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Original Research Article

Clinical Features and Outcomes of Idiopathic Pulmonary Fibrosis Patients Hospitalized for Pneumonia

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Abstract

Background: Idiopathic pulmonary fibrosis (IPF) is a chronic, progressive lung condition that exhibits the typical interstitial pneumonia histopathologic pattern. Despite a diverse natural history, the prognosis is dismal and the median survival following diagnosis is 2 to 3 years. IPF patients frequently experience acute respiratory problems. Acute exacerbations are the primary cause of acute respiratory events, followed by pulmonary infections such pneumonia and bronchitis. When an acute respiratory episode occurs, patients with IPF are typically hospitalized, albeit this relies on the availability of local medical resources. The importance of respiratory-related hospitalizations in IPF outcomes has just lately come to light. This is due in part to the high death rate associated with respiratory hospitalizations as well as the fact that hospitalization affects survival after discharge.

Aim: With the advent of the new, more inclusive definition of acute exacerbations, the goal of this study was to examine the clinical characteristics and outcomes of IPF patients hospitalized for pneumonia. It is critical to assess the importance of pneumonia in the management of Idiopathic Pulmonary Fibrosis (IPF) in light of the revised definition and new diagnostic criteria for acute exacerbations of Idiopathic Pulmonary Fibrosis (IPF), which proposed sub-categorization of acute exacerbations as "triggered".

Material and Method: We performed a retrospective cohort analysis in the Department of Respiratory Medicine on a series of IPF patients who had been hospitalized to the hospital for pneumonia. Clinical records served as the primary source for baseline demographic, clinical, and outcome information. All patients with IPF who were admitted to the hospital for pulmonary infections, including pneumonia and bronchitis, had their medical records reviewed retrospectively to determine the severity of their pneumonia using the A-DROP (Age, Dehydration, Respiratory failure, Orientation disturbance, and low blood pressure) scoring system. Every admission made by a patient who was admitted more than once during the study period was taken into account. Admissions that took place fewer than two weeks after the one before were, however, counted as a single continuous admission.

Results: 300 IPF cases were found to have been admitted to our hospital during the research period. Of them, 60 cases (19.9%) experienced an acute aggravation of IPF, while 50 cases (17.4%) developed pneumonia. The average age of the former group, 45 males (76.8%) and 15 females (23.2%), was 79.3 years. Prior to the development of pneumonia, steroid therapy, immunosuppressive therapy, and anti-fibrotic medications were used to treat IPF. Patients with IPF and pneumonia had considerably lower 30-day and in-hospital death rates than patients with acute IPF exacerbations identified in our hospital using the diagnostic criteria from 2016.

Conclusion: When IPF patients were admitted for pneumonia, their 30-day and in-hospital death rates were significantly lower than those with acute exacerbations identified using the diagnostic criteria from 2016. The 30-day mortality from pneumonia was substantially correlated with the A-DROP score. In the era of a new, larger definition of acute exacerbations, it is critical to distinguish between pneumonia and acute exacerbation.

Keywords: Idiopathic Pulmonary Fibrosis; Pulmonary Infection; High-Resolution Computed Tomography, Interstitial Pneumonia.

Introduction

Idiopathic pulmonary fibrosis (IPF) is a chronic, progressive lung condition that exhibits the typical interstitial pneumonia histopathologic pattern. 1 Despite a diverse natural history, the prognosis is dismal and the median survival following diagnosis is 2 to 3 years. [1,2] IPF patients frequently experience acute respiratory problems. Acute exacerbations are the primary cause of acute respiratory events, followed by pulmonary infections such pneumonia and bronchitis. 3 When an acute respiratory episode occurs, patients with IPF are typically hospitalized, albeit this relies on the availability of local medical resources. [3] The importance of respiratory-related hospitalizations in IPF outcomes has just lately come to light. This is due in part to the high death rate associated with respiratory hospitalizations as well as the fact that hospitalization affects survival after discharge. [4]

Idiopathic pulmonary fibrosis (IPF) is a special type of interstitial pneumonia that is chronically progressing and fibrosing with no recognized cause. [5] The clinical course of it can vary greatly. Many people have an unpredictable illness course, with periods of relative stability interspersed with episodes of rapid and frequently deadly decline, despite the fact that some patients endure a continuous progression of the disease over time. [6] According to previous definitions, an acute exacerbation of IPF is an idiopathic worsening of dyspnea that is radiologically indicated by the presence of bilateral ground glass abnormalities on a chest high-resolution computed tomography scan. [7] In clinical practice, it can occasionally be challenging to differentiate between acute exacerbations and respiratory illnesses like bacterial pneumonia. Acute exacerbations of IPF were proposed to be subcategorized as either "triggered" or "idiopathic" in the 2016 International Working Group Report. However, an acute exacerbation might still be identified even in the presence of a recognized trigger. According to the 2016 diagnostic criteria, pulmonary infection can cause an acute exacerbation, however clinical characteristics of IPF patients admitted for pneumonia have not been defined. [8]

Despite the limited knowledge we currently have of the etiology of AE-IPF, AE has clinical features with acute respiratory distress syndrome (ARDS). They both require more oxygen, show bilateral ground glass opacities or consolidation on imaging, and both exhibit diffuse alveolar injury on histology. [9-10] We are aware that ARDS can have a variety of reasons, and people with AE-IPF are probably no different. Furthermore, differential responses of IPF fibroblasts to stimuli in vitro compared to control fibroblasts show that IPF patients likely have maladaptive responses to lung injury. [11-12] An acute exacerbation in IPF patients frequently manifests as shortness of breath or deteriorating

exercise tolerance over the course of days to weeks, but typically less than one month. [13,14] The average number of days between the beginning of symptoms and hospital admission in a small group of 11 patients was 13 days. [15] Frequent symptoms include coughing (with or without sputum formation), fever, and flu-like symptoms. IPF patients frequently have pulmonary infections, which are a primary factor in respiratory hospitalization. But the characteristics of pulmonary infection in IPF are still not completely understood. In this study, the most prevalent microorganisms that cause respiratory hospitalizations in patients with IPF were identified using a retrospective investigation. IPF patients frequently have pulmonary infections, which are a primary factor in respiratory hospitalization. In this study, the most prevalent microorganisms that cause respiratory hospitalizations in patients with IPF were identified using a retrospective investigation. Blood samples, a fast test for the urine antigen of Legionella pneumophila serogroup or Streptococcus pneumoniae, Gram stain and sputum culture where available, and The JRS's A-DROP (Age, Dehydration, Respiratory Failure, Orientation Disturbance, and Low Blood Pressure) scoring system, which uses a 6-point scale (0–5), was used to assess the severity of pneumonia. [16-18]

Material and Methods

All IPF patients who were admitted to the hospital for lung infections, such as pneumonia and bronchitis, had their medical records retrospectively reviewed. Every admission made by a patient who was admitted more than once during the study period was taken into account. Admissions that took place fewer than two weeks after the one before were, however, counted as a single continuous admission.

In patients with at least 1 of the following: fever, a productive cough, or an abnormal white blood cell count, pneumonia was defined as newly acquired radiological consolidations or localized local ground-glass opacities on chest radiographs or chest high-resolution computed tomography (HRCT). A diagnosis of bronchitis was made in a symptomatic patient if the chest HRCT and/or radiograph were unaltered. The study excluded participants who had additional explanations for chest radiography abnormalities, such as acute exacerbation of IPF, congestive heart failure, pulmonary embolism, or malignancy. After careful deliberation with numerous specialists, patients with new bilateral ground-glass opacities that were consistent with an acute exacerbation of IPF were specifically excluded from the study.

300 IPF cases were found to have been admitted to our hospital during the research period. Of them, 60 patients (19.9%) (57) experienced an acute aggravation of IPF, while 50 cases (17.4%) had pneumonia. The average age of the former group, 40 males (76.8%) and 20 females (23.2%), was 79.3 years (range: 60- 94 years). Due to pneumonia, nine patients were admitted more than once: three patients had four episodes, and three patients had six episodes. 28 had NHCAP, whereas 28 had CAP. Prior to the development of pneumonia, steroid therapy, immunosuppressive therapy, and anti-fibrotic medications were used to treat IPF. The number of pneumonia-related hospitalizations increased throughout the winter and spring seasons: 20 in the spring, 9 in the summer, 10 in the fall, and 17 in the winter.

Clinical records served as the primary source for baseline demographic, clinical, and outcome information. Age, sex, lifestyle, pre-admission IPF therapies, concomitant conditions, laboratory data, percutaneous oxygen saturation, bacteriological tests, length of hospital stay, and 30-day or in-hospital mortality were all included in the data. The following tests were performed as part of

the initial microbiological evaluations: Gram stain and culture of sputum when available, aerobic and anaerobic conventional cultures of two blood samples, and a rapid test for the urinary antigen of Legionella pneumophila serogroup 1 or Streptococcus pneumoniae.

Statistical Analysis

Discrete numbers were used to represent categorical data and mean and SD were used to describe continuous variables. In order to compare differences in the clinical, laboratory, and HRCT data between survivors and non-survivors, categorical data were analyzed using the $\chi 2$ test or Fisher's exact test, while continuous data were analyzed using the Mann-Whitney U-test. Potential risk factors for 30-day and hospital mortality were identified using univariate and multivariate analysis with logistic regression models. The PSI score (I-V) was handled as a continuous variable in the mortality analyses. A P value of 0.05 or less was regarded as significant.

Result

300 IPF cases were found to have been admitted to our hospital during the research period. Of them, 60 cases (19.9%) experienced an acute aggravation of IPF, while 50 cases (17.4%) developed pneumonia. The average age of the former group, 45 males (76.8%) and 15 females (23.2%), was 79.3 years. Prior to the development of pneumonia, steroid therapy, immunosuppressive therapy, and anti-fibrotic medications were used to treat IPF. The number of pneumonia-related hospitalizations increased throughout the winter and spring seasons: 20 in the spring, 9 in the summer, 10 in the fall, and 17 in the winter.

Table 1: Microbes identified on hospital admission of 41 study cases with idiopathic pulmonary fibrosis and pneumonia.

Examination of sputum	**N=50**
Streptococcus pneumoniae	4
Moraxella catarrhalis	4
Haemophilus influenza	4
Staphylococcus aureus	3
MSSA	3
MRSA	0
Klebsiella pneumoniae	2
Pseudomonas aeruginosa	2
Acinetobacter baumanii	2
Escherichia coli	0
Enterobactor spp.	0
Urine antigen test	
Streptococcus pneumoniae	3/46
Legionella pneumophila	0/35
A positive culture from blood	1*/40

In our hospital, acute exacerbations of IPF were diagnosed based on the 2016 diagnostic criteria, and the 30-day and in-hospital mortality was considerably lower in those with IPF with pneumonia (14.3% and 17.9%, respectively) than in those with acute exacerbations (37.5% and 54.7%, respectively).

Table 2: Logistic regression analysis for risk factors associated with 30-day mortality in hospitalized cases with idiopathic pulmonary fibrosis and pneumonia

	Odds ratio	95% CI
Alcohol habit	18.55	0.77-520.25
Blood urea nitrogen, mg/dL	0.85	0.77-1.02
C-reactive protein, mg/dL	1.03	0.83-1.12
A-DROP score	55.0	1.44-1543.32

A multiple logistic regression analysis comprised the alcohol habit, BUN, CRP, and A-DROP scores. Albumin and SP-D were excluded from both analyses due to missing data. Only the A-DROP score was substantially linked to 30-day pneumonia mortality.

Discussion

In our IPF sample, acute exacerbations of IPF and pneumonia that required hospitalization were both linked to considerable morbidity, but the prognosis for the former was better than the latter. It is critical to assess the role of pneumonia in the treatment of IPF in light of the updated definition and new diagnostic standards for acute exacerbations of IPF7, which advocated sub-categorization of acute exacerbations as "triggered". In 163 IPF patients who presented with an abrupt (within 30 days) worsening of dyspnea necessitating hospitalization, acute exacerbation of IPF was the most common cause of respiratory-related hospitalizations (55.2%), followed by infection (31.3%). According to Teramachi et al [19] 's report, pneumonia (23%) and acute aggravation of IPF (29%) were the most common diagnoses among 122 patients hospitalized for acute respiratory deterioration. On the other hand, among 106 patients, Nishiyama et al.22 found that pneumonia (47%) and an acute exacerbation of IPF (29.4%) were the two most common reasons for respiratory-related hospitalizations in IPF. The frequency of respiratory-related hospitalization owing to pneumonia in IPF patients was demonstrated to be nearly equal to that of acute exacerbation, but frequency varied by research design and reasons for hospitalization.

According to Molyneaux et al. [20], individuals with IPF had a 3.4-fold higher concentration of Haemophilus sp. in their bronchoalveolar lavage fluid than did control subjects. Further research into the relationship between lung pathogens and the typical microbiota is highly encouraged. P. aeruginosa was the most frequently isolated pathogen across all hospitalizations, and it was discovered in 23% of patients where a causal pathogen was identified. This discovery could be the result of numerous factors. Patients with structural lung abnormalities, such as cystic fibrosis or bronchiectasis, are particularly affected by P. aeruginosa pneumonia. [21] IPF structural lung alterations, such as honeycombing and traction bronchiectasis, may have an impact on the microorganisms that cause the disease. The causal microorganisms, including P. aeruginosa, were not statistically significantly different between pneumonia associated with already-existing IPF radiological patterns and pneumonia that was separate from already-existing IPF radiological patterns. It has been demonstrated that immunocompromised people and patients who recently used antibiotics are more susceptible to developing P. aeruginosa pneumonia. [22]

Patients with IPF who require respiratory hospitalization had higher in-hospital mortality rates and lower post-discharge survival rates. [4] Furthermore, a deterioration in pulmonary function is not a requirement for respiratory hospitalization. Therefore, not only in

clinical trials but also in clinical practice, respiratory hospitalization should be acknowledged as an essential outcome measure. Understanding the features of pulmonary infections and improving treatment based on these findings may increase survival in people with IPF since pulmonary infections frequently cause respiratory hospitalizations in this patient population.

According to Yamazaki et al. [23] 48 IPF patients hospitalized for lung infections such pneumonia and bronchitis, gram-negative bacteria such as Haemophilus influenzae (14.5%), Pseudomonas aeruginosa (4.1%), and Klebsiella pneumoniae (4.1%) were the main culprits. They included bronchitis-causing bacteria, which would explain why our results and those of Oda et al. [24] differed.

According to Koizumi et al. [25], A-utility DROP's in CAP and NHCAP was comparable to that of PSI and CURB-65. The mortality of IPF patients hospitalized for pneumonia may therefore be predicted using this straightforward severity ranking system. [26]

As a result, the findings might not be relevant to people in other regions or to groups with IPF that were born more recently. Third, just a small percentage of individuals had pneumonia's cause determined. Although bronchoscopy-based protected respiratory sampling may be advised, we have had trouble getting samples, particularly from elderly people. Additionally, no PCR analysis was done to find the microorganisms that cause disease. It's possible that viruses, anaerobes, and certain unusual infections like Mycoplasma pneumonia went unnoticed.

Conclusion:

Conclusion: When IPF patients were admitted for pneumonia, their 30-day and in-hospital death rates were significantly lower than those with acute exacerbations identified using the diagnostic criteria from 2016. The 30-day mortality from pneumonia was substantially correlated with the A-DROP score. In the era of a new, larger definition of acute exacerbations, it is critical to distinguish between pneumonia and acute exacerbation. To determine other prognostic markers and the accountable lung microbiota, additional multicenter prospective investigations are required. We concluded that the majority of pathogens recovered from IPF patients who are hospitalized for lung infections are gram-negative bacteria. This contrasts with the gram-positive bacteria that are typically isolated from patients with community-acquired pneumonia. The PSI score may be a useful mortality predictor. Our findings might help in the selection of antibiotics for IPF patients with lung infections.

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