Patient-reported quality of life in fibrotic interstitial lung disease: novel assessments of self-management ability and affect

To the Editor:

Current medical therapy in the treatment of fibrotic interstitial lung disease (f-ILD) is focused on objective improvement or stabilisation of lung function decline as represented by raw or per cent predicted forced vital capacity (FVC % pred). Patient-reported quality of life (PR-QoL) outcomes, as measured from the viewpoint of how patients assess their own health-related well-being, have not been the primary targets of recent clinical trials. However, it has been reported that lung function (*i.e.* measured FVC % pred) in f-ILD correlates poorly with patient-reported well-being [1]. This study explored the degree to which two previously unassessed PR-QoL outcomes in f-ILD correlate with clinical and functional parameters, and a respiratory-related QoL instrument applied in a novel manner.

Institutional research review board approval was obtained prior to study initiation (Mayo Clinic IRB 17-005475). Patients with f-ILD of all aetiologies (>10% fibrosis as visually assessed on computed tomography (CT) imaging) seen at Mayo Clinic Rochester from January 2019 to February 2020 were prospectively recruited and enrolled after study consent. Demographics, fibrosis type, FVC % pred, per cent predicted diffusion capacity for carbon monoxide (D_{LCO} % pred), symptom duration, and radiological pattern were collected at presentation.

Enrolled participants completed four specific questionnaires. 1) Dyspnoea was assessed with the modified Medical Research Council score (mMRC) [2]. 2) Emotional affect or mood was measured by the positive and negative affect scale (PANAS), a 20-item scale measuring both positive and negative affect with a total positive to negative score ratio of >2.9 suggesting more positive affect (1-week recall period) [3]. 3) Self-management ability was assessed by the Self-Management Ability Score (SMAS-30), with a total score on a 100-point scale calculated as the average of the scores of the six subscales (higher numbers suggest better self-management, no reported recall period) [4]. 4) Respiratory-related QoL was defined by four original domains of the Chronic Respiratory Questionnaire (CRQ) (Dyspnoea, Emotional, Fatigue, and Self-mastery domains), a Physical summary domain (combined dyspnoea and fatigue domains), and Emotional Function domain (combined emotional and mastery domains) [5]. For each CRQ domain, a lower score suggested a greater degree of dysfunction on a 7-point scale with a 2-week recall period.

Baseline demographic, functional, and survey measurements were compared between idiopathic pulmonary fibrosis (IPF) and non-IPF patients. Regression analysis with LASSO was performed to delineate predictors of the CRQ subdomains and two summary CRQ scores. Statistical analysis was completed with SAS 9.0 (SAS Institute Inc., Cary, NC, USA) and two-sided p-values<0.05 were considered statistically significant.

167 patients were enrolled (median age 70 years, (interquartile range (IQR) 65–75 years); 41% female) with older age and greater frequency of usual interstitial pneumonia CT fibrosis pattern found in IPF patients, as presented in table 1. Non-IPF patients included connective tissue disease-related ILD (n=30), fibrotic hypersensitivity pneumonitis (n=34), unclassifiable fibrosis (n=32), occupational or drug-induced

TABLE 1 Baseline characteristics, patient-reported quality of life outcome comparisons, and LASSO predictor models of Chronic Respiratory Questionnaire (CRQ) domains

Parameter	IPF	Non-IPF	p-value[#]
Subjects n	53	114	
Age years	71 (68–76)	68 (61–75)	0.006
Female sex	12 (23%)	56 (49%)	0.001
FVC % pred	71 (61–82)	68 (55–85)	0.642
D_{LCO} % pred	46 (38–59)	50 (39–63)	0.214
Ever-smoker status	29 (55%)	60 (53%)	0.674
UIP radiological pattern on CT	47 (89%)	25 (22%)	<0.0001
Reported symptom duration months	24 (10–53)	18 (8–42)	0.215
6MWT distance m	363 (297–385); (n=22)	347 (268–469); (n=34)	0.687
mMRC dyspnoea scale (0–4)	2 (1–3)	3 (1–3)	0.147
PANAS Positive Score	34 (28–37)	33 (27–38)	0.776
PANAS Negative Score	12 (11–17)	15 (12–20)	0.043
PANAS ratio >2.9	23 (44%)	30 (28%)	0.042
SMAS-30 Taking Initiatives subscore (0–100)	70 (60–84)	68 (56–84)	0.508
SMAS-30 Investment behaviour subscore (0–100)	68 (56–78)	64 (52–80)	0.797
SMAS-30 Self-efficacy subscore (0–100)	92 (84–100)	92 (82–100)	0.539
SMAS-30 Total (0–100)	70 (59–80)	68 (59–80)	0.802
CRQ Dyspnoea	5.8 (4.1–6.6)	5.2 (3.4–6.2)	0.165
CRQ Fatigue	4.5 (3.5–5.3)	4.0 (3.0–5.0)	0.068
CRQ Emotional subscale	5.3 (4.5–6.0)	5.0 (4.1–5.9)	0.104
CRQ Mastery	5.5 (4.5–6.3)	5.3 (4.0–6.3)	0.179
CRQ Emotional Function (1–7)	5 (4.5–6)	5 (4.1–5.9)	0.104
CRQ Physical score	5.3 (3.9–5.7)	4.7 (3.2–5.5)	0.057

Data are presented as median (interquartile range) or n (%), unless otherwise stated. IPF: idiopathic pulmonary fibrosis; FVC: forced vital capacity; D_{LCO}: diffusion capacity for carbon monoxide; UIP: usual interstitial pneumonia; CT: computed tomography; 6MWT: 6-min walk test; mMRC: modified Medical Research Council; PANAS: positive and negative affect survey; SMAS-30: self-management assessment survey 30. [#]: comparison between IPF and non-IPF subjects.

(n=4), other idiopathic interstitial pneumonia (n=6), combined pulmonary fibrosis and emphysema (n=7), and fibrotic sarcoid (n=1). IPF and non-IPF f-ILD subtypes did not differ in terms of pulmonary function (FVC % pred and D_{LCO} % pred), duration of symptoms prior to study enrolment, and scores for the majority of surveyed PR-QoL end-points (table 1). Positive affect, as represented by a PANAS ratio >2.9, was found in a greater number of IPF than non-IPF patients (44% *versus* 28%, p=0.042). FVC % pred was selected in only two of the LASSO CRQ domain predictor models (CRQ Dyspnoea and Physical Summary domains) and accounted for 3–6% of unforced model variances. Investment behaviour assessed by SMAS-30 accounted for a higher degree of variance in the physically-oriented disease scores as highlighted by the Dyspnoea and Physical Summary CRQ scores (R square=0.23 and 0.33, respectively), while mood or affect (PANAS affect ratio) accounted for higher variances in the Emotional and Mastery CRQ domains (R square=0.54 and 0.34, respectively).

Several findings from this prospective cohort study are worth noting. We report for the first time CRQ results in a cross-section of f-ILD patients with a comparison of IPF and non-IPF subtypes. While further validation is needed, our study suggests feasibility in the use of this instrument for measuring individual and combined domains, including fatigue as a relevant patient-reported parameter. Newly assessed self-management ability and mood or affect also appeared to correlate with the respective Physical and Emotional domains of the CRQ. FVC % pred, on the other hand, explained 6% or less of the variance among CRQ LASSO predictor models, consistent with prior knowledge that lung function often does not correlate with PR-QoL outcomes. While similarly challenging in terms of unifying patient-reported and objectively measured disease status, there remains the implication that interventions targeting patient-centred end-points may still be applicable and pursued successfully independent of lung function severity or its course.

Our findings are also novel as PANAS and SMAS-30 have not been previously reported in f-ILD. The PANAS positive/negative ratio, also called the clinical positivity ratio, reflects an attitude of viewing the world in a more positive light, and in our study was predictive of the CRQ Emotional Function and Mastery domains. Self-management ability, in particular aspects of investment behaviour, was a relevant

component of the CRQ Dyspnoea and Physical Summary score. This subscale refers to the ability to allot time and action towards procuring and maintaining resources for coping with chronic illness and appears to predict sustaining a positive response to increased symptoms and functional limitations. SMAS-30 has been studied as a general assessment in healthy elderly patients and patients with COPD [6], but was not previously reported in f-ILD. Additional validation of both these instruments is needed in our cohort and may offer important insights into modifiable patient-centred attributes that potentially influence disease experience and improve QoL.

Indeed, interventions targeting PR-QoL outcomes need not exclude traditional therapies directed at FVC % pred and may in fact be synergistic when aligned. Treatment modalities such as exercise rehabilitation have shown efficacy in IPF and other f-ILD, with reductions in symptom burden and healthcare utilisation [7, 8]. A recent review of IPF patients eligible to start anti-fibrotic medications found up to 40% of surveyed physicians chose a "watch and wait" approach, either due to lack of symptoms or perceived additional clinical burden from drug-related adverse effects [9, 10]. Intolerance of drug-related adverse effects or the perception of inefficacy with ongoing loss of QoL are commonly encountered barriers to sustaining therapy. This obstacle may be tempered with directed exercise or health coaching programmes that encourage investment behaviour and self-efficacy, improving treatment tolerance and therefore possible disease response.

In conclusion, we report for the first time exploratory findings of the CRQ in patients with f-ILD and note its similarly poor correlation with objectively measured lung function (FVC % pred), as seen with other patient-reported outcome instruments and reported in the literature. However, self-management ability and mood or affect are two novel areas of assessment found to be correlated with clinically relevant CRQ domains, which may be modifiable and further studied to address and improve other aspects of PR-QoL outcomes.

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References

1   Swigris JJ, Kuschner WG, Jacobs SS, et al. Health-related quality of life in patients with idiopathic pulmonary fibrosis: a systematic review. Thorax 2005; 60: 588–594.

2   Bestall JC, Paul EA, Garrod R, et al. Usefulness of the Medical Research Council (MRC) dyspnoea scale as a measure of disability in patients with chronic obstructive pulmonary disease. Thorax 1999; 54: 581–586.

3   Watson D, Clark LA, Tellegen A. Development and validation of brief measures of positive and negative affect: the PANAS scales. J Pers Soc Psychol 1988; 54: 1063–1070.

4   Schuurmans H, Steverink N, Frieswijk N, et al. How to measure self-management abilities in older people by self-report. The development of the SMAS-30. Qual Life Res 2005; 14: 2215–2228.

5   Williams JE, Singh SJ, Sewell L, et al. Development of a self-reported Chronic Respiratory Questionnaire (CRQ-SR). Thorax 2001; 56: 954–959.

6   Benzo RP, Abascal-Bolado B, Dulohery MM. Self-management and quality of life in chronic obstructive pulmonary disease (COPD): The mediating effects of positive affect. Patient Educ Couns 2016; 99: 617–623.

7   Gomes-Neto M, Silva CM, Ezequiel D, et al. Impact of pulmonary rehabilitation on exercise tolerance and quality of life in patients with idiopathic pulmonary fibrosis: a systematic review and meta-analysis. J Cardiopulm Rehabil Prev 2018; 38: 273–278.

8   Dowman L, Hill CJ, Holland AE. Pulmonary rehabilitation for interstitial lung disease. Cochrane Database Syst Rev 2014; 2014: CD006322.

9   Maher TM, Molina-Molina M, Russell AM, et al. Unmet needs in the treatment of idiopathic pulmonary fibrosis-insights from patient chart review in five European countries. BMC Pulm Med 2017; 17: 124.

10 Cottin V, Wollin L, Fischer A, et al. Fibrosing interstitial lung diseases: knowns and unknowns. Eur Respir Rev 2019; 28: 180100.