

Idiopathic pulmonary fibrosis in a Swiss interstitial lung disease reference centre

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Summary

BACKGROUND: Idiopathic pulmonary fibrosis (IPF) differs substantially from other idiopathic interstitial pneumonias regarding disease trajectory and the appropriate management strategies, making meticulous diagnosis essential. However, patient characteristics and clinical practice vary between clinical trials, and real life and registries provide the opportunity to critically analyse current clinical practices in order to ultimately improve patient care.

METHODS: We aimed to identify characteristics of our baseline IPF cohort at initiation of a web-based registry for patients with idiopathic interstitial pneumonia. Baseline and 6-month follow-up data from all consecutive IPF patients consulting at our centre over 2 years were analysed.

RESULTS: Forty IPF patients were included for baseline and 23 for longitudinal analysis. Besides many similarities to other IPF populations, our cohort included considerably fewer women. Forced vital capacity impairment in our cohort was more severe and mortality prediction poorer than in clinical trials, which emphasises the importance to confirm the applicability of clinical trial results with data from real life settings.

CONCLUSION: Registries for rare diseases such as IPF are a valuable resource for studying the course of the disease under current compliance with diagnostic and treatment guidelines and to appreciate local epidemiological particularities.

Key words: *idiopathic interstitial pneumonia, idiopathic pulmonary fibrosis, registry, real life practice, gender differences, cohort study*

Introduction

Idiopathic pulmonary fibrosis (IPF) is the most frequent and severe form of idiopathic interstitial pneumonia (IIP) [1, 2]. Prompt and correct diagnosis of IPF is crucial, since antifibrotic drugs are approved for IPF only and its management differs from that of non-IPF IIPs [3, 4]. Although guidelines and national recommendations for di-

agnosis and treatment are available, real-life standards often diverge and information about regional discrepancies is sparse [5–8]. Specifically, in rare diseases, critical review of current standards by use of registry data can elucidate clinical reality and guide real-life practices.

The aim of this brief communication is to report characteristics of our baseline IPF cohort revealed at initiation of our web-based registry for patients with IIP.

Methods and results

We retrospectively analysed all consecutive IPF patients consulting at our Swiss reference centre over 2 years. Clinical data were collected and stored directly by means of electronic case report forms, with automatic plausibility checks, on a web-based platform (ALABUS[®], Alabus AG, Zug, Switzerland).

Data on demographics, risk factors, comorbidities, medication, symptoms, physical examinations, pulmonary function tests, 6-minute walk tests, arterial blood gas analysis, chest computed tomography (CT) scans, bronchoscopy (including bronchoalveolar lavage), surgical lung biopsy, multidisciplinary discussion and current therapy (including oxygen) were assessed. For the 6-month longitudinal observation, we collected those parameters again, plus rate of hospitalisations, exacerbations, and death. Approval by the local ethics committee was obtained for data acquisition (Swiss Ethics Committee, Bern, approval number KEK 246/15 PB_2016-01524).

Forty patients met the inclusion criteria. Longitudinal data 6 months after the first data entry were available for 23 patients. Seventeen patients were referred only for a second opinion or were lost to follow up for other reasons. Patient characteristics including exposures, symptoms at presentation, diagnostic tests, comorbidities and ILD severity are reported in [table 1](#).

Discussion

Interestingly, we found, that our IPF patients were almost exclusively men (98%), whereas other studies report a proportion of male patients ranging from 57% in Northern

Author contributions
SG and PZ contributed equally to this manuscript. MF designed the study. SG, PZ, and MF made substantial contributions to conception of the study and contributed to acquisition of data, analysis and interpretation of data acquired, analyzed data and prepared the manuscript. SB, AP, and TG contributed substantially by critical revision for important intellectual content; all authors have given final approval of the version to be published.

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Italy, to 78% in Germany [9–17]. Compared with women, men are at greater risk of developing IPF, and have faster disease progress and an increased mortality [2, 18, 19]. Traditionally men more frequently chose occupations that are associated with dust exposures. Exposure to agricultural, wood, stone and several metal dusts has been shown to increase IPF risk, more so in male smokers [20, 21].

Table 1: Patient characteristics at baseline including pulmonary function tests at follow-up.

Demographics	Sex, male	39 (98)	
	Race, Caucasian	37 (88)	
	Age, years	70 (43 to 85)	
Exposures	Ever smokers	32 (80)	
	Smoked pack-years	32.9 ± 16.6	
	Farming	4 (10)	
	Welding	4 (10)	
	Asbestos	4 (10)	
	Birds (droppings/feather)	3 (7.5)	
	Dust	2 (5)	
Symptoms	Dyspnoea only	8 (20)	
	Cough only	8 (20)	
	Dyspnoea and cough	19 (47.5)	
Investigations	Multidisciplinary discussion	20 (50)	
	Bronchoalveolar lavage	19 (48)	
	Transbronchial biopsy	6 (15)	
	Surgical lung biopsy	19 (48)	
Composite Index	GAP Index	4.45 ± 1.72	
	GAP Stage I	10 (26.3)	
	GAP Stage II	20 (52.6)	
	GAP Stage III	8 (21.1)	
Comorbidities	Lung cancer	3 (7.5)	
	Pulmonary hypertension	7 (17.5)	
	Pulmonary embolism	3 (7.5)	
	Arterial hypertension	13 (32.5)	
	Coronary artery disease	12 (30)	
	Obesity	10 (25)	
	Obstructive sleep apnoea	9 (22.5)	
	Gastroesophageal reflux	8 (20)	
	Depression	2 (5)	
	Baseline	Follow-up	p-value[#]
FVC, L	2.60 ± 0.83	2.46 ± 0.82	0.09
FVC, % predicted	65.1 ± 17.4	60.5 ± 16.9	0.12
FEV1, L	2.17 ± 0.67	2.08 ± 0.68	0.05
FEV1, % predicted	70.7 ± 18.4	66.3 ± 18.6	0.09
FEV1/FVC, %	84.1 ± 5.2	85.1 ± 7.2	0.58
DLCO	3.89 ± 1.6	3.69 ± 1.2	0.09
DLCO, % predicted	43.3 ± 17.9	40.7 ± 11.2	0.12

DLCO = diffusion capacity of the lung for carbon monoxide (ml/min/mm Hg/l); FVC = forced vital capacity; FEV1 = forced expiratory volume in 1 second; GAP = gender, age, physiology (FVC, DLCO) Data are presented as n (%) or mean ± standard deviation/median (range) * Pulmonary function data from our clinic available for 38 patients (2 tested externally). [#] Paired t-test comparing baseline and 6-month follow-up in 23 patients with available data

Nearly half of our patients reported occupational exposures and the majority were previous smokers. In Switzerland even now 30% of men and 24% of women smoke [22], although in the past this gender difference was more pronounced. Besides these exposure differences between genders, there are diverging theories hypothesising that the male predominance in IPF is due to differences in sex hormones, which has also been suggested by animal studies using the bleomycin model of lung fibrosis [23]. So far, no clinical studies on sex hormones as modulators of pulmonary fibrosis in humans are available. However, evidence on sex hormone receptor expression in fibrotic lung tissue is evolving [24]. The reason for the small number of women in our IPF population remains unclear; possible explanations are a regional underdiagnosis [25] or a more thorough exclusion of secondary causes of interstitial lung disease in women. Reasons for sex differences in IPF prevalence warrant further investigation.

Our IPF population had more severe lung function impairment (mean forced vital capacity [FVC] 65% predicted) compared with other registries and large clinical trial cohorts (FVC 71–82% predicted) [3, 9, 11, 26, 27]. Compared with our and other registries [9], the populations of the phase III pharmacological trials included more patients with GAP stage I (40%) and fewer with GAP stage III (9%) (GAP score based on gender, age, physiology) [26]. This indicates that patients in clinical trials have less severe disease and better prognosis compared with real life, and might suggest that our patients were diagnosed at later disease stages. Clinical trials on safety and efficacy of antifibrotic agents in real-world settings are emerging [28, 29] and further studies will hopefully confirm the benefit of antifibrotic medications in the general IPF population.

Age- and smoking-related comorbidities in IPF are highly prevalent and their management is challenging [30]. Comorbidities have a significant impact on quality of life, morbidity, and mortality, and even though IPF is a fatal disease every fifth IPF patient dies from unrelated causes [31]. In contrast to our observations, studies that specifically screen for comorbidities in their populations report higher prevalences [30, 32–37], which highlights the importance of specific screening in populations at risk.

We diagnose IPF according to the current ATS/ERS guidelines [5] and as previously described in our interstitial lung disease centre [38]. We found only 50% of our IPF cases were diagnosed by formal multidisciplinary team discussion. Even though this team approach is considered the gold standard for diagnosis [5, 6], in real-life practice it is still implemented poorly with only about 20% of cases diagnosed in multidisciplinary conferences [9, 11]. Possible reasons are the high demand on time and resources, and the current lack of clear guidance on the format of an ideal multidisciplinary team discussion [38–40].

Conclusion

We briefly summarised initial data from our local IPF cohort and the pilot study for an open-end, multicentre prospective observational cohort study including patients with IIP referred to specialised centres in Switzerland. Our data show that patient characteristics, diagnostic standards and treatments are mostly, but not in every aspect, consistent with international data and recommendations. Most

strikingly, there are almost no women diagnosed with IPF in our cohort. Registries for rare diseases offer opportunities to evaluate the real-life situation and contribute to more effective care for our patients.

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Competing interests

MF has received travel support, advisory board and speaker fees as well as research funding from Boehringer Ingelheim, Roche and Internune. TG has received advisory and speaker fees from BI and Roche. SB received travel support and advisory board fees from MSD, Roche and Bristol-Myers Squibb outside the submitted work, and grants from AstraZeneca outside the submitted work.

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