Risk Factors for ARDS in Patients Receiving Mechanical Ventilation for > 48 h*

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Background: **Low tidal volume (VT) ventilation for ARDS is a well-accepted concept. However, controversy persists regarding the optimal ventilator settings for patients without ARDS receiving mechanical ventilation. This study tested the hypothesis that ventilator settings influence the development of new ARDS.**

Methods: **Retrospective analysis of patients from the Multi Parameter Intelligent Monitoring of Intensive Care-II project database who received mechanical ventilation for ≥ 48 h between 2001 and 2005.**

Results: **A total of 2,583 patients required > 48 h of ventilation. Of 789 patients who did not have ARDS at hospital admission, ARDS developed in 152 patients (19%). Univariate analysis revealed high peak inspiratory pressure (odds ratio [OR], 1.53 per SD; 95% confidence interval [CI], 1.28 to 1.84), increasing positive end-expiratory pressure (OR, 1.35 per SD; 95% CI, 1.15 to 1.58), and VT (OR, 1.36 per SD; 95% CI, 1.12 to 1.64) to be significant risk factors. Major nonventilator risk factors for ARDS included sepsis, low pH, elevated lactate, low albumin, transfusion of packed RBCs, transfusion of plasma, high net fluid balance, and low respiratory compliance. Multivariable logistic regression showed that peak pressure (OR, 1.31 per SD; 95% CI, 1.08 to 1.59), high net fluid balance (OR, 1.3 per SD; 95% CI, 1.09 to 1.56), transfusion of plasma (OR, 1.26 per SD; 95% CI, 1.07 to 1.49), sepsis (OR, 1.57; 95% CI, 1.00 to 2.45), and VT (OR, 1.29 per SD; 95% CI, 1.02 to 1.52) were significantly associated with the development of ARDS.**

Conclusions: **The associations between the development of ARDS and clinical interventions, including high airway pressures, high VT, positive fluid balance, and transfusion of blood products, suggests that ARDS may be a preventable complication in some cases.** ***(CHEST 2008; 133:853–861)***

Key words: ARDS; lung injury; plateau pressure; tidal volume; transfusion; ventilator

Abbreviations: CHF = congestive heart failure; CI = confidence interval; F_{IO_2} = fraction of inspired oxygen; ICD-9 = *International Classification of Diseases, Ninth Revision*; MIMIC = Multi Parameter Intelligent Monitoring of Intensive Care; OR = odds ratio; PEEP = positive end-expiratory pressure; PIP = peak inspiratory pressure; PPLAT = plateau pressure; SAPS = Simplified Acute Physiology Score; VT = tidal volume

Patients in the ICU are commonly supported using mechanical ventilation for days to weeks. Studies[1–4] suggest that initial ventilator settings may affect patient outcome. In particular, patients with ARDS have lower mortality rates when ventilated at lower tidal volumes (VTs).[4] The idea that mechanical ventilator settings may greatly influence respiratory health and mortality has prompted clinicians to find protective measures for minimizing iatrogenic lung injuries. However, there have been few studies and no firm recommendations on the optimal settings for patients who require this intervention for reasons apart from respiratory failure. In fact, patients without respiratory failure make up a significant portion (20 to 30%) of all who are receiving mechanical ventilation in the ICU.[1,3]

There is increasing evidence that mechanical ventilation can trigger inflammatory pulmonary edema in both animal models[5] and human patients.[6,7] Both short-term endotracheal intubation and long-term mechanical ventilation are known to increase the risk for nosocomial pneumonia.[8] Some studies[9,10] have shown that higher VTs are associated with more cases of ARDS and acute lung injury in patients without the

disease at the outset. Others authors[11] show that ventilation with high pressures increases mortality rates in patients with ARDS. Positive end-expiratory pressure (PEEP) is hypothesized to have protective effects on the lungs during mechanical ventilation,[12,13] although randomized trials are equivocal in this area.

Due to the multitude and complexity of risk factors associated with ventilator-induced ARDS, it is necessary to analyze the disorder in large patient populations. In this study, we examined a large ICU database to find physiologic and ventilator-associated risk factors for ARDS. We hypothesized that initial ventilator settings as well as other, potentially preventable, risk factors may be associated with the development of ARDS in patients receiving mechanical ventilation for > 48 h but who did not have ARDS at the outset.

Materials and Methods

The Multi Parameter Intelligent Monitoring of Intensive Care-II Project Database

The Multi Parameter Intelligent Monitoring of Intensive Care (MIMIC)-II project was approved by the institutional review boards of the Massachusetts Institute of Technology and Beth Israel Deaconess Medical Center and granted a waiver of informed consent. The MIMIC-II database includes physiologic information from bedside monitors in the adult ICUs of Beth Israel Deaconess Medical Center. These data (heart rate, BP) were validated by ICU nurses on an hourly basis. The database also contains records of arterial blood gas levels and laboratory values, nursing progress notes, IV medications, fluid intake/output, and other clinical variables. Ventilator settings were documented by respiratory therapists at intubation and as ventilator settings were adjusted. Radiologic films were evaluated by specialists at the time of patient care, and written evaluations were recorded into the database. *International Classification of Diseases, Ninth Revision* (ICD-9) codes were documented for specific diseases as required by hospital staff on patient discharge. Currently, the database includes > 17,000 medical records collected between 2001 and 2005.[14] The distribution of patients from the MIMIC-II database is shown in Figure 1.

Patient Selection

We examined medical records of patients who received mechanical ventilation for > 48 h and who did not have ARDS at the outset of ventilation. To rule out cardiogenic causes of pulmonary edema, we excluded patients with evidence of congestive heart failure (CHF) during their hospital stay.

Definitions

The length of mechanical ventilation was defined as the duration of the first continuous ventilation period according to recorded ventilator settings. ARDS was diagnosed using the American European consensus conference criteria[15] (acute onset, Pao_2/fraction of inspired oxygen [Fio_2] < 200 mm Hg, bilateral infiltrates on chest radiograph, and no CHF). Pao_2/Fio_2 values were calculated by finding the ratio of each Pao_2 measurement to the nearest Fio_2 value available before the corresponding blood gas value (this difference was approximately 2 ± 1.9 h apart). Due to the absence of pulmonary wedge pressure in the majority of records (86%), patients with CHF were identified using ICD-9 code 428 and were excluded from the study. To be considered as without ARDS at the outset, patients must have had two Pao_2/Fio_2 values > 200 mm Hg in the first 12 h of mechanical ventilation. Development of ARDS was identified has having an acute drop in Pao_2/Fio_2 to < 200 mm Hg for at least 24 h with evidence of bilateral infiltrates and/or consolidations in the chest radiograph report. Reports from 24 h before to 72 h after the drop in Pao_2/Fio_2 ratio were independently evaluated by two expert intensivists for the presence of bilateral disease. A random sample of 25% of the radiographs was reviewed and in all cases confirmed findings from the report and were consistent with a diagnosis of ARDS. Discrepancies were settled by a joint evaluation of the overall data available but blinded to the exposure variables (*eg*, baseline mechanical ventilator settings).

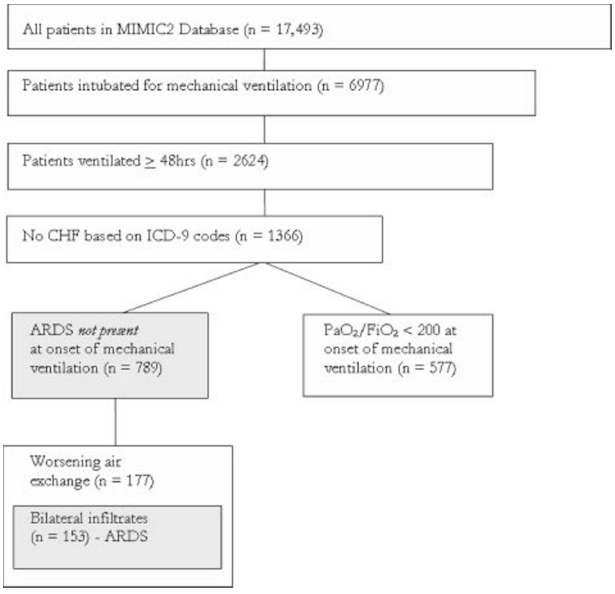

Figure 1. Patient distribution from the MIMIC-II database. Gray boxes indicate patients examined in this study.

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This work was supported in part by National Institutes of Health grant R01-EB001659.
None of the authors have any financial interests or potential conflicts of interest to disclose.
Manuscript received May 9, 2007; revision accepted December 18, 2007.

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DOI: 10.1378/chest.07-1121