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Understanding the Clinical Course Of Idiopathic Pulmonary Fibrosis

S17 THE BURDEN OF IDIOPATHIC PULMONARY FIBROSIS IN THE UNITED KINGDOM: A RETROSPECTIVE, MATCHED COHORT STUDY

[1]M Storm, [2]I Tran, [3]H Strongman, [2]J Fredriksson, [4]T Maher. *[1]IHS Life Sciences, Washington DC, USA; [2]Roche Products Ltd, Welwyn Garden City, UK; [3]Clinical Practice Research Datalink, London, UK; [4]Royal Brompton and Harefield NHS Foundation Trust, London, UK*

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Background Idiopathic pulmonary fibrosis (IPF) is a specific form of chronic, progressive fibrosing interstitial pneumonia which primarily affects older adults, for which very few treatments have existed. While attention has been paid to quantifying the rising incidence and prevalence of the disease, little has been done to quantify the impact of this disease on NHS resources and how this impact varies by setting.
Objective This study aims to identify health care utilisation patterns in the United Kingdom (UK) following IPF diagnosis.
Methods The Clinical Practice Research Datalink (CPRD) GOLD dataset for general practitioner office visits and the linked Hospital Episode Statistics (HES) datasets were analysed, covering the time period from January 1, 2000 to June 30, 2015. A matched cohort analysis was conducted, and frequency counts and regression analyses were used to quantify raw healthcare resource utilisation and understand the proportion of the utilisation that is attributable to IPF.
Results The results of this study indicate that IPF patients have significantly higher healthcare utilisation patterns than non-IPF patients. The regression results indicate that IPF leads to roughly 2.2 times as many GP visits, 8.7 times as many inpatient hospitalizations, and 2.4 times as many outpatient hospital visits per year (all p-values <0.0001), as well as increased referrals, prescriptions, and, in the post-diagnosis period, inpatient stay duration. Additionally, healthcare utilisation amongst these patients is dramatically higher in the year prior to IPF diagnosis, a pattern not witnessed in the matched cohort.
Conclusions IPF imposes a significant burden on the NHS despite its rare prevalence. IPF patients experience an across the board increase in healthcare utilisation, but the burden is particularly acute in the inpatient hospital setting. Additionally, the large increase in resource utilisation in the year prior to IPF diagnosis is evidence of the potential benefits to refining the diagnostic procedures.

S18 A WORKING DEFINITION AND NATURAL HISTORY OF 'MINIMAL' ILD

[1]R Ross Browne, [1]A Mathur, [2]A Marshal, [2]PA McFarlane, [2]GA Stewart, [2]J Sharkey, [2]G Ritchie, [2]M Jones, [2]JT Murchison, [2]N Hirani. *[1]University of Edinburgh, Edinburgh, UK; [2]Royal Infirmary of Edinburgh, Edinburgh, UK*

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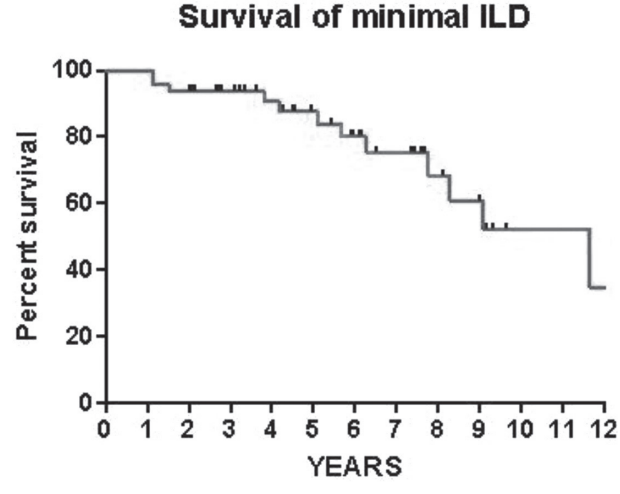
Background High resolution computed tomography (HRCT) scanning is able to detect abnormalities consistent with interstitial lung disease (ILD). However, if only a small proportion of lung is affected, radiologists variously report this as 'minimal', 'minor' or 'early' ILD. There is no definition of what constitutes 'minimal' ILD and the natural history of these patients is not known.
Aims To define 'minimal' ILD, test observer agreement with this definition and describe the characteristics and survival of these patients.
Hypothesis Minimal ILD can be defined by subjective quantification and has a benign course.
Methods Between 01.01.2002 and 31.12.2014 the Edinburgh Lung Fibrosis Database was prospectively populated with data for 1450 consecutively presenting patients with ILD. Of these, 56 were identified as presenting with 'minimal' disease according to HRCT. Three radiologists participated in a modified Delphi exercise and agreed on a definition of 'minimal' ILD. A sample (n = 38) of HRCT scans was provided to test inter- and intra-observer agreement according to this definition using Fleiss' Kappa statistics. Survival was assessed using Kaplan-Meier curves.
Results The Delphi exercise resulted in 'minimal' disease being defined as ILD involving <5% of the total lung volume and/or <10% of the lung peripheries. Using this definition, inter-observer and intra-observer agreement was moderate (kappa 0.42 and 0.58 respectively). Of the 56 subjects originally deemed as 'minimal' ILD, 48 were unanimously described as minimal disease by post-definition criteria. One subject was biopsied (consensus after biopsy, unclassifiable). Forty-seven subjects were not biopsied and none met ATS/ERS consensus criteria for diagnosing IPF. Most subjects had 'unclassifiable' disease, but the working diagnoses were; IPF or other fibrotic idiopathic interstitial pneumonia (IIP) (n = 34), IIP without fibrosis (n = 7) and connective-tissue disease associated ILD (n = 7). The median age was 69yrs, 56% were male and 23% had never smoked. The mean (SD) %pred lung function was; FEV_1 91.8% (19), VC 101% (18)



Abstract S18 Figure 1 Survival of minimal ILD

TCO 62% (19). The median survival was 11.6 years, and all deaths (n = 12) were attributable to respiratory disease.

Summary Defining 'minimal' ILD is feasible and there was moderate radiological agreement. Minimal ILD is relatively benign, but the associated mortality was of respiratory cause.

S19 THE IMPACT OF CLOTTING ABNORMALITIES ON THE NATURAL HISTORY OF IDIOPATHIC PULMONARY FIBROSIS: AN EXTENDED FOLLOW UP OF A POPULATION BASED COHORT

[1]V Navaratnam, [1]AW Fogarty, [1]T McKeever, [2]N Thompson, [3]G Jenkins, [3]SR Johnson, [4]M Kumaran, [4]K Pointon, [1]RB Hubbard. *[1]Division of Epidemiology and Public Health, University of Nottingham, Nottingham, UK; [2]Nottingham Respiratory Research Unit, Nottingham, UK; [3]Department of Respiratory Medicine, University of Nottingham, Nottingham, UK; [4]Department of Radiology, Nottingham University Hospitals NHS Trust, Nottingham, UK*

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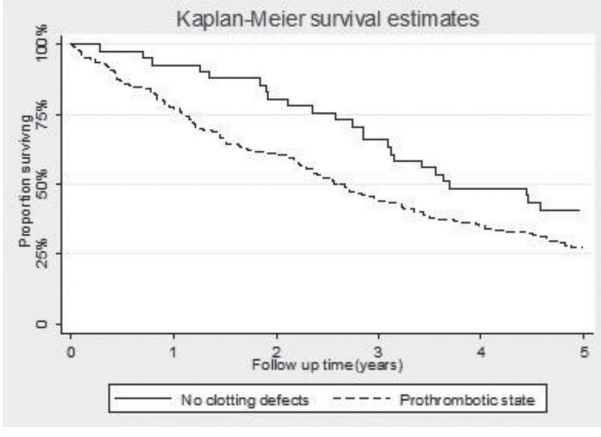
Background We have previously demonstrated that people with idiopathic pulmonary fibrosis (IPF) are more likely to have a prothrombotic state and that people with IPF and a prothrombotic state have a higher risk of death at a year's follow up. The aim of this study was to establish the impact of clotting abnormalities on the natural history of IPF with respect to median survival and lung function (forced vital capacity (FVC)).

Methods We recruited 211 incident cases of radiologically diagnosed definite or probable IPF and collected longitudinal information on pulmonary function tests done as part of routine care. All participants were tagged with the NHS Information Centre to enable us to collect data on mortality. Blood samples were tested for a prothrombotic state defined as at least one inherited or acquired clotting defect or marker of fibrinolytic dysfunction. Kaplan-Meir methods were used to calculate median survival. Random effects linear regression modelling was used to estimate decline in FVC.

Results Median follow-up was four years, during which 148 (70.1%) people died. Median survival in those with and without prothrombotic state was 2.7 and 3.7 years respectively (see Figure 1). We found evidence of effect modification between risk of death and follow-up time (p = 0.031). There was more than a three-fold increase risk of death in individuals with IPF and a prothrombotic state in the first half of follow-up (HR 3.36, 95% CI: 1.35 to 8.36), but this was reduced (HR 1.79, 95% CI: 1.08 to 2.94) in the second half. The estimated decline in FVC was 288mls (95% CI: 184 to 392mls) in those with normal clotting and 328mls (95% CI: 269 to 387mls) in those with one or more clotting defects.

Conclusions Coagulation dysfunction has an adverse impact on the natural history of IPF, both in terms of median survival and lung function decline. Our findings suggest that a prothombotic state may be a useful biomarker to predict prognosis as part of routine care.



Abstract S19 Figure 1 Kaplan-Meier survival estimates

S20 KBILD SCORES HAVE SIMILAR POWER TO PREDICT SURVIVAL AS PULMONARY PHYSIOLOGY IN INTERSTITIAL LUNG DISEASE

[1]C Sharp, [2]C Baggott, [3]SS Birring, [2]HI Adamali. *[1]Academic Respiratory Group, University of Bristol, Bristol, UK; [2]Bristol Interstitial Lung Disease (BILD) Service, North Bristol NHS Trust, Bristol, UK; [3]Division of Asthma, Allergy and Lung Biology, King's College London, London, UK*

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Background The KBILD questionnaire is an ILD health related quality of life (HRQL) tool. Its relationship with survival has not been assessed.

Aims Assess impact of KBILD scores on survival in a heterogeneous population with interstitial lung disease (ILD).

Methods Patients attending the Bristol ILD service with fibrotic ILDs completed KBILD questionnaires, full lung function and exercise testing. Survival analysis using univariable and multivariable Weibull regression with an accelerated time-failure form was used to assess the significance of KBILD scores to predict all cause mortality. Comparison was made with lung function from the same clinic visit. Results are reported as hazard ratio and time ratio.

Area under receiver operator characteristics (AUROC) curve analysis was used to assess sensitivity of KBILD for predicting 12-month mortality.

Results 175 patients, 58% IPF, 67.4% male, completed a KBILD questionnaire. Mean values were; age 71yrs, KBILD 61, FVC

Abstract S20 Table 1 Weibull regression results and c-statistic for 12-month mortality for variables

	Weibull univariable regression		Weibull multivariable regression			AUROC	
	Hazard Ratio	Significance	Hazard Ratio	Time Ratio*	Significance	c-statisitic	95% CI
Age (yrs)	1.05	0.003	1.06	0.96	0.001	0.646	0.511, 0.781
KBILD	0.98	0.005	0.98	1.01	0.022	0.654	0.531, 0.777
FVC (%)	0.97	<0.001	0.97	1.02	0.004	0.674	0.560, 0.788
Desaturation	2.64	0.002	2.00	0.61	0.038		
DLCO (%)	0.96	<0.001				0.680	0.554, 0.807
6MWD (m)	0.99	0.035				0.553	0.416, 0.690

TR – time ratio, AUROC – area under receiver operator characteristics curve, CI – confidence interval

Time ratio – The factor by which survival time changes for each 1 point change in a variable when all other variables are constant; eg. For each additional year of age, survival changes by a factor of 0.95