Periodontal condition in patients with rheumatoid arthritis

Abstract: The purpose of this clinical study was to investigate if periodontal disease and rheumatoid arthritis (RA) are associated. The study included 39 RA patients (test group) and 22 age- and gender-matched healthy individuals (control group). Questionnaires on general and oral health were applied and a complete periodontal exam, including visible plaque, marginal bleeding, attachment loss (AL) and number of teeth present, was also performed by a single calibrated examiner. Diabetes mellitus patients and smokers were excluded. RA patients had fewer teeth, higher prevalence of sites presenting dental plaque and a higher frequency of sites with advanced attachment loss. Although the prevalence of dental plaque was higher in the test group (Chi-square test, p = 0.0006), the percentage of sites showing gingival bleeding was not different (Fisher’s exact test, p > 0.05). Based on our results, we suggest that there is an association between periodontal disease and RA.

Descriptors: Periodontitis; Rheumatoid arthritis; Periodontal attachment loss.
Introduction

Periodontitis is an infection initiated by bacteria present in the dental biofilm, which is characterized by a chronic inflammation and is associated with destruction of both connective tissue and alveolar bone.\(^1\)

Rheumatoid arthritis\(^2\) (RA) is an autoimmune disease that affects several organs and systems and it is also associated with destruction of joint connective tissue and bone. Moreover, both periodontitis and RA present an imbalance between pro-inflammatory and anti-inflammatory cytokines, which is deemed responsible for the tissue damage. In this sense, both conditions are associated with destruction of bone, mediated by inflammatory cytokines such as interleukin-1, tumoral necrosis factor and prostaglandin E2.\(^2\)

A bidirectional relationship of RA and periodontitis may involve RA affecting the pathogenesis of periodontitis\(^3\) and vice-versa.\(^4\) There is still the possibility of a common genetic trait predisposing to both conditions\(^2\) (dysregulation of the inflammatory mechanisms).

Periodontitis might interfere with the pathogenesis of RA through bacteremia, presence of inflammatory mediators, bacterial antigens and immunoglobulins in the serum.\(^5\) Studies in rats\(^6\) and in humans\(^7\) involving rheumatoid factors (which are immunoglobulins) support this concept. High levels of serum rheumatoid factor are related to the activity, greater severity and less favorable course of RA.\(^5\) Moreover, periodontitis may have systemic repercussions with increased inflammatory mediator levels and frequent transitory bacteremias occurring over a prolonged period of time.\(^5\) Comprehension of a possible association between periodontitis and RA can be relevant for the medical care of RA patients.

RA may influence the pathogenesis of periodontitis through its motor and emotional impairment.\(^9\) Motor impairment may make it more difficult to perform adequate oral hygiene. The salivary flow reduction due to medication or secondary Sjögren syndrome may increase supragingival plaque formation in these individuals.\(^10\) Psychological alterations found among RA patients\(^11\) were suggested as risk indicators for periodontitis.\(^12\)

The literature regarding the relationship between periodontal disease and RA is controversial. The methodologies applied in the studies are as diverse as their results and conclusions.\(^3,10,13-17\) Hence the purpose of this study was to evaluate the association between periodontal disease and RA by assessing the periodontal status of patients with RA.

Material and Methods

This is a descriptive/observational and analytical study that follows a cross-sectional design, which was approved by the Ethics Committee, School of Medical Sciences, State University of Campinas (FCM-UNICAMP). All the volunteers signed a term of informed consent.

The inclusion criteria for the test and control groups were: both genders; age between 30 and 55 years, at least six teeth in the oral cavity. The exclusion criteria for both groups were: smoking; diabetes mellitus; individuals who had undergone periodontal treatment (including prophylaxis) and/or antibiotic therapy over the last three months, systemic diseases that require prophylactic antibiotic therapy and individuals who were undergoing orthodontic treatment.

Test group: patients with rheumatoid arthritis

This group was composed of 39 patients selected from the Outpatient Arthritis Unit, School of Medical Sciences, State University of Campinas (UNICAMP), and were diagnosed with RA in accordance with the Revised Criteria of the American College of Rheumatology.\(^18\) Specific inclusion criteria in this group were a diagnosis of RA for more than a year and the absence of other autoimmune diseases.

Control group: individuals without autoimmune disease

This was a convenience sample composed of 22 individuals from the staff of the State University of Campinas and São Paulo State University. The specific inclusion criterion for this group was the absence of RA or any other autoimmune disease.

Clinical procedures and data collection

Health questionnaire (general and oral)

All the volunteers answered a standardized questionnaire covering medical history, use of medica-
tion during the last three months, habits and oral hygiene measures.

**Periodontal assessment**

All the 61 volunteers underwent an oral cavity examination by the same operator, an experienced periodontist, previously trained regarding all periodontal parameters and calibrated for attachment loss (AL). AL was calculated by adding the values of probing depth (PD) and of the distance between the cemento-enamel junction (CEJ) and the gingival margin (GM), when the GM was located apically to the CEJ. When the GM was located coronally to the CEJ, the value of the CEJ-GM distance was subtracted from the value of PD. The weighted Kappa test was9 used to assess the concordance between the data of two consecutive periodontal exams performed one week apart.

The number of teeth present in the oral cavity was determined, followed by assessment of the visible plaque index (VPI), gingival bleeding index (GBI) and attachment loss (AL) (six sites per tooth). The data were tabulated in frequency distribution tables.

**Clinical parameters for assessing rheumatoid arthritis**

The patients’ clinical records were used to assess the rheumatologic condition of the individuals of the test group. They were classified in accordance with the duration of the disease, presence of osteoporosis, use of disease-modifying anti-rheumatic drugs (DMARDs) and the use of anti-inflammatory, steroidal and non-steroidal medication.

**Statistical analysis**

After determining the distribution (normal/non-normal) of the data, the groups were compared for age, sex and remaining teeth. VPI, GBI and AL data were set in frequency distribution tables. Non-parametric statistics were used. Values of p < 0.05 were considered statistically significant. Two statistical packages (Bioestat 3.0 – CNPq and Sociedade Civil Mamirauá, Belém, PA, Brazil; and G-power – Faul F & Erdfelder E., Bonn, Germany) were used for the analysis.

**Results**

Three males and 36 females composed the test group and the median age in this group was 46 years. Two male and 20 female composed the control group and the median age in this group was 44.5 years. The groups were uniform with regard to age (p = 0.2963) and sex (p = 0.6335) (Table 1).

The median number of remaining teeth in the control group was 24.5 teeth; in the test group, it was 20 teeth. This was a significant difference (Table 1).

All RA patients used DMARDs and only 4 did not use anti-inflammatory drugs (Table 1).

With regard to the periodontal parameters, the test group presented a higher prevalence of visible plaque sites (Table 2).

Although the test group presented a greater prevalence of visible plaque sites, the prevalence of inflamed gingival margins did not differ (test group: 92.3% of the individuals with GBI between 0 and 20%, and 7.7% of the individuals with GBI between 20% and 40%; control group: 95.5% and 4.5% respectively).

The value of the weighted Kappa test for the pa-

| Table 1 - Demographic data, oral and systemic characteristics of the individuals. |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|                                 | Test (n = 39)   | Control (n = 22) |
| Gender                         |                 |                 |                 |                 |                 |                 |
| Male                           | 7.7%            | 9.1%            | 7.7%            | 9.1%            |                  |                 |
| Female                         | 92.3%           | 90.9%           | 92.3%           | 90.9%           |                  |                 |
| Age (median/range)             | 46 / 30-55 years| 44.5 / 30-55 years|                  |                 |                  |                 |
| Remaining teeth (median/range) | 20 / 6-32 teeth*| 24.5 / 12-32 teeth|                  |                 |                  |                 |
| Duration of RA (median/range)  | 9 / 1-28 years  | –               |                  |                 |                  |                 |
| Osteoporosis                   | 17.9%           | –               |                  |                 |                  |                 |
| Sjögren syndrome               | 7.7%            | –               |                  |                 |                  |                 |
| Use of DMARDs                  | 100%            | –               |                  |                 |                  |                 |
| Use of NSAIDs                  | 10.2%           | –               |                  |                 |                  |                 |
| Use of SAIDs                   | 17.9%           | –               |                  |                 |                  |                 |
| NSAIDs + SAIDs                 | 61.5%           | –               |                  |                 |                  |                 |
| No use of AIDs                 | 10.2%           | 100%            |                  |                 |                  |                 |

*Mann-Whitney test indicates that the number of remaining teeth was significantly different between the groups (p = 0.0053). RA: rheumatoid arthritis, DMARDs: disease-modifying anti-rheumatic drugs, NSAIDs: non-steroidal anti-inflammatory drugs, SAIDs: steroidal anti-inflammatory drugs, AIDs: anti-inflammatory drugs.
The test group presented a higher frequency of sites presenting AL greater than or equal to 5 mm than the control group (Table 3). A power analysis was performed for the AL parameter (post hoc analysis: effect size d = 0.83, \( \Delta = 0.05 \), two tailed, power = 0.86, critical \( t \) (59) = 2, delta = 3.12 - t-test for means).

### Discussion

In the present study, test and control groups were uniform regarding age and gender. Smokers and diabetics were excluded since smoking and diabetes mellitus are considered risk factors for periodontitis. It is important to stress that one simply cannot avoid some of the confounding variables when studying the periodontal condition of RA patients. This is because RA itself and its medical treatment affect various organ systems. So, taking these confounding variables into account is of utmost importance for the analysis and discussion of our results.

Patients with the Sjögren syndrome (SS) secondary to RA were not excluded. The negative effect of the SS on the periodontal condition is a disputed issue. Its negative effect on oral bacterial clearance and on supragingival plaque accumulation may not have a major influence on AL since the extent and severity of periodontitis cannot be directly related to supragingival plaque accumulation.

Although there is some indication that osteoporosis may influence the progression of periodontitis, there is no conclusive data confirming this hypothesis. Therefore, individuals with this condition, who represent 17.9% of the test group, were not excluded.

## Tables

### Table 2 - Individuals of the test and control groups distributed into 5 classes of visible plaque index (VPI).

<table>
<thead>
<tr>
<th>Visible Plaque Index (VPI)</th>
<th>Test (n = 39)</th>
<th>Control (n = 22)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-20% n (%)</td>
<td>5 (12.8)</td>
<td>12 (54.5)</td>
</tr>
<tr>
<td>20-40% n (%)</td>
<td>12 (30.8)</td>
<td>9 (41)</td>
</tr>
<tr>
<td>40-60% n (%)</td>
<td>11 (28.2)</td>
<td>0 (0)*</td>
</tr>
<tr>
<td>60-80% n (%)</td>
<td>9 (23.1)</td>
<td>1 (4.5)*</td>
</tr>
<tr>
<td>80-100% n (%)</td>
<td>2 (5.1)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

*Chi square test of independence indicates that the distribution of the variable depends on the group to which the individual belongs (\( \chi^2 = 19.48 \), \( p = 0.0006 \)).

### Table 3 - Frequency distribution of periodontal sites according to attachment loss (AL).

<table>
<thead>
<tr>
<th>Attachment Loss (AL)</th>
<th>Test (n = 39)</th>
<th>Control (n = 22)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AL: 0-2 mm n (%)</td>
<td>3,252 (76.2)</td>
<td>2,409 (77.3)</td>
</tr>
<tr>
<td>AL: 3-4 mm n (%)</td>
<td>829 (19.4)</td>
<td>617 (19.8)</td>
</tr>
<tr>
<td>AL: 5 mm n (%)</td>
<td>185 (4.4)</td>
<td>88 (2.8)*</td>
</tr>
<tr>
<td>Total n (%)</td>
<td>4,266 (100)</td>
<td>3,114 (100)</td>
</tr>
</tbody>
</table>

*Chi square test of independence indicates that the distribution of the variable depends on the group to which the individual belongs (\( \chi^2 = 14.39 \), \( p = 0.007 \)).
Current evidence shows that there is great variation in periodontal disease severity both among different individuals and among different tooth types and sites in each tooth. Also, the distribution of severe periodontal disease is markedly skewed. Thus, we chose to represent the periodontal disease in the subjects of this study by a frequency distribution in three levels of severity, which yields a better description of destructive periodontal disease experience. Data analysis was performed by non-parametric tests because of the use of these frequency distributions and also because of the natural skewness of the distribution of severe periodontal disease.

The test group presented a higher frequency of sites with AL greater than or equal to 5 mm than the control group. RA patients might be predisposed to periodontitis since he or she presents a higher risk for infections (due to medication-induced immunosuppression) and for inflammatory-mediated tecidual destruction (due to an unbalanced cytokine expression profile). A higher VPI was observed in the RA group (p < 0.001), and this could have influenced AL in this group. However, our data do not support this assumption since we were unable to find any association between AL and VPI. Indeed, Loe et al. found that the extent and severity of periodontitis cannot be explained by the supragingival plaque distribution. Also, we were unable to find any difference in AL distribution between RA patients with osteoporosis and those who did not present bone mass alterations (data not shown).

All the RA patients in our sample used DMARDs and 89.75% used some type of anti-inflammatory drug for a long period of time (median time of RA diagnosis in the test group was 9 years) and these drugs might protect periodontal tissues from destruction. Based on this, less periodontal destruction (AL) would be expected in the test group. Thus, the finding of greater periodontal disease extent and/or severity among patients using these anti-inflammatory medications can be interpreted as indication of the strength of the effect of RA or of a predisposing genetic trait on periodontal disease pathogenesis, which is supported by the findings of a recent study. The analysis of the parameters of PD and bleeding on probing (data not shown) followed a similar distribution to that of the AL, presenting higher frequency of deeper and bleeding sites in the RA group.

Our results suggest an association between periodontitis and RA and more studies are needed to assess the possible relationship between these two conditions, especially prospective studies that can yield information regarding rates of progression of destructive periodontal disease in RA patients. Since patients with RA tend to present higher VPI and higher AL, they need a more strict periodontal follow up that includes motivation regarding oral hygiene measures, taking into consideration the motor limitation and psychological condition of these individuals.

### Conclusion
Based on the attachment loss distribution in our sample, we suggest that there is an association between periodontal disease and rheumatoid arthritis.

### Acknowledgments
The authors would like to acknowledge Dr. Marlene de Paula Ishi for the support in data collection, Professor Silvio Govone for the support on statistics and the Outpatient Dentistry Unit of the FCM-UNICAMP for providing the dental office for patients’ examination. This study was financially supported by the Coordination for the Improvement of Higher Education Personnel - CAPES.

### References