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Predictors of Mortality Among Patients Hospitalised with Acute Exacerbation of Interstitial Lung Disease: A Prospective Observational Study

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Abstract: Background: Acute exacerbation of interstitial lung disease (AE-ILD) is associated with substantial mortality. This study evaluated clinical, laboratory, and radiological predictors of in-hospital mortality.**Methods:**A prospective observational study involving 150 AE-ILD hospitalisations was analysed. Admission characteristics were compared between survivors and non-survivors.Univariable and multivariable logistic regression analyses were performed to evaluate mortality associations.**Results:** In-hospital mortality was 36.0% (54/150). Previous home oxygen therapy (OR=3.45; p=0.002), HRCT abnormalities involving >50% of the lungs (OR=3.18; p=0.004), diffuse HRCT abnormalities (OR=3.33; p<0.001), reduced PaO_2/FiO_2 (OR=1.21 per 50-mmHg decrease; p=0.038), and lower serum albumin (OR=1.46 per 0.5-g/dL decrease; p=0.046) were associated with mortality in univariable analyses. None of the three variables in the adjusted model remained statistically significant. The model demonstrated modest discrimination (AUROC=0.670).**Conclusion:** Respiratory impairment, extensive radiological abnormalities, and baseline disease severity were associated with in-hospital mortality, although independent prediction remained limited.

Keywords: Acute exacerbation; Interstitial lung disease; In-hospital mortality; Prognostic factors; High-resolution computed tomography.

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INTRODUCTION

Interstitial lung diseases (ILDs) are a diverse group of pulmonary diseases with different degrees of inflammation, fibrosis, and progressive loss of lung function. Acute exacerbation of interstitial lung disease (AE-ILD) is a clinically important deterioration that is accompanied by acute respiratory failure and mortality.

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Interstitial lung diseases (ILDs) are a diverse group of pulmonary diseases with different degrees of inflammation, fibrosis, and progressive loss of lung

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function. Acute exacerbation of interstitial lung disease (AE-ILD) is a clinically important deterioration that is accompanied by acute respiratory failure and mortality. In 2016, an international working group agreed that acute exacerbation of idiopathic pulmonary fibrosis (AE-IPF) is defined as an acute worsening of respiratory symptoms within 1 month, with the presence of new bilateral ground-glass opacities or consolidation on high-resolution computed tomography (HRCT) that cannot be explained by cardiac failure or fluid overload [1]. While described in IPF, similar acute exacerbations are found in other fibrotic ILD subtypes.

There is significant morbidity and mortality associated with acute exacerbations. In a retrospective study of 461 patients with IPF, Song et al. reported cumulative exacerbation rates of 14.2% and 20.7% at one and three years, respectively, and 50% in-hospital mortality among those who had acute exacerbation [2]. In a similar study, Moua et al. analysed 311 hospitalizations for acute respiratory deterioration in 220 patients with fibrotic ILD, and found high in-hospital mortality rates in both IPF and non-IPF groups. There were nearly threefold higher odds of in-hospital death with suspected acute exacerbation [3]. The results underscore the need to recognise patients who are at higher risk of adverse events when they are admitted to hospital.

The clinical impact of acute exacerbation goes beyond IPF. Suzuki et al. showed that acute exacerbations in non-IPF fibrotic ILD had a poor short-term prognosis similar to AE-IPF, with 90-day mortality rates of 38% and 47%, respectively [4]. Alhamad et al. also found that age, underlying IPF, decreased diffusing capacity, exercise intolerance, and acute exacerbation were significant factors in ILD patients' survival [5]. The observations indicate that there is a relationship between the underlying disease characteristics and the severity of acute respiratory deterioration, which affects prognosis.

Multiple clinical and radiological parameters have been studied for their predictive value for mortality. Singh et al. found lower baseline arterial oxygen tension and mechanical ventilation to be important predictors of poor outcome in a study of patients with acute exacerbation of connective tissue disease-associated ILD in India [6].
Enokida et al. showed that diffuse abnormalities on thoracic computed tomography were correlated with high short-term mortality, especially with severe respiratory failure [7]. In addition, Charokopos et al. highlighted the prognostic significance of the severity of respiratory failure, ventilatory support needs, and clinical risk stratification in AE-ILD patients admitted to intensive care [8].

Although there is increasing knowledge about AE-ILD, the prediction of mortality is still difficult due to the diversity of underlying ILD subtypes, respiratory impairment, inflammatory response, and radiological extent of the disease. There is limited evidence that incorporates the readily available admission parameters to assess in-hospital mortality, especially in Indian tertiary-care settings. Reliable clinical, laboratory and radiological markers could facilitate early risk stratification and clinical decision making.

Thus, the present study was designed to evaluate the clinical profile and in-hospital outcomes of patients admitted with acute exacerbation of interstitial lung disease, to determine the relationship between baseline clinical, laboratory and radiological data and mortality, and to identify baseline clinical, laboratory and radiological predictors of in-hospital death.

MATERIALS AND METHODS

Study design and setting

The study was a prospective observational study of patients admitted to the Department of Respiratory Medicine, Sawai Man Singh Medical College and Associated Hospitals, Jaipur, Rajasthan with the diagnosis of acute exacerbation of interstitial lung disease (AE-ILD). The study period was for 1 year in 2022–2023. The study included 150 index hospitalisations and the primary outcome was in-hospital mortality.

Study population and eligibility criteria

Patients were included if they were adults (aged 18 years or older) with a known or newly diagnosed interstitial lung disease who had acute deterioration of their respiratory function, which was consistent with acute exacerbation of interstitial lung disease (AE-ILD). Acute exacerbation was defined as the appearance of new or worsening respiratory symptoms, usually occurring within 1 month, with the appearance of new bilateral ground-glass opacities and/or consolidation on high-resolution computed tomography (HRCT) on top of the underlying interstitial lung abnormalities. The deterioration had to be not completely accounted for by cardiac failure or fluid overload.

Exclusion criteria were stable ILD without acute exacerbation, respiratory deterioration only due to cardiac failure, pulmonary embolism, pneumothorax, or another established alternative cause, and age <18 years. Suspected infection was not automatically an exclusion if the criteria for AE-ILD were met.

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Recruitment and assessment of patients

The recruitment system outlined consecutive screening of adult admissions to respiratory medicine wards and intensive care units. One index hospitalisation was provided by each patient. Baseline data consisted of demographic data, smoking history, comorbidities, underlying ILD subtype, previous exacerbations, home oxygen use, and prior use of corticosteroids, immunosuppressants, or antifibrotic agents. When available, historical FVC and diffusing capacity for carbon monoxide (DLCO) were taken into account. Admission clinical assessment comprised duration of respiratory deterioration, vital signs, oxygen saturation, initial oxygen delivery device, arterial blood gas parameters and suspected respiratory infection. When paired PaO_2 measurements and reliably documented FiO_2 values were available, the arterial oxygen tension to inspired oxygen fraction ratio (PaO_2/FiO_2) was calculated.

Laboratory parameters were haemoglobin, leukocyte count and differential, platelet count, C-reactive protein (CRP), lactate dehydrogenase (LDH), serum albumin, creatinine, blood urea, and electrolytes. Absolute differential counts were used to calculate the neutrophil-to-lymphocyte ratio.

HRCT findings included the underlying interstitial pattern, new ground-glass opacities/consolidation, extent of new pulmonary abnormalities (less than 25%, 25–50%, and greater than 50%) and diffuse versus non-diffuse distribution.

Outcome Assessment

The main outcome was in-hospital mortality for the index admission. Survival was defined as discharge alive or death during hospital stay. Secondary descriptive outcomes were intensive care admission, invasive mechanical ventilation, and hospital length of stay. Baseline data were compared between survivor and non-survivor groups.

Statistical Analysis

Data for continuous variables were presented as mean ± SD or median [IQR] and categorical variables were presented as frequencies and percentages. Welch's t-test or Mann–Whitney U test, chi-square test or Fisher's exact test was used as appropriate to compare survivors with non-survivors. Univariable and multivariable logistic regression analyses were conducted to determine the predictors of in-hospital mortality, and odds ratios (ORs) and 95% confidence intervals (CIs) were reported. Complete-case analysis was used to create the multivariable model, which contained age, PaO_2/FiO_2 ratio, and serum albumin. Model discrimination and calibration were assessed with AUROC, Brier score and calibration slope with bootstrap internal validation. Alternative predictor specifications were evaluated using sensitivity analyses. All statistical tests were two-tailed and $p<0.05$ was considered statistically significant.

Results

The study cohort comprised 150 index hospitalisations for acute exacerbation of interstitial lung disease. In-hospital death occurred in 54 (36.0%) admissions (95% CI, 28.8%–43.9%). ICU admission occurred in 68 (45.3%), and 18 (12.0%) received invasive mechanical ventilation. Median hospital stay was 10 days [Q1–Q3, 7–14]. Baseline characteristics are summarised in Table 1.

Admission laboratory, imaging and clinical characteristics by survival status are presented in Tables 2 and 3. In univariable logistic regression, prior home oxygen use, greater than 50% extent of new high-resolution computed tomography (HRCT) abnormalities, diffuse HRCT abnormalities, lower PaO_2/FiO_2 and lower serum albumin were associated with higher odds of death (Table 4).

The adjusted model included 83 admissions, with 35 (42.2%) in-hospital deaths. The 95% confidence intervals for age, PaO_2/FiO_2 and serum albumin included unity (Table 5 and Figure 1).

Apparent discrimination was modest (AUROC 0.670 [95% CI, 0.546–0.786]). The bootstrap optimism-corrected AUROC was 0.624, the corrected Brier score was 0.246 and the corrected calibration slope was 0.760 (Figure 2). Estimates remained imprecise when PaO_2/FiO_2 was log-transformed or replaced with respiratory rate (Supplementary Table S1).

Table 1. Baseline characteristics

Characteristic	Overall (N = 150)
Age, years	63.7 (10.7) [n=150]
Sex	Male 96 (64.0%) · Female 54 (36.0%) [n=150]
Body mass index, kg/m²	24.2 (4.0) [n=150]
Smoking status	Never 95 (63.3%) · Former 45 (30.0%) · Current 10 (6.7%) [n=150]
Smoking exposure, pack-years	20.1 [14.2, 26.9] [n=55]
Hypertension	59 (39.3%) [n=150]
Diabetes	26 (17.3%) [n=150]
Coronary artery disease	14 (9.3%) [n=150]

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Chronic kidney disease	15 (10.0%) [n=150]
Prior long-term oxygen therapy	34 (22.7%) [n=150]
Newly recognised ILD	21 (14.0%) [n=150]
Time since ILD diagnosis, months	24.0 [14.0, 40.0] [n=129]
Prior AE-ILD admission	39 (26.0%) [n=150]
ILD subtype	IPF 54 (36.0%) · Fibrotic HP 30 (20.0%) · CTD-ILD 29 (19.3%) · Non-IPF IIP 20 (13.3%) · Unclassifiable ILD 9 (6.0%) · Other fibrotic ILD 8 (5.3%) [n=150]
Prior systemic corticosteroids	51 (34.0%) [n=150]
Prior immunosuppression	25 (16.7%) [n=150]
Prior antifibrotic therapy	32 (21.3%) [n=150]
FVC, % predicted	64.1 (12.5) [n=97]
DLCO, % predicted	48.4 (13.1) [n=84]

Values are mean (SD), median [Q1, Q3], or n (%). Bracketed n gives the available denominator. Pack-years describe ever-smokers. ILD duration describes previously diagnosed cases. Historical FVC and DLCO use available tests.

Table 2. Admission laboratory and HRCT characteristics

Characteristic	Survived (n = 96)	Died (n = 54)	Test statistic	p-value	Effect estimate
Haemoglobin, g/dL	12.2 (1.7) [n=96]	12.6 (1.3) [n=54]	t=1.60 (132.3 df)	0.111	MD 0.40 [-0.09, 0.90]
Leukocytes, cells/µL	10881.0 [8723.8, 13578.8] [n=96]	12377.0 [9183.8, 14592.8] [n=54]	U=2949.0	0.163	Rank-biserial 0.14
Neutrophils, cells/µL	8890.5 [6692.0, 11727.5] [n=96]	10225.0 [7153.2, 12524.5] [n=54]	U=2975.5	0.134	Rank-biserial 0.15
Lymphocytes, cells/µL	1135.0 [800.2, 1521.5] [n=96]	1108.0 [746.0, 1628.0] [n=54]	U=2555.5	0.888	Rank-biserial -0.01
Neutrophil-to-lymphocyte ratio	7.7 [4.6, 13.7] [n=96]	8.8 [5.2, 13.9] [n=54]	U=2813.5	0.387	Rank-biserial 0.09
Platelets, ×10⁹/L	246.1 (62.1) [n=96]	253.6 (59.2) [n=54]	t=0.74 (114.5 df)	0.463	MD 7.55 [-12.76, 27.85]
C-reactive protein, mg/L	57.5 [33.1, 89.2] [n=96]	71.6 [44.5, 99.9] [n=54]	U=2989.0	0.121	Rank-biserial 0.15
LDH, U/L	366.0 [307.0, 477.0] [n=89]	423.0 [348.0, 539.2] [n=50]	U=2645.5	0.065	Rank-biserial 0.19
Albumin, g/dL	3.35 (0.47) [n=96]	3.19 (0.45) [n=54]	t=-2.06 (114.7 df)	0.041	MD -0.16 [-0.31, -0.01]
Creatinine, mg/dL	0.94 [0.76, 1.16] [n=96]	1.03 [0.90, 1.17] [n=54]	U=2967.0	0.143	Rank-biserial 0.14
Blood urea, mg/dL	39.8 [32.4, 45.3] [n=96]	42.9 [30.8, 53.0] [n=54]	U=2917.5	0.203	Rank-biserial 0.13
Sodium, mmol/L	136.9 (3.5) [n=96]	136.1 (4.1) [n=54]	t=-1.28 (97.8 df)	0.204	MD -0.84 [-2.16, 0.47]
Potassium, mmol/L	4.1 (0.4) [n=96]	4.0 (0.4) [n=54]	t=-1.14 (100.0 df)	0.258	MD -0.08 [-0.22, 0.06]
Baseline HRCT pattern	UIP 35 (36.5%) · NSIP 20 (20.8%) · Probable UIP 19 (19.8%) · Other 18 (18.8%) · Indeterminate 4 (4.2%) [n=96]	UIP 17 (31.5%) · Probable UIP 17 (31.5%) · Other 10 (18.5%) · NSIP 9 (16.7%) · Indeterminate 1 (1.9%) [n=54]	Monte Carlo χ^2=3.08 (4 df)	0.563	
New bilateral ground-glass opacity	92 (95.8%) [n=96]	51 (94.4%) [n=54]	Fisher exact	0.703	
New bilateral consolidation	45 (46.9%) [n=96]	21 (38.9%) [n=54]	χ^2=0.89 (1 df)	0.344	

Extent of new HRCT abnormalities	25–50% 49 (51.0%) · <25% 33 (34.4%) · >50% 14 (14.6%) [n=96]	25–50% 30 (55.6%) · >50% 19 (35.2%) · <25% 5 (9.3%) [n=54]	χ^2=15.41 (2 df)	<0.001	
Diffuse abnormalities	36 (37.5%) [n=96]	36 (66.7%) [n=54]	χ^2=11.78 (1 df)	<0.001	

Values are mean (SD), median [Q1, Q3], or n (%). Bracketed n gives the available denominator. MD is the mean difference (died minus survived), with 95% CI. Positive rank-biserial estimates indicate higher values among deaths.

Table 3. Admission clinical characteristics

Characteristic	Survived (n = 96)	Died (n = 54)	Test statistic	p-value	Effect estimate
Acute deterioration, days	7.0 [4.0, 10.0] [n=96]	6.0 [4.0, 9.0] [n=54]	U=2517.0	0.770	Rank-biserial -0.03
Respiratory rate, breaths/min	27.5 (5.4) [n=96]	28.3 (5.2) [n=54]	t=0.90 (113.8 df)	0.370	MD 0.80 [-0.97, 2.58]
Heart rate, beats/min	102.7 (12.1) [n=96]	105.2 (15.0) [n=54]	t=1.06 (92.3 df)	0.291	MD 2.53 [-2.20, 7.26]
Systolic BP, mmHg	125.2 (16.4) [n=96]	118.5 (15.9) [n=54]	t=-2.42 (112.9 df)	0.017	MD -6.63 [-12.05, -1.21]
Diastolic BP, mmHg	70.8 (12.3) [n=96]	68.0 (11.2) [n=54]	t=-1.43 (119.1 df)	0.155	MD -2.82 [-6.73, 1.09]
Temperature, °C	37.3 (0.5) [n=96]	37.3 (0.6) [n=54]	t=-0.10 (85.4 df)	0.917	MD -0.01 [-0.20, 0.18]
Fever	8 (8.3%) [n=96]	9 (16.7%) [n=54]	χ^2=2.39 (1 df)	0.122	
SpO_2 on initial device, %	94.0 [91.0, 95.8] [n=96]	93.5 [90.8, 95.2] [n=54]	U=2374.0	0.394	Rank-biserial -0.08
Initial oxygen device	Nasal cannula 33 (34.4%) · Room air 21 (21.9%) · Venturi mask 18 (18.8%) · Reservoir mask 13 (13.5%) · HFNO 7 (7.3%) · NIV 4 (4.2%) [n=96]	Reservoir mask 10 (18.5%) · HFNO 10 (18.5%) · Venturi mask 10 (18.5%) · Nasal cannula 9 (16.7%) · Room air 8 (14.8%) · NIV 7 (13.0%) [n=54]	Monte Carlo χ^2=12.81 (5 df)	0.024	
FiO_2, fraction	0.35 [0.21, 0.50] [n=50]	0.50 [0.38, 0.69] [n=35]	U=1166.5	0.008	Rank-biserial 0.33
PaO_2, mmHg	73.9 (15.9) [n=94]	72.6 (12.3) [n=54]	t=-0.58 (133.5 df)	0.565	MD -1.35 [-5.98, 3.28]
$PaCO_2$, mmHg	35.9 [31.0, 40.9] [n=94]	34.5 [29.6, 40.8] [n=54]	U=2402.5	0.591	Rank-biserial -0.05
Arterial pH	7.41 (0.05) [n=94]	7.42 (0.04) [n=54]	t=0.23 (116.3 df)	0.820	MD 0.00 [-0.01, 0.02]
PaO_2/FiO_2, mmHg	193.8 [133.8, 369.3] [n=48]	131.5 [95.3, 226.4] [n=35]	U=609.0	0.034	Rank-biserial -0.28
Suspected respiratory infection	45 (46.9%) [n=96]	24 (44.4%) [n=54]	χ^2=0.08 (1 df)	0.774	
Acute respiratory failure	69 (71.9%) [n=96]	46 (85.2%) [n=54]	χ^2=3.42 (1 df)	0.064	

Values are mean (SD), median [Q1, Q3], or n (%). Bracketed n gives the available denominator. PaO_2/FiO_2 uses paired PaO_2 and reliably documented FiO_2. MD is the mean difference (died minus survived), with 95% CI. Positive rank-biserial estimates indicate higher values among deaths.

Table 4. Univariable logistic regression

Predictor	Analysed n	Deaths	OR [95% CI]	Wald z	p-value
Age per 10 years	150	54	1.25 [0.91, 1.73]	1.39	0.166
PaO_2/FiO_2 per 50 mmHg lower	83	35	1.21 [1.01, 1.44]	2.07	0.038
Albumin per 0.5 g/dL lower	150	54	1.46 [1.01, 2.12]	1.99	0.046
LDH per 100 U/L higher	139	50	1.17 [0.94, 1.47]	1.38	0.167
CRP per doubling	150	54	1.31 [0.92, 1.88]	1.48	0.138
Respiratory rate per 5 breaths/min higher	150	54	1.15 [0.84, 1.58]	0.89	0.374
Home oxygen	150	54	3.45 [1.56, 7.60]	3.06	0.002
IPF versus other subtypes	150	54	1.56 [0.78, 3.10]	1.26	0.208

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New HRCT abnormalities >50%	150	54	3.18 [1.43, 7.05]	2.85	0.004
Diffuse HRCT abnormalities	150	54	3.33 [1.65, 6.72]	3.37	<0.001
FVC per 10 percentage points lower	97	38	1.27 [0.91, 1.78]	1.39	0.165
Suspected respiratory infection	150	54	0.91 [0.46, 1.77]	-0.29	0.774

Each row represents a separate model. Binary variables compare presence with absence unless specified. The >50% HRCT category is compared with ≤50%.

Table 5. Multivariable logistic regression

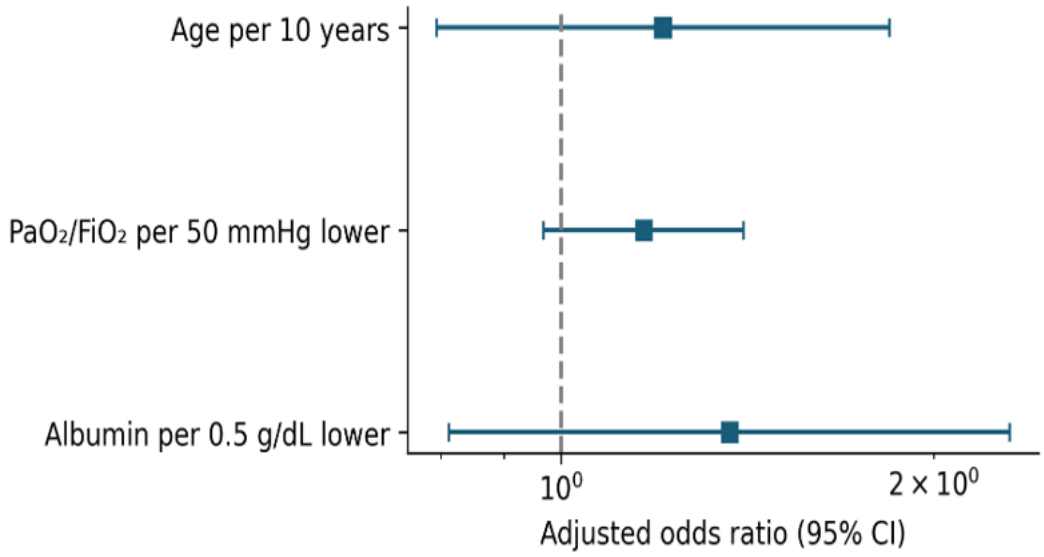
Predictor	Analysed n	Deaths	OR [95% CI]	Wald z	p-value
Age per 10 years	83	35	1.21 [0.79, 1.84]	0.88	0.377
PaO_2/FiO_2 per 50 mmHg lower	83	35	1.17 [0.97, 1.40]	1.63	0.103
Albumin per 0.5 g/dL lower	83	35	1.37 [0.81, 2.31]	1.18	0.239

All three terms were included simultaneously. The model used 83 complete records with 35 deaths. Odds ratios are scaled as indicated.

Supplementary Table S1. Sensitivity analyses

Model	Predictor	Analysed n	Deaths	OR [95% CI]	Wald z	p-value
Log_2 PaO_2/FiO_2 on primary sample	Age per 10 years	83	35	1.19 [0.78, 1.82]	0.82	0.411
	PaO_2/FiO_2 per halving	83	35	1.44 [0.86, 2.41]	1.39	0.165
	Albumin per 0.5 g/dL lower	83	35	1.38 [0.82, 2.34]	1.21	0.225
Age and albumin on primary sample	Age per 10 years	83	35	1.19 [0.78, 1.80]	0.82	0.413
	Albumin per 0.5 g/dL lower	83	35	1.55 [0.94, 2.55]	1.74	0.083
Respiratory-rate model on primary sample	Age per 10 years	83	35	1.19 [0.78, 1.80]	0.80	0.425
	Respiratory rate per 5 breaths/min higher	83	35	0.91 [0.61, 1.35]	-0.46	0.644
	Albumin per 0.5 g/dL lower	83	35	1.60 [0.96, 2.67]	1.79	0.074
Respiratory-rate model on full cohort	Age per 10 years	150	54	1.21 [0.88, 1.67]	1.16	0.247
	Respiratory rate per 5 breaths/min higher	150	54	1.12 [0.81, 1.55]	0.70	0.486
	Albumin per 0.5 g/dL lower	150	54	1.41 [0.97, 2.06]	1.80	0.072

PaO_2/FiO_2 was assessed on the original and logarithmic scales. Respiratory-rate models were fitted in the primary analysis subset and the full cohort.



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Figure 1. Adjusted associations with in-hospital mortality

Adjusted odds ratios and Wald 95% confidence intervals for the primary three-term model.

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Figure 2. Model discrimination and calibration

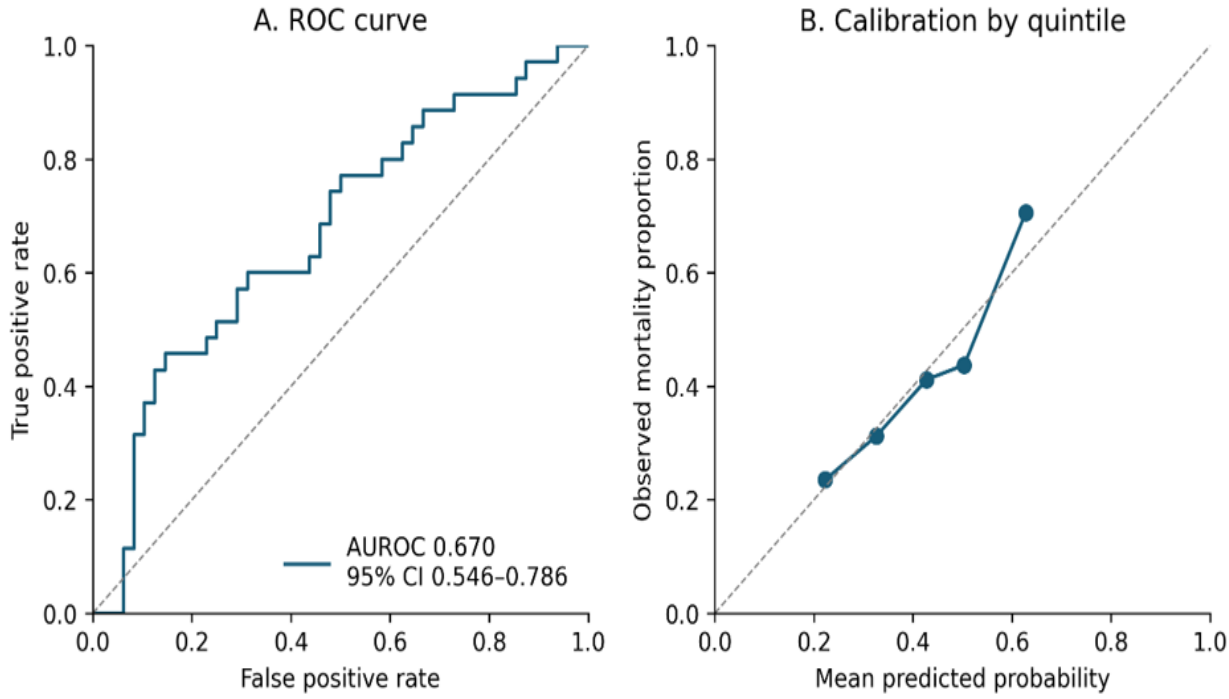


Figure 2. Model discrimination and calibration

Apparent ROC curve and grouped calibration for the 83 complete records. The diagonal in the calibration panel indicates agreement between predicted and observed risk.

DISCUSSION

In the present analysis, we evaluated factors associated with in-hospital mortality in 150 patients with acute exacerbation of interstitial lung disease (AE-ILD). In-hospital mortality was 36.0%, while 45.3% required intensive care and 12.0% received invasive mechanical ventilation. In univariable analysis, previous home oxygen therapy, extensive or diffuse high-resolution computed tomography (HRCT) abnormalities, reduced PaO_2/FiO_2 ratio, and lower serum albumin were associated with mortality. None of the three variables (age, PaO_2/FiO_2, and albumin) in the adjusted model had a statistically significant independent association. These results highlight the complexity of predicting mortality in AE-ILD, as underlying disease severity and acute respiratory dysfunction could play a role simultaneously.

The mortality rate in the current study was similar to those reported by some hospital-based studies. Choi et al. [9] evaluated 96 patients with AE-ILD from three tertiary hospitals and found that the in-hospital mortality rate was 24%. The mean age of their population was 70.1 years, and idiopathic pulmonary fibrosis (IPF) accounted for 60.4% of the cases. Likewise, Shi et al. [10] reported in-hospital and overall mortality of 43.1% and 63.8%, respectively, in 160 critically ill patients with ILD. Differences between these studies and the current analysis could be due to differences in underlying ILD subtypes, severity of admission, need for intensive care, and the length of follow-up.

Respiratory impairment was an important marker of adverse outcomes. The non-survivors group had a lower median PaO_2/FiO_2 ratio than the survivors group (131.5 mmHg compared to 193.8 mmHg; p=0.034), and each 50 mmHg decrease in PaO_2/FiO_2 ratio was associated with increased unadjusted odds of death (OR=1.21; 95% CI: 1.01–1.44). A similar study by Usui et al. [11] showed that the PaO_2/FiO_2 ratio was significantly lower in non-survivors with acute exacerbation of chronic fibrosing interstitial pneumonia (p=0.012). They also found systemic inflammatory response syndrome to be an independent mortality predictor (HR=6.28; p=0.015). The results indicate that the extent of the acute physiological deterioration could provide prognostic information beyond the diagnosis of underlying ILD.

This is further supported by the systematic review by Kamiya and Panlaqui [12] who included 37 studies that assessed prognostic factors in acute exacerbation of IPF. Lower PaO_2/FiO_2, increased lactate dehydrogenase (LDH), leukocytosis and use of pre-exacerbation oxygen therapy were all associated with death. In previous studies, adjusted hazard ratios of 2.34 and 3.68 were found for oxygen therapy. Similarly, unadjusted mortality odds were higher among those who used oxygen at

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home prior to the exacerbation (OR=3.45; 95% CI: 1.56–7.60; p=0.002). This association could indicate greater baseline physiological impairment and lower respiratory reserve prior to exacerbation.

Another significant finding was radiological severity. Mortality risk was higher for those with new HRCT abnormalities that involved more than 50% of the lungs (OR=3.18; p=0.004) or diffuse abnormalities (OR=3.33; p<0.001). Akira et al. [13] studied 64 exacerbation episodes in 58 patients with IPF and found peripheral, multifocal, and diffuse patterns of new pulmonary opacities. Of 58 patients with a first exacerbation, 25 patients died, and diffuse or multifocal abnormalities were associated with worse survival than peripheral abnormalities (OR=4.63; 95% CI: 1.90–11.28). Their results confirm the prognostic value of the distribution of acute pulmonary abnormalities.

Fujimoto et al. [14] also showed the usefulness of quantitative HRCT assessment in 60 AE-IPF patients. The HRCT severity score was an independent predictor of mortality (HR=1.13; 95% CI: 1.06–1.19; p=0.0002) and had an area under the receiver operating characteristic curve of 0.944. Patients with scores of ≥245 had significantly worse survival. The present analysis grouped the extent and distribution of new abnormalities into categories, unlike this detailed radiological scoring approach. However, the associations observed indicate that even the most basic HRCT classifications may provide clinically useful prognostic data.

It is important to take into account the influence of underlying ILD subtype. Salonen et al. [15] investigated 128 patients with acute exacerbations of fibrosing ILD (AEFI), of which 79 were patients with IPF. The median survival time after hospitalisation was 2.6 months in AE-IPF versus 21 months in other fibrotic ILDs (p<0.001). This survival difference remained after adjusting for demographic characteristics and pulmonary function (HR=2.39; 95% CI: 1.41–4.05). The current analysis revealed that IPF represented 36.0% of the patients, and was not significantly associated with in-hospital mortality in univariable regression (OR=1.56; p=0.208). This discrepancy may be due, in part, to differences in outcome definition and to the heterogeneous distribution of non-IPF subtypes.

Inflammatory abnormalities can also play a role in prognosis. Choi et al. [9] found that non-survivors had higher levels of CRP and LDH, and that an increase in Krebs von den Lungen-6 over one week was an independent predictor of death (OR=1.094; p=0.025). Concentrations of CRP and LDH, however, were not statistically significant in the present univariable analyses, but tended to be elevated in non-survivors. Kato et al. [16] studied 79 patients with acute exacerbations of chronic fibrosing idiopathic interstitial pneumonias, of which 34 were idiopathic, 25 were triggered by infections, and 20 were non-infection-triggered. The infection-related exacerbations showed better survival, and clinical type of exacerbation and radiological findings were linked to early mortality. These findings highlight the clinical diversity of AE-ILD and the need for further understanding of triggers for exacerbation.

In the present analysis, non-survivors had lower serum albumin levels (3.19 g/dL vs 3.35 g/dL; p=0.041), and lower levels of serum albumin were associated with death in univariable regression (OR=1.46 per 0.5 g/dL decrease; p=0.046). This association was, however, weakened after adjustment (OR=1.37; p=0.239). Likewise, the OR for the adjusted PaO_2/FiO_2 association was not statistically significant (OR=1.17; p=0.103). Modest discrimination was seen in the multivariable model (AUROC=0.670), which dropped to 0.624 after optimism correction. The findings suggest that a small number of admission factors may not be sufficient to represent the multi-faceted factors contributing to death.

The strengths of the methods are evaluation of clinically accessible admission parameters, systematic HRCT assessment, and internal validation of the prediction model. There were also significant limitations, such as the single-centre design, the fact that the ILD subtypes were not homogeneous and that PaO_2/FiO_2 was not available for all cases, resulting in the analysis of only 83 observations. There were relatively few deaths in this subset, which reduced the precision of the statistics and the number of predictors that could be assessed simultaneously. Additionally, in-hospital mortality rates do not include deaths that happen after discharge. Multicentre studies with longer follow-up, standardized radiological evaluation, and wider physiological and biochemical risk factors are required to improve the risk-stratification models in AE-ILD.

CONCLUSION

The in-hospital mortality rate in this analysis of acute exacerbation of interstitial lung disease (AE-ILD) was 36.0%. Impaired oxygenation, lower serum albumin, and previous home oxygen therapy, and extensive and diffuse HRCT abnormalities were associated with mortality in univariable analyses. After adjusting for these factors, however, there was no statistically significant independent association between age, PaO_2/FiO_2 ratio, or serum albumin. The multivariable model demonstrated moderate

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predictive ability, reflecting the complexity of the assessment of mortality risk in AE-ILD. These results suggest that larger prospective studies are needed to assess the severity of the respiratory disease, extent of radiology and baseline clinical parameters to better stratify the early risk of respiratory disease.

REFERENCES

1. Collard HR, Ryerson CJ, Corte TJ, Jenkins G, Kondoh Y, Lederer DJ, et al. Acute exacerbation of idiopathic pulmonary fibrosis. An international working group report. *Am J Respir Crit Care Med.* 2016;194(3):265–275. doi:10.1164/rccm.201604-0801CI.
2. Song JW, Hong SB, Lim CM, Koh Y, Kim DS. Acute exacerbation of idiopathic pulmonary fibrosis: incidence, risk factors and outcome. *Eur Respir J.* 2011;37(2):356–363. doi:10.1183/09031936.00159709.
3. Moua T, Westerly BD, Dulohery MM, Daniels CE, Ryu JH, Lim KG. Patients with fibrotic interstitial lung disease hospitalized for acute respiratory worsening: a large cohort analysis. *Chest.* 2016;149(5):1205–1214. doi:10.1016/j.chest.2015.12.026.
4. Suzuki A, Kondoh Y, Brown KK, Johkoh T, Kataoka K, Fukuoka J, et al. Acute exacerbations of fibrotic interstitial lung diseases. *Respirology.* 2020;25(5):525–534. doi:10.1111/resp.13682.
5. Alhamad EH, Cal JG, Alrajhi NN, AlBoukai AA. Acute exacerbation in interstitial lung disease. *Ann Thorac Med.* 2021;16(2):178–187. doi:10.4103/atm.atm_14_21.
6. Singh P, Thakur B, Mohapatra AK, Padhan P. Clinical features and outcome of acute exacerbation in connective tissue disease-associated interstitial lung disease: a single-center study from India. *Int J Rheum Dis.* 2019;22(9):1741–1745. doi:10.1111/1756-185X.13666.
7. Enokida K, Takihara T, Horio Y, Nakamura N, Kutsuzawa N, Takahashi M, et al. Combination of computed tomography imaging pattern and severity of respiratory failure as factors associated with prognosis for acute exacerbation of idiopathic chronic fibrosing interstitial pneumonia. *PLoS One.* 2023;18(2). doi:10.1371/journal.pone.0279878.
8. Charokopos A, Moua T, Ryu JH, Smischney NJ. Acute exacerbation of interstitial lung disease in the intensive care unit. *World J Crit Care Med.* 2022;11(1):22–32. doi:10.5492/wjccm.v11.i1.22.
9. Choi MG, Choi SM, Lee JH, Yoon JK, Song JW. Changes in blood Krebs von den Lungen-6 predict the mortality of patients with acute exacerbation of interstitial lung disease. *Sci Rep.* 2022;12:4916. doi:10.1038/s41598-022-08965-9
10. Shi S, Xiao Y, Qiu X, Li Y, Qiu Y, Zhou K, et al. Prognostic effects of clinical and CT imaging features on critically ill patients with interstitial lung disease hospitalized in respiratory intensive care unit. *Sci Rep.* 2019;9:17190. doi:10.1038/s41598-019-53865-0.
11. Usui Y, Kaga A, Sakai F, Shiono A, Komiyama KI, Hagiwara K, et al. A cohort study of mortality predictors in patients with acute exacerbation of chronic fibrosing interstitial pneumonia. *BMJ Open.* 2013;3(7). doi:10.1136/bmjopen-2013-002971.
12. Kamiya H, Panlaqui OM. Systematic review and meta-analysis of prognostic factors of acute exacerbation of idiopathic pulmonary fibrosis. *BMJ Open.* 2020;10(6). doi:10.1136/bmjopen-2019-035420.
13. Akira M, Kozuka T, Yamamoto S, Sakatani M. Computed tomography findings in acute exacerbation of idiopathic pulmonary fibrosis. *Am J Respir Crit Care Med.* 2008;178(4):372–378. doi:10.1164/rccm.200709-1365OC.
14. Fujimoto K, Taniguchi H, Johkoh T, Kondoh Y, Ichikado K, Sumikawa H, et al. Acute exacerbation of idiopathic pulmonary fibrosis: high-resolution CT scores predict mortality. *EurRadiol.* 2012;22(1):83–92. doi:10.1007/s00330-011-2211-6.
15. Salonen J, Purokivi M, Bloigu R, Kaarteenaho R. Prognosis and causes of death of patients with acute exacerbation of fibrosing interstitial lung diseases. *BMJ Open Respir Res.* 2020;7(1). doi:10.1136/bmjresp-2020-000563.
16. Kato M, Yamada T, Kataoka S, Arai Y, Miura K, Ochi Y, et al. Prognostic differences among patients with idiopathic interstitial pneumonias with acute exacerbation of varying pathogenesis: a retrospective study. *Respir Res.* 2019;20(1):287. doi:10.1186/s12931-019-1247-z.

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