The Impact of Genomic Classifier in Patients with Undiagnosed Interstitial Lung Disease

Diana Espinoza,[1] Regina Villalobos,[2] David Becnel,[1] Ramsy Abdelghani,[1] Rachel Herr,[1] Alejandro Aragaki,[3] Joseph Lasky,[1] Fayez Kheir[2]

1. Division of Pulmonary and Critical Care, Department of Medicine, School of Medicine, Tulane University, New Orleans, LA
2. Division of Pulmonary and Critical Care Medicine, Massachusetts General Hospital, Boston, MA
3. Division of Pulmonary, Critical Care and Sleep Medicine, University of Cincinnati Medical Center, Cincinnati, OH

BACKGROUND

- Interstitial lung diseases (ILDs) are collection of complex and heterogeneous diseases that can be challenging to diagnose.
- Genomic Classifier (GC) is a clinically validated molecular diagnostic test that identifies usual interstitial pneumonia (UIP), increasing diagnostic confidence for idiopathic pulmonary fibrosis.

RESEARCH QUESTION

- What is the impact of GC and lung cryobiopsy results on clinical management decisions in patients with fibrotic ILD where high-resolution computed tomography and clinical factors alone did not provide a definitive diagnosis.

METHODS

- A retrospective analysis of patients who underwent clinically indicated diagnostic bronchoscopy with cryobiopsy and GC testing at three medical centers. We assessed the change in management strategy and association between genomic UIP classification and disease progression.

RESULTS

TABLE 1
Patient characteristics and diagnoses stratified by genomic UIP classification

Baseline characteristics	gUIP Positive (n=42)	gUIP Negative (n=56)	p-value
Age, mean (SD)	71 (8)	61 (11)	<0.001
Male sex, n (%)	28 (66.7)	32 (57.1)	0.34
HRCT Pattern			
Probable UIP	12 (28.6)	6 (10.7)	0.02
Indeterminate UIP	30 (71.4)	39 (69.9)	0.85
Alternative Diagnosis	0 (0)	11 (19.6)	<0.001
Pulmonary Function			
FVC % predicted, mean (SD)	72 (15)	74(16)	0.28
DLCO % predicted, mean (SD)	52 (15)	53 (16)	0.75
Current or former smokers, n (%)	28 (66.7)	36 (64.3)	0.81
Diagnosis after cryobiopsy and gUIP testing			
Idiopathic Pulmonary Fibrosis	33 (78.6)	5 (11.9)	<0.001
Non-idiopathic pulmonary fibrosis	9 (21.4)	51 (91.1)	<0.001
Fibrotic hypersensitivity pneumonitis	4 (44)	4(7.8)	
Idiopathic non-specific interstitial pneumonia	1(11)	13(25.5)	
Unclassifiable ILD	2(22)	17(33)	
Connective tissue disease associated ILD	1(11)	9(17.6)	
Sarcoidosis	0(0)	3(5.9)	
Other ILD	1(11)	5(9.8)	

FIGURE 1
Algorithm showing the impact of cryobiopsy and genomic classifier information on patients' management

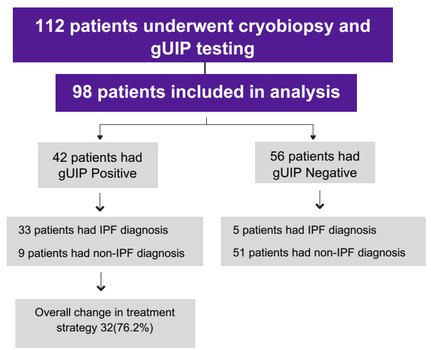


FIGURE 2
Bar plots that show the management plan in patient before and after procedure (cryobiopsy and genomic testing)

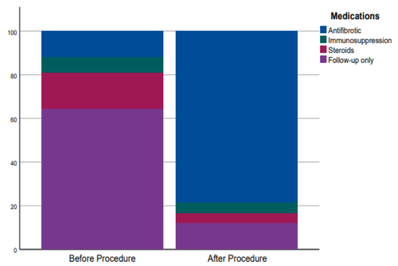
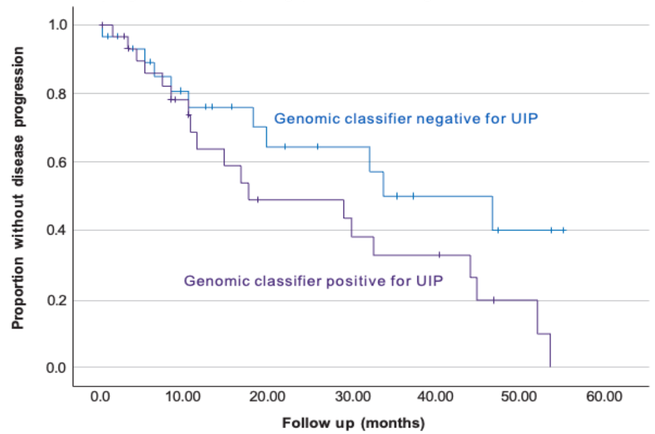


FIGURE 3
Kaplan-Meier plot for disease progression comparing patients with genomic classifier positive and negative for UIP pattern



Combining cryobiopsy and GC (positive for UIP) data, the management strategy changed for 25/42 patients (59.5%) in the cohort with gUIP positive. Nine patients out of 42 had indeterminate cryobiopsy results with gUIP positive leading to further change in treatment strategy of additional 7 cases. Overall, management strategy changed in 32/42 (76.2%) patients. There was a decrease in follow up without treatment from 64.3 % to 11.9% (P<0.001) as well as immunosuppressive drugs from 23.8% to 9.5% (P=0.06) and increase in antifibrotics drugs from 11.9% to 71.4% (P<0.001). In multivariable analysis, positive gUIP classification was associated with disease progression (hazard ratio 1.4, 95% CI 0.4–4.2; p=0.55), without reaching statistical significance.

INTERPRETATION

This study suggested that combined GC and cryobiopsy might impact therapeutic strategy without affecting prognosis prediction in patients with undiagnosed ILD. This could assist physicians in effectively managing patients to improve outcomes of patients with IPF.

Take-home Point
We found that adding genomic classifier for UIP to lung cryobiopsy had a meaningful impact on therapeutic strategy in patients with fibrotic interstitial lung disease.