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A New Tool to Assess Quality of Life in Patients with Idiopathic Pulmonary Fibrosis or Non-specific Interstitial Pneumonia*

Ein neuer Fragebogen zur Kennzeichnung der Lebensqualität bei Patienten mit idiopathischer Lungenfibrose und idiopathischer nicht-spezifischer interstitieller Lungenfibrose

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Bibliography

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ABSTRACT

Background Quality of life (QoL) is significantly impaired in patients with pulmonary fibrosis, however reliable tools to assess QoL issues specific for this group of patients are still missing. We thus aimed to develop a new questionnaire called “Quality of life in patients with idiopathic pulmonary fibrosis” (QPF) to measure QoL in patients with fibrotic idiopathic interstitial pneumonias (IIP).

Methods An item pool was created on the basis of a German expert group with support of patients suffering from pulmonary fibrosis. In a 1st step, this version of the questionnaire was completed by 52 patients with idiopathic pulmonary fibrosis (IPF) or non-specific interstitial pneumonia (NSIP). Following this, an item- and an exploratory factor analysis was carried out and a 2nd version created. In a multicenter validation study in a one-group pre-post design, the questionnaire was filled in by 200 patients with IIP (IPF = 190, iNSIP = 10) at 2 time points with an interval of 6 months. Cross-validation was carried out with the St. Georges Respiratory Questionnaire (SGRQ).

Results The mean age of the patients was 71.0 years (50–90 years), 82.5 % were male. Item analysis revealed that most of Cronbach alpha and selectivity values of QPF-scales could be considered as sufficient (e. g. QPF-scale “condition” [alpha = 0.827], “impairment” [alpha = 0.882]). At scale level, there were significant differences in terms of a deterioration or improvement in the QPF-condition and QPF-breathlessness scales and also in the SGRQ-activity scale. Analysis of construct validation of QPF and SGRQ showed moderate correlations between both questionnaires. A deterioration in health status from the patient’s and doctor’s perspective was seen in the scales “impairment”, “shortness of breath” and “health status” of the QPF. The QPF was able to detect a

* In memory to Prof. Dr. Franz Petermann, Bremen. He has accompanied this project until his early death in August 2019.

change in the patient's mood ("condition" scale) in the course of treatment.

Conclusion This newly developed questionnaire maps the special needs of the patients well. The QPF is suitable for screening of quality of life as well as for supplementing the medical history and for monitoring the course of disease in fibrotic IIPs.

ZUSAMMENFASSUNG

Hintergrund Die Lebensqualität (QoL) ist bei Patienten mit Lungenfibrose erheblich vermindert. Messinstrumente der QoL für diese spezielle Patientengruppe sind bislang nicht in ausreichender Art und Weise vorhanden. Deshalb entwickelten wir einen spezifischen Fragebogen bei Patienten mit Idiopathischer Lungenfibrose (IPF) und Nicht-spezifischer Lungenfibrose (NSIP).

Methoden Ein Fragenkatalog wurde von einer Expertengruppe der Deutschen Gesellschaft für Pneumologie für Patienten mit Idiopatischer Lungenfibrose und Nicht-spezifischer Lungenfibrose zusammengestellt. In einem ersten Schritt wurden diese Fragen an 52 Patienten dieser Krankheitsentitäten getestet und einer Item- und explorativen Faktor-Analyse unterzogen und anschließend so eine zweite Version des Fragenkatalogs erstellt und mit Patienten dieser Krankheitsentitäten diskutiert und evaluiert.

In einer multizentrischen Studie an 200 Patienten (IPF 190, NSIP 10) wurde der Fragebogen in einem Pre-post-Design zweizeitig in einem Abstand von 6 Monaten getestet. Ein Vergleich mit dem eingeführten St. Georges Respiratory Questionaire (SGRQ) wurde zeitgleich durchgeführt.

Ergebnisse Das mittlere Alter der Patienten betrug 71,0 Jahre (50–90 Jahre). Die Itemanalyse erfolgte mittels Cronbach's alpha und Werte für Befindlichkeit (alpha = 0.827) sowie Beinträchtigungen (alpha = 0.882) wurden als statistisch ausreichend angesehen.

Es wurden signifikante Änderungen in Bezug auf Verschlechterungen oder Verbesserungen in den Fragen zur „Befindlichkeit" und „Atemnot" und auch in der Skala „Aktivität" gefunden.

Der Vergleich mit dem SGRQ zeigte eine moderate Übereinstimmung beider Fragebögen. Eine Verschlechterung des Gesundheitsstatus aus der Patientenperspektive sowie aus der ärztlichen Perspektive wurde bei den Skalen „Beeinträchtigungen", „Atemnot" und „allgemeiner Gesundheitsstatus" analysiert.

Der Fragebogen zur Lebensqualität bei Patienten mit Idiopathischer Lungenfibrose und Nicht-spezifischer Lungenfibrose ist in der Lage, Änderungen der Lebensqualität im Verlauf der Erkrankung zu erkennen.

Background

Idiopathic pulmonary fibrosis (IPF) is a chronic, progressive, fibrosing interstitial pneumonia of unknown etiology. IPF affects elderly, predominantly male ex-smokers [1, 2]. Estimates of the prevalence of IPF range from 2 to 29 cases per 100,000, the incidence is approximately 10 per 100,000 in the general population [3]. The prevalence of IPF is increasing, whereby it is unclear whether this increase is influenced by geographical, ethnic or cultural factors, or whether improved diagnosis and demographic change play a role.

Despite the improved situation with antifibrotic drugs now available not only for IPF but also for other progressive fibrotic ILDs [4], the therapeutic options are still limited [5–7]. While antifibrotic therapy halts disease progression and may positively impact survival [3] prognosis remains poor and the burden of disease is still high. As the disease progresses, the patient's activities become more restricted due to increasing breathing difficulties. These significant limitations inevitably affect QoL [8–15]. In addition, there is evidence of associations between pulmonary fibrosis and depressive mood and a perceived impairment in independence [10, 11]. Nishiyama et al. [16, 17] identified dyspnea as the most important prognostic factor for assessing the QoL. Using focus groups, Swigris and colleagues [18] identified the factors that had the greatest impact on the QoL from a patient's perspective: symptoms, therapy procedures, sleep, exhaustion, future thoughts, employment, finances, dependency, family, sexuality, social involvement, mental and spiritual wellbeing and mortality.

To date, existing instruments for assessing QoL do not seem to be able to map the specific problems of patients with pulmonary fibrosis comprehensively [18, 19]. Currently available questionnaires assess more general, non-disease-specific aspects of QoL [20]. For example, the 15-item K-BILD questionnaire [21] covers quality of life-specific factors in a very general way. In the course of the item reduction from originally 71 to 15, essential aspects were excluded, such as coughing, medication, sleep and sexuality; according to the authors, this elimination inevitably led to a loss of information in favour of a low number of items. The disease-specific LQ questionnaires Chronic Respiratory Questionnaire (CRQ) [22] and St. George's Respiratory Questionnaire (SGRQ) [23] were both originally developed for patients with obstructive pulmonary diseases [9–11, 24–27] not including the perceptions of patients with IPF in its development. Swigris et al. [28, 29] validated the questionnaire for patients with IPF (L-IPF) [30] on a smaller sample (n = 125) and a short follow-up period of 14 days. However, fibrosing lung diseases cover a different range of symptoms; associated with thoracic tightness, shortness of breath and non-productive cough. Witt et al. [20] showed in their study with the help of the SF-36 a significantly lower QoL, mainly in people who received long-term oxygen therapy. Analyses on stable individuals showed a small proportion of significant changes in QoL. Only patients with significant changes in health status had significant changes in nearly all SF-36 dimensions. Berry et al. [31] compared patients with COPD and with pulmonary fibrosis and showed that despite comparable physiological condition or symptom severity,

patients with pulmonary fibrosis showed significantly poorer QoL values than patients with COPD (measured with SGRQ and SF-12).

We thus aimed to create a novel QoL measure to better reflect specific aspects in patients with fibrotic idiopathic interstitial pneumonias (IPF and iNSIP).

Methods

On the basis of an expert group from the German Society of Pulmonary Diseases (DGP) with support of patients suffering from pulmonary fibrosis (organized in the German patient support group Lungenfibrose e. V.) an item pool was created. This version of the questionnaire was initially completed by 52 patients with IPF or iNSIP. After returning and reviewing these questionnaires, an item- and an exploratory factor analysis was carried out. In addition, the feedback provided by patients and treating physicians was implemented. As a result, the questionnaire on QoL in patients with IPF and iNSIP (QPF) comprised 6 domains with 42 items (see version in **appendix**). As part of a multicenter validation study in a one-group pre-post design, the questionnaire was filled in by 200 patients with IIPs (IPF = 190, iNSIP = 10) at 2 time points with an interval of 6 months [32].

The sample size was determined on the basis of the planned statistical methods (two-sided testing, $\alpha = 0.05$, Power $1 - \beta = 0.95$). Assuming a conservative estimate of the Cohen effect size of 0.5, the sample size thus determined was n = 42. The pre-test showed that the surveyed patient group was very heterogeneous with regard to the QoL and also achieved extreme test values. In order to ensure a normal distribution and thus the representativeness of the data, the planned sample size was increased to n = 70. Considering a high drop-out and lost-to-follow-up rate, especially due to expected mortality, a sample size of n = 200 patients was calculated.

Item analyses were carried out as a procedure for test validation of the QPF. Differences in mean values were tested for significance using one-factor analysis of variance with repeated measurements. The internal consistency or reliability of the total values and scales was calculated using the Cronbach's alpha value (homogeneity index). Values below 0.5 are rated as unacceptable. In accordance with the convention, a "part-whole correction" was used to determine the selectivity, whereby items should have at least a better selectivity than +0.30.

Correlation effects between the individual QPF and SGRQ measurement methods were calculated using Pearson correlation coefficients. An error probability of < 5 % was determined on both sides.

As an external criterion, the physician's assessment of the disease course at both time points of measurement was used. For this purpose, the attending physician reflected on the clinical status and his knowledge of the patient's lung function (visual analogue scale).

For further criterion validation of the state of health of the patients, the degree of stress on their patients and an assessment of the progression of the disease were collected by the treating physicians. In order to check whether a change in the state of health can also be represented psychometrically, groups were formed with and without a clinically significant deterioration in the state of health (external criterion). The group with relevant changes in health status was formed on the basis of the following criteria:

- Deterioration of the subjectively assessed state of health at t2 by at least 50 % (patient's view, visual analogue scale in the QPF),
- Increased degree of stress at t2 by at least 50 % (doctor's judgment, visual analogue scale, doctor's questionnaire).

The QPF dataset had no missing values. Missing SGRQ items were handled according to the developers' instructions in the SGRQ manual.

The statistical evaluation was carried out with the statistics program IBM SPSS Statistics 22. The evaluation was carried out by protocol.

Recruitment

This study was approved by a central ethics committee (IRB 127/16 Ärztekammer Schleswig-Holstein). Data collection took place from February 2017 to December 2018 in seven tertiary care centers for ILD. Consecutive patients were recruited prospectively after giving written informed consent. The questionnaires were issued at the baseline (t1) during initial contact and six months later (t2) during a re-appointment in the same center. Questionnaires were filled out in a quiet room without distraction.

Inclusion criteria:

- IPF or iNISP according to diagnostic criteria of ATS/ERS (2011 for IPF and 2013 for iNSIP)
- sufficient knowledge of German, reading and writing skills, which makes it possible to fill out the questionnaires

Exclusion criteria:

- Significant respiratory infection in the past 4 weeks
- Significant comorbidity (e. g. severe CAD, heart failure) impeding QoL
- cognitive or linguistic restrictions that hinder the completion of the questionnaires

Instruments

The sociodemographic and medical data of the patients including age, gender, body weight and other chronic diseases were recorded using a self-developed questionnaire. As an external criterion, the patient's self-assessed state of health was recorded on the basis of a visual analogue scale, and the patient's prognosis through doctor's assessment.

The QoL was recorded using the newly developed QPF. This comprises 42 items with the 6 scales: 1. Condition, 2. Impairments, 3. Problems, 4. Shortness of breath, 5. Cough, 6. Health status

There is a 6-step answer format for items on scales 1 and 2, items on scales 3–5 are answered dichotomously (yes/no). Health status (scale 6) is assessed using a visual analog scale. This is 10 cm long, 10 points are awarded per centimeter, i. e. "My state of health is very good." gives 100 points, "My state of

health is very bad." results in 0 points. The final calculation is carried out by adding up the raw values to a total value (0–198 points). A higher score represents a better QoL.

The Saint George Respiratory Questionnaire (SGRQ, [22]) containing 50 items, was used to analyse the construct-validity. The SGRQ has been developed as a multidimensional survey tool for assessing the impairment of disease-specific QoLin adult patients with chronic obstructive pulmonary diseases. The operationalization of the disease-specific quality of life in chronic respiratory diseases takes place on the basis of three impairment areas, which are summarized on the scales symptoms (frequency and form of clinical symptoms), activity (everyday activities) and stress (due to illness and medication). A weighted scale value is determined for each of the three scales and for the entire test, which indicates the degree of impairment of the disease-specific QoLno impairment to "100" – maximum impairment.

Results

219 patients were recruited. 10 patients died during the 6-month-period, 9 patients were lost to follow up. Accordingly, data from 200 patients at t1 and t2 were collected. The mean age of the patients was 71.0 years (50–90 years), 82.5 % were male. Comorbidities (self-reported by the patients without control by the doctors) were frequent (36 % of patients) (▶ **Table 1**).

▶ **Table 1** Comorbidities.

	n	Percent
Diabetes	22	30.56
Arthrosis	8	11.11
Coronary Artery Disease	8	11.11
Hypertension	7	9.72
Asthma	5	6.94
Hypothyroidism	4	5.56
Rheumatism	3	4.17
Hay fever	2	2.78
Lung cancer	2	2.78
Cluster headache	1	1.39
COPD	1	1.39
Depression	1	1.39
Epilepsy	1	1.39
Glaucoma	1	1.39
Congestive heart disease	1	1.39
Heart failure	1	1.39
Ankylosing spondilitis	1	1.39
Prostata hyperplasia	1	1.39
GERD	1	1.39
Sleep apnea syndrome	1	1.39
total	72	100.00

Item analysis

The reliability according to Cronbach (homogeneity index) results in an alpha of 0.827 (unstandardized) for the QPF-scale "Condition" (7 items in total, n = 200). The alpha of this scale can be considered satisfactory. The selectivity indices range from 0.146 to 0.800. According to common criteria (selectivity = at least 0.3), however, the indices of the item "Condition-7" (selectivity = 0.146) must be rated as insufficient. The alpha of this scale increases to 0.858 by eliminating this item, which seems possible without losing information (▶ **Table 2**).

The QPF-scale "Impairment" has an alpha of 0.882 (6 items, n = 200). This value can be considered as sufficient. The selectivity is between 0.539 and 0.777. There is no reason to eliminate any item (▶ **Table 3**).

The QPF-scale "Problems" alpha was found to be too low at 0.457. The selectivity indices also did not meet the statistical requirements because they were below 0.3 in 10 of 11 items and thus had no discriminatory power. The following three items on the QPF "Problems" scale had very low levels of discrimination power (<0.15): "Have you noticed that your fingernails/toenails have changed?", "Do your fingers change color

▶ **Table 2** Indices of the QPF "Condition" scale.

In the past two weeks	Selectivity	Cronbach's Alpha if item is deleted
… I was happy and in a good mood	0.800	0.766
… I felt calm and relaxed	0.783	0.764
… I felt energetic and active	0.715	0.773
… I felt fresh and rested when I woke up	0.633	0.788
… my everyday life was full of things that interest me	0.695	0.779
… I was very afraid of how my illness would progress	0.303	0.848
… my family/friends was a big help	0.146	0.858

▶ **Table 3** Selectivity indices of the QPF impairment scale.

In the past six months I felt restricted	Selectivity	Cronbach's Alpha if item is deleted
... in my everyday activities, e. g. gardening, household.	0.733	0.857
... in my family life.	0.716	0.860
... when participating in public events, e. g. cinema, club.	0.777	0.849
... on vacation trips.	0.683	0.865
... through my tools, e. g. stair lift, oxygen device.	0.719	0.859
... through my medication.	0.539	0.886

▶ **Table 4** QPF "Problems" selectivity indices.

	Selectivity	Cronbach's Alpha if item is deleted
Have you noticed a "drop in performance" in the past six months?	0.266	0.406
Did you lose weight unintentionally?	0.184	0.431
Do you suffer from new night sweats?	0.152	0.442
Did you lose your appetite?	0.323	0.396
Are you tired unusually often?	0.277	0.392
Do you fall asleep unintentionally during the day?	0.190	0.431
Do you suffer from heartburn?	0.089	0.457
Did you notice that your fingernails/toenails have changed?	0.044	0.507
Do your fingers change color when it is cold?	0.149	0.442
Do you have swollen ankles in the evening?	0.188	0.433
Do you suffer from joint problems?	0.212	0.423

▶ **Table 5** Selectivity indices of the QPF "Cough" scale.

	Selectivity	Cronbach's Alpha if item is deleted
Do you suffer from irritable cough?	0.444	0.524
Do you cough after exertion?	0.469	0.514
Do you cough at night?	0.309	0.575
Do you cough mainly in the morning?	**0.226**	0.607
Do you have coughing attacks until you pass out?	**0.136**	0.616
Do you need a cough suppressant?	**0.234**	0.599
Do you have sputum?	0.423	0.532

when it is cold?" and "Do you have swollen ankles in the evening?" The whole scale "Problems" was eliminated (▶ **Table 4**).

The QPF "Cough" scale shows an alpha of 0.608. The selectivity indices are 0.136 to 0.469. The items "Do you mainly cough in the morning?", "Do you have coughing attacks until you pass out?" And "Do you need a cough suppressant?" have selectivity below 0.30 and therefore are insufficient (▶ **Table 5**).

The QPF-scale "Shortness of breath" also has a low internal consistency with alpha = 0.301. The items "I have no shortness of breath.", "I have shortness of breath when I exercise hard, e. g. in sports." and "I have shortness of breath at rest." have a selectivity below 0.30. Leaving out the item "I don't have difficulty breathing." would increase the alpha to 0.536 (▶ **Table 6**).

The "Shortness of breath" scale turns out to be problematic, the patients often answered implausible not matching the rest of the answers. Many patients answer "yes", i. e. the double negation was obviously misunderstood. Some patients also crossed out the "don't" in the question "I don't have difficulty breathing.".

▶ **Table 6** Selectivity indices of the QPF "Shortness of breath" scale.

	Selectivity	Cronbach's Alpha if item is deleted
I don't have difficulty breathing.	**–0.515**	0.536
I have difficulty breathing when I exert myself, e. g. during sports.	**0.090**	0.294
I have difficulty breathing with little effort, e. g. when climbing stairs.	0.302	0.107
I have shortness of breath at the slightest strain, e. g. when I dress or undress.	0.319	0.080
I have shortness of breath at rest.	**0.251**	0.226
Has your breathlessness worsened in the past 3 months?	0.315	0.077

▶ **Table 7** Scale differences of the QPF and SGRQ at t1 and t2.

	Mean value t1	Mean value t2	*P*-Value
QPF-scales (range)			
Total score (0–198)	97.11	95.36	0.400
Condition (0–35)	23.22	21.94	**0.044**
Impairment (0–30)	9.25	10.43	0.086
Problems (0–12)	3.71	3.75	0.880
Shortness of breath (0–7)	2.88	3.18	**0.032**
Cough (0–14)	4.23	4.13	0.476
Health status (0–100)	53.8	51.95	0.398
SGRQ-scales (range)			
Total score (0–100)	38.80	41.70	0.138
Symptoms (0–100)	41.82	40.84	0.683
Activity (0–100)	53.55	59.43	**0.019**
Burden (0–100)	38.80	31.63	0.256

Scale mean values QPF and SGRQ

▶ **Table 7** shows the mean scores of the QPF and SGRQ. The results of the one-factor analysis of variance with repeated measurements showed no significant changes in the point values at the level of the overall scores in the 6 months of observation in either method. However, one can see a small numerical decrease in the overall score in the QPF in the sense of a deterioration in the QoL. The SGRQ-total score increased over time, also indicating a deterioration in the QoL. At the scale level, there were significant differences in terms of a deterioration or improvement in the QPF-condition and QPF-breathlessness scales and also in the SGRQ-activity scale (see ▶ **Table 7**, bold cells).

Construct validation of QPF and SGRQ

As shown in ▶ **Table 8**, some scales of the QPF correlated moderately with those of the SGRQ. The corresponding scales also correlate with one another in a moderate significant manner. Some correlations are negative and thus indicate that there is an inverse relationship between scores of the QPF and SGRQ, which is to be assessed as a good match (high score means good QoL in QPF, bad QoL in SGRQ). The highest negative correlation was found between the scales "QPF-condition" and "SGRQ-total score". This could be seen as an indication that both instruments depict the construct of QoL very similarly. On the other hand, some correlations are positive, which means that a good QoL in the QPF is associated with a decreased QoL in the SGRQ. This could be due to the SGRQ being a condition specific measure but also due to the greater amount of items, especially those with a job-related theme, which are not relevant for the sample examined (the mean age of the patients was 71.0 years), and which produced some missing data.

Responsiveness

Global assessments (visual analogue scale) of the state of health of the patients, the degree of stress on their patient and an assessment of the progression of the disease were collected by the treating physicians. In order to check whether a (supposedly) real change in the state of health can also be represented psychometrically, groups were formed with and without a clinically significant deterioration in the state of health (external criterion) (see methods). The group with relevant

▶ **Table 8** Intercorrelations (Pearson correlation) of the SGRQ-scales with the QPF-scales (t1 data, n = 200).

	SGRQ Total score	SGRQ Symptoms	SGRQ Activity	SGRQ Burden
QPF Total score	−0.447[1]	−0.383[1]	−0.360[1]	−0.437[1]
QPF Condition	−0.593[1]	−0.515[1]	−0.463[1]	−0.057
QPF Impairment	0.527[1]	0.436[1]	0.466[1]	0.492[1]
QPF Problems	0.374[1]	0.352[1]	0.285[1]	0.364[1]
QPF Shortness of breath	0.571[1]	0.399[1]	0.540[1]	0.534[1]
QPF Cough	0.167[2]	0.279[1]	0.135	0.120
QPF Health status	−0.509[1]	−0.447[1]	−0.431[1]	−0.483[1]

[1] = P < 0.01
[2] = P < 0.05

▶ **Table 9** Differences in the mean of the scale with and without the external criterion "Deterioration in health status".

	Significance difference in mean values t1–t2 "No deterioration in health status" n = 138 *P*-Values	Significance difference in mean values t1–t2 "Deterioration in health" n = 62 *P*-Values
QPF-scales		
Total score	0.868	0.177
Conditions	0.199	0.124
Impairment	0.685	**0.028**
Problems	0.887	0.936
Shortness of breath	0.831	**0.002**
Cough	0.603	0.617
Health status	0.888	**0.035**

changes in health status (n = 62) was formed on the basis of special criteria (see methods).

As ▶ **Table 9** shows, a real deterioration in health status from the patient and doctor's perspective is seen in the scales "Impairment", "Shortness of breath" and "Health status" of the QPF.

As a further external criterion, the physicians' assessment of the disease course at both timepoints of measurement was used. At both measurement time points, 70 % of the patients were classified as "stable". In 66.5 % of the patients, there was no change, i. e. the patients were classified as stable or progressive at t1 and t2. In 17 % of the patients there was an improvement (t1 progressive, t2 stable), in 16.5 % a deterioration (t1 stable, t2 progressive) of the state of health. ▶ **Table 10** shows that the deterioration in health status (t1 stable, t2 progressive) can be shown in the scales "Impairment", "Shortness of breath", "Cough" and "Health status" of the QPF.

Discussion

The present study aimed to develop a disease-specific quality of life questionnaire (named QPF) for patients with fibrosing IIPs, i. e. IPF and NSIP, which would allow assessing particular issues on QoL in this patient group. The questionnaire represents the QoL in a real-life and patient-oriented manner. Advantages of our study were the large number of interviewed patients and the comparatively long follow-up period.

▶ **Table 10** Differences in scale mean with and without the external criterion "Prognosis".

	Significance difference in mean values t1–t2 "Improvement of prognosis" n = 34 *P*-Values	**Significance difference in mean values t1–t2 "Deterioration of prognosis" n = 34 *P*-Values**
QPF-scales		
Total	0.847	0.176
Conditions	0.190	0.124
Impairment	0.485	**0.020**
Problems	0.886	0.932
Shortness of breath	0.832	**0.001**
Cough	0.604	**0.017**
Health status	0.877	**0.022**

We used the Saint George Respiratory Questionnaire to cross-validate the QPF which is currently the most frequently used, particularly in validation studies.

The demographic features of the study population with a predominance of male sex (82.5 %) and a mean age of 71 years are characteristic of this patient group. While numbers of comorbidities were also representative of this patient population [33], some of the comorbid conditions might be underrepresented compared to other cohorts. However, the number and type of comorbidities were self-reported by the patients and may not reflect the general incidence [34].

It has to be taken into account that our patient group consists mainly of patients with a newly diagnosed lung disease. At this stage of the disease, it is unlikely that the health status will deteriorate within six months. At the other side there are died some patients in this time.

The analyses of the QPF revealed some problematic items which led to a reduction of the 6 scales with 42 items applied in this study to 5 scales with 23 items in a new and hopefully final version of the QPF. This new version will need to be validated again. The discriminatory power of the seventh item on the QPF-scale "Condition" ("In the last two weeks my family/friends was a big help.") had to be rated as insufficient with a discriminative power of 0.146). This item was thus eliminated because the low selectivity does not allow an assessment of how well it distinguishes between people with low and high burden of disease. In comparison, the analyses by Witt et al. using the SF-36 [20] showed a low sensitivity with regard to changes in QoL.

In the QPF "Cough" scale, the item "Do you have coughing attacks until you pass out?" is also characterized by a low selectivity. There may be an influence here from comorbidity with obstructive respiratory diseases. Two more items in this scale also had a low selectivity < .3 and were thus eliminated.

The QPF-scale "Problems" alpha was found to be too low. The selectivity indices also did not meet the statistical requirements because they were below 0.3 in 10 of 11 items and thus had no discriminatory power. The following three items on the QPF "Problems" scale had very low levels of discrimination power (< 0.15): "Have you noticed that your fingernails/toenails have changed?", "Do your fingers change color when it is cold?" and "Do you have swollen ankles in the evening?" The whole scale "Problems" was therefore eliminated. The questions mentioned tend to focus on differential diagnostic aspects and are therefore not relevant for assessing individual QoL.

There was no significant change after 6 months at the level of the overall scores in QPF or SGRQ but significant changes in several subscores: a deterioration in health status from the patient's and doctor's perspective was seen in the scales "impairment", "Shortness of breath" and "Health status" of the QPF. (▶ **Table 9**, ▶ **Table 10**). The same was true for the reduction in the overall score in the QPF in the sense of a deterioration and at the same time associated with an increase in the overall score in the SGRQ also indicating a deterioration of QoLs. The correlations of the QPF scales with those of the SGRQ are largely significant. The strongest correlations were found between the scales "QPF-condition" and "SGRQ-total". This could be taken as an indication that both instruments represent the construct QoL in a similar way.

In reality, it is usually difficult to find a suitable external criterion that tries to validate the patient's information about his or her QoL and to explain possible changes in the questionnaire. In the present study, global assessments (visual analogue scale) of the state of health of the patients, the degree of stress on the patient and an assessment of the progression of the disease were collected by the treating physicians. Studies have shown that the correlation between data on QoL and data on lung function is only moderate [35, 36]. With the help of lung function, extent of shortness of breath, frequency of coughing and distance covered in the 6-minute walk test, a maximum of 50 % explanation of the variance can be achieved. Conversely, this means that at least 50 % of the variance in QoL cannot be explained by these variables [35, 36]. Therefore, regarding the

responsiveness or sensitivity of the questionnaire, two other external criteria than lung-function were used to check whether the QPF can reflect clinically meaningful changes in QoL. A deterioration in health status was observed on the scales “impairment”, “shortness of breath”, “cough” and “health status”. This suggests that the QPF is sensitive to changes, which is particularly important for the patient group examined.

A limitation is that this questionnaire was validated in fibrosing IIPs and not in other forms of pulmonary fibrosis. However, the developers have chosen this large and uniform group of fibrosing ILDs and hypothesise that the QPF is also suitable for other entities which however has still to be proven. A Validation of the German Translation of this questionnaire is in press.

In conclusion, the QPF is a new questionnaire covering all important areas of QoL in patients with fibrosing IIPs. This questionnaire is suitable for both assessment of Qol and supplementing the medical history. The questionnaire appears to be also important for monitoring the progression of pulmonary fibrosis from the patient's point of view. The questionnaire can be used both in clinical trials and in clinical practice. Further validation studies are necessary, however.

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Conflict of interest

The authors declare that they have no conflict of interest.

References

[1] American Thoracic Society. European Respiratory Society. Idiopathic pulmonary fibrosis: diagnosis and treatment: international consensus statement. Am J Respir Crit Care Med 2000; 161: 646–664

[2] Raghu G, Collard HR, Egan JJ. An official ATS/ERS/JRS/ALAT statement: idiopathic pulmonary fibrosis: evidence-based guidelines for diagnosis and management. Am Resp Crit Care Med 2011; 183: 788–824

[3] Behr J, Prasse A, Wirtz H et al. Survival and course of lung function in the presence or absence of antifibrotic treatment in patients with idiopathic pulmonary fibrosis: long-term results of the INSIGHTS-IPF registry. Eur Respir J 2020; 56: 1902279

[4] Somogyi V, Chaudhuri N, Torrisi SE et al. The therapy of idiopathic pulmonary fibrosis: what is next? Eur Resp Rev 2019; 28: 195021

[5] Behr J, Günther A, Bonella F et al. S2k-Leitlinie Idiopathische Lungenfibrose - Update zur medikamentösen Therapie 2017. Pneumologie 2017; 71: 460–474

[6] King TEjr, Bradford WZ, Castro-Bernardini S et al. A phase 3 trial of pirfenidone in patients with idiopathic pulmonary fibrosis. N Eng J Med 2014; 370: 2083–2092

[7] Richeldi L, Costabel Selman M et al. Efficacy of a tyrosine kinase inhibitor in idiopathic pulmonary fibrosis. N Engl J Med 2011; 365: 1079–1087

[8] Bahmer T, Kirsten AM, Waschki B et al. Prognosis and longitudinal changes of physical activity in idiopathic pulmonary fibrosis. BMC Pulm Med 2017; 25: 104

[9] Chang JA, Curtis JR, Patrick DL et al. Assessment of health-related quality of life in patients with interstitial lung disease. Chest 2012; 116: 1175–1182

[10] De Vries J, Kessels BLJ, Drent M. Quality of life of idiopathic pulmonary fibrosis patients. Eur Resp J 2001; 17: 954–961

[11] De Vries J, Seebregts A, Drent M. Assessing health status and quality of life in idiopathic pulmonary fibrosis: which measure should be used? Respir Med 2001; 94: 273–278

[12] Glaspole I, Goh N, Hopkins P et al. Quality of life of patients with idiopathic pulmonary fibrosis (IPF) – what can the Australian IPF registry tell us? Am J Resp Crit Care Med 2014; 189: A1439

[13] King TEjr, Tooze JA, Schwarz MI et al. Predicting survival in idiopathic pulmonary fibrosis: scoring system and survival model. Am J Resp Crit Care Med 2001; 164: 1171–1181

[14] Kreuter M, Swigris J, Behr J. The clinical course of idiopathic pulmonary fibrosis and its association to quality of life over time: longitudinal data from the INSIGHTS-IPF registry. Resp Research 2019; 20: 59

[15] Kreuter M, Swigris J, Pittrow D et al. Health related quality of life in patients with idiopathic pulmonary fibrosis in clinical practice: INSIGHTS-IPF registry. Resp Res 2017; 18: 139

[16] Nishiyama O, Taniguchi H, Kondoh Y. A simple assessment of dyspnea as a prognostic indicator in idiopathic pulmonary fibrosis. Eur J Res Med 2010; 36: 1067–1072

[17] Nishiyamaa O, Taniguchia H, Kondoha Y et al. Health-related quality of life in patients with idiopathic pulmonary fibrosis. What is the main contributing factor? Res Med 2005; 99: 408–414

[18] Swigris JJ, Stewart AL, Gould MK et al. Patients’ perspectives on how idiopathic pulmonary fibrosis affects the quality of their lives. Health Qual Life Outcomes 2005; 3: 61

[19] Kreuter M, Ochmann U, Koschel D et al. Patientenfragebogen zur Erfassung der Ursachen interstitieller und seltener Lungenerkrankungen – klinische Sektion der DGP. Pneumologie 2018; 72: 446–457

[20] Witt S, Krauss E, Asunción NB et al. Psychometric properties and minimal important differences of SF-36 in Idiopathic Pulmonary Fibrosis. Resp Res 2019; 20: 47

[21] Kreuter M, Birrring SS, Wijsenbeek M et al. Deutschsprachige Validierung des „King’s Brief Interstitial Lung Disease (K-BILD)“. Lebensqualitätsfragebogens für interstitielle Lungenerkrankungen. Pneumologie 2001; 70: 742–746

[22] Guyatt GH, Berman LB, Townsend M et al. A measure of quality of life for clinical trials of chronic lung disease. Thorax 1987; 42: 773–778

[23] Jones PW, Quirk FH, Baveystock CM. The St. George’s Respiratory Questionnaire. Resp Med 1991; 85: 25–31

[24] Clark M, Cooper B, Singh S et al. A survey of nocturnal hypoxaemia and health related quality of life in patients with cryptogenic fibrosing alveolitis. Thorax 2001; 56: 482–486

[25] Martinez JAB, Martinez TY, Galhardo FPL et al. Dyspnea scales as a measure of health-related quality of life in patients with idiopathic pulmonary fibrosis. Med Sci Monit 2002; 8: 405–410

[26] Martinez TY, Pereira CA, dos Santos ML et al. Evaluation of the short-form 36-item questionnaire to measure health-related quality of life in patients with idiopathic pulmonary fibrosis. Chest 2000; 117: 1627–1632

[27] Swigris JJ, Wilson H, Esser D et al. Psychometric properties of the St George’s Respiratory Questionnaire in patients with idiopathic pulmonary fibrosis: insights from the INPULSIS trials. BMJ Open Respir Res 2018; 5: e000278

[28] Swigris JJ, Esser D, Wilson H et al. Psychometric properties of the St George's Respiratory Questionnaire in patients with idiopathic pulmonary fibrosis. Eur Respir J 2017; 49: 1601788

[29] Swigris JJ, Andrae DA, Churney T et al. Development and Initial Validation Analyses of the Living with Idiopathic Pulmonary Fibrosis Questionnaire. Am J Respir Crit Care Med 2020; 15: 1689–1697

[30] Graney B, Johnson N, Evans CJ et al. Living with idiopathic pulmonary fibrosis (L-IPF): Developing a patient-reported symptom and impact questionnaire to assess health-related quality of life in IPF. Am J Respir Crit Care Med 2017; 195: A5353

[31] Berry CE, Drummond MB, Han MK et al. Relationship between lung function impairment and health-related quality of life in COPD and interstitial lung disease. Chest 2012; 142: 704–711

[32] Kirsten D, de Vries U, Costabel U et al. Linguistic validation of the "German Lung Fibrosis Health Related Quality of Life Questionaire". Pneumologie 2021: doi:10.1055/a-1334-2745. Online ahead of print

[33] Raghu G, Amatto VC, Behr J et al. Comorbidities in idiopathic pulmonary fibrosis patients: a systematic literature review. Eur Res J 2015; 46: 1113–1130

[34] Raghu G, Freudenberger TD, Yang S et al. High prevalence of abnormal acid gastro-oesophageal reflux in idiopathic pulmonary fibrosis. Eur Resp J 2006; 27: 136–142

[35] Jones PW. Issues cocerning health-related quality of life in COPD. Chest 1995; 107: 187S–193S

[36] Jones PW, Brusselle G, Dal Negro W et al. Health-related quality of life in patients by COPD severity within primary care in Europe. Respir Med 2011; 105: 57–66