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The Clinical Value of Different Ultrasonographic Techniques in the Evaluation of Salivary Gland Involvement in Sjögren's Syndrome

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Abstract

Sjögren's syndrome (SS) is an autoimmune disease that most commonly affects the salivary and lacrimal glands. At present, diagnosis mainly relies on salivary gland biopsy, which is an invasive and relatively complex procedure. In recent years, ultrasonography, as a noninvasive and convenient imaging modality, has been widely applied in the evaluation of salivary gland diseases. By assessing glandular parenchymal characteristics and blood flow distribution, ultrasonography enables evaluation of salivary gland involvement. This article reviews the clinical value of different ultrasonographic techniques in assessing salivary gland lesions in patients with SS from two aspects—parenchymal changes and vascular alterations—and discusses their prospects for clinical application.

Keywords

Sjögren's Syndrome, Salivary Glands, Ultrasonography, Application Value

1. Introduction

Sjögren's syndrome (SS) is an autoimmune disease characterized by lymphocytic infiltration of exocrine glands. Its main clinical manifestations include xerostomia, xerophthalmia, and joint pain, and it may also involve multiple organs and systems throughout the body, such as the skin and mucosa, musculoskeletal system, and kidneys [1]. According to whether it is associated with other connective tissue diseases, SS is classified into primary Sjögren's syndrome (pSS) and secondary Sjögren's syndrome (sSS). The diagnostic criteria for SS commonly include the 2002 American-European Consensus Group criteria, the 2012 Sjögren's International Collaborative Clinical Alliance criteria, and the 2016 American College

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of Rheumatology/European League Against Rheumatism classification criteria. Auxiliary examinations include autoantibody testing, salivary flow rate measurement, labial gland biopsy, tear film break-up time, salivary gland ultrasonography (SGUS), and salivary gland scintigraphy. Because some of these examinations are invasive or involve radiation exposure, they are not suitable for repeated assessment or follow-up [2]. The pathological mechanism of salivary gland damage in SS mainly involves focal lymphocytic sialadenitis caused by lymphocytic infiltration. Progressive damage to acinar cells, together with inflammation-induced persistent ductal obstruction, accelerates acinar atrophy [3]-[5]. Although the etiologies of pSS and sSS differ, salivary gland involvement follows the same pathological process in both, ultimately leading to failure of salivary secretion. Different ultrasonographic techniques can sensitively detect and evaluate various aspects of salivary gland damage in SS, including structural destruction, tissue stiffness, and blood perfusion. However, the imaging manifestations of salivary gland involvement arise from common terminal pathological pathways—such as lymphocytic infiltration, glandular destruction, and fibrosis—and therefore lack specificity for the initial etiology of damage [6]-[9]. Consequently, SGUS can effectively assess the severity of salivary gland involvement in both pSS and sSS, with its core role being the quantification of glandular damage rather than etiological differentiation. Final differentiation between pSS and sSS still relies on comprehensive evaluation of systemic clinical manifestations and serological profiles, including disease-specific autoantibodies. As a simple, safe, and noninvasive examination method, SGUS has high clinical value in early diagnosis and follow-up of the disease.

2. Evaluation of Salivary Gland Parenchymal Changes Using Two-Dimensional Ultrasonographic Scoring and Shear Wave Elastography

SGUS mainly focuses on the parotid and submandibular glands, as the sublingual glands are small and cannot be accurately assessed by ultrasonography. Two-dimensional ultrasonographic scoring is primarily based on changes in gland size, contour, and internal echogenicity [10].

Currently, more than 30 different scoring systems have been reported. As early as 1992, De Vita *et al.* [11] identified heterogeneous echogenicity and the presence of hypoechoic or anechoic areas as characteristic features of SS and proposed a 0 - 3 point scoring system based on internal echogenicity (**Table 1**). However, because the grading of hypoechoic areas was not sufficiently detailed, the sensitivity and specificity of SS diagnosis varied widely among different studies [12]-[16]. In 2013, Cornec *et al.* [17] proposed a 0 - 4 point scoring system based on the size of hypoechoic areas and the presence of hyperechoic bands (**Table 2**). Each of the four glands was scored separately, and the highest score was taken as the final score. With a cutoff value of 2, the sensitivity and specificity for SS diagnosis were 62.8% and 95.0%, respectively. Salaffi *et al.* [18] scored the four glands individually using a 0 - 4 scale and summed the scores to form a 0 - 16 point system. With a cutoff of 6, the sensitivity and specificity were 75.3% and 83.5%, respectively. Hocevar *et al.* [19] proposed a more comprehensive 0 - 48 point scoring system (**Table 3**), with a sensitivity of 58.8% and a specificity of 98.7%.

Table 1. 0 - 3 point scoring system.

Score (points)	Ultrasonographic Findings
0	Homogeneous glandular echogenicity
1	Mildly inhomogeneous glandular echogenicity, with isolated hypoechoic areas
2	Markedly inhomogeneous glandular echogenicity, with distinct hypoechoic areas, and/or multiple punctate or linear hyperechoic
3	Large round or confluent hypoechoic areas, and/or linear hyperechoic bands, and/or multiple cysts or multiple calcifications

Table 2. 0 - 4 point scoring system.

Score (points)	Ultrasonographic Findings
0	Normal
1	Small hypoechoic areas, without hyperechoic bands
2	Multiple hypoechoic areas, diameter < 2 mm, with hyperechoic bands
3	Multiple hypoechoic areas, diameter 2 - 6 mm, with hyperechoic bands
4	Multiple hypoechoic areas, diameter > 6 mm, or multiple hyperechoic calcifications

Table 3. 0 - 48 point scoring system.

Ultrasonic Parameter	Score (points)	Ultrasonographic Findings
Parenchymal Echogenicity	0	Normal
	1	Decreased echogenicity
Parenchymal Homogeneity	0	Homogeneous
	1	Mildly inhomogeneous
	2	Markedly inhomogeneous
	3	Extremely inhomogeneous
Hypoechoic Areas	0	No hypoechoic areas
	1	Scattered hypoechoic areas
	2	Several hypoechoic areas
	3	Multiple hypoechoic areas
Hyperechoic Parotid Gland Bands	0	No hyperechoic bands
	1	Few hyperechoic bands
	2	Several hyperechoic bands
	3	Numerous hyperechoic bands

Continued

Submandibular Gland	0	No hyperechoic bands
	1	Presence of hyperechoic bands
Gland Border Definition	0	Well-defined borders
	1	Partially ill-defined borders
	2	ill-defined borders
	3	Borders not visible

Some studies have shown that the 0 - 16 scoring system better defines parenchymal echogenic changes and has higher specificity than the 0 - 48 system, although with lower sensitivity.

Given the large number of scoring systems and their susceptibility to operator subjectivity, Jousse-Joulin *et al.* convened 25 experts in 2019 to propose a simplified scoring system known as the 2019 Outcome Measures in Rheumatology Clinical Trials (OMERACT) scoring system [20]. This system uses two-dimensional ultrasonography to assign a four-grade semiquantitative score to salivary glands, ranging from 0 to 3:

- **Score 0**: normal parenchyma;
- **Score 1**: mild involvement, slight heterogeneity without hypoechoic/anechoic areas;
- **Score 2**: moderate involvement, moderate heterogeneity with focal hypoechoic/anechoic areas;
- **Score 3**: severe involvement, diffuse heterogeneity with extensive hypoechoic/anechoic areas throughout the gland.

If semiquantitative grading is not feasible, findings can be qualitatively classified as fatty infiltration (mild, score 1) or fibrotic echogenicity (severe, score 3). A score ≥ 2 by either method is defined as abnormal salivary gland involvement in SS.

In recent years, the OMERACT scoring system has been widely applied due to its high reproducibility and low operator dependence, demonstrating good sensitivity and excellent specificity for SS diagnosis [21], and serving as an effective predictor of disease severity [22]. Combined application of the OMERACT score with anti-SSA antibodies significantly improves overall diagnostic accuracy, particularly in increasing the negative predictive value [23]. When both results are negative, this combination can serve as an efficient strategy for excluding SS [24] [25]. Within the diagnostic framework of SS, SGUS is not an independent diagnostic criterion but an objective imaging tool for assessing glandular involvement. Therefore, the OMERACT score is not a primary diagnostic standard but a standardized method for quantitative evaluation of glandular damage.

Although two-dimensional ultrasonographic scoring is widely used clinically, it provides only morphological information and is subject to substantial subjectivity. Shear wave elastography (SWE) is a quantitative ultrasonographic technique for measuring tissue stiffness: the stiffer the tissue, the faster the propagation of shear waves, allowing calculation of elastic modulus values. Arslan *et al.* [26] measured salivary gland elasticity using SWE in 53 SS patients and 30 healthy volunteers and found statistically significant differences in mean elastic modulus values, enabling differentiation between SS patients and healthy individuals. Wang *et al.* [27] studied 62 SS patients and 44 non-SS patients, performing both ultrasonographic scoring and SWE measurements. They found that the combined diagnostic sensitivity and specificity of parotid gland ultrasonographic scoring plus SWE were 75.8% and 97.7%, respectively, while those for the submandibular gland were 79.0% and 86.4%. The combined diagnostic performance was superior to that of either modality alone, and SWE showed higher diagnostic value for the parotid gland. Therefore, in suspected SS patients with symptoms of dry mouth and dry eyes, parotid gland evaluation should be prioritized. Mo *et al.* [28] demonstrated that a matrix model based on two-dimensional ultrasonography and SWE results helps clinicians decide whether invasive examinations such as labial gland biopsy are necessary. Chen [29] found that the combination of ultrasonographic scoring and SWE is valuable for assessing SS disease activity and can provide useful indications of disease activity.

In summary, the combination of ultrasonographic scoring and SWE enables more refined assessment of parenchymal changes and provides a noninvasive, real-time, and convenient imaging approach for early SS diagnosis and evaluation of disease activity.

3. Evaluation of Salivary Gland Blood Flow Changes Using Color Doppler Ultrasonography and Contrast-Enhanced Ultrasound

Salivary glands have a rich and complex vascular system, and intraglandular blood flow is closely related to salivary secretion [30]. In SS, immune-mediated attacks on glandular parenchyma lead to autoantibody formation and immune complex deposition on vessel walls, triggering inflammation. This inflammatory process may disrupt coagulation and fibrinolysis balance, resulting in intravascular thrombosis. Autoantibodies may also interfere with endothelial cell and platelet function, thereby affecting blood flow.

Color Doppler ultrasonography (CDUS) detects frequency shifts caused by moving blood cells and uses color coding to superimpose real-time information on blood flow velocity and direction onto two-dimensional anatomical images, enabling visualization of vascular anatomy and hemodynamics within and around the gland. Spectral Doppler, guided by CDUS, displays detailed temporal changes in blood flow velocity within the sampling volume as a waveform, providing quantitative data. As early as 1994, Martinoli *et al.* [31] observed differences in intraparenchymal blood flow distribution between SS patients and non-SS individuals. Xu *et al.* [32] compared the resistance index (RI) of intraparotid small arteries between SS patients and controls and found reduced RI in affected parotid glands of SS patients. Before and after acid stimulation, the control group showed higher peak systolic velocity (PSV) and lower RI compared with baseline, whereas no significant changes were observed in the SS group. Tian *et al.* [33] compared hemodynamic parameters of the superficial temporal artery before and after acid stimulation in SS patients and controls. They found no significant changes in SS patients, while controls showed significant increases in PSV and end-diastolic velocity (EDV) and a significant decrease in RI after stimulation. The core pathological mechanism of salivary gland involvement in SS is lymphocyte-mediated chronic inflammation. Inflammatory factors can induce local microvascular dilation and increased permeability, leading to reduced resistance in small intraglandular arteries [34]. Reduced vascular resistance generally results in increased blood flow [35], which in turn alters the hemodynamics of supplying arteries. As a major branch supplying the parotid gland, the superficial temporal artery may indirectly reflect parotid blood flow status. Salivary secretion is mainly regulated by the autonomic nervous system. In healthy individuals, acid stimulation enhances salivary secretion, accompanied by dilation of intraglandular small arteries and increased blood supply, manifested sonographically as increased PSV and EDV and decreased RI [36]. In SS patients, the lack of significant hemodynamic changes after acid stimulation may be related to glandular destruction and functional impairment, resulting in diminished or absent physiological hyperemic responses [32].

Wang *et al.* [37] measured facial artery PSV, EDV, and RI bilaterally and found that EDV was significantly higher in middle-to-late-stage SS patients than in early-stage patients and healthy controls, suggesting progressive involvement of perisalivary vasculature with disease progression. In early SS, lymphocytic infiltration causes glandular edema, whereas in later stages, lobular structural changes and fibrosis become more pronounced. Because the parotid gland is not the sole target organ supplied by the superficial temporal and facial arteries, early disease may not cause significant hemodynamic changes. These findings indicate that CDUS has limited specificity for early SS but shows considerable potential for monitoring disease progression and therapeutic response.

Traditional CDUS is limited by strong angle dependence and low sensitivity to low-velocity flow, posing challenges in microcirculation assessment. Power Doppler ultrasonography (PDU), which detects the energy of Doppler signals rather than flow velocity and direction, overcomes angle dependence and significantly improves sensitivity to low-velocity flow. On this basis, high-resolution microvascular imaging techniques further suppress motion artifacts through advanced algorithms, enabling clearer and more stable visualization of low-velocity, low-volume microvascular flow.

Fethi Emre *et al.* [38] evaluated parotid and submandibular gland blood flow using PDU and superb microvascular imaging (SMI; Canon Medical Systems). Compared with PDU, SMI demonstrated higher sensitivity and specificity, and the vascularity index (VI) provided by SMI showed good reproducibility. These findings suggest that SMI is a reliable noninvasive adjunctive diagnostic tool that, when combined with clinical findings, laboratory data, and other imaging modalities, facilitates comprehensive and precise disease assessment.

Contrast-enhanced ultrasound (CEUS) is also widely used in the evaluation of tissue hemodynamics. By intravenous injection of contrast agents, CEUS allows intuitive visualization of microvascular perfusion within lesions. However, due to its relatively complex operation, cost, and potential allergic reactions to contrast agents, its clinical application and research in salivary gland diseases remain limited. Giuseppetti *et al.* [39] found that both baseline and post-acid stimulation enhancement of the parotid gland on CEUS were lower in SS patients than in controls. In SS patients, two-dimensional ultrasonography mainly showed scattered hypoechoic areas, which demonstrated no contrast enhancement, whereas in other diffuse parotid diseases, hypoechoic areas often exhibited mild enhancement [40]. Overall, CEUS shows very high sensitivity and specificity in the diagnosis of SS.

4. Summary and Perspectives

As a simple and noninvasive imaging modality, SGUS enables comprehensive evaluation of multiple salivary gland parameters. Two-dimensional ultrasonography, SWE, CDUS, and CEUS each have distinct advantages and limitations in SS diagnosis, summarized in **Table 4**. Gray-scale-based ultrasonographic scoring systems provide an initial assessment of structural parenchymal changes, while the addition of SWE enables quantitative evaluation of glandular stiffness, significantly improving diagnostic objectivity and accuracy. In terms of vascular assessment, CDUS and CEUS allow direct visualization of intraglandular and perisalivary blood flow distribution and provide quantitative hemodynamic parameters such as PSV, EDV, and RI. SMI further enhances sensitivity for detecting low-velocity, low-volume microvascular flow, enabling more precise visualization of microcirculation. The combined application of multiple ultrasonographic techniques not only facilitates early diagnosis and differential diagnosis of SS but also plays an important role in monitoring disease progression, assessing disease activity, and evaluating therapeutic efficacy.

SGUS has significant clinical value in SS diagnosis but still faces challenges and limitations. Currently, there is no internationally unified standard for image acquisition, scoring criteria, or result interpretation, which limits consistency and comparability across multicenter studies and clinical practice. Moreover, as a single imaging modality, SGUS has inherent limitations in sensitivity and specificity, particularly in early or atypical cases, where false-negative or false-positive results may occur. Future research should focus on developing multimodal imaging-based diagnostic models that integrate two-dimensional ultrasonographic scoring, SWE, CDUS, CEUS, and other techniques to obtain multidimensional glandular information. Combining imaging features with serological and histopathological indicators would enable comprehensive analysis from structural,

Table 4. Sensitivity, specificity, key advantages, and limitations of the four major ultrasound techniques.

Technique		Sensitivity (95% CI)	Specificity (95% CI)	Note (s)	Key Advantages	Limitations
Ultrasonography Scoring	0 - 4 Point Scoring System	0.78 (0.65 - 0.88)	0.95 (0.89 - 0.98)	1	Direct 2D structural visualization of glands; simple operation and high accessibility	High operator dependency; low sensitivity for early pathology; only provides 2D structural information.
	0 - 16 Point Scoring System	0.85 (0.79 - 0.89)	0.89 (0.83 - 0.93)			
	0 - 48 Point Scoring System	0.78 (0.61 - 0.89)	0.95 (0.86 - 0.98)			
SWE		0.80 (0.71 - 0.87)	0.87 (0.78 - 0.92)	2	Quantitative fibrosis assessment; disease staging evaluation	Affected by multiple variables (e.g., pressure, depth); non-specific for etiology; high device dependency.
CDUS(SMI)	Parotid Gland	0.875 (NR)	0.725 (NR)	3	Perfusion assessment; multi-parameter quantitative flow analysis	**Conventional CDUS:** Low sensitivity to slow flow; highly angle-dependent. **SMI:** Higher diagnostic value, yet more device-dependent.
	Submandibular Gland	0.825 (NR)	0.70 (NR)			
CEUS		0.875 (NR)	0.85 (NR)	4	Rich quantitative parameters; d emonstrated differential diagnostic utility	Invasive, high-cost, complex procedure; no structural assessment of glands

Notes: 1. Data from the meta-analysis by Zhou *et al.* (2018) [41]. 2. Data from the meta-analysis by Dai *et al.* (2024) [42]. 3. Data from Fethi Emre *et al.* (2020); NR indicates that confidence intervals were not reported [38]. 4. Data from Giuseppetti *et al.* (2005); NR indicates that confidence intervals were not reported [39].

functional, and immunological perspectives, thereby establishing a more robust diagnostic framework and maximizing diagnostic accuracy.

In conclusion, multiple ultrasonographic techniques have demonstrated significant value in the diagnosis and differential diagnosis of SS. With the continuous emergence of new ultrasonographic technologies and advances in standardization, ultrasonography is expected to play an increasingly precise and important role in early disease identification, assessment of disease progression, and monitoring of treatment response in Sjögren's syndrome.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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