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The role of noninvasive positive pressure ventilation in community-acquired pneumonia☆,☆☆,★

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ABSTRACT

Background: Despite the increasing use of noninvasive positive pressure ventilation (NIV) in the treatment of critically ill patients with respiratory failure, its role in the treatment of severe community-acquired pneumonia (CAP) is controversial. The aim of this study was to assess the use of NIV in patients with CAP requiring ventilation who are admitted an intensive care unit.

Methods: A retrospective cohort study of all consecutive patients admitted to 3 tertiary care, university-affiliated, intensive care units from January 2007 to January 2012 with the principal diagnosis of CAP and requiring positive pressure ventilation was carried out. The primary outcome was acute hospital mortality. Univariable and multivariable analysis were performed to assess the association between mode of ventilation and death as well as factors associated with failure of NIV.

Results: A total of 229 patients were admitted, with 20 patients excluded from the analysis because of do-not-resuscitate orders. Fifty-six percent of patients were initially treated with NIV. Of those, 76% failed NIV and required intubation and invasive ventilation. After adjusting for confounders, no difference in mortality was seen between patients who received NIV as first-line therapy in comparison with patients who received invasive ventilation (odds ratio [OR], 1.63; 95% confidence interval [CI], 0.81-3.28; $P = .17$). Multivariable analysis demonstrated a trend toward increased NIV failure for the patients who had higher Acute Physiology and Chronic Health Evaluation II scores ($P = .07$) and vasopressor use at 2 hours after initiation of positive pressure ventilation (OR, 7.5; 95% CI, 1.8-31.3, $P = .006$). In an adjusted analysis, patients who failed NIV had an increased odds of death when compared with patients who were treated with invasive ventilation (OR, 2.2; 95% CI, 1.0-4.8; $P = .03$).

Conclusion: Noninvasive pressure ventilation is frequently used in CAP but is associated with high failure rates. Mortality was not improved in the group of patients who received NIV as first-line therapy despite clinical characteristics that might have suggested a more favorable prognosis. Given the high rates of NIV use, high failure rates, and the hypothesis generating nature of the data in this study, further randomized studies are needed to better delineate the role of NIV in CAP.

1. Introduction

The use of noninvasive positive pressure ventilation (NIV) in the treatment for critically ill patients with respiratory failure has dramatically increased over the past decade. However, its role in the treatment of severe community-acquired pneumonia (CAP) is controversial due to high rates of reported treatment failure [1]. Despite this, NIV is commonly used in emergency departments and intensive care units (ICU) for treatment of CAP [2], with the goal of preventing intubation and invasive mechanical ventilation.

The strongest evidence of benefit from NIV has been observed in patients with hypercapneic respiratory failure from acute exacerbation of chronic obstructive lung disease [3], cardiogenic pulmonary edema [4], and immunocompromised patients with lung infiltrates [5]. Hospitalized patients with severe CAP frequently have high rates of these

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Data sharing: technical appendix and statistical code are available from corresponding author at Jason.shahin@mcgill.ca.

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comorbidities [6,7]. This confounds much of the published data on the use of NIV in CAP which is based on a few randomized and observational studies of small sample size [1,5,8–13]. Given the limited data, recently published clinical practice guidelines on evidence-based application of NIV made no recommendations on the use of NIV in severe CAP [14].

The role of NIV in pneumonia is therefore still unclear and warrants further evaluation. The objective of this study was to assess in a retrospective cohort study the application of NIV in patients with CAP in a critical care setting and identify clinical and laboratory parameters that would predict NIV failure.

2. Methods

2.1. Setting and study population

A retrospective cohort study of all consecutive patients admitted to 3 tertiary care, university-affiliated, ICUs during the period January 2007 to January 2012 with the principal diagnosis of CAP and placed on positive pressure ventilation was carried out. Data were abstracted by a trained data collector using a standardized data collection tool. The study was approved by the McGill University Health Centre Research Ethics Board.

The patients were identified via each center's ICU database. Positive pressure ventilation included both invasive (IV) and NIV but not continuous positive pressure ventilation (ie, continuous positive airway pressure). Patients who required at least 1 hour of positive pressure ventilation were included. All patients admitted to the ICU with a diagnosis of sepsis, hypoxic respiratory failure, or pneumonia were screened for inclusion. *Community-acquired pneumonia* was defined as being present if 3 of the following were present and the presence of a new chest x-ray infiltrate upon admission to hospital: white blood cell count >12 000 cells/mm^3 or white blood cell count <4000 cells/mm^3, or temperature >38°C or temperature <36°C, or symptoms suggestive of pneumonia.

Patients transferred to or from another hospital prior to critical care unit admission were excluded to avoid any missing data or confounding of care. Patients were also excluded if CAP was the not considered to be the most likely etiology of the patient's respiratory failure on presentation. If readmitted to the ICU, only data from the first admission was collected.

2.2. Data collection

The following data were collected: age sex, severity of illness, comorbidities, location prior to ICU admission, ventilation mode, location of initial positive pressure application, chest x-ray quadrant score, physiological parameters, time required to apply positive pressure ventilation, duration of positive pressure ventilation, ventilator settings, and therapies administered.

Severity of illness was defined using the Acute Physiology and Chronic Health Evaluation II (APACHE II) score [15]. Comorbidities were extracted from the patient's medical records. Severe cardiovascular disease was defined in order to capture a population with severe cardiovascular disease and was considered if severe left ventricular dysfunction (with an ejection fraction <45%) [16], severe right ventricular dysfunction, severe pulmonary hypertension with evidence of right ventricular failure dysfunction or requiring medical treatment, severe valvular heart disease, significant peripheral vascular disease requiring surgical intervention, or coronary artery disease not amenable to revascularization was present. Severe respiratory disease was considered if interstitial lung disease, neuromuscular disease, chronic obstructive lung disease, or any lung disease leading to home oxygen dependency was present. Renal disease was considered in any patient who was dialysis dependant or had evidence or intrinsic renal disease. Chronic liver disease was defined as any patient with evidence of cirrhosis or chronic liver injury that could lead to cirrhosis or liver failure. Hematologic Malignancy was considered in any patient known for lymphoma, leukemia, or a plasma cell disorder. Metastatic cancer was considered in patients known for a solid organ cancer with metastases. Immunologic dysfunction was defined as acquired/congenital immunodeficiency disorder, evidence of immune dysfunction secondary to bone marrow failure, chronic steroids (equivalent of prednisone 20 mg daily for at least 2 weeks), or history of opportunistic infections.

Location prior to admission was either the emergency department or hospital ward. Ventilation mode was defined as either invasive or noninvasive. Patients who received at least 1 hour of NIV were considered to have received NIV therapy. Patients who switched ventilatory modes after at least 1 hour were considered as being in the group of their initial ventilatory therapy. Physiology parameters were collected prior to initiation of ventilation and 2 hours after initiation of ventilation (or as close to 2 hours as possible but not exceeding 6 hours). Physiological parameters included hemodynamic support, heart rate, mean arterial pressure, respiratory rate, Pa_{O_2}/Fi_{O_2}, pH, and Pa_{CO_2}. Hemodynamic support was defined as requiring vasopressors or at least 2 L of fluid resuscitation over an hour. Arterial blood gas values were taken from arterial samples when available and otherwise from venous gasses for Pa_{CO_2} and serum pH. Data for ventilator settings consisted of mode of ventilation, peak inspiratory pressure, and end-expiratory pressures. Therapies administered in the first 24 hours of positive pressure application were collected and included bronchodilators, corticosteroids, antibiotics, and vasopressors.

Noninvasive and invasive ventilations were administered in a nonstandardized way and were at the discretion of the treating physician. Patients were admitted initially from the emergency department or the hospital ward. Noninvasive ventilation could have been initiated in the emergency department or ICU, but not on the hospital ward (as per hospital policy). The location of initial ventilation was documented. During the course of NIV, all patients were continuously monitored with electrocardiogram, blood pressure, and pulse oximetry. Noninvasive ventilation was administered (Respironics Vision BiPAP ventilator) through face masks.

The primary outcome was acute hospital mortality. Secondary outcomes were NIV failure and length of ICU and hospital stay. Noninvasive ventilation failure was noted if rescue IV through an endotracheal tube after at least 1 hour of NIV was needed or if death occurred while on NIV. We also identified complications that arose during the first 24 hours of positive pressure ventilation. These included renal failure and myocardial infarction. Renal failure was defined as a doubling of baseline creatinine or requiring renal replacement therapy. Myocardial infarction was defined as a rise in cardiac enzymes in conjunction with electrocardiogram changes and a clinical diagnosis by the treating physician.

2.3. Statistical analysis

An analysis of baseline characteristics was performed for the whole cohort and by mode of ventilation. In total, 20 patients with a do-not-resuscitate status were excluded from the cohort. The distributions of all variables were explored in the whole cohort and in each group of patients. The cohort of patients who were administered NIV were further categorized by failure or success of NIV. Continuous variables were analyzed using Student *t* test for parametric variables and Wilcoxan rank sum test for nonparametric variables. Categorical variables were analyzed using a χ^2 test.

A univariable analysis was conducted to assess the relationship between variables of interest and both mode of ventilation and noninvasive failure. A multivariable analysis was performed to assess the association between mode of ventilation and death while adjusting for confounders. Variables entered into the model were chosen based on a priori importance and from the univariable analysis, with a *P* value level of 0.1 chosen as the cutoff for accepting a variable into the model. The a priori variables were immune dysfunction, cardiovascular disease, and APACHE II score. Variables were then entered simultaneously with no statistical selection process applied. A second multivariable analysis was performed to assess the relationship between baseline characteristics, 2-hour physiological