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ORIGINAL RESEARCH

Association Between Mechanical Power and 28-Day All-Cause Mortality in Chronic Obstructive Pulmonary Disease Patients Undergoing Invasive Ventilation: Analysis of the MIMIC-IV Database

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Video Abstract

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Purpose: Increasing evidence suggests that mechanical power (MP) is associated with mortality among patients undergoing invasive mechanical ventilation. However, the relationship between MP and mortality in chronic obstructive pulmonary disease (COPD) patients undergoing invasive ventilation remains uncertain. The aim of this study was to investigate the association between MP and 28-day all-cause mortality among COPD patients undergoing invasive ventilation.

Patients and Methods: Data were obtained from the Medical Information Mart for Intensive Care (MIMIC-IV) database. COPD patients undergoing invasive ventilation were categorized into three categories based on MP tertiles to further assess the robustness of our results. The primary outcome was 28-day all-cause mortality. The relationship between MP and 28-day all-cause mortality in COPD patients undergoing invasive ventilation was performed to evaluate restricted cubic splines and Cox proportional hazards regression analysis. Receiver operating characteristic (ROC) curves and Kaplan-Meier survival analysis were employed to evaluate and visualize the predictive value of MP for 28-day all-cause mortality. Additionally, the optimal cut-off value of MP was determined. Finally, subgroup analysis was conducted to assess the robustness of the findings.

Results: 1704 COPD patients undergoing invasive ventilation (56.92% male) were included in the study. Based on the Cox regression analysis, MP was significantly associated with 28-day all-cause mortality risk in the unadjusted model (Model 1) [HR (95% CI) 1.04 (1.03–1.05), p<0.001]. However, as this is an observational study, causality cannot be inferred. Restricted cubic spline regression models revealed a linear rise in the risk of 28-day mortality as MP increased (P for non-linearity = 0.967). The area under the curve (AUC) for MP was 0.602. This study also identified an optimal cut-off value of 17.38 J/min for MP. Kaplan-Meier survival analysis demonstrated statistically significant differences in survival among invasive ventilation patients stratified by MP tertiles. Subgroup analysis of potential confounding factors indicated no significant interaction between MP and any subgroup (P for interaction: 0.114–0.967).

Conclusion: MP is associated with 28-day all-cause mortality in COPD patients undergoing invasive ventilation. The cut-off value of 17.38 J/min may serve as a reference point for clinicians in assessing disease severity. However, further research is needed to investigate the causal relationship between MP and mortality.

Keywords: mechanical power, chronic obstructive pulmonary disease, invasive ventilation, mortality, MIMIC-IV

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Introduction

COPD is a progressive and heterogeneous lung disease characterized by abnormalities in the airways and/or alveoli typically accompanied by persistent airflow limitation that is not fully reversible.[1] COPD is the third leading cause of death worldwide, affecting approximately 384 million people. Alarmingly, over half of individuals with COPD remain undiagnosed, making it a major public health issue that demands significant attention.[2–4] Studies suggest that COPD patients experience between 0.5 and 3.5 acute exacerbations per year, marked by worsening cough, increased sputum production, and escalating dyspnea.[5,6] The elevated rates of intensive care unit (ICU) admissions and mortality in acute exacerbations of COPD (AECOPD) place considerable economic and social strain on healthcare systems globally, a burden compounded by the increasing aging population.[7,8]

MP refers to the mechanical energy transmitted from the ventilator to the respiratory system, which can potentially lead to ventilator-induced lung injury (VILI). This results from the interaction between the load imposed by the ventilator and the load experienced by the lung parenchyma.[9] Currently, the most practical formula for bedside measurement in clinical settings is $MP = 0.098 \times V_t \times RR \times (PIP - 1/2DP)$, where V_t denotes tidal volume, RR stands for respiratory rate, PIP is peak inspiratory pressure, and DP refers to the driving pressure.[10] The growing recognition of MP as an important factor in ventilator induced lung injury (VILI) has made it an essential parameter in critical care settings. A study has suggested that variations in DP and MP are associated with 30-day mortality in patients with acute respiratory distress syndrome (ARDS), a condition marked by impaired pulmonary oxygenation.[11]

ARDS is a representative of diseases characterized by impaired pulmonary oxygenation. Its respiratory mechanics are characterized by decreased lung volumes and reduced compliance. Consolidated lung tissue cannot participate in gas exchange, while the remaining relatively normal lung tissue compensates by maintaining gas exchange.[12] In contrast, COPD is an obstructive lung disease marked by severe expiratory flow limitation and significant increases in lung volumes. The reduction in lung elastic recoil (due to emphysema) increases airway resistance, which causes dynamic hyperinflation of the lungs, shortened expiratory time and increased tidal volume, resulting in an elevated end-expiratory lung volume.[13] As the severity of AECOPD increases, more patients may require invasive mechanical ventilation due to severe gas exchange abnormalities or inadequate airway protection.[14] While studies have confirmed a relationship between MP and mortality in ARDS patients, the distinct respiratory mechanics of COPD compared to ARDS means the association between MP and mortality among COPD patients undergoing invasive ventilation remains unclear.

Building on this background, the purpose of this study was to investigate the association between MP and 28-day all-cause mortality among COPD patients undergoing invasive ventilation.

Materials and Methods

Data Source

Data were obtained from the MIMIC-IV database, which includes information collected from patients in the ICU at Beth Israel Deaconess Medical Center in Boston, Massachusetts.[15] Ethical considerations regarding patient privacy and confidentiality were addressed through deidentification. Access to the database and data extraction were performed by one of the authors, Haipeng Li, who has successfully passed an examination for a collaborative institutional training program (certification number: 13619655). Publicly accessible databases can be accessed and used by researchers with appropriate credentials. Additionally, the ethics committee (The Institutional Review Board of the Massachusetts Institute of Technology and Beth Israel Deaconess Medical Center) approved the database at its inception, eliminating the need for further informed consent.

Participant Selection Criteria

We included all consecutive patients (aged over 18 years) in the ICU with a primary diagnosis of COPD, identified using ICD-9 codes (code = 49,120, 49,121, 49122, and 496) and ICD-10 codes (code = J44, J440, J441, and J449) from the MIMIC-IV database. Patients were excluded based on the following criteria: (1) patients with multiple ICU admissions for COPD, with data extracted only from the first admission; (2) Patients with an ICU stay shorter than 24 hours; and (3) insufficient data on key variables such as respiratory rate, tidal volume, peak pressure, positive end-expiratory pressure

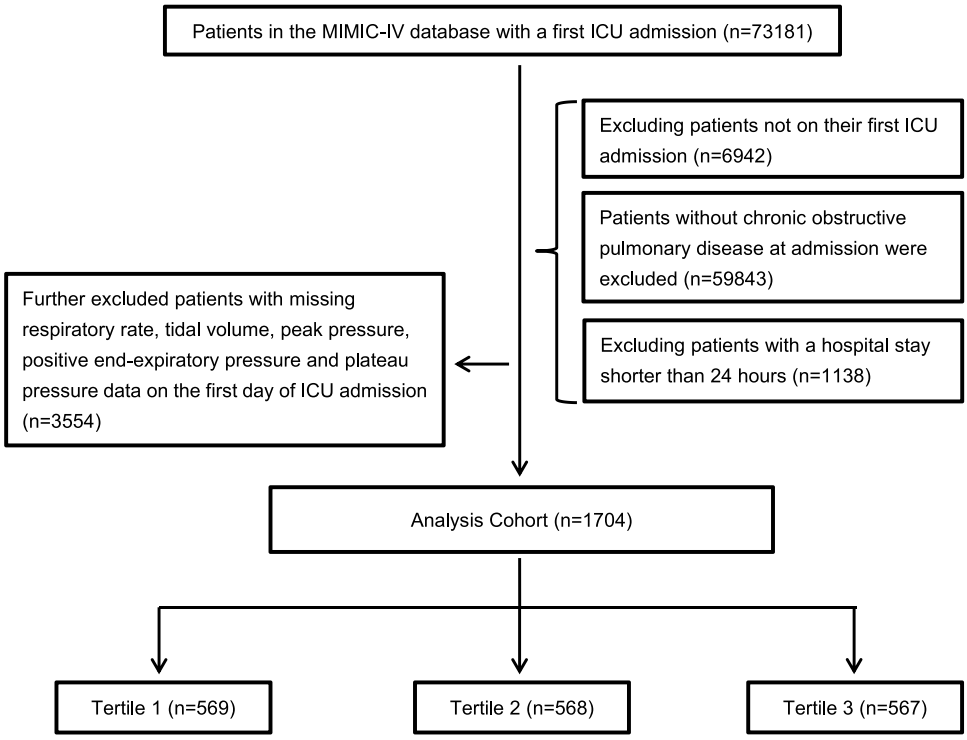

Figure 1 Flowchart of the study.
Notes: Mechanical power (J/min): Tertile 1 (1.20–11.49), Tertile 2 (11.49–16.17), Tertile 3 (16.17–98.65).
Abbreviations: ICU, intensive care unit; MIMIC-IV, Medical Information Mart for Intensive Care IV.

(PEEP), and plateau pressure during the first 24 hours in the ICU. Ultimately, 1704 patients were enrolled, and they were divided into three categories based on MP tertiles to further assess the robustness of our results. Figure 1 shows the patient screening flowchart.

Data Extraction

In this study, the software PostgreSQL (version 10.11) and Navicat Premium (version 12) were used to extract information. Age, gender, race, mortality and the length of ICU stay were extracted. The first dataset of vital signs, laboratory tests, comorbidity diseases and scoring systems were extracted from the first 24 hours of their admission to the ICU. Vital signs included heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean blood pressure (MBP), and temperature. Laboratory parameters included: white blood cell (WBC), red blood cell distribution width (RDW), hemoglobin (HGB), platelets, red blood cell (RBC), blood urea nitrogen (BUN), calcium, international normalized ratio (INR), sodium, potassium, prothrombin Time (PT), activated partial thromboplastin time (APTT), creatinine, and glucose. Acidity, partial pressure of oxygen (PO_2), Arterial Carbon Dioxide Pressure (PCO_2), total dioxide (TCO_2), and bicarbonate chemistry were extracted. The comorbidities diseases contained congestive heart failure (CHF), myocardial infarct, renal disease, severe liver disease, diabetes, malignant cancer and sepsis. Ventilator parameters include tidal volume (V_t), positive end-expiratory pressure (PEEP), respiratory rate (RR), peak inspiratory pressure (PIP) and driving pressure (DP). The MP was calculated using the following: $MP = 0.098 \times V_t \times RR \times (PIP - 1/2DP)$.[11] And driving pressure equals peak pressure minus PEEP.[16] Since mechanical power depends on multiple ventilator parameters, it can be influenced by various factors. To maximize the accuracy of the MP measurement, we utilized the average MP over the preceding 24 hours.

Primary Outcomes

The primary outcome of this study was 28-day all-cause mortality. Follow-up began on the date of ICU admission and ended on the date of death.

Statistical Analysis

Baseline characteristics were described and compared according to the tertiles of the MP. Continuous variables are presented as mean ± standard deviation (for normally distributed data) or medians with interquartile range (for skewed data), while categorical variables are presented as number (%). The chi-square test was used to assess intergroup differences for categorical variables, while one-way ANOVA was employed to evaluate intergroup differences for continuous variables with normal distribution. The mice package in R was employed to perform multiple imputation for missing data. The Classification and Regression Trees method was applied to generate five imputed datasets, with a random seed set to enhance the accuracy, stability, and reproducibility of the results. Cox proportional hazards models were used to calculate hazard ratios (HR) and 95% confidence intervals (CI) for the association between MP and the primary outcome, adjusting for various models. Confounding variables were selected based on a p-value <0.05 from univariate analysis, and clinically relevant variables associated with prognosis were included in the multivariate model. The Model 1 was unadjusted, while Model 2 was adjusted for age, gender, and race. Model 3 included a comprehensive set of covariates: age, sex, race, SBP, DBP, HR, SpO_2, glucose, PO_2, bicarbonate, BUN, calcium, creatinine, potassium, APTT, WBC, RDW, platelet count, HGB, myocardial infarction, CHF, renal disease, malignant cancer, severe liver disease, SOFA score, sepsis criteria, SAPS II score, and vasopressor use.

Additionally, this study used a restricted cubic spline regression model to examine the nonlinear association between MP and 28-day all-cause mortality. Receiver operating characteristic (ROC) curves were used to predict the 28-day all-cause mortality rate and identify the optimal cut-off value. Kaplan-Meier survival analysis was used to estimate endpoint disparities through groups differentiated by the tertiles of MP, and participants were classified into two groups according to the inflection point of MP to assess the incidence of endpoints defined by different levels of MP. A subgroup analysis was carried out to determine whether MP had a different impact on the 28-day all-cause mortality rate based on the varied subgroup. All statistical analyses were performed using R software (version 4.4.1), with a P-value <0.05 was considered statistically significant.

Results

Baseline Characteristics and Demographic Information

Table 1 presents the baseline characteristics of the participants stratified by MP tertiles. A total of 1704 patients were enrolled, with a mean age of 70.7 years (±10.9). Among these patients, 970 (56.9%) were male. The mean MP was 15.19 J/min (±7.0). In total, 372 patients (21.8%) experienced 28-day all-cause mortality. There were no significant differences among the different groups in terms of race, MBP, TCO_2, sodium, APTT, RDW, myocardial infarction, SBP, CHF, diabetes, renal disease, malignant cancer, severe liver disease, or the need for dialysis (P>0.05). As MP increased, several

Table 1 Baseline Characteristics of Patients Grouped by Mechanical Power[a]

Variables	Overall (N=1704)	T1 (N=569)	T2 (N=568)	T3 (N=567)	*P* Value
Age (years)	70.70 (10.90)	72.74 (10.74)	71.28 (10.20)	68.06 (11.20)	<0.001
Gender: male (n)	970 (56.9)	267 (46.9)	333 (58.6)	370 (65.3)	<0.001
Race (n)					0.054
White	1156 (67.8)	399 (70.1)	389 (68.5)	368 (64.9)	
Non white	548 (32.2)	170 (29.9)	179 (31.5)	199 (35.1)	
Vitals					
SBP (mmHg)	121.00 (25.10)	121.81 (23.28)	121.48 (26.03)	119.81 (25.98)	0.356
DBP (mmHg)	65.50 (18.20)	64.14 (16.81)	65.42 (18.62)	66.80 (18.99)	0.047
MBP (mmHg)	81.50 (18.20)	81.50 (16.63)	81.39 (18.69)	81.54 (19.08)	0.990
HR (beats/min)	86.90 (19.40)	83.29 (17.09)	86.16 (19.00)	91.13 (21.21)	<0.001
Temperature (°C)	36.60 (0.92)	36.47 (0.81)	36.54 (0.86)	36.65 (1.06)	0.003
SpO_2 (%)	97.30 (4.53)	98.20 (3.69)	97.42 (4.04)	96.20 (5.43)	<0.001

(*Continued*)

Table 1 (Continued).

Variables	Overall (N=1704)	T1 (N=569)	T2 (N=568)	T3 (N=567)	*P* Value
Laboratory events					
Glucose (mg/dL)	156.00 (67.70)	147.66 (56.61)	153.67 (64.11)	165.21 (79.39)	<0.001
pH	7.34 (0.11)	7.37 (0.09)	7.35 (0.10)	7.29 (0.12)	<0.001
PO_2 (mmHg)	195.00 (141.00)	228.21 (145.59)	204.73 (144.96)	151.94 (120.67)	<0.001
PCO_2 (mmHg)	49.40 (16.30)	45.08 (13.46)	49.01 (15.93)	53.98 (17.89)	<0.001
TCO_2 (mmol/L)	27.10 (6.38)	27.11 (5.99)	27.51 (6.48)	26.73 (6.63)	0.119
BC (mmol/L)	24.20 (5.36)	24.27 (4.89)	24.52 (5.46)	23.70 (5.68)	0.031
BUN (mg/dL)	28.30 (19.90)	25.48 (17.09)	27.28 (18.90)	32.18 (22.83)	<0.001
Calcium (mg/dL)	8.23 (0.86)	8.33 (0.85)	8.23 (0.81)	8.12 (0.91)	<0.001
Creatinine (mg/dL)	1.41 (1.28)	1.21 (1.09)	1.36 (1.14)	1.65 (1.52)	<0.001
Sodium (mEq/L)	139.00 (4.87)	139.18 (4.80)	138.77 (4.56)	138.51 (5.20)	0.065
Potassium (mEq/L)	4.38 (0.77)	4.27 (0.70)	4.35 (0.70)	4.52 (0.87)	<0.001
INR	1.50 (0.87)	1.43 (0.74)	1.47 (0.75)	1.59 (1.07)	0.007
PT (s)	16.20 (8.87)	15.63 (7.61)	15.98 (7.96)	17.09 (10.68)	0.015
APTT (s)	39.70 (25.9)	41.03 (28.42)	38.57 (24.67)	39.52 (24.53)	0.271
WBC (10^9/L)	13.50 (9.71)	12.29 (6.57)	13.30 (10.71)	14.89 (11.06)	<0.001
RBC (10^9/L)	3.55 (0.77)	3.39 (0.74)	3.54 (0.75)	3.72 (0.80)	<0.001
RDW (%)	15.20 (2.20)	15.18 (2.36)	15.27 (2.22)	15.25 (2.01)	0.785
Platelet (10^9/L)	202.00 (98.90)	193.31 (103.21)	202.13 (95.80)	211.83 (96.75)	0.007
HGB (g/L)	10.60 (2.26)	10.13 (2.13)	10.54 (2.20)	11.12 (2.35)	<0.001
Comorbidities					
Myocardial infarct (n)	448 (26.3)	156 (27.4)	157 (27.6)	135 (23.8)	0.258
CHF (n)	724 (42.5)	234 (41.1)	233 (41.0)	257 (45.3)	0.246
Diabetes (n)	617 (36.2)	211 (37.1)	201 (35.4)	205 (36.2)	0.837
Renal disease (n)	423 (24.8)	149 (26.2)	143 (25.2)	131 (23.1)	0.472
Malignant cancer (n)	175 (10.3)	59 (10.4)	58 (10.2)	58 (10.2)	0.995
Severe liver disease (n)	69 (4.05)	24 (4.2)	18 (3.2)	27 (4.8)	0.384
Scores					
SOFA	7.01 (3.61)	5.94 (3.19)	6.64 (3.19)	8.46 (3.91)	<0.001
Sepsis (n)	1260 (73.9)	341 (59.9)	428 (75.4)	491 (86.6)	<0.001
SAPS II	44.9 (14.1)	41.85 (12.40)	43.53 (12.69)	49.22 (15.78)	<0.001
Dialysis active (n)	1685 (98.9)	566 (99.5)	562 (98.9)	557 (98.2)	0.138
Vasopressor (n)	1200 (70.4)	371 (65.2)	386 (68.0)	443 (78.1)	<0.001
First day of ventilation parameters					
Tidal volume (mL)	465.00 (85.40)	435.90 (85.10)	470.27 (78.23)	488.92 (84.27)	<0.001
PIP (cmH2O)	22.90 (5.69)	18.51 (3.49)	22.36 (3.42)	27.93 (5.34)	<0.001
PEEP (cmH2O)	6.76 (2.72)	5.28 (1.02)	6.15 (1.73)	8.84 (3.36)	<0.001
RR (beats/min)	19.40 (4.27)	16.83 (3.06)	18.79 (3.18)	22.55 (4.29)	<0.001
PP (cmH2O)	18.60 (4.39)	15.83 (3.13)	18.07 (3.28)	21.77 (4.41)	<0.001
MP (J/min)	15.20 (7.03)	9.19 (1.66)	13.69 (1.30)	22.72 (7.01)	<0.001
Outcome (n)	372 (21.8)	100 (17.6)	104 (18.3)	168 (29.6)	<0.001

Notes: [a]Mechanical power (J/min): T1 (1.20–11.49), T2 (11.49–16.17), T3 (16.17–98.65).

Abbreviations: HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean blood pressure; RR, respiratory rate; pH, acidity; SpO_2, pulse oxygen saturation; PO_2, partial pressure of oxygen; PCO_2, arterial carbon dioxide pressure; TCO_2, total carbon dioxide; BC, bicarbonate chemistry; BUN, blood urea nitrogen; INR, international normalized ratio; PT, prothrombin time; APTT, activated partial thromboplastin time; WBC, white blood cell; RBC, red blood cell; RDW, red blood cell distribution width; HGB, hemoglobin; CHF, congestive heart failure; SOFA, sequential organ failure assessment; SAPS II, simplified acute physiology score II; PIP, peak inspiratory pressure; PEEP, positive end-expiratory pressure; PP, plateau pressure; MP, mechanical power; Outcome, death.

variables showed changes: age, SpO_2, pH, PO_2, bicarbonate, and calcium levels decreased, while DBP, HR, temperature, glucose, PCO_2, BUN, creatinine, potassium, INR, PT, WBC, RBC, platelet count, and HGB levels increased. Additionally, there was increased utilization of vasopressors and a higher incidence of sepsis. Table 2 lists the baseline

Table 2 Baseline Characteristics of the Survivors and Non-Survivors Groups

Variables	Overall (N=1704)	Survivor (N=1332)	Non-Survivor (N=372)	*P* Value
Age (years)	70.70 (10.90)	69.99 (10.55)	73.23 (11.71)	<0.001
Gender: male (n)	970 (56.9)	771 (57.9)	199 (53.5)	0.147
Race (n)				<0.001
White	1156 (67.8)	947 (71.1)	209 (56.2)	
Non white	548 (32.2)	385 (28.9)	163 (43.8)	
Vitals				
SBP (mmHg)	121.00 (25.10)	120.91 (24.08)	121.47 (28.62)	0.707
DBP (mmHg)	65.50 (18.20)	64.91 (17.64)	67.41 (19.91)	0.019
MBP (mmHg)	81.50 (18.20)	81.32 (17.44)	82.04 (20.52)	0.496
HR (beats/min)	86.90 (19.40)	85.49 (18.49)	91.76 (21.82)	<0.001
Temperature (°C)	36.60 (0.92)	36.56 (0.90)	36.54 (0.98)	0.763
SpO_2 (%)	97.30 (4.53)	97.53 (4.17)	96.36 (5.53)	<0.001
Laboratory events				
Glucose (mg/dL)	156.00 (67.70)	152.20 (62.39)	167.32 (83.07)	<0.001
pH	7.34 (0.11)	7.35 (0.10)	7.30 (0.13)	<0.001
PO_2 (mmHg)	195.00 (141.00)	210.11 (144.81)	140.90 (111.64)	<0.001
PCO_2 (mmHg)	49.40 (16.30)	48.86 (15.73)	51.12 (17.95)	0.018
TCO_2 (mmol/L)	27.10 (6.38)	27.52 (6.13)	25.67 (7.01)	<0.001
BC (mmol/L)	24.20 (5.36)	24.52 (5.14)	22.89 (5.93)	<0.001
BUN (mg/dL)	28.30 (19.90)	26.17 (18.71)	36.00 (22.21)	<0.001
Calcium (mg/dL)	8.23 (0.86)	8.25 (0.83)	8.14 (0.97)	0.031
Creatinine (mg/dL)	1.41 (1.28)	1.32 (1.17)	1.73 (1.55)	<0.001
Sodium (mEq/L)	139.00 (4.87)	138.88 (4.57)	138.64 (5.81)	0.402
Potassium (mEq/L)	4.38 (0.77)	4.37 (0.74)	4.42 (0.86)	0.301
INR	1.50 (0.87)	1.43 (0.66)	1.75 (1.34)	<0.001
PT (s)	16.20 (8.87)	15.57 (6.84)	18.60 (13.65)	<0.001
APTT (s)	39.70 (25.90)	38.92 (25.30)	42.53 (27.98)	0.018
WBC (10^9/L)	13.50 (9.71)	13.04 (8.86)	15.12 (12.17)	<0.001
RBC (10^9/L)	3.55 (0.77)	3.54 (0.76)	3.59 (0.82)	0.245
RDW (%)	15.20 (2.20)	15.04 (2.11)	15.91 (2.38)	<0.001
Platelet (10^9/L)	202.00 (98.90)	200.00 (93.71)	211.06 (115.22)	0.056
HGB (g/L)	10.60 (2.26)	10.58 (2.24)	10.67 (2.34)	0.490
Comorbidities				
Myocardial infarct (n)	448 (26.3)	341 (25.6)	107 (28.8)	0.247
CHF (n)	724 (42.5)	557 (41.8)	167 (44.9)	0.316
Diabetes (n)	617 (36.2)	481 (36.1)	136 (36.6)	0.922
Renal disease (n)	423 (24.8)	318 (23.9)	105 (28.2)	0.099
Malignant cancer (n)	175 (10.3)	112 (8.4)	63 (16.9)	<0.001
Severe liver disease (n)	69 (4.05)	39 (2.9)	30 (8.1)	<0.001
Scores				
SOFA	7.01 (3.61)	6.42 (3.25)	9.13 (4.00)	<0.001
Sepsis (n)	1260 (73.9)	936 (70.3)	324 (87.1)	<0.001
SAPS II	44.90 (14.10)	42.21 (12.65)	54.34 (14.75)	<0.001
Dialysis active (n)	1685 (98.9)	1319 (99.0)	366 (98.4)	0.450
Vasopressor (n)	1200 (70.4)	898 (67.4)	302 (81.2)	<0.001
First day of ventilation parameters				
Tidal volume (mL)	465.00 (85.40)	470.98 (85.43)	443.57 (81.95)	<0.001
PIP (cmH2O)	22.90 (5.69)	22.44 (5.33)	24.68 (6.54)	<0.001
PEEP (cmH2O)	6.76 (2.72)	6.56 (2.56)	7.45 (3.12)	<0.001
RR (beats/min)	19.40 (4.27)	18.87 (4.00)	21.24 (4.68)	<0.001
PP (cmH2O)	18.60 (4.39)	18.20 (4.12)	19.83 (5.06)	<0.001
MP (J/min)	15.20 (7.03)	14.57 (6.26)	17.43 (8.95)	<0.001

Abbreviations: HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean blood pressure; RR, respiratory rate; pH, acidity; SpO_2, pulse oxygen saturation; PO_2, partial pressure of oxygen; PCO_2, arterial carbon dioxide pressure; TCO_2, total carbon dioxide; BC, bicarbonate chemistry; BUN, blood urea nitrogen; INR, international normalized ratio; PT, prothrombin time; APTT, activated partial thromboplastin time; WBC, white blood cell; RBC, red blood cell; RDW, red blood cell distribution width; HGB, hemoglobin; CHF, congestive heart failure; SOFA, sequential organ failure assessment; SAPS II, simplified acute physiology score II; PIP, peak inspiratory pressure; PEEP, positive end-expiratory pressure; PP, plateau pressure; MP, mechanical power.

characteristics of the survival and non-survival groups. We observed that MP was significantly higher in the non-survival group (17.43 (8.95) vs 14.57 (6.26), P<0.001). Non-surviving ventilated COPD patients were older (P<0.001) and had lower SpO_2, while higher DBP, HR, SAPS II, and SOFA scores when compared to the 28-day survival group. In the non-survival group, dialysis and vasopressors were used in 98.4% and 81.2% of cases, respectively, and 87.1% of patients presented with sepsis. However, only 8.1% of non-surviving patients had concurrent severe liver disease, while 16.9% had malignant cancer. Laboratory indicators revealed that the non-survival group exhibited lower levels of pH, PO_2, TCO_2, bicarbonate, and calcium compared to the survival group. Conversely, glucose, BUN, creatinine, INR, PT, APTT, WBC, RDW, and HGB were all significantly higher in the non-survival group (P<0.05) than in the survival group. There were no discernible differences between the two groups for the remaining factors (P>0.05).

Cox Proportional Hazards Models and Restricted Cubic Spline Regression Models

Three distinct Cox regression models were constructed and shown in Table 3 to assess the impact of MP on the 28-day all-cause mortality rate among COPD patients undergoing invasive ventilation. Based on the Cox regression analysis, MP was positively associated with the 28-day all-cause mortality risk to the Model 1 [HR (95% CI) 1.04 (1.03–1.05), p<0.001]. Using the T1 group as the reference, HRs for T2 and T3 groups in Model 1 were [HR (95% CI) 1.04 (0.79–1.37), p = 0.758] and [HR (95% CI) 1.84 (1.43–2.35), p<0.001]. After adjusting for age, gender, and race in Model 2, higher MP values were associated with an increased risk of 28-day mortality [HR (95% CI) 1.05 (1.04–1.06), p<0.001]. In Model 3, which adjusted for covariates including age, sex, race, SBP, DBP, HR, SpO_2, glucose, PO_2, bicarbonate, BUN, calcium, creatinine, potassium, APTT, WBC, RDW, platelet count, HGB, myocardial infarction, CHF, renal disease, malignant cancer, severe liver disease, SOFA score, sepsis criteria, SAPS II score, and vasopressor use, a higher MP value was associated with an increased risk of 28-day all-cause mortality in the T3 group [HR (95% CI) 1.33 (1.01–1.75), p = 0.045], while the association was not statistically significant in the T2 group [HR (95% CI) 0.97 (0.74–1.29), p = 0.856]. The linear trend tests conducted on 28-day mortality revealed significant outcomes in all three models, with p for trend values of <0.001 in the Model 1 and Model 2, and 0.022 in Model 3. Restricted cubic spline regression models indicated a linear rise in the risk of 28-day mortality as MP increased (P for non-linearity = 0.967) (Figure 2). The results suggest that MP may be a potential indicator of 28-day all-cause mortality among COPD patients undergoing invasive ventilation.

ROC Curve Analysis and Kaplan–Meier Curve

Figure 3 shows ROC curves for the MP for forecasting 28-day all-cause mortality for COPD patients undergoing invasive ventilation. The AUC for MP was 0.602, suggesting a modest ability to predict 28-day all-cause mortality. This study simultaneously gained the best cut-off value of 17.38 J/min for MP, which had a sensitivity of 41.6% and a specificity of 76.12%. COPD patients undergoing invasive mechanical ventilation were divided into high MP group (MP ≥17.38 J/min, n = 473) and low MP group (MP <17.38 J/min, n = 1231) according to the cut-off value. The 28-day

Table 3 Cox Proportional Hazard Ratios (HR) for 28-Day All-Cause Mortality

	Model 1 hR (95% CI)	P Value	Model 2 hR (95% CI)	P Value	Model 3 hR (95% CI)	P Value
MP Continuous variable per unit	1.04 [1.03, 1.05]	<0.001	1.05 [1.04, 1.06]	<0.001	1.03 [1.01, 1.04]	<0.001
MP						
T1 (N=569)	1(Ref)		1(Ref)		1(Ref)	
T2 (N=568)	1.04 [0.79, 1.37]	0.758	1.13 [0.85, 1.48]	0.425	0.97 [0.74, 1.29]	0.856
T3 (N=567)	1.84 [1.43, 2.35]	<0.001	2.19 [1.71, 2.83]	<0.001	1.33 [1.01, 1.75]	0.045
P for trend	<0.001		<0.001		0.022	

Notes: MP (J/min): T1 (1.20–11.49), T2 (11.49–16.17), T3 (16.17–98.65). Model 1 was unadjusted; Model 2 was adjusted for age, sex, and race; Model 3 was adjusted for age, sex, race, systolic blood pressure, heart rate, pulse oxygen saturation, diastolic blood pressure, glucose, partial pressure of oxygen, bicarbonate, blood urea nitrogen, calcium, creatinine, potassium, activated partial thromboplastin time, white blood cell count, platelet count, red cell distribution width, myocardial infarction, hemoglobin, congestive heart failure, malignant cancer, renal disease, severe liver disease, sequential organ failure assessment score, sepsis criteria, simplified acute physiology score II score, and vasopressor use.

Abbreviations: HR, hazard ratio; CI, confidence interval; Ref, reference; MP, mechanical power.

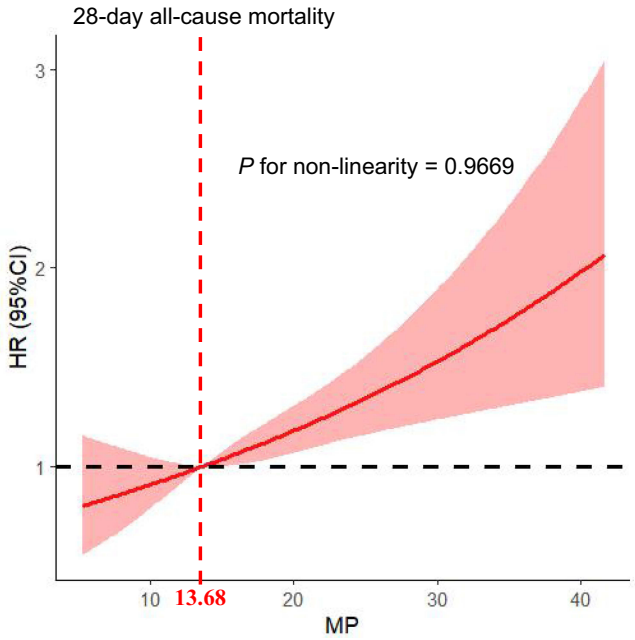

Figure 2 Restricted cubic spline regression analysis of mechanical power with 28-day all-cause mortality.
Notes: Heavy central lines represent the estimated adjusted hazard ratios, with shaded ribbons denoting 95% confidence intervals. The horizontal dotted lines represent the hazard ratio of 1.0. MP of 13.68 J/min was selected as the reference level represented by the vertical dotted lines. The p-value for non-linearity is 0.9669, suggesting a linear relationship. When MP is below 13.68 J/min, the 95% CI includes the HR = 1.0 line, indicating that the positive association between MP and 28-day all-cause mortality is not statistically significant in this range. Conversely, when MP exceeds 13.68 J/min, the 95% CI remains above the HR = 1.0 line, demonstrating a statistically significant positive association between MP and 28-day all-cause mortality.
Abbreviations: CI, confidence interval; HR, hazard ratio; MP, mechanical power.

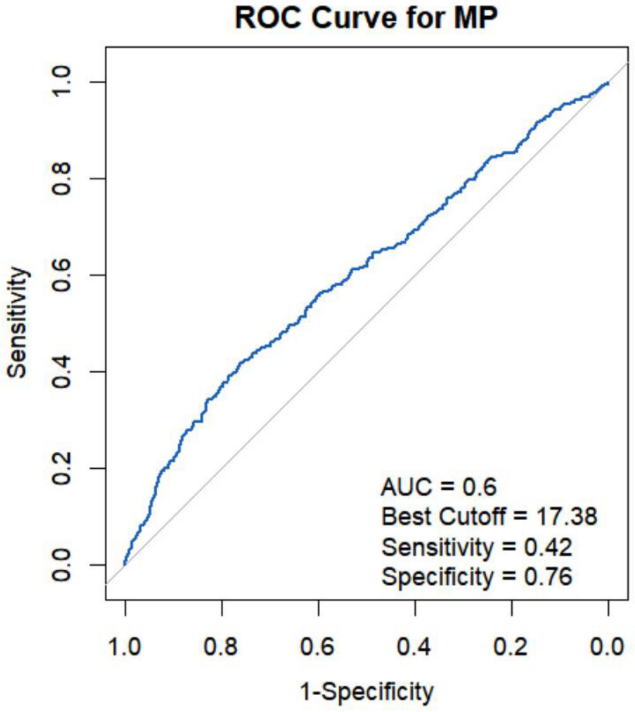

Figure 3 Receiver operating characteristic curve for mechanical power.
Abbreviations: AUC, area under the curve; ROC, receiver operating characteristic.

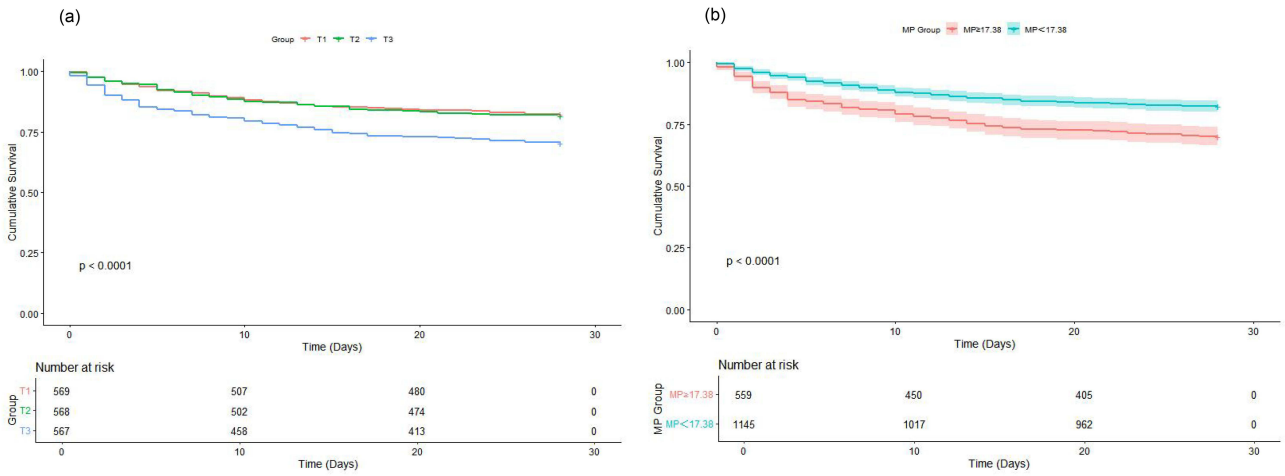

Figure 4 Kaplan–Meier survival analysis curves for all-cause mortality according to groups at 28 days. (**a**) Kaplan–Meier survival analysis curves for all-cause mortality according to the tertiles of MP; (**b**) Kaplan–Meier survival analysis curves for all-cause mortality according to the optimal cut-off value of MP.
Notes: MP tertiles: T1 (1.20–11.49), T2 (11.49–16.17), T3 (16.17–98.65).

survival rates for patients in the T1 and T2 groups were considerably greater than those in the T3 group (p<0.0001), according to the Kaplan-Meier survival analysis (Figure 4a). Figure 4b revealed that patients in the high MP (MP ≥17.38 J/min) group had a significantly higher mortality rate than those in the low MP (MP <17.38 J/min) group (P<0.0001). Figure 5 examines the stability of the relationship between MP and 28-day all-cause mortality across various subgroups among COPD patients undergoing invasive mechanical ventilation.

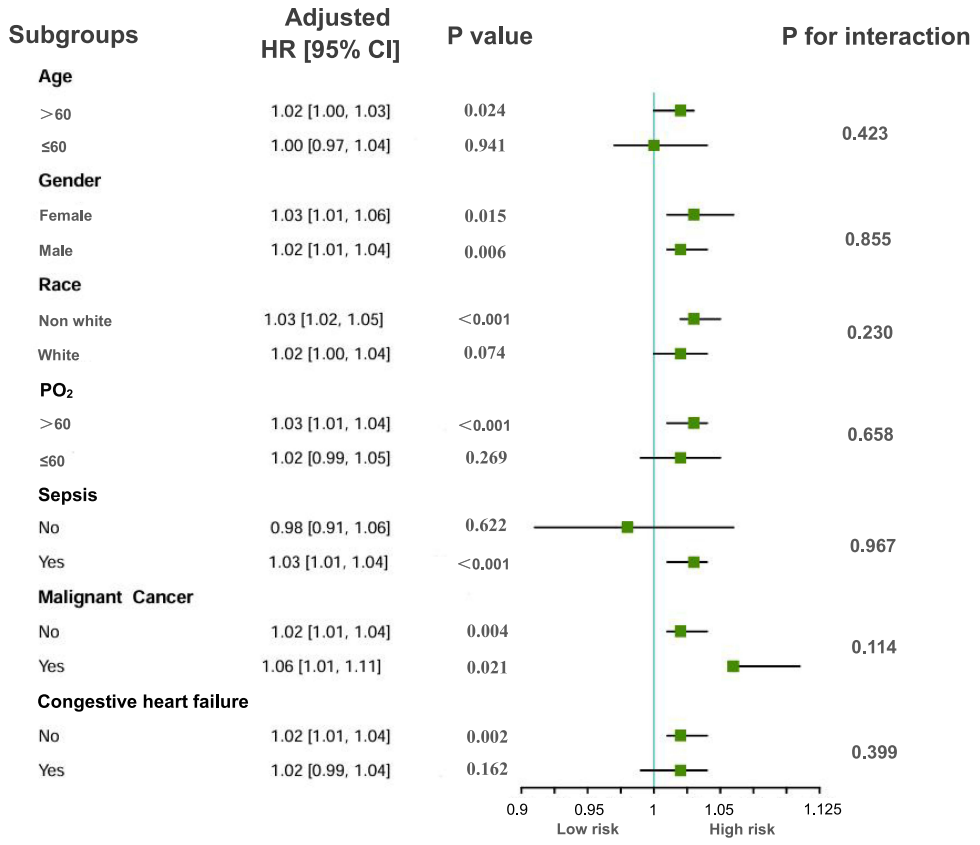

Figure 5 Forest plots of hazard ratios (HRs) for the 28 day all-cause mortality in different subgroups.
Abbreviations: PO_2, partial pressure of oxygen; CHF, congestive heart failure; CI, confidence interval.

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Subgroup Analysis

Upon stratified analysis considering factors such as age, gender, race, sepsis, PO_2, malignant cancer, and congestive heart failure, the forest plot (Figure 5) revealed no significant interaction between MP and subgroup (P for interaction: 0.114–0.967), suggesting that MP may be a potential indicator of 28-day all-cause mortality.

Discussion

In this study, we explore the association between MP and 28-day all-cause mortality among COPD patients undergoing invasive ventilation, using data from the MIMIC-IV database. Our research demonstrates that higher MP values are significantly associated with an increased risk of 28-day mortality in this cohort. Importantly, the association persists even after controlling for various confounding factors, indicating that MP may serve as a potential indicator of disease severity in COPD patients undergoing invasive mechanical ventilation.

Moreover, our analysis identified a cut-off value for high MP at 17.38 J/min, which provides a potentially valuable metric for assessing the severity of COPD patients undergoing invasive ventilation. However, we recognize that the sensitivity and specificity of this threshold are not perfect, as indicated by our results. Future studies are needed to refine and validate this threshold across diverse cohorts of mechanically ventilated COPD patients. This value may be a reference point for evaluating the severity of COPD patients undergoing invasive ventilation. By integrating MP thresholds into clinical practice, we may improve the identification of high-risk individuals who require intensified monitoring. However, the clinical utility of MP should be considered in conjunction with other parameters of mechanical ventilation to ensure that ventilatory support is neither excessive nor insufficient. Although the exact strategies to lower mortality based on MP are unclear, it may serve as an important parameter for risk stratification and guide clinicians in providing more personalized care.

Currently, MP has shown promise in predicting mortality across various diseases contexts, including ARDS. The findings[17] indicated that MP was independently linked to the ICU mortality among patients with comparable ARDS severity. Sarah Wahlster's research[18] revealed that in the initial stages of mechanical ventilation, the association between MP and hospital mortality was at its strongest. Furthermore, the findings from Huangpin Wu's team[19] revealed that MP was a significant factor linked to 28-day mortality in critically ill pneumonia patients requiring ventilation. A retrospective cohort study[20] demonstrated that the 24-hour variation in MP was an independent risk factor for ICU mortality in patients with acute respiratory failure after adjusting for confounding factors. Xiaofeng Jiang's study[21] involved sustained acute brain injury participant who needed invasive ventilation. The findings indicated that increased MP was linked to higher mortality rates in the ICU. However, given that COPD has unique pathological and respiratory mechanical characteristics, it remains uncertain whether there is a similar relationship between MP and mortality rates among COPD patients undergoing invasive ventilation. Consistent with our research findings, elevated MP may serve as a marker of the severity of underlying lung disease and respiratory dysfunction, potentially guiding clinical decision-making to prioritize intensive monitoring or more aggressive therapeutic approaches for high-risk patients. However, COPD is distinct from ARDS in its pathophysiology, and patients with COPD may tolerate higher levels of mechanical ventilation. Studies have shown that chronic hypercapnic COPD patients often experience improvements in hypercapnia and quality of life with appropriate mechanical ventilation, and long-term survival may be enhanced with optimal ventilatory support.[22,23]

The original MP calculation involves three important components.[24] The first key component is the elastance of the respiratory system, which relates to the energy associated with VT and ΔP. The second crucial component is airway resistance, which concerns the energy related to gas flow. The third component represents the energy required to overcome the surface tension caused by PEEP. Additionally, a simplified power equation has been proposed, which demonstrates a strong association with the original equation, while being more straightforward and not requiring pressure-volume curves. When calculated in patients without ARDS, the average difference was only 0.196 J/min.[25] This simplified power equation is used in this study.

The energy delivered to the respiratory system generates mechanical stress and strain during mechanical ventilation. This load is considered the intensity of mechanical ventilation and can be quantified as a value of MP.[25] In COPD

patients, higher MP values may be associated with more severe disease and a greater degree of ventilatory support required. However, MP itself does not directly cause lung injury or death. Rather, it reflects the intensity of mechanical ventilation and is associated with more severe respiratory dysfunction.[26,27] High MP values may signal the need for greater ventilatory support and potentially indicate worse outcomes in severe COPD cases, but it must be interpreted in the broader context of the patient's overall ventilatory status and the mechanical load being applied. In our study, we identified a critical threshold of 17.38 J/min for high MP in COPD patients undergoing invasive mechanical ventilation, based on ROC curve analysis. While statistically significant, this threshold's predictive value requires further validation.

Numerous studies have indicated that various blood biomarkers are associated with mortality in COPD patients. A relevant research found that serum anion gap is positively associated with all-cause mortality among COPD patients.[28] The red cell distribution width-to-platelet ratio is associated with the in-hospital mortality rate of AECOPD patients.[29] Furthermore, lower serum albumin levels are inversely associated with higher in-hospital mortality rates in COPD patients in the ICU.[30] Elevated blood urea nitrogen levels are associated with an increased risk of mortality in AECOPD patients.[31] However, despite the association between blood marker and mortality among COPD patients, there is currently no dedicated scoring system to evaluate the severity and risk stratification of COPD in patients undergoing mechanical ventilation. Developing such a system, which integrates MP and relevant biomarkers, would enhance risk stratification and improve patient management.

While our study found an association between high MP and increased mortality in COPD patients undergoing invasive ventilation, several limitations should be considered. First, our investigation is a retrospective cohort study reliant on data from the MIMIC-IV database. While we found a relationship between MP and mortality in this population, causality cannot be established. To confirm these findings, future multicenter, prospective, randomized double-blind controlled trials are necessary for verification. Second, despite utilizing multivariable Cox regression analysis and subgroup analyses, residual confounding factors may still affect clinical outcomes, potentially limiting the applicability of our results. When selecting patients from the MIMIC-IV database, we excluded COPD patients undergoing invasive mechanical ventilation due to missing data. This missing information could potentially impact the conclusions of the study. Although we included COPD patients undergoing invasive mechanical ventilation, we were unable to differentiate the methods of artificial airway establishment, such as nasal, oral, or tracheostomy intubation techniques. Lastly, the study did not statistically evaluate the use of sedatives or neuromuscular blockers in patients, preventing us from distinguishing whether they were in a sedated or awake state during mechanical ventilation. MP may be influenced by patients' spontaneous breathing; therefore, we attempted to minimize potential confounding factors by using the average MP over the preceding 24 hours. Finally, the MIMIC-IV database lacks specific data on the severity of COPD, such as detailed information on lung function or the MMRC grade. As COPD severity is known to influence patient outcomes, the absence of this information may limit the accuracy of our conclusions regarding the direct impact of MP on mortality. We were unable to account for the varying degrees of disease severity, which could lead to potential confounding effects. More severe COPD patients may be more prone to mortality irrespective of their MP levels, and the absence of such stratifications could impact the strength and generalizability of our findings. In future prospective studies, we plan to address this limitation by incorporating a more detailed stratification of COPD stages to explore their potential impact on the findings.

Conclusions

In summary, this study emphasizes that MP is associated with 28-day all-cause mortality in COPD patients undergoing invasive ventilation. The cut-off value of 17.38 J/min may serve as a reference point for clinicians in assessing disease severity. Further studies are needed to explore whether MP could be a useful monitoring parameter in COPD patients undergoing invasive ventilation management and to determine its potential impact on patient outcomes.

Abbreviations

COPD, chronic obstructive pulmonary disease; MIMIC-IV, medical information mart for intensive Care; ICU, intensive care unit; ARDS, acute respiratory distress syndrome; ROC, receiver operating characteristic; CI, confidence intervals; HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean blood pressure; RR, respiratory rate; pH, acidity; SpO_2, pulse oxygen saturation; PO_2, partial pressure of oxygen; PCO_2, arterial carbon dioxide pressure; TCO_2, total carbon dioxide; BC, bicarbonate chemistry; BUN, blood urea nitrogen; INR, international normalized ratio;

PT, prothrombin time; APTT, activated partial thromboplastin time; WBC, white blood cell; RBC, red blood cell; RDW, red blood cell distribution width; HGB, hemoglobin; CHF, congestive heart failure; SOFA, sequential organ failure assessment; SAPS II, simplified acute physiology score II; PIP, peak inspiratory pressure; PEEP, positive end-expiratory pressure; PP, plateau pressure; MP, mechanical power; Outcome, death.

Data Sharing Statement

In this study, the data used were obtained from the MIMIC-IV database, which is an open-access database. It can be accessed on the website after applying for and passing the eligibility certification exam: https://physionet.org/content/mimiciv/2.2/.

Ethics Approval and Informed Consent

The MIMIC-IV database has received ethical approval from the institutional review boards (IRB) at Beth Israel Deaconess Medical Center and the Massachusetts Institute of Technology Institutional Review Board. Due to the database's de-identification process, which addresses ethical considerations regarding patient privacy and confidentiality, the data can be used without compromising patient confidentiality. The Ethics Committee of the Guangdong Provincial Hospital of Chinese Medicine exempted our ethical review with the acceptance number ZM2024-376.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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