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Sleep disorders and other medical and socio-demographic factors in systemic scleroderma

Leyla Bagheri (1), Hoda Kavosi (2), Nasim Shokouhi (3), Shila Aghayani (4), Khosro Sadeghniiat Haghighi (5), Seyed Reza Najafizadeh (6)

(1) Department of Internal Medicine, Shahid Modarres Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran; (2) Rheumatology Research Center, Tehran University of Medical Sciences, Tehran, Iran; (3) Yas Hospital, Tehran University of Medical Sciences, Tehran, Iran; (4) Department of Rheumatology, Imam Khomeini Hospital Complex, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran; (5) Sleep Breathing Disorders Research Center, Tehran University of Medical Sciences, Tehran, Iran; (6) Rheumatology Research Center, Imam Khomeini Hospital, Tehran University of Medical Sciences, Tehran, Iran.

Abstract

We aimed to investigate sleep disorders in patients with systemic scleroderma (SSc) and its relationship with socio-demographic and medical factors and to provide a suitable solution to better control the disease and improve the quality of life in these patients. This cross-sectional study evaluated SSc patients seen at a rheumatology clinic from September 1, 2022, through April 1, 2023.The patients were examined by the main investigator of the project and entered the study after taking the medical history and meeting the criteria of ACR 2013 Classification Criteria. Pittsburgh Sleep Quality Index (PSQI), Insomnia Severity Index (ISI), Epworth Sleepiness Scale (ESS) and STOP-Bang Questionnaire were employed to investigate sleep disorders. A total of 103 patients were included in the study. The average age of the patients was 48.42 ± 12.4 years. PSQI showed lower quality of sleep scores among SSc (68% of patients), which was significantly related to the degree of skin stiffness in patients, telangiectasia, interstitial lung disease (ILD) in computed tomography (CT) scan, patient age, duration of the disease, and pulmonary artery pressure (PAP). STOP-Bang Questionnaire revealed that obstructive sleep apnea (OSA) was significantly associated with telangiectasia, ILD, patient age, disease onset age, disease duration, body mass index and PAP. Insomnia had a statistically significant relationship with telangiectasia, ILD and patient age. Drowsiness during daily activities was not significantly related to any of the individual variables and disease-related variables. Sleep disorders are common in patients with systemic scleroderma. Telangiectasia, ILD and patient age were related to all sleep quality disorders and respiratory apnea and insomnia. Furthermore, the amount of skin involvement significantly causes disturbances in the quality of sleep of patients, where in the group with diffuse skin stiffness, 80% of patients exhibited disturbances in the quality of sleep. Therefore, paying attention to sleep health can be an effective factor in improving the quality of life of patients with SSc.

Key Words: systemic scleroderma; sleep disorders; telangiectasia; quality of life.

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Scleroderma or systemic sclerosis (SSc) is a condition accompanied by restricted dermatological condition (e.g., abnormal skin thickening, and systemic involvement of internal organs (pulmonary hypertension (PH), interstitial lung disease (ILD), esophageal motility disorders, oropharyngeal dysfunction, etc.). This disease is characterized by immune dysfunction, vasculopathy and excessive collagen fibrosis.[1-6] The wide array of cardiopulmonary phenotypes in SSc has raised the hypothesis that scleroderma may be linked to sleep-disordered breathing (SDB).[5] This immune dysfunction has been previously described to be associated with difficulty sleeping and increased risk for sleep.[4,8-10] Few studies are available regarding potential factors associated with sleep problems in SSc. The findings of

existing studies have shown its correlation with esophageal dysmotility, dyspnea and restless leg syndrome, and fatigue as well as pain, the severity of reflux symptoms, worsening dyspnea, Gastrointestinal symptoms, and pruritus.[8,9,11-13]
Therefore, the current study aimed at assessing the association of sleep disturbance with socio-demographic and medical factors among patients with SSc. Understanding the factors potentially related to sleep problems in SSc is important to guide clinicians in the management of patients and improving overall quality of life and well-being.

Materials and Methods

Patients

We cross-sectionally evaluated patients seen at the rheumatology clinic, two tertiary referral centers of Iran, from September 1, 2022, through April 1, 2023, for scleroderma evaluation. Sufficient sample size was determined as 41 using G-power tool, considering a Type I error as low as 0.05, a power as high as 0.95, an effect size of 0.2 and a P of 0.7.
All experimental procedures were ethically approved by the ethics board of Vice-Chancellor of Research and Technology of Tehran University of Medical Sciences Research. All methods in our study were carried out in accordance with the Declaration of Helsinki. Informed consent was obtained from all subjects
The inclusion criteria were: SSc confirmed by 2 rheumatology specialists based on American College of Rheumatology (ACR) 2013 Classification criteria, Age 18 and above, and the ability to fill out questionnaires.
Exclusion criteria included: Psychological disorders such as major depression and psychosis (based on the patient's history and medical records), Primary cognitive impairment, Pregnancy, History of using sleeping pills, BMI > 35, and Patient's lack of consent to participate in the research. we excluded patients who received more or equal 5 milligrams of prednisolone.

Data Collection

Demographic data of the patients (age, gender, BMI, disease duration) and data related to the major symptoms and organ involvement of the disease including Raynaud's phenomenon, digital ulcers, skin stiffness, telangiectasia, ILD based on chest CT scan, forced vital capacity(FVC) percent predicted in spirometry, left ventricle ejection fraction percentage (EF%) by echocardiography ,pulmonary arterial pressure(PAP) measurement by right heart catheterization, gastroesophageal reflux, arthritis and/or arthralgia and renal crisis were collected by prepared questionnaires based on interview and registered patients files. Then the information was matched with the patient's medical records. In order to investigate sleep disorders in these patients, The Pittsburgh Sleep Quality Index (PSQI), Insomnia Severity Index (ISI), Epworth Sleepiness Scale (ESS) and STOP-Bang Questionnaire are used in the present study.
PSQI questionnaire was used to check sleep quality during the last month. This questionnaire contains 8 items, based on which a score higher than 5 indicates poor sleep quality. STOP-Bang questionnaire was employed to assess respiratory apnea and based on 5 questions, patients were divided into two groups with respiratory apnea and without it. The ESS questionnaire was used to check the amount of daily sleepiness, which includes 8 questions and is divided based on whether the patient falls asleep or not in different situations. The ISI

Table 1. *Frequency of sleep disorders based on standard questionnaires in patients with systemic scleroderma participating in the study.*

Variable	Condition	Frequency in systemic scleroderma patients	
		Percent (%)	**Number**
Sleep quality based on the Pittsburgh Questionnaire (PSQI)	≥ 5 is not a problem	(32)	33
	5 < Disturbance in sleep quality	(68)	70
Insomnia(ISI)	7-0 lack of sleep	(46.6)	48
	14-8 mild insomnia	(24.3)	25
	15-21 moderate insomnia	(25.2)	26
	22-28 severe insomnia	(3.9)	4
sleepiness (ESS)	≥ 10 without drowsiness	(93.2)	96
	< 10 severe drowsiness	(6.8)	7
Respiratory disorder and apnea while sleeping (Stop Bang)	<3 No risk of breathing apnea	(68.9)	71
	≥3 At risk of breathing apnea	(31.1)	32

Table 2. *The results of the relationship between sleep quality and quantitative variables in patients with SSc.*

Two-sample independent t-test	Disturbance in sleep quality	No disturbance in sleep quality	P-value
Age of the patient	51.17 ± 11.32	42.58 ± 12.75	0.001
Age of disease onset	38.37 ± 10.51	34.98 ± 12.46	0.154
FVC% predicted	70.86 ± 15.39	76.82 ± 16.34	0.075
Mann-Whitney test			
duration of illness	12.0 (6.0, 18.0)	6.0 (4.0, 10.0)	0.001
BMI	23.5 (20.6, 29.0)	21.08 (20.3, 25.2)	0.101
EF %	55.0 (55.0, 55.0)	55.0 (55.0, 55.0)	0.524
PAP mmHg <<<<	30.0 (27.0, 37.3)	27.08 (20.0, 30.0)	0.004

questionnaire also examines insomnia, which includes 7 questions, and based on scoring, patients are divided into no insomnia (scale 0-7), mild insomnia (scale14-8), moderate insomnia (scale15-21) and severe insomnia (scale 22-28). The datasets used or analyzed during the current study are available from the corresponding author on reasonable request.

Statistical analysis

We analyzed data with IBM SPSS version 20.0 (Chicago, IL, USA). The extracted information is analyzed with independent t test, chi square and regression analysis. Independent two-sample t-tests and Mann-Whitney were used for normally and no normally distributed variables. The level of statistical significance was set at $p<0.05$.

Results

Descriptive findings

Demographic information is shown in Table 1. Among 103 patients participating in the research, 86% of the patients were women and 14% of the patients were men. Based on the body mass index (BMI), 52% of the patients were within the normal weight range. This is while 35% of the patients were overweight and 13% of them were underweight. As shown in Table 1, the most common co-morbidities in SSc patients referring to the clinic were related to Raynaud's phenomenon (99%), skin stiffness (diffuse: 40.8%; limited: 58.3%), (Table 1). Furthermore, gastroesophageal reflux (76.7%), ILD (67%) and arthralgia/arthritis (65%) had a high prevalence among patients. Telangiectasia and digital ulcers had a prevalence of 38.8% and 30.1% among patients, respectively. The renal crisis was not observed in any of the patients referred to the clinic. Inappropriate sleep quality was the most common sleep disorder (68% prevalence) among the studied patients, followed by insomnia, severe insomnia: 3.9%, moderate insomnia: 26%; mild insomnia: 25%). 32% of patients were at risk of sleep apnea and 7% of patients had severe sleepiness during daily activities (Table 1).

Analytical findings

Fisher's and chi-square tests were employed to investigate the relationship between sleep quality and qualitative findings based on the PSQI questionnaire. Disturbance in sleep quality was significantly related to skin stiffness, telangiectasia and ILD, ($p<0.5$). The results of logistic regression showed that the chance of sleep quality disorder in people with ILD CT complication is 4.97 times higher than in people without this complication. The chance of sleep quality disorder in people with diffuse skin stiffness was 2.83 times higher than in people with limited skin stiffness.

The chance of having a disorder in the quality of sleep in those with telangiectasia was 7.67 times that of patients who did not have this complication (Supplementary materials Table 1).

In order to investigate the relationship between sleep quality and patients' condition based on the PSQI questionnaire, for quantitative findings, independent two-sample t-tests and Mann-Whitney tests were used for normal and non-normal data, respectively. Disturbance in sleep quality was significantly related to patients' age, duration of disease and pulmonary artery pressure (PAP) ($p<0.5$) (Table 2). Based on the Stop-Bang questionaire, the level of sleep apnea was found to be significantly associated with telangiectasia and ILD (Supplementary materials: Table 2).

The results of logistic regression showed that the chance of having sleep apnea in individuals with ILD CT complications was found to be 2.82 times higher than those without complications. The chance of having sleep apnea in people with telangiectasia was 3.47 times higher than those without this complication.

Table 3. *The results of the relationship between sleep apnea and quantitative variables in patients with SSc.*

Two-sample independent t-test	**At risk of sleep apnea**	**No risk of apnea**	**p-value**
Age of the patient	57.41 ± 9.42	44.37 ± 11.46	<.001
Age of disease onset	42.63 ± 9.61	34.88 ± 11.12	0.001
FVC % predicted	70.91 ± 16.43	73.61 ± 15.66	0.427
Mann-Whitney test			
duration of illness	13.0 (7.3, 21.8)	8.0 (4.0, 13.0)	0.002
BMI	24.5 (21.0, 31.9)	21.9 (20.3, 25.8)	0.013
EF %	55.0 (51.3, 55.0)	55.0 (55.0, 55.0)	0.683
PAP mmHg	31.5 (25.8, 39.5)	28.0 (25.0, 32.0)	0.024

Table 4. *The results of the relationship between sleepiness during daily activities and the quantitative variables.*

Two-sample independent t-test			
	With sleepiness	No sleepiness	p-value
Patient age	53.71 ± 11.10	48.03 ± 12.46	0.244
FVC% predicted	74.00 ± 15.71	72.68 ± 15.96	0.833
Mann-Whitney test			
	with sleepiness	No sleepiness	P-value
Age of disease onset	45.0 (40, 49.0)	34.0 (28.0, 46.5)	0.095
duration of illness	6.0 (5, 18.0)	10.0 (5.0, 16.0)	0.670
BMI	28.7 (21, 35.5)	22.2 (20.4, 26.5)	0.086
EF %	55.0 (50, 55.0)	55.0 (55.0, 55.0)	0.662
PAP(mmHg)	30.0 (28, 37.0)	29.0 (25.0, 35.0)	0.674

In order to investigate the association of sleep apnea with the condition of patients based on the Stop-Bang questionnaire, sleep apnea was significantly related to the age of the patients, the age of onset of the disease, the duration of the disease, BMI and PAP (Table 3).

Based on the ESS questionnaire, no significant relationship was found between sleepiness and any of the investigated variables in patients as revealed by Fisher's and chi-square tests (Supplementary materials: Table 3).

Based on the ESS questionnaire, no significant relationship was found between sleepiness and any of the investigated variables as revealed by independent two-sample t-tests and Mann-Whitney (Table 4).

Based on the ISI questionnaire and qualitative findings, a significant relationship was found between insomnia and telangiectasia and ILD (Supplementary materials: Table 4).

The one-way analysis of variance (ANOVA) showed that insomnia has a significant relationship only with the age of the patients (Table 5).

Post hoc Tukey test demonstrated that the average age of the normal insomnia group was significantly different from the subclinical insomnia and moderate insomnia groups ($p<.05$). As a matter of fact, the average age of individuals in the group with normal insomnia was 10.3

Table 5. *The results of ANOVA test to investigate the relationship between different groups of insomnia and quantitative parametric variables*

	Normal	Subclinical insomnia	Moderate insomnia	severe insomnia	p-value
Age of the patient	43.19 ± 12.02	53.56 ± 9.84	52.31 ± 12.16	53.75 ± 11.62	0.001
Age of disease onset	35.36 ± 11.13	37.96 ± 10.80	39.19 ± 10.93	43.75 ± 16.15	0.314
BMI	23.29 ± 4.36	23.46 ± 5.23	24.99 ± 6.39	27.88 ± 4.89	0.229
FVC % (predicted)	75.25 ± 15.17	67.60 ± 17.39	72.85 ± 16.08	74.75 ± 7.63	0.276

Table 6. *The results of the Kruskal-Wallis test regarding the relationship of different groups of insomnia with quantitative non-parametric variables.*

	Normal	Subclinical insomnia	Moderate insomnia	severe insomnia	P-value
Disease duration	6.0 (3.3, 10.0)	16.0 (7.5, 22.0)	13.0 (6.8, 17.3)	9.0 (4.3, 16.8)	<.001
EF %	55.0 (55.0, 55.0)	55.0 (55.0, 55.0)	55.0 (50.0, 55.0)	52.5 (46.3, 55.0)	0.036
PAP mmHg	27.0 (21.3, 30.0)	30.0 (27.0, 33.5)	36.5 (26.5, 40.3)	38.0 (30.5, 40.3)	0.001

Table 7. *Dunn's test.*

	Dunn's multiple comparisons test	Mean rank diff.	P-value
Disease duration	Normal vs subclinical insomnia	-30.0	<.001
	Normal vs moderate insomnia	-24.0	0.006
	Normal vs severe insomnia	-11.1	>.999
	Subclinical insomnia VS moderate insomnia	6.0	>.999
	Subclinical insomnia VS severe insomnia	18.8	>.999
	Moderate insomnia vs severe insomnia	12.9	>.999
EF %	Normal vs subclinical insomnia	-6.0	0.342
	Normal vs moderate insomnia	11.2	0.071
	Normal vs severe insomnia	22.0	0.098
	Subclinical insomnia VS moderate insomnia	17.2	0.016
	Subclinical insomnia VS severe insomnia	28.0	0.042
	Moderate insomnia vs severe insomnia	10.8	0.432
PAP mmHg	Normal vs subclinical insomnia	-14.1	0.056
	Normal vs moderate insomnia	-26	<.001
	Normal vs severe insomnia	-35.9	0.021
	Subclinical insomnia VS moderate insomnia	-11.9	0.154
	Subclinical insomnia VS severe insomnia	-21.8	0.174
	Moderate insomnia vs severe insomnia	-9.9	0.536

years lower compared to the group with subclinical insomnia. In addition, the average age difference between the normal group and the insomnia group was 9.12 years.

Due to the non-normality of the data in the insomnia groups, the non-parametric Kruskal-Wallis test was used, and the results showed that the studied groups have statistically significant differences in terms of the duration of the disease and the percentage of EF and PAP (Table 6). Dunn's test was used for pairwise comparisons using GraphPad Prism (Table 7).

Discussion

The present study was conducted with the aim of investigating sleep disorders and their relationship with socio-demographic and medical factors in patients with SSc referred to the two tertiary referral rheumatology clinics. In the current study, variables of individual characteristics such as gender of patients, age of patients, and body mass index (BMI) as well as characteristics of the disease including skin stiffness type, age of disease onset and duration of disease, telangiectasia, ILD and other organ involvement were separately analyzed for their relationship with various common types of sleep disorders. The results of the present study demonstrated that patients with SSc suffer from many sleep disorders. Our findings demonstrated a statistically significant relationship between skin stiffness, telangiectasia, ILD observation in CT scan, patient age, duration of illness and pulmonary artery pressure with sleep quality ($p<0.05$). Furthermore, patients who had lower pulmonary artery pressure had better sleep quality, less risk of sleep apnea, and less insomnia. In other words, the majority of patients with blood pressure higher than 27 mmHg suffered from one of the types of sleep disorders. It was also found that the presence of gastroesophageal reflux, forced vital capacity (FVC) percent predicted measures and having arthritis or arthralgia were not predictors of poor sleep. SBD increases with increasing age, likely owing to the physiological and physical changes. Additionally, increased comorbidity and its subsequent polypharmacy are linked to SDB with increasing age.[14] Nokes et al. (2019) reported that the only predictive variables for abnormal oximetry were age as revealed by regression analysis, which is considered to be associated with an increased risk of SDB, regardless of the presence of underlying lung disease.[5] Minic et al. (2014) revealed that older age and increased Epworth Sleepiness Scale were linked to an increased risk of SDB.[15] Obstructive sleep apnea is associated with an increased risk of pulmonary hypertension regardless of the presence of interstitial lung disease, so detection and treatment of sleep apnea in SSc patients is an important measure to prevent or postpone pulmonary hypertension and help to decrease morbidity and mortality in this group.[19] SSc has been described to be linked to lung complications including ILD, pulmonary hypertension, restrictive-ventilatory limitation and fibrosis associated with anatomic changes in the upper airways,[5] affecting sleep quality and sleep breathing movements. In clinical studies, it is also believed that SSc patients with polysomnography findings are at increased risk of sleep disorders. Prado et al. (2002) evaluated sleep disorders in SSc patients and found that SSc patients had decreased sleep efficiency, rapid-eye movement sleep, increased arousal index and slow-wave sleep, but not sleep apnea seemed to have an increased risk for sleep-disordered breathing in SSc.[10] This immune dysfunction has been previously described to be associated with difficulty sleeping and increased risk for sleep disturbance.[7-10]

Sleep disturbances have been found to be related to worsening dyspnea, depressed mood and severity of reflux symptoms in SSc patients.[9] Another study by Milette et al. (2013) reported that sleep disturbance in SSc was correlated with gastrointestinal symptoms, pain and pruritus.[7] Researchers have also shown that lower quality of sleep was found to be linked to pain, fatigue, depressive symptoms, and functional status among SSc patients.[16] In the same context, it has been shown that higher depression, fatigue and pain scores in patients with SSc were associated with functional disability.[17,18] Poor sleep quality not only can be associated with a functional disability but also is an important problem in childbearing women which can related to the incidence of diabetes during pregnancy.[20] The strong point of our study is the assessment of one the most important missed compliant of the SSc patients by nonaggressive and simple validated methods like questionnaires, of course, there are limitations to our study. it's more exact to do other procedures like polysomnography or measure inflammatory and fibrotic serum biomarkers in future studies. the impact of drugs like steroids and substances or smoking and alcohol consumption could be evaluated in other studies in the future.

In conclusion, it was found that low quality of sleep is a very common symptom in patients with SSc. Interestingly, the presence of gastroesophageal reflux, forced vital capacity (FVC) percent predicted measures and having arthritis or arthralgia were not predictors of poor sleep.

Our findings revealed a statistically significant relationship between skin stiffness, telangiectasia, ILD observation in CT scan, patient age, duration of illness and pulmonary artery pressure values with sleep quality. Sleep disorders in patients with SSc occur due to multifactorial origin and multidirectional disease-related variables such as degree of skin stiffness and respiratory involvement.

List of acronyms

ACR- American College of Rheumatology
BMI- body mass index
ESS -Epworth Sleepiness Scale
FVC- forced vital capacity
ILD- interstitial lung disease
ISI -Insomnia Severity Index
PH- pulmonary hypertension
PSQI -Pittsburgh Sleep Quality Index
SDB- sleep-disordered breathing
SSc -systemic scleroderma

Contributions of Authors

Study conception, design, methodology, data collection, formal analysis, writing original draft, review and editing done by LB, HK, SA, KSH and SRN. All authors read and approved the final edited manuscript.

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Conflict of Interest

The authors declare they have no financial, personal, or other conflicts of interest.

Ethical Publication Statement

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

Corresponding Author

Seyed Reza Najafizadeh, Rheumatology Research Center, Imam Khomeini Hospital, Tehran University of Medical Sciences, Tehran, Iran.
ORCID iD: 0000-0002-1860-9450
Email: najafisr@tums.ac.ir

E-mails and ORCID iD of co-authors

Leyla Bagheri : Leylabagheri90@gmail.com
ORCID iD: 0000-0002-7496-5417
Hoda Kavosi: h-kavosi@sina.tums.ac.ir
ORCID iD: 0000-0003-4762-6943
Nasim Shokouhi: shokouhinasim@ymail.com
ORCID iD :0000-0002-4746-8087
Shila Aghayani: shila.aghayani@yahoo.com
ORCID iD: 0000-0001-6002-079X
Khosro Sadeghniiat Haghighi: Sadeghniiat@yahoo.com
ORCID iD: 0000-0001-5242-5113

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Supplementary materials: Table 1. *The results regarding the relationship between sleep quality and patients' condition.*

		Sleep quality		Total	p-value
		No disturbance	disturbance		
Gender	Female	27	62	89	0.368
		81.80%	88.60%	86.40%	
	Male	6	8	14	
		18.20%	11.40%	13.60%	
Weight range	Underweight	5	8	13	0.519
		15.20%	11.40%	12.60%	
	Normal weight	19	35	54	
		57.60%	50.00%	52.40%	
	Overweight	9	27	36	
		27.30%	38.60%	35.00%	
Skin stiffness	does not have	1	0	1	0.017
		3.00%	0.00%	1.00%	
	Limited	24	36	60	
		72.70%	51.40%	58.30%	
	Diffuse	8	34	42	
		24.20%	48.60%	40.80%	
Raynaud's phenomenon	Does not have	0	1	1	1
		0.00%	1.40%	1.00%	
	Has it	33	69	102	
		100.00%	98.60%	99.00%	
Digital ulcers	does not have	23	49	72	0.975
		69.70%	70.00%	69.90%	
	Has it	10	21	31	
		30.30%	30.00%	30.10%	
Telangiectasia	does not have	29	34	63	<.001
		87.90%	48.60%	61.20%	
	Has it	4	36	40	
		12.10%	51.40%	38.80%	
ILD CT	does not have	19	15	34	<.001
		57.60%	21.40%	33.00%	
	Has it	14	55	69	
		42.40%	78.60%	67.00%	
Reflux	does not have	7	17	24	0.731
		21.20%	24.30%	23.30%	
	Has it	26	53	79	
		78.80%	75.70%	76.70%	
Arthralgia and/or arthritis	does not have	14	22	36	0.275
		42.40%	31.40%	35.00%	
	Has it	19	48	67	
		57.60%	68.60%	65.00%	

Supplementary materials: Table 2. *The results of the relationship between the risk of sleep apnea and the condition of patients.*

	category	Groups		Total	p-value
		No risk of sleep apnea	risk of sleep apnea		
Gender	Female	64	25	89	0.124
		90.10%	78.10%	86.40%	
	Man	7	7	14	
		9.90%	21.90%	13.60%	
Weight range	Underweight	10	3	13	0.230
		14.10%	9.40%	12.60%	
	Normal weight	40	14	54	
		56.30%	43.80%	52.40%	
	Overweight	21	15	36	
		29.60%	46.90%	35.00%	
Skin stiffness	does not have	1	0	1	0.174
		1.40%	0.00%	1.00%	
	limited	45	15	60	
		63.40%	46.90%	58.30%	
	diffuse	25	17	42	
		35.20%	53.10%	40.80%	
Raynaud's phenomenon	does not have	0	1	1	0.311
		0.00%	3.10%	1.00%	
	has it	71	31	102	
		100.00%	96.90%	99.00%	
Digital ulcers	does not have	49	23	72	0.820
		69.00%	71.90%	69.90%	
	has it	22	9	31	
		31.00%	28.10%	30.10%	
Telangiectasia	does not have	50	13	63	0.004
		70.40%	40.60%	61.20%	
	has it	21	19	40	
		29.60%	59.40%	38.80%	
ILD CT	does not have	28	6	34	0.039
		39.40%	18.80%	33.00%	
	has it	43	26	69	
		60.60%	81.30%	67.00%	
Reflux	does not have	15	9	24	0.458
		21.10%	28.10%	23.30%	
	has it	56	23	79	
		78.90%	71.90%	76.70%	
Arthralgia and/or arthritis	does not have	29	7	36	0.062
		40.80%	21.90%	35.00%	
	has it	42	25	67	
		59.20%	78.10%	65.00%	

Supplementary materials: Table 3. *The results of the relationship between sleepiness during daily activities and the qualitative variables.*

	Category	Groups		Total	p-value
		No sleepiness	With sleepiness		
Gender	Female	82	7	89	0.589
		85.40%	100.00%	86.40%	
	Man	14	0	14	
		14.60%	0.00%	13.60%	
Weight range	Underweight	13	0	13	0.463
		13.50%	0.00%	12.60%	
	Normal weight	51	3	54	
		53.10%	42.90%	52.40%	
	Overweight	32	4	36	
		33.30%	57.10%	35.00%	
Skin stiffness	does not have	1	0	1	1.000
		1.00%	0.00%	1.00%	
	limited	56	4	60	
		58.30%	57.10%	58.30%	
	diffuse	39	3	42	
		40.60%	42.90%	40.80%	
Raynaud's phenomenon	does not have	1	0	1	1.000
		1.00%	0.00%	1.00%	
	has it	95	7	102	
		99.00%	100.00%	99.00%	
Digital ulcers	does not have	68	4	72	0.427
		70.80%	57.10%	69.90%	
	has it	28	3	31	
		29.20%	42.90%	30.10%	
Telangiectasia	does not have	57	6	63	0.243
		59.40%	85.70%	61.20%	
	has it	39	1	40	
		40.60%	14.30%	38.80%	
ILD CT	does not have	32	2	34	1.000
		33.30%	28.60%	33.00%	
	has it	64	5	69	
		66.70%	71.40%	67.00%	
Reflux	does not have	22	2	24	0.663
		22.90%	28.60%	23.30%	
	has it	74	5	79	
		77.10%	71.40%	76.70%	
Arthralgia and/or arthritis	does not have	35	1	36	0.417
		36.50%	14.30%	35.00%	
	has it	61	6	67	
		63.50%	85.70%	65.00%	

Supplementary materials: Table 4. *The relationship of types of insomnia with patients' condition base on the Fisher's and Chi-2 tests.*

		Normal (n=48)	Subclinical insomnia (n=25)	moderate insomnia (n=26)	severe insomnia (n=4)	Total	p-value
Gender	Female	41	22	22	4	89	1
		85.40%	88.00%	84.60%	100.00%	86.40%	
	Man	7	3	4	0	14	
		14.60%	12.00%	15.40%	0.00%	13.60%	
Weight range	Underweight	7	2	4	0	13	0.717
		14.60%	8.00%	15.40%	0.00%	12.60%	
	Normal weight	26	15	12	1	54	
		54.20%	60.00%	46.20%	25.00%	52.40%	
	Overweight	15	8	10	3	36	
		31.30%	32.00%	38.50%	75.00%	35.00%	
Skin stiffness	does not have	1	0	0	0	1	0.11
		2.10%	0.00%	0.00%	0.00%	1.00%	
	limited	34	11	13	2	60	
		70.80%	44.00%	50.00%	50.00%	58.30%	
	diffuse	13	14	13	2	42	
		27.10%	56.00%	50.00%	50.00%	40.80%	
Raynaud's phenomenon	does not have	0	1	0	0	1	0.28
		0.00%	4.00%	0.00%	0.00%	1.00%	
	has it	48	24	26	4	102	
		100.00%	96.00%	100.00%	100.00%	99.00%	
Digital ulcers	does not have	33	20	15	4	72	0.222
		68.80%	80.00%	57.70%	100.00%	69.90%	
	has it	15	5	11	0	31	
		31.30%	20.00%	42.30%	0.00%	30.10%	
Telangiectasia	does not have	37	13	12	1	63	0.011
		77.10%	52.00%	46.20%	25.00%	61.20%	
	has it	11	12	14	3	40	
		22.90%	48.00%	53.80%	75.00%	38.80%	
ILD CT	does not have	24	3	6	1	34	0.003
		50.00%	12.00%	23.10%	25.00%	33.00%	
	has it	24	22	20	3	69	
		50.00%	88.00%	76.90%	75.00%	67.00%	
Reflux	does not have	10	6	8	0	24	0.649
		20.80%	24.00%	30.80%	0.00%	23.30%	
	has it	38	19	18	4	79	
		79.20%	76.00%	69.20%	100.00%	76.70%	
Arthralgia and/or arthritis	does not have	23	6	6	1	36	0.086
		47.90%	24.00%	23.10%	25.00%	35.00%	
	has it	25	19	20	3	67	
		52.10%	76.00%	76.90%	75.00%	65.00%	