Added value of the salivary gland ultrasonography OMERACT score in the ACR/EULAR classification criteria for Sjögren’s disease

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A B S T R A C T

Keywords: Sjögren’s disease
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OMERACT
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Objectives: To assess whether addition of the salivary gland ultrasonography (SGUS) OMERACT score influences the performance of the 2016 ACR/EULAR classification criteria for Sjögren’s disease (SjD) in daily clinical practice.

Methods: Patients visiting the Sjögren Expertise centre in the University Medical Center Groningen for a diagnostic trajectory because of a suspicion of SjD were included. SGUS was performed of both parotid and submandibular glands. ROC analysis was used to assess the accuracy to predict clinical diagnosis of SjD with the SGUS OMERACT score, and by adding the SGUS OMERACT score to the ACR/EULAR criteria. Furthermore, the performance of the SGUS OMERACT and total SGUS Hocevar score were compared.

Results: In total, 419 consecutive patients were included. ROC analysis of the highest SGUS OMERACT score out of all four salivary glands (range 0–3) showed good accuracy (AUC 0.849) to predict clinical diagnosis of SjD, comparable to the accuracy of the total SGUS OMERACT score (range 0–12; AUC 0.868) and total Hocevar score (range 0–48; AUC 0.864). When incorporating the highest SGUS OMERACT score (cut-off score of ≥2) as additional item in the ACR/EULAR criteria, accuracy remained excellent (AUC 0.974), and clinical diagnosis could be predicted with a sensitivity of 96.4% and specificity of 86.5%.

Conclusion: The accuracy of the ACR/EULAR classification criteria for predicting the clinical diagnosis of SjD remained excellent after incorporating the SGUS OMERACT score and extends the diagnostic options in patients suspected with SjD.

Introduction

Sjögren’s disease (SjD) is a chronic systemic autoimmune disease. The main characteristics are dryness symptoms of eyes and mouth, and lymphocytic infiltration of the lacrimal and salivary glands. Since SjD is a systemic disease, patients may experience a variety of symptoms such as fatigue, arthritis, interstitial lung disease or polyneuropathy [1]. Because of this heterogeneous nature and the often gradual development of SjD, establishing a timely diagnosis can be challenging.

In 2016, the American College of Rheumatology/European Alliance of Associations for Rheumatology (ACR/EULAR) classification criteria for SjD were developed to be able to identify a homogeneous group of SjD patients for research purposes [2]. If patients fulfill the entry criteria (dryness symptoms or any activity in the EULAR Sjögren’s Syndrome Disease Activity Index (ESSDAI)) and do not fulfill any of the exclusion criteria, these classification criteria can be applied. The criteria consist of 5 items including a salivary gland biopsy, presence of anti-SSA (each weighted with 3 points) and the objective dryness measurements (Ocular Staining Score (OSS) ≥5 in at least one eye, Schirmer’s test ≤5 mm/5 min in at least one eye, unstimulated whole saliva flow (UWS) ≤0.1 ml/minute, each weighted with 1 point). Patients with a total score of ≥4 are classified with SjD [2]. The clinical diagnosis of SjD is based on expert opinion after extensive evaluation of all diagnostic assessments.

Salivary gland ultrasonography (SGUS) is not included in the ACR/EULAR classification criteria, but is increasingly used in SjD. In past research, various SGUS scoring systems have been used. We have previously shown that combining the presence of anti-SSA antibodies and SGUS scored with the Hocevar score [3] is highly predictive for classification of patients according to the ACR/EULAR criteria [4]. However, the Hocevar score (range 0–48) is quite extensive, and may therefore not

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be feasible to routinely perform in all centres [5]. Recently, a novel semi-quantitative and simpler scoring system for SGUS was proposed by the international Outcome Measures in Rheumatology (OMERACT) working group [6]. This SGUS OMERACT score evaluates homogeneity and presence of hypoechoic areas in the parotid and submandibular glands (range 0–3 per gland) [6,7]. Incorporating this scoring system in the ACR/EULAR classification criteria might improve classification of SjD. It could even supplement or replace items such as the salivary gland biopsy, which is an invasive procedure for patients and is not always performed in secondary referral centres. Furthermore, the SGUS OMERACT scoring system may be more feasible to perform than the extensive Hocevar scoring system in daily clinical practice.

Therefore, the main objective of this study was to assess whether addition of the SGUS OMERACT score influences the performance of the 2016 ACR/EULAR classification criteria. Secondary objectives were to compare the performance of predicting clinical diagnosis of the SGUS OMERACT score to the Hocevar score, and to assess the performance of anti-SSA positivity combined with the SGUS OMERACT score.

Methods

Study design and research subjects

This retrospective cross-sectional study included consecutive patients who visited the University Medical Center Groningen (UMCG), a tertiary referral and expertise centre for SjD patients, between January 2017 and December 2021 for a diagnostic trajectory because they were suspected to have SjD. As part of the standardized SjD diagnostic trajectory, patients visited the rheumatologist, oral and maxillofacial surgeon, dental hygienist, and ophthalmologist. In addition, SGUS was performed by experienced ultrasonographers, who were well calibrated and showed high inter-observer reliability [5]. Furthermore, a biopsy was performed in a subgroup of patients based on clinical decision. All patients were included in this analysis, i.e., regardless of comorbidities and medication use. Patients below 18 years of age or patients of which the medical file did not clearly state the diagnosis were excluded. Furthermore, patients who did not comply to the sicca symptom or ESSDAI entry criteria of the ACR/EULAR classification criteria, and patients without SGUS data were excluded. Clinical diagnosis by the treating physician (SjD or non-SjD sicca patients) was used as gold standard. Patients diagnosed with incomplete SjD were classified as non-SjD sicca patients.

Outcome measurements

For all patients, demographic data were collected. The following outcome measurements were collected: fulfilment of the ACR/EULAR classification criteria for SjD (yes/no), including the criteria items: parotid or labial salivary gland biopsy (focus score ≥1), presence of anti-SSA antibodies, OSS, Schirmer’s test, and UWS [2]. Furthermore, SGUS was performed of both parotid and submandibular glands with the same ultrasonographic scanner (Esaote MyLabSeven, Genova, Italy) equipped with a high-resolution linear probe (4–13 MHz). The SGUS Hocevar score was assessed, which includes the parameters homogeneity, hypoechoic areas, echogenicity, hyperechoic reflections, and clearness of the salivary gland borders for both parotid glands and submandibular glands. The total score ranges from 0 to 48 [3]. A total Hocevar score of ≥15 was considered positive [9]. The Hocevar score was converted to the SGUS OMERACT score using a conversion table developed by two experienced ultrasonographers (AS and KD) (Supplementary Table S1 and S2). The SGUS OMERACT scoring system assesses the salivary glands on a grade from 0 to 3 based on the homogeneity of the gland and the presence of hypoechoic areas; grade 0 represents a normal gland, grade 1 mild inhomogeneity without hypoechoic areas, grade 2 moderate inhomogeneity with focal hypoechoic areas, and grade 3 severe inhomogeneity with diffuse hypoechoic areas [7]. The main analysis was based on the highest score out of all four salivary glands (range 0–3). Additionally, we assessed the total SGUS OMERACT score by adding up individual scores of all four salivary glands (range 0–12). When a salivary gland was resected in a patient, resulting in missing scores, the scores of the same gland on the contralateral side were extrapolated to the missing side, which seems a reliable approach supported by our previous study [9]. The optimal cut-off point for SGUS OMERACT score to be considered positive was analysed.

Validation of conversion table for SGUS OMERACT score

External validation of the conversion table for the SGUS OMERACT score was performed in the Registro de Sjogren Syndrome Longitudinal (RESULT) cohort [10]. Consecutive outpatients with SjD (n = 263) underwent ultrasonographic examination by an experienced reader (AS or KD). SGUS was performed real-time according to the Hocevar score and OMERACT score. The Hocevar score was converted to the SGUS OMERACT score using the conversion table by an independent and blinded researcher (DR). The agreement between the converted OMERACT score and the live-scored OMERACT score was excellent, with Cohen’s kappa (linear weighting) of 0.843 for highest OMERACT score out of all four salivary glands (range 0–3) and intra-class correlation coefficient (2-way mixed effects model, single measures, absolute agreement) of 0.931 for total OMERACT score (range 0–12). Bland-Altman plot revealed that the converted OMERACT scores were lower compared to the live scores, with mean difference of −0.62 (Supplementary Figure 1). The most frequent discrepancy was between score 2 for converted OMERACT versus score 3 for live scoring, indicating that the severity of lesions is most difficult to score [5]. The agreement for SGUS OMERACT score of ≥2 in at least one gland, indicative for Sjogren’s disease, was excellent with Cohen’s kappa of 0.873 (Supplementary Table S3).

Statistical analysis

SPSS version 28.0 was used to perform statistical analyses. Mean (±SD), median (IQR) and n (%) were used to describe normally distributed, non-normally distributed and categorical data, respectively. Independent samples t-test, Mann-Whitney U test or Chi-Square test were used to analyse differences between the SjD and non-SjD sicca patients’ group as appropriate. The accuracy to predict clinical diagnosis of SjD of several outcome measures were analysed using receiver operating characteristics (ROC) analyses. The following outcome measures were analysed: the highest SGUS OMERACT score, i.e. highest score out of all four salivary glands (range 0–3), total SGUS OMERACT score, i.e. sum of scores from all four salivary glands (range 0–12), total Hocevar score from all four salivary glands (range 0–48), the current ACR/EULAR classification criteria, the ACR/EULAR criteria with addition of the (highest/total) SGUS OMERACT score, and the ACR/EULAR criteria with addition of the total Hocevar score. The area under the curve (AUC) was interpreted as poor (<0.5 to 0.7), fair (0.7 to 0.8), good (>0.8 to 0.9) or excellent (>0.9 to 1.0) accuracy. Furthermore, different cut-off values for the (highest/total) SGUS OMERACT and the ACR/EULAR classification criteria scores were evaluated to find the optimal cut-off value to predict clinical diagnosis of SjD based on the highest Youden’s index, which was calculated as (sensitivity + specificity)/100 – 1. Sensitivity and specificity of the original and modified ACR/EULAR criteria sets, with clinical diagnosis as the gold standard, were determined and compared. Furthermore, the sensitivity and specificity of anti-SSA positivity combined with the (highest/total) SGUS OMERACT score were determined. P-values of <0.05 were considered as statistically significant.
Results

Baseline characteristics

In total, 476 consecutive patients with a suspicion of SjD completed the diagnostic trajectory at the UMCG. Fifty-seven patients were excluded because of the following reasons: a diagnosis was not clearly stated in the medical file (n = 40), SGUS data were missing (n = 9), SGUS data were incomplete (n = 4) or because they did not fulfil the entry criteria of the ACR/EULAR classification criteria (n = 4). Of the 419 eligible patients, 167 were diagnosed with SjD. The remaining 252 patients were not diagnosed with SjD (n = 233) or were diagnosed with incomplete SjD (n = 19).

A significant difference between SjD and non-SjD sicca patients was observed for all items of the ACR/EULAR criteria, as expected (Table 1). In the SjD group, 159 patients (95.2%) fulfilled the ACR/EULAR criteria versus 29 patients (11.5%) in the non-SjD sicca group. Age, sex and symptom duration were comparable between both groups.

All SGUS scores were significantly higher in the SjD group compared to non-SjD sicca patients (Table 2). Considering the highest SGUS OMERACT score, a median score of 2 [1.0–3.0] was found in the SjD group versus 1 [0.5–1.5] in the non-SJD sicca group. Median total SGUS OMERACT score was 7 [4–10] in the SjD group versus 1 [0–2] in the non-SjD sicca group. Median total Hocevar scores were 22 [13.5–30.5] versus 6 [3.5–8.5] in the SjD and non-SjD group (Table 2).

Performance of the ACR/EULAR classification criteria with addition of SGUS OMERACT score

The highest SGUS OMERACT score (range 0–3) could predict clinical diagnosis with good accuracy, with an AUC of 0.849 [95% CI 0.810–0.889]. An optimal cut-off point of ≥2 in at least one gland was found. When using highest SGUS OMERACT score of ≥2 in at least one gland as cut-off point, sensitivity was 74.9% and specificity 85.7% (Table 3). Furthermore, 125 of 167 patients (74.9%) in the SjD group, and 36 of 252 patients (14.3%) in the non-SjD sicca group reached this cut-off point (Table 2). The total SGUS OMERACT score (range 0–12) showed a marginally higher AUC of 0.868 [95% CI 0.830–0.905], and the Youden’s index was very similar for an optimal cut-off score of ≥4 or ≥5. With a cut-off point of ≥5, clinical diagnosis was predicted with a sensitivity of 68.3% and specificity of 91.7% (Table 3). Furthermore, 114 of 167 patients (68.3%) in the SjD group and 21 of 252 patients (8.3%) in the non-SjD sicca group reached this cut-off point (Table 2).

The current ACR/EULAR classification criteria showed excellent accuracy to predict clinical diagnosis, with an AUC of 0.966 [95% CI 0.950–0.982] (Fig. 1A). To incorporate the SGUS OMERACT score into the ACR/EULAR criteria, a weight of 1 point was allocated to a positive SGUS OMERACT score. With the highest SGUS OMERACT score of ≥2 as an additional item in the ACR/EULAR criteria, the AUC was 0.974 [95% CI 0.961–0.987]. Alternatively, with the total SGUS OMERACT score of ≥5 as additional item in the ACR/EULAR criteria, the AUC was 0.975 [95% CI 0.962–0.988].

The optimal cut-off score of ≥4 for the current ACR/EULAR classification criteria was confirmed, resulting in a sensitivity of 95.2% and a specificity 88.5% to predict clinical diagnosis (Table 3). With the addition of highest SGUS OMERACT score of ≥2 and the original cut-off score of ≥4 for the ACR/EULAR criteria, sensitivity was 96.4% and specificity 86.5%. With a stricter cut-off score of ≥5 for the ACR/EULAR criteria, sensitivity decreased to 86.2% and specificity increased to 96.8%. With addition of total SGUS OMERACT score of ≥5 and the original cut-off score of ≥4 for the ACR/EULAR criteria, a sensitivity of 95.8% and specificity of 88.1% was found. With a stricter cut-off score of

Table 1

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>SjD (n = 167)</th>
<th>Non-SjD sicca patients (n = 252)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>53 ± 14</td>
<td>53 ± 14</td>
<td>0.948</td>
</tr>
<tr>
<td>Sex (female)</td>
<td>146/167</td>
<td>220/252 (87.3)</td>
<td>0.970</td>
</tr>
<tr>
<td>Symptom duration (years)</td>
<td>5 [0.5–9.5]</td>
<td>5 [1–9]</td>
<td>0.624</td>
</tr>
<tr>
<td>Fulfilling ACR/EULAR criteria ≥4</td>
<td>159/167</td>
<td>29/252 (11.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FS ≥1 in salivary gland biopsy</td>
<td>111/137</td>
<td>19/155 (12.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Anti-SSA positive</td>
<td>134/167</td>
<td>31/250 (12.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ocular staining score ≥5*</td>
<td>34/167</td>
<td>15/252 (6.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Schirmer ≤5 mm</td>
<td>113/163</td>
<td>126/239 (52.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Unstimulated whole saliva &lt;0.1 ml/min</td>
<td>91/165</td>
<td>90/250 (36.0)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Data presented as mean ± SD, median [IQR] or n/total n (%).

* Scored in at least one eye.

Table 2

SGUS of study population.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>SjD (n = 167)</th>
<th>Non-SjD sicca patients (n = 252)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Highest SGUS OMERACT score (from all glands, range 0–3)</td>
<td>2 [1.0–3.0]</td>
<td>1 [0.5–1.5]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Highest SGUS OMERACT score ≥2 in ≥1 gland</td>
<td>125 (74.9)</td>
<td>36 (14.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total SGUS OMERACT score (range 0–12)</td>
<td>7 [4–10]</td>
<td>1 [0–2]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total SGUS OMERACT score ≥5</td>
<td>114 (68.3)</td>
<td>21 (8.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total Hocevar score (0–48)</td>
<td>22 [13.5–30.5]</td>
<td>6 [3.5–8.5]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total Hocevar score ≥15</td>
<td>105 (62.9)</td>
<td>11 (4.4)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Data presented as median [IQR] or n (%).

Table 3

Performance of SGUS scores, performance of original and modified ACR/EULAR criteria including SGUS scores, and the performance of SSA and SGUS scores to predict clinical diagnosis of SjD.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Youden’s index</th>
</tr>
</thead>
<tbody>
<tr>
<td>SGUS scores</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Highest SGUS OMERACT score ≥2 in ≥1 gland</td>
<td>74.9</td>
<td>85.7</td>
<td>0.606</td>
</tr>
<tr>
<td>Total SGUS OMERACT score ≥5</td>
<td>68.3</td>
<td>91.7</td>
<td>0.600</td>
</tr>
<tr>
<td>Original and modified ACR/EULAR criteria</td>
<td>59.9</td>
<td>97.2</td>
<td>0.571</td>
</tr>
<tr>
<td>Original ACR/EULAR criteria (cut-off ≥4)</td>
<td>95.2</td>
<td>88.5</td>
<td>0.837</td>
</tr>
<tr>
<td>ACR/EULAR criteria (cut-off ≥4) with highest SGUS OMERACT score ≥2 in ≥1 gland</td>
<td>86.2</td>
<td>96.8</td>
<td>0.830</td>
</tr>
<tr>
<td>ACR/EULAR criteria (cut-off ≥5) with highest SGUS OMERACT score ≥2 in ≥1 gland</td>
<td>95.8</td>
<td>88.1</td>
<td>0.839</td>
</tr>
<tr>
<td>ACR/EULAR criteria (cut-off ≥5) with total SGUS OMERACT score ≥5</td>
<td>84.4</td>
<td>97.2</td>
<td>0.816</td>
</tr>
<tr>
<td>ACR/EULAR criteria (cut-off ≥5) with total SGUS OMERACT score ≥5</td>
<td>95.8</td>
<td>87.7</td>
<td>0.835</td>
</tr>
<tr>
<td>ACR/EULAR criteria (cut-off ≥5) with total SGUS OMERACT score ≥5</td>
<td>81.4</td>
<td>97.2</td>
<td>0.786</td>
</tr>
<tr>
<td>SSA and SGUS OMERACT</td>
<td>64.1</td>
<td>98.4</td>
<td>0.625</td>
</tr>
<tr>
<td>SSA positivity and positive SGUS OMERACT (highest score ≥2 in ≥1 gland)</td>
<td>58.7</td>
<td>99.6</td>
<td>0.583</td>
</tr>
</tbody>
</table>

Data presented as median [IQR] or n (%).
The performance of the SGUS OMERACT score compared to the Hocevar score

The total Hocevar score had a very similar AUC compared to the SGUS OMERACT score (Hocevar: 0.864 vs. highest SGUS OMERACT: 0.849) (Fig. 1B). The sensitivity and specificity of Hocevar score of ≥5 to predict clinical diagnosis were 59.9% and 97.2%, respectively. With a stricter cut-off score of ≥4 for the ACR/EULAR criteria, a sensitivity of 95.8% and specificity increased to 97.2% (Table 3).

Presence of anti-SSA and SGUS OMERACT score

SSA seropositivity and highest SGUS OMERACT score of ≥2 could predict clinical diagnosis with a sensitivity of 64.1% and specificity of 98.4%. For SSA seropositivity and total SGUS OMERACT score of ≥5, this was 58.7% and 99.6% respectively (Table 3). In total, 107 of 167 (64.1%) patients in the SjD group had positive anti-SSA and reached highest SGUS OMERACT score of ≥2. In the non-SjD group, this was the case in 4 of 250 (1.6%) patients. Considering anti-SSA positivity and total SGUS OMERACT score of ≥5, 98 of 167 (58.7%) patients in the SjD group were positive for both. In the non-SjD sicca group, only one of 250 (0.4%) patients was positive for both. In the SjD group, only 15 of 167 (8.98%) patients were both anti-SSA negative and had highest SGUS OMERACT score of <2. In the non-SjD group, this was the case in 187 of 250 (74.8%) patients. When using total SGUS OMERACT score of <5, the number of patients negative for both anti-SSA and total SGUS OMERACT score was numerically higher in both the SjD group (n = 17) and non-SjD group (n = 199) compared to the highest SGUS OMERACT score.

In the subgroup in which a biopsy was performed (n = 292), two in the non-SjD group (n = 155) had a positive biopsy and SGUS OMERACT score when considering the cut-off point of ≥2 in ≥1 gland. In the SjD group, both items were positive in 87 of 137 (63.5%) patients. None of the non-SjD patients were both anti-SSA positive and reached the total SGUS OMERACT cut-off point of ≥5. In the SjD group, both items were positive in 80 of 137 (58.4%) patients.

Discussion

Our study aimed to assess whether addition of the SGUS OMERACT score influenced the performance of the 2016 ACR/EULAR classification criteria in predicting the clinical diagnosis of SjD patients in daily clinical practice. We demonstrated that the SGUS OMERACT score showed good accuracy to predict clinical diagnosis of SjD, and that the accuracy of the ACR/EULAR criteria with addition of the SGUS OMERACT score remained excellent, with a somewhat higher sensitivity and somewhat lower specificity. These results were consistent when considering the highest SGUS OMERACT score out of all four salivary glands, or when considering the sum from all four salivary glands.

When analysing the highest SGUS OMERACT score (range 0–3), a score of ≥2 in at least one gland was found as optimal cut-off point in predicting clinical diagnosis. For the total SGUS OMERACT score (range 0–12), the Youden’s index was very similar for an optimal cut-off value of ≥4 or ≥5. In practice, an optimal cut-off value of ≥5 is more relevant, as this means at least one gland must have a score of ≥2, demonstrating that at least moderate inhomogeneity with focal hypoechoic areas in either one of the submandibular or parotid glands is indicative of SjD. Comparing these two definitions, highest SGUS OMERACT score of ≥2 has somewhat higher sensitivity for predicting clinical diagnosis, whereas specificity is somewhat lower, compared to the total SGUS OMERACT score of ≥5. A smaller cross-sectional observational study showed similar results, with an optimal cut-off value of ≥2 in at least one gland for fulfilling the ACR/EULAR classification criteria [12].

The performance of the SGUS OMERACT score in our study is in line with prior studies, but these studies demonstrated higher cut-off values for the total SGUS OMERACT score for predicting fulfilment of the ACR/EULAR classification criteria [13,14]. One study showed an optimal...
The accuracy of the SGUS OMERACT score in predicting clinical diagnosis was comparable with the Holecvar score, even though the SGUS OMERACT score consists of fewer components. In clinical practice, implementing the SGUS OMERACT score can save time when performing SGUS. Previously, our group demonstrated excellent intra-observer reliability and good to excellent inter-observer reliability for the homogeneity and hypoechoic area components of the total Holecvar score, which are also the components included in the SGUS OMERACT score [5]. A European multicentre reliability study demonstrated excellent intra-observer reliability (kappa 0.87) and substantial inter-observer reliability (kappa 0.77) of the SGUS OMERACT score, regardless of the experience of the ultrasonographist [17]. The SGUS OMERACT score can therefore be considered feasible and reliable to assess involvement of the salivary glands in SjD patients.

Our study demonstrated that SSA seropositivity and SGUS OMERACT positivity (highest score of ≥2) could predict clinical diagnosis with a sensitivity of 64.1% and a specificity of 98.4%. This is in line with our previous findings. A study by Robin et al. also found a lower AUC of 0.705, with a cut-off of ≥2 in at least one gland [15]. In our study, the performance of highest SGUS OMERACT score of ≥2 and total SGUS OMERACT score of ≥5 was very similar, therefore we propose using SGUS OMERACT score ≥2 in ≥1 gland cut-off as this is the most feasible for the clinic.

The addition of the highest SGUS OMERACT score of ≥2 or total SGUS OMERACT score of ≥5 to the ACR/EULAR criteria yielded a comparable accuracy, sensitivity and specificity as the original ACR/EULAR criteria to predict clinical diagnosis. Increasing the modified ACR/EULAR criteria cut-off to ≥5 instead of ≥4 for both SGUS OMERACT scores, resulted in a decrease in sensitivity but increase in specificity. A small retrospective study showed similar results [15]. Previously, we analysed the addition of SGUS based on measurement of hypoechoic areas in one parotid and one submandibular gland to the ACR/EULAR criteria. Similarly, increasing the modified ACR/EULAR cut-off score to ≥5 led to a decrease in sensitivity and increase in specificity [16]. Because a cut-off score of ≥5 for the ACR/EULAR criteria would lead to less classification of SjD, using the current ACR/EULAR cut-off score of ≥4 with SGUS OMERACT as additional item (weight 1 point) would be preferred. Patients with SSA negativity and a negative biopsy could potentially classify as SjD in this case. However, within our study population, only 19 patients clinically diagnosed with SjD reached a score of 4 when taking out the focus score and anti-SSA, which was not the case for non-SjD patients. An important argument for adding the SGUS OMERACT score as an item to the ACR/EULAR criteria is that it improves the balance of the classification criteria. Currently, Schirmer’s test to assess function of the lacrimal glands and OSS as indicator of ocular surface dryness (punctate epithelial erosions or devitalized conjunctival cells) are included, while for the salivary glands only a functional test is part of the criteria (UWS). SGUS is a simple, non-invasive imaging procedure, and with the SGUS OMERACT score, this procedure is even less complex and time consuming than the SGUS Holecvar score.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Ethics statement

This study was conducted in accordance with the Declaration of Helsinki. The research protocol was approved by the Central ethics
Review Board non-WMO studies of the University Medical Center Groningen (CTc UMCG; 202200009), which waived the requirement of written informed consent. Data availability statement: Data are available from the University of Groningen-UMCG Institutional Data Access for researchers who meet the criteria for access to confidential data. The local ethics committees of the University Medical Center Groningen (UMCG) will maintain the ethical restrictions of the data. The Data Protection Officer of the UMCG will maintain the legal restrictions and appropriate codes of conduct. Permission is required prior to access. Data requests can be sent to Research Data Office University of Groningen: researchdata@rug.nl.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.semarthrit.2024.152473.

References