | 5 (1.4%) | 4 (1.1%) |
| At least one coronary obstruction, ≥ 50% | 28 (7.7%) | 80 (22.2%) | 126 (34.9%) |
| No catheterization | 3 (0.8%) | 10 (2.8%) | 23 (6.4%) |

| Table 2 - Distribution of cases in groups with obstructive coronary disease of any degree and no coronary disease relative to the absence of current periodontal disease or edentulism |
|-----------------|-----------------|-----------------|
|                  | No periodontal disease | Edentulism | Total |
| Obstructive disease (any degree) | 31 | 130 | 161 |
| Normal coronaries | 18 | 41 | 59 |
| Total | 49 | 171 | 220 |

p = 0.0989 OR = 0.6311 (95%CI 0.3834 to 1.039)

| Table 3 - Distribution of cases in groups with obstructive coronary disease of any degree and no coronary disease relative to the presence of current periodontal disease or edentulism |
|-----------------|-----------------|-----------------|
|                  | Periodontal disease | Edentulism | Total |
| Obstructive disease (any degree) | 85 | 130 | 215 |
| Normal coronaries | 20 | 41 | 61 |
| Total | 105 | 171 | 276 |

p = 0.3726 OR = 1.340 (95%CI 0.735 to 2.444)
levels of TNFα in later phases. Furthermore, in patients with less advanced periodontal inflammatory response decreased more rapidly compared to groups with more advanced periodontal disease.

The statistically significant association between obstructive coronary disease and active periodontal disease strongly suggests that periodontal disease be considered among the risk factors for the development of obstructive coronary disease. Therefore, considering the inflammatory aspects involved, it would represent a potential risk factor in the etiology and atherosclerotic plaque instability and cause acute coronary syndrome.

Studies that are prospective, controlled and have a larger number of patients are needed to further elucidate this issue.

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References


