Socioeconomic impact of acute exacerbations of IPF in Spain: prospective, observational, multicentric study (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].
- In Spain, IPF prevalence is estimated to be around 13 cases per 100,000 women and 20 per 100,000 men, affecting about 7,500 patients [2].
- The course of IPF includes acute exacerbations (AE-IPF) with an estimated incidence of 4.1 AE-IPF/100 patient-year [3,4] being, patients with a lower forced vital capacity (FVC) at higher risk of suffering AE-IPF [5].
- AE-IPF lead to a significant decline in lung function and are associated with high short-term mortality rates (around 50% [6] – 85% [5]). AE-IPF are associated with high use of healthcare resources and costs and important contributors to total annual IPF-related costs [7].

AIM

- This study aims to characterize the economic impact and the quality of life (QoL) of IPF patients associated with AE-IPF in Spain during a follow-up period of 12 months.

METHODS

Study design

- The OASIS Study is a descriptive, prospective, observational, multicentric real world data study based on newly collected data of patients with a confirmed diagnosis of IPF followed-up for one year in secondary care settings (Pulmonology Services).
- A total of 204 patients diagnosed with IPF according to 2011 ATS/ERS/JRS ALAT guidelines [1] who met the selection criteria were included from 28 sites in Spain from December 2017 to July 2018. The mean (SD) follow-up was 12.40 (1.07) months.
- AE-IPF was defined as an acute, clinically significant respiratory deterioration characterized by an evidence of new widespread alveolar abnormality. AE-IPF and its management-were registered in each visit.
- AE-IPF associated resources included direct health costs, non-health costs and indirect costs.
- FVC decline was estimated as relative change by means of: [(Final FVC % predicted – Initial FVC % predicted) / Initial FVC % predicted] x100
- QoL was assessed through three validated questionnaires:
  - **Saint George Respiratory Questionnaire (SGRQ).** It includes 50 items divided into three components (symptoms, activity, and impacts). Scores range from 0 (least limitations) – 100 (most).
  - **Euro-QoL-5 dimensions-5 levels (EQ-5D-5L) and EQ-visual analogue scale (EQ-VAS).** Index value scores range from -0.654 (worst QoL) to 1.000 (best QoL). EQ-VAS scores range from 0 (worst state) – 100 (best imaginable).
  - **Barthel index.** Scores capture patient's independence and range from 0 (totally dependent) – 100 (completely independent).

RESULTS

- A total of 204 consecutive IPF patients were included: 77% male, average age (SD) 70.8 (7.6) years. Patients were classified according if they had suffered at least 1 AE-IPF or not during the study period [exacerbated patients: n= 22 (10.8%); non-exacerbated patients n= 182 (89.2%)].
  - In the overall population, the mean (SD) number of AE-IPF by patient was 0.14 (0.44). Among patients who suffered AE-IPF, mean (SD) number of AE-IPF/patient was 1.27 (0.63) with a mean duration of 16.50 (18.38) days per event.
- 14/30 (46.7%) patients who died along the study had suffered at least 1 AE-IPF at some point during the study. 6/22 (27.3%) patients died during an AE-IPF.

Use of resources

- Use of resources and costs were estimated in the cost-evaluable population which included those patients with at least 6 months of follow-up (14 patients with AE-IPF and 166 patients without AE-IPF).
- Patients who suffered at least 1 AE-IPF made significantly more primary care visits along the study compared with patients who did not suffer AE-IPF (57.1% vs 28.3%; p=0.0245). Specialized care visits revealed no significant differences except for the nursing home visits, which were more common among AE-IPF patients (p=0.0056).
- Patients with at least 1 AE-IPF attended significantly more the hospital care area compared with patients without AE-IPF (need of emergency visit, number of visits, hospital admissions and number of hospitalizations) (p<0.0001 all of them). No statistically significant differences were found with regard to the days of hospitalization and need for ICU stay between groups (Table 1).

Table 1. *Summary of use of health-related resources in patients who suffered at least 1 AE-IPF and patients without AE-IPF during the study period.*

Use of resources along the study*	Patients with at least 1 AE-IPF N=14	Patients without AE-IPF N=166	p-value
Number of visits to primary care area, mean (SD)	0.57 (1.16)	0.08 (0.47)	0.0106
Number of visits in hospital care area, mean (SD)	2.07 (2.59)	0.22 (0.64)	<0.0001
Did the patient attend emergency room related to IPF? Yes n (%)	14 (100%)	14 (14.5%)	<0.0001
Did the patient require hospital admission related to IPF? Yes n (%)	11 (78.6%)	10 (6.0%)	<0.0001
Number of hospitalizations by patient, mean (SD)	2.29 (1.86)	0.13 (0.56)	<0.0001
Days of hospitalization, mean (SD)	7.25 (5.16)	9.00 (9.55)	0.7611
Need for ICU stay, Yes n (%)	1 (5.0%)	4 (19.0%)	0.3433

*Includes use of resources collected at study visits and due to AE-IPF. FVC: forced vital capacity; ICU: intensive care unit; IPF: idiopathic pulmonary fibrosis; n: number of patients; SD: standard deviation.

- 180 patients specified 334 pharmacological treatments related to IPF along the study. Of those treatments:
  - Antifibrotics represented 41% and 61.7% and systemic corticosteroids represented 12.8% and 4,7% among patients with and without AE-IPF, respectively.
- No differences were observed with regard to non-pharmacological treatments.
- With regard to direct non-health use of resources, transport use was required for 42.9% of patients with at least 1 AE-IPF compared with 6.6% of patients without exacerbations (p=0.0005).
- 50% of patients who suffered at least 1 AE-IPF required a caregiver compared with the 19.9% of those without AE-IPF (p=0.0092).

Costs

- Patients who experienced at least 1 AE-IPF showed a significantly higher annual cost of IPF compared to patients who did not suffer AE-IPF along the study (mean annual cost: ≥1AE-IPF: 31763.31€ vs no AE-IPF: 22977.90 €; p=0.0399) (Table 2).
  - Annual direct health IPF-related costs had the greatest weight in both groups, but they were statistically higher among patients who suffered at least 1 AE-IPF.
  - AE-IPF patients incurred on significantly higher final living costs compared with patients without exacerbations.
  - Pharmacological treatments were the cost with greatest weight on the total annual costs followed by the days of hospitalizations.

Table 2. *Annual IPF-related costs in patients who suffered at least 1 AE-IPF and patients without AE-IPF during the study period.*

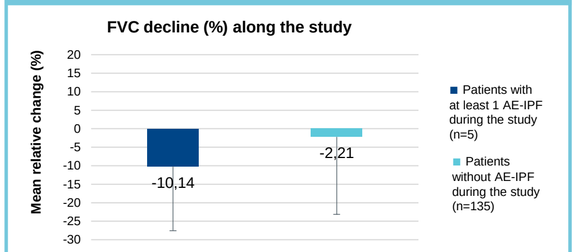
Annual costs per patient (euros)	AE-IPF: Patients with at least 1 AE-IPF N=14	AE-IPF: Patients without AE-IPF N=166	p-value
Total IPF-related costs (€), mean (SD)	**31763.31 (19766.75)**	**22977.90 (14831.92)**	**0.0399**
Direct health IPF-related costs (€), mean (SD)	**30978.82 (19158.61)**	**22701.91 (14607.84)**	**0.0488**
Primary care visits	44.26 (62.15)	29.07 (66.88)	0.4134
Secondary care visits (specialized care visits)	652.32 (591.41)	383.24 (302.03)	0.0041
Emergency visits (primary care visits)	42.77 (86.67)	6.31 (35.36)	0.0018
Emergency visits (hospital)	355.98 (444.38)	37.27 (110.48)	<0.0001
Hospitalizations- admission in emergency room	383.16 (443.40)	107.77 (803.24)	0.2077
Hospitalizations- days of hospitalization	7388.44 (7041.59)	953.04 (6165.60)	0.0003
Hospitalizations- in ICU	1262.79 (4724.94)	319.50 (2508.07)	0.2163
Outpatients tests (laboratory test, pulmonary function test, other examinations)	1317.05 (1289.07)	691.53 (540.18)	0.0004
Pharmacological treatment*	18405.23 (14594.68)	19662.93 (11881.29)	0.7092
Non-Pharmacological treatment*	151.83 (259.55)	401.60 (1353.74)	0.4926
End of life (palliative care)	975.00 (1168.33)	109.64 (488.72)	<0.0001
Direct non-health IPF-related costs (€), mean (SD)	**776.97 (1422.33)**	**236.43 (1145.78)**	**0.0981**
Indirect costs (€), mean (SD)	**7.52 (28.15)**	**39.56 (305.56)**	**0.6961**

*except treatments administered in hospitalization.
FVC: forced vital capacity; ICU: intensive care unit; IPF: idiopathic pulmonary fibrosis; n: number of patients; SD: standard deviation.

FVC decline

- FVC decline analysis was performed with those patients with paired data at start and at the end of the study.
- Patients who experienced at least 1 AE-IPF suffered a FVC decline along the study (12 months) 4.7 times greater than those patients who did not suffer any AE-IPF.
  - Mean relative change was -10.14 (17.41) in patients with ≥ 1 AE-IPF and -2.21 (20.95) in patients without AE-IPF (p=0.4385, not significant probably due to the small sample size in AE-IPF group, but clinically meaningful) (Figure 1).

Figure 1. *Relative FVC decline along the study (12 months of follow-up).*



FVC: forced vital capacity. Error bars describe standard deviation.

Quality of life

- Patients with at least 1 AE-IPF experienced a substantial decline of QoL compared with patients without AE-IPF (3-fold to 5-fold in all the questionnaires), although these differences did not reach statistical significance probably due to small sample in the exacerbation group (Table 3).
- IPF patients without AE-IPF also suffered statistically significant (p<0,05) impairment of QoL according to all the measured QoL scores except for the Barthel (p=0.0886) (Table 3).

Table 3. *QoL scores in patients who suffered at least 1 AE-IPF and patients without AE-IPF during the study period.*

Scores change (end of study vs baseline)	Patients with at least 1 AE-IPF	Patients without AE-IPF	p[1]
SGRQ –Overall score, mean (SD) [n]	9.11 (31.87) [n=8]	2.41 (12.66) [n=117]	*0.8126*
P[2] (change)	*0.5469*	*0.0013*	
EQ-5D-5L – Index value, mean (SD) [n]	-0.23 (0.42) [n=6]	-0.04 (0.18) [n=141]	*0.5821*
P[2] (change)	*0.6250*	*0.0182*	
EQ – VAS, mean (SD) [n]	-18.38 (21.14) [n=8]	-3.13 (15.96) [n=150]	*0.0500*
P[2] (change)	*0.0625*	*0.0148*	
Barthel – Overall score, mean (SD) [n]	-6.43 (28.68) [n=7]	-1.71 (10.36) [n=152]	*0.8719*
P[2] (change)	*0.6250*	*0.0886*	

1. P-value of the difference between groups (U-Mann-Witney); 2. P-value of the change (paired data Wilcoxon)

- In the whole sample, results from the linear regression revealed statistically significant association between QoL scores and change of FVC throughout the study. For each additional 1% of FVC:
  - SGRQ: mean overall score decreased 0.36250 points (p<0.0001),
  - EQ-5D-5L mean index value increases 0.00358 points (p<0.0001) and EQ-VAS increased 0.28802 points (p<0.0001),
  - Barthel: mean overall score increased 0.17684 points (p=0.0011),

indicating a significant relationship between FVC decline and loss in QoL.

CONCLUSIONS

- **AE-IPF events are associated with a substantial increase in the use of health resources.**
- **Suffering an AE-IPF often results in a quicker progression and FVC decline over time.**
- **Patients who suffered at least 1 AE-IPF showed a significant impairment of their QoL which is rapidly reduced compared with patients who did not suffer AE-IPF.**
- **Preventing or avoiding AE-IPF is important to reduce the use of health resources and FVC decline of IPF patients, as well as to preserve their QoL, thus lowering the economic impact of IPF.**

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