Two-dimensional shear wave elastography as an alternative method of ultrasound for major salivary gland evaluation in Sjögren's disease

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Abstract

Objective
This study aimed to investigate the performance of 2-dimensional shear wave elastography (2D-SWE) in the assessment of major salivary gland (MSG) involvement in patients with Sjögren's disease (SjD), compared with B-mode ultrasound (B-mode US), both individually and in combination, and to evaluate the association between elastography parameters and clinical and laboratory data.

Methods
This cross-sectional study included 52 patients with SjD and 48 age, sex and ethnicity-matched healthy controls. Clinical and laboratory characteristics of the patients were recorded. MSG were assessed by B-mode US, and 2D-SWE, in both parameters [elasticity and shear wave velocity (SWV)].

Results
B-mode US and SWE parameters revealed significant differences between patients with SjD and healthy controls. Analysis of the four MSG combined demonstrated that SjD patients had higher values of elasticity (15.2 ± 2.9 vs. 9.3 ± 0.8 kPa; $p<0.001$) and SWV (2.2 ± 0.2 vs. 1.8 ± 0.1 m/s; $p<0.001$) compared with controls. Both elasticity and SWV showed excellent diagnostic performance for SjD (AUC=0.982 and 0.983, respectively). Comparatively, the elastography parameters showed higher AUCs than B-mode US (AUC=0.852). Combining both methods provided superior predictive ability (AUC=0.985) compared to isolated use of B-mode US. No significant correlations were observed between SWE parameters and clinical or laboratory features, except for the glandular domain of the ESSDAI ($r=0.286$; $p=0.040$).

Conclusion
Elastography seems to be a promising tool for providing additional diagnostic value in SjD. 2D-SWE, either alone or in combination with B-mode US, may contribute to the assessment of MSG as a quantitative, non-invasive and feasible imaging method. However, further studies are needed to validate this technique.

Key words
Sjögren's disease, Sjögren's syndrome, major salivary glands, shear-wave elastography, B-mode ultrasound

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Introduction

Sjögren's disease (SjD) is a common chronic systemic autoimmune rheumatic disease, characterised by lymphoplasmacytic infiltration of exocrine glands that mainly affects the salivary and lacrimal glands, leading to immune-mediated secretory dysfunction, and generally presenting as xerostomia and xerophthalmia (1). Sicca symptoms, fatigue and joint pain occur in more than 80% of patients with this disease (2). In addition, systemic manifestations are present in almost 50% of patients, including pulmonary, articular, cutaneous, muscular, haematological, renal and neurological involvement (2, 3). An important and potentially life-threatening complication of SjD is B-cell non-Hodgkin lymphoma, which develops predominantly in the major salivary glands (MSG) (4, 5).

The prevalence of SjD varies widely around the world being estimated at 0.03% to 2.7%, and affects predominantly women between 40-60 years of age, in a variable proportion of 9-20:1. The variability and lack of specificity of signs and symptoms of the disease often lead to a delay in diagnosis (6), by which time there is frequently significant glandular damage (7).

The current classification criteria for SjD, established by the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) in 2016 (8), are based on clinical and laboratory abnormalities and do not include any imaging methods of the MSG.

Currently, B-mode US of MSG is one of the most often used imaging methods to assess structural alterations of the MSG with high accuracy in the diagnosis of SjD (9) However, there is wide variability in the diagnostic performances of B-mode US in different reports, likely due to the use of different scoring systems, as well as the subjective and operator-dependent nature of this method (10).

Elastography is a new complementary technique of the US to overcome the limitations of B-mode US in SjD (7). Several ultrasound elastography techniques have been developed using different excitation methods. There are two main modalities of elastography: strain imaging and shear wave imaging (SWI). SWI is a quantitative method that employs different technical approaches: transient elastography, and acoustic radiation force impulse (ARFI). ARFI-based techniques include point shear wave elastography (p.SWE), and 2-dimensional SWE (2D-SWE) (11-14).

SWE uses ARFI to generate shear waves. This technique reports the shear waves velocity (SWV) in metres per second (m/s) or converts the value into Young's modulus, a quantitative estimate of tissue elasticity, in kilopascals (kPa). Both SWV and the elasticity modulus increase with tissue stiffness and with loss of gland elasticity (11, 12). The most recent SWE technique is 2D-SWE, which allows the operator to be directed by both anatomical and tissue stiffness information. The sonographer chooses an adequate region of interest (ROI), as the most representative part of the gland (15). 2D-SWE accesses tissue stiffness over a much larger area than p.SWE and provides a numerical value (11, 14, 15). This objective quantitative result reduces the operator-dependency and subjectivity of this method (7, 16).

Some studies have shown that elastography may be useful for diagnosing SjD at stages when morphological abnormalities of the MSG are not yet present (17, 18), as well as for identifying patients with suspected parotid lymphoma (15, 19).

Based on the above, the current study aimed to evaluate the performance of 2D-SWE in assessing MSG involvement in patients with SjD, in comparison to B-mode US, both individually and in combination. Additionally, the study sought to explore the correlations between elastography parameters, and clinical and laboratory findings.

Material and methods

Study design and participants

This cross-sectional study, conducted between June 2024 and January 2025, included 52 consecutive patients aged 18 years or older with SjD, during their routine clinical care. All of whom met the 2016 ACR/EULAR classification criteria for SjD (8) and were under

regular follow-up at two tertiary rheumatology outpatient clinics specialising in SjD. Exclusion criteria included having another autoimmune rheumatologic disease, C hepatitis, human immunodeficiency virus infection, sialolithiasis, sarcoidosis, amyloidosis, IgG4-associated disease, lymphoma or other tumours of the MSG, and previous head or neck radiotherapy. The control group, matched to patients by age (± 3 years), sex, and ethnicity, was composed of 48 volunteers aged 18 years or older without rheumatologic autoimmune disease, salivary gland disease or sicca symptoms. Control participants were recruited among the patients' relatives and hospital staff during the study period. Matching was performed manually to ensure comparable distributions of demographic characteristics between groups.

All participants provided written informed consent, in accordance with the Declaration of Helsinki. The study protocol was approved by the Research Ethics Committee of the Federal University of Health Sciences of Porto Alegre (CAAE: 45083421.5.0000.5345), Irmandade da Santa Casa de Misericordia de Porto Alegre Hospital (CAAE: 45083421.5.3001.5335), and Pontifical Catholic University of Rio Grande do Sul, São Lucas Hospital (SLH) as a co-participant institution.

Clinical data
Clinical data including age, sex, ethnicity, disease duration, duration of symptoms and presence and duration of mouth dryness (<5 years; ≥5 years) were collected. Systemic disease activity was evaluated according to the EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) (20, 21) scored from 0–123 and divided into three groups: low activity (<5), moderate activity (5–13) and high activity (≥14). The glandular domain of the ESSDAI was classified into three categories (no activity, low activity and moderate activity) based on the degree of MSG enlargement. The patient-reported symptoms were recorded from the EULAR Sjögren Syndrome Patient Reported Index (ESSPRI) (22, 23) using the average of the scales for pain,

Table I. The OMERACT ultrasonographic grading system for diagnosing Sjögren's disease.

Grade	Descriptions
0	normal parenchyma
1	minimal change (mild inhomogeneity without anechoic/hypoechoic foci)
2	moderate change (moderate inhomogeneity with focal anechoic/hypoechoic foci surrounded by normal tissue)
3	severe change (diffuse inhomogeneity with anechoic/hypoechoic areas occupying the entire gland surface

Adapted from Jousse-Joulin *et al.* (25).

fatigue and dryness (0-10) and divided into two groups (<5 and ≥5). The ESSPRI Dryness Domain (0-10) was also classified into <5 and ≥5. The non-stimulated whole saliva flow rate (NSWSF) was measured in 15 min (≤0.1mL/min and >0.1mL/min) (24), and Schirmer's test in 5 min (≤5mm and >5mm). Labial salivary gland biopsy (LSGB) was performed (focus score ≥1 and <1) and immunological profiles including antinuclear antibodies (ANA), rheumatoid factor (RF), anti-SSA/Ro, and anti-SSB/La, were collected.

Ultrasound examination:
B-mode US and 2D SWE
Patients and controls underwent a standardised US evaluation in a single visit. All participants were examined in the supine position. The four major glands (bilateral parotid and submandibular glands) were assessed using B-mode US and 2D-SWE modalities. Routine B-mode US was performed before the 2D-SWE, with a portable, stand-alone US system (Aplio a / Canon Medical Systems, Otawara, Japan), equipped with elastography software and a 5–14 MHz linear transducer.

All imaging exams were carried out in the radiology department of SLH and were performed by the same physician, a board-certified radiologist, with over five years of experience in elastography, blinded to the clinical data of the subjects.
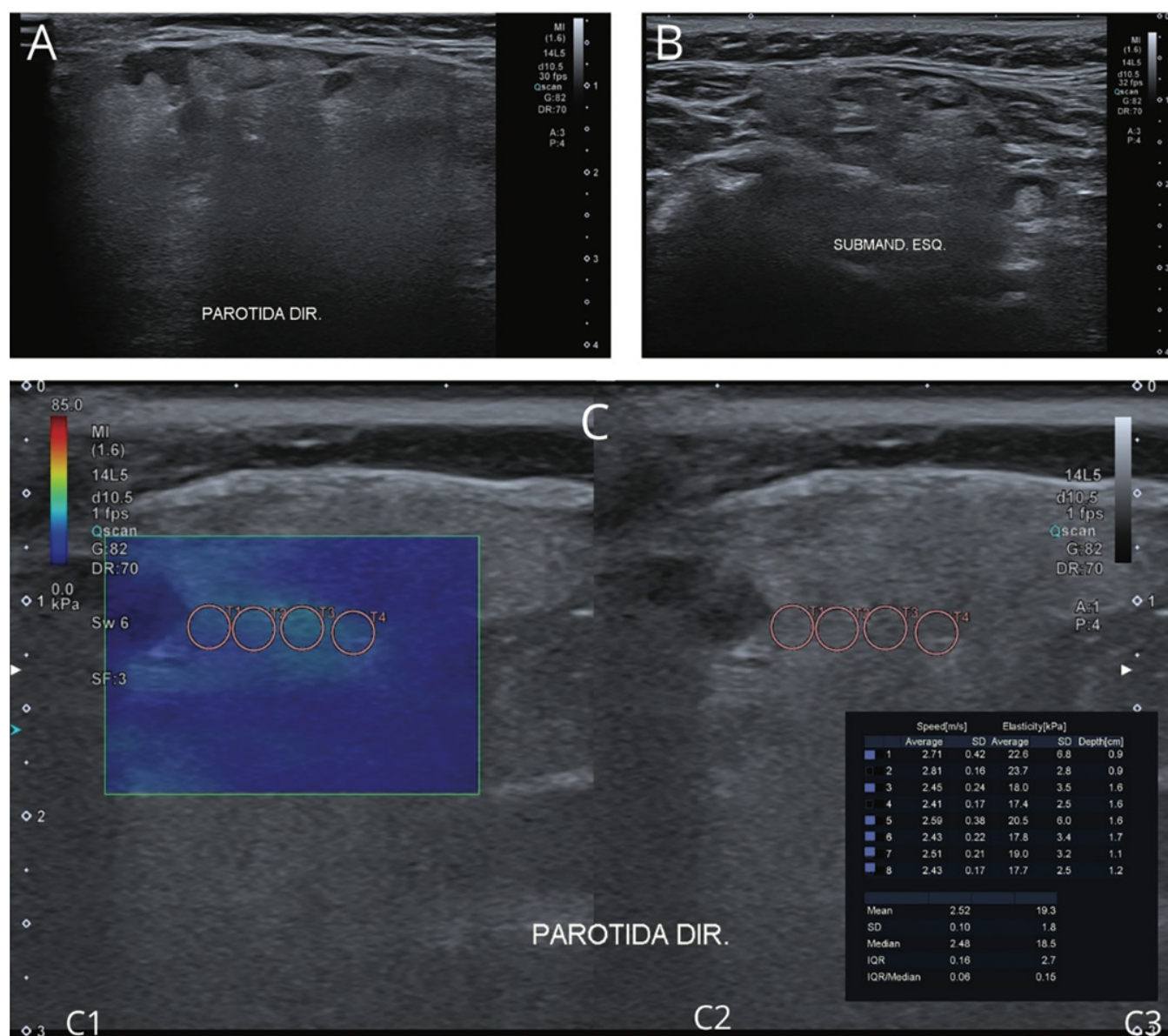
Imaging technique:
B-mode US Grading
The B-mode US of the MSG was evaluated in longitudinal and transverse planes, according to the scoring system of the Outcome Measures in Rheumatology Clinical Trials (OMERACT)

working group, for parotid and submandibular glands (grade 0–3) (25). Evaluation of echogenicity and homogeneity of each salivary gland was assessed and scored semi-quantitatively in four grades, as presented in Table I. The highest score was recorded as the total score for each patient. Grades 2 and 3 represent pathological changes, consistent with SjD alteration (25-27).

Imaging technique: 2D-SWE
The 2D-SWE of the MSG was performed after switching the echograph to the shear wave mode only in the transverse plane. MSG were identified under the guidance of grey-scale imaging. The transducer was placed perpendicular to the measurement area with an adequate quantity of ultrasound gel, and no pressure was applied to the examined tissue. Measurements were made using a ROI, measuring 1x1cm. The ROI was selected as the most representative part of the gland, without visible vessels and cystic areas. Following a 3-s interval to complete colour filling within the sampling frame, the acquired frame was stored. Eight consecutive measurements (quantification cursors) at two deep positions, in four lateral directions were placed within the ROI in the gland, each providing the values for SWV in m/s and an estimated elasticity value in kPa, defined with Young's modulus (tissue stiffness). The highest and lowest of all 8 measurements were eliminated. The remaining 6 measurements were taken for each gland and the averages of the SWV, and the elasticity modulus were calculated automatically by the ultrasound machine. For each salivary gland measurement (kPa), the interquartile range-to-median ratio (IQR/M) was maintained

Fig. 1. B-mode ultrasound and 2D-shear wave elastography of the major salivary glands in a patient with Sjögren Disease.
A: B-mode ultrasound grade 2 in the right parotid gland; **B**: B-mode ultrasound grade 3 in the left submandibular gland; **C**: 2D-shear wave elastography parameters in the right parotid gland [elasticity (kPa) and shear wave velocity (m/s)]; C1) colour-coded image with placement of the Q-box and four quantification cursors; C2) corresponding B-mode ultrasound image of the right parotid gland; C3) obtained values of the eight consecutive quantification cursors and the mean of the elasticity and the shear wave velocity of the six selected measurements.

below 30% to ensure measurement quality (14). The mean of the elasticity modulus and SWV measurements of the four glands, as well as the parotid and submandibular glands, separately, were used in the analysis. Examples of a B-mode US and a 2D-SWE scan of the salivary glands in the SjD group are presented in Figure 1.

Statistical analysis
Statistical analysis was performed using IBM SPSS Statistics software, version 21.0 (IBM Corporation, Armonk, NY, USA). The distribution of variables was assessed using the Shapiro-Wilk test. Categorical variables are described as absolute frequencies and percentages, while continuous variables are expressed as mean ± standard deviation (SD) when normally distributed, or as median and interquartile range (IQR) when asymmetrically distributed.

To compare patients with SjD and healthy control subjects, the chi-square test was used for categorical variables, and the Student's t-test for continuous variables with a normal distribution.

Comparisons of the mean values of elasticity and SWV among the parotid and submandibular glands were conducted using the paired Student's test.

The diagnostic performance of the evaluated methods was determined using Receiver Operating Characteristic (ROC) curves, including calculation of the area under the curve (AUC), sensitivity, and specificity. The Youden index was used to define the optimal cutoff points for distinguishing between individuals with and without SjD.

Logistic regression models were con-

structed to predict the presence of SjD. Parameters obtained from B-mode US, elasticity values, and a combined model integrating both variables were analysed separately. The predictive performance of the models was assessed through the odds ratio [Exp(B)] with corresponding 95% confidence intervals (95% CI), model fit (Nagelkerke's R^2), discriminative ability (AUC), and overall accuracy (proportion of correct classifications). Model comparisons were performed using the likelihood ratio test.

Correlations between clinical variables and SWE parameters related to SjD were assessed using Pearson's correlation coefficient for symmetrically distributed data and Spearman's correlation coefficient for asymmetrically distributed data. The significance level adopted for all analyses was 5% (α=0.05).

Results

A total of 100 participants were included in the study, comprising 52 patients with SjD and 48 healthy individuals. No statistically significant differences were observed between the groups regarding age, sex, and race (Table II).

Among patients with SjD, the median symptom duration was 13 years (IQR: 8–19), while the median time since diagnosis was 6 years (IQR: 3–11). The mean ESSPRI score was 6.1±2.2, with the dryness domain being the most affected. The median ESSDAI score was 6 (IQR: 2–11), with 44.2% of patients classified as having low disease activity, 34.6% as moderate activity, and 21.2% as high activity. In the glandular ESSDAI, 61.5% of patients exhibited no activity, while 38.5% presented low or moderate activity. A labial salivary gland biopsy (LSGB) was performed on 19 (36.5%) SjD patients, with a focus score of ≥1 in 14 (73.7%) of them. Additional clinical and laboratory characteristics are presented in Table III.

The B-mode US assessment revealed significant differences between patients with SjD and healthy individuals. Regarding B-mode US scores, 80.8% of SjD patients had grades 2–3 across the four glands, in contrast to only 10.4% of controls, however, 10 patients (19.2%) with SjD had grades 0–1 (Table IV).

The analysis of elastography para-meters, performed both collectively across all MSG and individually, for each gland, demonstrated statistically significant differences between patients with SjD and healthy controls. The analysis of the four MSG demonstrated that SjD patients had higher values of elasticity (15.2±2.9 *vs.* 9.3±0.8kPa; *p*<0.001) and SWV (2.2±0.2 *vs.* 1.8±0.1m/s; *p*<0.001) compared to controls. Similar findings were observed in specific analyses of the parotid and submandibular glands. Statistically significant differences were identified

Table II. Baseline characteristics of the study population.

	Sjögren's disease (n = 52)	Health subjects (n = 48)	*p*-value
Age (years), mean ± SD	59.6 ± 11.9	58.8 ± 14.7	0.755
Sex, n (%)			0.732
Female	51 (98.1)	47 (97.9)	
Race, n (%)			0.836
White	36 (69.2)	35 (72.9)	
Mixed-race	9 (17.3)	9 (18.8)	
Black	6 (11.5)	3 (6.3)	
Indigenous	1 (1.9)	1 (2.1)	

n: sample size; SD: standard deviation.

Table III. General clinic and laboratorial characteristics of Sjögren's disease patients.

	n=52
Time to symptom onset (years), median (IQR)	13 (8 – 19)
Diagnosis time (years), median (IQR)	6 (3 – 11)
Diagnosis time, n (%)	
< 5 years	18 (34.6)
5 – 10 years	19 (36.5)
> 10 years	15 (28.8)
Duration of xerostomia, n (%)	
< 5 years	4 (7.7)
≥ 5 years	48 (92.3)
ESSPRI total score, mean ± SD	6.1 ± 2.2
ESSPRI total score, n (%)	
< 5	16 (30.8)
≥ 5	36 (69.2)
ESSPRI dryness score, mean ± SD	6.5 ± 2.45
ESSPRI dryness score, n (%)	
< 5	9 (17.3)
≥ 5	43 (82.7)
ESSDAI, median (IQR)	6 (2 – 11)
ESSDAI, n (%)	
Low activity	23 (44.2)
Moderate activity	18 (34.6)
High activity	11 (21.2)
Glandular ESSDAI, n (%)	
No activity	32 (61.5)
Low activity	16 (30.8)
Moderate activity	4 (7.7)
NSWSF, n (%)	
≤ 0,1 mL/min	43 (82.7)
> 0,1 mL/min	9 (17.3)
Schirmer's test, n (%)	
≤5mm/5min	38 (73.1)
>5mm/5min	14 (26.9)
Positive ANA, n (%)	44 (84.6)
Positive RF, n (%)	25 (48.1)
Positive Anti-SSA/Ro antibody, n (%)	42 (80.8)
Positive Anti-SSB/La antibody, n (%)	19 (36.5)

n: sample size; SD: standard deviation; IQR: interquartile range; ESSPRI: EULAR Sjögren's Syndrome Patient Reported Index; ESSDAI: EULAR Sjögren's Syndrome Disease Activity Index; NSWSF: non-stimulated whole saliva flow; ANA: antinuclear antibody; RF: rheumatoid factor.

Table IV. Comparison between patients with Sjögren's disease and healthy individuals according to salivary gland ultrasound grades.

	Sjögren's diseas (n=52)	Healthy subjects (n=48)	p-value
Parotid + submandibular glands			< 0.001
B-mode US Grade 0 – 1	10 (19.2)	43 (89.6)	
B-mode US Grade 2 - 3	42 (80.8)	5 (10.4)	
Parotid glands			< 0.001
B-mode US Grade 0 – 1	16 (30.8)	46 (95.8)	
B-mode US Grade 2 - 3	36 (69.2)	2 (4.2)	
Submandibular glands			< 0.001
B-mode US Grade 0 – 1	20 (38.5)	44 (91.7)	
B-mode US Grade 2 - 3	32 (61.5)	4 (8.3)	

n: sample size; US: ultrasound. Chi-square test. Data presented as absolute value (%).

Table V. Elasticity and shear-wave velocity results in the study population.

	Sjögren's disease (n=52)	Healthy subjects (n=48)	p-value
Parotid + submandibular glands			
Elasticity (kPa)	15.2 ± 2.9	9.3 ± 0.8	< 0.001
Shear-wave velocity (m/s)	2.2 ± 0.2	1.8 ± 0.1	< 0.001
Parotid glands			
Elasticity (kPa)	15.7 ± 3.6	9.3 ± 1.1	< 0.001
Shear-wave velocity (m/s)	2.3 ± 0.3	1.8 ± 0.1	< 0.001
Submandibular glands			
Elasticity (kPa)	14.6 ± 3.1	9.3 ± 1.1	< 0.001
Shear-wave velocity (m/s)	2.2 ± 0.2	1.8 ± 0.1	< 0.001

n: sample size; kPa: kilopascals; m/s: meters per second.
p-values were obtained using Student's test. Data presented as mean ± standard deviation.

Table VI. ROC analysis of grades of B-mode ultrasound and elastography parameters for the diagnosis of Sjögren's disease.

	AUC	Cut-off point	Sensitivity (%)	Specificity (%)
Parotid + submandibular glands				
B-mode US	0.852	≥2.0	80.7	89.5
Elasticity (kPa)	0.982	9.90	98.1	83.3
Shear-wave velocity (m/s)	0.983	1.85	96.2	79.2
Parotid glands				
B-mode US	0.825	≥2.0	69.2	95.8
Elasticity (kPa)	0.972	10.05	98.1	79.2
Shear-wave velocity (m/s)	0.980	1.85	96.2	79.2
Submandibular glands				
B-mode US	0.766	≥2.0	61.5	91.7
Elasticity (kPa)	0.954	10.12	94.2	85.4
Shear-wave velocity (m/s)	0.950	1.85	94.2	85.4

AUC: area under the curve; US: ultrasound; kPa: kilopascals; m/s: meters per second.

between the parotid and submandibular glands in SjD patients regarding the elastic modulus ($p=0.022$) and SWV ($p=0.016$), suggesting a possible variation in tissue stiffness according to glandular location (Table V).

The elastography parameters of the four glands in the 10 SjD patients with B-mode US grades 0–1 also presented higher elasticity (13.8±2.9 vs. 9.2±0.6kPa; $p<0.001$) and SWV values (2.1±0.2 vs. 1.8±0.1m/s; $p<0.001$) compared to 43 controls with B-mode grades 0–1. Nonetheless, no significant differences were found between the group of patients with B-mode US grades 0–1 and 2–3 in elasticity (13.8±2.9 vs. 15.5±2.9kPa; $p=0.123$) or SWV (2.1±0.2 vs. 2.3±0.2 m/s; $p=0.107$).
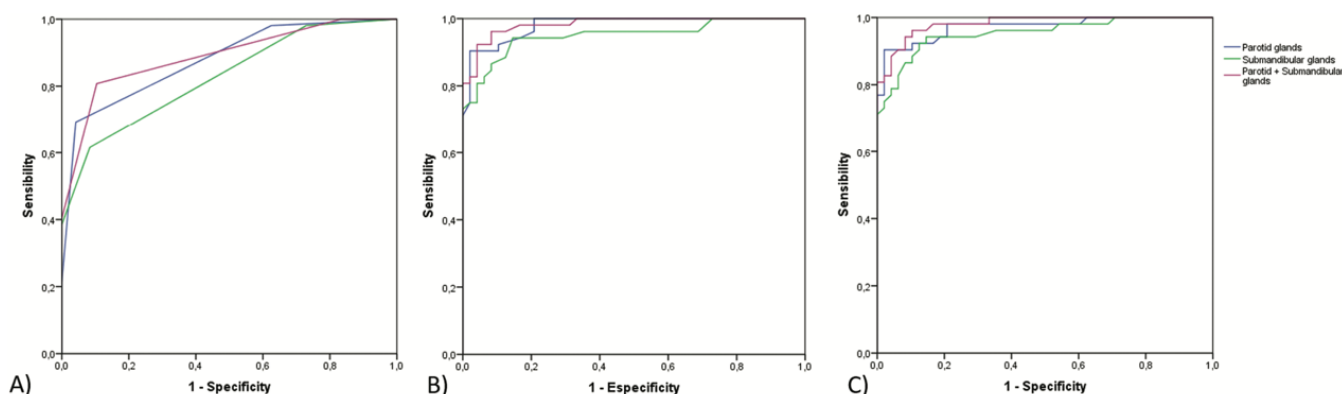
Considering the B-mode US score cut-off of ≥2, the assessment of the four salivary glands yielded a sensitivity of 80.7%, specificity of 89.5%, and AUC of 0.852 (95%CI: 0.771–0.932) for the diagnosis of SjD (Table VI, Fig. 2A). The ROC curve analysis of MSG elastography parameters demonstrated excellent diagnostic performance. The total glands showed an AUC of 0.982 (95%CI: 0.962–1.0) for elasticity, with a cut-off of 9.90kPa, sensitivity of 98.1%, and specificity of 83.3%. The SWV had an AUC of 0.983 (95%CI: 0.965–1.0), with a cut-off of 1.85 m/s, sensitivity of 96.2%, and specificity of 79.2%. The parotid SWV demonstrated the highest individual AUC of 0.980 (95%CI: 0.960–1.0) (Table VI, Fig. 2B and 2C). Comparatively the elastography parameters showed higher AUCs than B-mode US for diagnosing SjD across all four glands (Fig. 3).

The comparisons of elastography parameters with B-mode US grades (0–1 vs. 2–3) in parotid glands, among SjD patients, demonstrated a trend towards increased values of elasticity and SWV in higher grades, although none of the comparisons reached statistical significance (Table VII).
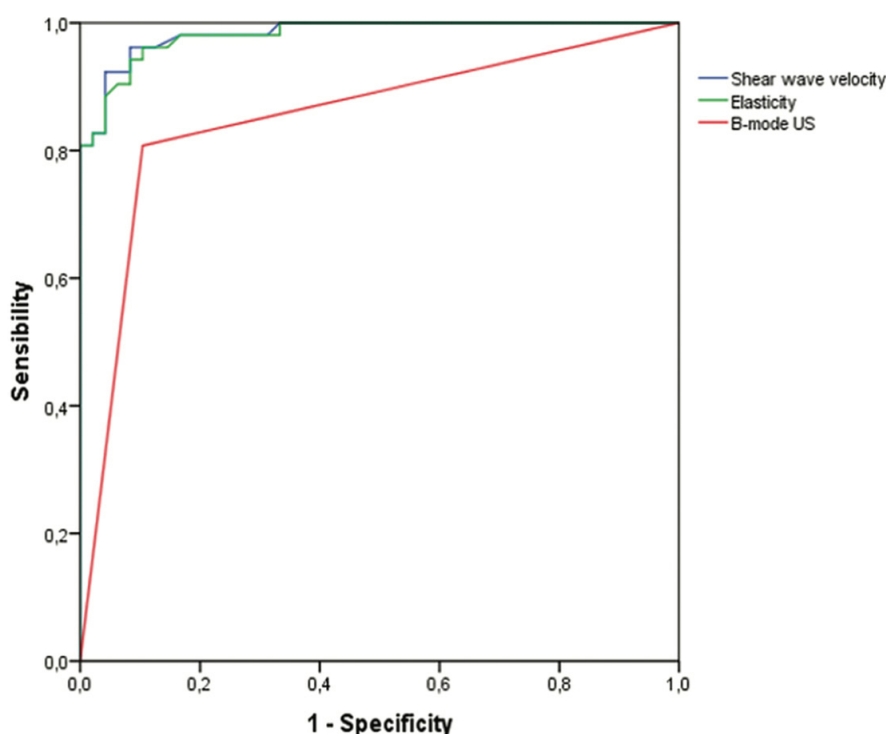
Table VIII presents a comparison of the different logistic regression models for predicting SjD, based on the evaluation of the four salivary glands using B-mode US and elastography. The combined model, integrating both methods, demonstrated the best predictive performance, with an AUC of 0.985 (95%CI: 0.967–1.0) and accuracy of 94%, and the highest Nagelkerke's R^2 value (0.890), indicating excellent discriminative ability.

Although the individual models, B-mode US and elasticity, also demonstrated high performance, with AUCs of 0.852 (95%CI: 0.771–0.932) and 0.982 (95%CI: 0.962–1.0), respectively, the combination of variables further increased the diagnostic accuracy. The comparison between models, performed using the likelihood ratio test, showed that adding the elasticity variable to the model containing only B-mode US resulted in a statistically significant improvement in model fit ($\Delta\chi^2=48.17$; df=1; $p<0.0001$). This

Fig. 2. Diagnostic performance of B-mode ultrasound and elastography parameters for Sjögren's disease in isolated and combined salivary glands. **A**: ROC curve of B-mode ultrasound; **B**: ROC curve of shear wave velocity; **C**: ROC curve of elasticity.

Fig. 3. ROC curves comparing the diagnostic performance of elastography parameters (elasticity and shear wave velocity) and B-mode ultrasound for differentiating Sjögren's disease patients from healthy controls, in four salivary glands.

The results demonstrated that the 2D-SWE of the MSG was an ultrasound modality with excellent diagnostic performance in discriminating between SjD patients and healthy controls, and that B-mode US also presented a very good performance. Furthermore, both techniques together are superior to B-mode US alone and slightly higher than SWE alone.

The importance of the B-mode US of the MSG evaluation as a diagnostic tool for SjD has been well established (10, 15). B-mode US according to the OMERACT score was used in our study to assess the MSG. This method showed very good performance in discriminating SjD patients from healthy controls, but approximately 20% of the patients had an inconclusive B-mode US score (<2) for SjD, which was consistent with the literature (10). The diagnostic efficacy of B-mode US for detecting salivary gland involvement in patients with early-stage SjD is limited as this method detects structural damage.

2D-SWE may be useful for diagnosing SjD at stages when morphological abnormalities are not yet present (17, 18). Since 2014 the elastography utility has been tested in the evaluation of MSG in SjD (28, 29) using different techniques and yielding varying results (18, 30-35). 2D-SWE is a more recent technique that has been used in MSG in SjD (19, 36, 37) with the advantage that the stiffness is measured over a much larger area (14). 2D-SWE demonstrated superior diagnostics performance compared to the other elastography techniques (15, 19, 36, 37). Furthermore,

finding indicates that combining both methods provides superior predictive ability compared to the isolated use of B-mode US. However, when comparing the model based solely on elasticity with the combined model, the difference was not statistically significant ($\Delta\chi^2$=2.10; df=1; *p*>0.05), suggesting that adding B-mode US to a model already containing elasticity does not provide a relevant additional gain in predicting SjD.

Finally, no significant correlations were observed between the elastography parameters and clinical or laboratory variables, except for the glandular domain of the ESSDAI, which showed a positive, albeit modest, correlation (r=0.286; *p*=0.040).

Discussion

The current study aimed to evaluate the diagnostic value of the most recent elastography technique, 2D-SWE, and B-mode US, of the MSG in the diagnosis of SjD and verify if there are any correlations between the SWE values and some disease characteristics.

Table VII. Comparison between elastography parameters and B-mode US grades of the parotid and submandibular glands in patients with Sjögren's disease.

	US Grade 0 e 1	US Grade 2 e 3	p-value
Parotid + submandibular glands			
Elasticity (kPa)	13.8 ± 2.9	15.5 ± 2.9	0.123
Shear-wave velocity (m/s)	2.1 ± 0.2	2.3 ± 0.2	0.107
Parotid glands			
Elasticity (kPa)	14.1 ± 2.8	16.1 ± 3.6	0.085
Shear-wave velocity (m/s)	2.2 ± 0.2	2.3 ± 0.3	0.066
Submandibular glands			
Elasticity (kPa)	13.5 ± 3.1	14.9 ± 3.1	0.218
Shear-wave velocity (m/s)	2.1 ± 0.2	2.2 ± 0.2	0.220

US: ultrasound; kPa: kilopascals; m/s: meters per second.
Independent samples t-test. Data presented as mean ± standard deviation.

Table VIII. Comparison of logistic regression models for predicting Sjögren's disease in the assessment of the four salivary glands.

Model	Exp(B) (95% CI)	Nagelkerke R²	AUC	Accuracy (%)
B-mode US	36.1 (11.4 – 114.6)	0.567	0.852	85
Elasticity	1.7 (2.3 – 12.8)	0.850	0.982	92
B-mode US + Elasticity	4.2 (0.68 – 28.47)	0.890	0.985	94
	0.253 (0.11 – 0.56)			

AUC: area under the curve; Exp(B): odds ratio; CI: confidence interval; US: ultrasound.

2D-SWE reduces the operator-dependency and subjectivity of the results and provides objective quantitative data (7). Although this technique has been employed since 2020, the studies varied in methodology. In the present study, all MSG were assessed, both collectively and individually, using two elastography parameters, thereby providing a more comprehensive evaluation. Therefore, it can be used for comparative purposes in different studies.

Our results showed that the elasticity modulus and SWV values of the MSG successfully separate SjD patients from controls demonstrating its usefulness in the diagnosis of SjD, which is consistent with the literature, both in works that used the same technique (7, 36-43) and in others that used different elastography techniques (18, 28, 30, 33, 44) The higher SWE values in patients compared to controls reflect the loss of elasticity and increase in stiffness of the MSG in SjD, as expected in a disease that causes inflammation and fibrosis in these glands. We compared patients with established SjD with healthy controls, which may have led to an overestimation of the results, although the sonographer was blinded to the diagnosis. Based on recent studies using 2D-SWE of the MSG in patients with SjD, Tromby et al. (45), stated that the diagnostic performance of this technique is promising. However, further experience and validation are still required (45).

The parotid SWV demonstrated the highest individual AUC of 0.980 (95%CI: 0.960–1.0) with a cut-off point for elasticity and SWV of 10.05 kPa and 1.85 m/s respectively, with sensitivity in the elasticity modulus of 98.1 % and specificity of 79.2%. Özer et al. (38) also found the highest AUC values for the parotid gland elasticity modulus (0.937;95%-CI: 0.901–0.973), with a sensitivity of 93.2% and specificity of 83.3%, but with higher cut-off points of SWE parameters (13.90kPa and 2.12m/s). Karadeniz et al. (7) found a parotid cut-off value of 10.3kPa for elasticity, with a sensitivity of 84.78% and specificity of 95.65%, and an AUC of 0.950 (95%-CI: 0.905–1.000) (7). Prata et al. (41) also found that the parotid AUC for SWV was greater than the submandibular AUC, with a cut-off point of 1.96 m/s, a value closer to our findings. The superior usefulness of the parotid SWE, as found in our study, has been demonstrated in many studies using different elastography techniques (18, 30, 34, 35, 38, 41, 44, 46). This discrepancy in gland affectation might be explained by differences in the histological composition of the salivary glands (18). Golder et al. (47) indicated that lymphocytic infiltrate was more severe in parotid glands than in submandibular glands in patients with SjD. Nonetheless, other studies did not find differences between MSG (17, 39, 40, 43) and few studies reported an elasticity AUC of the submandibular gland that was higher than the parotid gland (33, 42). These differences show the importance of evaluating the four glands together.

Differences in diagnostic performance and cut-off values between the present study and other studies with 2D-SWE may be due to patient demographics, user dependency, and diverse ultrasound device (13, 38). Different equipment can give different values of stiffness within the same tissue in the same patient (14).

In the current study, as well as in others in the literature, the comparison of B-mode US and SWE showed that SWE is better than B-mode US for the diagnosis of SjD patients (30, 38). However, Cheng et al. (39) found similar results with both methods, and Prata et al. (41) reported that B-mode US alone was superior to SWE alone.

Although none of the comparisons between elastography parameters and B-mode ultrasound grades (0–1 vs. 2–3) among patients with SjD showed statistically significant increases in elasticity or shear wave velocity values with higher grades, in the parotid gland alone, differences approaching the threshold of significance were observed for elasticity (p=0.085) and shear wave velocity (p=0.066). This finding highlights the need for larger sample sizes or longitudinal study designs.

Another important question is whether SWE can aid in identifying SjD patients before morphological abnormalities are detected on B-mode US. In our study, 10 patients with SjD and B-mode US grades 0–1 showed no significant difference from those with B-mode US grades 2–3 in either elasticity or SWV but had significantly higher SWE parameters compared with the 43 controls (grades 0–1) (p<0.001 for both para-

meters). These findings suggest that SWE may raise diagnostic suspicion in patients who do not yet have significant structural damage or have only mild MSG involvement (19, 42), even before morphological abnormalities are detected on B-mode US.

The combination of B-mode US and elastography modulus of the four glands demonstrated excellent diagnostic performance for SjD (AUC=0.985; 95%-CI:0.967–1.0) better than B-mode US alone, but similar to individual SWE values. These findings suggest that these techniques can complement each other, helping not only in the diagnosis of SjD, but also in monitoring the disease's progression and response to treatments. Other studies also found that the sum of these two methods showed better performance than using each one (17, 30, 34, 36, 39).

The final objective of our study was to explore potential correlations between SWE parameters and clinical or laboratory variables. Although the patients included in this study showed a relatively uniform distribution of ESSDAI scores and disease duration, we did not find significant correlations between elastography parameters and ESSDAI, disease duration, or most clinical and laboratory variables. Such correlations have also been rarely reported in previous studies (7, 30, 35, 36, 38). Interestingly, most prior studies also found no association with disease duration (7, 32, 35, 36, 38, 41), except for two (29, 48), suggesting that disease progression may vary among patients. Kimura-Hayama *et al.* (31) found correlations with ESSDAI, the ESSDAI glandular domain, NSWSF, and hypocomplementemia, but not with ESSPRI and with LSGB. Similarly, in our study, which included only 19 LSGB samples, no correlations were observed between SWE parameters and LSGB findings, in agreement with the results of Kimura-Hayama *et al.* (31) and other studies (7, 18, 30, 38). In line with the study by Kimura-Hayama *et al.* (31), Wang *et al.* (49), in a recent investigation assessing the value of SWE of the labial glands in patients with SjD for evaluating disease activity, also reported significant correlations between SWE and ESSDAI,

as well as with hypocomplementemia. Additionally, that study found positive correlations between SWE findings and elevated IgG levels, suggesting that elastography may serve as a potential prognostic marker in patients with SjD (49). In our study, no correlations were found between SWE parameters and ESSPRI, NSWSF, or Schirmer's test. The only significant correlation was observed with the glandular domain of the ESSDAI, suggesting that the elasticity modulus is positively associated with greater glandular activity of the disease. The present study has some limitations. First, this study included a limited number of patients and a female predominance, although this is comparable to other studies in the literature (32, 34, 38, 41). Second, we performed a histopathological correlation with SWE findings in a small number of patients. Third, our study only included healthy volunteers as a control group, and, finally, the major limitation of this study was the lack of assessment of interobserver variability. All B-mode US and SWE examinations were performed and interpreted by a single experienced radiologist who was blinded to the diagnosis, which ensured internal consistency but did not allow evaluation of reproducibility across different observers. In conclusion, the results of the current study showed that elastography seems to be a promising tool with additional diagnostic value in SjD. 2D-SWE alone or in combination with B-mode US may be beneficial in the assessment of MSG, as a quantitative, non-invasive, and feasible image method. However, these findings need to be validated in multicentre and larger studies, which adopt an accurate protocol to standardise this method, so that, in future, cut-off values can be established on different devices.

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