Invasive mechanical ventilation in patients with fibrosing interstitial pneumonia

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Objective: The prognosis of patients with idiopathic pulmonary fibrosis or fibrosing idiopathic nonspecific interstitial pneumonia undergoing invasive mechanical ventilation (MV) for acute respiratory failure is known to be poor. The issue of life support in these patients needs to be reconsidered in light of changes during the past decade in ventilator settings and in the management of acute exacerbation. We therefore aimed to reassess the prognosis of such patients.

Methods: We retrospectively assessed the outcomes of all medical patients with idiopathic pulmonary fibrosis or fibrosing idiopathic nonspecific interstitial pneumonia who required invasive MV in 3 university hospitals in the Paris area from January 2002 to April 2009.

Results: In total, 27 patients (mean age, 66 ± 12.8 years) required invasive MV in the intensive care unit: 8 (30%) were successfully weaned from MV, and 6 and 4 were discharged from the intensive care unit and the hospital, respectively. Survivals for patients who did not undergo lung transplant were 22%, 3.7%, and 3.7%, at 30 days, 6 months, and 12 months, respectively.

Conclusions: We confirm that use of invasive MV for acute respiratory failure in patients with idiopathic pulmonary fibrosis or fibrosing idiopathic nonspecific interstitial pneumonia is associated with a high mortality; however, a subset of patients may be discharged alive from the intensive care unit and hospital, providing an opportunity to consider lung transplant in case of eligibility. Our results suggest that invasive MV should not be systematically denied to these patients but discussed on a case-by-case basis. (J Thorac Cardiovasc Surg 2014;147:47-53)

The prognosis is poor for the most common idiopathic fibrosing interstitial pneumonias, idiopathic pulmonary fibrosis (IPF) and idiopathic nonspecific interstitial pneumonia (iNSIP) in its fibrotic form. In particular, the median survival after diagnosis of IPF is 2 to 3 years.[1] The clinical courses of IPF and iNSIP are usually slowly progressive but may be complicated by episodes of acute deterioration. During an episode of acute respiratory failure (ARF), the patient's condition may worsen despite symptomatic treatment, possible leading to referral to an intensive care unit (ICU) and the requirement of invasive mechanical ventilation (MV). Guidelines concerning the referral to the ICU and initiation of MV are lacking; however, the literature suggests that invasive MV for patients with IPF is appropriate when respiratory failure follows a surgical procedure but is questionable for medical patients because the short- or medium-term outcome is poor, according to several convergent studies.[2-7] This has led many intensivists to deny initiation of invasive MV in this setting[8]; however, most studies investigating outcomes after MV in fibrotic lung diseases involved patients who underwent MV back in the 1990s.

We aimed to reassess the prognosis of medical patients with idiopathic fibrosing interstitial pneumonias (IPF and iNSIP) who required invasive MV in the ICU. Our hypothesis was that the prognosis of these patients might have improved with time, at least with respect to the short-term (ICU) mortality because of developments in the past decade in ventilator settings and management of acute exacerbation in patients undergoing MV, as suggested in a recently published letter.[9] This question seems relevant because an improvement in even short-term prognosis could

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Abbreviations and Acronyms

ARF = acute respiratory failure
BAL = bronchoalveolar lavage
ECMO = extracorporeal membrane oxygenation
ICU = intensive care unit
IPF = idiopathic pulmonary fibrosis
iNSIP = idiopathic nonspecific interstitial pneumonia
LTx = lung transplant
MV = mechanical ventilation
V_T = tidal volume

GTS

allow access to lung transplant (LTx) for patients who are eligible for this procedure.[10] We conducted a retrospective study of patients with IPF in the ICUs of 3 university hospitals. We also investigated patients with fibrosing iNSIP because of their similarities in terms of clinical decision making at the time of admission to an ICU.

MATERIALS AND METHODS

This was a retrospective study of patients in 3 ICUs of teaching hospitals in the Paris area, particularly hospitals involved in care of interstitial pulmonary diseases (Bichat Hospital, Avicenne Hospital, Hôtel Dieu Hospital). We analyzed the medical charts of all patients with fibrosing idiopathic interstitial pneumonia (IPF or fibrosing iNSIP) who required invasive MV from January 2002 to April 2009. This study was approved by the ethics committee of the Société de Réanimation de Langue Française (project 08-263, June 18, 2009).

The diagnosis of IPF was based on histologic evaluation (surgical lung biopsy, transbronchial biopsy, or autopsy) indicative of usual interstitial pneumonia and the absence of an identifiable cause (professional exposure, drug toxicity, identified connective tissue disease). In the absence of histologic evaluation, patients had to fulfill all major criteria and at least 3 of the 4 minor criteria of the American Thoracic Society (ATS) and European Thoracic Society.[11] Diagnosis of fibrosing iNSIP was based on a histologic evaluation indicative of a fibrotic pattern of nonspecific interstitial pneumonia in the absence of an identifiable cause (drug toxicity, infection, connective tissue disease) as proposed by the consensus conference of the American Thoracic Society and European Respiratory Society published in 2002.[1] Invasive MV was defined as the use of MV through an endotracheal tube (orotracheal, nasotracheal intubation, or tracheostomy). All selected patients had undergone invasive MV for ARF or hemodynamic failure. Patients with MV who were admitted to the ICU for simple monitoring after a surgical procedure or a bronchoscopy were excluded.

Data Gathering

We recorded data from medical charts.

Characteristics of patients at baseline. Baseline data included age, sex, body mass index, smoking habit, comorbidities (ischemic heart disease, systemic hypertension, and diabetes), diagnosis (IPF or fibrosing iNSIP), type of histologic evidence if available, disease duration, results from most recent pulmonary function tests (including vital capacity, total lung capacity, ratio of forced expiratory volume in 1 second to vital capacity, carbon monoxide diffusing capacity), blood gas analysis, pulmonary hypertension at baseline (defined as mean pulmonary arterial pressure >25 mm Hg at the right heart catheterization or arbitrarily as systolic pulmonary arterial pressure >50 mm Hg when measured by echocardiography at rest[12]), requirement of long-term oxygen therapy, use of corticosteroids or immunosuppressive therapy at the time of admission, curative anticoagulation therapy, and registration on a waiting list for LTx.

Characteristics on admission to the ICU. ICU admission data included Simplified Acute Physiology Score II, Acute Physiology and Chronic Health Evaluation II score, and reason for ICU admission.

Management in the ICU. ICU management data included time elapsed between admission and the beginning of invasive MV, use of noninvasive ventilation before intubation, ventilator settings after intubation (ventilation mode, tidal volume [V_T] expressed in mL/kg ideal body weight, level of positive end-expiratory pressure, plateau pressure), need for systemic catecholamines within 24 hours after intubation, best Pao_2/fraction of inspired oxygen ratio and best $Paco_2$ within 24 hours after intubation, type of microbiologic respiratory sampling if available obtained before or soon after intubation (bronchoalveolar lavage [BAL], protected distal sampling, tracheal aspirate), type of antibiotics received after admission in the ICU, use of high-dose intravenous "pulse" methylprednisolone, introduction of immunosuppressive drugs, use of curative anticoagulation therapy, treatment with N-acetylcysteine, use of inhaled nitric oxide after intubation, requirement of extracorporeal membrane oxygenation (ECMO) at any time during the ICU stay, weaning from MV, performance of LTx during the ICU stay, and discharge from versus death in the ICU.

Characteristics after the ICU stay. Data collected after the ICU stay included discharge from the hospital versus death in the hospital and LTx.

Survival. Survivals were determined at 30 days, 6 months, and 12 months after ICU admission.

Data Review

Clinical, biologic, and radiologic data were reviewed retrospectively by 2 investigators (S.G. and H.M.) to determine the cause of admission to the ICU. The diagnosis of bacterial pneumonia was based on radiographic evidence of new infiltrates and significant concentration of bacteria in respiratory specimens ($>10^4$ colony-forming units/mL on BAL, $>10^3$ colony-forming units/mL on protected distal sampling, $>10^6$ colony-forming units/mL on tracheal aspirate). Diagnosis of *Pneumocystis* pneumonia was based on the presence of *Pneumocystis jirovecii* in BAL fluid. Diagnosis of acute exacerbation of IPF was based on criteria defined by Collard and colleagues[13]: (1) onset or recent increase of dyspnea (<30 days), (2) appearance of ground-glass opacities or superimposed condensation on preexisting reticular opacities and honeycombing, (3) absence of infectious precipitating factor, and (4) absence of another identifiable cause (eg, heart failure, pulmonary embolism, pneumothorax).

Successful weaning from MV was defined as extubation or ability to breathe spontaneously for 24 hours on tracheostomy cannula. ICU survival and hospital survival were defined as discharge of the patient from the ICU and hospital, respectively.

Statistical Analysis

Statistical analysis involved use of GraphPad Prism 5 (GraphPad Software, San Diego, Calif). Categoric data are described by number and percentage and were compared by χ^2 test. The distribution of continuous data was tested by the Kolmogorov-Smirnov test. Continuous data with normal distribution are described by mean ± SD and were compared with the Student *t* test. Continuous data with nonnormal distribution are described by median with interquartile range (25%-75%) and were compared with the Mann-Whitney *U* test. The Kaplan-Meier estimator was used to estimate survival.

RESULTS

Baseline Characteristics of Patients

Baseline patient characteristics were determined by analysis of charts for 27 patients (23 men; mean age,