Assessment Of The Quality Of Life Of Patients With Idiopathic Pulmonary Fibrosis In Spain: Results From The OASIS Study

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INTRODUCTION

- Idiopathic pulmonary fibrosis (IPF) is a chronic, progressive and fatal disease of unknown cause, occurring primarily in older adults, limited to the lungs, and associated with the histopathologic and/or radiologic pattern of usual interstitial pneumonia. [1]
- As the disease progresses, lung function declines with the consequent worsening of dyspnea and quality of life (QoL) impairment. [2]
- It is estimated that IPF affects about 7,500 people in Spain. [3]

AIM

- This study aims to estimate the QoL of IPF according to forced vital capacity (FVC) % predicted at baseline in adult patients along 12 months.
- Secondary objectives aimed to explore the determinants of QoL and QoL variation according to FVC decline over 12 months.

METHODS

Study design

- The OASIS Study is a prospective, observational, multicentric study based on newly collected data of patients with a confirmed diagnosis of IPF in secondary care settings (Pulmonology Services) followed during 12 months.
- As per clinical practice, three visits per patient were performed (baseline, the closest visit to 6 months –T6- and 12 months after baseline –T12-).
  - The inclusion period was from December 2017 to July 2018. The mean (standard deviation (SD)) follow-up were 12.40 (1.07) months.
- A total of 204 consecutive patients ≥ 40 years of age diagnosed with IPF according to last ATS/ERS/JRS/ALAT IPF guideline [1], who met the selection criteria were included from 28 sites in Spain.
- Patients were classified in 3 groups according to their FVC % predicted at baseline: FVC < 50 %, FVC 50-80% and FVC >80%.
- QoL was assessed through three validated QoL questionnaires:
  - **Saint George Respiratory Questionnaire (SGRQ):** a specific instrument to measure impact on overall health, daily life, and perceived well-being in patients with obstructive airways disease. It includes 50 items divided into three components (symptoms, activity, and impacts). Scores range from 0-100, where 0 is the least limitations and 100 is most limitations.
  - **Euro-QoL-5 dimensions-5 levels (EQ-5D-5L):** a questionnaire to assess health status through value scores in 5 domains (mobility, self-care, usual activities, pain or discomfort, and anxiety or depression) and a visual analogue scale (VAS). Index value scores range from -0.654 (worst QoL) to 1.000 (best QoL). VAS scores of health status range from 0-100, where 0 is the best state and 100, the worst state.
  - **Barthel index:** ordinal scale to measure performance of the patient on his/her activities of daily living. Scores range from 0-100, where 0 is a totally dependent patient and 100 a completely independent patient.
- Bivariate exploratory methods and multivariate linear models were used to explore factors related to QoL.
- To estimate QoL variation associated to FVC decline, patients were classified according to their relative FVC decline along 12 months in 3 subgroups: >10%, 10% to 5% and <5%.

RESULTS

Population characteristics

- 204 consecutive IPF patients were included: 77% male, average age (SD) 70.8 (7.6) years (Table 1).
- At baseline, FVC % predicted was <50%, 50–80% and >80% in 10.8%, 74.5% and 14.7% of patients, respectively (Table 1).
- Mean (SD) time between IPF diagnosis and baseline visit was 1.92 (1.85) years [23.19 (22.31) months] (Table 1).
- In general, most of the patients (>70%) were not active workers during the study. Among patients with less impaired lung function (FVC % predicted <80%), 26.7% of the patients were active workers (Table 1).

Table 1. *Characteristics of patients at baseline.*

Characteristic	FVC <50% N=22	FVC 50-80% N=152	FVC >80% N= 30
Sex, n (%)			
Male	18 (81.8%)	120 (78.9%)	19 (63.3%)
Female	4 (18.2%)	32 (21.1%)	11 (36.7%)
Age (years), mean (SD)	70.32 (8.52)	71.36 (7.21)	68.33 (8.54)
Time since IPF diagnosis to baseline visit (years), mean (SD)	2.00 (1.69)	1.95 (1.91)	1.73 (1.67)
Smoking habit, n (%)			
Non smokers	8 (36.4%)	48 (31.6%)	8 (26.7%)
Former smokers[2]	14 (63.6%)	101 (66.4%)	20 (66.7%)
Smokers	0 (0.0%)	3 (2.0%)	2 (6.7%)
IPF associated comorbidities, n (%)			
Yes	18 (81.8%)	110 (72.4%)	19 (63.3%)
No	4 (18.2%)	42 (27.6%)	11 (36.7%)
Occupational or environmental exposure factors, n (%)			
Yes	10 (45.5%)	75 (49.3%)	12 (40.0%)
No	12 (54.5%)	73 (48.0%)	18 (60.0%)
Unknown	0 (0.0%)	4 (2.6%)	0 (0.0%)
Lung function, mean (SD)			
FVC post BD (L)	1.68 (0.41)	2.53 (0.63)	3.34 (0.94)
FVC post BD (%)	50.00 (10.02)	75.95 (13.33)	98.23 (16.65)
Six-minute walk test, mean (SD)			
Distance (m)	376.45 (122.65)	449.78 (92.71)	472.55 (103.70)
Patients receiving antifibrotic treatment, n (%)			
Yes	16 (72.7%)	129 (84.9%)	21 (70.0%)
No	6 (27.3%)	23 (15.1%)	9 (30.0%)
Employment status, n (%)			
Active worker	2 (9.1%)	14 (9.2%)	8 (26,7%)
Not active worker	20 (90.9%)	138 (90.8%)	22 (73.3%)

BD: bronchodilator; FVC: forced vital capacity; IPF: idiopathic pulmonary fibrosis; L: litre; n: number of patients; SD: standard deviation.

SGRQ

- The mean (SD) overall SGRQ score was 32.51 (16.55) at T0, with statistically significant differences between FVC predicted groups (p=0.0013). At T12, patients with FVC<50% had statistically significantly more limitations than FVC>80% patients by means of overall SGRQ score (p=0.0233) (Table 2).
- Results from the total sample showed a significant decrease in SGRQ score along the study (p=0.0015) (Table 2).
  - Patients with a baseline FCV % predicted of 50-80% reported a statistically significant worsening of their SGRQ scores (p<0.001). In contrast, patients in both extreme FVC % predicted groups did not show a decrease in their QoL.

Table 2. *SGQR scores (baseline, T12 and change along the study) according to FVC % predicted at baseline*

	Total N=125	FVC<50% N=10	FVC 50-80% N=96	FVC>80% N=19	p[1]
Overall score					
T0					
Mean (SD)	32.51 (16.55)	46.46 (13.60)	32.84 (16.26)	23.50 (14.30)	0.0013
T12					
Mean (SD)	35.35 (19.44)	40.15 (21.49)	36.81 (19.49)	25.43 (15.44)	0.0362
CHANGE T12 - T0					
Mean (SD)	2.84 (14.49)	-6.30 (27.86)	3.97 (13.04)	1.93 (10.38)	0.8265
p[2] (change)	0.0015	1.0000	0.0027	0.0799	

[1] Kruskal-Wallis test; [2] Wilcoxon (paired data). FVC: forced vital capacity; IPF: idiopathic pulmonary fibrosis; n: number of patients; SD: standard deviation.

EQ-5D-5L and EQ-VAS

- At baseline, the mean (SD) index value was 0.81 (0.18), with statistically significant differences between FVC predicted groups reflecting a worse QoL in patients with a less preserved lung function (p=0.0107) (Table 3).
- The mean (SD) EQ–VAS (0-100) score was 68.05 (18.83) at T0 with statistically significant lower scores in patients with lower FVC% predicted (p=0.0176) (Table 3).
- Results from the total sample showed a significant decrease patients' health status and EQ-VAS along the study mainly driven by the significant decline observed in patients from the FCV % predicted group 50-80% (p-value of change T12-T0 <0.001 in both) (Table 3).
  - Changes in health status and EQ-VAS were not statistically significant among patients from FVC <50% and FVC>80%.

Table 3. *EQ-5D-5L index value and EQ-VAS scores (baseline, T12 and change along the study) according to FVC % predicted at baseline*

	Total	FVC<50%	FVC 50-80%	FVC>80%	p-value
EQ-5D-5L Index value, n	**147**	**12**	**117**	**18**	
T0					
Mean (SD)	0.81 (0.18)	0.69 (0.17)	0.82 (0.17)	0.85 (0.24)	0.0107
T12					
Mean (SD)	0.76 (0.25)	0.64 (0.34)	0.77 (0.24)	0.82 (0.22)	0.1649
CHANGE T12 – T0					
Mean (SD)	-0.05 (0.19)	-0.05 (0.36)	-0.05 (0.18)	-0.02 (0.11)	0.4181
p[2] (change)	0.0126	0.6772	0.0044	0.5999	
EQ-VAS (0-100), n	**158**	**13**	**125**	**20**	
T0					
Mean (SD)	68.05 (18.83)	60.00 (16.20)	67.54 (19.35)	76.50 (14.15)	0.0176
T12					
Mean (SD)	64.15 (20.24)	61.15 (22.47)	63.04 (20.41)	73.00 (15.84)	0.1218
CHANGE T12 – T0					
Mean (SD)	-3.91 (16.52)	1.15 (20.63)	-4.50 (17.07)	-3.50 (8.13)	0.4083
p[2] (change)	0.0036	0.6113	0.0037	0.0646	

[1] Kruskal-Wallis test; [2] Wilcoxon (paired data). FVC: forced vital capacity; IPF: idiopathic pulmonary fibrosis; n: number of patients; SD: standard deviation.

Barthel Index

- At baseline, the mean (SD) overall Barthel index score was 97.96 (6.57) at T0, being 100 an independent patient (Table 4).
  - No significant differences were observed between FVC % predicted groups at baseline.
  - Results did not reveal significant changes along the study neither significant differences with regard to Barthel index score change between FVC groups.

Table 4. *Barthel Index (baseline, T12 and change along the study) according to FVC % predicted at baseline*

	Total N=159	FVC<50% N=11	FVC 50-80% N=127	FVC>80% N=21	p[1]
Overall score					
T0					
Mean (SD)	97.96 (6.57)	97.73 (5.18)	98.15 (6.69)	96.90 (6.61)	0.4190
T12					
Mean (SD)	96.04 (11.64)	92.73 (15.39)	96.26 (11.07)	96.43 (13.15)	0.6318
CHANGE T12 - T0					
Mean (SD)	-1.92 (11.61)	-5.00 (14.49)	-1.89 (11.36)	-0.48 (11.82)	0.4082
p[2] (change)	0.0915	0.3750	0.0929	0.8125	

[1] Kruskal-Wallis test; [2] Wilcoxon (paired data). FVC: forced vital capacity; IPF: idiopathic pulmonary fibrosis; n: number of patients; SD: standard deviation.

Determinants of QoL

- Factors related with the decrease of the IPF- related QoL scores were estimated for the SGRQ and for the EQ-5D-5L and EQ-VAS. Results revealed significant associations in patients with FVC 50-80%:
  - Regarding lung function:
    - » For each additional unit in the 6MWD start O2 saturation at T0, the EQ-VAS decreased 1.45 points (p=0.0351)
    - » For each additional unit in the FVC rate change by year (T12), EQ-5d-5L index value increased 0.0022 (p=0.0056).
  - To not use non-pharmacological treatment (eg.: oxygen therapy) was associated with a lower QoL:
    - » Overall SGRQ score was 13.07 points lower in patients not receiving non-pharmacological treatment (p=0.0008).
    - » EQ-VAS score was 14.07 points higher in patients not receiving non-pharmacological treatment (p=0.0031) suggesting that the use of supplementary oxygen may improve IPF patients' QoL.
  - For each additional unit in the Barthel score at baseline, the overall SQGR score decreased by 0.37 points (p=0.0400) and the EQ-5D-5L index value decreased by 0.0055 points (p=0.0491).

QoL variation associated with FVC decline

- Patients with higher relative FVC decline reported increased worsening of their QoL throughout the study (T0-T12) both for the mean global change in the overall SGRQ scores (p=0.0716) and in EQ-VAS (p=0.0814) (Table 5).

Table 5. *QOL variation (overall SGRQ and EQ-VAS) according to relative FVC decline.*

	FVC decline (Relative change)			
	>10%	From 10% to 5%	<5%	P-value
Absolute change overall SGRQ score (T0-T12), n	36	20	64	
Mean (SD)	6.09 (14.95)	4.32 (11.24)	-0.53 (13.35)	0.0716
Absolute change EQ-VAS score (T0-T12), n	24	31	85	
Mean (SD)	-7.86 (19.60)	-4.39 (11.71)	0.29 (15.33)	0.0814

CI: confidence interval; FVC: forced vital capacity; IPF: idiopathic pulmonary fibrosis; n: number of patients.

CONCLUSIONS

- **Patients with lower FVC% predicted at baseline had more limitations and worse QoL than patients with a less impaired lung function.**
- **Throughout the study, patients with a higher FVC decline reported a higher QoL loss highlighting the importance of preventing FVC decline.**
- **Slowing disease progression is relevant to preserve patients' QoL and independence.**

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