Infection and Drug Resistance

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ORIGINAL RESEARCH

Impact of Endotracheal Intubation Timing on Clinical Outcomes in Patients with Severe Pneumonia: A Single-Center Retrospective Cohort Study

Wen-Hui Bai[1], Li Cheng[2]

[1]Department of Hepatobiliary Surgery, Eastern Campus, Renmin Hospital of Wuhan University, Wuhan, Hubei, 430200, People's Republic of China; [2]Department of Critical Care Medicine, Eastern Campus, Renmin Hospital of Wuhan University, Wuhan, Hubei, 430200, People's Republic of China

Correspondence: Li Cheng, Email 304558638@qq.com

Purpose: To compare clinical outcomes between early (<24 hours) and delayed (≥24 hours) mechanical ventilation (MV) in adults with severe pneumonia.

Methods: In this single-center, multi-ward retrospective cohort study, 827 adults with severe pneumonia requiring MV were admitted to the intensive care unit (ICU) between January 2022 and December 2024. Patients were divided into an early MV group (<24 hours after ICU admission) and a delayed MV group (≥24 hours after ICU admission) according to the timing of endotracheal intubation. Propensity score matching (PSM) was performed to balance baseline characteristics (age, PSI score, APACHE II score, comorbidities). The primary outcome was 28-day all-cause mortality. Secondary outcomes included ICU length of stay, duration of MV, and incidence of related complications.

Results: After PSM, 274 patients were included per group. Compared with the delayed MV, early MV was associated with significantly lower 28-day mortality (42.7% vs 51.8%; HR=0.735, 95% CI: 0.567–0.954; P=0.032), shorter ICU stay (11 vs 13 days; P=0.043), shorter MV duration (141 vs 145 h; P=0.018), and lower rates of tracheostomy at ICU discharge (30.7% vs 39.4%; P=0.032) and continuous renal replacement therapy (CRRT) requirement (23.4% vs 31.0%; P=0.044). In the unmatched cohort, cox regression showed that early MV was independently associated with lower ICU mortality (HR=0.767, 95% CI: 0.615–0.956; P=0.018).

Conclusion: In critically ill patients with severe pneumonia receiving MV in the ICU, early initiation of invasive mechanical ventilation was associated with lower 28-day mortality.

Keywords: severe pneumonia, endotracheal intubation, timing, mechanical ventilation, mortality, propensity score matching

Introduction

Severe pneumonia remains a leading cause of intensive care unit (ICU) admission and mortality, primarily driven by profound hypoxemic respiratory failure.[1] Although mechanical ventilation effectively supports gas exchange, it carries significant risks, including ventilator-associated lung injury and complications related to airway management and sedation.[2–4] Thus, determining the optimal timing for endotracheal intubation-balancing clinical benefits against potential risks-is a critical yet challenging decision in the management of severe pneumonia.

Existing evidence on intubation timing largely originates from studies of mixed populations with acute hypoxemic respiratory failure or sepsis, yielding inconsistent conclusions.[5–7] Recent work suggests that delayed intubation may worsen outcomes. For example, in patients with acute hypoxemic respiratory failure, intubation delayed >12 hours after high-flow oxygen failure was associated with increased 28-day mortality,[8] potentially due to ongoing lung injury from spontaneous breathing before the initiation of lung-protective ventilation.[9] Similarly, earlier mechanical ventilation (MV) after ICU admission has been linked to lower mortality in septic patients.[10] Although the timing of intubation has been

https://doi.org/10.2147/IDR.S595644
Received: 27 January 2026
Accepted: 24 March 2026
Published: 27 March 2026

recognized as an important factor influencing outcomes in patients with severe pneumonia, the definitions of "early" and "delayed" intubation remain inconsistent across the literature. Based on our institutional clinical practice, the first 24 hours after admission represent a critical window for reassessing disease progression and the response to initial therapy. Moreover, several previous studies have adopted the 24-hour threshold and demonstrated its value in predicting prognosis.[11,12] Accordingly, this study used 24 hours after ICU admission as the cut-off to define early versus delayed intubation.

Using a single-center, multi-ward retrospective design and propensity score matching (PSM) to balance baseline characteristics, we evaluated 28-day mortality, ICU length of stay, and duration of MV in adults with severe pneumonia. Compared with previous studies,[8,10] this study offers several novel aspects: inclusion of a broad spectrum of severe pneumonia patients from multiple wards, enhancing generalizability, and the use of PSM combined with multivariable Cox regression to provide a more robust assessment, and the development of a nomogram based on independent risk factors as a practical tool for individualized risk assessment. We hypothesize that earlier intubation in severe pneumonia is associated with improved survival and better clinical outcomes. Our findings aim to provide more targeted evidence to guide this critical clinical decision.

Materials and Methods

Study Design and Patient Population

A total of 827 adult patients with severe pneumonia who were admitted between January 2022 and December 2024 were enrolled. All patients received invasive MV and were from three ICUs within our hospital: the General ICU (20 beds), the Respiratory ICU (12 beds), and the Emergency ICU (15 beds). All three ICUs followed unified protocols for severe pneumonia management. Pneumonia was classified according to the site of acquisition: community-acquired pneumonia (CAP),[13] hospital-acquired pneumonia (HAP),[14] and nursing home-acquired pneumonia (NHAP)[15] with distributions of 55.1% (n=456), 33.3% (n=275), and 11.6% (n=96), respectively. All patients were followed until hospital discharge or death, with the final follow-up date of January 31, 2025. Baseline characteristics and relevant auxiliary examination data were collected following ICU admission. Patients were classified into early (<24 h after ICU admission) or delayed (≥24 h) MV groups. The study flow diagram is shown in Figure 1. This study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Renmin Hospital of Wuhan University (Approval No. WDRY2026-K055).

Inclusion Criteria for Severe Pneumonia:[16] Severe pneumonia was diagnosed according to established criteria,[16] defined as meeting either one major criterion or at least three minor criteria. Major Criteria: ① Requirement for endotracheal intubation and MV; ② septic shock hypotension requiring vasopressor support despite adequate fluid resuscitation. Minor Criteria: ① Respiratory rate ≥ 30 breaths/min; ② oxygenation index (PaO_2/FiO_2 ratio) ≤ 250 mmHg; ③ radiographic evidence of multilobar infiltrates; ④ impaired consciousness or disorientation; ⑤ blood urea nitrogen ≥ 20 mg/dL; ⑥ leukopenia (white blood cell count < 4×10^9/L); ⑦ thrombocytopenia (platelet count < 100×10^9/L); ⑧ hypothermia (core body temperature < 36°C); ⑨ hypotension requiring aggressive fluid resuscitation.

Exclusion Criteria: ① Age ≤ 18 years; ② not undergoing invasive MV; ③ ICU length of stay ≤ 3 days; ④ loss to follow- up or incomplete key auxiliary examination data.

Acute respiratory distress syndrome (ARDS) was diagnosed at ICU admission according to the Berlin definition,[17] based on clinical, radiographic, and oxygenation parameters at that time rather than after endotracheal intubation. Therefore, the occurrence of ARDS in this study reflects the severity of baseline respiratory failure at ICU admission.

Exposure Variable

Timing of endotracheal intubation: Early MV was defined as the initiation of invasive mechanical ventilation <24 hours after ICU admission, and delayed MV as ≥24 hours after ICU admission. ICU admission time was selected as the starting point for timing primarily due to its data reliability in retrospective studies and comparability with previous research.[11,12]

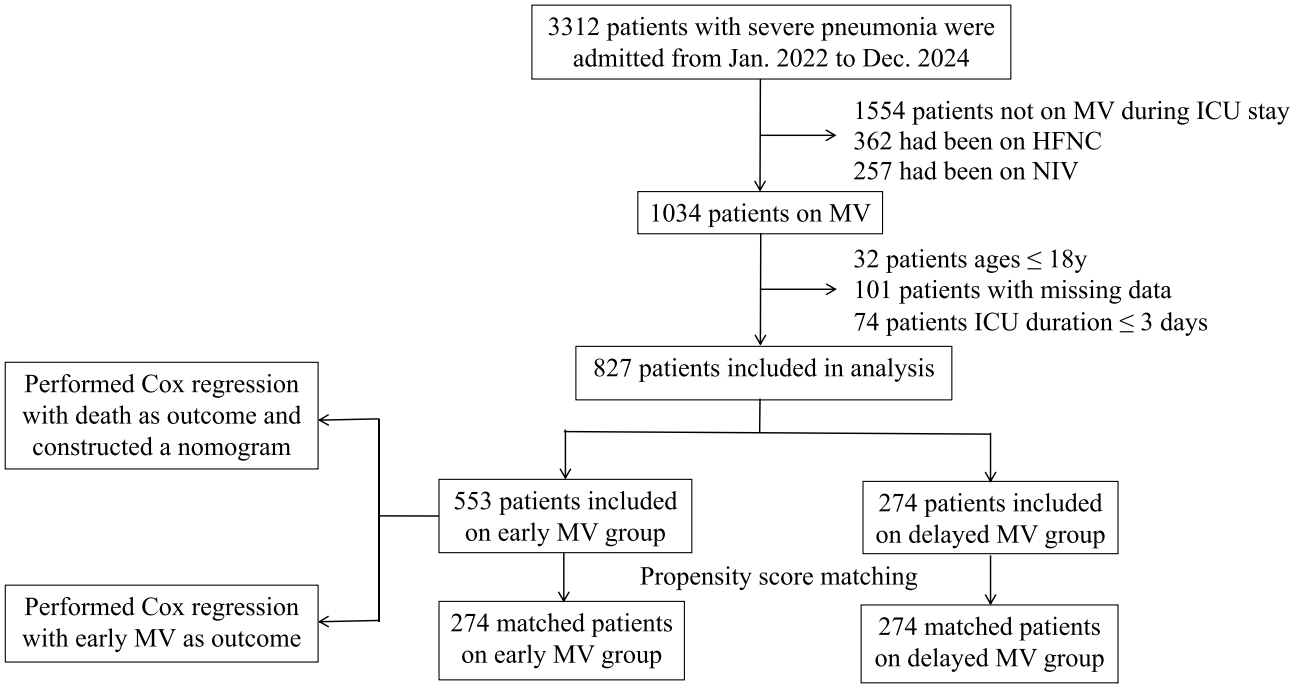

Figure 1 Study flowchart.

Outcomes

Primary Outcome: 28-day all-cause mortality. Secondary Outcomes: Hospital and ICU length of stay; duration of MV; incidence of complications, including ARDS, sepsis, acute myocardial injury, acute kidney injury, central nervous system injury, and deep vein thrombosis. Requirement for organ support at ICU discharge, including supplemental oxygen via nasal cannula, high-flow humidified oxygen therapy, tracheostomy, and continuous renal replacement therapy (CRRT).

PSM

PSM was applied to balance baseline characteristics between the two groups before intervention. Matching variables included: Demographics (sex and age); Presenting symptoms (fever, cough, dyspnea, myalgia, chest tightness, diarrhea, impaired consciousness); medical history (chronic lung disease, hypertension, diabetes, coronary heart disease, cerebrovascular disease, digestive system diseases, chronic kidney disease, immune disorders, malignancy); pathogen category (Gram-positive bacteria, Gram-negative bacteria, viruses, fungi, and culture-negative results); invasive therapies within 24 h of ICU admission [extracorporeal membrane oxygenation (ECMO), CRRT, and prone positioning ventilation]; auxiliary tests within 24 h of ICU admission: laboratory [complete blood count, hepatic and renal function, coagulation profile, cardiac injury markers, heart failure biomarkers, inflammatory markers, and arterial blood gas analysis]; imaging [chest imaging results, derived severity scores including pneumonia severity index (PSI) score, acute physiology and chronic health evaluation II (APACHE II) score, mean arterial pressure (MAP), and PaO_2/FiO_2 ratio].

Propensity scores were derived from a logistic regression model. Patients in the early and delayed MV groups were matched 1:1 without replacement using nearest-neighbor matching with a caliper width of 0.010. Matching quality was assessed using standardized mean differences (SMD), with SMD <10% indicating adequate balance between groups. The caliper width was chosen to maximize sample retention while ensuring close matching. Sensitivity analysis via the Hosmer-Lemeshow test yielded a post-matching p-value of 0.183, indicating good model fit and balanced covariate distribution. Compare the baseline characteristics before and after PSM (Supplementary Tables 1 and 2).

https://doi.org/10.2147/IDR.S595644

Statistical Analysis

Categorical variables were presented as frequencies (percentages), continuous variables as medians with interquartile ranges (IQRs). Group comparisons were performed using the Mann–Whitney *U*-test for continuous variables and the chi-square or Fisher's exact test for categorical variables, as appropriate. Outcomes were reported as hazard ratios (HRs) with 95% confidence intervals (CIs).

The post-hoc power calculation demonstrated that, with a two-sided alpha of 0.05 and 274 patients per group, the study had 83.2% power to detect the observed mortality difference (42.7% vs 51.8%), indicating sufficient sample size to assess the primary outcome.

In the unmatched cohort, multivariate Cox proportional hazards regression models were used to identify factors associated with 28-day all-cause mortality and with the decision for early MV, respectively. Results from the mortality model were visualized using a forest plot and a nomogram; the early ventilation decision model was presented with a forest plot. The optimal cut-off for risk stratification based on the nomogram score was determined using X-tile software. Kaplan-Meier survival curves were plotted, and between-group differences were assessed with the Log rank test. To evaluate potential unmeasured confounding, an E-value was calculated via an online tool.[18] A two-sided p-value < 0.05 was considered statistically significant. All analyses were conducted using R software (version 4.1.3).

Results

Comparison of Baseline Characteristics

The baseline characteristics of the unmatched cohort are presented in Table 1. Compared to the Delayed MV group, the early MV group had a significantly higher prevalence of fever, myalgia, chest tightness, impaired consciousness, and hypertension (all $P < 0.05$). Conversely, the delayed MV group showed a higher proportion of patients with diabetes, chronic kidney disease, malignancy, Gram-positive or Gram-negative bacteria detection, pulmonary infiltrates involving >50% of the lung field, and use of prone positioning ventilation (all $P < 0.05$). Among all 827 patients, 9 (1.1%) received ECMO support during ICU stay.

Following PSM, 274 patients from the early MV group were successfully matched 1:1 with 274 patients from the delayed MV group. Post-matching characteristics were summarized in Table 1. After matching, the early MV group had a significantly higher proportion of male patients, and those presenting with impaired consciousness, while the delayed MV group had a higher proportion of patients with a history of diabetes and chronic kidney disease, as well as a higher median APACHE II score (all $P < 0.05$).

Comparison of Baseline Laboratory and Examination Findings

Baseline laboratory and examination findings of the unmatched cohort are shown in Table 2. Compared to the delayed MV group, the early MV group exhibited significantly higher white blood cell count (WBC), aspartate aminotransferase (AST), urea, B-type natriuretic peptide (BNP), troponin I (cTnI), prothrombin time (PT), activated partial thromboplastin time (APTT), D-dimer, arterial blood pH, and PaO_2/FiO_2 ratio (all $P < 0.05$). In contrast, the delayed MV group demonstrated higher platelet count (PLT), direct bilirubin (DBIL), albumin (ALB), lactate dehydrogenase (LDH), creatine kinase (CK), and body temperature (all $P < 0.05$).

Following PSM (274 patients per group), post-matching results were summarized in Table 2. The delayed MV group maintained significantly higher lactate dehydrogenase, blood lactate, and mean arterial pressure compared to the early MV group (all $P < 0.05$).

Clinical Outcomes

In the unmatched cohort, the early MV group had significantly lower ICU mortality (43.4% vs 51.8%, $P = 0.022$), shorter ICU length of stay (11 vs 13 d, $P = 0.039$), and shorter MV duration (138 vs 145 h, $P = 0.005$) compared to the delayed MV group (Table 3). However, the early MV group had a higher incidence of concurrent ARDS (76.5% vs 70.1%, $P = 0.047$). Conversely, the delayed MV group showed higher rates of sepsis (55.5% vs 44.3%, $P = 0.002$), myocardial injury (70.8% vs 62.2%, $P = 0.015$), central nervous system injury (27.7% vs 14.6%, $P < 0.001$), other complications (14.6% vs

Table 1 Baseline Characteristics of Study Population

Variables [(%)/[M(Q_L, Q_U)]]	Unmatched Cohort (n=827)				Propensity Score-Matched Cohort (n=548)			
	Early MV (n=553)	Delayed MV (n=274)	*P* value	SMD (%)	Early MV (n=274)	Delayed MV (n=274)	*P* value	SMD (%)
Male/Female (n)	378/175	190/84	0.773	2.1	212/62	190/84	0.034	1.6
Age								
18~49y	61 (11.0)	35 (12.8)	0.446	4.7	30 (10.9)	35 (12.8)	0.509	4.4
50~59y	81 (14.6)	44 (16.1)	0.594	3.8	47 (17.2)	44 (16.7)	0.731	3.0
60~69y	155 (28.0)	60 (21.9)	0.058	15.9	62 (22.6)	60 (21.9)	0.837	2.7
70~79y	163 (29.5)	77 (28.1)	0.682	3.1	73 (26.6)	77 (18.1)	0.702	3.2
≥80y	93 (16.8)	58 (21.2)	0.127	11.0	62 (22.6)	58 (21.2)	0.679	0.9
Clinical symptoms								
Fever	224 (40.5)	142 (51.8)	0.002	22.0	123 (44.9)	142 (51.8)	0.104	9.1
Cough	206 (37.3)	115 (42.0)	0.190	9.6	104 (38.0)	115 (42.0)	0.337	8.1
Dyspnea	238 (43.0)	111 (40.5)	0.489	5.9	106 (38.7)	111 (40.5)	0.662	3.0
Systemic myalgia	130 (23.5)	29 (10.6)	0.000	42.0	37 (13.5)	29 (10.6)	0.294	9.5
Chest discomfort	186 (33.6)	63 (23.0)	0.002	25.3	61 (22.3)	63 (23.0)	0.838	1.7
Diarrhea	45 (8.1)	17 (6.2)	0.320	35.4	21 (7.7)	17 (6.2)	0.501	2.3
Altered consciousness	95 (17.2)	32 (11.7)	0.039	30.2	50 (18.2)	32 (11.7)	0.031	9.1
Others	23 (4.2)	16 (5.8)	0.283	18.6	18 (6.6)	16 (5.8)	0.723	0.0
Medical history								
Chronic lung disease	96 (17.4)	39 (14.2)	0.252	10.1	46 (16.8)	39 (14.2)	0.409	8.4
Hypertension	235 (42.5)	151 (55.1)	0.001	11.0	152 (55.5)	151 (55.1)	0.932	0.7
Diabetes	136 (24.6)	107 (39.1)	0.000	29.6	85 (31.0)	107 (39.1)	0.049	9.7
Coronary heart disease	108 (19.5)	60 (21.9)	0.426	8.3	55 (20.1)	60 (21.9)	0.600	3.6
Cerebrovascular disease	61 (11.0)	26 (9.5)	0.496	17.6	40 (14.6)	26 (9.5)	0.066	3.2

(*Continued*)

https://doi.org/10.2147/IDR.S595644

Table 1 (Continued).

Variables [(%)/[M(Q_L, Q_U)]]	Unmatched Cohort (n=827)				Propensity Score-Matched Cohort (n=548)			
	Early MV (n=553)	Delayed MV (n=274)	*P* value	SMD (%)	Early MV (n=274)	Delayed MV (n=274)	*P* value	SMD (%)
Digestive system disease	42 (7.6)	19 (6.9)	0.732	11.0	25 (9.1)	19 (6.9)	0.346	4.0
Chronic kidney disease	162 (29.3)	103 (37.6)	0.016	2.4	80 (29.2)	103 (37.6)	0.037	3.4
Autoimmune disease	12 (2.2)	7 (2.6)	0.728	2.4	8 (2.9)	7 (2.6)	0.793	0.0
Malignancy	40 (7.2)	37 (13.5)	0.003	4.7	31 (11.3)	37 (13.5)	0.437	4.9
Others	15 (2.7)	10 (3.6)	0.459	16.3	10 (3.6)	10 (3.6)	-	8.3
Type of pathogen								
Gram-positive bacteria	118 (21.3)	77 (28.1)	0.031	6.3	60 (21.9)	77 (28.1)	0.094	0.0
Gram-negative bacteria	217 (39.2)	117 (42.7)	0.000	19.3	108 (39.4)	117 (42.7)	0.434	6.2
Viruses	22 (4.0)	12 (4.4)	0.784	1.9	14 (5.1)	12 (4.4)	0.688	0.0
Fungi	51 (9.2)	23 (8.4)	0.694	21.2	20 (7.3)	23 (8.4)	0.634	9.0
Negative	239 (43.2)	119 (43.4)	0.954	0.5	108 (39.4)	119 (43.4)	0.340	7.3
Extent of bilateral infiltrates > 50%	368 (66.5)	201 (73.4)	0.047	5.1	182 (66.4)	201 (73.4)	0.077	5.5
Treatments								
ECMO	5 (0.9)	4 (1.5)	0.712[a]	4.6	4 (1.5)	4 (1.5)	-	0.0
CRRT	212 (38.3)	117 (42.7)	0.227	43.4	98 (35.8)	117 (42.7)	0.096	9.5
Prone ventilation	108 (19.5)	107 (39.1)	0.000	32.5	99 (36.1)	107 (39.1)	0.480	9.3
PSI score	121.0 (109.0, 145.0)	129.0 (113.0, 152.0)	0.092	13.1	123.0 (112.0, 142.0)	129.0 (113.0, 152.0)	0.132	9.5
APACHE II score	21.0 (18.0, 26.0)	21 (17.0, 25.0)	0.123	8.4	20.0 (18.0, 23.0)	21 (17.0, 25.0)	0.033	6.8

Note: [a]P-value for continuity-corrected Chi-square test.

Abbreviations: ECMO, Extracorporeal Membrane Oxygenation; CRRT, Continuous Renal Replacement Therapy; PSI, Pneumonia Severity Index; APACHE II, Acute Physiology and Chronic Health Evaluation II score.

https://doi.org/10.2147/IDR.S595644

Table 2 Baseline Laboratory Results of Study Population

Variables [M(Q_L, Q_U)]	Unmatched Cohort (n=827)				Propensity Score-Matched Cohort (n=548)			
	Early MV (n=553)	Delayed MV (n=274)	*P* value	SMD (%)	Early MV (n=274)	Delayed MV (n=274)	*P* value	SMD (%)
WBC (×10^9/L)	11.0 (7.5, 15.6)	10.5 (7.1, 15.1)	0.586	3.1	11.4 (8.4, 16.0)	10.5 (7.1, 15.1)	0.098	9.5
N (×10^9/L)	9.8 (6.4, 13.8)	8.9 (5.7, 14.0)	0.384	7.9	10.1 (6.7, 14.3)	8.9 (5.7, 14.0)	0.150	0.4
L (×10^9/L)	0.6 (0.3, 0.9)	0.6 (0.3, 0.9)	0.303	3.0	0.6 (0.4, 0.9)	0.6 (0.3, 0.9)	0.980	7.6
PLT (×10^9/L)	156.0 (97.0, 219.5)	171.0 (110.0, 241.0)	0.017	12.1	182.5 (110.0, 228.0)	171.0 (110.0, 241.0)	0.448	2.3
PCT (μg/L)	0.9 (0.3, 4.0)	1.1 (0.2, 7.9)	0.381	33.6	1.0 (0.2, 3.6)	1.1 (0.2, 7.9)	0.807	9.7
CRP (mg/L)	72.3 (16.4, 164.1)	83.7 (23.5, 185.6)	0.082	9.3	70.0 (15.4, 177.6)	83.7 (23.5, 185.6)	0.541	2.5
IL-6 (pg/mL)	45.3 (17.4, 104.1)	33.7 (17.0, 100.4)	0.246	6.6	42.3 (0.0, 9.7)	33.7 (17.0, 100.4)	0.176	3.2
ALT (U/L)	25.0 (14.0, 48.0)	21.0 (14.0, 40.0)	0.431	0.3	17.0 (11.7, 100.5)	21.0 (14.0, 40.0)	0.883	4.0
AST (U/L)	37.5 (22.0, 75.0)	32.0 (22.0, 56.9)	0.026	12.1	34.0 (20.0, 61.0)	32.0 (22.0, 56.9)	0.898	3.8
TBIL (μmol/L)	10.7 (7.4, 19.3)	12.6 (8.8, 18.0)	0.088	48.6	11.1 (6.7, 13.9)	12.6 (8.8, 18.0)	0.105	0.1
DBIL (μmol/L)	4.4 (2.9, 7.8)	5.1 (3.5, 8.1)	0.034	34.7	4.8 (2.6, 5.8)	5.1 (3.5, 8.1)	0.096	9.3
ALB (g/L)	30.5 (27.5, 34.4)	32.2 (28.5, 37.4)	0.000	25.0	31.9 (28.9, 36.9)	32.2 (28.5, 37.4)	0.954	9.5
Urea (mmol/L)	11.8 (7.1, 18.7)	9.7 (6.8, 18.2)	0.049	4.5	11.7 (6.8, 17.7)	9.7 (6.8, 18.2)	0.479	0.8
Cr (μmol/L)	81.0 (60.0, 158.0)	89.0 (60.0, 178.0)	0.095	6.9	84.0 (58.0, 159.0)	89.0 (60.0, 178.0)	0.568	1.3
eGFR (mL/min)	69.1 (31.0, 97.7)	80.4 (36.6, 99.2)	0.068	13.7	79.8 (36.6, 100.1)	80.4 (36.6, 99.2)	0.699	7.0
LDH (U/L)	320.0 (239.0, 420.0)	342.0 (253.0, 507.0)	0.002	17.0	329.5 (232.0, 429.0)	342.0 (253.0, 507.0)	0.045	4.7
CK (U/L)	6.8 (3.1, 18.9)	9.3 (4.6, 21.5)	0.002	2.8	7.4 (3.0, 18.9)	9.3 (4.6, 21.5)	0.062	9.8
BNP (ng/L)	2137.0 (493.0, 6162.5)	1335.0 (435.9, 3879.0)	0.018	52.1	1085.0 (314.0, 3738.0)	1335.0 (435.9, 3879.0)	0.030	1.3
cTnI (gl/L)	0.1 (0.0, 25.7)	0.1 (0.0, 9.7)	0.016	56.8	0.1 (0.0, 9.9)	0.1 (0.0, 9.7)	0.365	9.1
PT (s)	12.8 (11.6, 15.0)	12.5 (11.5, 13.8)	0.022	5.1	12.6 (11.4, 14.5)	12.5 (11.5, 13.8)	0.828	0.0
APTT (s)	32.3 (27.7, 38.9)	31.0 (26.8, 35.6)	0.007	6.8	31.9 (27.2, 37.4)	31.0 (26.8, 35.6)	0.214	4.2
D-dimer (mg/L)	6.2 (2.3, 11.2)	4.3 (1.5, 11.2)	0.025	10.4	4.6 (2.2, 9.5)	4.3 (1.5, 11.2)	0.341	3.9

(*Continued*)

https://doi.org/10.2147/IDR.S595644

Table 2 (Continued).

Variables [M(Q_L, Q_U)]	Unmatched Cohort (n=827)				Propensity Score-Matched Cohort (n=548)			
	Early MV (n=553)	Delayed MV (n=274)	*P* value	SMD (%)	Early MV (n=274)	Delayed MV (n=274)	*P* value	SMD (%)
Lac (mmol/L)	1.7 (1.2, 2.5)	1.7 (1.3, 2.3)	0.858	1.1	1.6 (1.2, 2.4)	1.7 (1.3, 2.3)	0.041	1.7
PH	7.4 (7.3, 7.5)	7.4 (7.3, 7.5)	0.024	69.3	7.4 (7.3, 7.5)	7.4 (7.3, 7.5)	0.057	9.0
T (°C)	36.9 (36.5, 37.5)	37.3 (36.6, 38.1)	0.000	1.8	37.2 (36.7, 38.1)	37.3 (36.6, 38.1)	0.942	1.5
HR (bpm)	94.0 (81.0, 110.0)	101.0 (80.0, 116.0)	0.136	10.5	96.0 (82.0, 110.0)	101.0 (80.0, 116.0)	0.347	6.4
MAP (mmHg)	87.0 (80.0, 96.0)	88.0 (80.0, 97.0)	0.935	2.0	87.0 (79.0, 96.0)	88.0 (80.0, 97.0)	0.037	0.8
P/F (mmHg)	170.0 (122.0, 262.0)	154.0 (102.0, 242.0)	0.003	23.1	162.0 (114.0, 227.0)	154.0 (102.0, 242.0)	0.338	5.4

Abbreviations: WBC, white blood cell count; N, neutrophil count; L, lymphocyte count; PLT, platelet count; PCT, procalcitonin; CRP, C-reactive protein; IL-6, interleukin-6; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALB, albumin; Cr, creatinine, eGFR, estimated glomerular filtration rate; LDH, lactate dehydrogenase; CK, creatine kinase; BNP, B-type natriuretic peptide; cTnI, cardiac troponin I; PT, prothrombin time; APTT, activated partial thromboplastin time; Lac, lactate; pH, potential of hydrogen; T, temperature; HR, heart rate; MAP, mean arterial pressure; P/F, ratio of arterial oxygen partial pressure to fractional inspired oxygen.

https://doi.org/10.2147/IDR.S595644

9.6%, P = 0.032), and higher proportions of patients requiring tracheostomy (39.4% vs 29.8%, P = 0.006) and CRRT (31.0% vs 24.4%, P = 0.043) at ICU discharge.

After PSM, early MV remained associated with lower ICU mortality (42.7% vs 51.8%; HR = 0.735, 95% CI: 0.567–0.954; P = 0.032), shorter ICU stay (11 vs 13 d; P = 0.043), and shorter MV duration (141 vs 145 h; P = 0.018), and lower rates of tracheostomy at ICU discharge (30.7% vs 39.4%; P=0.032) and CRRT requirement (23.4% vs 31.0%; P=0.044) (Table 3). The early MV group continued to show a higher incidence of concurrent ARDS (77.7% vs 70.1%; P = 0.041). The delayed MV group maintained higher rates of sepsis (55.5% vs 45.1%; P = 0.016). After matching, there were no significant differences in total hospital stay, incidence of myocardial injury, acute kidney injury, central nervous system injury, deep vein thrombosis, other complications, or the need for supplemental oxygen therapy (all P > 0.05).

The Kaplan-Meier survival curves demonstrated significantly better 28-day cumulative survival in the early MV group (log-rank P = 0.005; HR = 1.339, 95% CI: 1.088–1.647; Figure 2).

Cox Regression for Factors Associated with 28-Day Mortality

In the unmatched cohort, early MV was identified as an independent protective factor against 28-day all-cause mortality in the multivariable Cox regression model (adjusted HR = 0.767, 95% CI: 0.615–0.956, P = 0.018; Figure 3). The model demonstrated good overall fit (Likelihood Ratio Test: χ^2 = 64.74, P < 0.001). The calculated E-value was 2.020, indicating moderate robustness to potential unmeasured confounding.

Six variables were retained in the final model: early MV, duration of MV, age ≥ 80 years, APACHE II score, presence of deep vein thrombosis (DVT), and lactate level. A nomogram based on these variables was constructed to facilitate individualized mortality risk assessment (Figure 4). In this model, prolonged MV duration, age ≥ 80 years, higher APACHE II score, DVT, and elevated lactate were associated with increased mortality, whereas early MV was the sole protective factor.

The model exhibited strong discriminative performance, with a concordance index (C-index) of 0.801 (95% CI: 0.786–0.815), Using X-tile analysis, patients were stratified into low-, intermediate-, and high-risk groups based on nomogram scores, with predicted mortality probabilities of < 59.8%, 67.2–73.9%, and > 73.9%, respectively. Kaplan-Meier survival curves confirmed progressively lower survival across risk strata (log-rank P < 0.001; Figure 5).

Variables Associated with the Decision for Early MV

To identify factors influencing the clinical decision to early MV, we performed a Cox regression analysis with early MV as the endpoint. The final multivariate model included 8 variables: age ≥ 80 years, impaired consciousness at presentation, history of malignancy, long-term dialysis, concurrent ARDS, MAP level, APACHE II score, and pulmonary infiltrates involving >50% of the lung area (Figure 6).

The analysis showed that impaired consciousness, concurrent ARDS, higher APACHE II score, and extensive pulmonary infiltrates (>50% lung involvement) were significantly associated with early MV. Conversely, age ≥ 80 years, history of malignancy, long-term dialysis, and higher MAP were associated with delayed MV (all P < 0.05). The model demonstrated strong overall significance (Likelihood Ratio Test χ^2 = 82.07, P < 0.001) and excellent discriminative performance (C-index = 0.827, 95% CI: 0.812–0.842, P < 0.001).

Discussion

This single-center retrospective cohort study investigated the impact of early versus delayed invasive mechanical ventilation on outcomes in patients with severe pneumonia. After PSM, early MV was significantly associated with lower 28-day mortality, shorter duration of MV, and lower rates of tracheostomy and CRRT requirement. Multivariable Cox regression analysis confirmed that early MV was independently associated with lower ICU mortality. In clinical practice, determining the optimal intubation timing requires consideration of multiple factors: the 24-hour threshold aligns with the window for reassessing initial treatment response, and intubation decisions should integrate respiratory rate, oxygenation status, hemodynamics, and clinical deterioration trends, and clinical judgment of high risk should prompt earlier intubation. The 24-hour cut-off may serve as a reference framework, but individualized assessment remains paramount.

Table 3 Outcomes of Study Population

Variables [(%)/[M(QL, QU)]]	Unmatched Cohort (n=827)			Propensity Score-Matched Cohort (n=548)			
	Early MV (n=553)	Delayed MV (n=274)	P value	Early MV (n=274)	Delayed MV (n=274)	HR (95% CI)	P value
Outcome (Death/Survival)	240/313	142/132	0.022	117/157	142/132	0.735 (0.567–0.954)	0.032
Hospital duration (days)	15.0 (10.0, 22.0)	16.0 (11.0, 21.0)	0.522	14.0 (10.0, 21.5)	16.0 (11.0, 21.0)		0.171
ICU duration (days)	11.0 (7.0, 18.0)	13.0 (8.0, 18.0)	0.039	11.0 (7.0, 17.0)	13.0 (8.0, 18.0)		0.043
MV duration (h)	138.0 (91.0, 182.0)	145.0 (98.0, 233.0)	0.005	141.0 (107.3, 178.0)	145.0 (98.0, 233.0)		0.018
Complication (s)							
ARDS	423 (76.5)	192 (70.1)	0.047	217 (77.7)	192 (70.1)	1.131 (1.042–1.585)	0.041
Sepsis	245 (44.3)	152 (55.5)	0.002	119 (45.1)	152 (55.5)	1.339 (1.054–1.700)	0.016
Acute myocardial injury	344 (62.2)	194 (70.8)	0.015	180 (65.7)	194 (70.8)	1.077 (0.814–1.442)	0.199
Acute kidney injury	276 (49.9)	145 (52.9)	0.415	148 (54.0)	145 (52.9)	1.091 (0.875–1.483)	0.797
Central nervous system injury	81 (14.6)	76 (27.7)	0.000	68 (24.8)	76 (27.7)	0.928 (0.722–1.194)	0.437
Deep vein thrombosis	284 (51.4)	153 (55.8)	0.224	137 (50.0)	153 (55.8)	1.077 (0.951–1.211)	0.171
Others	53 (9.6)	40 (14.6)	0.032	37 (13.5)	40 (14.6)	1.035 (0.942–1.410)	0.712
At ICU discharge							
Nasal cannula oxygen therapy	312 (56.4)	148 (54.0)	0.512	149 (54.4)	148 (54.0)	0.879 (0.692–1.117)	0.932
High-flow nasal cannula	241 (43.6)	126 (46.0)	0.512	124 (47.0)	126 (46.0)	1.012 (0.792–1.294)	0.819
Tracheostomized	165 (29.8)	108 (39.4)	0.006	84 (30.7)	108 (39.4)	1.345 (1.036–1.746)	0.032
CRRT	135 (24.4)	85 (31.0)	0.043	64 (23.4)	85 (31.0)	1.180 (1.015–1.522)	0.044

Abbreviations: ICU, intensive care unit; ARDS, acute respiratory distress syndrome; CRRT, continuous renal replacement therapy.

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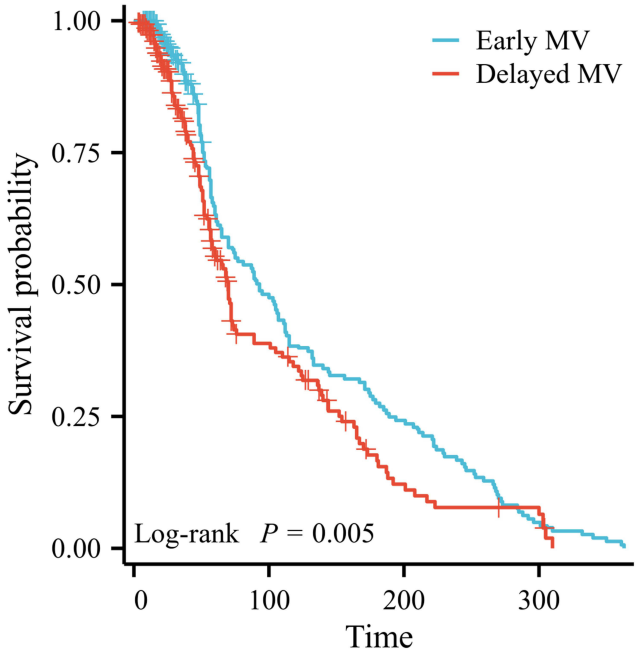

Figure 2 Comparison of 28-day cumulative survival between early and delayed MV groups in patients with severe pneumonia.

Characteristics	Total(N)	HR(95% CI) Univariate analysis	P value Univariate analysis	HR(95% CI) Multivariate analysis	P value Multivariate analysis
Timing of MV	827				
0	274	Reference		Reference	
1	553	0.791(0.643 - 0.974)	0.027	0.767 (0.615 - 0.956)	0.018
MV duration (h)	827	1.001 (1.000 - 1.002)	0.014	1.001 (1.000 - 1.002)	0.037
Age ≥ 80y	827				
0	676	Reference		Reference	
1	151	1.678 (1.330 - 2.116)	< 0.001	1.569 (1.236 - 1.992)	< 0.001
Diabetes mellitus	827				
0	584	Reference		Reference	
1	243	1.258 (1.016 - 1.558)	0.036	1.129(0.908 - 1.405)	0.276
PSI score	827	1.013 (0.979 - 1.048)	0.456		
APACHE II score	827	1.032 (1.015 - 1.049)	< 0.001	1.029(1.012 - 1.047)	< 0.001
Sepsis	827				
0	420	Reference		Reference	
1	407	1.659 (1.352 - 2.037)	< 0.001	1.766 (1.426 - 2.189)	< 0.001
Deep vein thrombosis	827				
0	390	Reference		Reference	
1	437	1.502 (1.208 - 1.866)	< 0.001	1.425 (1.139 - 1.782)	0.002
Lactate (mmol/L)	827	1.037(1.003 - 1.073)	0.034	1.036 (1.001- 1.072)	0.041
Fungal infection	827				
0	753	Reference			
1	74	1.137 (0.803 - 1.609)	0.471		

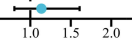

Figure 3 Multivariable Cox regression model for predicting ICU mortality in the unmatched cohort.

In this study, patients in the early MV group presented with greater illness severity at ICU admission but had lower 28-day mortality than those in the delayed MV group. This suggests that early initiation of invasive MV is associated with timely interruption of respiratory failure progression and prevention of multi-organ failure resulting from prolonged hypoxia, which may offset the negative prognostic impact of initial disease severity. Thus, for patients with greater illness severity, early intubation may represent an effective proactive intervention rather than waiting for further deterioration before rescue intubation. The incidence of ARDS was higher in the early MV. Since ARDS was diagnosed at ICU admission according to the Berlin definition,[17] this difference reflects greater baseline respiratory failure in the early MV, which is associated with a greater tendency for clinicians to intubate within 24 hours. This finding suggests that early intubation is prevention of ARDS progression rather than being a consequence of ARDS developing after intubation.

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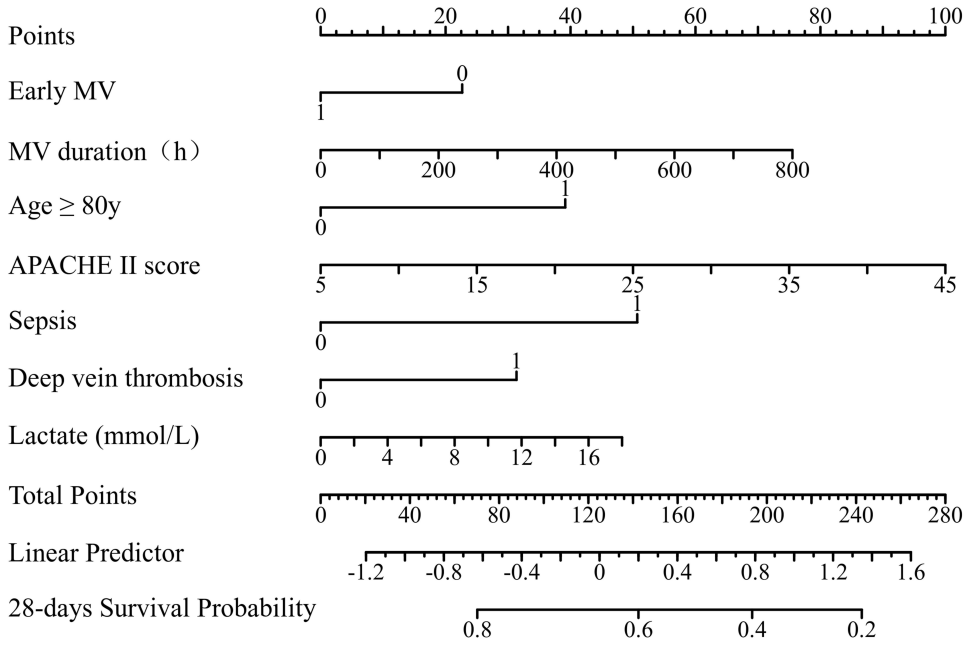

Figure 4 Nomogram for predicting ICU mortality.

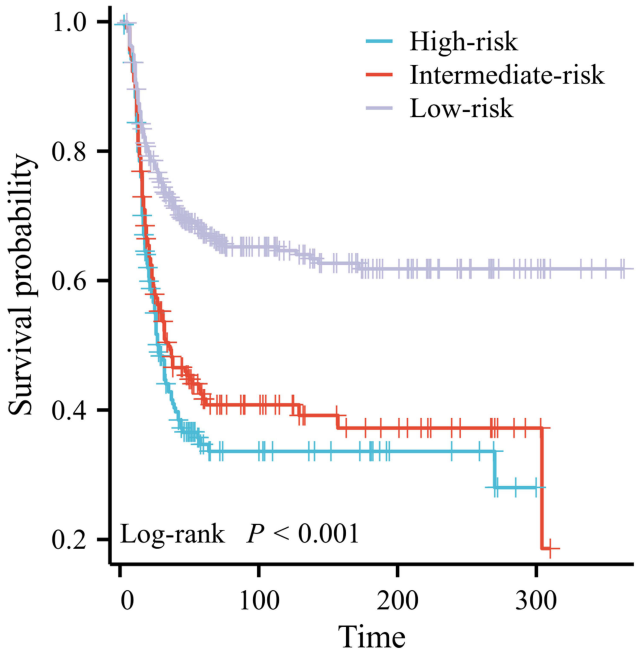

Figure 5 Comparison of survival curves among low-, intermediate-, and high-risk patient groups.

Collectively, These findings support the clinical value of early recognition of respiratory failure and timely intervention in patients with severe pneumonia.

Although some studies have compared intubation timing in critically ill patients, conclusions vary across disease contexts. A secondary analysis of a multicenter prospective study in 735 patients with septic shock found no significant

Characteristics	Total(N)	HR(95% CI) Univariate analysis	P value Univariate analysis	HR(95% CI) Multivariate analysis	P value Multivariate analysis
Age ≥ 80y	827				
0	676	Reference		Reference	
1	151	0.736 (0.579 - 0.936)	0.012	0.786 (0.617 - 0.999)	0.049
Encephalopathy	827				
0	700	Reference		Reference	
1	127	1.305 (1.093 - 1.557)	0.003	1.382 (1.154 - 1.656)	< 0.001
Malignancy	827				
0	750	Reference		Reference	
1	77	0.535 (0.394 - 0.737)	< 0.001	0.517 (0.376 - 0.710)	< 0.001
Regular dialysis	827				
0	682	Reference		Reference	
1	145	0.647 (0.486 - 0.862)	0.003	0.666 (0.499 - 0.889)	0.006
ARDS	827				
0	324	Reference		Reference	
1	503	1.305 (1.084 - 1.572)	0.005	1.246 (1.032 - 1.503)	0.022
Mean arterial pressure (mmHg)	827	0.995 (0.990 - 1.001)	0.093	0.993 (0.988 - 0.998)	0.011
PSI score	827	1.005 (0.976 - 1.035)	0.74		
APACHE II score	827	1.018 (1.003 - 1.032)	0.016	1.015 (1.001 - 1.030)	0.036
Extent of bilateral infiltrates	827				
0	258	Reference		Reference	
1	569	1.204 (1.008 - 1.438)	0.04	1.224 (1.022 - 1.467)	0.028

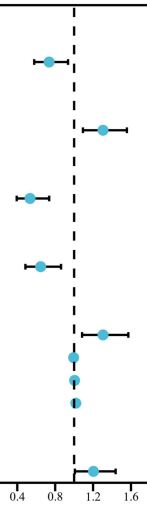

Figure 6 Multivariable Cox regression analysis for early MV groups on the unmatched study population.

difference in hospital mortality or length of stay between early and delayed MV groups.[19] Conversely, a prospective cohort study of 457 patients with ARDS reported significantly higher 60-day mortality in the delayed MV group.[20] Similarly, among immunocompromised patients with acute respiratory failure, early intubation was associated with lower mortality.[21] Studies on COVID-19 patients further suggested that delayed intubation was associated with increased mortality.[11,22] The findings of the present study align closely with the majority of these previous studies.

Early MV was significantly associated with shorter ICU length of stay, possibly by interrupting the cycle of hypoxemia-induced multi-organ injury and systemic inflammation.[1] Supporting evidence suggests that delayed intubation is associated with prolonged intense spontaneous breathing, which is linked to worsening lung injury and respiratory muscle fatigue, as well as extended weaning time.[23] These findings are consistent with the conclusions of the present study. Therefore, early intubation may be associated with improved patient survival, optimized healthcare resource utilization, and a more rapid recovery process.

Early MV was associated with a lower requirement for CRRT. The underlying mechanisms may involve the following aspects. First, severe hypoxemia can directly impair renal medullary oxygenation and induce inflammation and vasoconstriction, serving as an independent risk factor for acute kidney injury.[24,25] Second, during delayed intubation, intense spontaneous breathing efforts are associated with "respiratory muscle steal", which may compromise venous return and cardiac output and is linked to reduce renal perfusion.[26] Furthermore, early MV may be associated with interrupt the progression from respiratory failure to sepsis and multiple organ dysfunction, with sepsis being a leading cause of acute kidney injury in ICU patients.[27] Although some studies suggested that MV itself is associated with reduced renal blood flow and increased sympathetic activity, which may affect renal function,[28] a study on COVID-19 patients demonstrated a trend toward lower CRRT requirement in the early intubation cohort compared to the delayed intubation cohort (10% vs 29%, P = 0.07),[29] which aligns with our findings. This observation suggests that the early respiratory support may be associated with benefits beyond pulmonary protection, including potential renoprotective effects.

The incidence of sepsis was lower in the early MV than in the delayed MV. This finding may be related to the rapid correction of severe hypoxemia and excessive work of breathing with early invasive ventilation, which is associated with interruption of the key pathways through which these factors are linked to a systemic inflammatory response and tissue perfusion injury, and may be associated with inhibition of the progression from severe pneumonia to sepsis.[10] However, current evidence regarding this association remains inconsistent. Some studies supported that early intervention improved sepsis outcomes,[10] while others have found that delayed intubation did not significantly increase sepsis risk[30] and that premature intubation might be associated with iatrogenic infections due to increased exposure to ventilator-associated pneumonia.[19] Furthermore, early MV was also associated with a lower rate of tracheostomy, which may be attributable to

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the shorter overall duration of MV, as ventilation time is a key factor associated with the need for tracheostomy.[31] In summary, this study provides evidence that early MV is associated with lower risks of systemic infection and long-term airway complications in patients with severe pneumonia.

Cox regression in the unmatched cohort identified early MV as the only factor significantly associated with lower 28-day mortality, with the derived nomogram showing good discriminative ability (C-index = 0.801). The model shows that within the real-world, unmatched cohort, where baseline characteristics differed, the association between early MV and survival was independent of age, disease severity, and other complications. This suggests that the observed association of early intubation with survival is primarily associated with an active interventional approach, rather than merely reflecting less severe baseline illness in these patients.

In addition to examining the impact of intubation timing on outcomes, this study aimed to identify the key clinical factors associated with ICU physicians' decision to proceed with early intubation. The results indicated that impaired consciousness, high APACHE II score, pulmonary infiltrates involving >50% of the lung area, and concurrent ARDS were significant predictors associated with the decision for early MV. This finding aligns with the conclusions of a large observational study's prediction model, which included factors such as glasgow coma scale (GCS) score, central cyanosis, signs of respiratory muscle fatigue, lactate level, vasopressor dose, pH, and impaired airway clearance, collectively accounting for approximately 60% of the variance in early intubation decisions.[32] This highlights that a composite picture of deteriorating multi-system physiological status serves as the primary driver associated with clinicians' tendency toward active intervention. However, the decision to initiate MV is not solely based on objective parameters; it is a multidimensional process integrating clinical evidence, physician experience, resource availability, and the clinical environment. A mixed-methods study delving into the decision-making pathway for intubation in sepsis-associated acute respiratory failure emphasized that patient baseline status, clinical disease characteristics, and hospital/system-level factors are dynamically and collectively associated with the timing and manner of intervention.[33] Therefore, an optimal decision requires not only the acute recognition of physiological deterioration but also careful consideration within the broader clinical context and resource framework.

This study has several limitations. First, as a single-center, retrospective study, it cannot fully avoid unmeasured confounding and residual bias, despite the use of PSM and the calculation of an E-value to control for known confounders. Notably, clinicians may perform early intubation based on their anticipation of patient deterioration (treatment bias/indication bias), which may lead to an overestimation of the benefits of early intubation. PSM can only balance measured confounders, while unmeasured factors such as clinician judgment cannot be fully excluded. Therefore, the results should be interpreted with caution, and future prospective studies are needed to further validate the findings. Second, although using a 24-hour threshold to dichotomize intubation timing facilitates clinical application, it may not accurately capture the optimal intervention window based on dynamic physiological deterioration and limits the analysis of differences across finer time gradients. Third, the study only included patients with severe pneumonia who ultimately received MV; therefore, the findings should not be directly generalized to patients with other types of respiratory failure or those who successfully avoided intubation through non-invasive support. Finally, the retrospective design restricted the in-depth evaluation of operational details such as non-invasive ventilation settings and the protocols for escalating oxygen therapy, which may limit a more nuanced interpretation of the potential mechanisms underlying delayed intubation.

Conclusion

This single-center retrospective cohort study showed that early MV was associated with lower 28-day mortality, shorter duration of MV, and shorter ICU length of stay in patients with severe pneumonia. These findings suggest that early intubation may confer clinical benefits; however, due to the limitations of the study design, causality cannot be inferred. Future prospective studies or randomized controlled trials are needed to further validate these findings.

Disclosure

The author(s) report no conflicts of interest in this work.

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