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ORIGINAL ARTICLE

Divergent perspectives: exploring the relationships between St. George's Respiratory Questionnaire and outcome measures in systemic sclerosis–associated interstitial lung disease

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Abstract

Introduction/objectives Controversy exists regarding the concordance of patient-reported outcome measures (PROMs) with other assessment parameters in systemic sclerosis–associated interstitial lung disease (SSc-ILD). This study aims to explore the association between the St. George's Respiratory Questionnaire (SGRQ) and various outcome measures in patients with SSc-ILD within a real-world cross-sectional setting.

Method Patients with SSc-ILD were consecutively recruited from our SSc cohort. Simultaneous administration of SGRQ, scleroderma Health Assessment Questionnaire (sHAQ), respiratory visual analog scale (R-VAS), pulmonary function tests (PFTs), and the 6-min walking test (6-MWT) was conducted. The total extent of lung fibrosis was quantified using high-resolution computed tomography (HRCT) images. Relationships between SGRQ and functional, radiographic, and other patient-reported outcome measures were analyzed.

Results The total SGRQ score demonstrated correlations with forced vital capacity (FVC) and R-VAS ($r=-0.397$, $p=0.016$ and $r=0.418$, $p=0.027$, respectively). Symptom score correlated with ILD-extension ($r=0.430$, $p=0.005$); activity score correlated with FVC and R-VAS ($r=-0.502$, $p=0.002$ and $r=0.395$, $p=0.038$, respectively); impact score correlated with R-VAS ($r=0.386$, $p=0.043$). In patients with fibrosis extent exceeding 20%, total SGRQ score was associated with sHAQ and R-VAS ($r=0.398$, $p=0.049$; $r=0.524$, $p=0.021$, respectively), activity score with R-VAS ($r=0.478$, $p=0.038$), and impact score with 6-MWT-D and R-VAS ($r=-0.489$, $p=0.034$; $r=0.545$, $p=0.016$, respectively). The symptom score and activity score demonstrated optimal performance in identifying patients with interstitial lung disease (ILD) extent exceeding 20% and forced vital capacity (FVC) less than 70% (area under the curve [AUC] 0.799, $p=0.002$, and AUC 0.792, $p=0.03$, respectively).

Conclusions Our study reveals varying degrees of correlation between SGRQ and distinct outcome measures. Given the incomplete alignment of SGRQ with other outcome measures, an integrative approach utilizing existing criteria as complementary tools is recommended.

Key Points

- *Patient-reported outcome measures (PROMs) derive from patients' subjective evaluations of the impact of the disease on their daily activities, social interactions, and psychological well-being.*
- *PROMs frequently serve as outcome measures in randomized controlled trials, yet conflicting findings have emerged in relation to primary outcomes.*
- *This study aims to assess the appropriateness and interrelation of PROMs with both radiological and functional outcome measures, providing insight into the current state of our patients in a real-life context. The investigation delves into the compatibility of these measures with each other.*

Keywords Interstitial lung disease · Patient-reported outcome measure · Systemic sclerosis

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Introduction

Systemic sclerosis (SSc) is a multifaceted autoimmune disorder characterized by autoimmunity, vasculopathy, and fibrosis affecting both the skin and internal organs [1]. Among its various manifestations, interstitial lung disease

(ILD) emerges as a significant and relatively prevalent complication, impacting approximately 80% of patients, with a progressive course observed in 25 to 30% of cases. Unfortunately, SSc currently lacks a definitive cure, and ILD stands as a leading cause of SSc-related mortality [2]. Nevertheless, recent years have witnessed substantial progress in the treatment of systemic sclerosis–related interstitial lung disease (SSc-ILD). Identifying high-risk patients, early detection of ILD, and employing effective monitoring tools are pivotal for discerning individuals who may benefit from therapeutic interventions [3, 4].

In the routine follow-up of SSc-ILD patients, various outcome measures are employed to correlate with disease activity and trajectory. Traditional measures such as computed tomography (CT) scanning, pulmonary function testing (PFTs), and the 6-min walking test (6-MWT) are routinely utilized by physicians to evaluate treatment efficacy. However, there is an increasing recognition of patient-reported outcome measures (PROMs) that delve into patients' perspectives. These measures provide a comprehensive assessment of daily activities, social interactions, and psychological well-being, offering insights into the impact of drug effectiveness and side effects on patients' lives [5, 6]. The St. George's Respiratory Questionnaire (SGRQ), a widely employed PROM, is designed to gauge impaired health and quality of life in lung diseases. It encompasses assessments of disease-related symptoms, physical activities, and the impact of the disease and treatment on daily life [7]. Although initially developed for obstructive pulmonary disease, the SGRQ has found extensive use in evaluating patients with primary respiratory disorders and lung involvement in connective tissue diseases [8, 9] [10–12]. In studies focused on SSc-ILD, PFTs, CT, and the 6-MWT are explicitly designated as primary outcomes, thereby establishing their prominence in clinical practice. Patient-reported outcome measures (PROMs) are also incorporated into SSc-ILD investigations, serving as secondary endpoints. The utilization of PROMs in these studies aims to gather valuable insights into optimizing the measurement of therapeutic efficacy, improving lung function, and impeding or delaying progressive functional deterioration [13–17].

Given the scarcity of studies concurrently integrating functional, radiological, and patient-reported outcomes in real-world datasets and exploring their interrelationships, our study seeks to contribute objective data regarding their applicability in clinical practice. Specifically, we have investigated the association between PROMs reflecting patients' satisfaction/dissatisfaction and both functional and radiological measures in individuals with SSc-ILD. The primary aim is to assess the adequacy of these outcome measures in evaluating the current state of our patients and their compatibility with each other in real-life scenarios.

Methods

Patient selection

This study was designed as a cross-sectional investigation and was carried out at the Kocaeli University Rheumatology Clinic between 2022 and 2023. A total of 84 SSc-ILD patients in our cohort were screened. After excluding the patients who met the exclusion criteria and those who declined to participate in the study, 48 patients were ultimately included in the study. We consecutively enrolled patients with SSc-ILD from our SSc cohort, adhering to the 2013 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) systemic sclerosis classification criteria [18]. We included limited or diffuse cutaneous SSc patients in any stage of the disease without a limitation in disease duration [19]. ILD was defined radiologically by the presence of reticulation, traction bronchiectasis, honeycomb cysts, ground-glass opacities or airspace consolidation, other interstitial lung abnormalities, or any of the recognized patterns of interstitial pneumonias reported in the context of SSc [20].

We excluded individuals with non-fibrotic abnormalities, including severe anemia from any etiology including scleroderma renal crisis (SRC) or comorbidities that might influence and interact with the outcome measures, acute infection, pulmonary edema, pleural effusion, and severe emphysema, as determined by visual assessment based on high-resolution computed tomography (HRCT) images. In cases where doubt arose regarding acute abnormal findings (such as infection), pulmonary involvement was confirmed through supportive findings in subsequent HRCT scans. Additionally, patients with a diagnosis of other respiratory disorders, including asthma or chronic obstructive pulmonary disease, malignancy, and significant pulmonary hypertension defined by prior clinical or echocardiographic evidence of significant right heart failure or the need for parenteral therapy, were also excluded.

We documented the demographic characteristics, as well as clinical and laboratory findings, of the patients. Disease duration was computed as the duration between the onset of the first non-Raynaud symptom and the enrollment date. Recorded variables comprised Raynaud's phenomenon, skin and musculoskeletal involvement, history of pulmonary arterial hypertension (PAH) or renal crisis, and gastrointestinal symptoms (including dysphagia, reflux, early satiety, constipation, and diarrhea). The extent of skin involvement was evaluated utilizing the modified Rodnan skin score (mRSS) [21]. Pulmonary hypertension was defined as a mean pulmonary arterial pressure of ≥ 20 mm Hg, precapillary pulmonary hypertension as pulmonary vascular resistance of ≥ 2 Wood units, and a pulmonary capillary wedge pressure of ≤ 15 mmHg on right-sided heart catheterization

[22, 23]. The renal crisis was characterized as a sudden onset of severe hypertension (systolic blood pressure (BP) ≥ 180 mmHg and/or diastolic BP ≥ 100 mmHg) without an alternative etiology, with or without microangiopathic anemia or a decline in renal function [23]. We included the SSc patients with overlap syndromes, and the overlap syndromes were defined as instances where patients met the classification criteria for one or more connective tissue diseases (CTDs) simultaneously with SSc.

This study complied with the Declaration of Helsinki and was approved by the Kocaeli University School of Medicine Ethics Committee, Kocaeli, Turkey, with project number KOU/GOKAEK 2023/129.

Outcome measures

We enrolled patients with SSc-ILD during routine clinical visits. SGRQ, sHAQ, respiratory VAS (R-VAS), PFTs, and 6-MWT were administered concurrently. Each patient was provided with a thorough explanation of the study's content and objectives. Upon obtaining their consent, participants were then requested to complete the questionnaires (sHAQ, respiratory-VAS and St. George's Respiratory Questionnaire) under the supervision of the investigator (EB) with a brief explanation of the terms which the patients had difficulty in understanding, ensuring strict adherence to the rules of self-administered questionnaires. HRCT scans conducted within the last 3 months prior to inclusion were retrieved from the hospital's electronic picture archiving and communication system (PACS).

Functional outcome measures

Pulmonary function testing (PFTs) Spirometry was performed following the instructions of American Thoracic Society (ATS) and European Respiratory Society recommendations for the standardization of spirometry [24]. From the spirometric measures, forced vital capacity (FVC) and diffusion capacity of the lung for carbon monoxide (DLCO) were used for evaluation.

6-minute walking test (6-MWT) 6-MWT was performed in accordance with the instructions of ATS recommendations [25]. The walking distance, pre-test oxygen saturation, pre-test heart rate, pre-test blood pressure, post-test oxygen saturation, post-test heart rate, and post-test blood pressure were recorded.

Radiological outcome measures

Extent of fibrosis on chest CT An experienced observer (SD) scored the scans independently, blinded to clinical and lung function information, as described by Goh et al. [3]. HRCT images were scored at five levels: (1) the origin of great vessels, (2) main carina, (3) pulmonary venous confluence, (4) halfway between the third and fifth section, (5) immediately above the right hemidiaphragm. The total extent of interstitial lung disease was estimated to be the nearest 5% in each of the five sections, with the global extent of disease on HRCT computed as the mean of the scores.

Patient-reported outcome measures

Scleroderma Health Assessment Questionnaire (sHAQ) The standard disability index of sHAQ is a self-administered questionnaire comprising 20 items divided into eight domains: dressing and grooming, arising, eating, walking, hygiene, reach, grip, and activities. The answers for each question range between without any difficulty (0), with some difficulty (1), with much difficulty (2), and unable to do (3). The highest scores of the questions in each domain are added and then divided by 8 to determine the sHAQ. When the patient needs any devices or the help of somebody for activities in any of the domains, it is automatically scored 2. The Turkish version of the sHAQ has already been validated and adapted [26].

Visual analog scale (VAS) The sHAQ was constructed by the addition of the five following questions related to symptoms: "In the past week, how much have your—Raynaud's phenomenon, digital ulcers, gastrointestinal symptoms, lung symptoms, and overall scleroderma symptoms—interfered with your activity?" The answer is marked on a VAS with a length of 15 cm. The ends of the line are "does not interfere" and "very severe limitations." The final VAS score is calculated by multiplying the value by 0.2. The score ranges from 0 to 3, representing a minimum to maximum limitation, respectively. The value of each VAS score is reported separately [26].

St. George Respiratory Questionnaire (SGRQ) St. George's Respiratory Questionnaire [7] was developed to measure the impact on overall health, daily life, and perceived well-being in patients with respiratory disease. It comprises 76 items under three main domains: symptoms, activity, and impact. The symptom domain relates to items that question the cough, wheezing, and shortness of breath. The activity domain evaluates the physical activities that cause shortness of breath. The impact domain includes work-life challenges, drug side effects, health-related expectations, and challenges in daily life. Each section is individually scored on a scale of 0 (excellent) to 100 (extremely poor) and summed up to a total score, with higher scores representing worse quality of life. The Turkish version of the sHAQ has already been validated and adapted [27].

Statistical analysis

Descriptive statistics for clinical and demographic characteristics of the patients were presented as frequency and percentage (%) for categorical variables and mean with standard deviation (mean ± SD) or median with interquartile range (median [IQR = Q3–Q1]) according to the distribution of the continuous variables.

The Spearman's rank correlation coefficients were used to examine the degree of associations between the functional (FVC, DLCO, 6-MWT), radiographic (extent of the pulmonary fibrosis on chest CT), and patients reported outcome scores (sHAQ, pulmonary VAS, and SGRQ). Correlations less than or equal to 0.29 were considered low; between 0.30 and 0.49, as moderate; and greater than or equal to 0.50, as high [28]. The receiver operating characteristic (ROC) curve was used to evaluate the performance of SGRQ to determine the presence of patients with ILD extent higher than 20% and with FVC lower than 70%. We used the Mann–Whitney *U* test to show how the variables changed between the groups we separated according to the extent of fibrosis in HRCT.

Statistical analyses were performed using the SPSS version 20.0 software package (IBM Inc., Chicago, IL, USA). Two-sided *p* values less than 0.05 were considered statistically significant ($p < 0.05$).

Results

Study population

Forty-eight patients with SSc-ILD, 83.3% ($n = 40$) of which were female with a mean age of 57.8 ± 11.2, were included. The mean disease duration from the onset of RF and non-RF symptom was 12 ± 7.4 and 9.9 ± 4.9 years, respectively. Based on the medication regimen, 6.3% ($n = 3$) of patients were administered conventional synthetic disease-modifying antirheumatic drugs, 20.9% ($n = 10$) were administered azathioprine, and 60.4% ($n = 29$) were administered mycophenolate mofetil. Table 1 describes the patients' demographic data; clinical characteristics; and functional, radiological, and patient-reported outcome measures.

The association of the outcome measures

The relationship between the SGRQ and sHAQ with functional and radiological parameters are shown in Table 2. Total SGRQ score correlated with FVC and R-VAS ($r = -0.397$, $p = 0.016$ and $r = 0.418$, $p = 0.027$, respectively); symptom score correlated with ILD-extension ($r = 0.430$, $p = 0.005$); activity score correlated with FVC and R-VAS ($r = -0.502$, $p = 0.002$ and $r = 0.395$, $p = 0.038$, respectively); impact score correlated with R-VAS ($r = 0.386$, $p = 0.043$).

When we analyzed the interrelationship of variables other than SGRQ, we found that FVC was associated with ILD extent, post-test-SO_2 and R-VAS ($r = -0.422$, $p = 0.007$; $r = 0.431$, $p = 0.016$ and $r = -0.369$, $p = 0.045$, respectively). DLCO correlated with post-test-SO_2 ($r = 0.425$, $p = 0.038$). R-VAS was associated with post-test-SO_2 and HAQ ($r = -0.418$, $p = 0.033$ and $r = 0.444$, $p = 0.010$, respectively) (Table 3).

Total SGRQ score, symptom score, and impact score were higher in the patients with extensive lung fibrosis on HRCT (45.7 ± 17.6 vs 31.3 ± 16.6, $p = 0.017$; 46.1 ± 23.2 vs 22.6 ± 16.5, $p = 0.001$; 37.3 ± 19.7 vs 22.3 ± 14.9, $p = 0.015$, respectively). FVC was lower in these patients than those with less extensive fibrosis on HRCT (73.7 ± 13.8 vs 89.9 ± 19.2, $p = 0.010$) (Table 4). We also investigated the relationship between the SGRQ with the other PROMs, functional and radiological outcomes in patients with a pulmonary fibrosis extension of > 20% in HRCT (Table 5). Total SGRQ score was associated with sHAQ and R-VAS ($r = 0.398$, $p = 0.049$; $r = 0.524$, $p = 0.021$, respectively), activity score with R-VAS ($r = 0.478$, $p = 0.038$), and impact score with 6-MWT-D and R-VAS ($r = -0.489$, $p = 0.034$; $r = 0.545$, $p = 0.016$, respectively).

The results of ROC curve analysis for evaluating the performance of SGRQ to determine the presence of patients with ILD extent higher than 20% revealed fair results for total SGRQ, symptom, and impact scores (AUC 0.726, 0.799, 0.728, and *p* values 0.017, 0.002, 0.016, respectively). However, the result was bad for the activity score, with an AUC of 0.599 and $p = 0.297$. The analysis for evaluating the performance of SGRQ to determine the presence of patients with FVC less than 70% revealed fair results for total SGRQ and activity scores (AUC 0.724, 0.792, and *p* values 0.024, 0.03, respectively). The results were bad for symptom and impact scores (AUC 0.659, 0.617, and *p* values 0.109, 0.235, respectively) (Fig. 1). We selected the symptom score for ILD extent > 20% and activity score for FVC < 70% to determine cutoff scores. A symptom score of 28.21 showed a sensitivity of 77% and specificity of 73%. An impact score of 54 showed a sensitivity of 87% and specificity of 62%.

Discussion

PROMs are designed to capture the positive and negative impact of changes in health conditions as perceived by patients in the context of their daily lives, encompassing efforts to maintain work, social, and family activities. The

Table 1 Demographic data, disease subtypes, SGRQ, SDA, and other findings of the patients

		Frequency (*n*, %)/mean ± SD
Gender (female)		40/48 (83.3%)
Age		57.8 ± 11.2
Disease duration (years)		
	After RF	12 ± 7.4
	After non-RF symptom	9.9 ± 4.9
Disease subtype		
	Limited	18/48 (37.5%)
	Diffuse	28/48 (58.3%)
	Sine scleroderma	2/48 (4.2%)
Smokers (active)		8/48 (16.7%)
Smoking (packs-year)		5.52 ± 12.9
Overlap		4/48 (8.3%)
Pulmonary hypertension		3/48 (6.3%)
Gastrointestinal involvement		28/48 (58.3%)
Digital ulcer		10/48 (20.8%)
Sclerodactyly		45/48 (93.7%)
Calcinosis		5/48 (10.4%)
Telangiectasia		40/48 (83.3%)
ANA		46/48 (95.8%)
Scl-70		32/48 (66.7%)
ACA		4/48 (8.3%)
Total SGRQ score		40.4 ± 18.4
Symptom score		37.5 ± 23.7
Activity score		56.3 ± 24.3
Impact score		31.8 ± 19.3
HAQ		1.06 ± 2.94
R-VAS		0.99 ± 0.86
6MWT-D		372 ± 785
Pre-test-SO_2		96.3 ± 11.7
Post-test-SO_2		93.9 ± 4.9
FVC		79 ± 17.4
DLCO		53.4 ± 15.9
ILD extent		26 ± 12
Capillaroscopy		
	Normal	1/48 (1.2%)
	Early scleroderma pattern	9/48 (10.8%)
	Active scleroderma pattern	15/48 (18%)
	Late scleroderma pattern	10/48 (12%)
	Non-specific changes	5/48 (6%)

RF Raynaud's phenomenon, *ANA* anti-nuclear antibody, *ACA* anti-centromere antibody, *SGRQ* total St. George Score, *HAQ* health assessment questionnaire, *R-VAS* respiratory visual analog scale; *6-MWT-D* 6-min walk test distance, *Pre-test-SO_2* oxygen saturation before the 6MWT, *Post-test-SO_2* oxygen saturation after the 6MWT, *FVC* forced vital capacity, *DLCO* diffusing capacity of the lungs for carbon monoxide, *ILD* interstitial lung disease

significance of patient-reported outcomes is on the rise, and they are increasingly employed as secondary endpoints in trial designs and endpoint designations. Beyond assessing daily activities, these outcomes provide a means to evaluate overall well-being and treatment adherence. However, despite the benefits of certain interventions on lung function outcomes, many studies have not demonstrated a corresponding improvement in the quality of life [29]. Consequently, the incorporation of patient-reported outcomes into routine clinical practice has been limited. Our study seeks to investigate various outcome measures and their immediate relationship with the SGRQ in our patients within a real-life setting.

Our study revealed associations between the SGRQ and various outcomes at different levels. Notably, we observed an association between FVC and both the total SGRQ and the activity score sub-item of SGRQ. However, no such association was found between FVC and the other sub-items, namely symptom and impact scores. FVC stands out as a well-established and widely utilized outcome measure for diagnosing and monitoring ILD patients in both clinical practice and randomized controlled trials [30]. Despite its imperfections, sensitivity to comorbidities, dependence on patient compliance, technician training, and equipment calibration, FVC remains the prevailing conventional measure for assessing the flow-resistive properties of the lung [31]. Patients with SSc-ILD may experience discomfort, particularly during exercise, potentially resulting in elevated scores in the activity sub-item. This increase may indirectly manifest in the total SGRQ score. Patient-reported outcomes primarily serve to longitudinally monitor patients' responses in clinical trials. However, in a substantial proportion of these studies, changes in FVC with treatment do not consistently correlate with improvements in patient-reported outcome measures. For instance, the Scleroderma Lung Study II demonstrated significant improvement with both cyclophosphamide and mycophenolate mofetil treatments at 21 and 24 months, using an inferential joint model. Despite this improvement, a positive significant correlation was observed between the change in FVC and patient-reported scales from baseline to the 24th month [13]. Conversely, the SENSCIS trial did not show a significant difference between the trial arms, and the INBUILD trial demonstrated only marginal changes on the K-BILD questionnaire over the 52-week period [6, 32]. Our study did not identify an association between DLCO and SGRQ scores, aligning with Outcome Measures in Rheumatology (OMERACT) recommendations against using diffusion measurements to assess lung physiology in randomized controlled trials. DLCO's greater variability and less reliable reproducibility, even with laboratory quality control procedures, make it less favorable compared to FVC [33]. Furthermore, the lack of association with DLCO may be influenced by emphysematous changes

Table 2 The relationship between the St. George's Respiratory Questionnaire (SGRQ) and the other PROMs and functional and radiological outcomes

$N=48$	Total SGRQ score		Symptom score		Activity score		Impact score	
	r	*p*	*r*	*p*	*r*	*p*	*r*	*p*
FVC	−0.397	0.016	−0.139	0.419	−0.502	0.002	−0.306	0.070
DLCO	−0.168	0.401	0.013	0.947	−0.363	0.063	−0.154	0.444
ILD extent	0.298	0.058	0.430	0.005	0.160	0.318	0.252	0.112
6MWT-D	−0.233	0.208	0.150	0.422	−0.235	0.203	−0.326	0.073
Pre-test-SO_2	0.075	0.690	0.068	0.718	−0.014	0.939	0.134	0.472
Post-test-SO_2	−0.017	0.930	−0.098	0.600	−0.071	0.704	0.133	0.474
HAQ	0.265	0.103	0.065	0.692	0.220	0.178	0.283	0.081
R-VAS	0.418	0.027	0.309	0.110	0.395	0.038	0.386	0.043

SGRQ total St. George Score, *FVC* forced vital capacity, *DLCO* diffusing capacity of the lungs for carbon monoxide, *ILD* interstitial lung disease, *6-MWT-D* 6-min walk test distance, *Pre-test-SO_2* oxygen saturation before the 6MWT, *Post-test-SO_2* oxygen saturation after the 6MWT, *HAQ* health assessment questionnaire, *R-VAS* respiratory visual analog scale

Table 3 The interrelationship of variables other than St. George's Respiratory Questionnaire (SGRQ)

		FVC	DLCO	ILD extent	6MWT-D	Pre-test-SO_2	Post-test-SO_2	HAQ	R-VAS
FVC	*r*								
	p								
DLCO	*r*	0.305							
	p	0.101							
ILD extent	*r*	−0.422	−0.064	1.000					
	p	0.007	0.737						
6MWT-D	*r*	−0.036	0.024	0.073	1.000				
	p	0.847	0.913	0.665					
Pre-test-SO_2	*r*	0.154	0.347	−0.085	−0.015	1.000			
	p	0.410	0.096	0.612	0.927				
Post-test-SO_2	*r*	0.431	0.425	−0.291	−0.152	0.283	1.000		
	p	0.016	0.038	0.076	0.363	0.085			
HAQ	*r*	−0.155	−0.125	0.072	0.056	0.240	−0.107	1.000	
	p	0.352	0.512	0.634	0.746	0.159	0.535		
R-VAS	*r*	−0.369	0.067	0.203	−0.339	−0.021	−0.418	0.444	1.000
	p	0.045	0.746	0.257	0.091	0.919	0.033	0.010	

SGRQ total St. George Score, *FVC* forced vital capacity, *DLCO* diffusing capacity of the lungs for carbon monoxide, *ILD* interstitial lung disease, *6-MWT-D* 6-min walk test distance, *Pre-test-SO_2* oxygen saturation before the 6MWT, *Post-test-SO_2* oxygen saturation after the 6MWT, *HAQ* health assessment questionnaire, *R-VAS* respiratory visual analog scale

due to tobacco use or pulmonary hypertension on the test results [30].

Our study did not establish a significant relationship between the sHAQ and the SGRQ, except for the respiratory visual analog scale (R-VAS) score. This observation might be attributed to the lower weighting of questions related to strenuous activities in sHAQ, which many patients find challenging to perform. Consequently, the challenges arising from respiratory difficulties may be overshadowed by the prominence of other relatively simpler tasks [26]. In contrast, the R-VAS, inquiring about the extent to which respiratory system-related complaints interfered with daily activities over the past week, featured a question closely aligned with the total SGRQ and its sub-items such as activity and impact scores. This association persisted even when analyzing the data of patients with lung fibrosis extent exceeding 20%, with a marginal association observed for sHAQ. These findings underscore that R-VAS serves as a PROM that is not only easy to implement but also provides information consistent with the SGRQ and its sub-items. This supports the broader adoption of R-VAS in SSc-ILD patients, offering a time-efficient approach while yielding valuable and meaningful data.

Our study did not reveal a significant relationship between the 6-MWT and the SGRQ, except for a correlation with the impact score in patients with a prevalence of lung

Table 4 The distribution of PROMs and functional and radiological outcomes in patients with fibrosis prevalence below and above 20% on HRCT

	ILD extent on HRCT		*p*
	< %20	≥ %20	
Total SGRQ score	31.3 ± 16.6	45.7 ± 17.6	0.017
Symptom score	22.6 ± 16.5	46.1 ± 23.2	0.001
Activity score	50.3 ± 29.5	59.8 ± 20.5	0.301
Impact score	22.3 ± 14.9	37.3 ± 19.7	0.015
FVC	89.9 ± 19.2	73.7 ± 13.8	0.010
DLCO	53.4 ± 20.8	52.4 ± 14.3	0.872
ILD extent	12.5 ± 5.14	32.8 ± 7.86	< 0.001
6MWT-D	365 ± 77.5	375 ± 80.4	0.738
Pre-test-SO_2	96.5 ± 1.05	96.3 ± 1.82	0.856
Post-test-SO_2	95.5 ± 2.47	93.1 ± 5.65	0.141
HAQ	1.83 ± 5.08	0.69 ± 0.74	0.543
R-VAS	0.63 ± 0.62	1.14 ± 0.90	0.166

SGRQ total St. George Score, *FVC* forced vital capacity, *DLCO* diffusing capacity of the lungs for carbon monoxide, *ILD* interstitial lung disease, *6-MWT-D* 6-min walk test distance, *Pre-test-SO_2* oxygen saturation before the 6MWT, *Post-test-SO_2* oxygen saturation after the 6MWT, *HAQ* health assessment questionnaire, *R-VAS* respiratory visual analog scale

fibrosis exceeding 20%. In interpreting this result, we strive to maintain consistency with the broader understanding of 6-MWT in SSc patients. The role of this measurement in SSc patients remains uncertain due to inconclusive findings that have failed to establish a definitive relationship between disease status and 6-MWT [34] [35]. Systemic sclerosis is a systemic disorder characterized by various extrapulmonary features, including skin fibrosis, musculoskeletal involvement, heart complications, and anemia. These factors may contribute to significant disability, thereby complicating the interpretation of the 6-MWT [36]. In alignment with the prevailing consensus, we acknowledge the limitations of this test's utility in patients with SSc-ILD and refrain from drawing extensive conclusions based on our supportive yet limited results.

We observed an association between the extent of fibrosis on HRCT scans and symptom scores. In contrast to the post hoc analysis of the SENSCIS trial, where patients with fibrosis exceeding 30% reported significant differences in all SGRQ scores compared to those with fibrosis between 10 and 30%, our study demonstrated this association in only one sub-item of the SGRQ [37]. Unexpectedly, this association disappeared in the analysis of patients with a prevalence of fibrosis exceeding 20%. The extent of fibrosis on HRCT is commonly employed in both clinical research and practice to evaluate disease severity, making this discrepancy somewhat perplexing [38]. There is currently insufficient evidence to determine whether PROMs such as the SGRQ may be scored differently than expected in severely ill SSc-ILD patients. Alternatively, heterogeneity in disease severity may contribute to the conflicting results observed in PROMs. Further research is warranted to elucidate the nuanced relationship between HRCT-quantified fibrosis and patient-reported symptom scores in SSc-ILD patients, especially those with severe disease manifestations.

One of the limitations of our study is the absence of an evaluation of changes in these parameters over time to understand the disease trajectory. Additionally, the small number of patients is acknowledged as another limitation. However, it is crucial to recognize that SSc-ILD is inherently rare, and our findings are based on data from a single center. Despite these limitations, our study sought to explore conflicting results in real-life clinical practice. While PROMs may not consistently reflect disease activity, their correlation with other parameters such as FVC and fibrosis prevalence on HRCT in SSc has not been

Table 5 The relationship between the St. George's Respiratory Questionnaire (SGRQ) and the other PROMs and functional and radiological outcomes in patients with a pulmonary fibrosis extension of > 20% in HRCT

N = 32	Total SGRQ score		Symptom score		Activity score		Impact score	
	r	*p*	*r*	*p*	*r*	*p*	*r*	*p*
FVC	−0.166	0.449	0.172	0.433	−0.400	0.059	−0.060	0.786
DLCO	0.007	0.977	0.228	0.347	−0.221	0.362	−0.047	0.847
ILD extent	−0.009	0.967	0.098	0.634	0.031	0.881	−0.109	0.595
6MWT-D	−0.404	0.086	−0.197	0.420	−0.328	0.170	−0.489	0.034
Pre-test-SO_2	0.096	0.696	0.155	0.527	−0.096	0.691	0.150	0.540
Post-test-SO_2	0.113	0.646	0.366	0.123	−0.019	0.940	0.155	0.527
HAQ	0.398	0.049	−0.016	0.941	0.313	0.128	0.374	0.066
R-VAS	0.524	0.021	0.261	0.280	0.478	0.038	0.545	0.016

SGRQ total St. George Score, *FVC* forced vital capacity, *DLCO* diffusing capacity of the lungs for carbon monoxide, *ILD* interstitial lung disease, *6-MWT-D* 6-min walk test distance, *Pre-test-SO_2* oxygen saturation before the 6MWT, *Post-test-SO_2* oxygen saturation after the 6MWT, *HAQ* health assessment questionnaire, *R-VAS* respiratory visual analog scale

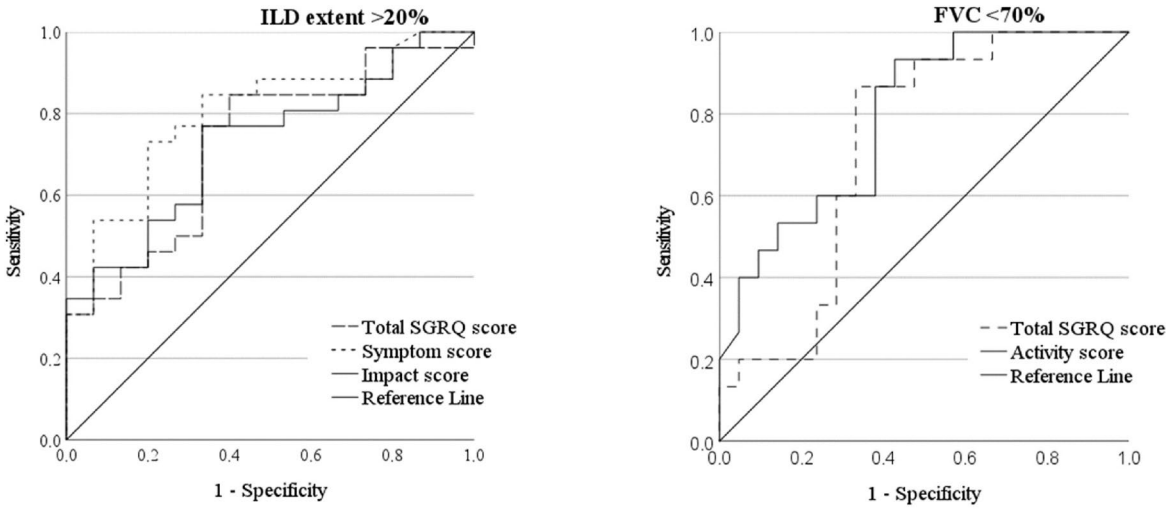

Fig. 1 ROC curve analysis for evaluating the performance of SGRQ and sub-items to determine the presence of patients with ILD extent higher than 20% and FVC less than 70%. Graph shows the test variables with significant results for ROC curve

extensively investigated before. Analyzing their relationship with other parameters at baseline and longitudinally in trials may contribute to elucidating the contradictions observed in the results. The study, despite its limitations, serves as an initial step toward understanding the complex interplay between PROMs and objective clinical measures in SSc-ILD.

Conclusion

In this cross-sectional study, we observed varying degrees of association between the SGRQ and different outcome measures. While the SGRQ did not align entirely with the radiological and functional assessment measures in our patients, it demonstrated compatibility with certain outcomes, particularly FVC, ILD extent, and the R-VAS. In patients with SSc-ILD, various common experiences associated with SSc, such as fatigue, myopathy, physical deconditioning, multifactorial pain, reflux, systemic inflammation, insomnia, and common general comorbidities, could potentially complicate the perception of expected pulmonary symptoms and influence the performance of outcome measures. Based on our findings, utilizing existing outcome measures as complementary to each other appears to be the most prudent approach. Until the deficiencies of existing measures are addressed or new measures are developed, this integrated approach can provide a more nuanced and thorough assessment of systemic sclerosis-related interstitial lung disease.

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Data availability The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Compliance with ethical standards

Disclosures None.

Ethics approval This study adhered to the principles of the Declaration of Helsinki and received approval from the Kocaeli University School of Medicine Ethics Committee in Kocaeli, Turkey, with project number KOU/GOKAEK 2023/129.

Consent to participate Written informed consent was obtained from all patients who participated in this study.

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