SARCOIDOSIS VASCULITIS AND DIFFUSE LUNG DISEASES 2025; 42 (2): 16342 DOI: 10.36141/svdld.v42i2.16342

Mental health burden in progressive pulmonary fibrosis and idiopathic pulmonary fibrosis: Depression and anxiety

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Abstract. *Background and aim:* Progressive pulmonary fibrosis (PPF) is an umbrella term for several interstitial lung diseases, excluding idiopathic pulmonary fibrosis (IPF), characterized by the progressive proliferation of fibrous tissue within the lung interstitium. This study aimed to assess the prevalence of depressive and anxiety symptoms among PPF or IPF patients and their repercussions on health-related quality of life (HRQL). *Methods:* Thirty-seven patients undergoing treatment at the Institute for Pulmonary Diseases of Vojvodina, Serbia were enrolled. The SGRQ assessed quality of life, while the DASS-21 questionnaire evaluated anxiety and depressive symptoms. Sociodemographic and clinical factors were correlated with questionnaire outcomes, and the influence of anxiety and depressive symptoms on quality of life was examined. *Results:* Anxiety symptoms were detected in 56.75% of patients and were more prevalent in patients previously diagnosed with depression and/or anxiety. Depressive symptoms were detected in 45.95% of patients and were more pronounced in the patients with longer duration of disease, and positive history of malignancies. Stress symptoms were linked to lower PaO2 values and were detected in 37.84% of participants. HRQL was moderately to severely decreased and was lower in patients who, in addition to PPF or IPF, also suffered from other respiratory diseases, and was statistically significantly associated with lower DLCO values. A statistically significant correlation has been proven between the presence of anxiety, depressive, and stress symptoms and HRQL, as measured through the "Symptoms" and "Impact" subscales of the SGRQ. *Conclusions:* Anxiety and depressive symptoms are highly prevalent among PPF and IPF patients, exerting substantial impacts on their quality of life.

Key words: anxiety, depression, quality of life, pulmonary fibrosis, idiopathic pulmonary fibrosis

Introduction

Progressive pulmonary fibrosis (PPF) is marked by extensive fibrous tissue proliferation in the lung interstitium (1). Initially linked to idiopathic pulmonary fibrosis (IPF), PPF now includes various non-IPF interstitial lung diseases (ILDs) with progressive fibrosis, such as idiopathic interstitial pneumonias, fibrotic hypersensitivity pneumonitis, exposure-related

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Accepted: 5 December 2024
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ILDs (asbestosis, silicosis), drug-induced ILDs, autoimmune ILDs, sarcoidosis, and unclassifiable ILDs (1-3). Diagnosis of PPF requires at least two of the following three criteria: worsening of symptoms (dyspnea, persistent cough, fatigue), functional decline (an absolute decline in forced vital capacity (FVC) and diffusion lung capacity for carbon monoxide (DLCO) by at least 5% and 10%, respectively, in the previous year), and radiological progression (increased extent or diameter of traction bronchiectasis or bronchiolectasis, new ground-glass opacities and reticular changes, worsening honeycombing, or lobar volume loss) (3). While novel antifibrotic therapies for IPF (such as nintedanib and pirfenidone) and for other forms of PPF (such as nintedanib) are primarily intended to slow disease progression, they may not improve symptoms and health-related quality of life (HRQL), although emerging insights, such as those from a recent study by He et al. (4), indicate that nintedanib may reduce anxiety and depressive symptoms in IPF patients by improving clinical symptoms, daily activities, and quality of life. Additionally, these conditions present with significant comorbidities impacting survival and HRQL, including psychological disorders (5). Anxiety and depressive symptoms are frequently encountered in IPF patients, with 25-50% of IPF patients experiencing depressive symptoms and up to 60% anxiety symptoms (6,7). Key factors in developing mood disorders include dependence on others for daily activities and self-care, social isolation due to the inability to participate in social events, distancing from family and friends, and the inevitable worsening of primary disease symptoms over time (8). Additionally, inadequate or insufficient information about the nature of the disease long after diagnosis can contribute to anxiety (9). Even though the significance of depression and anxiety in chronic pulmonary conditions, such as chronic obstructive pulmonary disease and asthma, is well established and documented (10), there is still insufficient data on their prevalence and impact on patients with ILDs. Considering this, our study aimed to assess the prevalence and impact of these symptoms in PPF and IPF patients, exploring correlations with quality of life, disease course, and sociodemographic factors.

Methods

The study was conducted as a cross-sectional observational study that included 37 participants – 23 IPF patients and 14 PPF patients, all aged 18 years and older. Data were collected between November 2023 and January 2024 from patients treated at the Institute for Pulmonary Diseases of Vojvodina (IPDV), the reference center for ILDs treatment in the Autonomous Province of Vojvodina, Serbia. As a research instrument, a battery of questionnaires was used, including a questionnaire on patients' sociodemographic characteristics (age, gender, education, monthly income, employment, and marital status), the previously validated Saint George's Respiratory Questionnaire (SGRQ) to assess patients' HRQL, and the Depression, Anxiety and Stress Scale (DASS-21) to evaluate anxiety, depressive, and stress symptoms. The SGRQ is a standardized tool for measuring the frequency and characteristics of respiratory symptoms and assessing the mental well-being of patients with respiratory diseases (11). It enables comparisons of health status between population groups and measures changes in health status during specific therapies. The questionnaire includes 50 questions divided into three sections: "Symptoms" (8 questions) – covering the frequency and intensity of respiratory symptoms (shortness of breath, persistent cough, fatigue); "Activities" (16 questions) – focusing on specific activities that induce shortness of breath (sitting quietly, washing or dressing, moving around the house, climbing stairs, etc.); and "Impact" (25 questions) – addressing social and psychological aspects affected by respiratory difficulties. Results were obtained for each section and as an overall score, ranging from 0 to 100, with a higher score indicating a poorer condition of the participants. The DASS-21 is a standardized psychometric instrument that distinguishes between symptoms of anxiety, depression, and stress (12). It consists of 21 questions, with seven questions each corresponding to anxiety, depressive, and stress symptoms. Each response obtained is valued from 0 to 3 points, where "0" indicates "does not apply to me at all," and "3" indicates "applies to me most of the time." By summing individual responses, the total score categorized the severity of different symptoms as "normal," "mild," "moderate," "severe," or "very severe" (13). In addition to these questionnaires, data were retrieved from the information system of the IPDV, relating to the underlying type of ILD of each participant, time since diagnosis, therapy, and current lung function parameters – FVC, DLCO, and partial pressure of oxygen (PaO2) at rest; we defined hypoxemia as a PaO_2 between 8.0

and 9.5 kPa, whereas chronic hypoxemic respiratory failure was defined as a PaO_2 below 8.0 kPa. Participants' consent to participate in the study was obtained by signing a previously prepared Informed Consent for Participation in the Study. The research was conducted in accordance with the principles of the Helsinki Declaration and approved by the Ethics Committee of IPDV, decision no. 24-VII/1 dated November 24, 2023. Statistical analysis included descriptive statistics and hypothesis testing. Frequencies, percentages, sample mean, and arithmetic mean (M) were used to describe parameters of interest. Standard deviation (SD) was used as a deviation value from the mean. The minimum and maximum values of the sample of numerical variables were also presented. One-way analysis of variance (ANOVA) was used to test differences between parameters. Differences between two modalities of a qualitative variable at a certain numerical value were tested using the t-test for large independent samples. Pearson's correlation coefficient was used to examine the relationship between two numerical variables. Statistical processing and data analysis were performed using the SPSS statistical package (Statistical Package for the Social Science, ver. 25.0), and the significance level of the obtained results was interpreted at the level of $P \leq 0.05$.

Results

Sociodemographic data of participants and general data on primary disease

The study included 37 patients, with an average age of 62.16±10.38 years (ranging from 36 to 80 years). The majority of participants were in the age category of 55 to 80 years. There was a slight predominance of male participants. Most participants had completed secondary education, were retired, had monthly incomes ranging from 30,000 to 60,000 RSD (Serbian dinar, approximately $290-570), and were married. Analysis of smoking status revealed that the majority were former smokers (48.6%), 37.8% were non-smokers, and 13.5% were active smokers. IPF was the most common diagnosis (62.2%), followed by PPF with systemic sclerosis and hypersensitivity pneumonitis. The average disease duration was 1.7 years. The average measured FVC was 75.70% (±21.58%), DLCO 40.68% (±14.61%), and PaO2 9.60 kPa (±1.34). Normal FVC values (>80%) were found in 51.4% of patients. All patients had reduced DLCO values, with severe reduction in 45.9%, moderate reduction in 43.2%, and mild reduction in 10.8%. Chronic hypoxemic respiratory failure was present in 8.1% of patients, hypoxemia in 37.8%, and 54.1% had preserved pulmonary gas exchange. Pharmacological treatment primarily involved antifibrotic drugs, with pirfenidone and nintedanib being equally used. The most commonly used immunosuppressive drug in PPF patients was azathioprine. A detailed analysis of the sociodemographic data and data regarding the primary disease is presented in Table 1.

Comorbidities were present in more than two-thirds of participants (70.3%). The most common comorbidities were cardiovascular diseases (64.9%), respiratory diseases (32.4%), and diabetes mellitus (13.5%). Gastrointestinal diseases were reported by 8.1% of participants, previous venous thromboembolism by 5.4%, and malignancies by 2.7%. Previously diagnosed anxiety and/or depression was present in only four patients (10.8%), while two patients (5.4%) were prescribed with antidepressive drugs, and five patients (13.5%) took anxiolytic drugs.

Average values on the DASS-21 questionnaire and correlations with other variables

Symptoms of depression, anxiety, and stress were measured using the DASS-21 questionnaire. The highest score was on the item "I felt that I was rather touchy" (M = 1.46, SD = 1.14), and the lowest on "I felt scared without any good reason" (M = 0.41, SD = 0.69). Average scores for depressive symptoms were M = 10.70 (±10.34), anxiety M = 10.65 (±8.22), and stress M = 13.41 (±9.36). The overall average score was 34.76±27.92. Depressive symptoms were detected in 45.95% of participants, with 18.92% scoring for moderate depression, 10.81% for mild depression, and 8.11% each for severe and extremely severe depression. Anxiety symptoms were detected in 56.75% of participants, with 5.4% showing mild anxiety, 21.62% moderate, 8.11% severe, and 21.62% extremely severe. Stress symptoms were the least prevalent, found in 37.84% of participants, with 16.22% having moderate and severe stress scores, 5.4% mild stress, and none with extremely severe stress. Statistical tests (Student's t-test and One-Way ANOVA) revealed a significant correlation between higher scores on depressive symptoms and longer disease duration (P = 0.029). The highest

Table 1. Sociodemographic and clinical features of the sample

		Frequency	Percentage
Age categories	36-55 years	7	18.9%
	55-80 years	30	81.1%
Gender	Female	17	45.9%
	Male	20	54.1%
Education	Master's degree/Doctorate	1	2.7%
	Bachelor's/Integrated Academic Studies	3	8.1%
	Primary School	4	10.8%
	Vocational Studies	5	13.5%
	Secondary School	24	64.9%
Employment	Unemployed	5	13.5%
	Employed	9	24.3%
	Retired	23	62.2%
Monthly income	>100.000 RSD	5	13.5%
	<30.000 RSD	7	18.9%
	60.000-100.000 RSD	7	18.9%
	30.000-60.000 RSD	18	48.6%
Marital status	Single	2	5.4%
	Divorced	4	10.8%
	Widower/Widow	7	18.9%
	Married	24	64.9%
Primary pulmonary disease that led to progressive pulmonary fibrosis	SLE	1	2.7%
	UCTD	2	5.4%
	UILD	2	5.4%
	HP	4	10.8%
	SSc	5	13.5%
	IPF	23	62.2%
Antifibrotic therapy	None	2	5.4%
	Pirfenidone	17	45.9%
	Nintedanib	18	48.6%
Immunosuppressive therapy	Methotrexate	1	2.7%
	Oral steroids	2	5.4%
	Azathioprine	3	8.1%
	None	31	83.8%

Abbreviations: IPF – idiopathic pulmonary fibrosis, HP – hypersensitivity pneumonitis, SLE – systemic lupus erythematosus, SSc – systemic sclerosis, UCTD – undifferentiated systemic connective tissue disease, UILD – unclassifiable interstitial lung disease, RSD – Serbian dinar.

level of depressive symptoms was observed in participants with a disease duration of 1-2 years (M = 17.00±13.47), followed by those with over 2 years (M = 8.40±7.86), and those with less than a year (M = 6.60±5.42) (Table 2). No significant correlations were found between mental health dimensions (depression, anxiety, stress) and sociodemographic factors. No significant differences were found in the expression of anxiety, depressive, and stress symptoms among patients with different types of ILDs, or among those using different antifibrotic and immunosuppressive drugs. Smoking status also did not affect the expression of these symptoms. Participants with previously diagnosed depression or anxiety had significantly higher scores on all three sections of the DASS-21 questionnaire compared to those without such diagnoses. Patients with prescribed antidepressive drugs (but not anxiolytic drugs) had significantly higher depression scores on the DASS-21 questionnaire compared to those not on antidepressive drugs (P = 0.043). Detailed results are shown in Table 2. Patient with a previous history of malignancy (with no active malignancy at the time of the study) also had significantly higher depression scores (M = 38.00) compared to those without malignancy (M = 9.94±9.39, P = 0.006). It is important to note that this patient did not have a prior diagnosis of anxiety or depression. However, this finding should

Table 2. Correlation of depression, anxiety, and stress symptoms with PPF duration, previous diagnosis of anxiety and/or depression, and use of anxiolytics and antidepressants

		Depression			Anxiety			Stress		
		M	SD	P	M	SD	P	M	SD	P
PPF/IPF duration (in years)	0 1 2+	6,60 17,00 8,40	5,42 13,47 7,86	0,029*	11,00 12,00 9,33	8,76 8,66 7,88	0,707	13,60 15,00 12,00	9,47 9,63 9,50	0,719
Previously diagnosed anxiety and/or depression	No Yes	9,15 23,50	9,54 8,23	0,007*	9,64 19,00	8,04 4,16	0,029*	12,06 24,50	8,61 8,70	0,010*
Therapy with anxiolytic drugs	No Yes	9,75 16,80	10,02 11,45	0,159	10,19 13,60	8,17 8,88	0,396	12,38 20,00	8,99 9,90	0,090
Therapy with antidepressive drugs	No Yes	9,89 25,00	9,79 12,73	0,043*	10,17 19,00	8,11 7,07	0,142	13,09 19,00	9,37 9,90	0,392

Abbreviations: M – arithmetic mean, SD – standard deviation, P – statistical significance, * – statistically significant, PPF – progressive pulmonary fibrosis, IPF – idiopathic pulmonary fibrosis.

be interpreted cautiously as only one participant had a diagnosed malignancy. The presence of other comorbidities was not significantly associated with the degree of anxiety, depressive, and stress symptoms compared to patients without these comorbidities.

FVC and DLCO values were not significantly associated with differences in anxiety, depressive, and stress symptoms. However, patients with chronic hypoxemic respiratory failure had significantly higher stress levels on the DASS-21 questionnaire (M = 18.00±5.29) compared to those with hypoxemia (M = 8.14±6.35) and those with normal pulmonary gas exchange (M = 16.40±10.11; P = 0.022).

Average values on the SGRQ and correlations with other variables

The overall composite score on the SGRQ measuring quality of life was M = 48.58 (±20.35). The highest scores were on the "Activities" subscale M = 64.67 (±21.94), followed by "Symptoms" M = 45.68 (±20.65), and the lowest on the "Impact" subscale M = 39.95 (±22.41). Statistical analysis showed that sociodemographic variables did not affect the HRQL of patients with PPF or IPF, as measured by the composite score on the SGRQ and its subscales. The same was concluded for variables related to the primary lung disease (diagnosis, disease duration, use of antifibrotic and immunosuppressive therapy). While most comorbidities did not significantly affect HRQL (including previously diagnosed anxiety and/or depression, and use of anxiolytics and antidepressants), there was a significant difference between the presence of other respiratory diseases and lower scores on the "Symptoms" subscale of the SGRQ. Patients with other respiratory diseases had worse scores (M = 35.85 ±14.54) compared to those without (M = 50.40±21.71; P = 0.043). The results of comorbidity impact on quality of life are detailed in Table 3.

Comparison of values obtained on the SGRQ and values of DLCO revealed that severely reduced DLCO was associated with the highest values achieved on the SGRQ (M = 55.99±18.75, P = 0.043), while subjects with moderately reduced DLCO achieved slightly lower values, and those with mildly reduced DLCO achieved the lowest SGRQ values (M = 29.74 ±22.94).

The association between quality of life and depressive and anxiety symptoms

Pearson's correlation coefficient was used to examine whether mental status and quality of life were significantly correlated. Analysis of the results presented in Table 4 revealed that the manifestation of depressive symptoms was in a statistically significant positive correlation with overall quality of life (r = 0.351, P = 0.033) and the "Impact" subscale within the SGRQ (r = 0.345, P = 0.036). The manifestation of anxiety symptoms was in a statistically significant positive correlation with overall quality of life (r = 0.520, P = 0.001), the "Symptoms" (r = 0.531, P = 0.001), and "Impact" (r = 0.560, P = 0.000) subscales, while the manifestation of stress symptoms was in a statistically significant correlation with the "Symptoms" subscale (r = 0.389, P = 0.017).

Table 3. The relationship between SGRQ subscales and the presence of various comorbidities

		SGRQ overall score			SGRQ Symptoms			SGRQ Activity			SGRQ Impact		
		M	SD	P	M	SD	P	M	SD	P	M	SD	P
RD	No	49,76	22,91	0,619	50,40	21,71	0,043*	66,10	23,80	0,575	39,91	25,08	0,991
	Yes	46,13	14,16		35,85	14,54		61,70	18,03		40,01	16,49	
CVD	No	54,49	20,25	0,452	46,89	16,90	0,396	69,76	24,56	0,507	47,88	21,79	0,337
	Yes	46,06	20,56		46,25	22,26		62,84	20,86		36,05	22,60	
MD	No	48,64	20,64	0,923	45,74	20,94	0,916	64,63	22,25	0,945	40,05	22,72	0,867
	Yes	46,60			43,48			66,19			36,17		
DM	No	49,17	20,61	0,665	46,48	20,28	0,559	65,80	22,74	0,437	40,15	22,26	0,890
	Yes	44,84	20,40		40,57	24,77		57,47	15,82		38,63	26,06	
GID	No	47,35	20,40	0,220	44,28	20,71	0,168	63,56	22,48	0,305	38,67	22,07	0,250
	Yes	62,53	16,43		61,56	13,73		77,31	8,08		54,39	25,76	
VTE	No	49,28	20,64	0,393	46,57	20,33	0,280	64,77	22,45	0,912	40,92	22,66	0,273
	Yes	36,44	10,57		30,14	28,23		62,98	13,23		22,85	4,09	
other[a]	No	48,15	20,24	0,822	44,29	20,79	0,479	65,17	20,91	0,811	39,20	22,04	0,728
	Yes	49,93	21,89		50,00	20,80		63,12	26,19		42,25	24,76	

Abbreviations: M – arithmetic mean, SD – standard deviation, P – statistical significance, * - statistically significant, RD – respiratory diseases (other than progressive pulmonary fibrosis), CVD – cardiovascular diseases, MD – malignant diseases, DM – diabetes mellitus, GID – gastrointestinal diseases, VTE – venous thromboembolism, [a] – osteoporosis, psoriasis, rosacea, benign prostate hyperplasia, hepatitis B.

Table 4. Association between quality of life (measured by SQRQ) and participants' mental health (measured by DASS-21)

		DASS-21 Depression	DASS-21 Anxiety	DASS-21 Stress	SGRQ Overall Score	SGRQ Symptoms	SGRQ Activity	SGRQ Impact
DASS-21 Depression	r	1	0.661**	0.555**	0.351*	0.295	0.281	0.345*
	p		0.000	0.000	0.033	0.077	0.092	0.036
DASS-21 Anxiety	r	0.661**	1	0.769**	0.520**	0.531**	0.289	0.560**
	p	0.000		0.000	0.001	0.001	0.082	0.000
DASS-21 Stress	r	0.555**	0.769**	1	0.295	0.389*	0.149	0.302
	p	0.000	0.000		0.077	0.017	0.380	0.069
SGRQ Overall Score	r	0.351*	0.520**	0.295	1	0.755**	0.898**	0.971**
	p	0.033	0.001	0.077		0.000	0.000	0.000
SGRQ Symptoms	r	0.295	0.531**	0.389*	0.755**	1	0.576**	0.678**
	p	0.077	0.001	0.017	0.000		0.000	0.000
SGRQ Activity	r	0.281	0.289	0.149	0.898**	0.576**	1	0.795**
	p	0.092	0.082	0.380	0.000	0.000		0.000
SGRQ Impact	r	0.345*	0.560**	0.302	0.971**	0.678**	0.795**	1
	p	0.036	0.000	0.069	0.000	0.000	0.000	

Abbreviations: r – Pearson's coefficient, P – statistical significance.

Discussion

This study investigated the prevalence of anxiety and depressive symptoms, HRQL, and their correlations within a cohort of ILD patients diagnosed with either PPF or IPF. Results indicated a high prevalence of anxiety and depressive symptoms in our sample, which can be explained by several factors. The chronic and progressive nature of these disorders often leads to severe respiratory disability, necessitating long-term oxygen therapy, which can create a constant sense of uncertainty and fear about the future (5,14). Persistent symptoms like dyspnea, chronic cough, and fatigue significantly impair daily functioning and quality of life (6). While our study did not directly correlate those symptoms with anxiety and depressive symptoms, it is evident that they can limit social engagement and contribute to isolation, increasing the risk of mental health issues (15). The median survival time for IPF patients is typically 3-5 years after diagnosis, which can exacerbate feelings of hopelessness and helplessness (6). Patients are usually forced to abandon their professional roles and hobbies, leading to identity crisis and emotional distress. Frequent medical visits, hospitalizations, and the side effects of medications can heighten anxiety and depressive symptoms. There may also be biological links between chronic lung diseases and mental health disorders, as systemic inflammation, can affect mood regulation (16). Our study found that anxiety and depressive symptoms were more pronounced in patients with longer disease durations, a history of anxiety/depression, comorbid malignancies, and chronic respiratory insufficiency. The observed increase in depressive symptoms, which peaks 1–2 years after diagnosis and subsequently decreases in patients with disease duration over 2 years, may indicate an initial psychological impact of PPF or IPF that lessens over time as patients develop coping mechanisms, resulting in relatively lower depressive symptom scores. As expected, patients with a history of anxiety and/or depression demonstrated a higher prevalence of mood disorder symptoms, even if they were receiving treatment for these conditions. This finding indicates that the current management of psychiatric disorders in these patients may be inadequate. The correlation between a history of malignancy and increased depressive symptoms aligns with research indicating a higher prevalence of mood disorders in cancer patients, even post-treatment (17). Although the DASS-21 is increasingly used in research, comparisons with other studies can be challenging due to varying assessment tools. A Belgian study using the Patient Health Questionnaire

(PHQ-9) and the General Anxiety Disorder Assessment (GAD-2) reported lower prevalence rates for IPF patients (17.6% for anxiety, 16% for depressive symptoms) than ours, with significant decline in the anxiety levels over time (18). In other studies, the prevalence of anxiety and depressive symptoms in IPF patients was somewhat higher – 21.4% for anxiety and 25.9% for depressive symptoms in a Korean study (6), 22.3% for borderline or definite depression in a Japanese study (19), 35% for anxiety and 37% for depression in a United Kingdom study (14), 33.3% for anxiety and 37% for depressive symptoms in a Turkish study (20), while another Turkish study found that over 50% of IPF patients had moderate to severe depression, and 40% had severe anxiety (21). In the study by Rajpoot et al. (22), the total DASS-21 score for patients with ILD was 35.56±22, which is approximately the value obtained in our study (M = 34.76±27.92). Various studies employ different instruments to assess the presence of anxiety and depressive symptoms. However, these questionnaires are designed just to detect these symptoms but are not sufficient as standalone tools for diagnosing these conditions. Another interesting observation is the limited number of studies examining anxiety and depressive symptoms in PPF (non-IPF) patients. This may be attributed to the fact that the term PPF has only recently been adopted. The somewhat higher prevalence rates of anxiety and depressive symptoms observed in our study may be due to the inclusion of PPF patients with systemic connective tissue diseases, who exhibit a higher prevalence of anxiety and depressive symptoms (23), regardless of pulmonary manifestations. On the other hand, the usual interstitial pneumonia (UIP), a radiological and pathohistological pattern often associated with IPF as well as with many different non-IPF fibrotic ILD, has been shown to have a worse prognosis compared to non-UIP patterns, potentially contributing to more pronounced symptoms of anxiety and depression in these patients. However, in our study, there was no statistical difference in experiencing such symptoms among different types of ILD. This is similar to the results from the study by Yalniz et al., where there was no significant difference on the Hamilton Anxiety and Depression Scale (HADS) total scores in IPF and non-IPF patients (24), with similar results obtained from one Korean study (25). The SGRQ revealed a moderate to severe impact of the disease on HRQL, particularly in the 'Activities' section, which is somewhat expected, as these patients experience significant limitations in physical activities due to respiratory symptoms that can severely affect daily life. High 'Symptoms' scores reflect the chronic nature of PPF symptoms like cough and dyspnea, which contribute to psychological distress and reduced physical function. Although 'Impacts' scores were lowest, they still indicate significant effects on social interactions, emotional health, and engagement in enjoyable activities. Kreuter et al. reported average SGRQ values of 45.9±19.7 (20), which does not differ significantly from the scores achieved by our respondents, and the individual questionnaire categories were in the same order as in our study. Swigriss et al. found moderate to strong correlations between the 'Activities' subscale and lung function parameters (FVC, DLCO) and gas analyses, while correlations for 'Symptoms' and 'Impacts' were weaker. FVC was statistically the most significant predictor of condition deterioration in IPF patients (26). Lower DLCO values and the presence of additional respiratory diseases were predictors of poorer HRQL, with patients exhibiting severe DLCO reductions reporting significant respiratory difficulties. These results are expected, as patients with severely reduced DLCO have the most pronounced respiratory difficulties, consequently leading to the development of mood disorders and impairment of HRQL (7). Moreover, the presence of other respiratory diseases, such as chronic obstructive pulmonary disease, asthma, and pulmonary hypertension, can exacerbate functional limitations and symptomatic burden in ILD patients, further lowering HRQL (27,28). Other predictors were shown to be not significantly correlated with HRQL. Matsuda et al. reported that male gender was associated with milder "Symptoms" subscale scores, though not to lower composite SGRQ score (19), while Han et al. found that male gender was associated with a lower degree of dyspnea and a better emotional life, but greater physical activity limitations (29). However, our study did not find statistically significant correlations between gender and SGRQ scores. Glaspole et al. observed that SGRQ scores were 15.67-15.77 points higher in patients with rehospitalization or mortality, and each 1% FVC decline raised the SGRQ score by 0.30, primarily affecting the 'Activity' domain (30). Due to the study design, unfortunately, we cannot compare these data with our results. In our study, we found a correlation between anxiety and depressive

symptoms and lower HRQL. Previous studies in IPF patients from Greece (5), Australia (30) and Japan (19) also found correlation between depressive symptoms and HRQL measured by SGRQ. Another Japanese study by Sokai et al. using the SGRQ-I (a version of the SGRQ adapted for IPF patients) indicated that depressive and anxiety symptoms were key factors affecting HRQL, alongside physiological and functional impairments (31).

Given the persistent association between depressive and anxiety symptoms and reduced HRQL, a systematic approach to mental health assessment and treatment is essential for managing ILD patients effectively. Routine mental health screening should be incorporated into standard care protocols, with questionnaires such as those used in our study, as well some other questionnaires (HADS, PHQ-9, GAD-2), administered periodically by trained healthcare professionals, such as nurses or psychologists, to monitor for early signs of anxiety and depression. For patients who screen positive, a multidisciplinary team that includes pulmonologists, psychiatrists, psychologists, and potentially social workers could offer a range of therapeutic interventions. Evidence-based treatments like cognitive-behavioral therapy, pharmacotherapy, and tailored respiratory rehabilitation programs could be provided, targeting both the psychological and physical challenges. Artificial intelligence (AI) and telemedicine may also hold potential for enhancing the assessment and management of depressive and anxiety symptoms in these patients. For instance, these technologies can enable regular psychological screenings, facilitate virtual cognitive-behavioral therapy sessions, and monitor treatment adherence, all of which could improve access to mental health care for patients with PPF or IPF who may have limited mobility due to respiratory symptoms. Finally, the study we conducted has certain limitations. The greatest limitation undoubtedly pertains to the small number of participants included in the study, which is somewhat understandable given the rarity of the diseases categorized under umbrella term of PPF. Another limitation, to some extent, may also be the study design itself, and the inability to prospectively monitor the presence of anxiety and depressive symptoms in these patients, as well as their quality of life using the questionnaires employed. Although the participants filled out the questionnaires independently, there is always the possibility that they did not truthfully answer a certain number of questions. Further research involving a larger number of participants and longitudinally tracking their condition over a longer period is necessary to determine the potential use of the SGRQ and DASS-21 questionnaire as reliable instruments for predicting disease progression and treatment success.

Conclusions

In this study, we found a high prevalence of depressive and anxiety symptoms among PPF patients, alongside reduced HRQL, with both mood disorders correlating with lower quality of life. These findings suggest several important clinical implications. Integrating regular mental health screening into the management of PPF and IPF patients is essential. Early detection of anxiety and depression can facilitate timely interventions, potentially improving these symptoms and enhancing overall quality of life. A multidisciplinary approach, involving pulmonologists, mental health professionals, and rehabilitation specialists, is crucial for the comprehensive care of ILD patients.

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

Authors' Contribution: JJ, DŽ and MM: Conceptualization; JJ, DŽ, MM and AM: Methodology, Validation; JJ, DŽ and MM: Investigation, Writing – Original Draft Preparation; JJ, DŽ, MM, VD, MI, AM, SPM, TP and SKL: Writing – Review and Editing; JJ, DŽ and MM: Visualization.

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