Surfactant Lipid Profiles Distinguish Idiopathic Pulmonary Fibrosis

Spela Kokelj[1], Sanna Kjellberg[2], Mats Josefson[3], Anna-Carin Olin[2], Emily Krantz

[1] Lungkliniken, Sahlgrenska Universitetssjukhuset, [2] Arbets- och miljömedicin, Avd för samhällsmedicin och folkhälsa, Inst för medicin, Sahlgrenska Akademin, Göteborgs Universitet, [3] Global Product Development, Pharmaceutical Technology & Development, AstraZeneca

Idiopathic pulmonary fibrosis (IPF) is a chronic, progressive lung disease with a poor prognosis and limited diagnostic and prognostic biomarkers. This study aimed to characterize the surfactant lipid composition in patients with IPF compared with healthy controls and to evaluate its relationship with lung function.

Exhaled particles from the small airways were collected non-invasively from 9 patients (3 females) with IPF (cases) and from 26 healthy controls (12 females), using the PExA method. Samples were analyzed for surfactant lipids using liquid chromatography-tandem mass spectrometry (LC MS/MS). Patients with IPF also underwent spirometry and diffusion capacity testing (DLCO). PCA and OPLS were used to identify discriminatory lipids.

The median age of cases was higher as compared to controls (71 years (IQR 62-76) vs. 62 years (IQR 60-65), $p = 0.013$). A total of 92 different lipid species belonging to 8 classes were detected, of which 64 species differed between groups (q-value < 0.05) (Figure 1). Compared with controls, IPF cases exhibited higher proportions ($p < 0.001$) of Lysophosphatidylcholines (LPC), Phosphatidylcholines (PC), and Sphingomyelins (SM), and lower proportions ($p < 0.001$) of Phosphatidylethanolamines (PE), Ether-linked Phosphatidylethanolamines (PE O), and Phosphatidylglycerols (PG). No significant difference was observed in the proportion of Phosphatidylinositols (PI) ($p = 0.469$). Multivariate analyses (OPLS) identified 11 lipid species that were significantly associated with DLCO in the IPF cases ($Q2 = 0.23$, $R2X = 0.40$).

Patients with IPF showed a distinct surfactant lipid profile compared with healthy individuals, characterized by marked shifts in multiple lipid classes. The association between specific lipid species and reduced DLCO suggests that surfactant composition may reflect disease-related dysfunction in the small airways. Non-invasively collected surfactant lipids represent a novel biomarker approach that requires larger validation studies and may inform mechanistic research on alveolar lipid dysfunction in IPF.

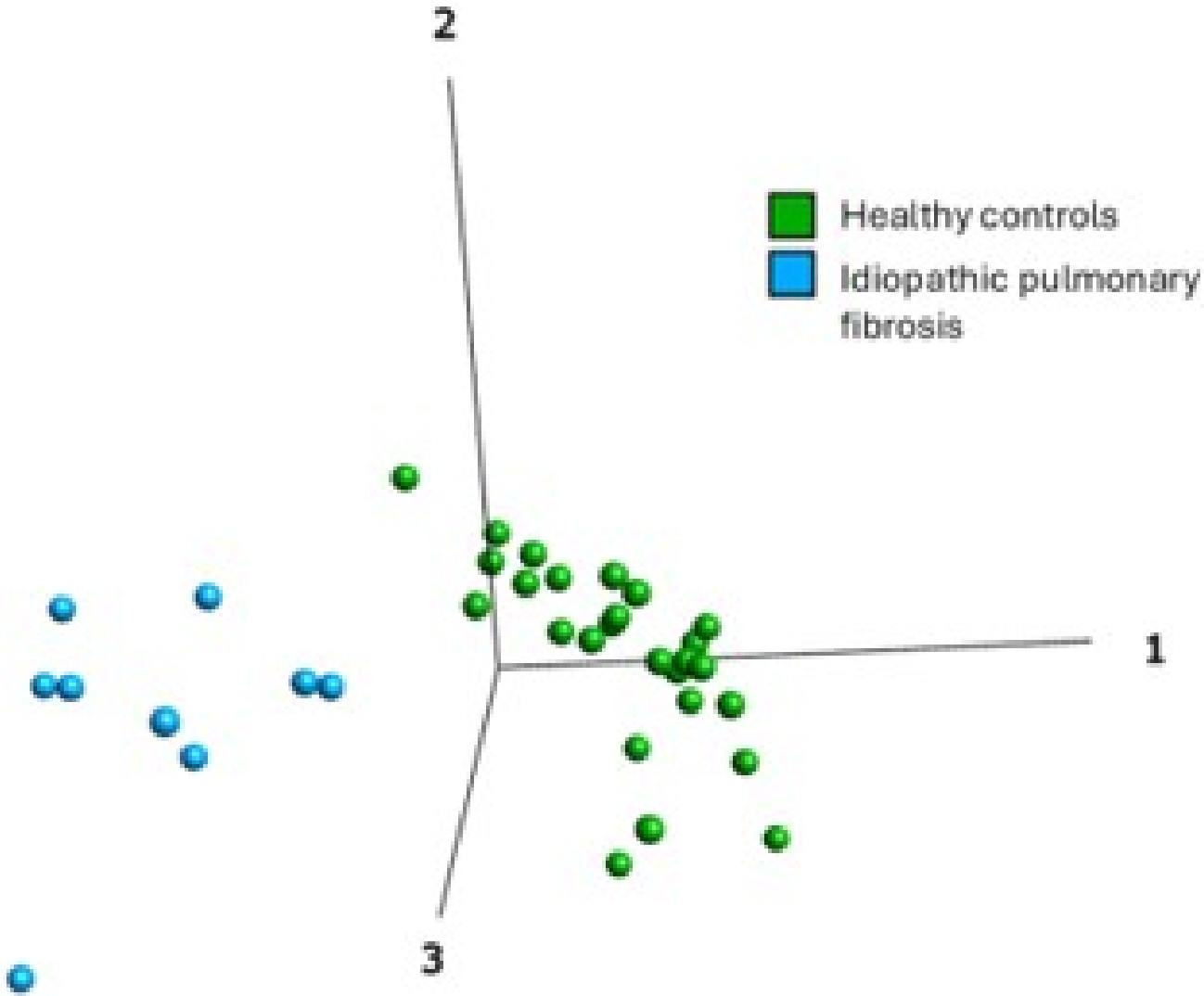

Figure 1. Principle Component Analysis (PCA) plot of patients with IPF (blue) and healthy controls (green). 62 out of 92 surfactant lipid species selected based on a Mann-Whitney statistical test ($q < 0.05$) were found to discriminate patients with IPF from healthy controls in a PCA plot by visual inspection.