

Noninvasive Sphingolipid Profiling May Help Differentiate Fibrotic Interstitial Lung Diseases

Glenview, IL (October 12, 2026) – Sphingolipid profiles found in plasma and exhaled breath condensate differed between patients with idiopathic pulmonary fibrosis (IPF) and fibrotic hypersensitivity pneumonitis (fHP), suggesting a potential noninvasive approach to help characterize fibrotic interstitial lung disease.

Fibrotic interstitial lung disease (f-ILD) encompasses multiple conditions, including IPF and fHP, which require different therapeutic strategies but can have overlapping clinical, radiographic, and pathologic features. Sphingolipids are bioactive lipids involved in membrane structure, immune regulation, and fibrogenic signaling and have been implicated in ILD pathobiology. Researchers evaluated sphingolipid signatures in plasma and exhaled breath condensate (EBC) in patients with IPF and fHP and assessed their associations with clinical characteristics and disease severity.

Researchers analyzed plasma samples from 40 patients with fHP, 33 with IPF, and 28 healthy controls. EBC was analyzed in a subset of 18 patients with fHP, 20 with IPF, and 11 healthy controls. Diagnoses were confirmed through multidisciplinary ILD conference review. Targeted sphingolipid profiling was performed using high-performance liquid chromatography–tandem mass spectrometry.

Sphingolipid profiles differed significantly between patients with fibrotic ILD and healthy controls in both plasma and EBC, with additional subtype-specific signatures distinguishing fHP from IPF. In plasma, DHSO and ceramide C24:0 were significantly different between disease subtypes. In EBC, sphingomyelin C24:1, ceramide C24:0, and sphingomyelin C18:0 also distinguished fHP from IPF.

Several sphingolipid species were also associated with measures of disease severity. Among patients with IPF, sphingolipids in both plasma and EBC correlated with gender-age-physiology (GAP) score, while EBC hexosylceramide C18:1 was also associated with diffusing capacity of the lungs for carbon monoxide (DLCO) and forced vital capacity (FVC). Among patients with fHP, sphingolipids were associated with GAP-ILD and FVC.

“Differentiating IPF from fibrotic hypersensitivity pneumonitis remains a major clinical challenge,” said Jon Mullholand, MD, CHEST 2026 presenting author. “Noninvasive sphingolipid profiling in plasma and exhaled breath condensate may complement multidisciplinary evaluation by improving disease classification and providing biologically relevant markers of severity in fibrotic ILD.”

The findings support further study of sphingolipid profiling in plasma and EBC as a potential noninvasive biomarker approach for disease characterization in fibrotic ILD. The

associations with physiologic measures of disease severity may also provide additional information about disease characteristics.

Further results will be presented at the CHEST Annual Meeting 2026 as part of the ILD: Clinical Roundup rapid fire original investigation presentations titled, *Noninvasive Sphingolipid Profiling Distinguishes IPF From Fibrotic Hypersensitivity Pneumonitis*. The [study abstract](#) can be viewed on the CHEST® journal website.