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BRIEF REPORT

Ultrasound salivary gland involvement in Sjogren's syndrome vs. other connective tissue diseases: is it autoantibody and gland dependent?

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Abstract

Abstract

This study aims to investigate ultrasound (US) findings on salivary glands (SG) in patients with Sjögren syndrome (SS) vs. other connective tissue diseases (CTDs) and to assess the relationship of SGUS abnormalities with autoantibody profile in both groups. We enrolled 81 patients, 45 diagnosed with SS (39 with primary SS, 6 with secondary SS) and 36 diagnosed with other CTDs. All patients underwent a prospective evaluation of sicca symptoms, a Schirmer's test, and a B-mode US assessment of the parotid and submandibular glands, all blinded to the diagnosis. Each SG was semi-quantitatively scored 0–3; a grade ≥ 2 was considered pathological. SGUS involvement was classified as normal or pathological at the patient level and for each pair at the gland level. In addition, a total SGUS score of 0–12 and a parotid/submandibular score of 0–6 were calculated for each patient. Autoimmunity laboratory data were also obtained. All SGUS scores were higher in SS patients than in those with CTD ($p < 0.001$) and significantly more SS patients showed a pathological global ($p < 0.001$), parotid ($p < 0.001$), or submandibular ($p = 0.001$) US score compared with CTD patients. In SS patients, the presence of autoantibodies was significantly associated with pathological SGUS and higher scores, particularly at the parotid level, while in CTD patients, xerostomia and a pathological Schirmer's test were associated with pathological US and higher scores at the submandibular level ($p < 0.05$). SGUS showed a different grade of abnormality, site involvement, and associated autoantibody profile in SS patients as compared with other CTD.

Key Points

- *Patients with SS and other CTDs showed different grades of SGUS abnormality.*
- *Patients with SS and other CTDs showed different gland involvement and associated autoantibody profiles.*
- *Anti-Ro60 and anti-Ro52 Ro60 positivity were associated with the severity of parotid involvement in SS patients.*

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Introduction

Sjogren's syndrome (SS) is an autoimmune disease characterized by inflammation of the exocrine glands that produces such common symptoms as sicca syndrome, which consists of dry eyes (xerophthalmia) and dry mouth (xerostomia), frequently accompanied by musculoskeletal or other extraglandular manifestations, all of which can greatly impact patient quality of life [1, 2].

There is a substantial body of evidence supporting the use of salivary gland (SG) ultrasound (US) as an effective technique for assessing major SG involvement in SS, especially for diagnostic purposes [3–9], being parenchymal inhomogeneity and the presence of internal hypo/anechoic areas the most discriminative features. SGUS is well tolerated, non-invasive, inexpensive, non-irradiating, and widely available in rheumatology outpatient clinics [10]. Moreover, the combination of pathological SGUS with the presence of anti-Ro/SSA antibodies has been shown to be highly predictive of primary SS classification in patients with sicca syndrome [8]. However, SGUS findings remain little studied in other CTDs [4, 11–13] despite the fact that sicca symptoms and anti-Ro/SSA antibodies may be present in these diseases.

Therefore, the objectives of this single-center, cross-sectional, observational study were to investigate US findings in parotid and submandibular glands in patients with SS vs. other CTDs and to compare the relationship between SGUS abnormalities and autoantibody profile in both groups.

Patients and methods

Patients

We enrolled patients who consecutively attended the rheumatology outpatient clinic of the Hospital Universitario Fundación Jiménez Diaz (Madrid, Spain) from February to June 2018 and who fulfilled the following inclusion criteria: they had been diagnosed with SS or had been diagnosed with systemic lupus erythematosus (SLE), systemic sclerosis (SSc), mixed connective tissue disease (MCTD), or undifferentiated connective tissue disease (UCTD) without a diagnosis of SS. The diagnosis of SS was made in accordance with the American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) classification criteria for pSS [14], while the other CTDs were diagnosed according to the classification criteria for each disease [15–18]. The study was conducted according to the World Medical Association Declaration of Helsinki and was approved by the Ethics Committee of the Hospital Universitario Fundación Jiménez Díaz. All patients signed informed consent prior to participating in the study.

Clinical assessment

All patients underwent a Schirmer's test blinded to the diagnosis and the SGUS findings. Furthermore, the American-European Consensus Group questionnaire [19] was administrated to all patients in order to prospectively collect sicca symptoms (i.e. xerostomia and xerophthalmia).

Ultrasound assessment

All patients underwent a B-mode US assessment of the parotid and submandibular glands by two investigators together (GLP and EN), blinded to the diagnosis and clinical and laboratory data, using a real-time scanner (LOGIQ E9, GE Medical Systems Ultrasound and Primary Care Diagnostics, Wauwatosa, WI, USA) equipped with a multifrequency linear matrix array transducer (6–15 MHz). Gray-scale settings were optimized beforehand and standardized for the whole study. The settings were as follows: frequency 15 MHz, gain 51 dB, and dynamic range 57 dB. The patients were scanned in a supine position with the neck slightly extended and turned away from the examined side. The parotid glands were examined in longitudinal and transverse planes, according to the 2017 EULAR standardized procedures for ultrasound imaging in rheumatology [20].

Each SG was semi-quantitatively scored (0–3) according to their homogeneity and echogenicity, with some variations from previously published scores [21–23], as follows: grade 0, homogeneous punctiform parenchymal pattern, isoechoic to normal thyroid gland; grade 1, mild global hypoechoic inhomogeneity of the parenchymal pattern, without abnormal hypo/anechoic areas; grade 2, moderate inhomogeneity of the parenchymal pattern, with focal abnormal rounded or irregular-shaped hypo/anechoic areas; grade 3, severe inhomogeneity of the parenchymal pattern, with extensive presence of abnormal rounded or irregular-shaped hypo/anechoic areas. According to previous studies [11, 12, 21, 24], a SG score ≥ 2 was considered pathological. Thus, global SGUS involvement at the patient level was dichotomously classified as non-pathological (i.e., normal or non-specific changes) if both parotid and submandibular glands scored < 2, or pathological if any parotid or submandibular gland scored ≥ 2. In addition, US involvement of each pair of parotid and submandibular glands were also dichotomously scored non-pathological if both

parotid or submandibular glands, respectively, scored < 2, or pathological if any parotid or submandibular gland, respectively, scored ≥ 2.

For each patient we calculated a 0–12 total SGUS score, obtained from the sum of the single scores of the four glands. Furthermore, each pair of glands were scored separately from 0 to 6. Moreover, for each patient with an SG score ≥ 2, we classified their SGUS involvement into two patterns: (A) predominance of abnormal rounded hypo/anechoic areas and (B) predominance of abnormal irregular-shaped hypo/anechoic areas. Representative US images of the scoring and patterns are shown in Fig. 1a, b.

Laboratory investigations

For all patients, in addition to routine blood tests (e.g., leucocytes, complement, immunoglobulins), we collected serological data. Antinuclear antibodies (ANA) were studied by Indirect Immunofluorescence (IIF) on Hep2 cells (INOVA; screening dilution 1/80). Anti-Ro/SSA (total Ro, Ro52 and/or Ro60 kDa) and anti-La/SSB antibodies were detected either by ALBIA

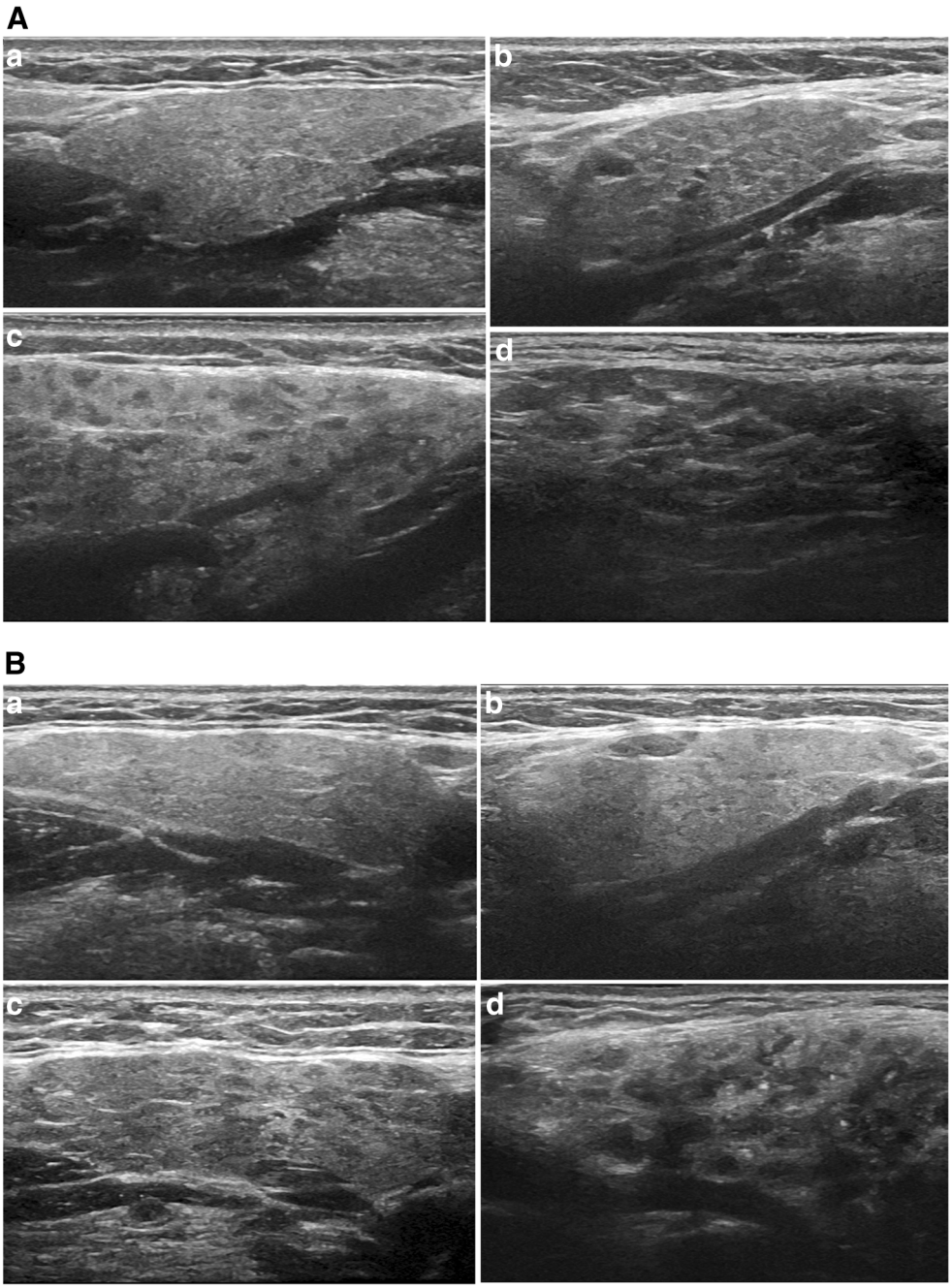

Fig. 1 **a** Ultrasound images of the scores (0–3) in patients with SS. a Submandibular gland, grade 0; b, submandibular gland, grade 1; c, submandibular gland, grade 2 (pattern A); d, submandibular gland, grade 3 (pattern B). **b** Ultrasound images of the scores (0–3) in patients with CTD without SS. a, Submandibular gland, grade 0; b, submandibular gland, grade 1; c, submandibular gland, grade 2 (pattern B); d, submandibular gland, grade 3 (pattern A)

(Bioplex2200®-Arbitrary Index (AI); Biorad®) or fluoroimmunoassay (ELiA-U/mL, Thermo®). Rheumatoid factor (RF) was measured by nephelometry (positive, > 14 U/ml).

Statistical analysis

Statistical analyses were performed using the statistical package IBM SPSS Statistics 23.0 or R and R Studio, version 3.5.1. Quantitative variables are summarized as mean, standard deviation (SD) minimum and maximum, or as median and interquartile range (IQR, Q_1–Q_3). Qualitative variables are summarized as absolute frequencies and percentages. For quantitative variables, comparisons between groups were performed by Student's *t* test for independent samples or Mann–Whitney *U* test, depending on their distribution and the size of the groups. For qualitative variables, a chi-squared test or a Fisher exact test was used; two-tailed tests were used in all contrasts. The significance level was set at p value < 0.05.

Results

Demographics, clinical, and laboratory features in SS and CTD patients

We enrolled 81 patients of whom 45 (42 females and 3 males; mean ± SD (range) age, 56 ± 12 years (30–81)) had a diagnosis of SS (39 primary SS; 6 associated with SLE (5 patients) or SSc (1 patient)) and 36 (35 females and 1 male; mean ± SD (range) age, 51.8 ± 12.7 years (20–73)) had a diagnosis of CTD (18 SLE, 11 SSc, 2 MCTD, and 5 UCTD) and had not been diagnosed with secondary SS. The subtypes of anti-Ro/SSA antibodies (i.e., anti-Ro 52 and anti-Ro60) were available in 35 SS patients (77.8%) and in all CTD patients.

Table 1 shows the comparison of clinical and laboratory features between SS and CTD patients. The two groups were distinguished by the presence of sicca findings and the autoantibody profile.

Comparison of SGUS findings between SS and CTD patients

Table 2 displays the SGUS findings in SS and CTD patients. All SGUS scores were higher in SS than in CTD patients. In addition, significantly more SS patients showed a pathological global, parotid, and submandibular US score compared with CTD patients. Considering the maximal grade assigned to any gland, in the SS group, 0 patients (0%) showed grade 0; 10 (22.2%) grade 1; 24 (53.3%) grade 2; and 11 (24.4%) grade 3. In the CTD group, this distribution was as follows: 2 patients (5.6%) grade 0; 24 (66.7%) grade 1, 8 (22.2%) grade 2; and 2 (5.6%) grade 3. Thus, grade 1 was significantly more frequent in CTD patients, while grades 2 and 3 were much more common in SS patients ($p < 0.001$). The presence of the two pathological patterns was not significantly different in the SS (pattern A, 21 patients (60%); pattern B, 14 patients (40%)) vs. the CTD group (pattern A, 5 patients (50.0%); pattern B, 5 patients (50%)) ($p = 0.572$).

Association between SGUS scores and clinical features and autoantibody profile

Table 3 shows the SGUS scores according to clinical features and autoantibody profile in the SS and CTD populations. In the former, RF positivity was significantly associated with higher total, parotid, and submandibular US scores, ANA positivity and double anti-Ro52 Ro60 positivity with higher total and parotid US scores, and anti-Ro60 positivity with a higher parotid US score. In the CT group, the presence of xerostomia and a pathological Schirmer's test were significantly associated with a higher US score at the submandibular level.

Association between abnormality of SGUS and clinical features and autoantibody profile

Supplementary Tables 1 and 2 show the association between pathological global, parotid and submandibular US, and clinical and autoimmunity features for the SS and CTD groups, respectively. In the SS group, the presence of pathological US at any gland was significantly associated with ANA, RF, and anti-Ro52 Ro60 positivity, the latter also being associated with pathological parotid US. In the CTD group, the presence of xerostomia and a pathological Schirmer's test were associated with pathological submandibular US. Neither in the SS group nor in the CTD group were there significant differences between patients with or without pathological SGUS with respect to age (mean ± SD, 55.5 ± 12.2 vs. 62.0 ± 7.6 (p = 0.255) for the SS group; 51.9 ± 13.8 vs. 51.5 ± 5.1 (p = 0.625) for the CTD group) and disease duration (median (IQR), 80.0 (17.5–156.0) vs. 19.0 (4.5–79.0) for the SS group ($p = 0.255$); 96.0 (22.8–133.8) vs. 42.5 (10.0–198.0) for the CTD group ($p = 0.625$)).

Discussion

We compared the SGUS findings in an SS population vs. a CTD population with a prevalence of sicca symptoms in half to two thirds of cases but without a diagnosis of SS, in a clinical setting.

In agreement with previous studies [4, 9, 11, 24, 25], the autoimmunity status expressed by RF, ANA, and anti-Ro positivity was associated with the grade of SGUS involvement in our SS population. However, to the best of our knowledge, there are no previous studies that have reported the relationship between

Table 1 Comparison of clinical and laboratory features between patients with SS and CTD

Clinical, laboratory, and US parameters	SS $n = 45$	CTD $n = 36$	p values
Age (years; mean ± SD)	56 ± 12	51.8 ± 12.7	0.128
Gender (female, *n* (%))	42 (93)	35 (97)	0.63
Disease duration (months; median (IQR))	79 (16–144)	96 (20.3–132)	0.575
Presence of xerophthalmia (*n* (%))	41 (91.1)	20 (55.6)	< 0.001
Presence of xerostomia (*n* (%))	35 (77.8)	18 (50)	0.009
Pathological Shirmer's test (*n* (%))	39 (86.7)	24 (66.7)	0.031
Schirmer's test (mm; median (IQR))	1 (1–1)	1 (0–1)	0.033
Leukocytes (n/mm^3; mean ± SD)	5105.5 ± 1730.1	5711.7 ± 1516.9	0.102
C3 level (mg/dl; mean ± SD)	123 ± 21.2	108 ± 35.0	0.017
C4 level (mg/dl; mean ± SD)	21.6 ± 8.6	23.6 ± 10.2	0.334
Presence of hypergammaglobulinemia (*n* (%))	18 (40)	9 (25)	0.155
IgG level (mg/dl; mean ± SD)	1434 ± 439.1	1171 ± 366.3	0.005
ANA positivity (*n* (%))	43 (95.6)	33 (91.7)	0.470
ANA titer (median (IQR))	640 (240–640)	320 (80–640)	0.141
RF positivity (*n* (%))	28 (62.2)	2 (5.6)	< 0.001
RF titer (U/ml; median (IQR))	22 (11–45.5)	9 (7–12)	< 0.001
Anti-Ro/SSA positivity (*n* (%))	42 (93.3)	18 (50)	< 0.001
Anti-Ro/SSA titer[a] (U/ml; median (IQR))	1 (1–1)	0.5 (0–1)	< 0.001
Anti-Ro60 positivity (*n* (%))	29 (82.9)	14 (38.9)	< 0.001
Anti-Ro60 titer[a] (U/ml; median (IQR))	1 (1–1)	0 (0–1)	< 0.001
Anti-Ro52 positivity (*n* (%))	29 (82.9)	10 (27.8)	< 0.001
Anti-Ro52 titer[a] (U/ml; median (IQR))	1 (1–1)	0 (0–1)	< 0.001
Anti-Ro52 Ro60 positivity (*n* (%))	26 (74.3)	6 (16.7)	< 0.001
Anti-La/SSB positivity (*n* (%))	26 (57.8)	4 (11.1)	< 0.001
Anti-La titer[a] (U/ml; median (IQR))	0 (0–1)	0 (0–0)	< 0.001
Anti-Ro52 Ro60 La positivity (*n* (%))	14 (40)	2 (5.6)	0.001

SS, Sjögren syndrome; *CTD*, connective tissue disease; *ANA*, antinuclear antibodies; *RF*, rheumatoid factor; *SD*, standard deviation; *IQR*, interquartile range

[a] Semiquantitative assessment

SGUS changes and the specificity of anti-Ro antibodies; i.e., anti-Ro60 and anti-Ro52 in SS patients. In our study, anti-Ro60 positivity and mainly double anti-Ro52 Ro60 positivity, but not anti-Ro52, were associated with the severity of SGUS, particularly parotid involvement in SS patients. These results suggest that future studies should assess the added value of anti-Ro specificity in the identification of SS.

Consistent with the study by Luciano et al. [11], our SS population showed greater SGUS involvement than patients with other CTDs. However, we found a mild grade of gland parenchymal hypoechoic inhomogeneity in a high percentage (66.7%) of CTD patients. This finding has been frequently described in patients with a variety of disorders but has been considered non-specific for SS [11, 12]. Nevertheless, the

Table 2 Comparison of US findings between patients with SS and CTD

US findings	SS $n = 45$	CTD $n = 36$	p values
Pathological global SGUS (any gland) (*n* (%))	35 (77.8)	10 (27.8)	< 0.001
Pathological parotid US (*n* (%))	28 (62.2)	5 (13.9)	< 0.001
Pathological submandibular US (*n* (%))	29 (64.4)	10 (27.8)	0.001
Total SGUS score 0–12, median (IQR)	6 (4–8)	4 (2–4)	< 0.001
Parotid US score 0–6, median (IQR)	3 (2–4)	1 (0–2)	< 0.001
Submandibular US score 0–6, median (IQR)	4 (2–4)	2 (2–2)	< 0.001

SS, Sjögren syndrome; *CTD*, connective tissue disease; *SG*, salivary gland; *US*, ultrasound; *IQR*, interquartile range

Table 3 SGUS scores according to clinical features and autoantibody profile

		Absence of xerophthalmia				Presence of xerophthalmia				*p* values
		n	Q_1	Median	Q_3	*n*	Q_1	Median	Q_3	
Total SGUS score 0–12	SS group	4	6.0	6.0	7.5	41	4.0	6.0	8.5	0.856
	CTD group	16	2.0	3.0	4.0	20	2.0	4.0	4.0	0.208
Parotid US score 0–6	SS group	4	2.3	3.5	4.0	41	2.0	3.0	4.0	0.651
	CTD group	16	0.0	1.0	2.0	20	0.0	2.0	2.0	0.504
Submandibular US score 0–6	SS group	4	2.3	3.5	4.0	41	2.0	4.0	4.5	0.727
	CTD group	16	2.0	2.0	2.0	20	2.0	2.0	3.0	0.118
		Absence of xerostomia				Presence of xerostomia				*p* values
		n	Q_1	Median	Q_3	*n*	Q_1	Median	Q_3	
Total SGUS score 0–12	SS group	10	4.0	6.0	6.8	35	5.0	6.0	8.0	0.295
	CTD group	18	2.0	3.5	4.0	18	2.0	4.0	4.3	0.500
Parotid US score 0–6	SS group	10	1.5	2.5	4.0	35	2.0	3.0	4.0	0.291
	CTD group	18	0.0	2.0	2.0	18	0.0	0.5	2.0	0.696
Submandibular US score 0–6	SS group	10	2.0	2.5	4.5	35	3.0	4.0	4.0	0.361
	CTD group	18	2.0	2.0	2.0	18	2.0	2.0	3.3	0.024
		Normal Schirmer's test				Pathological Schirmer's test				*p* values
		n	Q_1	Median	Q_3	*n*	Q_1	Median	Q_3	
Total SGUS score 0–12	SS group	6	2.8	5.0	7.5	39	5.0	6.0	8.0	0.225
	CTD group	12	2.0	3.5	4.0	24	2.0	4.0	4.0	0.637
Parotid US score 0–6	SS group	6	0.8	2.5	4.0	39	2.0	3.0	4.0	0.371
	CTD group	12	0.0	2.0	2.0	24	0.0	0.5	2.0	0.493
Submandibular US score 0–6	SS group	6	2.0	2.0	4.3	39	3.0	4.0	4.0	0.149
	CTD group	12	2.0	2.0	2.0	24	2.0	2.0	3.0	0.018
		ANA negativity				ANA positivity				*p* values
		n	Q_1	Median	Q_3	*n*	Q_1	Median	Q_3	
Total SGUS score 0–12	SS group	2	2.0	2.0	2.0	43	5.0	6.0	8.0	0.020
	CTD group	3	2.0	2.0	4.0	33	2.0	4.0	4.0	0.356
Parotid US score 0–6	SS group	2	0.0	0.0	0.0	43	2.0	3.0	4.0	0.023
	CTD group	3	0.0	0.0	0.0	33	0.0	2.0	2.0	0.065
Submandibular US score 0–6	SS group	2	2.0	2.0	2.0	43	2.0	4.0	4.0	0.079
	CTD group	3	2.0	2.0	4.0	33	2.0	2.0	2.0	0.461
		RF negativity				RF positivity				*p* values
		n	Q_1	Median	Q_3	*n*	Q_1	Median	Q_3	
Total SGUS score 0–12	SS group	17	3.0	4.0	7.5	28	6.0	6.5	9.0	0.013
	CTD group	34	2.0	3.5	4.0	2	4.0	7.0	10.0	0.098
Parotid US score 0–6	SS group	17	0.0	2.0	4.0	28	2.0	3.0	4.0	0.040
	CTD group	34	0.0	1.0	2.0	2	2.0	3.5	5.0	0.063
Submandibular US score 0–6	SS group	17	2.0	3.0	4.0	28	3.0	4.0	5.0	0.034
	CTD group	34	2.0	2.0	2.0	2	2.0	3.5	5.0	0.203
		Anti-Ro/SSA negativity				Anti-Ro/SSA positivity				*p* values
		n	Q_1	Median	Q_3	*n*	Q_1	Median	Q_3	
Total SGUS score 0–12	SS group	3	2.0	6.0	10.0	42	4.0	6.0	8.0	0.765
	CTD group	18	2.0	4.0	4.0	18	2.0	3.5	4.0	0.621
Parotid US score 0–6	SS group	3	0.0	2.0	4.0	42	2.0	3.0	4.0	0.360
	CTD group	18	0.0	1.0	2.0	18	0.0	1.5	2.0	0.892
Submandibular US score 0–6	SS group	3	2.0	4.0	6.0	42	2.0	3.5	4.0	0.657
	CTD group	18	2.0	2.0	3.0	18	2.0	2.0	2.0	0.294
		Anti-Ro60 negativity				Anti-Ro60 positivity				*p* values
		n	Q_1	Median	Q_3	*n*	Q_1	Median	Q_3	
Total SGUS score 0–12	SS group	6	2.0	3.5	7.0	29	4.5	6.0	8.0	0.070
	CTD group	22	2.0	4.0	4.0	14	2.0	3.0	4.0	0.489

Table 3 (continued)

Parotid US score 0–6	SS group	6	0.0	1.0	2.5	29	2.0	3.0	4.0	0.026
	CTD group	22	0.0	1.0	2.0	14	0.0	1.0	2.0	0.986
Submandibular US score 0–6	SS group	6	2.0	2.5	4.5	29	2.0	4.0	4.0	0.468
	CTD group	22	2.0	2.0	3.0	14	2.0	2.0	2.0	0.210
		Anti-Ro52 negativity				Anti-Ro52 positivity				*p* values
		n	Q_1	Median	Q_3	*n*	Q_1	Median	Q_3	
Total SGUS score 0–12	SS group	6	2.8	5.0	7.0	29	4.0	6.0	8.0	0.269
	CTD group	26	2.0	4.0	4.0	10	2.0	3.5	5.3	0.672
Parotid US score 0–6	SS group	6	0.8	2.0	4.0	29	2.0	3.0	4.0	0.297
	CTD group	26	0.0	1.0	2.0	10	0.0	1.5	2.5	0.595
Submandibular US score 0–6	SS group	6	2.0	2.0	4.5	29	2.0	4.0	4.0	0.277
	CTD group	26	2.0	2.0	2.3	10	2.0	2.0	2.3	0.745
		Anti-La/SSB negativity				Anti-La/SSB positivity				*p* values
		n	Q_1	Median	Q_3	*n*	Q_1	Median	Q_3	
Total SGUS score 0–12	SS group	19	4.0	6.0	8.0	26	5.0	6.0	8.3	0.347
	CTD group	32	2.0	3.0	4.0	4	4.0	4.0	5.5	0.094
Parotid US score 0–6	SS group	19	0.0	3.0	4.0	26	2.0	3.0	4.0	0.260
	CTD group	32	0.0	0.5	2.0	4	2.0	2.0	3.5	0.037
Submandibular US score 0–6	SS group	19	2.0	4.0	4.0	26	2.8	3.5	4.3	0.786
	CTD group	32	2.0	2.0	2.8	4	2.0	2.0	2.0	0.537
		No double anti-Ro positivity				Double anti-Ro positivity				*p* values
		n	Q_1	Median	Q_3	*n*	Q_1	Median	Q_3	
Total SGUS score 0–12	SS group	9	2.5	4.0	6.0	26	5.0	6.5	8.3	0.016
	CTD group	30	2.0	4.0	4.0	6	2.0	3.0	6.5	0.791
Parotid US score 0–6	SS group	9	0.0	2.0	3.0	26	2.0	3.5	4.0	0.021
	CTD group	30	0.0	1.0	2.0	6	0.0	1.0	4.0	0.665
Submandibular US score 0–6	SS group	9	2.0	2.0	3.5	26	2.8	4.0	4.3	0.055
	CTD group	30	2.0	2.0	2.3	6	2.0	2.0	2.5	0.876
		No triple anti-Ro/La positivity				Triple anti-Ro/La positivity				*p* values
		n	Q_1	Median	Q_3	*n*	Q_1	Median	Q_3	
Total SGUS score 0–12	SS group	21	3.5	6.0	8.0	14	5.0	7.0	8.5	0.197
	CTD group	34	2.0	3.5	4.0	2	4.0	5.0	6.0	0.131
Parotid US score 0–6	SS group	21	0.5	2.0	4.0	14	2.0	3.5	4.5	0.130
	CTD group	34	0.0	1.0	2.0	2	2.0	3.0	4.0	0.081
Submandibular US score 0–6	SS group	21	2.0	3.0	4.0	14	2.8	4.0	4.3	0.519
	CTD group	34	2.0	2.0	2.3	2	2.0	2.0	2.0	0.672

SG, salivary gland; *US*, ultrasound; *SS*, Sjögren syndrome; *CTD*, connective tissue disease; *ANA*, antinuclear antibodies; *RF*, rheumatoid factor

hypothesis that a less-aggressive inflammatory process than that of SS, with a potentially different pathogenic mechanism of SG damage in each CTD, could be a reasonable explanation and warrants further study. In addition, we detected moderate or severe SGUS changes, mainly at the submandibular glands, in almost a third (27.8%) of CTD patients. Indeed, these changes were significantly associated with the presence of xerostomia and pathological Schirmer's test. Since we did not perform a minor salivary gland biopsy at the time of the study due to its observational nature, it could be argued that some of our CTD patients with moderate or severe SGUS involvement actually had undiagnosed SS.

Interesting data emerged from our results regarding the different involvement of parotid and submandibular glands in SS and CTD patients. The former showed a similar involvement of both anatomic sites, although the presence of anti-Ro60 and anti-Ro52 Ro60 autoantibodies was associated mainly with parotid involvement. Conversely, the CTD group showed a clear predominance for submandibular involvement, which was associated with xerostomia and a pathological Schirmer's test. While these findings need to be confirmed in larger populations, the potential differences in site involvement could yield new insights into the pathophysiology of SG involvement in SS and other CTDs.

One of the main limitations of our study stems from the modest sample size of the population which, although sufficient to demonstrate relevant differences between SS and CTD patients, discouraged additional logistic regression analyses. In addition, the CTD population included essentially different diseases.

In conclusion, this study provided data on the different autoantibody profiles and gland involvements associated with SGUS abnormalities in SS vs. other CTD patients.

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Compliance with ethical standards

Disclosures None.

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