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Development of a multi-biomarker risk score based on serum proteins by the Prognostic Lung Fibrosis Consortium (PROLIFIC)

Idiopathic pulmonary fibrosis, Personalised medicine, Translational science

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Introduction: PROLIFIC has developed a set of well-qualified assays to measure serum proteins linked to prognosis in idiopathic pulmonary fibrosis (IPF).

Aims & Objectives: To select and combine the most prognostic biomarkers into a multi-marker algorithm and risk score.

Methods: Concentrations of 12 biomarkers were measured in serum collected from IPF patients at the time of enrollment (baseline) into the Pulmonary Fibrosis Foundation Patient Registry (N=657). Statistical analyses were performed to define a composite binary outcome of reaching an estimated 10% relative decline in % predicted forced vital capacity (FVC), death, or lung transplant in one year. Penalized logistic regression was used to select prognostic biomarkers using the LASSO method. The resulting model was used to derive a risk score which was evaluated by the ROC curve for its prediction ability. All the statistical analyses were adjusted for sex, age, BMI, anti-fibrotic medication, and % predicted DLCO.

Results: Five biomarkers (SP-D, sICAM-1, TNC, CXCL13, and MMP-7) were selected to form the risk score, which was significantly associated with the binary outcome (p = 9.30e-07 and AUC= 0.754). The

quartiles of the individual risk scores show clear separation among the transplant-free and 10% FVC reduction-free survival rates.

Conclusions: A multi-marker algorithm selected important biomarkers that are consistent with the findings from single-marker analyses, and also developed a subject-level prognostic biomarker-based score for both FVC decline and transplant-free survival in one year.