



# Periodontal disease defects and mandibular cortical index in lupus patients

Defeitos ósseos periodontais e índice da cortical mandibular em pacientes com lúpus

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## ABSTRACT

**Introduction:** Systemic lupus erythematosus is an autoimmune disease that affects multiple organs. It is well known that lupus patients have higher risk of osteoporosis, but if the disease affects mandibular cortical bone and alveolar bone is not fully established. **Objective:** The objective of this study was to evaluate periodontal disease defects and mandibular osteoporotic alterations in patients with lupus as compared to healthy patients using panoramic radiographs. **Material and Methods:** The panoramic radiographs of 72 patients with lupus and 360 healthy patients were evaluated for the presence of bone loss secondary to periodontal disease, classified as horizontal and vertical bone loss. We also assessed mandibular osteoporotic alterations by using the mandibular cortical index. Logistic regression analysis was applied to estimate the risk of mandibular osteoporotic alterations as well as horizontal and vertical bone loss in patients with lupus as compared to healthy patients. **Results:** There were no statistically significant differences between groups in the presence of horizontal bone defects and mandibular cortical indexes. However, patients with lupus demonstrated that patients with lupus were 2.17 more likely to present vertical bone loss than healthy patients. **Conclusions:** Patients with lupus might have higher risk of vertical bone loss than healthy patients due to pathophysiology of their disease. Further larger prospective studies should be performed to confirm our findings.

## KEYWORDS

Panoramic radiograph; Periodontal disease; Osteoporosis, Systemic Lupus Erythematosus; Cutaneous Lupus Erythematosus; Bone mineral density.

## RESUMO

**Introdução:** Os lúpus eritematoso sistêmico é uma doença autoimune que afeta múltiplos órgãos. Pacientes com lúpus têm maior risco de osteoporose, mas é necessário elucidar-se como a doença afeta o esqueleto maxilo-mandibular. **Objetivo:** O objetivo deste estudo foi avaliar defeitos ósseos por doença periodontal e alterações osteoporóticas mandibulares em pacientes com lúpus, em comparação com pacientes saudáveis, utilizando-se radiografias panorâmicas. **Material e Métodos:** As radiografias panorâmicas de 72 pacientes com lúpus e 360 pacientes saudáveis foram avaliadas quanto à presença de defeitos ósseos verticais e horizontais por doença periodontal. Foram também avaliadas as alterações osteoporóticas da mandíbula por meio do índice da cortical mandibular. A regressão logística foi aplicada para estimar o risco de alterações osteoporóticas mandibulares, bem como a perda óssea horizontal e vertical em pacientes com lúpus, em comparação com pacientes saudáveis. **Resultados:** Não houveram diferenças estatisticamente significativas entre os grupos no tocante à presença de defeitos ósseos horizontais quanto à redução da densidade mineral óssea aferida por meio do índice da cortical mandibular. No entanto, pacientes com lúpus apresentaram 2,17 mais risco à perda óssea vertical do que pacientes saudáveis. **Conclusões:** Pacientes com lúpus podem ter maior risco de apresentar defeito ósseo vertical do que pacientes saudáveis devido à fisiopatologia de sua doença. Novos estudos prospectivos devem ser realizados para confirmar estes achados.

## PALAVRAS-CHAVE

Radiografia panorâmica; Doença periodontal; osteoporose; Lupus sistêmico eritematoso; Lupus cutâneo eritematoso; Densidade mineral óssea.

## INTRODUCTION

Systemic Lupus Erythematosus (SLE) is an autoimmune disease with heterogeneous features that may affect multiple organs and presents with a wide range of clinical and laboratory abnormalities [1,2]. SLE frequently leads to permanent damage and, although it can have periods of remission, there is no cure. [3] SLE has distinct subdivisions according to the degree of impairment or organ involvement. One of these subdivisions is Cutaneous Lupus Erythematosus (CLE), which can occur independently or with SLE [4].

The disease affects 30-50/10,000 individuals worldwide [5] and over 90% of patients are women [3]. Life expectancy has improved in patients with lupus patients due to pharmaceutical advances. However, bone loss associated with low-impact fragility fractures and morbidity has considerably increased in lupus patients over time.[3] Osteoporosis occurs in 10-68% of patients with particularly SLE [6].

Osteoporosis is an osteometabolic disease that leads to low bone mineral density (BMD) [7] and, similarly to lupus, affects mostly women. The diagnosis of osteoporosis is obtained by dual energy x-ray absorptiometry (DEXA), which is a reliable and accurate test. However, a DEXA scan is expensive and not accessible in developing countries [8]. Hence, a number of screening tools have been created to detect patients at increased risk of osteoporosis, such as radiomorphometric indexes in panoramic radiographs.

A panoramic radiograph is a radiographic examination frequently used as the initial examination in dental clinics [9]. With panoramic radiographs, is it possible to evaluate the mandibular cortical index (MCI). The MCI assesses the morphological appearance of the cortical bone at the

mandibular endosteal margin [10], and it is a useful screening tool to evaluate risk of osteoporosis [8,9,11-14].

Panoramic radiographs are also a valuable tool to screen for periodontal disease. [15,16] Although intraoral radiographs are the most ideal for the evaluation of periodontal tissue, particularly bone involvement [17], panoramic radiographs present advantages over intraoral radiographs, such as low cost, convenience and reduced radiation exposure [17-19]. Furthermore, digital panoramic radiographs improve the evaluation of periodontal bone tissue since they can provide better visualization of structures with tools such as the ability to enlarge or contrast and brightness changes [20,21].

Thus, the objective of this study was to evaluate periodontal disease defects (horizontal and vertical bone loss) and mandibular osteoporotic alterations (using MCI) in patients with lupus (SLE and CLE) as compared to healthy patients of the same age and gender, using panoramic radiographs.

## MATERIAL AND METHODS

*Study participants and inclusion and exclusion criteria*

This retrospective study was conducted with 72 patients who had a confirmed diagnosis of lupus (from the Dermatology Department, Ambulatory of Collagenosis and Stomatology, Hospital das Clínicas de São Paulo, Brazil) and 360 healthy patients (from São Paulo University Dentistry School, Brazil) who underwent panoramic radiographic examinations for dental treatment. Patients with lupus were diagnosed with SLE and/or CLE. Approval was obtained from the Ethics Committee at São Paulo University Dentistry and Medicine School (number 2.701.761). The guidelines of Helsinki were followed in this investigation.

Panoramic radiographic examinations with technical failures were excluded. The healthy patients were selected randomly using the following criteria: for each lupus patient, five non-lupus patients with the same gender and age were selected.

MCI assessments were performed independently by three experienced radiologists two weeks apart to avoid memory bias. Intraobserver reliability was assessed between measurements. The radiologists assessed the appearance of the cortical bone at the mandibular endosteal margin on both sides of the mandible, between the mental foramen to the posterior limit of the angle of the mandible, using the Klemmeti classification [12]. This classification is as follows: C1 = normal, seen as a sharp and marked continuous endosteal margin; C2 = moderately eroded, seen as evidence of lacunar resorption and C3 = severely eroded, seen as obvious reduction of mandibular bone mineral density.

The presence of periodontal bone loss was classified as “horizontal” or “vertical” according to the appearance of alveolar bone of the remaining teeth and considering six distinct areas for descriptive purposes: anterior inferior, anterior superior, posterior superior left, posterior superior right, posterior inferior left and posterior inferior right. Furthermore, the number of missing teeth was also evaluated.

A control group of 360 healthy individuals was created using panoramic radiographs performed for dental treatment. The control group was matched with the patients with lupus for age, sex and number of missing teeth (we accepted a difference of no more than + two missing teeth or years in age for each patient selected). For each patient with lupus, five matched healthy individuals with panoramic radiographs were searched for individually in the Dentistry University database.

### *Statistical Analysis*

Normality of the variables was assessed using the Shapiro–Wilk test. Logistic regression was used to assess the risk of low MCI in panoramic radiographs (represented by MCI C2 and C3 classifications) and presence of periodontal disease (horizontal and vertical bone defects in panoramic radiographs) in patients with and without lupus. Risk estimates were reported as odds ratios (OR) with 95% confidence intervals (CIs).

Intra- and inter-observer agreement was assessed using the Kappa test for MCI and presence of periodontal disease defects.

All statistical analyses were performed using the IBM SPSS Statistics 24 software (SPSS, Inc., Chicago, IL, USA).

## **RESULTS**

As the variables were not normal ( $p = 0.000$ ), data are presented as median values and interquartile ranges when applicable.

### *Descriptive data*

Table 1 depicts the number and age of patients, as well as their treatment and systemic comorbidities (number of patients using medication that affects bone metabolism, such as corticosteroids; number of patients with systemic disease, such as diabetes), as well as median number of missing teeth, number of patients with low MCI (classified as MCI 2 and 3) and patients with periodontal disease (vertical or horizontal bone loss detected in panoramic radiographs). Table 2 shows descriptive data regarding the number of remaining teeth and periodontal bone loss according to the aforementioned classification (anterior inferior area, anterior superior area, posterior superior left area, posterior superior right area, posterior inferior left area, posterior inferior right area).

**Table 1** - Descriptive data of study patients. Number of patients, median age of the patients, number of patients using medication that affects bone metabolism, number of patients with other systemic disease, median number of missing teeth, number of patients with mandibular cortical index 2 or 3, number of patients with periodontal disease (horizontal and/or vertical bone defects detected in panoramic radiographs)

	n	Age	Medication that affects bone metabolism	Comorbidities	Missing teeth	MCI2and3	Periodontal disease
<b>SLE</b>	7	36(IR69)	7	29	8(IR12)	1	7
<b>CLE</b>	59	64(IR9)	31	3	27(IR8)	24	42
<b>SLE + CLE</b>	6	46(IR39)	6	10	11(IR22)	4	5
<b>All lupus patients</b>	72	46(IR27)	44	42	16 (IR19)	29	54
<b>Control group</b>	360	46(IR20)	0	0	16(IR17)	74	203

Abbreviations: SLE: patients with Systemic Erythematosus Lupus, CLE: patients with Cutaneous Lupus Erythematosus, SLEÜCLE: Patients with systemic and cutaneous lupus, MCI: mandibular cortical index, IR: interquartile range.

**Table 2** - Descriptive data of periodontal bone loss in the sample studied reported as the number of patients with a regional bone loss

Area	Lupus patients		Healthy patients	
	Horizontal bone loss	Vertical bone loss	Horizontal bone loss	Vertical bone loss
<b>Anterior inferior</b>	45	2	136	5
<b>Anterior superior</b>	26	4	86	10
<b>Posterior superior left</b>	16	9	101	7
<b>Posterior superior right</b>	19	4	93	1
<b>Posterior inferior right</b>	20	5	105	8
<b>Posterior inferior left</b>	21	6	114	5

<sup>a</sup>The same patient can have more than one alteration. Patients without any detectable bone loss were not included.

### Statistical assessment results

The Kappa test for MCI and periodontal disease showed significant values of 0.88 ( $p = 0.001$ ) and 0.91 ( $p = 0.000$ ), respectively. No statistically significant differences were observed after logistic regression for horizontal defects and MCI, seen in Table 3. However, patients with lupus demonstrated 2.17 more chances to present vertical bone loss than healthy patients.

**Table 3** - Logistic regression results

Variables	OR (95% CI)	p*
<b>Horizontal bone loss</b>		
<b>Absence</b>	1	
<b>Presence</b>	0.79 (0.36 – 1.71)	0.55
<b>Vertical bone loss</b>		
<b>Absence</b>	1	
<b>Presence</b>	2.17 (0.90 – 5.25)	0.08
<b>MCI</b>		
<b>Normal</b>	1	
<b>Low</b>	2.17 (0.90 – 5.25)	0.08

Abbreviations: OR: odds ratio; CI: confidence interval

## DISCUSSION

In the present study, we found that patients with lupus do not have a higher risk of horizontal bone loss or low MCI (MCI classifications 2 and 3) when compared to healthy patients. However, patients with lupus presented 2.17 higher risk of vertical bone loss than healthy patients ( $p = 0.08$ ).

Lupus is a chronic inflammatory disease with multiple osteometabolic effects that lead to increased osteoclastic activity and decreased osteoblastic activity. [3] Furthermore, vitamin D deficiency is more prevalent in patients with lupus [22], who usually avoid sun exposure, as ultraviolet light is a trigger to disease flare [23]. The role of vitamin D in bone metabolism is well known, and vitamin D accelerates bone metabolism and prevents osteoporotic fractures. [24] Additionally, chronic kidney disease, which is frequent in lupus patients, can lead to altered calcium and vitamin D homeostasis [25].

Although it is well established that lupus may lead to dysfunction of multiple organs [26], few studies have investigated association with periodontal disease [26,27] and none have examined mandibular bone mineral density using MCI assessment. To our knowledge, this is the first investigation using the mandibular cortical index in this group of patients.

Osteoporosis is a common complication of lupus, [28] and mandibular bone can reflect systemic osteoporotic alterations [29-31], which can be analyzed by radiomorphometric indexes, such as MCI in panoramic radiographs. Moreover, MCI has been already significantly inversely correlated with DEXA results in several studies [11,12,14]. In this investigation, surprisingly, patients with lupus did not show a higher risk of low MCI. This finding may be related to the young median age of the patients (46 years old) or to the small

sample size. No direct comparisons between our study findings and other investigations were performed, as this is the first study related to lupus using this methodology.

Previous studies have shown that patients with lupus have a higher risk [26,32] or prevalence [27] of periodontal disease and have suggested that periodontal disease seems to develop earlier [33]. However, other studies using clinical examination had contradictory results and concluded that rates of periodontal disease are similar in patients with lupus and healthy patients [32].

There are no prior studies that specifically associate vertical bone loss with lupus, which the major finding of our study. Alveolar bone loss due to periodontal disease is cumulative, and its measurement is essential to determine the severity of the diagnosis [34]. Vertical alveolar bone loss is often associated with aggressive periodontal disease, in which bone loss can be on one, two, three or all sides of the tooth [35].

Patients with lupus are more likely to have osteoporosis due to drugs, such as corticosteroids. Corticosteroids, commonly used in treatment of SLE, play a role in increasing osteoporosis risk, since this type of medication affects bone metabolism, changing the balance between osteoclasts and osteoblasts to favor bone loss. [36] A possible explanation for increased vertical bone loss in patients with lupus may be associated with lupus treatment, although not all patients in our sample were on corticosteroids.

Some studies of patients with lupus showed that these patients have more periodontal complications [26,27,32]. Periodontal complications are associated with higher level of pro-inflammatory cytokines and a heightened count of *Actinobacillus actinomycetemcomitans*. As lupus patients has elevated levels of pro-inflammatory cytokines

[37], is expected that they have higher risk to develop periodontal disease. The significant increase in periodontitis in patients with lupus might be related to their susceptibility to periodontal disease by its inherent host response due to the disease itself [38,39].

The limitations of the present investigation are the small sample size and the retrospective nature of the study. Prior studies examining periodontal disease in patients with lupus reported conflicting results [40-42]. High variance in the clinical research criteria for severity of periodontal disease might play a role in the results.

## CONCLUSIONS

In conclusion, the role of corticosteroids in patients with lupus and periodontal disease is still unclear, and MCI assessment did not show any statistically significant difference in lupus patients as compared to healthy controls. Patients with lupus might have higher risk of vertical bone loss than healthy patients due to the pathophysiology of the disease, and perhaps lupus may have a synergistic effect, worsening periodontal disease and making it more aggressive. In the future, larger prospective studies should be performed to confirm our findings.

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