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Early bronchoscopy in severe pneumonia patients in intensive care unit: insights from the Medical Information Mart for Intensive Care-IV database analysis

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Background: Pneumonia frequently leads to intensive care unit (ICU) admission and is associated with a high mortality risk. This study aimed to assess the impact of early bronchoscopy administered within 3 days of ICU admission on mortality in patients with pneumonia using the Medical Information Mart for Intensive Care-IV (MIMIC-IV) database.

Methods: A single-center retrospective analysis was conducted using the MIMIC-IV data from 2008 to 2019. Adult ICU-admitted patients diagnosed with pneumonia were included in this study. The patients were stratified into two cohorts based on whether they underwent early bronchoscopy. The primary outcome was the 28-day mortality rate. Propensity score matching was used to balance confounding variables.

Results: In total, 8,916 patients with pneumonia were included in the analysis. Among them, 783 patients underwent early bronchoscopy within 3 days of ICU admission, whereas 8,133 patients did not undergo early bronchoscopy. The primary outcome of the 28-day mortality between two groups had no significant difference even after propensity matched cohorts (22.7% vs. 24.0%, P=0.589). Patients undergoing early bronchoscopy had prolonged ICU (P<0.001) and hospital stays (P<0.001) and were less likely to be discharged to home (P<0.001).

Conclusions: Early bronchoscopy in severe pneumonia patients in the ICU did not reduce mortality but was associated with longer hospital stays, suggesting it was used in more severe cases. Therefore, when considering bronchoscopy for these patients, it's important to tailor the decision to each individual case, thoughtfully balancing the possible advantages with the related risks.

Key Words: bronchoscopy; intensive care units; mortality; pneumonia

Original Article

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INTRODUCTION

Pneumonia, which causes alveolar and distal airway inflammation, is a significant global public health challenge. This condition is responsible for notable morbidity, mortality, and healthcare costs worldwide [1,2]. Not only is pneumonia a frequent reason for intensive care unit (ICU) admission, but it also often escalates into severe complications. Patients with

pneumonia might require interventions such as mechanical ventilation, renal replacement therapy, and even extracorporeal membrane oxygenation [3,4]. Although early and appropriate antibiotic treatment can lead to favorable outcomes, many patients do not respond as expected. In these instances, pneumonia can lead to hemodynamic compromise owing to exacerbated respiratory failure or sepsis. Effective disease management requires constant monitoring, adjustment for concurrent medical conditions, and tailoring of treatment to the specific causative organism.

A crucial consideration when managing pneumonia in the ICU setting is the accurate and rapid identification of the pathogenic organisms causing the infection. The repercussions of ill-timed or incorrect therapy in ICU patients can be severe, leading to increased mortality rates, longer hospital stays, and rising costs [5,6]. In recent years, the use of flexible bronchoscopy in ICUs has increased notably [7]. Employing early bronchoscopy for patients with severe pneumonia in the ICU can serve both diagnostic and therapeutic goals [8,9]. The procedure allows clinicians to gather samples from the lower respiratory tract for microbiological and cytological testing. It aids in identifying causative pathogens, allowing for more precise antimicrobial treatment [10]. Furthermore, bronchoscopy can help distinguish pneumonia from other causes of respiratory failure. It can also be instrumental in clearing airway secretions and may enhance ventilation and oxygenation [8]. Although bronchoscopy has merits, its invasiveness must be recognized. The procedure can lead to complications such as hypoxemia, bleeding, and infection. Moreover, sedation of the patient for the procedure can present additional risks, especially in the critically ill [11].

In our endeavor to understand the diagnostic significance of microbiological and cytological tests and how they shape patient management, we examined the Comprehensive Medical Information Mart for Intensive Care-IV (MIMIC-IV) database. Our objective was to gauge the impact of early bronchoscopy, conducted within the first 3 days of ICU admission, on the outcomes of ICU patients diagnosed with severe pneumonia.

MATERIALS AND METHODS

The study was an analysis of a third-party anonymized publicly available database with preexisting institutional review board approval.

KEY MESSAGES

- This study assessed the effectiveness of early bronchoscopy within 3 days of intensive care unit (ICU) admission using the Medical Information Mart for Intensive Care-IV (MIMIC-IV) database.
- Early bronchoscopy in ICU patients with severe pneumonia did not significantly alter the 28-day mortality rate.
- It's important to carefully consider the potential benefits and associated risks of bronchoscopy for patients with severe pneumonia, tailoring the decision for each one.

Study Design, Participants, and Data Source

We used the MIMIC-IV database to construct a web-based database with MySQL, spanning from 2008 to 2019. Data was extracted using a Structured Query Language (SQL) to retrieve pertinent patient details, including sociodemographic characteristics, vital signs, laboratory measurements, complications, and specifics of microbiology and antibiotic use. We defined severe pneumonia, potentially life-threatening form of pneumonia, as requiring therapy in ICU. We focused on adult patients (aged ≥18 years) who were admitted to the ICU with a pneumonia diagnosis determined using the International Classification of Diseases, Ninth Revision codes. Only the initial ICU admission data were considered for patients with multiple hospital or ICU admissions. In instances where patient data were recorded multiple times, only the first measurement was considered. We selected 8,916 patients with pneumonia from the MIMIC-IV database. These patients were subsequently divided into two groups: an early bronchoscopy group (783 patients) and a non-early bronchoscopy group (8,133 patients).

The MIMIC database, initiated in 2003, emerged from a collaboration between institutions such as the Beth Israel Deaconess Medical Center, Massachusetts Institute of Health, and National Institutes of Health Technology. The MIMIC is a pre-eminent open-source, free clinical database for critical care and emergency departments. We used MIMIC-IV (version 1.0), which captured data from 2008 to 2019. Before accessing the database, we completed the necessary training and obtained the required certification. Given the non-clinical nature of our project and the anonymization of all protected health information, individual patient consent was not required.

Data Collection

Demographic and ICU admission data including age, sex, weight, height, admission day, discharge details, ICU admission, and discharge times were collected. Within 24 hours of admission, we collected the initial vital signs and laboratory data. The initial vital signs upon ICU admission, including heart rate, temperature, blood pressure (BP), respiratory rate (RR), and oxygen saturation (SpO_2), were documented. Laboratory findings encompassed parameters like white blood cell count, hemoglobin level, platelet count, and arterial blood gas test results.

Data Outcomes and Definitions

The main outcome was the 28-day mortality rate after ICU admission. The secondary outcomes were in-hospital mortality, mortality rates at 90 and 180 days, lengths of ICU and hospital stay, and home discharge rates. Early bronchoscopy was identified when the procedure was performed within the first 72 hours of ICU admission, with the bronchoscopy event starting time serving as the identifier.

Propensity Score Matching

Propensity score matching was used to address the confounding factors and balance the distribution of covariates in the two cohorts. Age, sex, SpO_2, RR, and mean BP were matched to form a propensity score-matched cohort.

Statistical Analysis

Data extracted from the MySQL database were analyzed using Excel 2019 (Microsoft) and R (version 4.3.1, The R Foundation for Statistical Computing). Descriptive statistics were used to describe baseline characteristics. Continuous variables are represented either as mean values with standard deviations for normally distributed data or as median values with an interquartile range for non-normally distributed data. Categorical variables were expressed as the number of patients and percentage of the group to which they belonged.

To address confounding factors and ensure a balanced covariate distribution between the cohorts, we employed propensity score matching. Factors, such as age, sex, SpO_2, RR, and mean BP, were matched to form a propensity score-matched cohort. A $P<0.05$ was considered statistically significant.

RESULTS

Baseline Characteristics

Table 1 presents the baseline characteristics of the study population. Out of the 8,916 patients screened, the mean age was 65±16, with 55.9% being male. The majority of ICU-admitted patients were emergency cases (83.0%). Among them, 1,698 patients underwent bronchoscopy during hospital admission, 1,464 underwent bronchoscopy in the ICU, 783 received early bronchoscopy within 3 days of ICU admission, while 8,133 did not undergo bronchoscopy or early bronchoscopy within 3 days of ICU admission.

Group Comparisons

The early bronchoscopy group comprised younger individuals with a higher proportion of males. Arterial blood gas analysis indicated that the early bronchoscopy group had lower levels of partial pressure of oxygen (PaO_2) and arterial SpO_2, as well as higher levels of partial pressure of carbon dioxide ($PaCO_2$) (Table 2).

Propensity Score Matching

Propensity score matching was conducted on 775 patients, resulting in a 1:1 matched group for analysis (Table 3). The

Table 1. Baseline characteristics

Variable	Value (n=8,916)
Age (yr)	65±16
Male	4,985 (55.9)
Weight (kg)	76.4 (63.6–92.0)
Height (cm)	170.0 (160.0–178.0)
Admission type[a]	
Emergency	7,402 (83.0)
Elective	1,514 (17.0)
Insurance	
Medicaid	703 (7.9)
Medicare	4,446 (49.9)
Other	3,767 (42.2)
Marital status	
Married	3,720 (46.0)
Single	2,537 (31.4)
Divorced	613 (7.6)
Widowed	1,216 (15.0)
Weekend admission	2,567 (28.8)

Values are presented as mean±standard deviation, number (%), or median (interquartile range).
a) Emergency indicates unplanned medical care and Elective indicates a previously planned admission.

Table 2. Vital signs and laboratory findings

Variable	Non-early bronchoscopy (n=8,133)	Early bronchoscopy (n=783)	P-value
Age (yr)	67 (55–78)	63 (51–74)	<0.001
Male (%)	4,505 (55.4)	480 (61.3)	0.002
Vital sign at ICU admission			
Systolic blood pressure (mm Hg)	121.0 (105.0–139.0)	122.0 (106.0–139.0)	0.338
Diastolic blood pressure (mm Hg)	67.0 (57.0–80.0)	67.0 (57.0–79.0)	0.763
Mean arterial pressure (mm Hg)	85.0 (74.0–99.0)	86.0 (74.0–98.0)	0.612
Temperature (°C)	36.8 (35.2–38.0)	36.8 (35.0–38.1)	0.535
Heart rates (beats/min)	92.0 (79.0–107.0)	93.0 (80.0–107.0)	0.335
Respiratory rates (beats/min)	20.0 (17.0–25.0)	20.0 (16.0–25.0)	0.900
SpO_2	97.0 (94.0–100.0)	97.0 (93.0–100.0)	0.196
Arterial blood gas analysis			
pH	7.4 (7.3–7.4)	7.4 (7.3–7.4)	<0.001
PaO_2 (mm Hg)	109.0 (78.0–192.0)	104.5 (75.0–181.0)	0.041
$PaCO_2$ (mm Hg)	40.0 (34.0–48.0)	43.0 (37.0–52.0)	<0.001
SaO_2 (mm Hg)	97.0 (94.0–98.0)	96.0 (93.0–98.0)	0.089
Laboratory finding			
White blood cell ($\times 10^9$/L)	11.4 (7.9–15.9)	12.0 (8.4–16.6)	0.012
Hemoglobin (g/L)	10.4 (8.8–12.0)	10.5 (9.0–12.1)	0.063
Platelet ($\times 10^9$/L)	195.0 (136.0–268.0)	201.5 (138.5–278.5)	0.109
Prothrombin time (INR)	1.3 (1.1–1.6)	1.2 (1.1–1.6)	0.002
Sodium (mEq/L)	138.0 (135.0–141.0)	139.0 (135.0–141.0)	0.297
Potassium (mEq/L)	4.1 (3.7–4.6)	4.1 (3.7–4.6)	0.960
Chloride (mEq/L)	103.0 (99.0–107.0)	104.0 (100.0–108.0)	0.005
HCO_3^- (mEq/L)	23.0 (20.0–26.0)	24.0 (20.0–26.0)	0.001
Serum osmolality (mOsm/L)	295.0 (283.0–309.0)	294.0 (282.0–303.0)	0.536
BUN (mg/dl)	22.0 (14.0–37.0)	20.0 (13.0–31.5)	<0.001
Creatinine (mg/dl)	1.0 (0.7–1.6)	1.0 (0.7–1.4)	<0.001
Glucose (mg/dl)	130.0 (106.0–169.0)	134.0 (106.0–169.0)	0.387
AST (IU/L)	39.0 (24.0–81.0)	38.0 (23.0–75.5)	0.545
ALT (IU/L)	27.0 (16.0–54.0)	29.0 (16.0–54.5)	0.714
Albumin (g/dl)	2.9 (2.5–3.4)	2.9 (2.4–3.2)	0.002
Total bilirubin (mg/dl)	0.6 (0.4–1.2)	0.6 (0.3–1.1)	0.300
CRP (mg/dl)	101.8 (42.4–180.5)	91.5 (38.0–155.5)	0.581

Values are presented as median (interquartile range) or number (%).
ICU: intensive care unit; SpO_2: oxygen saturation; PaO_2: partial pressure of oxygen; $PaCO_2$: partial pressure of carbon dioxide; SaO_2: arterial oxygen saturation; INR: international normalized ratio; HCO_3^-: bicarbonate; BUN: blood urea nitrogen; AST: aspartate aminotransferase; ALT: alanine aminotransferase; CRP: C-reactive protein.

primary outcome of the 28-day mortality between two groups had no significant difference even after propensity matched cohorts (22.7% vs. 24.0%, P=0.589). Prior to propensity score matching, the non-early bronchoscopy group had a significantly higher 180-day mortality rate than the early bronchoscopy group (17.1% vs. 14.2%, P=0.043). However, after propensity score matching, no significant difference in mortality was observed between the two groups. The bronchoscopy group had a longer mean length of ICU stay (3.1 days [1.6–8.5] vs. 8.2 days [4.9–14.1], P<0.001), a longer length of hospital stay (11.5 days [6.0–19.8] vs. 15.0 days [9.7–23.7], P<0.001), and a lower proportion of patients discharged to their homes compared to the non-early bronchoscopy group (115 [14.8%] vs. 71 [9.2%], P<0.001).

DISCUSSION

Despite its retrospective nature and potential concerns re-

Table 3. Patient outcome analysis with propensity score matching

Variable	Non-early bronchoscopy	Early bronchoscopy	P-value
Original cohort data	(n=8,133)	(n=783)	
Primary outcome			
28-Day mortality	1,882 (23.1)	188 (24.0)	0.613
Secondary outcome			
In-hospital mortality	1,673 (20.6)	180 (23.0)	0.122
90-Day mortality	2,675 (32.9)	253 (32.3)	0.772
180-day mortality	1,389 (17.1)	111 (14.2)	0.043
Length of ICU stay (day)	3.1 (1.6–7.8)	8.2 (4.9–14.1)	<0.001
Length of hospital stay (day)	10.9 (6.0–19.3)	15.0 (9.6–23.7)	<0.001
Discharge to home	1,044 (12.9)	71 (9.1)	0.003
Propensity matched data	(n=775)	(n=775)	
Primary outcome			
28-Day mortality	176 (22.7)	186 (24.0)	0.589
Secondary outcome			
In-hospital mortality	155 (20.0)	178 (23.0)	0.174
90-Day mortality	248 (32.0)	251 (32.4)	0.913
180-Day mortality	127 (16.4)	109 (14.1)	0.229
Length of ICU stay (day)	3.1 (1.6–8.5)	8.2 (4.9–14.1)	<0.001
Length of hospital stay (day)	11.5 (6.0–19.8)	15.0 (9.7–23.7)	<0.001
Discharge to home	115 (14.8)	71 (9.2)	0.001

Values are presented as number (%) or median (interquartile range). Age, sex, oxygen saturation (SpO_2), respiration rate, and mean blood pressure were matched for the propensity score-matched cohorts.
ICU: intensive care unit.

garding data accuracy, this study is fortified by its extensive MIMIC-IV database. Its primary objective was to investigate the role of early bronchoscopy in patients with severe pneumonia. The hypothesis was that early bronchoscopy would provide both diagnostic and therapeutic advantages, potentially reducing mortality rates. Regarding the baseline characteristics of the patients, there were no statistically significant variations observed based on the type of admission, marital status, or insurance coverage. The study's findings showed no significant difference in 28-day mortality between the two groups, even after adjusting for confounding factors through propensity score matching. Notably, patients who underwent early bronchoscopy experienced prolonged ICU and hospital stays, and a reduced likelihood of being discharged directly to their homes post-hospitalization. These extended durations in hospitalization and ICU stays among patients with severe pneumonia may reflect the severity of their condition. It is possible that the group selected for early bronchoscopy inherently consisted of individuals with more severe clinical presentations and poorer prognoses.

The management of pneumonia, especially in the ICU, involves a multitude of complications. The initial selection of therapies for pneumonia can be complex because of the diverse etiology of the condition, which involves a range of causative organisms, including bacteria, viruses, and fungi [12]. Moreover, the rising prevalence of antibiotic-resistant bacteria poses challenges in treatment decisions [13,14]. Challenges in care are further emphasized by the diversity in patient responses, presence of underlying comorbidities, and possibility of rapid escalation to septic shock or acute respiratory distress syndrome. Such difficulties highlight the importance of prompt and precise diagnostic evaluations for direct therapy, while acknowledging the multifaceted complexity of the treatment of severe pneumonia.

In recent years, bronchoscopy has seen increased use in managing pneumonia among ICU patients. The percentage of bronchoscopy use among hospitalizations treated with invasive mechanical ventilation increased from 9.5% in 2012 to 10.8% in 2018 [7]. The combined diagnostic and therapeutic potentials of this technology have contributed to its widespread adoption [15]. Understanding the pathogens associated with pneumonia is crucial for providing targeted empiric antibiotic therapy, preventing the emergence of antimicrobial resistance through selection pressure, and reducing healthcare costs [1]. Early bronchoscopy allows direct lower respiratory tract observation, aiding in pneumonia diagnosis. It also enables microbial organism identification through sample collection [12]. Real-time visualization, direct sample retrieval, and therapeutic interventions such as lavage make bronchoscopy a potential game changer in ICU pneumonia management [9]. This highlights the growing understanding of bronchoscopy as a flexible tool for treating pneumonia, even with the requisite safety measures.

Previous studies have suggested potential benefits of early bronchoscopy in specific patient populations, such as mechanically ventilated patients with aspiration pneumonia [16,17]. Diagnostic bronchoscopy for ventilator-associated pneumonia in the ICU is associated with shorter duration of antibiotic use [18]. For immunocompromised patients, bronchoscopy improved diagnosis and change in management but not improved hospital mortality [19]. In other study, fiberoptic bronchoscopy in a respiratory ICU contributed in clinical management but also showed higher mortality [20].

While bronchoscopy offers several diagnostic and therapeutic benefits in pneumonia management, it has inherent limitations. The risks associated with this procedure can be

severe, particularly in critically ill patients. Complications such as hemodynamic changes, hemorrhage, pneumothorax, and temporary hypoxemia have been observed [21,22]. Additionally, there are concerns regarding the possibility of aerosol formation, which has the potential to increase the risk of infection transmission, particularly in instances of viral pneumonia. A systematic review, however, found no statistically significant association between bronchoscopy and the transmission of acute respiratory infections [23]. Furthermore, the requirement of sedation may pose challenges in some patient groups [24]. It is therefore essential to adopt a cautious approach while using bronchoscopy because of its inherent limitations, to ensure that the possible advantages are carefully evaluated in relation to the associated hazards.

This study exhibits several limitations. Firstly, it is important to acknowledge that this is a retrospective study, originally designed without a primary focus on investigating the role of early bronchoscopy in ICU patients. Secondly, while the inclusion of a large number of patients can offer advantages in terms of statistical power, it may inadvertently compromise the precision of data at the individual patient level. For instance, determining the intent of bronchoscopy (therapeutic or diagnostic) for each patient can be challenging, and using the diagnosis at the time of admission may not always accurately capture pneumonia as the primary concern. Additionally, the study lacked detailed data for comparing the specific microbial species identified through bronchoscopy with the corresponding antibiotic prescriptions. Moreover, our analysis did not incorporate adjustments for the severity of pneumonia or the overall condition of ICU-admitted patients. Variables such as CURB-65 (confusion, uremia, respiratory rate, BP, age ≥65 years), Pneumonia Severity Index, Acute Physiology and Chronic Health Evaluation (APACHE) scores, intubation status, mechanical ventilation usage, and vasopressor administration were not simultaneously considered to account for variations in disease severity. While propensity score matching was employed to mitigate differences between patient groups, it may not have comprehensively accounted for all potential confounding variables. Our study try to offer valuable insights into the potential role of early bronchoscopy in severe pneumonia patients within the ICU setting. However, it is essential to acknowledge these limitations. Further prospective randomized trials are warranted to validate our findings and definitively elucidate the impact of early bronchoscopy on patient outcomes in severe pneumonia.

In conclusion, our study, based on a large ICU database, did not reveal a mortality reduction advantage associated with early bronchoscopy performed within the first 3 days for patients with severe pneumonia. Given that the early bronchoscopy group had longer ICU and hospital stay and a lower rate of discharge to home, it can be inferred that bronchoscopy was primarily performed in patients with more severe pneumonia. Therefore, when considering bronchoscopy for these patients, it's important to tailor the decision to each individual case, thoughtfully balancing the possible advantages with the related risks.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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Conceptualization: YP. Data curation: CA, YO. Formal Analysis: CA, YP. Funding acquisition: YP. Methodology: all authors. Project administration: YP. Visualization: CA. Writing–original draft: CA, YP. Writing–review & editing: CA, YP.

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