OPEN SOURCE IMAGING CONSORTIUM MEMBER CHALLENGE

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The Brainomix e-ILD CT algorithm outperforms traditional lung function parameters in predicting outcomes for patients with idiopathic pulmonary fibrosis

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OBJECTIVES

The interstitial lung diseases (ILDs) are a group of disorders in which the architecture of the lungs is disrupted; in some cases, this leads to irreversible and progressive fibrosis. Idiopathic pulmonary fibrosis (IPF) is the archetypal progressive fibrosing lung disease in which there is relentless decline in lung function and an estimated life expectancy of 5 years from diagnosis. Two antifibrotic drugs, nintedanib and pirfenidone reduce the rate of lung function (forced vital capacity (FVC)) decline by approximately 50%. However, even in the context of IPF, the most homogeneous of the ILDs, there is individual variability in disease trajectory such that it is not possible to provide prognostic information at diagnosis. Furthermore, the currently accepted primary endpoint in IPF clinical trials, change in FVC, is afflicted by measurement variability of at least 10%. It is no longer ethical to perform placebo-controlled trials for patients with IPF and so demonstrating incremental improvements above standard of care poses a major challenge to the pharmaceutical industry. There is therefore a pressing need to discover and validate novel biomarkers such that clinical trials can be enriched for patients more likely to deteriorate. This will allow clinical trials to be shortened, sample sizes to be reduced and therapeutic responses above standard of care to be identified.

Brainomix (Oxford, UK) has developed e-ILD, an AI-powered image processing module to quantify imaging biomarkers on thoracic CT scans of patients with fibrosing lung disease. In this study we used e-ILD to analyse serial imaging of IPF patients from the Open-Source Imaging Consortium (OSIC) database to validate imaging biomarkers of progressive fibrosis and their association with clinical baseline parameters and survival.

METHODS

Using the OSIC database, we applied an artificial intelligence, machine learning approach to the analysis of CT scans from patients with a diagnosis of IPF or IPF/CPFE. We considered only those with full lung coverage and contemporaneous FVC and diffusion capacity of the lung for carbon monoxide (DLco) measurements (within 12 weeks of acquisition). The input to e-ILD is the 3D image data, from a single CT scan, without any other clinical information. The output of the processing includes a weighted reticulovascular (WRV) score which quantifies the extent of the lung affected by reticulo-vascular abnormalities.

We used transplant free survival, a surrogate for lung function decline in patients with IPF, as the primary endpoint for our analyses. Patients without vital status data were censored at the time of the last datapoint. We used Cox proportional hazards regression to model the relationship between lung function tests, biomarkers and transplant-free survival. The prognostic value of the markers/models was assessed using Harrell's C-Index. To investigate the added value of imaging markers, we adjusted for lung function parameters in the Cox regression models. Imaging and lung function data were assessed at baseline and follow-up studies. The relative change from baseline to follow-up was also assessed, accounting for the time between the two points.

RESULTS

Data was analysed from 296 IPF patients with a baseline CT, contemporaneous lung function tests and outcome data and of these, 120 patients who also had follow up data. The mean follow-up interval was 54 (SD 13) weeks. At baseline the C-Index was 0.66 for FVC. The best performing baseline e-ILD CT biomarker was the WRV score which had a C-Index of 0.75. The prognostic performance of the e-ILD WRV score was maintained when additionally adjusting for FVC and DLco. We dichotomised patients into low and high e-ILD WRV score groups using the median value as a threshold. The observed mortality risk was four times greater in the high WRV group (HR 4.0 CI 2.8-5.7, $p<0.001$). By categorising patients based on the median FVC of the cohort at 80% predicted, the prognostic performance was half as good (HR 2.0, CI 1.4-2.8, $p<0.001$). When analysing the prognostic value of the relative change between baseline and follow-up, FVC achieved a C-Index of 0.56 for predicting survival from that point onwards. However, by adding the e-ILD WRV score, this increased to 0.63. Thirty-one patients (22%) experienced a relative FVC decline of at least 10%. The e-ILD WRV score at baseline significantly predicted the likelihood of FVC decline of at least 10% (OR 5.8 CI 1.5 – 22.3, $p=0.01$, C-index 0.71).

CONCLUSIONS

Our data suggest that imaging biomarkers derived from a baseline CT scan can better predict outcomes in patients with IPF than FVC even when controlling for lung function parameters. Combining change in imaging biomarkers and FVC between two timepoints outperforms change in FVC alone for predicting outcomes suggesting that imaging and lung function testing identify independent and complementary factors associated with outcomes. Furthermore, the e-ILD WRV score was able to accurately predict patients who subsequently experienced a relative decline in FVC of 10%.

In conclusion, we demonstrate that novel automated imaging biomarkers from e-ILD, specifically the e-ILD WRV score predicts lung function decline and survival in IPF patients from a baseline CT scan. In the setting of a clinical trial, combining automated imaging biomarkers with physiology may improve patient selection and definition of treatment response compared to traditional clinico-physiological markers alone.