Poster

A multivariable protein-inclusive predictor of death or lung transplant in patients with idiopathic pulmonary fibrosis: data from the IPF-PRO Registry

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A multivariable protein-inclusive predictor of death or lung transplant in patients with idiopathic pulmonary fibrosis: data from the IPF-PRO Registry

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INTRODUCTION

- Idiopathic pulmonary fibrosis (IPF) is a progressive fibrosing interstitial lung disease with an unpredictable course Identifying prognostic biomarkers remains an unmet need.

AIM

- To examine associations between select circulating proteins and respiratory death or lung transplant, and the variable importance of these proteins as predictors of this outcome, in patients with IPF.

METHODS

Study cohort

- The cohort was drawn from the IPF-PRO Registry, a multicenter US registry that enrolled patients with IPF that was diagnosed or confirmed at the enrolling center in the past 6 months.[1]
- These analyses were based on data from 299 patients followed for a median of 39.9 months.

Analyses

- Using plasma samples taken at enrollment, 50 proteins were quantified using multiplexed ELISA. Data were $\log_2$ transformed prior to analysis.
- Multivariable Cox regression modelling with the elastic net penalty was used to identify candidate predictors for the composite outcome of respiratory death or lung transplant:
  - firstly, considering only variables used to calculate GAP index (sex, age, FVC % predicted, DLco % predicted)[2]
  - secondly, considering these variables, oxygen use at rest and oxygen use with activity
  - thirdly, considering these six clinical factors and protein measurements.
- To assess model performance, time-dependent C-indices were calculated at 6, 12, and 24 months of follow-up.

CONCLUSIONS

- In patients with IPF, select circulating proteins strongly associated with the risk of mortality and conferred information independent of clinical measures.
- These data support the idea that, with further optimization, multiprotein-inclusive algorithms may provide meaningful risk stratification in patients with IPF.

RESULTS

Patient characteristics at enrollment (n=299)

Age (years)	70 (65, 75)
Male	223 (75%)
White	280 (94%)
Past/current smoker	203 (68%)
FVC % predicted	69.7 (60.9, 80.2)
DLco % predicted	40.5 (31.6, 49.4)
Use of oxygen at rest	61 (20%)
Use of antifibrotic drug	167 (56%)

Values are median (Q1, Q3) or n (%). Information on oxygen use was not available for 1 patient.

Model performance

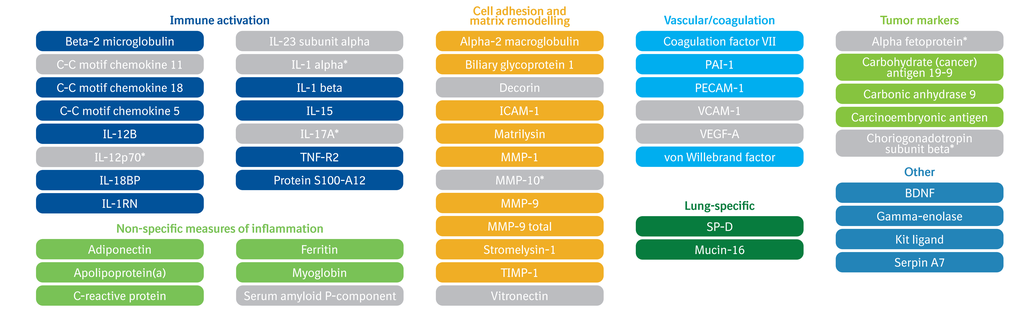
- 124 patients (41.5%) experienced respiratory death or lung transplant.
- The best fit protein-inclusive model selected 37 proteins and all six clinical factors as predictors of respiratory death or lung transplant.
  - More parsimonious models using fewer proteins were explored, but the C-index deteriorated and approached that observed with clinical factors only.

C-indices for respiratory death or lung transplant

Model	6 months	12 months	24 months
GAP variables only	0.71 (0.68, 0.75)	0.72 (0.67, 0.75)	0.72 (0.68, 0.76)
GAP variables and oxygen use	0.73 (0.69, 0.77)	0.73 (0.69, 0.77)	0.73 (0.70, 0.77)
Best-fit protein-inclusive model*	0.78 (0.73, 0.82)	0.77 (0.73, 0.81)	0.76 (0.73, 0.79)

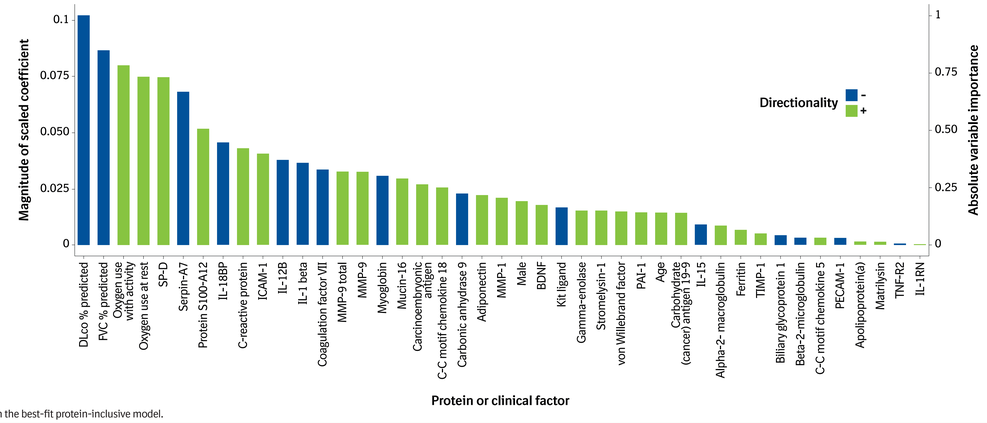
C-indices (95% CI).
*Selected all clinical factors (GAP variables, oxygen use with activity, oxygen use at rest) and 37 of 50 proteins considered.

Proteins selected by best-fit protein-inclusive model



Proteins in grey were not selected by the model. *Removed from analyses due to missingness >25%.

Variable importance of proteins and clinical factors as predictors of respiratory death or lung transplant



From the best-fit protein-inclusive model.

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2. Ley B et al. Ann Intern Med 2012;156:684–691.

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IPF-PRO Registry enrolling centers: Albany Medical Center, Albany, NY; Baylor College of Medicine, Houston, TX; Baylor University Medical Center at Dallas, Dallas, TX; Cleveland Clinic, Cleveland, OH; Columbia University Medical Center/New York Presbyterian Hospital, New York, NY; Duke University Medical Center, Durham, NC; Froedtert & The Medical College of Wisconsin Community Physicians, Milwaukee, WI; Houston Methodist Lung Center, Houston, TX; Lahey Clinic, Burlington, MA; Loyola University Health System, Maywood, IL; Lynchburg Pulmonary Associates, Lynchburg, VA; Medical University of South Carolina, Charleston, SC; National Jewish Health, Denver, CO; NYU Medical Center, New York, NY; Piedmont Healthcare, Austell, GA; Pulmonary Associates of Stamford, Stamford, CT; PulmonIx LLC, Greensboro, NC; Renovatio Clinical, The Woodlands, TX; Salem Chest and Southeastern Clinical Research Center, Winston Salem, NC; South Miami Hospital, South Miami, FL; St. Joseph's Hospital, Phoenix, AZ; Stanford University, Stanford, CA; Temple University, Philadelphia, PA; The Oregon Clinic, Portland, OR; Tulane University, New Orleans, LA; UNC Chapel Hill, Chapel Hill, NC; University of Alabama at Birmingham, Birmingham, AL; University of California, Davis, Sacramento, CA; University of California Los Angeles, Los Angeles, CA; University of Chicago, Chicago, IL; University of Cincinnati Medical Center, Cincinnati, OH; University of Louisville, Louisville, KY; University of Miami, Miami, FL; University of Michigan, Ann Arbor, MI; University of Minnesota, Minneapolis, MN; University of Pennsylvania, Philadelphia, PA; University of Pittsburgh, Pittsburgh, PA; University of Virginia, Charlottesville, VA; UT Southwestern Medical Center, Dallas, TX; Vanderbilt University Medical Center, Nashville, TN; Vermont Lung Center, Colchester, VT; Wake Forest University, Winston Salem, NC; Washington University, St. Louis, MO; Weill Cornell Medical College, New York, NY; Wilmington Health and PMG Research, Wilmington, NC; Yale School of Medicine, New Haven, CT.

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