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EXTENDED REPORT

Scoring hypoechogenic areas in one parotid and one submandibular gland increases feasibility of ultrasound in primary Sjögren's syndrome

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ABSTRACT

Objective To assess whether ultrasonographic scoring of (i) both parotid and submandibular salivary glands and (ii) all individual components of the Hocevar scoring system, is needed for classifying patients as primary Sjögren's syndrome (pSS).

Methods Ultrasound examination of the major salivary glands (sUS) was performed in 204 consecutive patients clinically suspected (n=171) or diagnosed (n=33) with pSS. Parenchymal echogenicity, homogeneity, hypoechogenic areas, hyperechogenic reflections and salivary gland posterior border were scored in left and right parotid and submandibular glands. Logistic regression analyses were performed to assess which glands and sUS components contributed significantly to classification as pSS or non-pSS according to the 2016 American College of Rheumatology-European League Against Rheumatism (ACR-EULAR) criteria.

Results 116 (57%) patients were classified as pSS, the remaining as non-pSS. Instead of scoring both sides (area under the curve; AUC=0.856, Nagelkerke R²=0.526), multivariate analysis showed that sUS scoring of only right (AUC=0.850; R²=0.518) or left (AUC=0.852; R²=0.511) parotid and submandibular glands is sufficient to predict ACR-EULAR classification. Moreover, all individual components of the Hocevar scoring system significantly predicted classification. Multivariate analysis showed that parenchymal echogenicity and hypoechogenic areas contributed independently to ACR-EULAR classification (AUC=0.857; R²=0.539). Scoring these components in one parotid and one submandibular gland highly predicted ACR-EULAR classification (AUC=0.855; R²=0.539). Scoring only hypoechogenic areas on one side showed almost similar results (AUC=0.846; R²=0.498).

Conclusion sUS examination of parotid and submandibular glands on one side is sufficient to predict classification of patients according to the ACR-EULAR criteria. To further increase feasibility of sUS in outpatient clinics worldwide, only hypoechogenic areas can be scored.

INTRODUCTION

Primary Sjögren's syndrome (pSS) is a chronic, systemic autoimmune disease with inflammation of the exocrine glands being the most common feature, leading to keratoconjunctivitis sicca and a sensation of oral dryness (xerostomia). Extreme

fatigue and several extraglandular manifestations are also common.^{1,2}

Ultrasound of major salivary glands (sUS) is an upcoming imaging technique to assess the involvement of major salivary glands in pSS. It is gaining more acceptance in daily clinical practice, as it is non-irradiating, non-invasive and easy to perform.^{3–6}

A meta-analysis has recently identified 33 scoring systems used to evaluate the major salivary glands in patients with SS.³ This heterogeneity within the scoring systems was related to the type of salivary glands examined, the ultrasonographic characteristics evaluated and the cut-off points applied. The scoring system of Hocevar *et al*⁷ is the most extensive and has previously been applied in several studies.^{6–10} However, this scoring system is time consuming and therefore less feasible in daily clinical practice. In order to become part of the routine in daily clinical practice in the outpatient rheumatologic clinics worldwide, sUS should be as easy, fast and efficient as possible. Previously, more simple scoring systems have been used,^{11–14} but none of these systems were constructed on the basis of a multivariate regression model.

According to the Outcome Measures in Rheumatology Clinical Trials (OMERACT) filter, three aspects are considered important when it comes to the applicability of a new diagnostic method, that is, truth, discrimination and feasibility.¹⁵ Truth questions whether sUS measures what is intended. Discrimination evaluates whether sUS differentiates between situations of interest. Both aspects were previously investigated in our validity and reliability studies.^{6,10} Feasibility examines whether sUS can be applied easily, given constraints in time, money and interpretability. Since time is precious in daily clinical practice, the feasibility of sUS could be increased by reducing the number of glands and/or the number of components scored. Therefore, the aim of this study was to assess whether ultrasonographic scoring of (i) both parotid and submandibular glands and (ii) all five components of the Hocevar scoring system,⁷ is needed for classifying patients as pSS.

MATERIALS AND METHODS

Patients

In this cross-sectional study derived from our daily clinical practice, consecutive patients clinically

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suspected or diagnosed with pSS were included. The largest group consisted of tertiary referrals with clinical suspicion of pSS, referred to the University Medical Center Groningen (UMCG) for evaluation at our multidisciplinary Sjögren's expertise centre. The remaining part were participants of our Registry of Sjögren syndrome in Umcg—Longitudinal (RESULT) cohort, in which consecutive patients with pSS are included. All patients were aged ≥ 18 years and underwent a full (diagnostic) workup, including an ultrasound of the major salivary glands. Patients with an incomplete workup or an associated systemic autoimmune disease (eg, rheumatoid arthritis, systemic lupus erythematosus) were excluded.

Ultrasonography

The ultrasonographic scanner (Esaote MyLabSeven, Genova, Italy), equipped with a high-resolution linear scanner (4–13 MHz) was used. During the examination, patients were lying in supine position, with their neck slightly extended and head turned towards the opposite side. The scoring system by Hocevar *et al*⁷ was used and the following components were investigated in both parotid and submandibular salivary glands: (i) parenchymal echogenicity compared with thyroid gland or when there was co-incident thyroid gland disease compared with surrounding anatomical structure, graded 0–1; (ii) homogeneity, graded 0–3; (iii) presence of hypoechogenic areas, graded 0–3; (iv) hyperechogenic reflections, graded 0–3 in the parotid glands and 0–1 in the submandibular glands and (v) clearness of salivary gland border, graded 0–3. Ultrasonographic examination was performed by three well-trained ultrasonographers (AJS, KD and JFN). These ultrasonographers previously showed good to excellent interobserver reliability and excellent intraobserver reliability on the total Hocevar score.⁶

ACR-EULAR criteria

Patients were classified as pSS or non-pSS according to the recently published 2016 American College of Rheumatology-European League Against Rheumatism (ACR-EULAR) classification criteria.¹⁶ Routinely, all items of these criteria were assessed, including serology and histopathology. To assess fulfilment of the salivary gland histology item, labial as well as parotid glands biopsy results were considered.^{17 18}

Statistical analysis

Descriptive parameters were expressed as number of patients (%) for categorical data and mean (SD) for continuous data. Mann-Whitney U test was used to evaluate the differences in ultrasound scores between pSS and non-pSS patients according to the ACR-EULAR criteria. Associations between different ultrasound scores were analysed using Spearman's correlation coefficient (ρ); ρ was interpreted as poor (0.0–0.2), fair (0.2–0.4), moderate (0.4–0.6), good (0.6–0.8) or excellent (0.8–1.0) association.¹⁹ Receiver operating characteristic (ROC) analysis was performed to determine the accuracy of sUS to predict classification according to the ACR-EULAR criteria. Area under the curve (AUC) was interpreted as no discrimination (0–0.5), poor (0.5–0.7), fair (0.7–0.8), good (0.8–0.9) or excellent (0.9–1.0) accuracy.²⁰

The Hocevar total score (four glands, five components) was evaluated using univariate logistic regression analysis with ACR-EULAR classification as dependent variable. Univariate and multivariate logistic regression analyses applying the Forward Wald method were performed for ultrasound total score for (i) all separate glands, (ii) all individual components

Table 1 Characteristics of the study population

Characteristics	Total group (n=204)	pSS (n=116)	non-pSS (n=88)
Age, years	52.2 (13.8)	53.5 (12.8)	50.4 (14.8)
Females	174 (85.3%)	100 (86.2%)	74 (84.1%)
Parotid gland biopsy, focus score $\geq 1^*$	64 (40.3%)	61 (68.5%)	3 (4.3%)
Labial gland biopsy, focus score $\geq 1^*$	52 (52.0%)	47 (81.0%)	5 (11.9%)
Anti-SSA antibodies	106 (52.0%)	104 (89.7%)	2 (2.3%)
UWS ≤ 0.1 mL/min	113 (55.4%)	87 (75.0%)	26 (29.5%)
OSS $\geq 5^{\dagger}$	63 (31.0%)	55 (47.4%)	8 (9.2%)
Schirmer's test ≤ 5 mm/5 min†	144 (71.3%)	98 (84.5%)	46 (53.4%)
Ultrasound total score	16.9 (11.6)	23.2 (11.5)	8.7 (4.5)
Right parotid and submandibular glands	8.6 (6.1)	11.9 (6.1)	4.4 (2.4)
Left parotid and submandibular glands	8.3 (5.7)	11.3 (5.6)	4.3 (2.5)

Data are expressed as number of patients (%) or mean (SD).

OSS was missing in two patients and Schirmer's test was missing in one patient. Data were complete for anti-SSA antibody status, UWS and the ultrasonographic examination.

*A parotid gland biopsy was performed in 159 out of the 204 patients and a labial gland biopsy was performed in 100 out of the 204 patients. In 75 patients, both biopsies were performed. In 20 patients, there was no salivary gland biopsy performed. In these patients, the outcome of a biopsy would not influence classification as pSS or non-pSS according to the ACR-EULAR criteria.

†In at least one eye.

UWS, unstimulated whole saliva; OSS, ocular staining score.

of the Hocevar scoring system and (iii) combining i and ii.⁷ The explained variance was evaluated using Nagelkerke R^2 . IBM SPSS Statistics V.23 (SPSS, Chicago, Illinois, USA) was used to perform the statistical analyses. P values < 0.05 were considered to be statistically significant.

RESULTS

Between October 2014 and February 2017, 224 consecutive patients were evaluated in our multidisciplinary Sjögren's expertise centre. Twenty patients had to be excluded because of incomplete workup (n=14) or presence of an associated systemic autoimmune disease (n=6). Of the 204 included patients, mean age was 52 (13.8) years and 85% were female (table 1). This cohort consisted of tertiary referrals with clinical suspicion of pSS (n=171), and patients previously diagnosed with pSS from our RESULT cohort (n=33). A salivary gland biopsy was available in 184 patients. In the remaining 20 patients, the result of the biopsy would not influence classification as pSS or non-pSS and therefore these patients were not willing to undergo a salivary gland biopsy as part of the routine diagnostic workup. In this cohort, 116 (57%) patients were classified as pSS according to the ACR-EULAR criteria.

Online supplementary figure 1 shows ultrasonographic images of normal submandibular and parotid glands and images of submandibular and parotid glands suggestive of pSS. Ultrasound scores of all four glands differed significantly between pSS and non-pSS patients (online supplementary figure 2).

Scoring only one parotid and one submandibular gland is sufficient

In the total group, there were very high correlations between the ultrasound scores of both parotid glands ($\rho=0.909$), both submandibular glands ($\rho=0.868$) and between the combination

Figure 1 Association of ultrasound total scores between (A) right vs left parotid glands; (B) right vs left submandibular glands; (C) left parotid vs left submandibular glands; (D) right parotid vs right submandibular glands and (E) right parotid and submandibular glands vs left parotid and submandibular glands. Spearman's ρ is shown for (i) total group, (ii) American College of Rheumatology-European League Against Rheumatism (ACR-EULAR) positive group and (iii) ACR-EULAR negative group.

of left parotid and submandibular glands versus the right parotid and submandibular glands ($\rho=0.926$; [figure 1](#)). In other words, patients who scored high on their left parotid gland also scored high on their right parotid gland and the same is true for the submandibular glands.

Correlations between the ultrasound scores of the left parotid and left submandibular gland ($\rho=0.731$) as well as the right parotid and right submandibular gland ($\rho=0.734$) were slightly

lower ([figure 1](#)). In summary, the ultrasound scores of the same type of salivary glands are interchangeable (ie, right vs left parotid gland; right vs left submandibular gland), but this is not always true for the score of the different types of glands (ie, parotid vs submandibular gland).

The accuracy of sUS to predict ACR-EULAR classification based on the original Hoyer score (four glands, five components) was good (AUC=0.856; [figure 2](#)). Accuracy was

Figure 2 Receiver operating curves (ROC) (A–D) 4 glands, 5 components* compared with: (A) 2 glands, 5 components*, right and left; (B) 4 glands, 2 components†; (C) 2 glands, 2 components†, right and left and (D) 2 glands, 1 component‡, right and left. *5 components: parenchymal echogenicity, homogeneity, hypoechogenic areas, hyperechogenic reflections and salivary gland posterior border. †2 components: parenchymal echogenicity and hypoechogenic areas. ‡1 component: hypoechogenic areas.

comparable when only the scores of the right parotid and right submandibular gland ($AUC=0.850$), or only the scores of the left parotid and left submandibular gland ($AUC=0.852$) were included (figure 2).

In the univariate analysis, the explained variance (R^2) for the total Hocevar score of all four glands was 0.526 (table 2 and table 3). sUS scores of all individual glands significantly predicted ACR-EULAR classification, with R^2 ranging from 0.419 for the left parotid gland to 0.473 for the left submandibular gland (table 2B).

In the multivariate analysis, only the sUS scores of the right parotid and left submandibular gland independently predicted ACR-EULAR classification ($R^2=0.527$), due to high correlation

between both parotid glands and between both submandibular glands. When only the right parotid and right submandibular gland ($R^2=0.518$) or only the left parotid and left submandibular gland ($R^2=0.511$) were included, this resulted in models with equally high explained variance. In summary, scoring of only one side is enough to predict ACR-EULAR classification. Whether left or right side is scored does not make any difference.

Scoring only parenchymal echogenicity and hypoechogenic areas is sufficient

The distribution of scores for the individual Hocevar components differed significantly between pSS and

Table 2 Logistic regression analyses of separate major salivary glands and Hocevar components to predict ACR-EULAR criteria classification as pSS or non-pSS

	Univariate analysis OR (95% CI)	P value	R ²	Multivariate analysis OR (95% CI)	P value
A. Overall Hocevar score					
Total Hocevar score (0–48)	1.216 (1.148 to 1.288)	<0.001*	0.526	Not applicable	
B. Separate major salivary glands					
Right parotid gland (0–13)	1.765 (1.488 to 2.094)	<0.001*	0.449	1.415 (1.156 to 1.732)	0.001*
Left parotid gland (0–13)	1.718 (1.467 to 2.013)	<0.001*	0.419	–	†
Right submandibular gland (0–11)	1.854 (1.554 to 2.211)	<0.001*	0.472	–	†
Left submandibular gland (0–11)	1.913 (1.587 to 2.307)	<0.001*	0.473	1.538 (1.241 to 1.906)	<0.001*
C. Individual components of Hocevar score					
Parenchymal echogenicity (0–4)	4.350 (2.402 to 7.878)	<0.001*	0.433	2.279 (1.173 to 4.428)	0.015*
Homogeneity (0–12)	1.592 (1.395 to 1.816)	<0.001*	0.451	–	†
Hypoechoic areas (0–12)	1.683 (1.456 to 1.946)	<0.001*	0.505	1.453 (1.229 to 1.718)	<0.001*
Hyperechoic reflections (0–8)	2.101 (1.600 to 2.760)	<0.001*	0.236	–	†
Salivary gland posterior border (0–12)	1.793 (1.462 to 2.200)	<0.001*	0.315	–	†

*Statistically significant.

†Not included in the multivariate model (based on Forward Wald method).

ACR-EULAR, American College of Rheumatology-European League Against Rheumatism; pSS, primary Sjögren's syndrome.

non-pSS patients (online supplementary figure 3). In univariate analysis, all individual components significantly predicted ACR-EULAR classification. ACR-EULAR classification was predicted best by hypoechoic areas ($R^2=0.505$). The correlation between the components homogeneity and hypoechoic areas was very high ($p=0.927$; table 4), suggesting that these two components measure the same and that scoring both is not necessary. The multivariate analysis, including all five components measured in all four glands, showed that only parenchymal echogenicity and hypoechoic areas independently predicted ACR-EULAR classification ($R^2=0.539$), with a good AUC of 0.857.

Scoring two glands and one or two components increases feasibility of ultrasound in pSS

Taking into account only the right parotid and right submandibular glands, the results of the univariate analysis of the individual components of the Hocevar scoring system were similar compared with the model including all four glands (table 2B). In the multivariate analysis, only parenchymal echogenicity and

hypoechoic areas independently predicted ACR-EULAR classification ($R^2=0.539$), with a good AUC of 0.855 (figure 2). Taking into account only the left parotid and left submandibular glands, similar results were found (table 2C; figure 2).

Thus, sUS examination of parotid and submandibular glands on one side and scoring parenchymal echogenicity and hypoechoic areas, is sufficient to predict classification of patients according to the ACR-EULAR criteria.

However, this system can be simplified even further by only scoring the hypoechoic component of the Hocevar system, without decreasing the accuracy. When only scoring the hypoechoic areas of the right parotid and right submandibular glands, the explained variance was 0.498, with a good AUC of 0.846. The explained variance and accuracy were again similar for the left parotid and left submandibular glands (figure 2).

DISCUSSION

We proved that ultrasound scoring of hypoechoic areas in one parotid and one submandibular gland is enough to predict ACR-EULAR classification of patients with or without pSS.

Table 3 Logistic regression analyses of Hocevar components in the right and left glands to predict ACR-EULAR classification as pSS or non-pSS

	Univariate analysis OR (95% CI)	P value	R ²	Multivariate analysis OR (95% CI)	P value
A. Overall Hocevar score					
Total Hocevar score (0–48)	1.216 (1.148 to 1.288)	<0.001*	0.526	Not applicable	
B. Individual components of Hocevar system for right parotid and submandibular glands					
Parenchymal echogenicity (0–2)	15.024 (4.988 to 45.249)	<0.001*	0.427	5.188 (1.533 to 17.558)	0.008*
Homogeneity (0–6)	2.400 (1.872 to 3.077)	<0.001*	0.444	–	†
Hypoechoic areas (0–6)	2.694 (2.034 to 3.552)	<0.001*	0.498	2.031 (1.490 to 2.770)	<0.001*
Hyperechoic reflections (0–4)	3.242 (2.006 to 5.238)	<0.001*	0.188	–	†
Salivary gland posterior border (0–6)	2.669 (1.872 to 3.804)	<0.001*	0.292	–	†
C. Individual components of Hocevar system for left parotid and submandibular glands					
Parenchymal echogenicity (0–2)	13.779 (5.088 to 37.314)	<0.001*	0.404	4.071 (1.369 to 12.103)	0.012*
Homogeneity (0–6)	2.443 (1.894 to 3.152)	<0.001*	0.430	–	†
Hypoechoic areas (0–6)	2.589 (1.984 to 3.379)	<0.001*	0.471	1.989 (1.458 to 2.713)	<0.001*
Hyperechoic reflections (0–4)	3.552 (2.206 to 5.720)	<0.001*	0.214	–	†
Salivary gland posterior border (0–6)	2.996 (2.039 to 4.402)	<0.001*	0.291	–	†

*Statistically significant.

†Not included in the multivariate model (based on Forward Wald method).

ACR-EULAR, American College of Rheumatology-European League Against Rheumatism; pSS, primary Sjögren's syndrome.

Table 4 Spearman's correlation coefficients for individual Hocevar components

	Homogeneity	Hypoechoogenic areas	Hyperechoogenic reflections	Salivary gland posterior border
A. Right and left parotid and submandibular glands				
Parenchymal echogenicity	0.736	0.729	0.508	0.582
Homogeneity	–	0.927	0.574	0.624
Hypoechoogenic areas	–	–	0.603	0.593
Hyperechoogenic reflections	–	–	–	0.511
B. Right parotid and submandibular glands				
Parenchymal echogenicity	0.725	0.718	0.494	0.573
Homogeneity	–	0.921	0.540	0.602
Hypoechoogenic areas	–	–	0.556	0.568
Hyperechoogenic reflections	–	–	–	0.503
C. Left parotid and submandibular glands				
Parenchymal echogenicity	0.728	0.730	0.427	0.552
Homogeneity	–	0.921	0.517	0.613
Hypoechoogenic areas	–	–	0.520	0.589
Hyperechoogenic reflections	–	–	–	0.413

Thus far, there is no agreement regarding which ultrasonographic scoring system should be used in the evaluation of major salivary glands of patients suspected or clinically diagnosed with pSS. Based on a recent meta-analysis,³ the Hocevar scoring system⁷ was incorporated in our daily clinical practice to address all relevant aspects of sUS, since this system appeared to most comprehensive and was therefore also recently applied in our reliability and validity studies.^{6,10} As mentioned before, more simple scoring systems have been used previously,^{11–14} but, to the best of our knowledge, none of these simpler scoring systems were constructed applying a multivariate regression model. Ideally, in every rheumatologic outpatient clinic around the world the same scoring system for evaluation of salivary glands in the diagnostic workup of pSS should be applied. In order to reach such a goal, an essential first step was to perform a multivariate logistic regression analysis using the results of the most comprehensive scoring system commonly applied.⁷ Having access to a reliable, simpler sUS scoring system would greatly increase the feasibility of sUS as a routine procedure to be applied in the diagnostic workup of patients with pSS.

There was an excellent correlation between the ultrasound scores of the right and left parotid glands and the ultrasound scores of the right and left submandibular glands. Correlation between ultrasound scores of parotid and submandibular glands was somewhat lower, in agreement with previous reports.²¹ These results indicate that scoring of the two parotid glands is interchangeable and the same applies to both submandibular glands, but that ultrasound scores of the parotid compared with the submandibular glands can differ within patients. In some patients, the parotid glands are more affected, whereas in others the submandibular glands are more affected. Therefore, ultrasound abnormalities might be underdiagnosed in a subgroup of patients when only parotid glands or only submandibular glands are taken into account. This is confirmed by the multivariate regression model, in which only one parotid gland and one submandibular gland were found to independently contribute to ACR-EULAR classification as pSS or non-pSS. Our results therefore show that scoring of one side is adequate, but that the parotid as well as the submandibular gland should be scored.

Previously, studies found more pathological changes in the submandibular glands compared with the parotid glands in patients suspected with pSS.^{22,23} Takagi *et al* therefore suggested to reduce the sUS examination to only the submandibular glands in order to

save time.²² On the other hand, very recently it was suggested to measure only the parotid glands with a simplified scoring system.¹⁴ Based on our results, we cannot confirm either suggestion. Furthermore, neither of these studies performed multivariate regression analyses to actually proof their statements.

Another important reason to include sUS examination of the parotid glands, besides that it was included in our model, is that suspicion of the presence of a mucosa-associated lymphoid tissue lymphoma in the parotid gland might rise at an earlier stage. We therefore recommend to compile a global view of all four glands, especially when patients experience unilateral complaints, but to actually score only one side. With this global view, unilateral and bilateral morbidities of the salivary glands can be distinguished, increasing the specificity of the examination.

At group level, all five individual components of the Hocevar scoring system were significant predictors of ACR-EULAR classification. However, the differences in explained variance were quite large, that is, with the lowest value for hyperechoogenic reflections and the highest value for hypoechoogenic areas, indicating that not every component is equally highly predictive of ACR-EULAR classification. In the multivariate analysis, parenchymal echogenicity and hypoechoogenic areas were found to independently predict ACR-EULAR classification. It might even be considered to measure only hypoechoogenic areas of one parotid and one submandibular gland, since parenchymal echogenicity added only slightly to the explained variance and diagnostic accuracy. Taking into account the reliability of the individual components of the Hocevar score, reducing the scoring system to only hypoechoogenic areas increases the applicability even more. Recently, we showed that the interobserver reliability of hypoechoogenic areas was good ($\kappa > 0.7$). In contrast, the reliability of parenchymal echogenicity was only fair.⁶ Two other studies showed similar results even though slightly different scoring systems were applied.^{24,25} Both articles also contain ultrasonographic images of major salivary glands with different stages of ultrasonographic abnormalities suggestive of pSS.^{24,25}

Previously, it was assumed that the presence of hypoechoic rounded multiple parenchymal lesions is a pathognomonic feature of pSS and that only evident parenchymal inhomogeneity is of true diagnostic value.^{12,13} We agree with these assumptions. In the Hocevar scoring system, homogeneity and hypoechoogenic areas are scored separately. On the other hand, in the scoring system used by Theander and Mandl,¹² only parenchymal homogeneity is measured. However, when taking a closer

look at their scoring system, in fact a combination of homogeneity and hypoechogenic areas is scored.¹² Approximately the same component was measured in a German cohort.¹³ In our study, the correlation between homogeneity and hypoechogenic areas was excellent. Therefore, it can indeed be interpreted that both components measure the same concept in salivary glands of patients suspected or diagnosed with pSS. When there is a homogenous gland, there are no hypoechogenic areas present and when the gland is very inhomogeneous, this is usually due to the presence of hypoechogenic areas and less due to the presence of hyperechogenic reflections.

Reduction of the examination duration has the advantage that the sUS examination is easier to learn and takes less time to perform in clinical practice. By increasing the feasibility of sUS, it will facilitate outpatient rheumatologic clinics worldwide to integrate the ultrasound in the daily clinical practice when it comes to evaluating patients clinically suspected or diagnosed with pSS. We demonstrated that it is adequate to measure only one out of five components of the Hocevar scoring system, in only one side, without recommending a particular side.

The next step, before incorporation of sUS in the classification criteria is possible, would be to define exactly how to score hypoechogenic areas and decide the optimal cut-off point based on data from multiple centres.

In conclusion, in our cohort study derived from daily clinical practice, we showed that it is sufficient to measure parenchymal echogenicity and hypoechogenic areas in one parotid and one submandibular gland to predict classification as pSS or non-pSS according to the ACR-EULAR criteria. Taking into account the relatively small difference in diagnostic accuracy as well as the reliability of the individual ultrasound components, we pose that only measuring hypoechogenic areas in one parotid and one submandibular gland also is sufficient. As the severity of sUS findings in the parotid and submandibular glands may differ, one parotid and one submandibular gland of either the left or the right side should be scored. Simplification of sUS scoring will increase the feasibility of sUS in daily clinical practice and will facilitate worldwide implementation of the ultrasound in the outpatient rheumatologic clinics.

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