Diagnostic role of lung biopsy in early pulmonary fibrosis with preserved lung function: a multicentre observational study

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Background

Early and accurate diagnosis in fibrosing interstitial lung diseases (ILDs) enables timely antifibrotic therapy. When high-resolution CT (HRCT) shows minimal or indeterminate fibrosis and lung function is preserved, imaging alone may be insufficient. Prior work suggests tissue acquisition can disclose histologic usual interstitial pneumonia (UIP) despite limited, non-specific HRCT changes, improving diagnostic confidence and management.

Methods

We conducted a retrospective, multicentre observational study of consecutive adults evaluated between January 2024 and January 2026 at two Italian ILD referral centres. Inclusion criteria were HRCT patterns suggestive of ILD (indeterminate/probable UIP, NSIP, BIP, or ILA) and preserved pulmonary function (normal spirometry; diffusing capacity [DLCO] normal or moderately reduced). Exclusions were definite UIP on HRCT, coagulopathy, haemodynamic instability, diffuse bullous disease, and severe hypoxaemia. All cases underwent multidisciplinary discussion (MDD). Tissue was obtained by transbronchial lung cryobiopsy (TBLC) or, selectively, surgical lung biopsy (SLB). The primary endpoint was biopsy diagnostic yield; secondary endpoints were MDD diagnostic yield, radiology–histology concordance, and post-biopsy diagnostic reclassification.

Results

Fifty-four patients were included (median age 69 years, IQR 55–85; 81% male; 74% current/former smokers). Median FVC% and FEV1% were 105 (IQR 80–135) and 109 (IQR 75–144), respectively. DLCO was ≥80% in 42/54 (78%) and 60–79% in 12/54 (22%). TBLC was performed in 49/54 (92%) and SLB in 4/54 (7%).

Biopsy was diagnostic in 52/54 (96.3%), indeterminate in 1/54 (1.9%), and non-diagnostic in 1/54 (1.9%); MDD yielded a final diagnosis in 53/54 (98.1%).

Among 44 patients with HRCT “indeterminate for UIP,” histology showed UIP in 33/44 (75.0%), with additional diagnoses including UIP with features of BIP (3/44, 6%), NSIP (2/44, 5%), HP (2/44, 5%), smoking-related interstitial fibrosis (2/44, 5%), smoking-related ILD (1/44, 2%), and one indeterminate (1/44, 2%). All three “probable UIP” cases were histologic UIP.

In other HRCT categories (NSIP, BIP, other), histology enabled targeted reclassification (e.g., fibrotic HP, organizing pneumonia, SRIF, silicosis) in 3/4 cases (75%), with one non-diagnostic result.

Procedures were undertaken in experienced centres; although safety was not a primary outcome, feasibility was favourable. Limitations include absence of a control group and potential selection bias intrinsic to high-volume centres.

Conclusions

In early pulmonary fibrosis with preserved lung function, lung tissue acquisition—predominantly via TBLC—achieves a high diagnostic yield, frequently uncovers histologic UIP in HRCT-indeterminate presentations, and materially reclassifies diagnoses beyond imaging alone. Integration of histology within MDD facilitates earlier identification of IPF and may enable prompt therapy with potential benefits for progression, symptoms, quality of life, and prognosis.