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ORIGINAL ARTICLE

Evaluation of subclinical atherosclerosis by ultrasound radiofrequency data technology in patients with primary Sjögren's syndrome

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Abstract

Primary Sjögren's syndrome (pSS) is a chronic inflammatory autoimmune disease, and inflammation is highly associated with atherosclerosis and increased cardiovascular risk. Carotid intima-media thickness (CIMT) and arterial stiffness measurements are commonly used to detect subclinical atherosclerosis. The aim of this study was to non-invasively demonstrate the presence of subclinical atherosclerosis in patients with pSS through these measurements, using ultrasound (US) radiofrequency (RF) data technology. 30 pSS patients as the study group and 30 age-and sex-matched healthy volunteers as the control group were included in this study. The age of the participants in the entire sample ranged from 18 to 60 years, and no primary cardiovascular risk factors were present, such as diabetes mellitus, hypertension, hyperlipidemia, or obesity. The participants in the study and control groups were evaluated with doppler ultrasonography. Arterial stiffness and CIMT measurements were made from the bilateral common carotid arteries (CCA) using US RF data technology. No statistically significant difference was identified between the patients with pSS and the controls in terms of the right, left, and mean CCA IMT; the right side distensibility coefficient (DC) and compliance coefficient (CC); or the right- and left-side α and β stiffness indices values ($p > 0.05$). Compared to the control subjects, the pSS patients had higher right and left side pulsed wave velocity (PWV), the mean value of the right and the left sides α stiffness index, β stiffness index, and PWV ($p < 0.05$). The pSS patients' left DC, left CC, and the mean value of the right and left sides DC and CC were lower than controls ($p < 0,05$). It was found that patients with pSS show evidence of subclinical atherosclerosis. To determine this situation in patients with pSS, CIMT and PWV measurements may serve as a guide. Radiofrequency data technology represents a non-invasive approach to the accurate and quantitative measurement of CIMT elevation and decreases in vascular elasticity.

Keywords Arterial stiffness · Carotid intima-media thickness · Primary Sjögren's syndrome · Subclinical atherosclerosis · Ultrasound radiofrequency data technology

Introduction

Sjögren's syndrome (SS) is a systemic autoimmune and chronic rheumatologic disease that causes secretory dysfunction as a result of lymphocytic infiltration of salivary and lacrimal glands [1]. The resulting dryness of the eyes and mouth is termed sicca syndrome. In addition to sicca syndrome, there may be many organ and system involvements such as joint, skin, lung, and peripheral nervous system [1, 2]. The syndrome may present as a prmiary disease (pSS) or be associated with other autoimmune rheumatic diseases, such as systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and systemic sclerosis, which define secondary SS [1–3]. The prevalence of pSS is 61/100,000, with an incidence of 6.92/100,000 [1, 2].

Atherosclerosis is a chronic inflammatory vascular disease that can lead to morbidity and mortality due to circulatory problems [4]. Inflammation plays a role in the onset and progression of atherosclerosis, and systemic inflammation has been shown to increase the risk of cardiovascular system

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diseases by accelerating atherosclerosis [5–8]. In addition to traditional risk factors, inflammation is a significant independent contributor to cardiovascular risk [9]. Increased levels of inflammatory markers (e.g., erythrocyte sedimentation rate, C-reactive protein, and interleukin-6) have been associated with cardiovascular morbidity and mortality [7].

Arterial stiffness is a term used to indicate qualitatively the reduction in the elastic properties (compliance and distensibility) of the vessel wall, which is an early sign of structural and functional changes in the vessel wall [7]. Systemic inflammation has been shown to cause premature arterial stiffness as the cause of accelerated atherosclerosis [7, 8]. An increased arterial stiffness leads to a decrease in the buffer capacity of the arteries and an increase in pulse pressure and pulse wave velocity (PWV) [7]. PWV is one of the most commonly used methods for the measurement of arterial stiffness [7, 8], which is an independent predictor of cardiovascular disease and a proven indicator of cardiovascular morbidity and mortality [6, 7].

Carotid intima-media thickness (CIMT) can be measured simply, non-invasively and reproducibly measured through B-mode carotid ultrasound, and so it is widely used around the world [10]. The measurement of CIMT is suggested as an important biomarker for the detection of the presence and progression of subclinical atherosclerosis [10, 11]. CIMT is a strong predictor of future cerebral and cardiovascular events, independent of age, gender, and cardiovascular risk factors [10, 11].

Ultrasound (US) radiofrequency (RF) data technology is a novel sonographic method for the evaluation of vascular disease, especially subclinical atherosclerotic changes [12, 13]. During the US examination, the pulsation of the arterial wall can be automatically tracked using RF energy and is less dependent on the experience of the operator [14]. It combines the advantages of B-mode imaging (visual morphology) with integrated RF-data technology for the quantitative assessment of the properties of the walls of blood vessels. So, it has enabled the automatic and accurate measurement of CIMT and arterial elasticity [12]. This technology also provides feedback on the measurement quality and makes measurements at the micrometer level [12, 13], while in other methods, the measurement results are determined in millimeters [13].

Compared to the genaral population, patients with rheumatic disease face an increased risk of atherosclerotic events and the development of cardiovascular comorbidities [9, 15]. The epidemiology and pathogenesis of cardiovascular events in rheumatic diseases are especially well-studied in terms of their relation with rheumatoid arthritis, and also systemic lupus erythematosus, ankylosing spondylitis, gout, psoriatic arthritis, and vasculitides [9, 15]. Although the pathogenic mechanisms and clinical expressions of cardiovascular comorbidities vary among different rheumatic diseases, atherosclerosis seems to be a shared factor [9].

The relationship between pSS and atherosclerosis is not as clear as in RA and SLE, as the number of studies into the effects of pSS on CIMT, especially on arterial stiffness, are limited. To the best of our knowledge there has been no research to date using US RF data technology in pSS. Accordingly, the aim of this study is to carry out CIMT and arterial stiffness measurements in the pSS patient sample using US RF data technology.

Materials and methods

Patient selection Thirty pSS patients (the study group), who were admitted to our rheumatology outpatient clinic and 30 age- and sex-matched healthy volunteers (the control group) were included in the study. All of the pSS patients fulfilled the American-European consensus group criteria for SS [16], and those who had been treated for pSS for at least 1 year were included in this study. The patients and controls were aged between 18 and 60 years. The exclusion criteria for both groups were as follows: hypertension, diabetes mellitus, dyslipidemia, obesity, primary cardiovascular or cerebrovascular disease, chronic obstructive pulmonary disease, acute or chronic renal insufficiency, hepatic insufficiency, use of antihypertensives, antidiabetics, lipid-lowering treatments, or any vasoactive drugs.

Symptom duration refers to the period between the point at which the first symptoms of the disease were identified and the date on which the patient was accepted into the study. Duration of diagnosis and treatment is defined as the time between the date on which PSS was first diagnosed and treatment was begun and the date on which the patient was accepted into the study.

The study protocol was approved by the Clinical Trials Ethics Committee and was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from each participant.

Ultrasonographic assessment

The systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured by the oscillometric method in the US unit of the radiology clinic after approximately 10 min of resting (M-6; Omron Healthcare Company, Ltd., Kyoto, Japan). The pulse pressure was calculated by subtracting the diastolic BP from the systolic BP. Height (meters), weight (kilograms), and body mass index (BMI; kilograms per square meter) measurements for the patient and control groups were recorded in the US unit on the same day as the CIMT measurements.

Patients' identification information and their SBP and DBP values were recorded in the US device, which functioned on a MyLab 60 platform (Esaote SpA, Genoa, Italy) with a high-resolution 12-MHz linear sequence transducer (LA523). The device was equipped with RF Quality Intima-Media Thickness Analysis and RF Quality Arterial Stiffness Analysis software, which worked with the RF method. IMT measurements were obtained from B-mode examinations by using US RF monitoring technology (RF Quality Intima-Media Thickness Analysis) from the distant common carotid arteries (CCA) wall at a 10-mm distal segment, where appropriate images were obtained from the longitudinal plane and no plaque was visualized. To run the software, first, the Tools button on the device was tapped. The same button was tapped once more on the pop-up screen to activate the RF Quality Intima-Media Thickness Analysis software. After 6 cardiac cycles, the software calculated a real-time mean IMT value and its standard deviation (Fig. 1). Afterward, measurement was tapped to numerically show IMT values of both CCAs, as presented in Fig. 2.

After IMT measurements were completed, the Tools button was tapped again, and the RF Quality Arterial Stiffness Analysis software was selected. Using this software, arterial wall movements were monitored by RF signals at systolic and diastolic phases during 6 cardiac cycles in B mode examinations. The RF quality arterial stiffness analysis technology provides a list of stiffness parameters calculated by measuring the arterial distension waveform combined with the brachial artery BP. These parameters are calculated using the following formulas [17, 18]. The parameters D and DD refer to the diastolic diameter and the change in diameter during systole, respectively. Ps and Pd are the SBP and DBPs; DP is the pulse pressure; and r is the blood density.

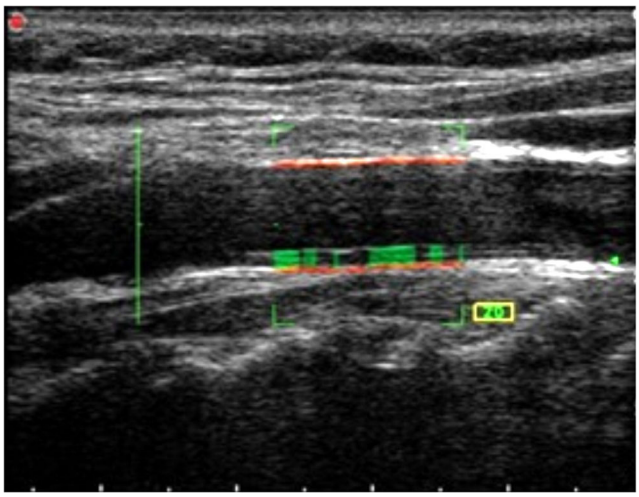

Fig. 1 Left CCA quality intima-media thickness analysis. The red line represents the RF signal following the anterior edge of the media-adventitia interface,and the green line represents the RF signal following the anterior edge of the lumen-intima interface

LEFT QIMT		
LEFT QIMT :	1256	µm
RIGHT QIMT		
RIGHT QIMT :	934	µm
QIMT (RF)		
QIMT (RF) :	1256	µm
SD :	20	µm
DIAMETER :	7.9	mm
SD :	0.45	mm
WIDTH :	13.9	mm
QIMT TABLE:	HOWARD (WHITE)	
EXPECTED QIMT:	---	µm

Fig. 2 Intima-media thickness measurement results for both CCAs. At standard deviation values of 20 µm and lower, the color of the box next to the measurement area turned green, and the measurements were obtained at those values. QIMT indicates Quality Intima-MediaThickness Analysis

1. The distensibility coefficient (DC) refers to the absolute change in vessel diameter during systole for a given pressure change. The DC will be lower if the artery is stiffer. It is calculated by the following formula:

$$\mathrm{DC} = \frac{2 \cdot D \cdot \Delta D + \Delta D^2}{D^2 \cdot \Delta P}.$$

2. The compliance coefficient (CC) is the relative change in the vessel diameter during systole for a given pressure change. The CC will be lower if the artery is stiffer. It is calculated by the following formula:

$$\mathrm{CC} = \frac{\pi \cdot \left(2 \cdot D \cdot \Delta D + \Delta D^2\right)}{4 \cdot \Delta P}.$$

3. The parameter α relates the cross-sectional area change to the driving pressure and is calculated as follows:

$$\alpha = \frac{D^2 \cdot \ln(P_s/P_d)}{2 \cdot D \cdot \Delta D + \Delta D^2}.$$

4. The parameter β indicates the degree of atherosclerosis, and it increases in the presence of atherosclerosis:

$$\beta = \frac{D \cdot \ln(P_s/P_d)}{\Delta D}.$$

5. The parameter PWVβ is the travel speed of the pulsed wave. PWVβ will be higher if the artery is stiffer:

$$\mathrm{PWB}\,\beta = \sqrt{\frac{D^2 \cdot \Delta P}{\rho \cdot \left(2 \cdot D \cdot \Delta D + \Delta D^2\right)}}.$$

Figures 3 and 4 show the quality arterial stiffness analysis of the right CCA and atherosclerosis values of both CCAs.

Statistical analysis

The research data was uploaded into the digital environment and evaluated with SPSS (Statistical Package for Social Sciences) program for Windows 22.0 (SPSS Inc., Chicago, IL). Descriptive statistics were expressed as mean ± standard deviation (min-max), frequency, and percentages. Visual (histograms and probability diagrams) and analytical methods (Shapiro-Wilk Test) were used to check whether or not the variables were normally distributed. For normally distributed variables, a Student's *T* test was used to check any statistically significant differences between two independent groups. As a statistical method for abnormally distributed variables, the Mann-Whitney *U* test was used to measure the statistical significance between two independent groups, and a Wilcoxon Marked Rank Test was used to measure statistical significance between two dependent groups. The relationships between variables were analyzed using Spearman's correlation coefficients. A p value of < 0.05 was considered statistically significant.

Results

The study group comprised 30 pSS patients and the control group comprised 30 healthy volunteers. There was no significant difference between the groups in terms of demographic or clinical characteristics (Table 1) or laboratory parameters (Table 2). Across the entire group of patients, the mean duration of the disease was 4.7 years, with a range of 1 to 20 years. The symptom, diagnosis, and treatment durations and rheumatologic test results of the study group are summarized in Table 3.

All of the patients were being treated with hydroxychloroquine 400 mg/day, while one patient was receiving azathioprine 100 mg/day (for hematological involvement) and another patient was receiving methotrexate 10 mg/week (for articular involvement) in addition to hydroxychloroquine. None of the of pSS patients suffered from pulmonary or vascular involvement.

No statistically significant difference was identified between the patients with pSS and the controls in terms of the right, left, and mean CCA IMT; the right side DC and CC; or the right- and left-side α and β stiffness indices values ($p > 0.05$). Compared to the control subjects, the pSS patients had higher right- and left-side PWV, the mean value of the right and the left sides α stiffness index, β stiffness index, and PWV ($p < 0.05$). The pSS patients' left DC, left CC, and the mean value of the right and left sides DC and CC were lower than controls ($p < 0.05$). These measurement parameters are shown in Table 4.

No statistically significant correlations were found between the C-reactive protein, erythrocyte sedimentation rate values, symptom duration, diagnosis, and treatment duration of the patients with pSS and their mean IMT, DC, CC, and PWV values, and α and β stiffness indices ($p > 0.05$; Table 5).

Discussion

Atherosclerosis is a chronic inflammatory disease characterized by intense immunological activity; it is widespread and leads to morbidity and mortality along with the development of circulatory problems (ex: coronary artery disease and cerebrovascular disease) [4, 5]. In addition to traditional risk factors, chronic inflammation has become recognized as a contributory factor in the development of chronic diseases, including cardiovascular disease [5, 9]. The concept of inflammation playing a role in the initiation and progression of atherosclerosis is now mature [5].

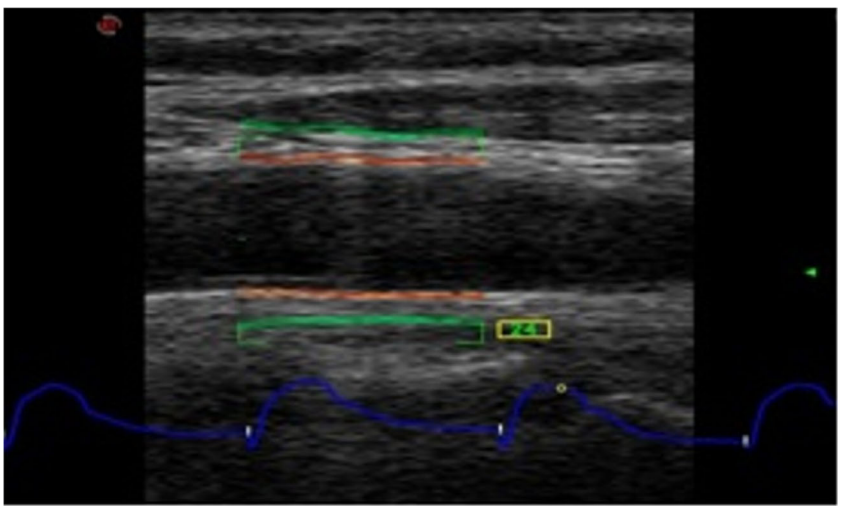

Fig. 3 Quality arterial stiffness analysis of the right CCA. The red and green lines represent the RF signals following the anterior edge of the lumen-intima and media-adventitia interfaces, respectively

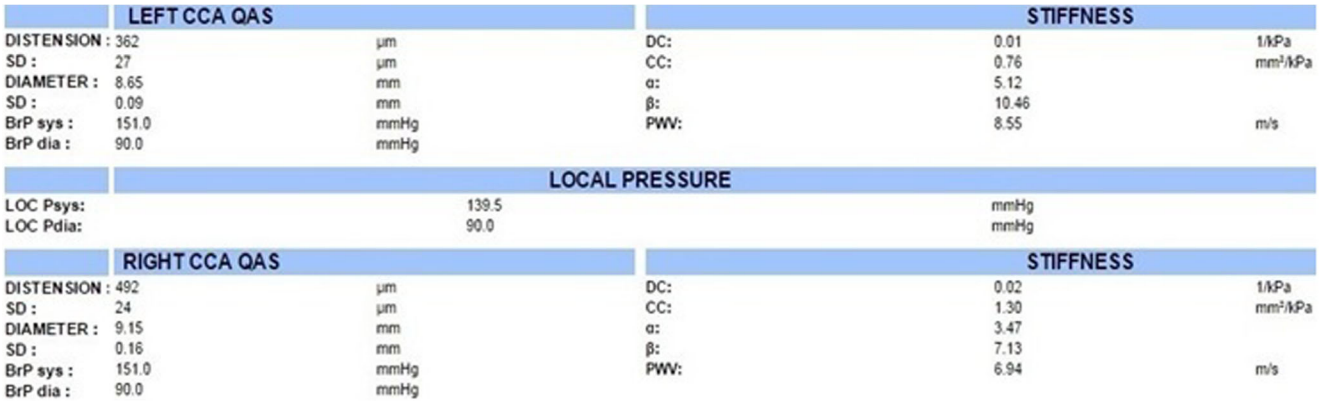

Fig. 4 Atherosclerosis values for both CCAs. Radiofrequency Quality Arterial Stiffness Analysis (QAS) technology includes a list of arterial stiffness parameters calculated by combining the blood pressure (BrP) measurements obtained from the arm and arterial distention waveforms. These parameters are defined as the distensibility coefficient (DC), compliance coefficient (CC), a stiffness index, β stiffness index, and pulsed wave velocity (PWV)

Compared with the general population, patients with autoimmune diseases such as rheumatic diseases are at increased risk of developing several comorbidities, of which cardiovascular comorbidities are the most common and have the major effect on mortality [9, 19, 20]. The increased atherosclerotic risk and cardiovascular diseases have been well established in autoimmune rheumatic diseases such as RA and SLE [20–22]. pSS is an autoimmune disorder that is characterized by chronic multisystem inflammation with shared pathophysiology with RA and SLE. However, there are limited data about the relationship between pSS and cardiovascular diseases [20–23].

Small case-control studies have demonstrated that pSS may be associated with cardiovascular and metabolic abnormalities. Vaudo et al. [24] compared 37 female pSS patients with 35 healthy control subjects and showed an increased rate of subclinical atherosclerosis in pSS patients, based on carotid and femoral USGs. In another study, abnormalities of serum lipid profile were described in 46 patients with pSS [25]. Gerli et al. [26] found that endothelium-dependent flow-mediated vasodilation rates were similar in the pSS and control groups, although the nitroglycerin-mediated vasodilatation rate was lower in the pSS group, and concluded that the functional impairment of the arterial wall may sustain the early phases of atherosclerotic damage.

Bartoloni et al. compared 788 female pSS patients with 4774 age-matched healty women in terms of cardiovascular events and risk factors. They found a significant increase in the prevalance of cerebrovascular disease and myocardial infarction [27]. Theander et al. saw no increased cardiovascular mortality in patients with pSS in a prospective cohort study [28]. In a study, researchers compared pSS patients with control subjects and found similar prevalence of cardiovascular disease (11 versus 10%) [19]. In another study, no association between pSS and an increased risk of subsequent acute myocardial infarction and ischemic stroke was identified [23, 29]. Zöller et al. conducted a nationwide follow-up study in Sweden and observed an increased incidence of coronary disease and no increased risk of cerebrovascular disease in patients with pSS [30, 31].

In the present study, no statistically significant difference was identified between the patient and control groups in terms of CIMT measurements. In a study by Zardi et al., CIMT values were similar in the pSS and control group [32]. In their study, cases with hypertension in the patient and control group were included. In a study conducted by Garcia et al. [33],

Table 1 Demographic and descriptive clinical characteristics of patients with pSS and healthy control participants

	pSS ($n = 30$) mean ± SD (min-max)	Control ($n = 30$) mean ± SD (min-max)	p
Age (year)	41.4 ± 9.4 (26–54)	38.7 ± 8.3 (27–57)	0.222[a]
BMI (kg/m^2)	25.6 ± 3.6 (18.6–29.7)	24.1 ± 2.98 (20.7–29.8)	0.101[b]
SBP (mm Hg)	116.4 ± 9.5 (94–129)	114.2 ± 7.6 (103–129)	0.326[b]
DBP (mm Hg)	78.6 ± 5.9 (64–85)	76.4 ± 5.5 (70–91)	0.125[b]
Pulse (beats/min)	76.6 ± 5.8 (66–85)	77.8 ± 6.1 (70–89)	0.456[b]

SD standard deviation, *BMI* body mass index, *SBP* systolic blood pressure, *DBP* diastolic blood pressure

[a] Mann-Whitney *U* test

[b] Student's *t* test

Table 2 Distribution of laboratory parameters between patients with pSS and healthy control participants

	pSS ($n = 30$) mean ± SD (min-max)	Control ($n = 30$) mean ± SD (min-max)	p^a
Glucose (mg/dl)	84.5 ± 6.3 (75–97)	81.9 ± 5.2 (70–91)	0.203
CRP (mg/L)	3.3 ± 2.0 (1–8.8)	3.8 ± 2.2 (1–7.7)	0.616
ESR (mm/h)	20.0 ± 17.4 (2–77)	12.2 ± 5.5 (3–19)	0.169
Total Cholesterol (mg/dl)	163.3 ± 25.5 (113–198)	150.0 ± 54.8 (0–198)	0.695
Triglycerides (mg/dl)	97.1 ± 37.8 (39–182)	79.4 ± 33.2 (38–171)	0.053
LDL (mg/dl)	106.5 ± 23.3 (71–149)	111.0 ± 20.4 (71–158)	0.429
HDL (mg/dl)	51.0 ± 13.0 (30–91)	53.0 ± 11.8 (28–78)	0.366

SD standard deviation, *CRP* C-reactive protein, *ESR* erythrocyte sedimentation rate, *LDL* low-density lipoprotein, *HDL* high-density lipoprotein

[a] Mann-Whitney *U* Test

values of CIMT above 0.9 mm were evaluated as a thickening of the arterial wall, and only two cases (4.1%) were found to have such high values, although it should be noted that there was no control group in this study, and that the study included patients with cardiovascular risk factors. Akyel et al. identified no significant difference between the PSS and control groups in terms of CIMT values [34]. This research has appropriate exclusion criteria and a healthy control group. Both in this respect and in terms of results, it is similar to our study.

In the three previous studies, CIMT values were statistically significantly higher in the pSS group than in the control group [24, 35, 36], although the cases with cardiovascular risk factors were included in both groups in all three studies, and it is necessary to keep this situation in mind when interpreting the results. In a study by Atzeni et al. [37] that did not include patients and controls with cardiovascular risk factors, CIMT values were found to be higher in the pSS group than in the healthy control group, but not to a statistically significant degree.

No significant correlation was identified between the mean CIMT values and CRP, ESR, symptom duration, diagnosis, and treatment durations in our study, which resembles previous studies in which CIMT levels were higher in the pSS group [24, 36, 37].

Left/right alpha and beta stiffness indices were not significantly different between the two groups, despite being higher in the patient group. However, the mean alpha and beta stiffness indices were statistically higher in the patient group. Right, left, and mean PWV values were significantly higher in the pSS group than in the healthy control group. Other stiffness indicators are DC and CC values. In the patient group, the right-side DC and CC values were lower but not statistically significant. Left-side DC, left-side CC, and the mean DC and CC values were significantly lower in the study group. In a study by Cicek et al. [38], aortic strain and aortic distensibility were significantly lower in patients with SS when compared to the control group, and the authors concluded that a significant relationship existed between atherosclerosis and left ventricular diastolic dysfunction in patients with SS. In a study by Sabio et al. [39], PWV was found to be significantly higher in the pSS group than in the control group, although in this study, both the patient and control groups had participants with primary cardiovascular risk factors such as hypertension and diabetes mellitus. In another study, it was reported that both right and left PWV values and the β stiffness index were significantly higher in the pSS patients than in the controls [37]. In a study by Demirci et al. [40], it was found that carotid-femoral PWV rates were significantly higher in patients with pSS than in the healthy controls, although the study included patients using antihypertensive and antihyperlipidemic medication.

Table 3 In pSS group, symptom duration, diagnosis and treatment duration, and results of rheumatologic tests

Symptom duration, year mean ± SD (min-max)	6.3 ± 4.6 (2–20)
Diagnosis and treatment duration, year mean ± SD (min-max)	4.7 ± 4.6 (1–20)
ANA, *n* (%)	
Negative	2 (6.7)
Positive	28 (93.3)
Granular	23 (82.1)
Homogen	4 (12.3)
Nucleolar	1 (3.6)
RF, *n* (%)	
Negative	16 (53.3)
Positive	14 (46.7)
Anti-SSA, *n* (%)	
Negative	4 (13.3)
Positive	26 (86.7)
Anti-SSB, *n* (%)	
Negative	19 (63.3)
Positive	11 (36.7)

SD standard deviation, *ANA* antinuclear antibodies, *RF* rheumatoid factor

Table 4 Distribution of carotid artery hemodynamic parameters between patients with pSS and healthy control participants

	pSS ($n = 30$) mean ± SD (min-max)	Control ($n = 30$) mean ± SD (min-max)	p^a
Right CIMT (μm)	475.5 ± 79.5 (295–612)	505.0 ± 105.5 (333–757)	0.496
Right DC (1/kPa)	0.022 ± 0.012 (0.01–0.05)	0.028 ± 0.012 (0.01–0.07)	0.064
Right CC (mm^2/kPa)	0.79 ± 0.39 (0.18–1.66)	0.99 ± 0.47 (0.20–2.16)	0.098
Right-α Stiffness Index	5.0 ± 2.9 (1.9–15.6)	4.2 ± 3.1 (0–13.8)	0.101
Right-β Stiffness Index	10.2 ± 5.9 (3.8–31.4)	8.7 ± 6.1 (3.0–27.7)	0.121
Right PWV (m/s)	7.4 ± 2.0 (4.5–12.6)	6.4 ± 2.0 (3.7–12.2)	*0.045*
Left CIMT (μm)	519.4 ± 92.4 (345–725)	492.0 ± 118.1 (50–692)	0.460
Left DC (1/kPa)	0.021 ± 0.011 (0–0.04)	0.031 ± 0.016 (0–0.08)	*0.013*
Left CC (mm^2/kPa)	0.778 ± 0.399 (0.04–1.57)	1.080 ± 0.52 (0.05–2.50)	*0.012*
Left-α Stiffness Index	6.6 ± 10.2 (1.7–57.2)	5.6 ± 11.5 (1.4–65.6)	0.060
Left-β Stiffness Index	13.4 ± 20.3 (3.6–114.5)	11.3 ± 23.1 (2.9–131.6)	0.062
Left PWV (m/s)	7.9 ± 4.2 (4.6–27.1)	6.6 ± 3.8 (3.6–24.9)	*0.011*
Mean CIMT (μm)	497.5 ± 64.7 (320–638)	498.5 ± 92.6 (242–658)	0.888
Mean DC (1/kPa)	0.022 ± 0.009 (0.01–0.04)	0.029 ± 0.013 (0.01–0.08)	*0.014*
Mean CC (mm^2/kPa)	0.78 ± 0.30 (0.21–1.32)	1.04 ± 0.46 (0.26–2.28)	*0.029*
Mean-α Stiffness Index	5.8 ± 5.5 (2.4–31.6)	4.9 ± 6.4 (1–36)	*0.017*
Mean-β Stiffness Index	11.7 ± 11 (4.9–63.4)	10.0 ± 12.7 (3–72.6)	*0.021*
Mean PWV (m/s)	7.6 ± 2.5 (5.1–18)	6.5 ± 2.5 (3.6–16.4)	*0.003*

SD standard deviation, *CIMT* carotid intima-media thickness, *DC* distensibility coefficient, *CC* compliance coefficient, *PWV* pulsed wave velocity

[a] Mann-Whitney *U* test

No significant correlation was found between the mean alpha stiffness index, mean beta stiffness index, mean PWV values and ESR, CRP, symptom duration, diagnosis/treatment duration. In this respect, our study resembles those of Sabio et al. and Atzeni et al. [37, 39]. In another study, PWV was positively correlated with CRP levels [40].

In our study, stiffness-related values were significantly higher in the patient group, although this was not detected in the CIMT values. Functional abnormalities can precede anatomic changes [34], and this means that increased arterial stiffness can precede increased CIMT values. Some authors have suggested that endothelial functional impairments linked to inflammation prevail in the early phases of the disease, whereas structured arterial wall damage is established in long-term disease (duration of more than 10 years) [26, 41]. The mean diagnosis and treatment duration in our patient

Table 5 Relationship between symptom duration, diagnosis and treatment duration, CRP and ESR levels for patients with pSS and their hemodynamic parameters

$n = 30$		Symptom duration	Diagnosis and treatment duration	CRP	ESR
Mean IMT (μm)	r	− 0.187	− 0.284	− 0.178	− 0.263
	p	0.322	0.128	0.346	0.161
Mean DC (1/kPa)	r	− 0.230	− 0.294	− 0.007	− 0.169
	p	0.222	0.114	0.972	0.371
Mean CC (mm^2/kPa)	r	− 0.134	− 0.265	− 0.146	− 0.158
	p	0.479	0.156	0.442	0.403
Mean-α Stiffness Index	r	0.142	0.216	0.034	0.107
	p	0.455	0.252	0.860	0.573
Mean-β Stiffness Index	r	0.143	0.217	0.033	0.112
	p	0.451	0.249	0.862	0.554
Mean PWV (m/s)	r	0.120	0.186	0.067	0.060
	p	0.528	0.326	0.727	0.753

CRP C-reactive protein, *ESR* erythrocyte sedimentation rate, *IMT* intima-media thickness, *DC* distensibility coefficient, *CC* compliance coefficient, *PWV* pulsed wave velocity, *r* Spearman's correlation coefficient

group was 4.7 years, but if we re-evaluate our patients when this time reaches an average of 10 years, we can detect statistically significant elevations in CIMT values.

Our study had few limitations, the most important of which was the small number of patients in the sample. In the present study, the exclusion criteria were the most important reason for the low number of patients, as all patients with cardiovascular risk factors were excluded from the study. This meant that we could only see the effects of pSS on our selected variables. Another limitation was that the study was single-centered.

In conclusion, in the present study, it was found that patients with pSS show evidence of subclinical atherosclerosis. To determine this situation in patients with pSS, measurements of CIMT and PWV may serve as a guide. We believe that there is a need for comparative studies in which the number of cases is higher to better determine the CIMT measurements in pSS patients at more significant levels. Radiofrequency data technology can be considered an appropriate non-invasive method for the accurate and quantitative measurement of CCA intima-media thickness elevations and decreases in vascular elasticity.

Compliance with ethical standards

The study protocol was approved by the Clinical Trials Ethics Committee and was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from each participant.

Disclosures None.

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