Association of patient-reported outcome measures with lung function and mortality in fibrotic interstitial lung disease: a prospective cohort study

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Shareable abstract (@ERSpublications)
Baseline and short-term serial changes in patient-reported outcome measures (PROMs) may correlate with pulmonary function change and mortality risk. Their use may improve the care of patients and serve as clinical outcomes in research studies. https://bit.ly/3SAYEgM

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Abstract

Background Patient-reported outcome measures (PROMs) may provide clinicians and researchers with direct insights into disease impact and patient well-being. We assessed whether selected PROMs and their domains are associated with baseline and longitudinal changes in lung function and can predict mortality in patients with fibrotic interstitial lung disease (f-ILD).

Methods A single-centre prospective study of adult patients with f-ILD enrolled over 3 years was conducted assessing baseline and short-term changes in PROMs. Three questionnaires, the modified Medical Research Council dyspnoea scale (mMRC), Chronic Respiratory Questionnaire (CRQ) and Self-Management Ability Scale (SMAS-30) were administered at planned intervals and assessed for their association with baseline clinical findings, change in lung function (% predicted forced vital capacity (FVC%) and diffusion capacity of the lung for carbon monoxide (D_{LCO}%)) and all-cause mortality.

Results 199 patients were enrolled with a mean PROM follow-up of 9.6 months. When stratified by FVC % quartiles at presentation, lower mMRC (less dyspnoea), higher CRQ Physical and Emotional domain (better health-related quality of life) and higher total SMAS-30 scores (better self-management ability) were associated with higher FVC%. Short-term changes in all three PROMs appeared to be associated with changes in FVC% and D_{LCO}%. Adjusted and unadjusted baseline and serial PROM changes were also predictive of mortality.

Conclusions Baseline and serial assessments of PROMs were associated with changes in lung function and predicted death in patients with f-ILD. PROMs may strengthen comprehensive assessments of disease impact in clinical practice as well as support patient-centred outcomes in research.

Introduction

Patients with fibrotic interstitial lung disease (f-ILD) commonly experience poor health-related quality of life (HRQoL) [1]. Current treatments in f-ILD may mitigate loss of lung function but have less measured impact on symptom burden or patient well-being [2–4]. A desire to better manage symptom burden and slow or stabilise lung function decline has been reported by patients with f-ILD [5, 6]. Further study is needed to implement measurement tools that sufficiently capture disease experience and assesses their association with functional outcomes or as targets of treatments themselves [7, 8].

Patient-reported outcome measures (PROMs) are proctored or self-administered questionnaires that directly elicit the impressions or insights of patients regarding their symptom burden or HRQoL [9–11]. Prior studies in interstitial lung disease (ILD) have reported mixed association of PROMs with presenting lung function or radiological findings [1, 12] Most interventional studies still include PROMs as secondary or adjunctive

outcomes as often required by local governing or oversight bodies [7, 11, 13]. Discordance of PROMs with physiological end-points has been reported and is believed to be attributable to several factors. These include shorter observational periods, heterogeneity of disease severity in assessed populations, and varied fidelity or subjectivity of PROMs across multi-national or multicultural settings [11]. To better understand how an intervention might additionally impact patient well-being, assessing PROM change as disease progresses may be helpful. We hypothesise that physiologic, emotional and psychological domains as longitudinally assessed by PROMs may be associated with changes in lung function and/or predict mortality. This may further support their use in clinical practice and in research as feasible end-points.

Methods

Patient selection

Institutional review board approval was obtained prior to study initiation (IRB 17-005475). A prospective study of adult patients with f-ILD seen at our institution was conducted from 6 September 2018 to 18 August 2021. Patients referred with f-ILD to our clinic were randomly screened, approached for participation and consented. Inclusion criteria were age >18 years and 10% or more radiological fibrosis on chest computed tomography. No exclusions were made for f-ILD subtype, functional severity or treatment history. Baseline demographics (age, sex, smoking history), disease diagnosis or aetiology (idiopathic pulmonary fibrosis (IPF) *versus* others) and pulmonary function testing (PFT) defined as % predicted forced vital capacity (FVC%) and diffusion capacity for carbon monoxide (D_{LCO}%) were collected on all participants. PFTs were performed at the discretion of treating clinicians based on clinical indication and collated if completed within 4 weeks of PROMs. Total follow-up occurred from the time of enrolment to the end of the study period or date of death. Patient deaths (all-cause) were confirmed in the medical record.

PROMs

PROMs were obtained at study enrolment (baseline), 3, 6 and 12 months for patients with IPF (given suspected higher rate of natural disease progression) and at baseline, 6 and 12 months for patients with non-IPF diagnoses, either as paper questionnaires provided in-person at clinic visits or mailed to patients' homes. Mean duration of PROM follow-up was defined as baseline measure at enrolment to last available measure, up to 1 year. Follow-up after the first year occurred for an additional 12–24 months based on timing of enrolment into the 3-year study period or date of death if prior to this.

Three PROMs were selected for assessing dyspnoea, respiratory-related quality of life and self-management ability.

The modified Medical Research Council dyspnoea scale (mMRC) is a five-item dyspnoea assessment scale with a score range of 0 to 4 [14]. Higher scores suggest greater degree of dyspnoea. The minimal clinically important difference (MCID) is a change of 1 point in either direction, suggesting worsening (increasing score) or improving dyspnoea (decreasing score). Prior studies support mMRC scores correlating with HR-QoL and mortality in both COPD and ILD patients [15–17].

The Chronic Respiratory Questionnaire (CRQ) is a validated 20-item questionnaire assessing four domains of respiratory-related quality of life: Dyspnoea, Fatigue, Emotion and Mastery. Individual items are scored *via* a seven-point Likert scale, with lower scores representing greater impairment [18–20]. The MCID is 0.5 for any of the domains or combined summary scores [21–23]. Our study used the physical summary score (combining the mean scores of the Dyspnoea and Fatigue domains) and Emotional function score (combining the mean scores of the Emotion and Mastery domains) as primary end-points [24]. The CRQ has been reported in ILD [25–28] and was chosen for its inclusion of a fatigue domain and more general assessment of chronic lung disease, reflecting the expected heterogeneity of the available f-ILD study population.

The Self-Management Ability Scale (SMAS-30) is a 30-item questionnaire used to assess participant self-management ability, including several health behaviours that contribute to well-being including self-efficacy, investment behaviour and taking initiative [29]. A total score on a 100-point scale is calculated as the mean of the six subscales, with a higher score suggesting better self-management ability. The recall period is 3 months with no reported MCID. Self-management ability has been recently evaluated in ILD [25, 30] with the current study rationale being to correlate disease severity or progression with either gain or loss in ability to cope or manage such changes.

Statistical analysis

Study data were collected and managed using REDCap (Research Electronic Data Capture), a secure, web-based software platform designed to support data capture for research studies as hosted by our

institution. Continuous data were presented as mean±SD or median and interquartile range (IQR 25–75%). Categorical data were summarised as counts and percentages. Baseline comparisons were made between IPF and non-IPF patients using Chi-square for categorical and ANOVA for continuous variables. PROM stratification and comparisons were made based on presenting FVC% cut-offs (severe <50%, moderate 50–59%, mild 60–79%, normal ⩾80%) using ANOVA. Baseline clinical (age, sex, FVC% and D_{LCO}%) and PROM findings were assessed for their association with mortality using adjusted and unadjusted logistic regression, with PROMs adjusted for *a priori* covariables of age, male sex and FVC%. Association of PROM change with change in FVC% and D_{LCO}% was assessed with a mixed effects model, adjusting for age, sex, IPF diagnosis and months on study as fixed effects and individual subjects as random effects. A mixed effects model also accounts for missing data at all intervals, so long as missingness is considered random. Baseline and short-term changes in PROMs as predictors of mortality were assessed using adjusted Cox proportional hazards regression for baseline measures and time-dependent Cox proportional hazards modelling adjusted for age and IPF diagnosis. p-values <0.05 were considered statistically significant. Statistical analysis was completed using R (R Core Team (2021) www.R-project.org/).

Results

Patient characteristics

Of 304 patients screened, 199 completed consent and were enrolled (76 did not return consents, 29 declined). 78 were female (39.2%) with a mean age of 68.8 years (range 32–88 years) (table 1). 65 were diagnosed with IPF (33%), representing the largest f-ILD subtype. IPF patients were older and male. Additional f-ILD diagnoses included connective tissue disease-associated ILD (CTD-ILD) (17.6%), fibrotic hypersensitivity pneumonitis (20.6%), and atypical or unclassifiable ILD (19.1%) (figure 1). As our site is a national tertiary referral centre, enrolled patients resided throughout the USA and represented 27 states, dominated by the mid-West. Most patients in the cohort were also former smokers (52.0%) with only 3% endorsing active tobacco use at the time of diagnosis. Mean FVC% and D_{LCO}% were 71.1 ±19.8% (range 19–133) and 49.8±17.3% (range 19−102), respectively, with no difference in presenting lung function between IPF and non-IPF patients. Overall mortality for the study period was 20.1%, with more deaths occurring in IPF than non-IPF patients (29.2% *versus* 15.7% respectively, p=0.025). Mean duration of PROM follow-up was 9.6 months (range 2.6–18.2), with 46% of IPF and 63% of non-IPF patients completing all pre-planned PROM assessment intervals (figure 2). Missing PROMs for the IPF and non-IPF cohorts during the 12-month assessment period were due to death in 13 patients and 16 patients respectively, with unreturned or incomplete reports in the remainder (see supplementary table S1 for interval missingness).

Baseline PROM and FVC% severity

When comparing baseline PROMs among f-ILD subgroups, there was greater dyspnoea for non-IPF patients than IPF as measured by mMRC (2.2 *versus* 1.8, p=0.038). CRQ Physical (4.9 *versus* 4.5, p=0.027) and Emotional function domain scores (5.3 *versus* 4.9, p=0.03) were also higher in patients with

TABLE 1 Patient baseline demographics

	Whole cohort	IPF	Non-IPF	p-value
Patients n	199	65	134	
Age years, mean±SD	68.8±9.2	72.0±6.6	67.3±9.9	<0.001
Female, n (%)	78 (39.2)	14 (21.5)	64 (47.8)	<0.001
FVC % predicted, mean±SD	71.1±19.8	73.9±20.8	69.8±13.4	0.171
D_{LCO} % predicted, mean±SD	49.8±17.3	47.5±15.5	50.9±18.1	0.205
Smoking status, n (%)				0.495
Current	6 (3.0)	1 (1.5)	5 (3.8)	
Former	103 (52.0)	37 (56.9)	66 (49.6)	
Never	89 (44.9)	27 (41.5)	62 (46.6)	
Mortality, n (%)	40 (20.1)	19 (29.2)	21 (15.7)	0.025
mMRC, mean±SD	2.1±1.2	1.8±1.2	2.2±1.1	0.038
CRQ Physical, mean±SD	4.6±1.3	4.9±1.3	4.5±1.3	0.027
CRQ Emotional, mean±SD	5.0±1.1	5.3±1.2	4.9±1.1	0.030
SMAS-30 total, mean±SD	71.6±12.2	72.4±12.0	71.2±12.4	0.501

IPF: idiopathic pulmonary fibrosis; non-IPF: non-idiopathic pulmonary fibrosis; FVC: forced vital capacity; D_{LCO}: diffusion capacity of the lungs for carbon monoxide; mMRC: Medical Research Council Dyspnoea Scale; CRQ: Chronic Respiratory Questionnaire; SMAS-30: Self-Management Ability Scale.

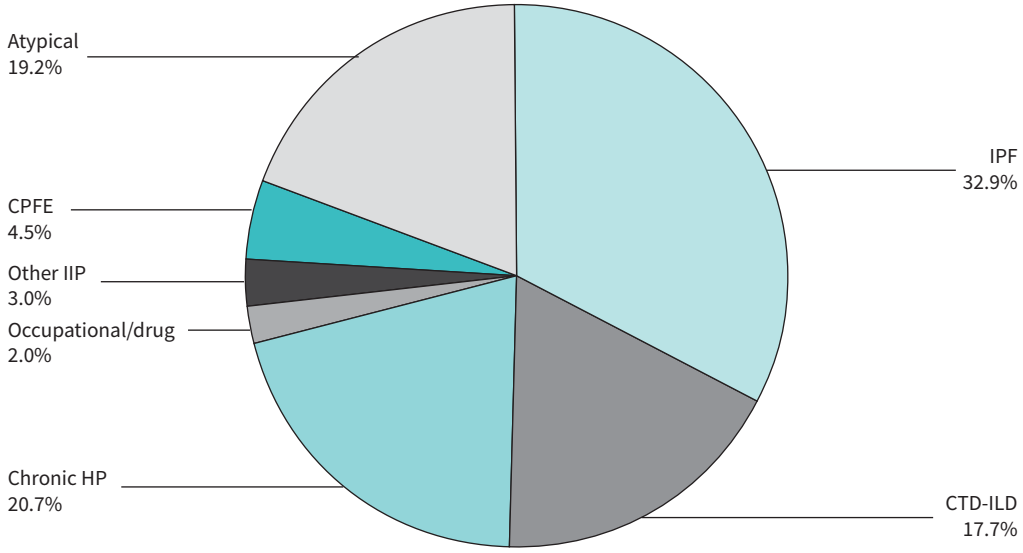

FIGURE 1 Cohort diagnosis of fibrotic interstitial lung disease by type. CPFE: combined pulmonary fibrosis and emphysema; IIP: idiopathic interstitial pneumonia; HP: hypersensitivity pneumonitis; IPF: idiopathic pulmonary fibrosis; CTD-ILD: connective tissue disease-associated interstitial lung disease.

IPF (better respiratory-related QoL), while SMAS-30 total scores (72.4 *versus* 71.2, p=0.501) did not differ (table 1). PROMs for the whole cohort, when stratified by FVC% cut-offs (severe <50%, moderate 50–59%, mild 60–79% or normal ⩾80% of predicted), were higher for mMRC scores and lower for CRQ Physical, CRQ Emotional and SMAS-30 total scores as FVC% decreased. These findings suggest overall less dyspnoea and improved HRQoL at higher FVC% cut-offs (table 2).

Association of PROM change with change in FVC% and D_{LCO}%

Change in PROMs were associated with change in FVC% and D_{LCO}% using a mixed effects model, adjusted for age, sex, IPF diagnosis and time on study (months) as fixed effects and individual patients as random effects. With other parameters being constant, a 1 point change in PROM score was associated with an estimate change in FVC% and D_{LCO}% at each time point (table 3). Changes in all four PROMs were associated with change in FVC% (table 3). For example, a 1 point increase in the CRQ Physical summary score reflected an estimate increase in FVC% of 3.53% (2.30–4.75) (p<0.001) when adjusted for sex. A similar 1 point increase in mMRC correlated with a drop of 3.48% on FVC% (−4.76 to −2.20) (p<0.001). Intraclass correlation coefficients (ICC), representing the proportion of variance explained by the PROM predictor model, ranged from 90.5% to 91.3%. Sensitivity analysis with the addition of SMAS-30 to the CRQ Physical PROM model (noting CRQ Physical and SMAS-30 were moderately correlated in this cohort (r=0.577)) found positive change in the CRQ Physical score still remained predictive of higher FVC% (estimate 3.43 (2.11–4.76), p<0.001; data not shown). Mixed effects modelling

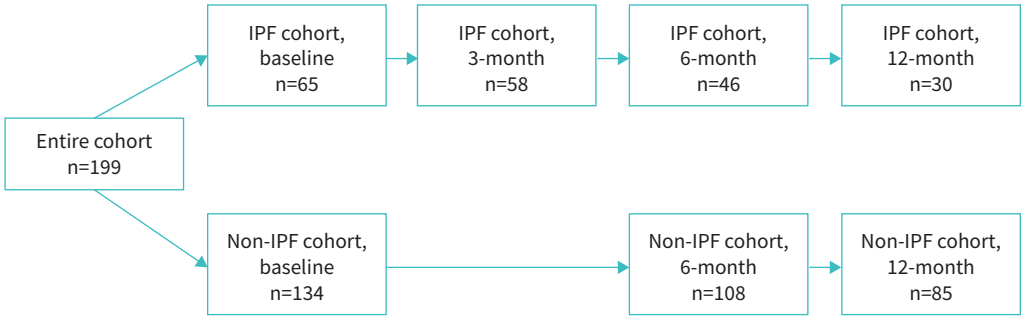

FIGURE 2 Patients completing patient-reported outcome measures at baseline and on all prior and subsequent assessment intervals. IPF: idiopathic pulmonary fibrosis.

TABLE 2 Baseline PROM findings stratified by FVC% severity

PROM	FVC <50%	FVC 50–59%	FVC 60–79%	FVC ⩾80%	p-value
mMRC	2.5±1.0	2.9±0.7	2.2±1.1	1.4±1.1	<0.001
CRQ Physical	4.1±1.3	3.8±1.3	4.6±1.3	5.2±1.1	<0.001
CRQ Emotional	4.8±1.1	4.5±1.1	5.0±1.1	5.5±1.0	<0.001
SMAS-30 total	68.7±11.3	70.3±11.5	70.0±12.3	75.8±12.2	0.0151

Data are presented as mean±SD. PROM: patient-reported outcome measure; FVC: forced vital capacity; mMRC: Medical Research Council Dyspnoea Scale; CRQ: Chronic Respiratory Questionnaire; SMAS-30: Self-Management Ability Scale.

for D_{LCO}% suggested similar predictive characteristics for all PROMs, with ICC ranges of 83.7% to 89.2% (table 3).

Baseline patient characteristics and PROMs as predictors of death

Baseline demographic, PFT and PROM findings were assessed as predictors of death using univariable and multivariable logistic regression. Age, male sex, FVC% and D_{LCO}% were analysed as independent predictors. Age trended towards significance (unit OR 1.04 (1.0–1.09), p=0.053) with presenting FVC% (unit OR 0.96 (0.94–0.98), p <0.001) and D_{LCO}% (unit OR 0.93 (0.89–0.96), p<0.001) being significant predictors of death, noting decreased risk for each unit increase (table 4).

All baseline PROMs were predictive of death on univariable analysis. Presenting SMAS-30 had the lowest Akaike information criterion and Bayesian information criterion, suggesting better model fit. For every 1-unit increase in the SMAS-30 total score at presentation, a patient was 6% less likely to die during the study period (p<0.001). Baseline PROMs adjusted for *a priori* covariables of age, male sex and FVC remained predictive of death. Increased risk of death was also associated with higher presenting mMRC scores (OR 1.53 (1.03–2.35), p=0.04) and lower CRQ Physical (OR 0.67 (0.49–0.91), p=0.01) and Emotional scores (OR 0.61 (0.41–0.88), p=0.01) (table 4).

Change in PROMs as predictors of death

Cox proportional hazards analysis and time-adjusted Cox regression models for internal time-varying covariables were pursued to assess baseline and change in PROMs as predictors of death (table 5). Adjustments were made for *a priori* covariables of age and IPF diagnosis. All baseline PROMs were predictive of death on Cox proportional hazards analysis, with higher mMRC and lower CRQ domain and SMAS-30 scores being associated with increased risk of death (mMRC HR 1.87 (1.34–2.6), p<0.001). Time-adjusted Cox regression models using PROMs as time-varying covariables found serial change in all PROMs was also predictive of death ((mMRC, HR 2.17 (1.51–3.12), p<0.001); CRQ Physical and Emotional domain scores (HR 0.57 for both; p<0.001); SMAS30 HR 0.95 (0.93–0.97, p<0.001)).

TABLE 3 Mixed effects model assessing association of PROM change with change in FVC% and D_{LCO}%[#]

	Estimate	95% CI	p-value
FVC % change			
mMRC	−3.45	−4.73– −2.17	<0.001
CRQ Physical	3.50	2.27–4.73	<0.001
CRQ Emotional	3.02	1.62–4.41	<0.001
SMAS-30 total	0.16	0.03–0.29	0.015
D_{LCO} % change			
mMRC	−4.85	−6.10– −3.61	<0.001
CRQ Physical	3.59	2.33–4.85	<0.001
CRQ Emotional	2.71	1.29–4.13	<0.001
SMAS-30 total	0.14	0.01–0.27	0.039

PROM: patient-reported outcome measure; FVC: forced vital capacity; D_{LCO}: diffusion capacity of the lungs for carbon monoxide; mMRC: Medical Research Council Dyspnoea Scale; CRQ: Chronic Respiratory Questionnaire; SMAS-30: Self-Management Ability Scale. [#]: adjusted for age, IPF diagnosis and months on study as fixed effects and individual subjects as random effect.

TABLE 4 Baseline clinical and PROM predictors of death

Univariable analysis	Odds ratio	95% CI	p-value
Age years	1.04	1.0–1.09	0.053
Sex, male	1.66	0.80–3.60	0.185
FVC% (unit OR)	0.96	0.94–0.98	<0.001
D_{LCO}% (unit OR)	0.93	0.89–0.96	<0.001
PROMs	**Odds ratio**	**AIC, BIC**	**p-value**
mMRC	1.85	165.19,171.53	0.002
CRQ Physical	0.64	167.05, 173.39	0.002
CRQ Emotional	0.64	169.23, 175.57	0.007
SMAS-30 total	0.94	161.37, 167.71	<0.001
Multivariable analysis: PROMs adjusted for age, sex and FVC%	**Odds ratio**	**95% CI**	**p-value**
mMRC	1.53	1.03–2.35	0.04
CRQ Physical	0.67	0.49–0.91	0.01
CRQ Emotional	0.61	0.41–0.88	0.01
SMAS-30 total	0.93	0.90–0.96	<0.001

PROM: patient-reported outcome measure; FVC: forced vital capacity; D_{LCO}: diffusion capacity of the lungs for carbon monoxide; mMRC: Medical Research Council Dyspnoea Scale; CRQ: Chronic Respiratory Questionnaire; SMAS-30: Self-Management Ability Scale.

Discussion

Our study suggests selected baseline and short-term serial changes in PROMs were associated with concomitant pulmonary function change and predictive of mortality. A diverse cohort of f-ILD patients was prospectively assessed at specific short-term intervals and followed up to 3 years for concurrent PFT and all-cause mortality outcomes. In this cohort, non-IPF patients appeared to have worse dyspnoea at baseline, though for both groups, presenting PROM findings were associated with presenting FVC severity. Longitudinal change in PROMs was associated with change in FVC and D_{LCO}, with baseline and short-term serial measures predicting mortality even after adjustment for known correlates (*e.g.*, age, male sex and FVC%). These findings add to the growing literature on the utility of PROMs for initial and serial assessment of patients with f-ILD, in both clinical and research settings.

Our study utilised the mMRC, CRQ and SMAS-30 questionnaires which have been previously reported in f-ILD or chronic lung disease patients as baseline correlates of symptomatology or disease impact. The mMRC has been validated in IPF and f-ILD and found to be associated with other clinical parameters including 6-minute walk distance and the post-exercise Borg score [31, 32]. As a simple assessment of

TABLE 5 Changes in PROMs as predictors of death; Cox proportional hazards model for baseline and time-based change in PROMs (adjusted for age and IPF diagnosis)

	Hazard ratio	95% CI	p-value
Baseline PROM (proportional hazards)			
mMRC	1.87	1.34–2.60	<0.001
CRQ Physical	0.61	0.48–0.77	<0.001
CRQ Emotional	0.61	0.47–0.78	<0.001
SMAS-30 total	0.94	0.91–0.96	<0.001
Change in PROM (time varying)			
mMRC	2.17	1.51–3.12	<0.001
CRQ Physical	0.57	0.45–0.71	<0.001
CRQ Emotional	0.57	0.44–0.73	<0.001
SMAS-30 total	0.95	0.93–0.97	<0.001

PROM: patient-reported outcome measure; mMRC: Medical Research Council Dyspnoea Scale; CRQ: Chronic Respiratory Questionnaire; SMAS-30: Self-Management Ability Scale.

dyspnoea, its feasibility in clinical and research settings and known MCID are relevant to our diverse study population. The CRQ has been previously described in a cross-sectional study of f-ILD patients which suggested feasibility for measuring individual and combined domains of patient symptomatology and impacts [25, 26]. It has also been used as a primary HRQoL outcome in prior pulmonary rehab studies [33, 34]. While a recent meta-analysis suggests the more commonly used HRQoL assessment tools in IPF and f-ILD are the St. George's Respiratory Questionnaire (SGRQ) and Short Form-36 [35], like the CRQ, neither were originally derived in ILD patients. We specifically selected the CRQ given its relative feasibility (20 questions) for serial assessments and capture of a specific fatigue domain, largely missing in other lung disease assessment tools. Lastly, self-management ability is a vital component to patient well-being and has been recently reported in patients with IPF [30].

Most systematic data reflecting the use of PROMs in IPF or f-ILD have been derived from interventional studies [9, 10]. PROMs have served primarily as secondary outcomes in randomised controlled trials. Unfortunately, few medical treatments have shown positive impact on PROMs even when there was positive impact on PFT decline. Several explanations for this include the historical use of PROMs derived from other chronic lung diseases, shorter measurement periods, or local cultural, population or linguistic differences given the international scope of larger studies, and heterogeneity of patient experience with disease impact. Additionally, mixed association of PROMs with presenting lung function or radiological findings has also been reported [11, 13]. A systematic review of seven studies involving patients with IPF found poor association between dyspnoea or HRQoL measures and pulmonary function [1]. Tzanakis and colleagues [12] on the other hand compared the fidelity of several PROM and HRQoL measures in IPF and control patients and found good association with FVC and total lung capacity using the SGRQ. A recent study by Kim *et al.* [36] assessed seven PROMs, including King's Brief Interstitial Lung Disease (K-BILD), mMRC, SGRQ and the University of California San Diego shortness of breath questionnaire (UCSD-SOBQ) in patients with IPF every 3 months for 12 months and reported better association in those with FVC $\geqslant$75% for several of the PROMs. PROMs may also diverge despite similar FVC cut-offs as disease severity worsens [37]. Our data involving a diverse group of f-ILD subtypes and severities found better dyspnoea and CRQ scores in patients with IPF who were older and male. While counter-ntuitive, this may reflect patient expectations of lower physical activity level at later stages in life (retirement for example) or less emotional or psychological impact in early clinical disease or those with longer disease duration and opportunities to cope. However, our study did find strong correlations between PROMs and concurrent lung function not only at baseline but over time. Exploration of serial changes in PROMs and their correlation with lung function may better target patient-centred outcomes for practice and research studies.

In addition to correlating with PFT parameters, PROMs also appeared to be associated with mortality. A prior study involving patients with IPF assessed the association of SGRQ scores at enrolment with death or lung transplantation over the initial study period [38]. After adjustments for potential confounding variables, higher symptom burden and lower physical activity scores were associated with increased risk of death or transplant at 1 year. Data from the Australian IPF Registry found lower scores on the SGRQ, UCSD-SOBQ and patient-reported cough severity were predictive of mortality on multivariable analyses adjusted for demographic and FVC findings [39]. Use of the mMRC as an independent predictor of death has been reported [17] though not seen in a subsequent study by Kim *et al.* [36], which showed stronger associations with K-BILD and SGRQ. Most studies are limited in their lack of serial PROM assessments, with our data demonstrating short-term changes in PROMs being predictive of mortality in IPF and non-IPF f-ILD subtypes.

Our study has several limitations. Despite a prospective design, not all questionnaires were obtained from all patients at each time interval, either due to non-response, incomplete or response errors, or death. Mixed effects and time-based models were used to adjust for this with individual patients as random effects to account for repeated measures. Immortal time bias should also be considered in terms of data acquisition. Our choice of PROMs, although pre-determined at study onset, reflects only one approach to assessing patient symptom burden or HRQoL. As there is no widely accepted PROM in common clinical use for patients with f-ILD, we chose those with potential for novel insights (self-management ability) as well as feasibility. Associations were also described for a broad or pragmatic prospective cohort reflecting most referral or tertiary practices (our patients were predominantly from the mid-West but included multiple US regions and states referred to our institution for consultation and care). Nonetheless, more data are needed to assess the generalisability of our findings as derived from a single tertiary or referral institution, where patient demographics, disease type or severity may vary and impact findings. Noting this, we made statistical adjustments for the expected heterogeneity of typical predictor variables and still found association of selected PROMs with PFT and mortality outcomes.

Conclusion

Our findings support the use of selected PROMs such as mMRC, CRQ or SMAS-30 in patients with f-ILD as baseline or longitudinal correlates of lung function and mortality. Clinical practice and research outcomes in f-ILD may be strengthened with PROMs as part of comprehensive assessments of disease burden and patient-centred responses to treatments and interventions.

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Ethics statement: Prospective observational study with patient contact, should guarantee patient anonymity and protection of health data.

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