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The comparative effectiveness of noninvasive and invasive ventilation in patients with pneumonia☆

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ABSTRACT

Purpose: To compare the outcomes of patients hospitalized with pneumonia treated with noninvasive ventilation (NIV) and invasive mechanical ventilation (IMV).
Materials and methods: Using the HealthFacts multihospital electronic medical record database, we included patients hospitalized with a diagnosis of pneumonia and treated with NIV or IMV. We developed a propensity model for receipt of initial NIV and assessed the outcomes in a propensity-matched cohort, and in a covariate adjusted and propensity score weighted models.
Results: Among 3971 ventilated patients, 1109 (27.9%) were initially treated with NIV. Patients treated with NIV were older, had lower acuity of illness score, and were more likely to have congestive heart failure and chronic pulmonary disease. Mortality was 15.8%, 29.8% and 25.9.0% among patients treated with initial NIV, initial IMV and among those with NIV failure. In the propensity matched analysis, the risk of death was lower in patients treated with NIV (relative risk: 0.71, 95% CI: 0.59–0.85). Subgroup analysis showed that NIV was beneficial among patients with cardiopulmonary comorbidities (relative risk 0.59, 95% CI: 0.47–0.75) but not in those without (relative risk 0.96, 95% CI: 0.74–0.1.25)NIV failure was significantly ($p = 0.002$) more common in patients without cardiopulmonary conditions (21.3%) compared to those with these conditions (13.8%).
Conclusions: Initial NIV was associated with better survival among the subgroup of patients hospitalized with pneumonia who had COPD or heart failure. Patients who failed NIV had high in-hospital mortality, emphasizing the importance of careful patient selection monitoring when managing severe pneumonia with NIV.

1. Background

Each year in the United States, nearly one million patients with acute respiratory failure (ARF) are treated with invasive mechanical ventilation (IMV) [1]. Up to 40% of mechanically ventilated patients die in the hospital [2,3], and some of these deaths are directly attributable to complications of the ventilator [4]. In selected groups of patients with ARF, noninvasive mechanical ventilation (NIV) reduces the need for endotracheal intubation leading to better outcomes. While most of the published evidence on the effectiveness of NIV to avoid intubation applies to patients with acute COPD exacerbation [5-8] or acute cardiopulmonary edema [9,10], NIV has become a common treatment in patients with ARF regardless of etiology [11-14].

Pneumonia is the leading infectious cause of hospitalization in U. S. and results in over one million admissions annually. Between 58% and

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87% of patients with severe pneumonia develop ARF. Mortality among patients with pneumonia who require intensive care unit admission ranges from 15 to 51%. The effectiveness of NIV in pneumonia is controversial since it is associated with high treatment failure rates compared to other causes of ARF [15,16] and because mortality rate associated with NIV failure is high [17]. This risk is particularly concerning for patients with no prior respiratory or cardiac condition (known as 'de novo' acute respiratory failure) [14,17-19]. In addition, several studies have found that pneumonia is an independent risk factor for NIV failure in patients hospitalized with acute COPD exacerbation or asthma [8,20,21]. Thus, professional guidelines recommend caution in using NIV in immunocompetent patients with ARF due to pneumonia given insufficient evidence of its efficacy [22].

Only one other study has examined the role of NIV in patients with pneumonia needing ventilatory assistance, however it included only patients older than 65 years of age admitted to an intensive care unit [23]. Therefore, we aimed to compare the outcomes of patients with pneumonia initially treated with NIV to those initially treated with IMV using a large multihospital electronic medical record database that contains results of laboratory testing.

2. Methods

2.1. Design and setting

We conducted a retrospective cohort study of patients hospitalized between January 1, 2009 and December 31, 2012 using Cerner HealthFacts (Cerner Corporation, Kansas City). Data in HealthFacts is extracted directly from the EMR from hospitals in which Cerner has a data use agreement. Encounters may include pharmacy, clinical and microbiology laboratory, admission and billing information. All admissions, medication orders and dispensing, laboratory orders and specimens are date and time stamped, providing a temporal relationship between treatment patterns and clinical information. Cerner Corporation has established Health Insurance Portability and Accountability Act-compliant operating policies to establish de-identification for Health Facts. The dataset was used extensively for research [24,25].

(Additional details about HealthFacts database in eAppendix).

2.2. Study population

The inclusion/exclusion criteria aimed to identify a cohort of patients with pneumonia eligible for either NIV or IMV for whom laboratory and medication data was available. This reduced the risk of misclassification from criteria based only on ICD-9 codes and allowed us to calculate a severity risk score at admission. From a cohort of patients with a principal discharge diagnosis of pneumonia or a secondary diagnosis of pneumonia when accompanied by a principal diagnosis of acute respiratory failure or sepsis, we included patients who were 18 years or older and received NIV or IMV on the day of admission. (ICD-9 codes in eAppendix 2) To increase the specificity of the diagnosis of pneumonia, we restricted the analysis to those patients treated with antibiotics within 48 h of admission. Since the dataset does not contain information about advance directives, we excluded patients older than 80 years and patients on palliative care or hospice at the time of admission, as they are less likely to be intubated if NIV is unsuccessful. We verified this assumption by analyzing this cohort of patients separately. (Results in eAppendix). Since we wanted to estimate mortality risk at the time of admission, we excluded patients who did not have results of WBC testing within 24 h of admission, and patients without laboratory data. We also excluded patients with obstructive sleep apnea since it would not be possible to differentiate chronic use of NIV from treatment for acute respiratory failure; and patients with a contraindication for NIV. We further excluded patients transferred to or from another facility because their initial form of ventilation and their outcomes could not be ascertained. For patients with multiple eligible admissions during the study period, we randomly selected 1 admission for inclusion into the study cohort.

2.3. Treatment variable

We defined initial NIV and initial IMV based on the first method of ventilation and noted changes in ventilation therapy (if any) over time. We used ICD-9 procedure codes to identify ventilation modality (93.90 for NIV and 96.7× and 96.04 for IMV). Of note, ICD-9 procedure codes do not contain information about the number of hours per day that the ventilation method was used.

When NIV and IMV were recorded on the same day with neither recorded for the following day, we assumed IMV followed NIV.

2.4. Patient and hospital characteristics

We recorded patient age, gender, and insurance status and the hospital characteristics (e.g., teaching status, number of beds) of each hospitalization. We recorded chronic comorbidities based on the software provided by the Healthcare Costs and Utilization Project of the AHRQ [26,27]. We calculated an overall comorbidity score as described by Gagne et al. [28].

We collected several variables to assess illness severity at the time of admission. First, we calculated the Laboratory Acute Physiology Score (LAPS), which uses the results of laboratory testing at the time of admission to quantify the risk of inpatient mortality. The LAPS has been internally and externally validated and has a high performance (c statistic of 0.83) in various subpopulations. It integrates 14 laboratory tests, including arterial blood gas results, into a single continuous score, which ranges between 0 and 256; higher LAPS scores are associated with greater likelihood of mortality (detailed information about LAPS in eAppendix) [29-31]. We also collected information on the number of prior hospitalizations, NIV or IMV use in the year before the index admission; vasopressor use during first 24 h of admission; and initial care venue including intensive care unit, intermediate care, or general medical ward (all treatments received in the emergency room are rolled in the admission encounter and cannot be separately identified). We classified pneumonia as community acquired or healthcare associated using the methodology used by other authors [32,33].

2.5. Outcomes

The primary outcome was in-hospital mortality. Secondary outcomes were NIV failure, length of hospital stay, and all-cause 30-day readmission among survivors.

NIV failure was defined as treatment with IMV following exposure to NIV. We required that NIV be followed by IMV on the same or subsequent day.

Using ICD-9 diagnosis codes, we identified complications that arose during hospitalization (not present at admission) which included myocardial infarction, cardiopulmonary arrest, and pneumothorax.

2.6. Statistical analysis

To describe the study population, we calculated frequencies and proportions for categorical data, means, standard deviations, or medians and interquartile ranges (IQR) for continuous variables. We compared characteristics of patients who received initial NIV or IMV using absolute standardized differences. All standardized differences >10% were deemed important.

To assess the impact of initial mode of ventilation on outcomes, we first developed a propensity score for receipt of initial NIV using a GEE model accounting for patient clustering within hospitals. Predictor variables included patient demographics, comorbidities, prior admission