



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

Marion Couderc, Anne Tournadre, Sylvain Mathieu, Bruno Pereira, Martin Soubrier, Jean Jacques Dubost

► To cite this version:

Marion Couderc, Anne Tournadre, Sylvain Mathieu, Bruno Pereira, Martin Soubrier, et al.. Do the salivary glands of patients with systemic sclerosis show ultrasonographic modifications suggestive of Sjögren's syndrome?. *Annals of the Rheumatic Diseases*, 2019, pp.annrheumdis-2019-215777. 10.1136/annrheumdis-2019-215777 . hal-02343567

HAL Id: hal-02343567

<https://hal.science/hal-02343567>

Submitted on 2 Nov 2019

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

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

Marion Couderc,¹ Anne Tournadre,¹ Sylvain Mathieu,¹ Bruno Pereira,² Martin Soubrier,¹ Jean Jacques Dubost¹

¹Rheumatology, CHU Clermont-Ferrand, Clermont-Ferrand, France

²DRCI Biostatistical department, University Hospital, Clermont-Ferrand, France

Correspondence to Mrs Marion Couderc, Rheumatology, CHU Clermont-Ferrand, Clermont-Ferrand 63000, France; mcouderc@chu-clermontferrand.fr

Contributors MC: conception and design of the work, acquisition, analysis and interpretation of the data, drafting the work, revising and final approval. AT: contribution to the conception and interpretation of the data, revising and

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.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval French CPP n°AU1292-07/10/2016, ANSM n°2016-A01256-45.

Provenance and peer review Not commissioned; internally peer reviewed.

© Author(s) (or their employer(s)) 2019. No commercial re-use. See rights and permissions. Published by BMJ.



To cite Couderc M, Tournadre A, Mathieu S, *et al.* *Ann Rheum Dis* Epub ahead of print: [please include Day Month Year]. doi:10.1136/annrheumdis-2019-215777

Received 24 May 2019

Accepted 25 May 2019

Ann Rheum Dis 2019;0:1–2. doi:10.1136/annrheumdis-2019-215777

REFERENCES

- 1 Ferdowsi N, Huq M, Stevens W, *et al.* Development and validation of the scleroderma clinical Trials Consortium damage index (SCTC-DI): a novel instrument to quantify organ damage in systemic sclerosis. *Ann Rheum Dis* 2019;78:807–16.
- 2 Kobak S, Oksel F, Aksu K, *et al.* The frequency of sicca symptoms and Sjögren's syndrome in patients with systemic sclerosis. *Int J Rheum Dis* 2013;16:88–92.
- 3 Avouac J, Sordet C, Depinay C, *et al.* Systemic sclerosis-associated Sjögren's syndrome and relationship to the limited cutaneous subtype: results of a prospective study of sicca syndrome in 133 consecutive patients. *Arthritis Rheum* 2006;54:2243–9.
- 4 Avouac J, Airò P, Dieude P, *et al.* Associated autoimmune diseases in systemic sclerosis define a subset of patients with milder disease: results from 2 large cohorts of European Caucasian patients. *J Rheumatol* 2010;37:608–14.
- 5 Cornec D, Jousse-Joulin S, Pers J-O, *et al.* Contribution of salivary gland ultrasonography to the diagnosis of Sjögren's syndrome: toward new diagnostic criteria? *Arthritis Rheum* 2013;65:216–25.
- 6 Baldini C, Mosca M, Della Rossa A, *et al.* Overlap of ACA-positive systemic sclerosis and Sjögren's syndrome: a distinct clinical entity with mild organ involvement but at high risk of lymphoma. *Clin Exp Rheumatol* 2013;31:272–80.