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Do the salivary glands of patients with systemic sclerosis show ultrasonographic modifications suggestive of Sjögren's syndrome?

The paper by Ferdowsi *et al*, reported a 23-item composite damage index to quantify organ damage in systemic sclerosis (SSc).¹ In this index, sicca symptoms (item 3) play an important

role (weight score=3). Actually, sicca symptoms are frequently reported by patients with SSc (7.5%–68%) and could be due to a fibrosis process of the salivary glands (SGs).^{2–4} In recent years, ultrasonography (US) of the parotid and submandibular glands has been widely used for identifying SG modifications in patients with primary Sjögren's syndrome (pSS). In order to assess modifications in the SG echostructure in patients with SSc and compare them with those of patients with pSS or controls with sicca symptoms, we prospectively enrolled patients with SSc fulfilling the American College of Rheumatology/European League against Rheumatism (ACR/EULAR) 2013 classification criteria, patients with pSS according to the ACR/EULAR 2016 classification criteria, and controls with sicca symptoms. Bilateral parotid and submandibular ultrasound was performed on every patient by the same operator (MC) blinded to the diagnosis. The inhomogeneity of each of the four major SGs in B-mode was graded using the Cornec *et al* scoring system (scale of 0 to 4) as previously described.⁵ The highest grade among the four glands was suggestive of Sjögren's syndrome if ≥ 2 .

A total of 108 patients were included in the study: SSc (n=25), pSS (n=48) and controls (n=35). The characteristics of the patients are shown in table 1. When comparing the pSS and controls, the performance of an US echostructure grade ≥ 2 for the diagnosis of pSS was good (sensitivity: 75%, specificity: 91.4%, positive predictive value: 92.3%, negative predictive value: 72.7%). Among the 25 patients with SSc, 9 had a history of or had a current digital ulcer, 8 had interstitial lung disease, 6 received an immunosuppressant (methotrexate (n=4), mycophenolate mofetil (n=2)), 2 received hydroxychloroquine, and 5 received glucocorticoids (all at a daily dose ≤ 10 mg), 40% complained of xerostomia and 36% of xerophthalmia, Schirmer's test was ≤ 5 mm in 5 min in 9/17 (53%), and 8/17 (47.1%) had an unstimulated salivary flow ≤ 0.1 mL/minute. The lengths of parotid and submandibular glands were smaller in patients with SSc versus controls after adjustment for age and sex ($p=0.02$ and $p=0.04$, respectively). In the SSc group, 7 (28%) had a salivary gland ultrasound (SGUS) grade ≥ 2 (n=5, grade 3; n=2, grade 4). Five (71%) of the 7 patients with SSc with SGUS grade ≥ 2 were anticentromere antibody (ACA)-positive compared with 4/18 (22%) patients with SSc with SGUS scores of 0–1 ($p=0.02$). None of these seven patients with US abnormalities suggestive of pSS had anti-Ro 60/SSA or La/SSB antibodies.

To date, this is the first study assessing morphological echostructure modifications of the major SGs in patients with SSc. According to our results, more than a quarter of patients with SSc, especially those with ACA, had inhomogeneity of the parotid and submandibular parenchyma that is evocative of pSS. We cannot exclude that the SGUS inhomogeneity is a SSc-related manifestation, especially in patients with SSc with ACA. These observations could more probably represent a distinct ACA-positive SSc/Sjögrenoverlap syndrome, as previously described, that salivary gland ultrasound could identify in a simple and non-invasive way.⁶

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Table 1 Clinical and biological characteristics of the patients

Characteristics	SSc (n=25)	pSS (n=48)	Controls (n=35)
Age, years, mean \pm SD	64.8 \pm 9.5	62.1 \pm 12.4	55 \pm 15
Female, n (%)	22 (88)	46 (95)	34 (97)
Disease duration, years	10.6 \pm 11.3	10.6 \pm 7.8	6.5 \pm 6.3
Treatments			
Immunosuppressive therapy, n (%)	7 (28)	4 (8.3)	2 (5.7)
Hydroxychloroquine, n (%)	2 (8)	12 (25)	4 (11.4)
Glucocorticoids, n (%)	5 (20)	5 (10.4)	2 (5.9)
Clinical signs			
Xerostomia, n (%)	10 (40)	48 (100)	30 (85)
Xerophthalmia, n (%)	9 (36)	43 (89)	29 (82)
Clinical parotid enlargement, n (%)	0	3 (6.4)	2 (5.7)
Raynaud phenomenon, n (%)	25 (100)	6 (12.5)	5 (14.3)
Inflammatory arthralgia, n (%)	14 (56)	11 (22.9)	30 (85.7)
Laboratory tests			
Schirmer's test ≤ 5 mm, n (%)	9/17 (53)	38/47 (80.9)	8/32 (25)
Unstimulated salivary flow ≤ 0.1 mL/min, n (%)	8/17 (47.1)	41/47 (87.2)	16/33 (49.5)
ANA $\geq 1/160$, n (%)	24 (96)	36 (75)	17 (49)
Anti-Ro 52/SSA, n (%)	4 (16)	24 (50)	2 (5.7)
Anti-Ro 60/SSA, n (%)	2 (8)	26 (54)	0
Anti-La/SSB, n (%)	0	14 (29.2)	0
Rheumatoid factor, n (%)	3/22 (14)	16/39 (41)	2/35 (5.7)
Antitopoisomerase, n (%)	10 (40)	1 (2.1)	0
ACA, n (%)	9 (36)	3 (6.3)	0
ESR, med (Q1–Q3), mm at first hour	16(11–21)	11(6–28)	8(5–14)
CRP, mean (Q1–Q3), mg/L	2.9 (2.9–8)	2.9 (0.5–3.8)	2.9 (0–6.5)
Focus score ≥ 1 (labial salivary gland), n (%)		41/46 (89)	3/27 (11)
SGUS features			
Parotid length, mean \pm SD, mm	41.5 \pm 7.8	42.5 \pm 6.5	45.9 \pm 5.2
Parotid width, mean \pm SD, mm	37 \pm 5.8	35.8 \pm 6.5	39 \pm 5.9
Submandibular surface area, mean \pm SD, cm ²	2 \pm 0.8	1.8 \pm 0.5	2.2 \pm 0.7
Submandibular length, mean \pm SD, mm	26.7 \pm 5.8	28.4 \pm 5.7	30.1 \pm 4.3
US grade max, n (%)			
0 or 1	18 (72)	12 (25)	32 (91.4)
≥ 2	7 (28)	36 (75)	3 (8.6)

ACA, anticentromere antibody; ANA, antinuclear antibody; CRP, C reactive protein; ESR, erythrocyte sedimentation rate; SGUS, Salivary gland ultrasound; SSA, Sjögren's-Syndrome-related-antigen type A antibody; SSB, Sjögren's-syndrome-related-antigen type B antibody; SSc, systemic sclerosis; US, ultrasonography; pSS, primary Sjögren's syndrome.

final approval. SM: contribution to the conception and interpretation of the data, revising and final approval. BP: contribution to the conception, statistical analysis and interpretation of the data, revising and final approval. MS: contribution to the conception and interpretation of the data, revising and final approval. JJD: conception and design of the work, interpretation of the data, drafting the work, revising and final approval.

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