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The frequency of obstructive sleep apnea in patients with primary Sjogren's syndrome

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Abstract

Introduction There is a lack of information about the frequency of obstructive sleep apnea (OSA) in primary Sjogren's syndrome (pSS). Using all-night polysomnography (PSG), this study aimed to investigate the frequency of OSA in pSS and the factors affecting the frequency of OSA in this condition.

Methods Consecutive patients with pSS who presented to the Collagen Tissue Diseases follow-up polyclinic of the Department of Chest Diseases between 1 April 2019 and 31 December, 2020, were included in the study. Demographic characteristics, chronic diseases, smoking history in pack-years, anthropometric data, Epworth Sleepiness Scale score, pulmonary function test parameters, current thorax computed tomography findings, and PSG data were recorded. The control group was created by the retrospective screening of patients admitted to the sleep polyclinic and who underwent PSG but did not have pSS.

Results OSA was detected in 37 (84%) of 44 patients with pSS who underwent PSG. Of 37 patients with OSA, 25 (68%) had moderate or severe OSA. Snoring and witnessed apneas, REM%, snoring index, and maximum apnea and maximum hypopnea duration were statistically significantly lower in the pSS group compared with the control group ($p < 0.001$, $p = 0.003$, $p = 0.025$, $p = 0.001$, $p = 0.028$, and $p = 0.035$, respectively).

Conclusion The frequency of OSA in patients with pSS was 84%, with a decrease in REM%. Although a correlation between symptoms suggesting OSA and the presence of radiological lung involvement, spirometry, and DLCO values with OSA could not be demonstrated, physicians are recommended to be attentive for the presence of OSA in all patients with pSS and to investigate OSA using PSG.

Keywords OSA · Primary Sjogren's syndrome · PSG · Frequency · Sjogren's syndrome

Introduction

Sjögren's syndrome (SS) is a chronic autoimmune disease of unknown cause, characterized by glandular and extraglandular involvement, most commonly affecting the salivary and lacrimal glands, and lymphocytic infiltration of exocrine glands [1]. It is referred to as primary SS (pSS) if it occurs alone without any other connective tissue disease. The prevalence of pSS is approximately 0.1–0.5% in the population. It can occur at any age, with the first highest incidence at 20–30 years and the second peak in the 50s. pSS is seen 9–10 times more commonly in women than in men [2]. The most common symptoms are dry mouth and eyes. Dryness in the upper respiratory tract and all airway mucosa, inflammation, deterioration of mucociliary clearance, and increased mucus viscosity cause the related symptoms. Subjective findings such as excessive daytime sleepiness (EDS), body pain, and depression, especially fatigue, are common in patients with pSS, and their etiopathogenesis have not been elucidated [1, 3].

Obstructive sleep apnea (OSA) occurs due to complete or partial obstruction of the upper airways during sleep. It is characterized by snoring, apnea, nocturnal desaturation, and EDS [4]. Symptoms, cognitive disorders, and fatigue can be seen due to nighttime respiratory events and complications. The main problem in OSA is upper respiratory

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tract narrowing. There are many mechanical and inflammatory causes in the pathophysiology of this narrowing. Its prevalence in the adult population is 4% in men and 2% in women [5].

Primary SS can cause airway involvement, especially upper airway involvement, with lymphocytic infiltration. It causes dryness in the entire respiratory tract mucosa by affecting the airway gland structures. Thus, it has been hypothesized that pSS facilitates upper airway collapse and may increase the risk of OSA by contributing to its pathophysiology. Symptoms such as EDS and fatigue in patients with pSS may be due to the underlying OSA. The prevalence of fatigue symptoms, which is also common in OSA, was found to be 38–88% in pSS patients, while it was 0.007–2.8% in the general population [6]. On the other hand, it has not been demonstrated whether or not radiologic lung involvement and the decrease in respiratory functions contribute to the risk of OSA in patients with pSS.

Sleep-related problems and sleep disorders in pSS have been investigated frequently, but there are few studies on the use of polysomnography (PSG) in investigating sleep-disordered breathing [7, 8]. There is scant information about the frequency of OSA in pSS. This study aimed to investigate the frequency of OSA in pSS and its affecting factors using all-night PSG, which is the gold standard test in the diagnosis of OSA.

Materials and method

The study was planned as a prospective, controlled, cross-sectional study. Ethics committee approval for the study was obtained from the Ethics Committee of Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty (IRB No. 604.01.01–45638).

Participants

The study group was formed from consecutive patients with pSS who presented to the Collagen Tissue Diseases follow-up polyclinic of the Department of Chest Diseases between 1 April 2019 and 31 December 2020 pSS was diagnosed by the rheumatology department according to the guidelines [9]. The patients were evaluated according to the inclusion criteria (diagnosis of pSS, age 18 years or older, and agreement to participate in the study obtained with written consent) and exclusion criteria (the association of another connective tissue disease or chronic diseases such as idiopathic pneumonia with interstitial involvement, sarcoidosis, amyloidosis, acromegaly, heart failure, active cancer, pregnancy, insufficient sleep time in PSG, or technically unsuitable PSG data).

Demographic characteristics, chronic diseases, smoking history in pack-year terms, anthropometric data, dry mouth, dry eye, snoring, witnessed apnea, and EDS of all patients was questioned and recorded. Salivary gland biopsy, dry eye assessment test (Schirmer test), serologic tests (anti-Ro/SSA, anti-La/SSB, RF, ANA) were recorded before diagnosing pSS. Epworth Sleepiness Scale (ESS) scores, pulmonary function test (PFT) parameters [spirometry and diffusing capacity of the lung for carbon monoxide (DLCO)], current thorax computed tomography (CT) findings, and PSG data were recorded.

The control group was created with the retrospective assessment of patients admitted to the sleep polyclinic during the study period who had PSG but were not diagnosed as having pSS. Female, non-pregnant patients aged over 18 years with normal chest radiography and acceptable PSG results without any connective tissue diseases such as sarcoidosis, amyloidosis, acromegaly, and active cancer diagnoses were included.

Anthropometric data

The height (cm), weight (kg), and body mass index (BMI) (kg/m^2) of the patients were recorded. Neck circumference (cm) was measured at the level of the cricothyroid membrane and recorded. BMI was classified as normal (18.5–24.9 kg/m^2), overweight (25–29.9 kg/m^2), and obese (> 30 kg/m^2) [10].

Polysomnography

All-night polysomnography (PSG) recording of all patients included in the study was performed with SOMNOscreen plus system (SOMNOscreen, SOMNOmedics, Germany). PSG records were evaluated by two different experts at different times, according to the AASM's "Manual for Scoring Sleep-Version 2" scoring criteria update in 2012, and a report was written for each patient with a consensus. During recording, electroencephalography (EEG), electrooculography (EOG), electromyography (EMG), electrocardiography (ECG) electrodes, nasal cannula, thermistor, abdominal and chest belts, tracheal microphone, pulse oximeter, and position sensor were used based on the AASM 2007 recording protocol. Sleep duration, efficiency, duration, and percentages of sleep phases, sleeping time, and percentages in the supine and non-supine positions were noted. All respiratory events, apnea and hypopnea indexes (AHI) per sleep hour, fingertip oxygen saturation follow-up values, and oxygen desaturation indexes (ODI) were recorded. For scoring hypopnea, the criterion of a 50% or more decrease in airflow lasting at least 10 s and accompanying a 3% decrease in oxygen saturation or arousal was used. Apnea was defined as an interruption of the airflow for 10 s [11]. For sufficient

PSG registration, at least 4 h of sleep time and at least 60% sleep efficiency were accepted.

AHI was used to define OSA. Patients with AHI ≥ 5 were considered as having OSA, and those with an AHI of 5–14, 15–29, and ≥ 30 were classified as having mild, moderate, and severe OSA. Rapid eye movement (REM)-dependent OSA was described as AHI being ≥ 5 with AHI < 5 during the non-REM period and AHI during the REM period being twice as much it was during the non-REM period [12, 13]. Similarly, "Position-dependent OSA" was described as AHI ≥ 5 with AHI < 5 in the supine position and AHI in a supine position being more than twice as much as it was in the non-supine position [12, 13].

The ESS was used to determine the patients' EDS subjectively, and its score was recorded. The ESS is an easy-to-use questionnaire consisting of 8 questions [14]. Each question is scored between 0 and 3 points. The total scores varied between 0 and 24, and EDS was considered to be present with ESS over 10 points.

PFT Spirometry and DLCO tests results [forced vital capacity (FVC), FVC%, forced expiratory volume in 1 s (FEV1), FEV1%, FEV1/FVC, FEV1/FVC%, DLCO, alveolar volume (VA), DLCO/VA, DLCO/VA% values] were recorded. The tests were conducted using a ZAN 100 Flow Handy II device according to the European Respiratory Society and American Respiratory Society (ERS/ARS) criteria [15, 16].

Thorax CT Chest radiographs of the control group and thorax CT reports of the pSS group were recorded. Pleural effusion, interstitial involvement patterns on thoracic CTs [non-specific interstitial pneumonia (NSIP), lymphocytic interstitial pneumonia (LIP), usual interstitial pneumonia (UIP), organized pneumonia (OP)], presence of bronchiectasis, and the number of segments involvement was assessed by two expert radiologists. Evaluations were made at different times, and the final report was written by ensuring a common consensus for each patient. Ten segments were evaluated in the right lung, and eight segments were evaluated in the left lung according to the final report.

Statistics and analysis

All analyses were performed using the SPSS v21 (SPSS Inc., Chicago, IL, USA) program. The compliance of quantitative variables to normal distribution was checked using the Kolmogorov–Smirnov test. Quantitative variables are summarized using mean ± standard deviation and median (lowest value—most considerable value), and qualitative variables are summarized as frequency (percentage). According to the pSS and control groups, analysis of quantitative variables was performed using the independent samples *t* test or the Mann–Whitney *U* test according to their suitability to normal distribution. According to OSA weight status, analysis of quantitative variables was performed using the Kruskal–Wallis test based on the conformity to normal distribution. Bonferroni correction was used for binary comparisons. Qualitative variables were analyzed using the chi-square test or Fisher's exact test. Values of $p < 0.05$ were considered statistically significant.

Results

Eighty-one patients with pSS were evaluated within the specified time interval. A total of 47 patients who met the inclusion criteria were included in the study; three patients were excluded due to insufficient sleep time. From among 740 patients who underwent PSG (486 M/254 F), 88 female patients without pSS were selected for the control group (see Fig. 1: Flow chart). The demographic characteristics of the pSS group are given in Table 1. Table 1 also shows the symptoms, laboratory findings, Schirmer test result, salivary gland biopsy result, spirometry test, and DLCO values of the pSS group. Anti-Ro/SSA positivity (57%) was the most common among the rheumatological markers examined. Dry mouth (66%) and dry eyes (75%) were also common symptoms.

An interstitial involvement pattern was detected in 15 (34%) of the 44 patients with pSS (Table 1). No pleural effusion was detected in any patient.

OSA was detected in 37 (84%) of 44 patients [no OSA:7 (16%); mild OSA:12 (27%); moderate OSA:19 (43%); severe OSA:6 (14%)] with pSS who underwent PSG. A statistically significant relationship was found between the presence of OSA and age, BMI, and being overweight or obese ($p = 0.016$, $p = 0.016$, and $p = 0.012$, respectively). Complaints suggestive of OSA, presence, and extent of radiological lung involvement, spirometry and DLCO values were not associated with OSA in the pSS group (Table 2).

There was no statistical difference between the control group and the pSS group in terms of age, gender, BMI, weight, height, obesity, neck circumference, comorbidities, smoking history in pack-years, and smoking status (Table 3).

There was no statistical difference between pSS and control groups in terms of OSA frequency [37 of 44 patients (84%) in the pSS group; 68 of 88 patients (77%) in the control group, $p = 0.359$], also there was no statistical difference in terms of OSA severity and AHI values (mean AHI value, 15.1 ± 11.4 in the pSS group; 17.4 ± 15.6 in the control group, $p = 0.820$) (Table 3). Snoring, witnessed apnea, REM%, snoring index, and maximum apnea and maximum hypopnea duration were statistically significantly lower in

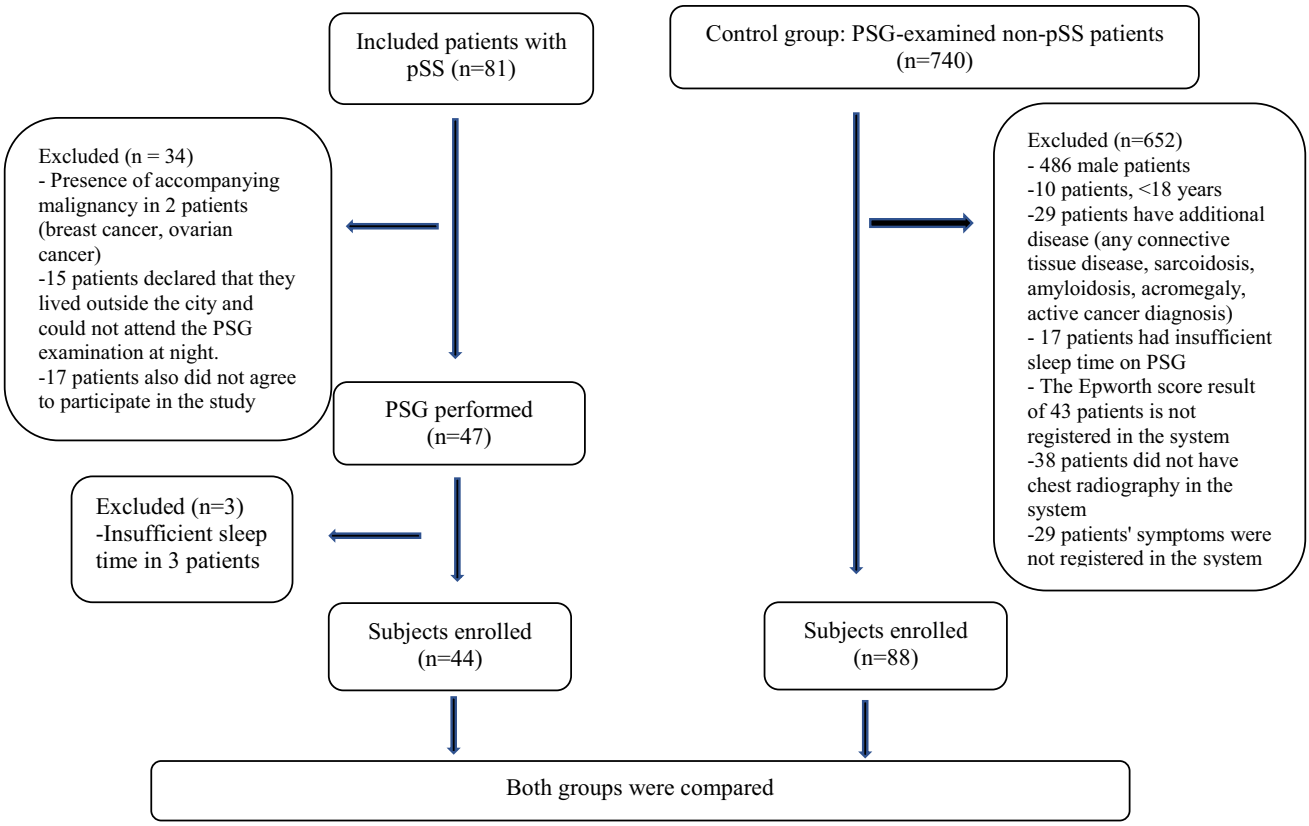

Fig. 1 Flow chart

the pSS group compared with the control group ($p < 0.001$, $p = 0.003$, $p = 0.025$, $p = 0.001$, $p = 0.028$, and $p = 0.035$, respectively) (Table 3).

Discussion

Our study found that the frequency of OSA was 84% in patients with pSS, and REM%, snoring index, maximum apnea, and hypopnea time decreased in patients with pSS with OSA. Symptoms suggesting OSA, radiologic pulmonary involvement, spirometry, and DLCO values were not found to be associated with OSA.

In pSS, there are two studies investigating OSA with PSG. In the study of Usmani et al., which consisted of 28 patients with pSS and 18 healthy controls, 64% of the patients had OSA. In the study of Jülich et al., not including a control group of 14 patients with pSS, 28.5% were diagnosed as having OSA [7, 8]. In our study, this rate was 84.1%. The high ratio of moderate and severe OSA were remarkable. This high rate shows that the presence of OSA is substantial in patients with pSS and requires attention.

It has been reported that OSA is most common at the ages of 40–60 years in the general population [17]. No relationship was found between age and OSA in Jülich et al.'s study [8]. In our study, a significant relationship was found between age and the presence of OSA. Studies with more extensive series are needed on this subject.

It has been reported that the risk and severity of OSA increase with increased BMI [18]. In patients with pSS, Jülich et al. reported that BMI was not associated with OSA [8]. However, in our study, a relationship was found between BMI and the presence and severity of OSA in patients with pSS. Our result shows that BMI is associated with OSA risk in patients with pSS, similar to the normal population. It may be necessary to be more careful in terms of OSA in overweight and older pSS patients.

Neck circumference is a risk factor for OSA in the general population [19]. In pSS, neck circumference has not been investigated previously. Regarding rheumatologic diseases, Gundogdu et al. found no relationship between neck circumference and the presence of OSA in patients with systemic sclerosis [20]. In our study, the increase in neck circumference was not associated with OSA risk in pSS.

The risk of OSA is increased in heavy smokers [21]. No study has examined the relationship between smoking and OSA in patients with pSS. In our study, smoking status

Table 1 Clinical, demographic, laboratory, pulmonary function tests, and radiologic characteristics of patients with pSS

Parameters	
Female/male, *n*	42/2
Age (year), mean ± SD	56.3 ± 13.3
Body mass index (kg/m^2), mean ± SD	29.0 ± 4.6
Neck circumference (cm), mean ± SD	35.0 ± 2.8
Duration of illness (year), mean ± SD	5.8 ± 4.5
Smoking	
Never smoker (%), mean ± SD	68 ± 9
Former smoker (%), mean ± SD	21 ± 4
Current smoker (%), mean ± SD	11 ± 4
Smoking (pack-year), mean ± SD	4.6 ± 9.1
pSS laboratory, *n* (%)	
RF positivity	14 (32)
ANA positivity	20 (46)
Anti-Ro/SSA positivity	25 (57)
Anti-La/SSB positivity	14 (32)
Shirmer test positivity, *n* (%)	25 (57)
Salivary gland biopsy supporting pSS, *n* (%)	26 (59)
Symptoms suggestive of pSS, *n* (%)	
Dry mouth	29 (66)
Dry eyes	33 (75)
Pulmonary function tests	
FVC (L), mean ± SD	2.70 ± 0.74
FVC (%), mean ± SD	101.6 ± 16.9
FEV1 (L), mean ± SD	2.15 ± 0.56
FEV1 (%), mean ± SD	96.0 ± 17.4
FEV1/FVC (%), mean ± SD	79.7 ± 6.9
DLCO (mL/min/mmHg), mean ± SD	16.8 ± 6.0
DLCO (%), mean ± SD	75.3 ± 23.2
Radiologic findings, *n* (%)	
Interstitial involvement	15 (34)
Number of segments involved, mean ± SD	12.9 ± 3.4
Comorbidities, *n* (%)	
Diabetes mellitus	7 (16)
Hypertension	15 (34)
Cardiovascular disease	3 (7)
Symptoms suggestive of OSA, *n* (%)	
EDS	33 (75)
Snore	13 (30)
Witnessed apnea	27 (61)

ANA anti-nuclear antibody, *DLCO* carbon monoxide of the lung diffusing capacity, *EDS* excessive daytime sleepiness, *FEV1* forced vital capacity 1. Second; *FVC* forced vital capacity, *OSA* obstructive sleep apnea syndrome, *pSS* primary Sjögren syndrome, *RF* rheumatoid factor

and pack-year smoking were not associated with OSA in patients with pSS.

Jülich et al. found a positive correlation between dry mouth and AHI values in patients with pSS ($p = 0.002$); there was no relationship between dry eye and OSA. It was commented that dry airways might cause OSA by increasing airway tension [8]. Dry mouth can be a guide in predicting the risk of OSA as an indicator of upper respiratory tract dryness, but Jülich et al.'s study included 14 patients. In our study, no relationship was found between the symptoms of dry mouth and eyes and OSA. Studies with more extensive series are needed on this subject.

Salivary gland biopsy in pSS may be an indicator of upper airway inflammation. In our study, no relationship was found between OSA and the presence of salivary gland biopsy supporting SS. No comparison could be made because there no other studies have investigated this issue.

Snoring and witnessed apnea were not examined in studies evaluating OSA in pSS [7, 8]. In our study, when patients with and without OSA were compared, no difference was found regarding the frequency of snoring and witnessed apnea. Also, the frequency of witnessed apnea and snoring and the snoring index value in PSG were significantly lower in patients with pSS compared with the control group. These findings suggest that witnessed apnea and snoring may be insufficient in predicting the presence of OSA in pSS. For this reason, we recommend that patients with pSS without snoring and witnessed apnea should also be evaluated using PSG for the presence of OSA.

EDS is the most common symptom in patients with OSA in the general population, also a common symptom in pSS. In a systematic review, Hackett et al. determined that there was more EDS in patients with pSS than in healthy controls. It was thought that EDS seen in pSS might be related to sleep disorders [22]. Gudbjörnsson et al. showed that the pSS group had five times more EDS than RA and three times more than the healthy control group [23]. Usmani et al. found that EDS was significantly higher in patients with pSS than in controls ($p = 0.014$) [7]. By contrast, we found no relationship between OSA and EDS in patients with pSS.

In the study of Usmani et al. no relationship was found between ESS score and AHI in patients with pSS, and in the study of Jülich et al., no relationship was found between the ESS score and the presence of OSA [7, 8]. Similarly, in our study, we found no relationship between ESS scores and the presence and severity of OSA in the pSS group.

No study has investigated the relationship between PFT parameters and OSA in patients with pSS. In our study, no relationship was found between the presence of OSA in pSS and the results of spirometry and DLCO. Not only pSS but also generally under the title of interstitial lung disease (ILD), how respiratory functions affect OSA is a question that remains unanswered. Mermigkis et al. investigated sleep-disordered breathing in patients with Idiopathic Pulmonary Fibrosis (IPF) and a partial relationship was found between low FVC and AHI, and a statistically significant relationship was found between FVC and REM AHI. This

Table 2 Relationship between the presence of OSA and clinical, demographic, laboratory, pulmonary function tests, and radiologic features in patients with pSS

Parameters	pSS-OSAS (-) (*n*=7)	pSS-OSAS (+) (*n*=37)	*p*
Sex Female/Male	6/1	36/1	0.296
Age (year), mean±SD	44.9 ± 11.8	58.4 ± 12.5	***0.016****
Body Mass Index (kg/m^2), mean±SD	24.8 ± 5.6	29.8 ± 4.0	***0.016****
Normal (BMI <25), n (% mean)	4 (28.6)	4 (10.8)	
Overweight (BMI <30), n (% mean)	2 (28.6)	15 (40.5)	***0.012****
Obese (BMI <40), n (% mean)	1(14.3)	18 (48.7)	
Neck circumference (cm), mean±SD	33.1 ± 2.5	35.3 ± 2.8	0.092
Duration of illness (year), mean±SD	5.7 ± 3.2	5.8 ± 4.8	0.619
Smoking			
Smoking (pack-year), n (% mean)	1.7 ± 4.9	5.1 ± 9.7	0.286
Never smoker n (% mean)	6 (85.8)	24 (64.9)	
Former smoker n (% mean)	0 (0)	9 (24.3)	0.343
Current smoker n (% mean)	1 (14.3)	4 (10.8)	
pSS lab, n (% mean)			
RF positivity	2 (28.6)	12 (32.4)	0.999
ANA positivity	2 (28.6)	18 (48.7)	0.355
Anti-Ro/SSA positivity	6 (85.7)	19 (51.4)	0.119
Anti-La/SSB positivity	1 (14.3)	13 (35.1)	0.270
Schirmer test positivity, n (% mean)	3 (42.9)	22 (59.5)	0.443
Salivary gland biopsy supporting pSS, n (% mean)	5 (71.4)	21 (56.8)	0.682
Symptoms, n (% mean)			
Dry mouth	5 (71.4)	24 (64.9)	0.999
Dry eyes	3 (42.9)	30 (81.1)	0.054
Pulmonary function tests			
FVC (L), mean±SD	3.03 ± 0.68	2.64 ± 0.75	0.112
FVC (%), mean±SD	96.0 ± 10.9	102.6 ± 17.8	0.360
FEV1 (L), mean±SD	2.33 ± 0.48	2.11 ± 0.57	0.211
FEV1 (%), mean±SD	87.8 ± 7.8	97.6 ± 18.3	0.177
FEV1/FVC (%), mean±SD	78.1 ± 6.0	80.0 ± 7.1	0.327
DLCO (mL/min/mmHg), mean±SD	18.8 ± 6.2	16.4 ± 6.0	0.320
DLCO (%), mean±SD	77.6 ± 21.3	74.9 ± 23.7	0.642
Radiological findings, n (%)			
Interstitial involvement	2 (28.6)	13 (35.1)	0.401
UIP	0 (0.0)	6 (16.2)	0.586
LIP	0 (0.0)	4 (10.8)	0.999
NSIP	1 (14.3)	2 (5.4)	0.413
OP	1 (14.3)	1 (2.7)	0.296
Number of segments held	1.7 ± 4.9	4.5 ± 6.5	0.294
Bronchiectasis	1 (14.3)	12 (32.4)	0.654
Comorbidities, n (%)			
Diabetes mellitus	1 (14.3)	6 (16.2)	0.999
Hypertension	1 (14.3)	14 (37.8)	0.393
Cardiovascular disease	0 (0.0)	3 (8.1)	0.999
Symptoms suggestive of OSA, n (%)			
EDS	5 (71.4)	28 (75.7)	0.999
Snore	3 (42.9)	24 (64.9)	0.402
Witnessed apnea	1 (14.3)	12 (32.4)	0.654
ESS, mean ± SD	5.4 ± 3.3	5.8 ± 4.2	0.821

*: $p<0.05$

ANA Anti-nuclear antibody; *BMI* Body mass index; *DLCO* carbon monoxide diffusion of the lung capacity; *FEV1* Forced vital capacity 1. Second; *FVC* Forced vital capacity; *EDS* excessive daytime sleepiness; *ESS* Epworth Sleepiness Scale; *LIP* Lymphocytic interstitial pneumonia; *NSIP* Non-specific intestinal pneumonia; *OP* organized pneumonia; *OSA* Obstructive sleep apnea syndrome; *pSS* Primary Sjögren Syndrome; *RF* Rheumatoid factor; *UIP* usual interstitial pneumonia

Table 3 Comparison of pSS and control group in terms of demographics, presence of OSA, and PSG findings

Parameters	pSS group ($n=44$)	Control ($n=88$)	p
Sex female/male	42/2	88/0	0.109
Age (year), mean ± SD	56.3 ± 13.3	54.0 ± 8.6	0.296
Body mass index (kg/m^2), mean ± SD	29.0 ± 4.6	28.5 ± 4.0	0.543
BMI classification			
Normal (≤ 18.5BMI < 25), *n* (% mean)	8 (18)	18 (21)	
Overweight (≤ 25 BMI < 30), *n* (% mean)	17 (39)	40 (46)	0.593
Obese (BMI ≥ 30), *n* (% mean)	19 (43)	30 (34)	
Neck circumference (cm), mean ± SD	35.0 ± 2.8	36.1 ± 3.1	0.053
Smoking (pack-year) mean ± SD	4.6 ± 9.1	7.3 ± 11.9	0.190
Smoking classification, *n* (%)			
Never smoker	30 (68)	51 (58)	
Former smoker	9 (21)	13 (15)	0.108
Current smoker	5 (11)	24 (27)	
Comorbidities, *n* (%)			
Diabetes mellitus	7 (16)	20 (23)	0.492
Hypertension	15 (34)	29 (33)	0.999
Cardiovascular disease	3 (7)	2 (2)	0.333
Symptoms suggestive of OSA, *n* (%)			
EDS	33(76)	56 (64)	0.264
Snore	**27 (61)**	**82 (93)**	***< 0.001****
Witnessed apnea	**13 (30)**	**45 (51)**	**0.030***
ESS, mean ± SD	5.7 ± 4.0	6.7 ± 5.0	0.577
OSA frequency, *n* (%)	37 (84)	68 (77)	0.359
OSA severity, *n* (%)			
No	7 (16)	20 (23)	
Mild	12 (27)	11 (13)	0.150
Moderate	19 (43)	38 (43)	
Severe	6 (14)	19 (22)	
REM-dependent OSA	6 (14)	6 (7)	0.213
Position-dependent	6 (14)	16 (18)	0.680
PSG findings, *n* (%)			
Obstructive apnea	39 (89)	73 (83)	0.548
Central apnea	9 (21)	17 (19)	0.999
Mixed apnea	4 (9)	9 (10)	0.999
Hypopnea	42 (96)	87 (99)	0.999
SaO2 number below 90%	28 (64)	67 (76)	0.193
Sleep efficiency (%)	74.1 ± 12.1	74.5 ± 11.5	0.841
REM (%), mean ± SD	**12 ± 7**	**15 ± 7**	***0.025****
Stage 1 (%), mean ± SD	9 ± 8	8 ± 7	0.088
Stage 2 (%), mean ± SD	58 ± 12	59 ± 19	0.549
Stage 3 (%), mean ± SD	21 ± 12	19 ± 8	0.688
AHI, mean ± SD	15.1 ± 11.4	17.4 ± 15.6	0.820
Time to fall asleep (min), mean ± SD	33.3 ± 28.4	41.5 ± 32.7	0.059
Snoring index, mean ± SD	**50.8 ± 106.3**	**124.4 ± 173.1**	***0.001****
Max apnea time (s), mean ± SD	**21.7 ± 16.2**	**30.5 ± 25.6**	***0.028****
Max hypopnea time (s), mean ± SD	**65.8 ± 30.1**	**78.5 ± 33.3**	***0.035****
ODI, mean ± SD	17.5 ± 13.4	18.2 ± 14.6	0.931
REM AHI, mean ± SD	28.5 ± 20.4	26.5 ± 19.9	0.503
NREM AHI, mean ± SD	13.4 ± 11.1	15.5 ± 16.2	0.948
Supine AHI, mean ± SD	20.2 ± 18.8	26.1 ± 24.5	0.319
Non-supine AHI, mean ± SD	9.5 ± 10.8	11.2 ± 13.3	0.544

*$p < 0.05$

AHI apnea–hypopnea index, *BMI* body mass index, *EDS* excessive daytime sleepiness, *ESS* Epworth Sleepiness Scale, *NREM* non-rapid eye movement, *ODI* oxygen desaturation index, *OSA* obstructive sleep apnea syndrome, *PSG* polysomnography, *pSS* primary Sjögren syndrome, *REM* rapid eye movement

was interpreted as that the risk of sleep apnea might increase in patients with IPF with decreased lung function tests, especially in REM [24]. Lancaster et al. reported no correlation between PFT parameters and AHI in IPF. It was argued that the reason for this might be that the tests were performed sitting rather than in the lying position, which would better reflect the lung volumes during sleep [25]. Pihtili et al. found no relationship between AHI and PFT results in ILD [26]. Although our result is specific to pSS, it is similar to Lancaster et al. and Pihtili et al.; no comparison could be made because there are no data on patients with pSS in the literature.

No studies have investigated the relationship between radiologic lung involvement and OSA in pSS. In ILD, decreased lung volumes, increased respiratory workload, hypoxemia, and increased airway resistance can increase airway collapse during sleep, especially during the REM period, and may cause OSA to occur [26]. AHI was found to be higher in ILD with severe radiologic involvement in the study of Pihtili et al. [26]. In our study, no increase was found in the frequency of OSA in 15 (34.1%) patients with pSS with radiologic pulmonary involvement. There was no relationship between the presence and severity of radiologic involvement and the presence of OSA. These data are the first in the literature; new studies on this subject will be instructive.

Studies show that patients with pSS and controls have similar total sleep times [7, 27, 28]. Gudbjörnsson et al. found that patients with pSS slept significantly less than patients with rheumatoid arthritis and healthy controls [23]. In our study, patients with pSS had similar total sleep times to the controls. This may be because our control group consisted of patients who had undergone PSG for some reason, rather than being completely healthy. New studies are needed on this subject.

In a study, it was reported that in patients with pSS, the time to fall asleep was longer than for controls [7, 23]. In our study, the time to falling asleep in patients with pSS was similar to that of the control group. Gudbjörnsson et al. and de Goodchild et al. reported that sleep efficiency was significantly lower in the pSS group than in the control group [23, 27]. In our study, patients with pSS were similar to the control group in terms of sleep efficiency.

Gudbjörnsson et al. found that the duration of stage 1 sleep in patients with pSS was long, and the duration of other stages was similar to that of controls [23]. Usmani et al. found no difference between a control group and a pSS group in terms of sleep times [7]. Looking at other ILDs, it is reported that REM and stage 3 sleep percentage decreased in patients with IPF, scleroderma, and sarcoidosis [26]. Prado et al. reported that stage 3 sleep duration increased and REM sleep percentage decreased in patients with scleroderma [29]. In our study, the percentage of REM sleep time of patients with pSS was lower than in the control group, whereas other sleep times were found to be similar to the control group. It was also found that the maximum apnea duration, maximum hypopnea duration, and snoring index were decreased in the pSS group compared with the control group. The short duration of maximum apnea and hypopnea in patients with pSS may explain the witnessed apnea and snoring symptoms and the significantly lower snoring index compared with controls. Short apnea and hypopneas may not cause snoring. The most striking points of sleep architecture in patients with pSS were shortened REM sleep duration, shortened maximum apnea, and hypopnea duration. In addition, total sleep time, time to fall asleep, and sleep efficiency are also important components of sleep architecture. These parameters may be explanatory in the symptoms of fatigue and EDS in pSS, but more studies are still needed on this subject.

In two studies investigating OSA in pSS, the ODI value was not examined [7, 8]. In our study, no difference was found between the pSS and control groups in terms of ODI.

Our study's most important limitation is that the retrospectively created control group does not reflect the healthy population. However, such a control group could not be established due to the ethical and cost problems of performing PSG tests on healthy individuals, the closure of PSG laboratories caused by the SARS-CoV-2 virus pandemic, and the difficulty of finding patients. However, the rate of moderate and severe OSA is high in pSS patients (68% of 37 patients with OSA), similar to the control group. On the other hand, our study's strength is that it is the first study to examine the frequency of OSA in patients with pSS including radiologic findings of lung involvement, spirometry, and DLCO parameters.

To conclude, the frequency of OSA in patients with pSS was 84%, with a decrease in REM%. Although a correlation between symptoms suggestive of OSA and the presence of radiologic lung involvement, spirometry, and DLCO values with OSA could not be demonstrated, we recommend that physicians be alert for the presence of OSA in all patients with pSS and investigate OSA using PSG.

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Author contributions E.K. and S.B. designed the study. E.K. and S.B. wrote the main manuscript text. E.K, S.B., S.U., and B.M. collected the data and reviewed the manuscript. B.M. analyzed the data. All authors read and approved the final manuscript.

Data availability The data used to support the findings of this study are available from the corresponding author upon request.

Declarations

Ethics approval Ethics committee approval for the study was obtained from the Ethics Committee of Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty (IRB No. 604.01.01–45638). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and were conducted according to the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.
Informed consent Written informed consent was obtained from all individual participants included in the study.

Conflicts of interest The authors declare that they have no conflict of interest.

Disclosure All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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