CHEST

Patients With Fibrotic Interstitial Lung Disease Hospitalized for Acute Respiratory Worsening

A Large Cohort Analysis

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BACKGROUND: Acute respiratory worsening (ARW) requiring hospitalization in patients with fibrotic interstitial lung disease (f-ILD) is common. Little is known about the frequency and implications of ARW in IPF and non-IPF ILD patients hospitalized for acute exacerbation (AE) vs known causes of ARW.

METHODS: All consecutive patients with f-ILD hospitalized with ARW at our institution from 2000 to 2014 were reviewed. ARW was defined as any worsening of respiratory symptoms with new or worsened hypoxemia or hypercapnia within 30 days of admission. Suspected AE was defined using modified 2007 American Thoracic Society/European Respiratory Society criteria. Known causes of ARW were reviewed and collated along with in-hospital and all-cause mortality postdischarge.

RESULTS: A total of 220 patients (100 with IPF and 120 non-IPF) composed 311 admissions for ARW. Suspected AE (SAE) comprised 52% of ARW admissions, followed by infection (20%), and subacute progression of disease (15%). In-hospital mortality was similar in patients with IPF vs patients without (55 vs 45%, $P = .18$), but worse in suspected AE admission types (OR, 3.1 [1.9-5.14]). One-year survival after last ARW admission for the whole cohort was 22%, despite only 27% of patients presenting with baseline oxygen requirement at admission and a mean admission Charlson Comorbidity Index score of 5.4 (expected 1-year survival, 89%). Survival after discharge was similar between SAE and secondary ARW admission types in both IPF and non-IPF patients.

CONCLUSIONS: Among patients with f-ILD, hospitalization for ARW appears associated with significant in-hospital and postdischarge mortality regardless of underlying fibrotic lung disease or non-AE cause of acute respiratory decline. CHEST 2016; 149(5):1205-1214

KEY WORDS: acute respiratory decline; fibrotic interstitial lung disease; hospitalization

ABBREVIATIONS: AE = acute exacerbation; ARW = acute respiratory worsening; CCIS = Charlson Comorbidity Index Score; CTD-ILD = connective tissue disease-interstitial lung disease; f-ILD = fibrotic interstitial lung disease; IPF = idiopathic pulmonary fibrosis; SAE = suspected acute exacerbation

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FUNDING/SUPPORT: This study was funded in part by the Brewer Award for Research in Idiopathic Pulmonary Fibrosis.

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DOI: http://dx.doi.org/10.1016/j.chest.2015.12.026

Patients with fibrotic interstitial lung disease (f-ILD) commonly present with acute respiratory worsening (ARW) requiring hospital admission. Although acute exacerbation (AE) in idiopathic pulmonary fibrosis (IPF)[1] is associated with high in-hospital mortality, AE has also been described in patients with non-IPF or secondary fibrotic lung diseases.[2-5] Suspected AE (SAE) again is a diagnosis of exclusion, whose differential is broad and may include infectious and cardiac causes for acute respiratory decline.

Although the frequency and morbidity of AE in IPF has been reported,[6-11] there are few data regarding SAE or secondary ARW outcomes in patients with non-IPF fibrotic lung disease. We postulated that (1) hospitalized patients with non-IPF disease would fare better than those with IPF; (2) those with secondary ARW or possibly modifiable causes for admission would have better inpatient prognosis; and (3) postdischarge survival for SAE admission would fare worse compared with admissions for secondary ARW as AE may represent rapid progression in underlying fibrotic disease. To better understand this, we reviewed consecutive patients admitted to our institution with f-ILD suffering from respiratory deterioration and compared outcomes in IPF and patients without IPF.

Methods

Definitions of Fibrotic Lung Disease and Patient Characteristics

Mayo Clinic Institutional Review Board approval was obtained (#12-010133). A search of the electronic medical records from January 1, 2000, to December 31, 2014, was performed for consecutive patients with suspected or known lung fibrosis and hospital admission for ARW using the search terms "lung fibrosis" and "acute respiratory failure." Each admission was reassessed by study members for IPF diagnosis as defined by recent international criteria.[12] Non-IPF cases were further categorized into one or more of seven listed disease subsets by study group consensus (see Table 1 and e-Appendixes 1 and 2 for case definitions).

Patient demographic and hospital data were collected at ILD diagnosis and ARW admission. A Charlson Comorbidity Index Score (CCIS) at the time of each admission was calculated using a previously described protocol.[13]

Definitions of Admission Type

ARW was defined as any acute worsening of respiratory symptoms with new or worsened hypoxemia or hypercapnia within 30 days of admission. AE was defined by 2007 American Thoracic Society/European Respiratory Society criteria,[1] with the definition broadened to include patients without IPF and those without previously known or established fibrotic disease at admission. Given the retrospective nature of our study, all AE was considered suspected, with the definition broadened to include patients whom did not undergo chest CT scan but had new bilateral superimposed infiltrate or consolidation on admission chest radiograph. We also included those who did not undergo bronchoscopic or endotracheal assessment of infection but presented without clinical features of infection including fever or cough, with subsequent negative sputum and blood culture studies.[14] Other admission types were further defined by study group consensus as presented in Table 2 and e-Appendixes 1 and 2.

In-Hospital Management

Diagnostic tests performed during hospitalization were reviewed and included chest CT scan, echocardiogram, and bronchoscopy. Bronchoscopy results were defined as positive for acute infection if infectious agents were identified on microbiologic studies in the right clinical context. Transthoracic echocardiogram done at any time during hospitalization was reviewed for presenting right ventricular systolic pressure (in mm Hg) and left ventricular ejection fraction (percent). High or pulse dose IV steroids was defined as methylprednisolone (or its equivalent) given at a dose $>$ 500 mg daily for a minimum of 3 days. Admission code status, hospital death, and discharge disposition were also reviewed.

Statistical Analysis

Statistical analysis was performed on JMP Software (Version 10.0). For the purposes of broad clinical analysis, patients were stratified by diagnosis (IPF or non-IPF) and admission (AE vs secondary ARW) type. Univariable and multivariable logistic regression for predictors of in-hospital mortality was performed using a priori covariables of age at admission, smoker status, baseline percent predicted FVC, and admission CCIS. Survival analysis for all-cause mortality was done using Kaplan-Meier method with log rank. In all analyses, two-sided P values $<$ .05 were considered statistically significant.

Results

Study Population

Two hundred and sixty-six patients were identified in the initial cohort, with 220 meeting inclusion criteria. These patients accounted for 311 unique ARW admissions. Population demographics are presented in Table 1. IPF accounted for 46% of presenting fibrotic lung disease followed by connective tissue disease-interstitial lung disease (CTD-ILD) (25%). Nearly one-third of patients (29%) presented without prior f-ILD diagnosis at the time of admission. Among previously diagnosed patients with fibrotic-ILD, 42 (27%) were on oxygen 2 L or more for longer than 8 h per day at the time of first ARW admission.

Admission Type and Hospitalization Characteristics of IPF and Non-IPF ILD

Table 2 outlines characteristics of 311 unique admissions for ARW. Patients with IPF were statistically older at admission (73.1 vs 65.2, P $<$ .0001) with median time from ILD diagnosis to first hospitalization for ARW