Association of quantitative lung fibrosis (QLF) score with the severity and progression of progressive pulmonary fibrosis (PPF)

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INTRODUCTION

- Progressive pulmonary fibrosis (PPF) is a term that is generally used to describe progressive lung fibrosis in patients with a fibrosing interstitial lung disease (ILD) other than idiopathic pulmonary fibrosis (IPF).[1]
- The prognostic value of quantitative measures of lung fibrosis on high-resolution computed tomography (HRCT) in patients with PPF has not been established.

AIM

- To evaluate associations between quantitative scores derived from HRCT scans and the severity and progression of PPF in patients in the ILD-PRO Registry.

METHODS

The ILD-PRO Registry
- Patients enrolled in the ILD-PRO Registry had an ILD other than IPF, reticular abnormality and traction bronchiectasis (with or without honeycombing) on an HRCT scan and/or lung biopsy, and met criteria for ILD progression within the prior 24 months.[2] Patients were followed prospectively while receiving usual care.

HRCT
- HRCT images taken within the 24 months prior to enrollment or up to 90 days post-enrollment were analyzed using a machine learning algorithm[3,4] to derive the following scores, expressed as percentages of total lung involvement:
  – Quantitative lung fibrosis (QLF) (fibrotic reticulation patterns with architectural distortion)
  – Quantitative ground glass (QGG)
  – Quantitative honeycomb cysts (QHC)
  – Quantitative ILD (QILD) (sum of QLF, QGG and QHC scores).
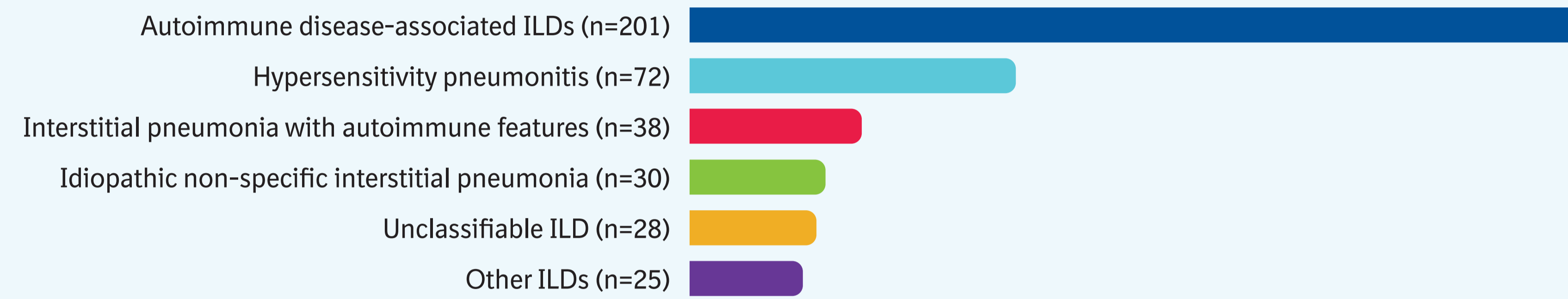- Median (Q1, Q3) time from the HRCT scan to enrollment was 5.1 (2.2, 9.4) months.

Analyses
- Associations between tertiles of each quantitative HRCT score and measures of disease severity at enrollment were assessed using linear or ordinal proportional odds logistic regression.
- Associations between tertiles of each quantitative HRCT score at enrollment and ILD progression (relative decline in FVC % predicted ≥10%, lung transplant, or death) were analyzed using Cox proportional hazard models.

CONCLUSIONS

- Among patients with PPF in the ILD-PRO Registry, patients with worse QLF scores had worse disease severity at enrollment. Patients with worse QLF scores had a significantly increased risk of ILD progression during follow-up in unadjusted analyses, but not in analyses adjusted for sex, age and disease severity at enrollment. There were no significant associations between other HRCT-derived scores and the risk of ILD progression.
- These data support a structure–function relationship between the extent of fibrosis on HRCT and physiologic measures in patients with PPF.

RESULTS

Types of ILD

- Autoimmune disease-associated ILDs (n=201)
- Hypersensitivity pneumonitis (n=72)
- Interstitial pneumonia with autoimmune features (n=38)
- Idiopathic non-specific interstitial pneumonia (n=30)
- Unclassifiable ILD (n=28)
- Other ILDs (n=25)

N=395. One patient had missing data.

Associations between QLF tertiles and measures of disease severity at enrollment

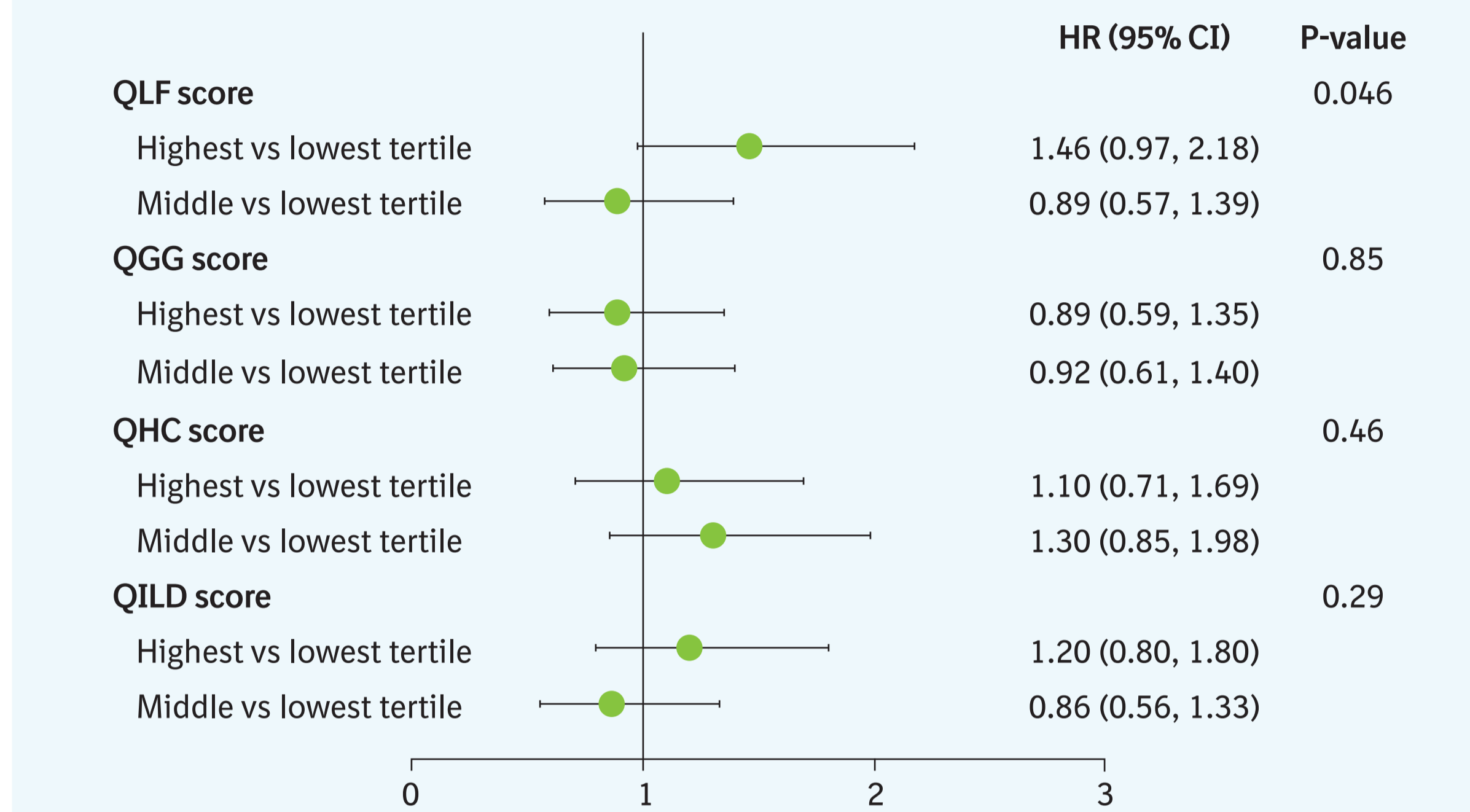|	Effect size for QLF tertile		
	Highest vs lowest tertile	Middle vs lowest tertile	P-value
FVC % predicted	−18.62 (−22.61, −14.63)	−9.71 (−13.65, −5.76)	<0.001
DLco % predicted	−17.49 (−20.99, −13.98)	−11.11 (−14.59, −7.62)	<0.001
GAP stage	9.13 (5.15, 16.21)	2.48 (1.51, 4.10)	<0.001
Oxygen use	10.39 (5.98, 18.05)	2.22 (1.26, 3.88)	<0.001

Cut-off for lowest tertile: <10.7%. Cut-off for highest tertile: ≥20.5%.
Data for FVC % predicted and DLco % predicted are mean difference (95% CI). Data for GAP stage and oxygen use are odds ratio (95% CI) and parameterized as "worse" versus "better" health status.

Associations between QHC tertiles and measures of disease severity at enrollment

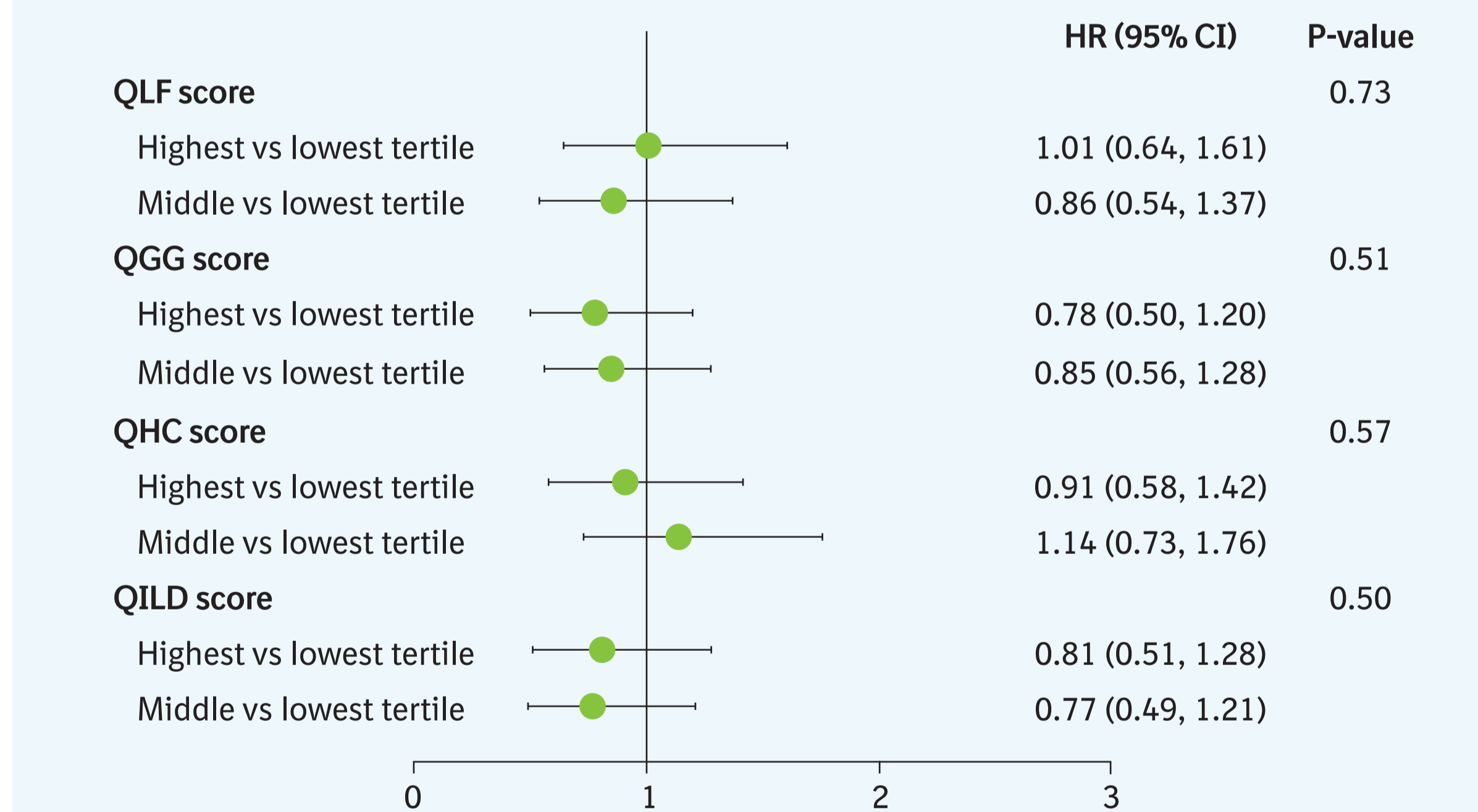|	Effect size for QHC tertile		
	Highest vs lowest tertile	Middle vs lowest tertile	P-value
FVC % predicted	2.62 (−1.88, 7.12)	4.22 (−0.13, 8.58)	0.16
DLco % predicted	1.19 (−2.87, 5.25)	1.45 (−2.50, 5.39)	0.75
GAP stage	1.59 (0.96, 2.65)	1.52 (0.93, 2.48)	0.14
Oxygen use	1.44 (0.88, 2.36)	1.24 (0.77, 2.02)	0.34

Cut-off for lowest tertile: <0.02%. Cut-off for highest tertile: ≥0.48%.
Data for FVC % predicted and DLco % predicted are mean difference (95% CI). Data for GAP stage and oxygen use are odds ratio (95% CI) and parameterized as "worse" versus "better" health status.

Associations between QGG tertiles and measures of disease severity at enrollment

	Effect size for QGG tertile		
	Highest vs lowest tertile	Middle vs lowest tertile	P-value
FVC % predicted	−8.58 (−12.89, −4.27)	−6.99 (−11.27, −2.71)	<0.001
DLco % predicted	−5.94 (−9.89, −2.00)	−1.73 (−5.62, 2.16)	0.011
GAP stage	1.60 (0.97, 2.64)	1.36 (0.84, 2.23)	0.17
Oxygen use	2.38 (1.47, 3.88)	1.70 (1.04, 2.79)	0.002

Cut-off for lowest tertile: <18.5%. Cut-off for highest tertile: ≥28.0%.
Data for FVC % predicted and DLco % predicted are mean difference (95% CI). Data for GAP stage and oxygen use are odds ratio (95% CI) and parameterized as "worse" versus "better" health status.

Associations between QILD tertiles and measures of disease severity at enrollment

	Effect size for QILD tertile		
	Highest vs lowest tertile	Middle vs lowest tertile	P-value
FVC % predicted	−16.76 (−20.84, −12.69)	−8.68 (−12.71, −4.66)	<0.001
DLco % predicted	−14.66 (−18.30, −11.01)	−8.34 (−11.98, −4.70)	<0.001
GAP stage	6.08 (3.52, 10.51)	2.08 (1.27, 3.41)	<0.001
Oxygen use	8.64 (5.04, 14.81)	2.39 (1.38, 4.13)	<0.001

Cut-off for lowest tertile: <32.2%. Cut-off for highest tertile: ≥51.4%.
Data for FVC % predicted and DLco % predicted are mean difference (95% CI). Data for GAP stage and oxygen use are odds ratio (95% CI) and parameterized as "worse" versus "better" health status.

Unadjusted associations between tertiles of quantitative scores at enrollment and time to ILD progression

	HR (95% CI)	P-value
QLF score		0.046
Highest vs lowest tertile	1.46 (0.97, 2.18)	
Middle vs lowest tertile	0.89 (0.57, 1.39)	
QGG score		0.85
Highest vs lowest tertile	0.89 (0.59, 1.35)	
Middle vs lowest tertile	0.92 (0.61, 1.40)	
QHC score		0.46
Highest vs lowest tertile	1.10 (0.71, 1.69)	
Middle vs lowest tertile	1.30 (0.85, 1.98)	
QILD score		0.29
Highest vs lowest tertile	1.20 (0.80, 1.80)	
Middle vs lowest tertile	0.86 (0.56, 1.33)	

Median follow-up was 17.3 months; 133 patients (33.7%) had ILD progression.

Adjusted associations between tertiles of quantitative scores at enrollment and time to ILD progression

	HR (95% CI)	P-value
QLF score		0.73
Highest vs lowest tertile	1.01 (0.64, 1.61)	
Middle vs lowest tertile	0.86 (0.54, 1.37)	
QGG score		0.51
Highest vs lowest tertile	0.78 (0.50, 1.20)	
Middle vs lowest tertile	0.85 (0.56, 1.28)	
QHC score		0.57
Highest vs lowest tertile	0.91 (0.58, 1.42)	
Middle vs lowest tertile	1.14 (0.73, 1.76)	
QILD score		0.50
Highest vs lowest tertile	0.81 (0.51, 1.28)	
Middle vs lowest tertile	0.77 (0.49, 1.21)	

Adjusted for sex, age, FVC % predicted and oxygen use (at rest, with exertion, none) at enrollment.
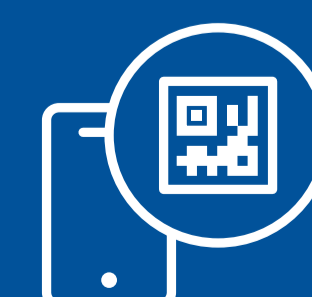Median follow-up was 17.3 months; 133 patients (33.7%) had ILD progression.

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