Salivary gland ultrasound findings are associated with clinical and serologic features in primary Sjögren's syndrome patients

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Dear Editor,

Primary Sjögren's syndrome (pSS) is a multisystem disease characterized by focal lymphocytic infiltration of the exocrine glands. Over the past years, three sets of diagnostic criteria have been proposed[1,2]. However, none of these included salivary gland ultrasound (SGUS). SGUS is a simple and noninvasive technique that allows us to classify the echogenicity, homogeneity and degeneration of the glandular parenchyma. To date, there is an increasing evidence supporting the association of SGUS findings with serological features in pSS patients[3-6]. Therefore, the aim of our study is to investigate the association of SGUS findings with clinical and analytical features of pSS patients.

A total of 54 patients diagnosed with pSS, fulfilling both the 2016 ACR/EULAR and 2002 AECG criteria, underwent SGUS evaluation. Ultrasound (US) examination was performed by a single rheumatologist experienced in SGUS. The parenchymal homogeneity of bilateral parotid and submandibular glands was graded using a simple semi-quantitative score ranging from 0 to 4, as previously described[7]. Briefly, grade 0 was a gland similar to normal thyroid parenchyma, grade 1 was a gland with slight inhomogeneity, grade 2 was a gland with mild inhomogeneity, without echogenic bands, grade 3 indicated a gland with evident inhomogeneity, with echogenic bands and grade 4 indicated gross inhomogeneity. Patients were classified into two groups according to the highest US score obtained. The grades 1 and 2 were considered to be normal and grades 3 and 4 to represent pathological SGUS findings. Demographics, European League Against Rheumatism Sjögren's Syndrome Disease Activity Index (ESSDAI) and laboratorial data were collected. Parametric, non-parametric and multivariate logistic regression were used, with statistical significance defined as $p < 0.05$.

The mean age of patients was 57.5±13.3 years and median disease duration was 5.0 [IQR (2.75-11.25)] years. The majority of the study population were women (96%) and 35% of patients had pathological SGUS findings. The main serological features were antinuclear antibodies (ANAs) positivity in 94.4% of patients, anti-SSA antibody in 83.3%, rheumatoid factor (RF) in 51.9% and anti-SSB antibody in 42.6%. An ESSDAI > 5 was found in 9 patients (16.7%). The differences between the two groups are depicted in table 1. Multivariate logistic regression revealed that anti-SSB (odds ratio [OR] = 6.6, 95% [CI] 1.7 to 25.8, p = 0.006) was independently associated with the presence of pathological features in SGUS.

In some studies, the disease duration was suggested to be related to the presence of pathological SGUS findings based on the hypothesis that a longer disease duration could be associated with more salivary gland damage. However, our results showed no association. Thus, pathological SGUS findings might not be associated with disease duration but instead with a more severe subtype of pSS[3]. The relationship between SGUS scores and disease activity has been demonstrated in previous studies[3-5]. We also found that pathological SGUS findings were significantly associated with a high disease activity. However, we could not determine which type of extra glandular involvement was more frequent in the pathological group. Recent studies also reported that high SGUS scores were related to more frequent positivity of ANAs, anti-SSA and RF[2-4,8-9]. Despite this, we did not obtain statistically different results regarding ANAs and anti-SSA positivity. Although the new 2016 criteria withdrew the anti-SSB antibody from use due to its low specificity, in the present study we observed that the anti-SSB was identified as a strong and independent factor associated with pathological

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TABLE I. COMPARISON OF DEMOGRAPHICS, CLINICAL AND SEROLOGIC FEATURES OF PRIMARY SJOGREN'S SYNDROME ACCORDING TO SALIVARY GLAND ULTRASOUND

	Pathological SGUS (n=19)	Normal SGUS (n=35)	p value
Age, years (mean +/- SD)	54.3±12.6	59.2±13.5	0.497
Mean disease duration, years	6.6±6.1	7.7±5.2	0.976
ESSDAI (IQR)	2.2 (0-5)	0.9 (0-1)	**0.044**
Erythrocyte sedimentation rate (mean +/- SD)	36.3±22.1	22.7±15.8	0.160
Antinuclear antibody, n (%)	19 (100)	32 (91.4)	0.544
Anti-SSA, n (%)	18 (94.7)	27 (77.1)	0.137
Anti-SSB, n (%)	14 (73.7)	9 (25.7)	**0.001**
Rheumatoid factor, n (%)	14 (73.7)	14 (40.0)	**0.018**
Hypergammaglobulinemia, n (%)	12 (63.2)	14 (40)	0.104
β2-microglobulin, mg/L (mean +/- SD)	2.9±0.9	2.2±0.7	0.378
Complement 3, mg/dL (mean +/- SD)	115.1±28.9	120.7±24.5	0.938
Complement 4, mg/dL (mean +/- SD)	21.6±6.0	21.9±8.1	0.165
Hydroxychloroquine treatment, n (%)	15 (78.9)	21 (60.0)	0.229

ESSDAI: European League Against Rheumatism Sjögren's Syndrome Disease Activity Index; SGUS: Salivary Gland Ultrasound; IQR: Interquartile Range

SGUS findings.

Some limitations should be noted. The SGUS was performed by a single examiner who, despite having sufficient expertise in the examination, was not blinded to the diagnosis. A labial salivary gland biopsy could have added more data, but only a few of our patients had histological results.

Further and larger studies are needed to support our findings.

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