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Are ultrasonographic scoring systems of the salivary gland in primary Sjögren's syndrome suitable for examination of Type2 diabetes mellitus patients with sicca?

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Abstract

Objective This study aimed to compare the salivary gland ultrasonography(SGUS) findings in patients with primary Sjögren's Syndrome (pSS) and diabetes mellitus(DM) patients with sicca symptoms and to examine the relationship between salivary gland ultrasonography (SGUS) findings with clinical and laboratory parameters.

Methods In this study, 34 patients with pSS and 34 DM patients with sicca symptoms were included. In all patients, bilateral parotid, and submandibular gland ultrasonography (totally 272 glands) was performed by blinded rheumatologist, using the Hocevar and the Outcome Measures in Rheumatology (OMERACT) scoring system. Clinic and ultrasonographic variables were compared between groups. The association between SGUS score and disease duration was analyzed by correlation analysis.

Results Patients with pSS presented significantly higher SGUS scores than patients with DM (the Hocevar score; 20.93(± 9.65) vs. 3.82(± 3.71); $p < 0.05$, the OMERACT score; 5.96(± 2.30) vs. 2.07(± 1.65); $p < 0.05$, respectively). In patients with pSS, the submandibular gland scores were significantly higher than the parotid gland scores (right; $p < 0.05$ vs. left; $p < 0.01$) while DM patients showed significantly higher parotid gland scores (right; $p < 0.05$ vs. left; $p < 0.05$). In pSS patients, the SGUS scores were associated with disease duration ($r = 0.57$; $r = 0.50$; $p < 0.05$), symptom duration ($r = 50$; $r = 0.47$; $p < 0.05$), and the European League Against Rheumatism Sjögren's Syndrome Patient Reported Index (ESSPRI)-dryness score ($r = 0.35$, $r = 0.36$; $p < 0.05$). However, in DM patients, the SGUS scores are highly correlated with the ESSPRI-dryness ($r = 0.74$, $r = 0.72$; $p < 0.05$) and HbA1C level ($r = 0.91$, $r = 0.86$; $p < 0.05$).

Conclusions This study demonstrated that major salivary gland involvement was more severe and correlated with disease duration, and submandibular gland was dominantly affected in pSS. Contrarily, in DM patients, salivary gland involvement was milder, parotid dominant and related to level of dryness and HbA1C, rather than disease duration when compared to pSS,

Keywords Salivary gland, Ultrasonography, Primary Sjögren's syndrome, Inflammation, Diabetes mellitus, Sicca symptoms

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Introduction

Primary Sjögren syndrome (pSS) is a chronic autoimmune disease that mainly affects the exocrine glands [1]. Type 2 diabetes mellitus (DM) is also an autoimmune disease involving not only the pancreas but also salivary glands [2]. In both diseases, sicca symptoms due to different mechanisms are common [1, 2].

The use of salivary gland ultrasonography (SGUS) has become widespread in the diagnosis and follow-up of pSS [3–5]. Further, SGUS findings were associated with some clinical (disease activity) and laboratory (antinuclear antibody (ANA), Anti-Ro, immunoglobulin G levels etc.) markers in pSS patients [6, 7].

Sicca symptoms seriously affect quality of life in DM patients. These patients suffer severely from sicca symptoms that can be a confounding factor with pSS. In DM, fewer US-based studies have shown abnormalities in the major salivary glands [8, 9]. These studies revealed several US findings as enlargement of glands, echogenicity, homogeneity, indefinity of posterior border [8, 9]. By ultrasonography, identification of the differences in salivary gland involvement between the pSS and DM may be useful in diagnosis, differential diagnosis, prognosis and overlap situations.

When we look at the literature, we come across that comparison of salivary gland ultrasound features of pSS patients with other connective tissue diseases and Sjögren's mimics [10–12]. However, to our knowledge, there is no study comparing the major SGUS findings between pSS and DM.

In this direction, we aimed to compare the SGUS findings in patients with pSS and DM patients with sicca symptoms and to examine the relationship between these findings with clinical and laboratory parameters in the current study.

Materials and methods

Patients and study design

This cross-sectional study was performed in the Rheumatology Clinic of Ankara University between November 2021 and April 2022. Thirty-four pSS patients and age-matched 34 patients Type 2 DM suffering from sicca symptoms (xerostomia and/or xerophthalmia) and meeting were included in study. In order to be eligible for inclusion in the study, participants had to be between the ages of 18 and 65, fulfill the disease criteria (2016 American Colleges of Rheumatology/ European League Against Rheumatism (ACR/EULAR) Classification Criteria for pSS, and 2011 American Diabetes Association (ADA) Criteria for DM), and agree to participate in the study. All subjects were informed about the aim of the study and accepted written informed consent.

Exclusion criteria were defined as; age under 18 years, sicca symptoms related to hepatitis C infection, previous head, and neck ionization radiation, acquired immunodeficiency syndrome, amyloidosis, sarcoidosis, graft versus host disease, immunoglobulin G4-related disease, concomitant secondary rheumatic disease, malign/pre-malign disease in parotid or submandibular glands, current use of drugs that might decrease salivary gland function, current smokers, and operation of the salivary gland. Also, in case of having pSS and Type 2 DM concomitantly, the patient was excluded from the study.

The sample size of study was calculated by G-power v3.1.9.4 (Heinrich-Heine-Universität, Düsseldorf, Germany) with a power of 80% and a two-sided significance level of 0.05 as 34 subjects for each group [13]. This study was approved by the Ankara University Ethics Committee (Protocol number: İ10-597-22). During the study period, the World Medical Association Helsinki Declaration and Good Clinical Practices Guidelines were followed.

Clinical and laboratory measurements

The demographic and clinical characteristics including age, body mass index, cigarette usage, disease, and symptom duration, the first symptom of patients, current symptoms, drugs and comorbidities, history of parotitis were collected. In the physical examination, the presence of hyperlobulation of tongue, and sialomegaly were noted. Cardiac and respiratory auscultation were also performed.

Laboratory measurements of the patients including rheumatoid factor (RF), ANA, anti-Ro (SS-A) and anti -La (SS-B), glycated hemoglobin A 1c (HbA1C; for DM patients), the results of unstimulated whole saliva flow rate (ml/ 15 min), Schirmer's test (mm/5 min), and minor labial gland biopsy (focus score) were recorded from the electronic health records.

Disease activity indices

Disease activity of patients with pSS was measured by the European League Against Rheumatism Sjögren Syndrome Patient Reported Index (ESSPRI), and the European League Against Rheumatism Sjögren Syndrome Disease Activity Index (ESSDAI). The ESSPRI-dryness was also considered to DM patients for measuring level of sicca symptoms. The ESSPRI was a patient-based numerical scale for pain, fatigue, and dryness. The overall ESSPRI score was the arithmetic mean of 0–10 points from the three items [14].

The ESSDAI was a physician-centered clinical index that consists of 12 domains which are cutaneous, respiratory, renal, articular, muscular, peripheral nervous system, central nervous system, hematological, glandular, constitutional, lymphadenopathic, and biological. Each domain is graded 3–4 levels of activity. Each activity level had a numeric value from 0 to 18 [15]. These two indices

were validated in numerous studies and used as a gold standard to measure disease activity of pSS patients [16].

Salivary gland ultrasonography assessments

The Hocevar and the Outcome Measures in Rheumatology Clinical Trials (OMERACT) scoring systems were used for US examination of major salivary glands. The ultrasonographic evaluation of bilateral parotid and submandibular glands were done by a rheumatologist (AK; eight-year experience of US and advanced EULAR-endorced US certificate) blinded to diagnose of the patients (Fig. 1). The US examination was performed by The LOGIQ P5® (GE-114118SU3, General Electric Healthcare, USA) with a multifrequency (6–18 MHz) linear probe with supine position as mentioned in the literature [5].

The Hocevar was a semiquantitative scoring system to investigate salivary gland pathologies [5]. These US pathologies were parenchymal echogeneity (0 or 1), presence of hypoechogenic areas (0,1,2 or 3), homogeneity (0,1,2 or 3), hyperechogenic reflection (0,1,2,or 3), and clearness of salivary gland border (0,1,2 or 3). The total scores of four salivary glands were calculated as the overall Hocevar score [5].

The OMERACT pSS working group achieved a four-grade semi-quantitative scoring system for evaluating US lesions of four major salivary glands [17]. The scoring of system was defined as; grade 0, normal; grade 1, mild inhomogeneity without anechoic or hypoechoic areas;

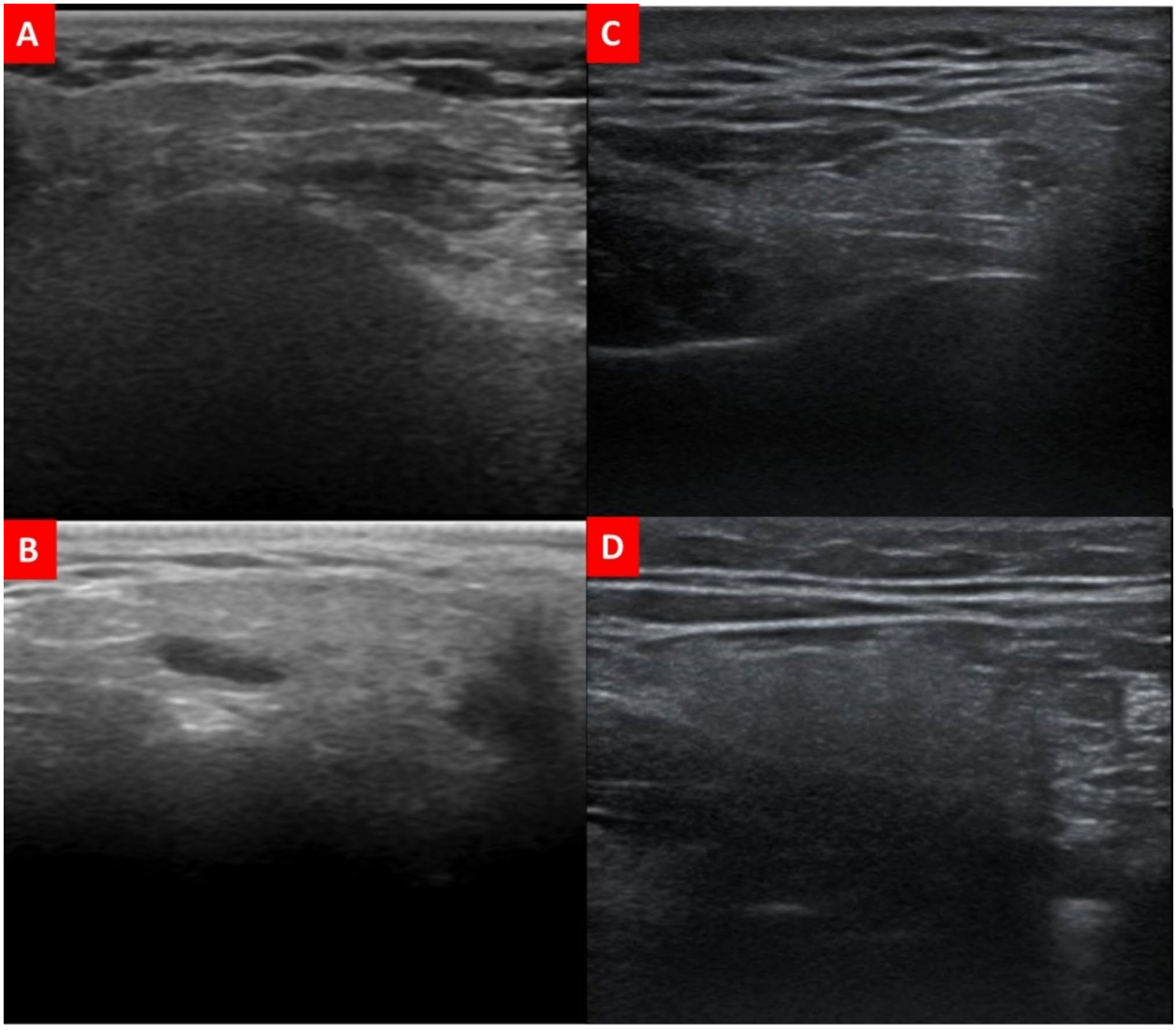

Fig. 1 Ultrasound images of salivary glands. (**A**) parotid gland and (**B**) submandibular gland in pSS patient, moderate hypoechoic areas, hyperechoic reflections, and inhomogeneity more marked in submandibular gland; (**C**) parotid gland and (**D**) submandibular gland in DM patient, mild in homogeneity and hyperechoic reflections more marked in parotid gland

grade 2, moderate inhomogeneity with focal anechoic or hypoechoic areas; grade 3, severe inhomogeneity with diffuse an- or hypoechoic areas occupying the entire gland or fibrous gland [17]. This scoring system was valid and reliable [4, 17].

Statistical analysis

Descriptive analysis of the study was reported, including mean, median, standard deviation, interquartile range, frequency distribution, and percentage. The conformity of continuous variables for normal distribution was evaluated using visual (histogram and probability graphs) and analytical methods (Kolmogorov-Smirnov test). To compare clinical characteristics, laboratory measurements, and SGUS scores between the pSS and DM groups, the independent sample *t*-test (normally distributed continuous variables) and the Mann-Whitney *U* test (non-normally distributed variables) were used. Within each group, comparisons of parotid and submandibular gland SGUS scores were also done with Mann-Whitney- *U* test and demonstrated with violin plots using the GraphPad Prism 5 software program (GraphPad Software Inc. ®; San Diego, CA, USA). All statistical analyses were done using the Statistical Package for Social Sciences (SPSS) V25.0 statistical software (IBM Corp.®, SPSS Inc.; Chicago, IL, USA).

For correlating the SGUS scores (the Hocevar and OMERACT SGUS total score) with clinical variables, Pearson's correlation analysis was used for the normally distributed variables and Spearman's correlation analysis was performed for the non-normally distributed variables. Correlation coefficients (r) were rated as follows; very high (0.80-1.00), high (0.50–0.79), moderate (0.30–0.49), and low (<0.30) [18]. For all comparisons, the significance level was set at $p<0.05$.

Results

The demographic and clinical characteristics of patients were shown in Table 1. The mean age, BMI, symptom, and disease duration were similar in groups ($p>0.05$). Around one-third of the pSS patients, xerophtalmia (11; 32.2%) and xerostomia (10; 29.4%) were the first symptoms of disease, whereas sicca symptoms were identified in 11.7% of DM patients as the first symptom. The current xerostomia was common in both groups while xerophthalmia, history of parotitis, sialomegaly, and arthralgia were more common in patients with pSS. Also, unstimulated whole saliva flow rate (30; 88.2% vs. 13; 38.2%, $p<0.05$) and the results of Schirmer's test (32; 94.1% vs. 9; 26.5%, $p<0.05$) were significantly lower in pSS patients than the patients with DM.

Regarding the disease activity score, the mean ESSDAI was 9.34 (±1.20), and the mean ESSPRI-total score was 6.82 (±0.30) in pSS patients. Among the ESSPRI domains, the mean ESSPRI-pain score was 7.21 (±0.25) and the mean ESSPRI-fatigue score was 7.0 (±0.32).

Table 1 Demographic and clinical characteristics of pSS and diabetic patients

	pSS patients($n=34$)	DM patients with sicca($n=34$)
Age, mean(±SD)	53.90(±9.70)	52.25(±7.65)
BMI, mean(±SD)	27.91(±3.91)	28.08(±4.74)
Symptom duration, mean(±SD)	9.43(±4.47)	9.35(±5.85)
Disease duration, mean(±SD)	7.68(±4.01)	8.46(±6.31)
First symptom, n(%)		
-Xerophthalmia	11(32.3%)[¥]	4(11.7%)
-Xerostomia	10(29.4%)[¥]	4(11.7%)
-Non-sicca	23(67.6%)	22(73.5%)
Current Xerostomia, n(%)	31(91.1%)	34(100%)
Current Xerophthalmia, n(%)	27(79.4%)[¥]	5(14.7%)
History of parotitis, n(%)	8(23.5%)[¥]	2(5.8%)
Sialomegaly, n(%)	8(23.5%)[¥]	3(8.8%)
Hyperlobulation of tongue, n(%)	4(11.7%)[¥]	2(5.8%)
Arthralgia, n(%)	32(94.1%)[¥]	11(32.3%)
RF positivity, n(%)	6(17.6%)[¥]	3(8.8%)
ANA positivity, n(%)	29(85.2%)[¥]	6(17.6%)
Anti-Ro (SS-A) positivity, n(%)	24(70.5%)[¥]	0(0.0%)
Anti-La (SS-B) positivity, n(%)	17(50.0%)[¥]	0(0.0%)
HbA1C level (%), mean(±SD)	-	5.86(±0.72)
Unstimulated whole saliva flow rate ≤ 0.1 ml/m, n(%)	30(88.2%)[¥]	13(38.2%)
Schirmer's test ≤ 5 mm/5 m in at least one eye, n(%)	32(94.1%)[¥]	9(26.5%)
Lymphocytic sialadenitis with focus score ≥ 1, n(%)	34(100%)	-

BMI, body mass index; ANA, anti-nuclear antibody; SGUS, salivary gland ultrasonography

[¥]$p<0.05$, *significance level*

Table 2 Disease activity index scores of patients

	pSS patients($n=34$)		DM patients with sicca($n=34$)	
	Mean (± SD)	**Median (IQR)**	**Mean (± SD)**	**Median (IQR)**
ESSDAI	9.34 (± 1.20)	7.0 (4.25–12.75)	-	-
ESSPRI-total	6.82 (± 0.30)	7.1 (6.25–9.5)	-	-
ESSPRI-pain	7.21 (± 0.25)	7.5 (7.0–8.0)	-	-
ESSPRI-dryness	6.25 (± 0.35)	7.0 (5.25-8.0)	4.21 (± 1.75)	4.5 (3.25–5.75)
ESSPRI-fatigue	7.0 (± 0.32)	7.0 (6.0–8.0)	-	-

ESSPRI, European League Against Rheumatism Sjögren Syndrome Patient Reported Index; ESSDAI, European League Against Rheumatism Sjögren Syndrome Disease Activity Index; IQR, interquartile range

Table 3 SGUS scores of both groups

	pSS patients($n=34$)	DM patients with sicca($n=34$)
The Hocevar SGUS score (total), mean(± SD)	20.93(± 9.65) ¥	3.82(± 3.71)
-right parotid, mean(± SD)	4.62(± 2.73) ¥	1.25(± 1.17)
-left parotid, mean(± SD)	4.34(± 2.57) ¥	1.25(± 1.08)
-right submandibular, mean(± SD)	6.06(± 3.07) ¥	0.67(± 0.41)
-left submandibular, mean(± SD)	6.31(± 2.95) ¥	0.64(± 0.43)
The OMERACT SGUS score (total), mean(± SD)	5.96(± 2.30) ¥	2.07(± 1.65)
-right parotid, mean(± SD)	1.28(± 0.77) ¥	0.71(± 0.59)
-left parotid, mean(± SD)	1.21(± 0.65) ¥	0.78(± 0.62)
-right submandibular, mean(± SD)	1.68(± 0.82) ¥	0.44(± 0.25)
-left submandibular, mean(± SD)	1.78(± 0.83) ¥	0.47(± 0.32)

BMI, body mass index; ANA, anti-nuclear antibody; SGUS, salivary gland ultrasonography ¥ *$p<0.05$, significance level*

While the mean ESSPRI-dryness score was 6.25 (±0.35) in the pSS patients, it was 4.21 (±1.75) in DM patients. The other descriptive values of the disease activity score were presented in Table 2.

In the pSS group, the Hocevar and OMERACT SGUS total scores were significantly higher (20.93(±9.65) vs. 3.82(±3.71); $p<0.05$ and 5.96(±2.30) vs. 2.07(±1.65); $p<0.05$, respectively) than DM group. Additionally, on both sides and on both salivary glands, the mean SGUS scores of the pSS patients were significantly higher compared to DM patients (Table 3).

Figures 2 and 3 demonstrated the comparisons of the Hocevar and the OMERACT SGUS scores between ipsilateral salivary glands (parotid vs. submandibular) within each group. By both scores, in pSS patients, bilateral submandibular glands were significantly more commonly involved than the ipsilateral parotid glands. However, the parotid glands were significantly affected more in DM patients.

The correlation analysis between the Hocevar-OMERACT SGUS scores and the potential parameters was illustrated in Fig. 4. The Hocevar score was strongly correlated with the OMERACT score in two groups ($r=0.93$, $p<0.01$; $r=0.92$, $p<0.01$ respectively). In pSS patients, both SGUS scores were highly associated with disease ($r=0.57$, $p=0.001$; $r=0.50$, $p=0.004$) and symptom duration ($r=0.50$, $p=0.002$; $r=0.47$, $p=0.006$). In DM patients, the SGUS scores were strongly correlated with the ESSPRI-dryness ($r=0.74$, $p<0.05$; $r=0.72$, $p<0.05$) and HbA1C level ($r=0.91$, $p<0.05$; $r=0.86$, $p<0.05$).

Table 4 showed the comparison of SGUS scores according to HbA1C level in the DM group. In DM patients with HbA1C level ≥ 5.7, mean US scores of salivary glands were significantly higher than in those with HbA1C level below 5.7 ($p<0.05$).

Discussion

This study observed that according to SGUS scores, the involvement of parotid and submandibular glands in patients with pSS was more severe than DM patients. It was also stated that in pSS patients, salivary gland involvement was submandibular gland predominant, which was associated with disease & symptom duration and ESSPRI-dryness score. On the other hand, in DM patients, it was parotid predominant and was highly correlated with ESSPRI-dryness score and HbA1c levels.

The SGUS is a non-invasive diagnostic procedure to measure involvement of major salivary glands in pSS [19, 20]. In the literature, many studies reported that the use of SGUS would contribute to diagnosis [21, 22] and classification of pSS (2016 ACR/EULAR criteria) [23, 24]. Additionally, it was stated that the SGUS scores (the OMERACT score, Hocevar score etc.) were associated with various clinic-pathological outcomes of pSS patients [6, 25–29]. Even, the literature suggested that this method assisted to salivary gland biopsy and might replace biopsy [30, 31].

Similar to current studies, our findings presented that both SGUS scores were positively correlated with disease and symptom duration in pSS. Also, there was a moderate

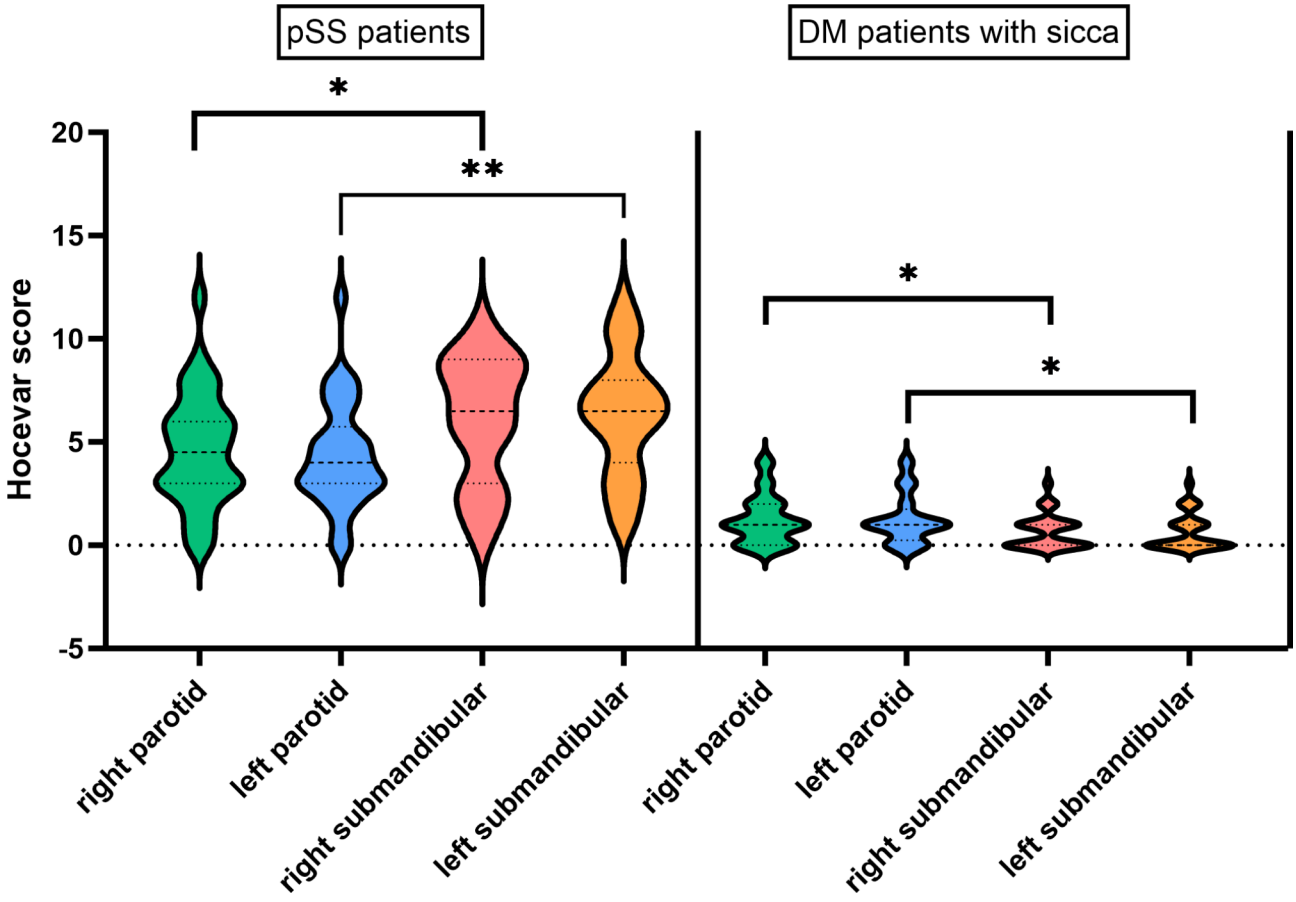

Fig. 2 Comparisons of the Hocevar SGUS scores with respect to salivary glands
* $p < 0.05$; ** $p < 0.01$

correlation between SGUS score and ESSPRI-dryness score. However, in our study, the association between the sonographic scores and ESSDAI, ESSPRI-total, ESSPRI- pain, and ESSPRI-fatigue scores were almost weak. Although the studies showed the association between the SGUS score and serology (e.g., anti-Ro antibody), pathology (e.g., focus score), and clinical outcomes [6, 25, 27, 28], the relationship between non-sicca symptoms and the severity of salivary gland involvement is not yet clear [32, 33]. Frequency and severity of non-sicca symptoms were very heterogeneous and may not always correlate with SGUS score [32, 34]. In the current concept of pSS, the SGUS scores may vary among clinical phenotypes [34, 35]. Even in this case, SGUS may be helpful to disease phenotyping and stratification of patients.

In our patients with pSS, involvement of submandibular gland was more severe than parotid gland. La Paglia et al. presented that patient with pSS showed a parotid gland dominant involvement which was associated with anti-Ro60, and anti-Ro52-60 autoantibodies compared to other connective tissue diseases [12]. However, to the best of our knowledge, there were no previous studies on predilection of salivary gland involvement between pSS and DM patients. Our DM patients with sicca symptoms represented more severe parotid gland involvement compared to submandibular gland. The new data based on salivary gland dominance (parotid vs. submandibular) between pSS, and DM might play a crucial role for understanding of the pathology.

In contrast to the pSS group, the SGUS scores were not associated with disease and symptom duration in DM patients. However, in these patients, the ESSPRI-dryness and HbA1C level were highly correlated to both SGUS scores. Also, the SGUS were observed to be higher in our diabetic patients with elevated HbA1c levels. Gupta et al. showed that ultrasonographic measurements (mostly dimensional parameters) of parotid glands in diabetic patients were higher compared to healthy subjects, and they increased with raised HbA1C levels [8]. Also, the authors stated longer duration of diabetes and treatment with oral agents or insulin were not associated with SGUS measurements [8]. The reason of this result may be the inverse relation between disease duration and good glycemic control (HbA1C level) [36]. The prospective studies may be more likely to clarify this relation rather than cross-sectional studies.

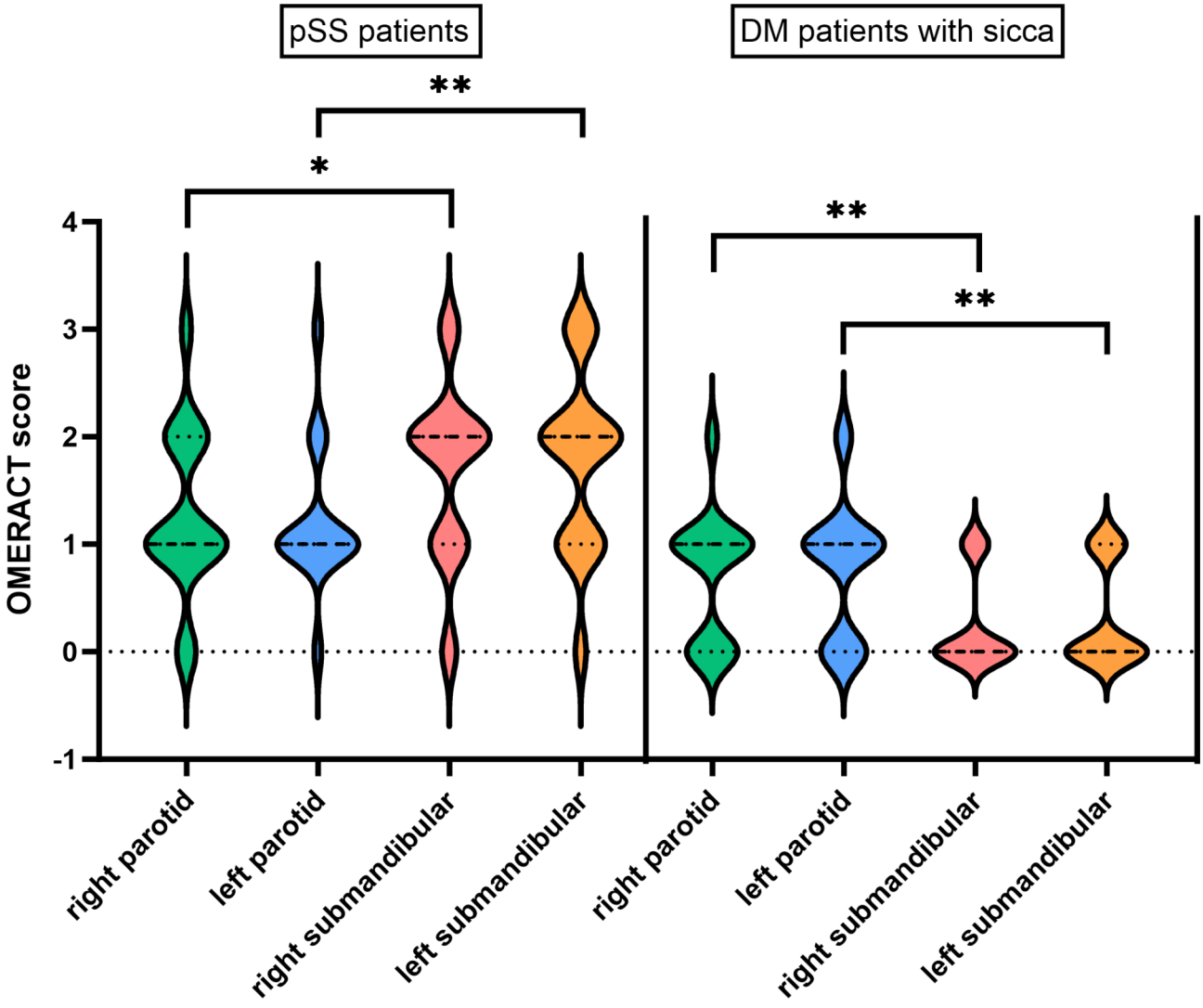

Fig. 3 Comparisons of the OMERACT SGUS scores with respect to salivary glands
* $p < 0.05$; ** $p < 0.01$

In DM patients, the main discriminative ultrasonographic features of salivary glands were declared as echogenicity, homogeneity, posterior border, and the size of glandular area by Badarinza et al. [9]. The authors did not measure SGUS in pSS patients in this study.

The prominent factors of salivary gland dysfunction of DM could be damage to the gland parenchyma, alterations in the microcirculation to the salivary glands, dehydration, disturbances in glycemic control, and autonomic neuropathy [37]. In our study, we investigated diabetics' salivary glands regarding SGUS scores of pSS. Although pSS and DM are distinct diseases affecting the salivary gland with varied pathological mechanisms, they are both autoimmune diseases [20, 37, 38]. We now know that DM affects not only endocrine but also exocrine glands such as salivary and lacrimal glands. It can be suggested that the ultrasonographic characteristics observed in patients with DM may be attributed to the interplay of pathophysiological factors influencing salivary gland function, as previously discussed.

The possible mechanism behind ultrasonic changes in salivary glands was declared only in a few studies [8, 9, 39, 40]. Even if the salivary glands in healthy individuals are described as homogeneous, they often appear non-homogeneous on ultrasound because of vascularity, especially in the submandibular gland [9, 41]. Conversely, Gupta et al. stated increased parenchymal homogeneity of patients with DM [8]. A recent study revealed a decrease in vascularization of the major salivary glands in diabetic patients compared to healthy subjects [39]. Reduced vascularization may be responsible for this homogeneity. Also, another study suggested that the reason for the homogeneity seen in the glands of diabetics may be due to increased fat deposition [9]. The same

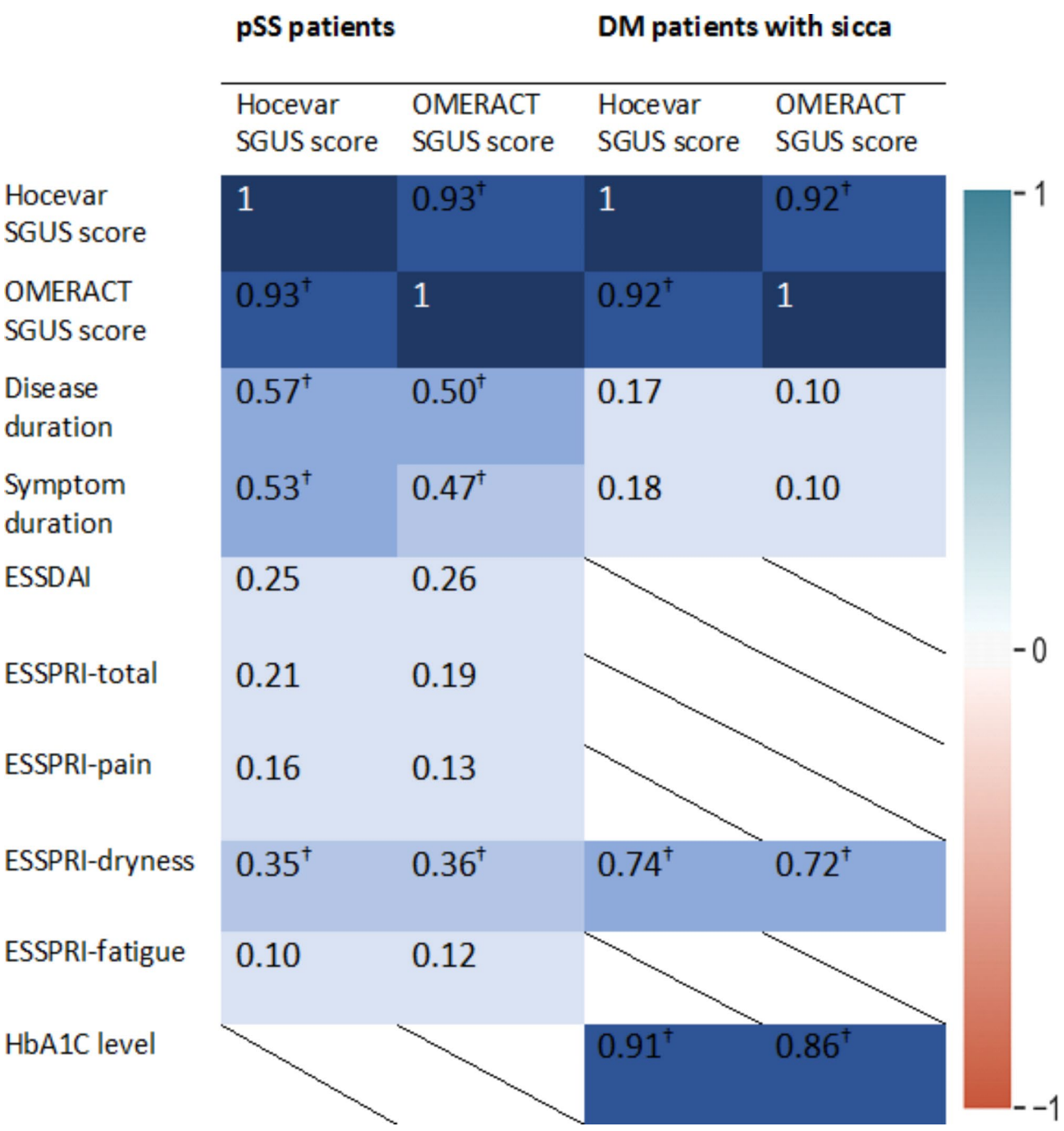

Fig. 4 Correlations between clinical variables and SGUS scores in groups
Correlation analysis was done by Pearson's and Spearman's rho correlation. Results were presented as correlation coefficient (r); †*p* value was < 0.05

study proposed fibrosis as a reason for increased echogenicity [9]. In support of this, a histopathologic study showed acinar enlargement and fat deposition in salivary glands of diabetics [42]. The sialomegaly caused by acinar cell enlargement is likely to compensate for hyposalivation [40]. Further, the probable cause of decreased vascularization in the salivary glands of diabetic patients is impaired microcirculation. Even if this works, there is a lack of clarity about the pathological mechanisms of how DM contributes to these structural changes.

Xerostomia is a subjective symptom that DM patients mostly suffer from. Hyposalivation is an objective sign when salivary flow rates are under 0.1 mL/min at rest or 0.7 mL/min under stimulation [38]. In DM patients, xerostomia was not always associated with salivary flow rate. Compatible with the literature, all DM patients had

Table 4 Comparison of SGUS scores with respect to HbA1C levels in DM patients

	HbA1C level (%)		
	< 5.7 (*n* = 21)	**≥ 5.7 (*n* = 13)**	***P***
The Hocevar SGUS score (total), mean(± SD)	1.28(± 1.12)	6.35(± 3.79)	**< 0.001**
-right parotid, mean(± SD)	0.52(± 0.51)	2.00(± 1.17)	**< 0.001**
-left parotid, mean(± SD)	0.57(± 0.51)	1.92(± 1.26)	**0.001**
-right submandibular, mean(± SD)	0.14(± 0.36)	1.21(± 0.80)	**< 0.001**
-left submandibular, mean(± SD)	0.07(± 0.26)	1.24(± 0.89)	**< 0.001**
The OMERACT SGUS score (total), mean(± SD)	1.00(± 0.87)	3.14(± 1.56)	**< 0.001**
-right parotid, mean(± SD)	0.42(± 0.51)	1.00(± 0.55)	**0.009**
-left parotid, mean(± SD)	0.50(± 0.51)	1.07(± 0.61)	**0.013**
-right submandibular, mean(± SD)	0.06(± 0.12)	0.50(± 0.51)	**0.001**
-left submandibular, mean(± SD)	0.07(± 0.26)	0.57(± 0.51)	**0.003**

HbA1C, glycated hemoglobin A 1c; BMI, body mass index; ANA, anti-nuclear antibody; SGUS, salivary gland ultrasonography, The value of p < 0.05 is expressed in bold.

xerostomia while only 38.2% of them considered a low salivary slow rate in this study. Also, xerophthalmia was only described in 14.7% of DM patients. Further, our DM patients had lower frequency of history of parotitis, sialomegaly, and hyperlobulation of tongue compared to pSS patients. These results suggested that several factors might be capable of xerostomia such as drugs, metabolic disorders, or psychological conditions in addition to diabetes related ones.

To our knowledge, there exists no valid ultrasonographic scale to examine salivary gland involvement in DM patients. Therefore, in this study, we used SGUS scores developed for Sjogren's syndrome to investigate salivary glands of DM patients with sicca symptoms. In other words, we aimed to test to what extent these scoring systems can be used for examining the salivary glands of DM patients. When using these scores, it could be suggested that the salivary gland ultrasound findings due to DM was not able to be fully demonstrated, and we may express it as a limitation of the study. Another limitation of study might be lacking a healthy control group. SGUS results of healthy individuals might clarify differentiation in ultrasonographic pathologies of patients, especially in diabetics.

Conclusion

This study revealed that DM negatively affects the salivary glands, especially parotid glands with respect to ultrasonographic evaluation. Also, this involvement was associated with high dryness score and poor glycemic control. Conversely, patients with pSS have more severe involvement of salivary glands which was submandibular dominant and positively related with symptom and disease duration. In practice, clinicians should carefully consider about concomitant DM when interpreting SGUS results of patients with pSS.

Abbreviations

(pSS) Primary Sjogren's Syndrome
(DM) Diabetes mellitus
(OMERACT) Outcome Measures in Rheumatology
(SGUS) Salivary gland ultrasonography
(ESSPRI) European League Against Rheumatism Sjogren's Syndrome Patient Reported Index
(ANA) Antinuclear antibody
(ACR/EULAR) American Colleges of Rheumatology/ European League Against Rheumatism
(ESSDAI) European League Against Rheumatism Sjogren Syndrome Disease Activity Index

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Author contributions
All authors contributed to the study conception and design. Material preparation and data collection were performed by [AK], [AG], [IS] and [ŞA]. Statistical analysis was performed by [AK] and [IS]. The first draft of the manuscript was written by [AK]. All authors commented on previous versions of the manuscript. All co-authors read and approved the final manuscript.

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Data availability
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request. Raw and analyzed data are located in data storages at Ankara University.

Declarations

Ethics approval and consent to participate
During the study, the World Medical Association Helsinki Declaration and Good Clinical Practices Guidelines were followed. This study was approved by the Ankara University Ethics Committee (Protocol number: İ10-597-22). Reporting of this trial was conducted according to the STROBE (Strengthening the reporting of observational studies in epidemiology) checklist from the EQUATOR Network. The preliminary results of this study have been published as an abstract at the European Congress of Rheumatology (EULAR) 2022. The informed consent was obtained from all participants.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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