ILD predictors of outcome, disease progression and survival

Background

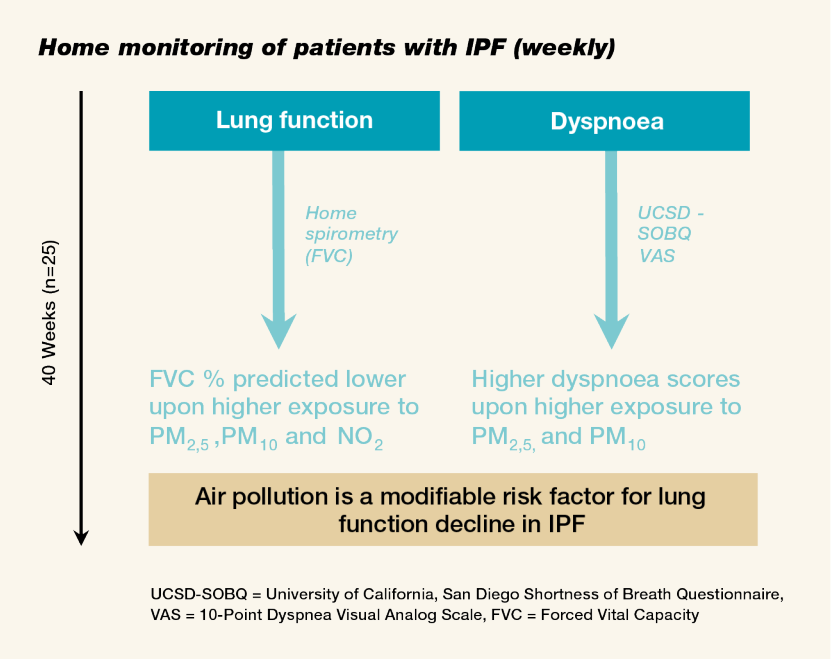
Although treatment options that delay disease progression are available, idiopathic pulmonary fibrosis (IPF) ultimately remains a fatal disease with an estimated 5-year survival rate of 20-30%. Disease progression is notoriously unpredictable, can be slow or rapid, and may be unexpectedly accelerated by acute IPF exacerbations.[1] In order to facilitate a more reliable prognosis for patients, it is necessary to gain a better understanding of the factors that contribute to the course of disease. Hence, predictors and biomarkers for IPF progression, patient outcomes and survival are of great clinical interest.

Risk factors in IPF

While the precise disease aetiology of IPF is unknown, several patient-related (e.g. male gender, old age, smoking)[2] and environment-related (e.g. inhalation of fine dust)[3] risk factors have been proposed. Ongoing research aims to improve our understanding of the factors that contribute to IPF development and progression.

Air pollution

Increased exposure to ambient air pollution (NO_2, O_3, $PM_{2,5}$ and PM_{10}) assessed by home monitoring is associated with reduced forced vital capacity (FVC), worse dyspnoea, and faster disease progression.[4]



Exposure to dust contributes to the aetiology of IPF. Prevention by reducing workplace exposure could potentially attenuate up to 13% of IPF disease burden.[5]

Helicobacter pylori infection

Helicobacter pylori serum antibody (≥2.3 U/ml) was identified as a risk factor for acute exacerbations in IPF (prospective study, n=142).[6]

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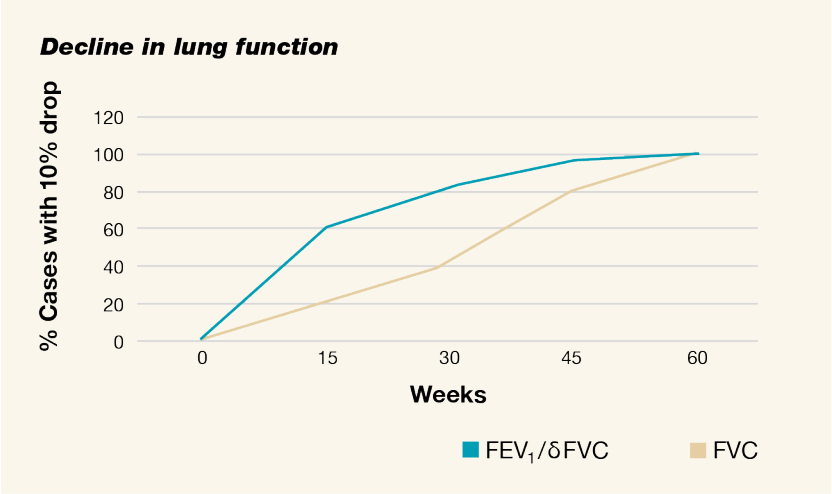
ILD highlights from the ATS 2017 congress
May 19th – May 24th / Washington, DC

Forced expiratory volume in one second to the change in forced vital capacity (FEV_1/δFVC) ratio and disease progression

The course of disease can vary considerably among IPF patients, and decline in FVC has in the past been viewed as a predictor of disease progression, since even a small decline in FVC indicates a deterioration in patient outcome.[7]

In a retrospective, post-hoc analysis of the RAINIER trial control arm (n=248), a prodromal decline in FVC % predicted over 14 weeks was identified as a risk factor for disease progression in IPF.[8]

Patients who showed a 10% decline in FVC during the PANTHER trial were selected (n=85). Time to 10% change in baseline FVC was compared to time to 10% change in baseline FEV_1/δ FVC ratio. A 10% decline in FEV_1/δ FVC ratio may be an earlier marker of disease progression in IPF than FVC alone.[9]



New IPF staging

Until recently, several staging systems were applied to predict survival of ILD patients: the GAP model (gender, age, physiology variables), ILD-GAP (Interstitial lung disease-gender, age, physiology) and CPI (composite physiologic index). In addition, baseline DL_{CO} is associated with length of remaining lifetime.[10] A new staging system for prediction of mortality in IPF was designed based on data from 65 patients in a retrospective analysis (2008-2015). In the new staging system, patients are divided into 3 stages based on changes in BMI and %FVC (baseline value minus 1-year value) and respiratory hospitalisation within one year. The new BFR staging system showed a clear survival difference between stages in the analysed cohort of IPF patients.[11]

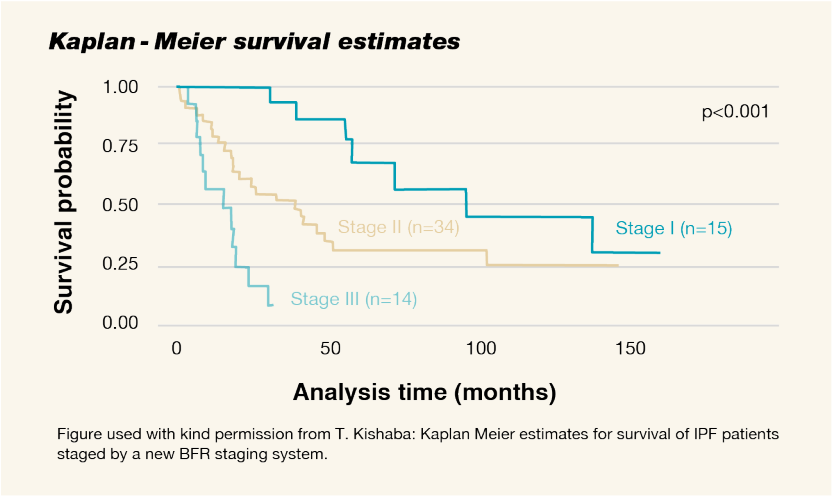


Figure used with kind permission from T. Kishaba: Kaplan Meier estimates for survival of IPF patients staged by a new BFR staging system.

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Interstitial pneumonia with autoimmune features (IPAF)

Patients with interstitial lung disease (ILD) may have features of connective tissue disease (CTD), but lack diagnostic findings of a specific CTD. A recent European Respiratory Society/American Thoracic Society research statement proposed criteria for patients with interstitial pneumonia with autoimmune features (IPAF). Patients with IIP and undifferentiated CTD-ILD were assessed for IPAF criteria to characterize features and domains, comparing survival to other ILD cohorts. IPAF was associated with a worse survival than CTD-ILD ($p<0.001$), but mildly improved compared to IPF. IPAF with non-usual interstitial pneumonia (non-UIP) pattern was associated with improved survival compared to IPAF with UIP.[12,13]

% IPAF patients positive for each domain

Clinical IPAF domain (47-62.5%)
- Inflammatory arthritis
- Reynaud's phenomena
- Mechanic's hands

Serological IPAF domain (91.1-93.0%)
- Anti-tRNA-synthetase
- Antinuclear antibody ≥1:320
- Anti-Ro Anti (SSA)
- Rheumatoid factor

Morphological IPAF domain (79.0-98.2%)
- Non-specific interstitial pneumonia pattern
- Vasculopathy
- Airways disease
- Pleural disease

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