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The modified effect of mechanical ventilation setting on relationship between fluid balance and hospital mortality for sepsis patients: a retrospective study

Dawei Zhou[1*], Yi Lv[1], Chao Wang[1] and Dan Li[1]

Abstract

Background Fluid supplement may be affected by ventilatory management due to physiological interaction between heart and lung. The aim of the present study was to explore the effects of ventilator strategies on the relationship of fluid balance and hospital mortality for sepsis patients.

Methods This was a retrospective cohort study included sepsis patients with invasive mechanical ventilation (MV) over 24 h from Medical Information Mart for Intensive Care (MIMIC) IV database. The accumulative fluid balance increased by 6 h intervals were calculated as fluid intake minus fluid output. The modes (assisted or controlled) and levels (high or low) of positive end-expiratory pressure (PEEP) of MV every 6 h were recorded. The modification effect for modes and levels of PEEP on the relationship of fluid balance and hospital mortality were tested by multivariable regression models, respectively.

Results A total of 4466 sepsis patients with invasive MV were included, of which hospital mortality was 26.5%. Fluid balance seemed to have U-shape relationship with hospital mortality. The majority of patients used controlled ventilation at the beginning, and switched to assisted ventilation gradually; however, the PEEP level did not change a lot during the first 24 h. The relationship between fluid balance and hospital mortality was not modified by the ventilator mode; while the PEEP level may modify the relationship.

Conclusions For sepsis patients admitted to ICU with invasive MV, the PEEP level, but not the mode of MV, appeared to modify the relationship of fluid balance and hospital mortality. The setting of mechanical ventilation may be an important consideration for fluid therapy.

Keywords Sepsis, Mechanical ventilation, Positive end-expiratory pressure, Fluid balance, Hospital mortality

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Introduction

Sepsis is life-threatening organ dysfunction due to a dysregulated host response to infection, which constitutes a substantial global health burden with high rates of morbidity and mortality [1, 2]. Fluid supplement and mechanical ventilation (MV) are ubiquitously used in intensive care unit (ICU) for sepsis patients [3–5]. Notwithstanding, both fluid supplement and mechanical ventilation are double-edged swords. Although fluid supplement is essential for expanding intravascular volume and improving perfusion pressure for sepsis patients undergoing MV [6, 7], fluid overload is associated with poor outcome both for adult and pediatric critically ill patients [8, 9]. MV could improve oxygen and carbon dioxide as well as reduce work of breathing [10]. However, it could also cause hemodynamic instability [11, 12].

Heart-lung interaction between the cardiovascular and the respiratory system may may impact the lung microvessels and have significant hemodynamic consequences [13, 14]. The setting of MV, including modes (assisted or controlled) or levels (high or low) of positive end expiratory pressure (PEEP), could change intrathoracic pressures and impact on cardiovascular physiology due to the heart-lung interplay [15, 16]. The mismatch between fluid and setting of MV could worsen the clinical conditions [15]. However, the clinical evidence of crosstalk between fluid supplement and MV setting and impact of the interaction on patient outcomes was scarce.

The aim of the study was to investigate if the association between fluid balance and hospital mortality for sepsis patients was modified by the setting of mechanical ventilation, including the modes (assisted and controlled) and levels (high and low) of PEEP for MV. The hypothesis was that the relationship of fluid balance and mortality may be different according to different setting (ventilation mode and PEEP) of mechanical ventilation.

Methods

Setting

The Medical Information Mart for Intensive Care IV (MIMIC-IV) database, which was a contemporary electronic health record (EHR) dataset covering a decade of admissions between 2008 and 2019, was used for the present study. The description of this database can be found elsewhere. Use of the MIMIC-IV database has been approved (certification number: 28795067) by the institutional review boards of Beth Israel Deaconess Medical Center (Boston, MA) and the Massachusetts Institute of Technology (Cambridge, MA). This present study was exempted from institutional review board approval due to the retrospective design, lack of direct patient intervention, and the security schema.

Study population

All patients in MIMIC-IV database admitted to ICU were included. As for those who admitted to hospital or ICU for more than once, only the first stay admitted to hospital and ICU was taken into consideration. Patients were excluded for the following reasons: (1) Not sepsis diagnosis; (2) Not received mechanical ventilation; (3) The duration of mechanical ventilation less than 24 h; (4) No ventilator setting data recorded; (5) No fluid, including fluid input and fluid output; (6) Patients with no body weight data.

Clinical variables

The demographic variables included age, sex, weigh, and height. The body mass index was calculated as the weight to be divided by the square of height. The comorbidity was depicted by Charlson comorbidity score (CCI).

Data were extracted on the following information during the first 24 h of ICU admission: arterial blood gas (the minimum and maximum pH, Pao2, Paco2, the ratio arterial oxygen partial pressure to fractional inspired oxygen, lactate, and base excess), sequential organ failure assessment (SOFA), simplified acute physiology score (SAPS) ii score, use of vasopressors, and use of continuous renal replacement therapy (CRRT). The primary outcome was hospital mortality, defined as death during the hospitalization. The hospital and ICU length of stay were defined the duration in hospital and ICU, respectively. The "Kidney Disease: Improving Global Outcomes" (KDIGO) was used to define acute kidney injury.

The setting of ventilator during the first 24 h after ICU admission was recorded every 6 h, including the mode (assisted or controlled) of mechanical ventilation, positive end expiratory pressure (PEEP), tidal volume and minute volume. Four periods of ventilator setting were generated, which were 0–6 h, 6–12 h, 12–18 h, and 18–24 h. First, the ventilation mode was divided into mode of allowing spontaneous breathing (e.g., Pressure Control Ventilation (PCV), Volume Control Ventilation (VCV), Pressure Regulated Volume Control (PRVC), Mandatory Minute Ventilation (MMV), Synchronized Intermittent Mandatory Ventilation (SIMV)) and mode of mandating spontaneous breathing (e.g., continuous positive airway pressure (CPAP), pressure support ventilation (PSV), proportional assist ventilation (PAV)). Second, patients who received allowing spontaneous breathing mode with a set RR equal to the actual RR (actual RR = set RR) were considered as controlled mode. Patients with spontaneous breathing activity were considered as assisted mode, including the mode with mandating spontaneous breathing or allowing spontaneous breathing mode and their actual RR was greater than the set RR. The algorithm was displayed in supplemental Fig. 1. The low PEEP was defined as PEEP level less than or equal to 10 cmH2O,

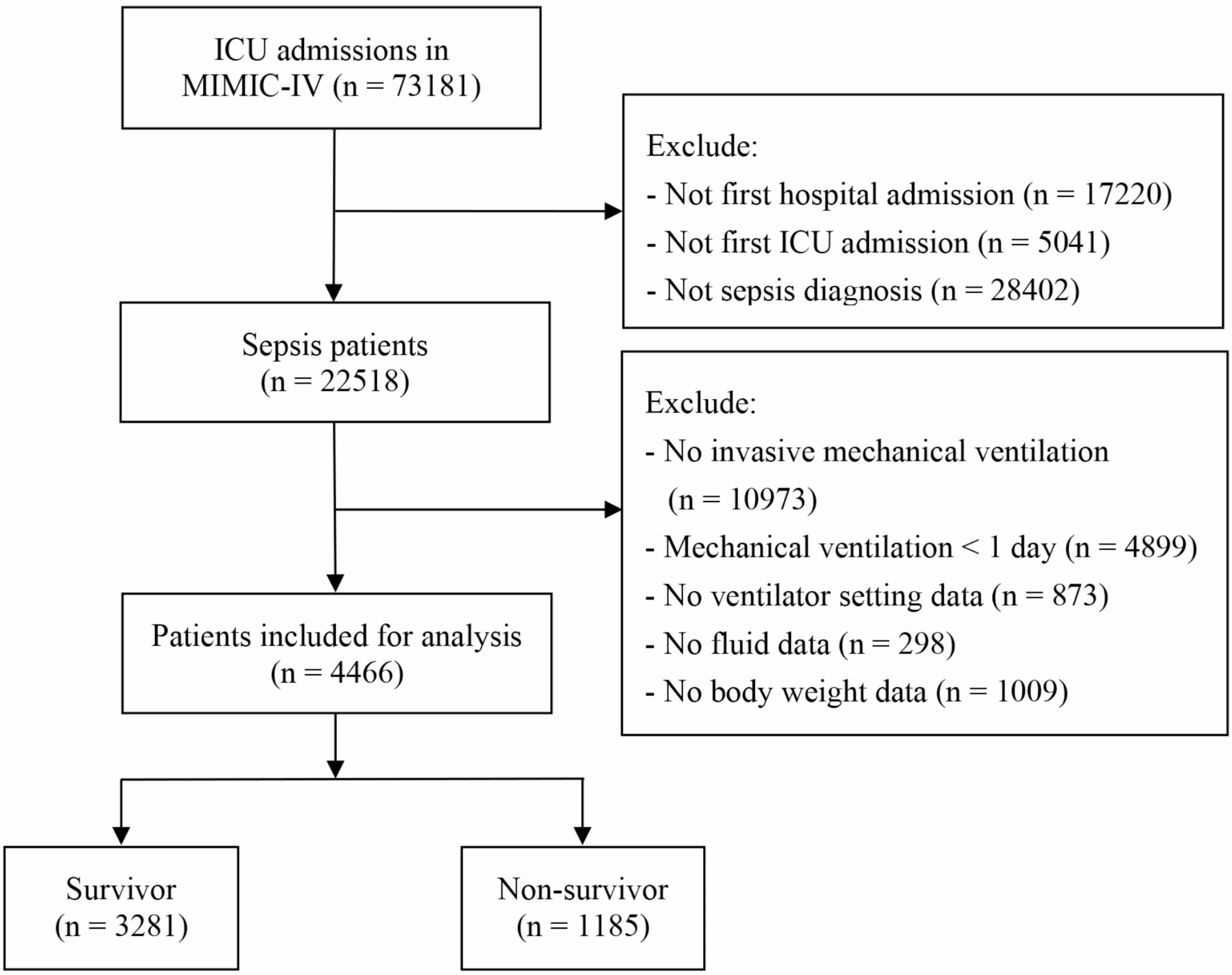

Fig. 1 Flow chart of patient selection

while the high PEEP was defined as PEEP level over 10 cmH2O based on the empirical practice for PEEP selection [17, 18].

Fluid input included intravenous fluids (crystalloid or colloid fluid), oral fluids, medications, and blood products. Fluid output included urine output, drainage fluid, and gastrointestinal fluid. The fluid balance was calculated as the difference of fluid input and output. The variables of fluid (fluid input, fluid output, and fluid balance) during the first 24 h were accumulated every 6 h. Four periods of fluid balance were generated, including the first 6 h (0–6 h), the first 12 h (0–12 h), the first 18 h (0–18 h), and the first 24 h (0–24 h), which corresponded to the periods (0–6 h, 6–12 h, 12–18 h, and 18–24 h) of ventilator setting, respectively.

Statistical analysis

The continuous variables were reported as mean and standard deviation (SD) or median and interquartile range (IQR) according to normality test, and compared with Student's t-test and Wilcoxon-rank-sum test, respectively. Categorical variables were expressed as numbers and percentages and were compared with Chi-square test or Fisher's exact test as appropriate.

The baseline characteristics and clinical parameters between survivors and non-survivors during hospitalization were compared. The Sankey diagram was used to describe the time course of mode of mechanical ventilation as well as PEEP usage. To assess the association of fluid balance with hospital mortality, multivariable logistic regression was performed for each fluid balance group. The restrictive cube spline was used to investigate the non-linear relationship between fluid balance and hospital mortality. The confounders included age, sex, Charlson comorbidity index, SOFA score, mode of mechanical ventilation, PEEP, and use of CRRT. To investigate whether mode of mechanical ventilation (assisted or controlled, and high or low PEEP) would modify the effect of fluid balance and hospital mortality, the multivariable logistic regression with restrictive cube spline

Table 1 Comparison of characteristics between survivors and non-survivors

	Total (*n* = 4466)	Survivors (*n* = 3281)	Non-survivors (*n* = 1185)	*P* value
Age (years)	65 (52, 76)	63 (51, 74)	69 (57, 80)	< 0.001
Sex				0.107
female	1877 (42)	1355 (41)	522 (44)	
male	2589 (58)	1926 (59)	663 (56)	
Weight (kg)	82 (68, 98)	83 (69, 100)	79 (67, 95)	< 0.001
Height (cm)	170 (163, 178)	170 (163, 178)	168 (160, 178)	0.003
BMI (kg/m^2)	29.0 (25.1, 34.3)	29.1 (25.1, 34. 5)	28.4 (24.7, 33.7)	0.031
Charlson comorbidity index	5 (3, 7)	5 (2, 7)	6 (4, 8)	< 0.001
Arterial blood gas for the first day				
Minimum pH value	7.29 (7.2, 7.37)	7.3 (7.22, 7.37)	7.26 (7.16, 7.36)	< 0.001
Maximum pH value	7.41 (7.37, 7.46)	7.42 (7.37, 7.46)	7.4 (7.35, 7.46)	< 0.001
Minimum Pao$_2$	86 (69, 116)	88 (71, 119)	81 (64, 108)	< 0.001
Maximum Pao$_2$	207 (137, 334)	210 (139, 338)	201 (134, 326)	0.091
Minimum Paco$_2$	34 (30, 40)	35 (30, 40)	33 (28, 38)	< 0.001
Maximum Paco$_2$	46 (40, 55)	46 (40, 55)	46 (40, 56)	0.818
Minimum P/F ratio	178 (112, 270)	182 (117, 276)	163 (101, 258)	< 0.001
Maximum P/F ratio	319 (228, 420)	320 (232, 418)	315 (210, 428)	0.092
Minimum Base Excess	-4 (-9, 0)	-3 (-8, 0)	-6 (-12, -1)	< 0.001
Maximum Base Excess	0 (-3, 2)	0 (-2, 3)	0 (-4, 2)	< 0.001
Minimum Lactate	1.5 (1, 2.2)	1.4 (1, 1.9)	1.8 (1.2, 3.15)	< 0.001
Maximum Lactate	2.5 (1.5, 4.6)	2.3 (1.4, 4)	3.4 (1.8, 6.6)	< 0.001
SOFA score	7 (5, 10)	7 (4, 10)	9 (6, 12)	< 0.001
SAPS ii score	43 (34, 55)	41 (32, 51)	51 (40, 63)	< 0.001
Acute kidney injury				< 0.001
KDIGO stage 0	406 (9)	353 (11)	53 (4)	
KDIGO stage 1	543 (12)	433 (13)	110 (9)	
KDIGO stage 2	1781 (40)	1456 (44)	325 (27)	
KDIGO stage 3	1736 (39)	1039 (32)	697 (59)	
Use of vasopressors	2220 (50)	1484 (45)	736 (62)	< 0.001
Use of CRRT	366 (8)	209 (6)	157 (13)	< 0.001
ICU length of stay (days)	7 (4, 13)	7 (5, 13)	6 (3, 11)	< 0.001
Hospital length of stay (days)	13 (8, 22)	15 (10, 24)	7 (3, 14)	< 0.001

Data are median (interquartile range) or no./total (%)

BMI body mass index, ICU intensive care unit, KDIGO Kidney Disease: Improving Global Outcomes, P/F arterial oxygen partial pressure to fractional inspired oxygen, SAPS simplified acute physiology score, SOFA sequential organ failure assessment

was used. The interaction effect were explored in the multivariable models.

The PostgreSQL (www.postgresql.org) was used to extract data. The P value less than 0.05 was considered as the statistically significant. R software (4.0.1, www.r-project.org) was used for all the statistical analyses with the packages of "tidyverse" and "rms".

Results

The MIMIC-IV database recorded 73,181 ICU admissions. After exclusion, a total of 4466 patients were included for analysis, with 3281 survivors and 1185 non-survivors (Fig. 1). The hospital mortality was 26.5%. The median age was 65 years [interquartile range (IQR), 52–76 years] and 58% was male (Table 1). The non-survivors had higher age (69 VS 63 years, $P < 0.001$) and higher CCI (6 VS 5, $P < 0.001$). The non-survivors had higher lactate ($P < 0.001$), low P/F ratio ($P < 0.001$), higher SOFA score (9 VS 7, $P < 0.001$) and SAPS ii score (51 VS 41, $P < 0.001$). There was no doubt that the non-survivors had higher percentage of acute kidney injury, use of vasopressors, and use of CRRT. However, the non-survivors had lower ICU and hospital length of stay.

During the first 6 h, the majority of patients used controlled ventilator mode (66%) and low PEEP (78%) strategy. More and more patients were changed to assisted ventilator mode, with 32% assisted ventilator mode during 0–6 h, 42% during 6–12 h, 45% during 12–18 h, and 47% during 18–24 h (Fig. 2). However, the time course of PEEP strategy was similar (Fig. 3). Compared with survivors, the non-survivors had higher percentage of controlled ventilator mode and higher PEEP strategy during periods of 12–18 h and 18–24 h (Table 2). The non-survivors had lower tidal volume ($P < 0.001$) and higher minute volume ($P < 0.001$) (Supplemental Table 1).

The fluid balance during the first 6 h, 12 h, 18 h, and 24 h were 2.5 ml/kg, 6.6 ml/kg, 8.6 ml/kg, and 9.6 ml/kg, respectively (Table 2). The non-survivors had higher fluid input, lower fluid output, and higher fluid balance during the first 6, 12, 18, and 24 h. The multivariable models showed the non-linear relationship of fluid balance and hospital mortality (Fig. 4, Supplemental Table 2). During the first 6 and 12 h, lower fluid balance were associated with higher estimated hospital mortality. However, during the first 18 and 24 h, both lower and higher fluid balance were both associated with higher estimated hospital mortality. The ventilator mode (assisted or controlled) had no modification effect on the relationship of fluid balance and hospital during all the four periods (Fig. 5, Supplemental Table 3). During the first 6 and 12 h, the higher fluid balance was associated with higher hospital mortality for low PEEP patients, but not for high PEEP patients (Fig. 6,, Supplemental Table 4). During the first 18 and 24 h, the higher fluid balance was associated with

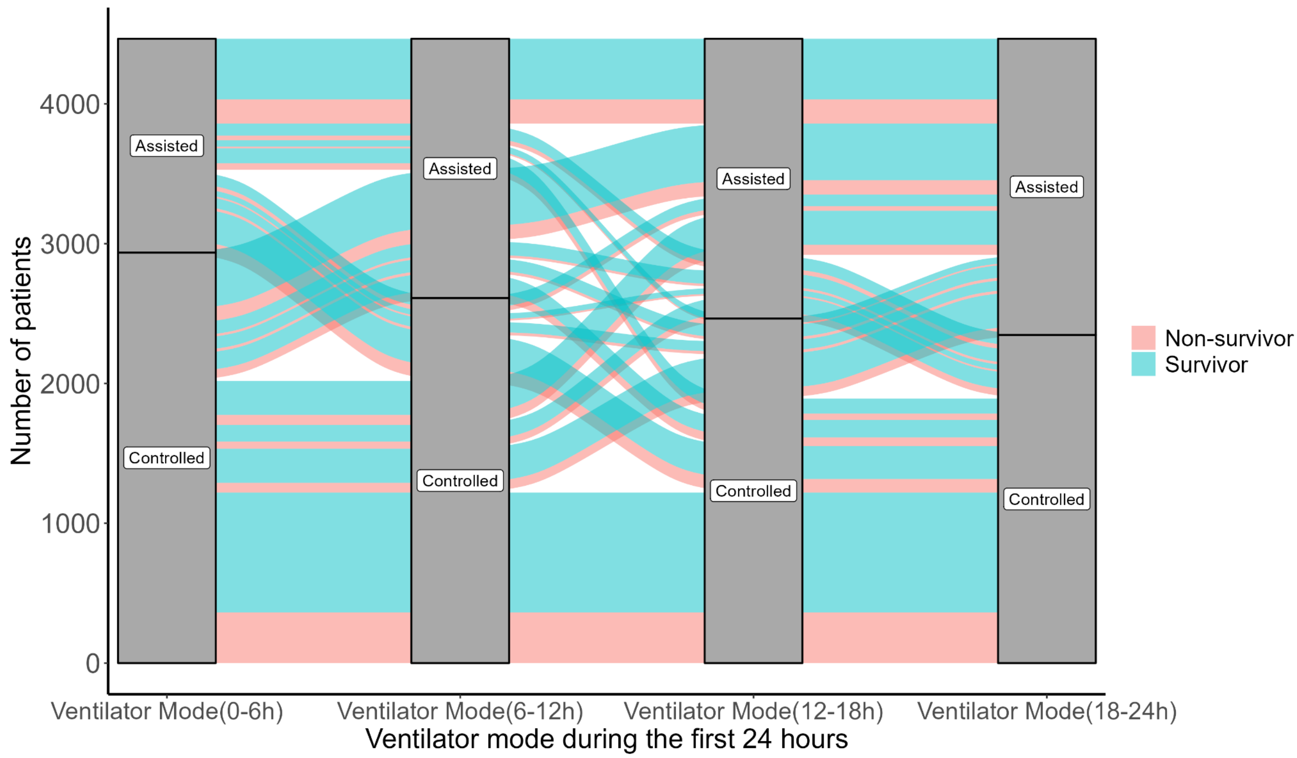

Fig. 2 The time course for mode of mechanical ventilation during the first 24 h between survivors and non-survivors

higher hospital mortality for high PEEP patients, but not for low PEEP patients (Fig. 6,, Supplemental Table 4).

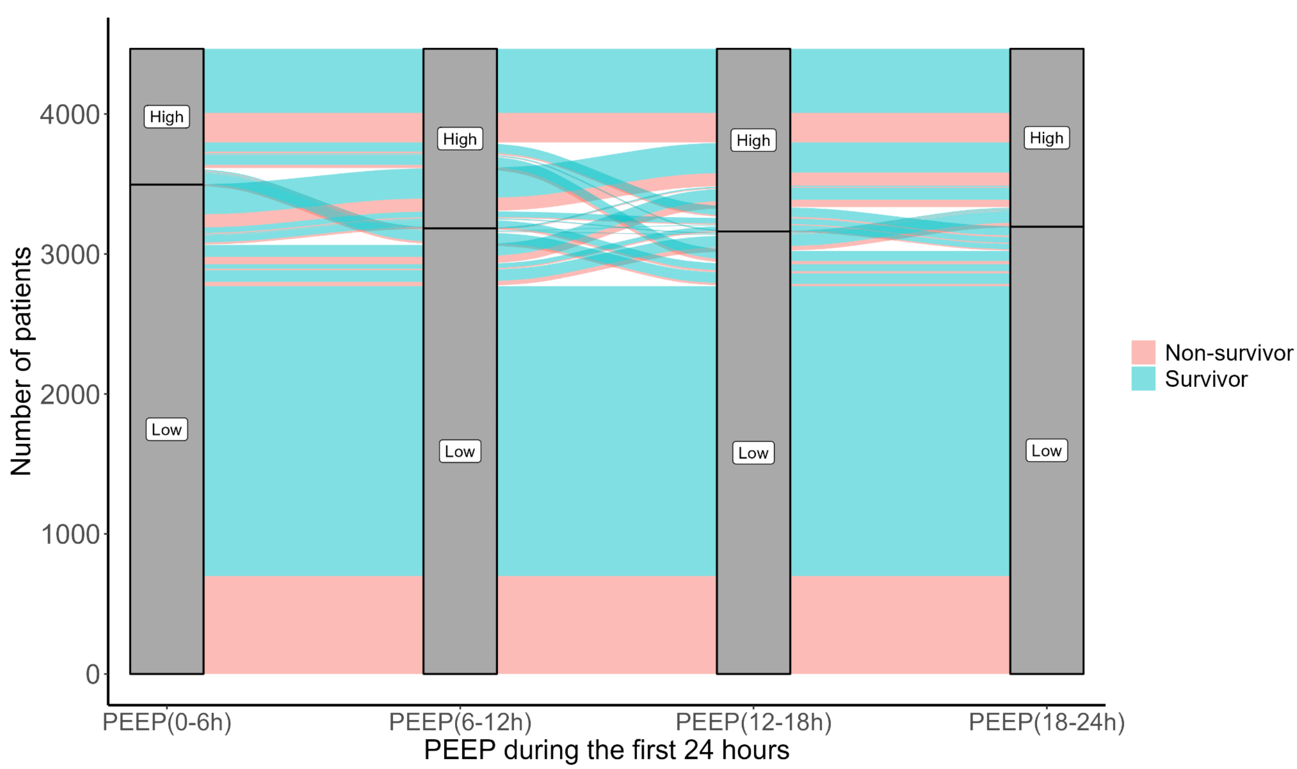

Fig. 3 The time course for PEEP of mechanical ventilation during the first 24 h between survivors and non-survivors. PEEP positive end-expiratory pressure

Table 2 Ventilator mode and fluid data between survivors and non-survivors

	Total (*n* = 4466)	Survivors (*n* = 3281)	Non-survivors (*n* = 1185)	*P* value
Ventilator mode (0–6 h)				0.143
Assisted	1530 (34)	1103 (34)	427 (36)	
Controlled	2936 (66)	2178 (66)	758 (64)	
PEEP (0–6 h)				0.214
Low PEEP	3496 (78)	2584 (79)	912 (77)	
High PEEP	970 (22)	697 (21)	273 (23)	
Ventilator mode (6–12 h)				0.089
Assisted	1855 (42)	1388 (42)	467 (39)	
Controlled	2611 (58)	1893 (58)	718 (61)	
PEEP (6–12 h)				0.043
Low PEEP	3183 (71)	2366 (72)	817 (69)	
High PEEP	1283 (29)	915 (28)	368 (31)	
Ventilator mode (12–18 h)				0.016
Assisted	2001 (45)	1506 (46)	495 (42)	
Controlled	2465 (55)	1775 (54)	690 (58)	
PEEP (12–18 h)				< 0.001
Low PEEP	3161 (71)	2369 (72)	792 (67)	
High PEEP	1305 (29)	912 (28)	393 (33)	
Ventilator mode (18–24 h)				< 0.001
Assisted	2119 (47)	1616 (49)	503 (42)	
Controlled	2347 (53)	1665 (51)	682 (58)	
PEEP (18–24 h)				< 0.001
Low PEEP	3195 (72)	2412 (74)	783 (66)	
High PEEP	1271 (28)	869 (26)	402 (34)	
Fluid in during the first 6 h (ml/kg)	8.0 (2.6, 20.5)	7.7 (2.6, 19.6)	9.4 (2.8, 22.9)	0.004
Fluid in during the first 12 h (ml/kg)	17.7 (7. 6, 37.4)	17.2 (7.4, 36.6)	19.5 (8.4, 40.9)	0.002
Fluid in during the first 18 h (ml/kg)	25.1 (11.8, 48.7)	24.2 (11.5, 46.4)	27.0 (12.8, 55.4)	< 0.001
Fluid in during the first 24 h (ml/kg)	31.5 (16.0, 57.9)	30.2 (15.6, 55.5)	34.7 (17.3, 69.1)	< 0.001
Fluid out during the first 6 h (ml/kg)	5.0 (2.2, 9.7)	5.3 (2.5, 10.0)	4.2 (1.3, 8.6)	< 0.001
Fluid out during the first 12 h (ml/kg)	10.7 (5.7, 18.4)	11.4 (6.4, 19.0)	9.0 (4.0, 15.9)	< 0.001
Fluid out during the first 18 h (ml/kg)	16.0 (9.1, 26.4)	17.0 (10.1, 27.4)	13.2 (6.3, 23.6)	< 0.001
Fluid out during the first 24 h (ml/kg)	21.8 (12.5, 34.2)	23.1 (14.0, 35.8)	17.5 (8.6, 30.4)	< 0.001
Fluid balance during the first 6 h (ml/kg)	2.5 (-3.0, 14.3)	2.0 (-3.2, 13.1)	4.0 (-2, 17.3)	< 0.001
Fluid balance during the first 12 h (ml/kg)	6.6 (-4.7, 24.8)	5.6 (-5.3, 23.1)	8.9 (-2.7, 30.2)	< 0.001
Fluid balance during the first 18 h (ml/kg)	8.6 (-6.7, 31.1)	6.8 (-7.7, 27.9)	13.2 (-3.2, 39.4)	< 0.001
Fluid balance during the first 24 h (ml/kg)	9.6 (-8.5, 34.5)	7.5 (-10, 31.2)	16.4 (-4.5, 46.9)	< 0.001

Data are median (interquartile range) or no./total (%)

PEEP positive end expiratory pressure

Discussion

The major findings of the study were summarized as: (1) the majority of patients used controlled ventilation at the beginning, and switched to assisted ventilation as times went on; however, the PEEP level was almost the same during the first 24 h after admission. (2) cumulative

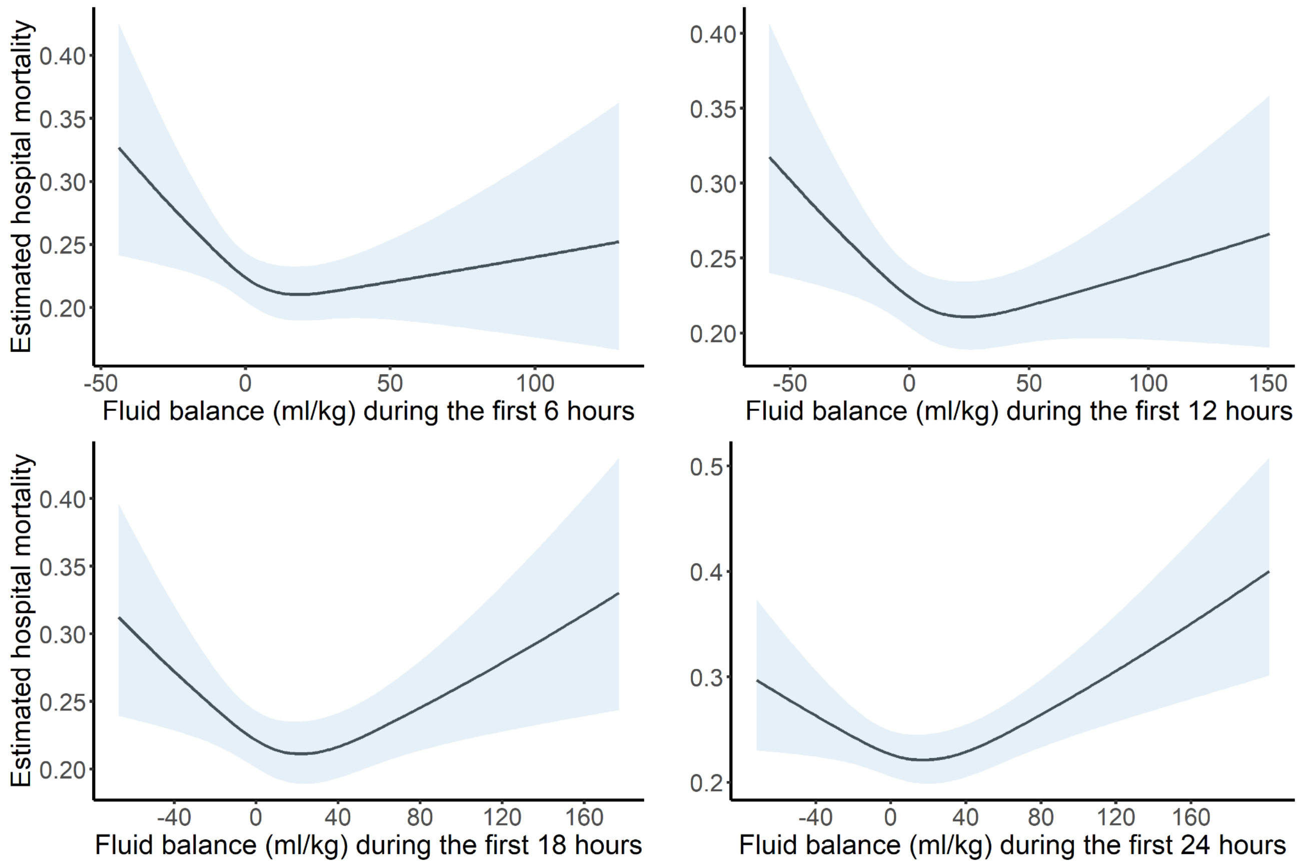

Fig. 4 The relationship between fluid balance during the first 6 h, 12 h, 18 h, and 24 h and hospital mortality, respectively. Multivariable regression models were used. The confounders included age, sex, Charlson comorbidity index, SOFA score, mode of mechanical ventilation, PEEP, and use of CRRT (Supplemental Table 2). CRRT, continuous renal replacement treatment, PEEP positive end-expiratory pressure, SOFA, sequential organ failure assessment

negative fluid balance was associated with hospital mortality, while the cumulative positive fluid balance was associated with mortality only during the first 18 and 24 h. (3) the relationship between fluid balance and hospital mortality was not modified by the ventilator mode. (4) cumulative positive fluid balance was associated with mortality for patients with high PEEP but not low PEEP during the first 18 and 24 h; while cumulative negative fluid balance was associated with mortality for patients with low PEEP but not high PEEP during the first 6 and 12 h.

Assisted mode of MV is common in patients with ARDS during the first 48 h [19], which has been shown to improve gas exchange, hemodynamics, peripheral muscle and diaphragm function and is associated with reduced sedation [20–22]. However, assisted mode may cause or worsen acute lung injury if spontaneous effort is vigorous, which was also called patient self-inflicted lung injury (P-SILI) [23, 24]. The proportion of assisted mode was slightly lower than "LUNG SAFE" study, which may be attributed to short time (24 h in the present study). Compared with period of 0–6 h, the proportion of assisted mode increased during periods of the 6–12 h, 12–18 h, and 18–24 h. At the beginning, patients with controlled or assisted ventilation had similar mortality. Further, patients with assisted mode had lower hospital mortality as time went on. The proportion of patients with high PEEP level was relatively low. In "LUNG SAFE" study, 82.6% received a PEEP of less than 12 cmH2O, which was comparable with the present study [25]. There was a small increase for proportion of high PEEP level during the 6–12 h period compared with 0–6 h period. However, the proportion of high PEEP level was similar during the rest time. Similarly, the PEEP level was not associated with hospital mortality at the beginning; however, patients with low PEEP level had lower mortality as time went on, which may be a reflection of disease improvement.

The U-shaped relationship was found between fluid balance and hospital mortality in the present study, which was in line with the previous studies [26–28]. As we all known, four phases were suggested for shock treatment, including salvage, optimization, stabilization, and de-escalation phases [29]. In the salvage phase of shock resuscitation, fluid resuscitation (within the first 3 h) was associated with a greater number of survivors for severe

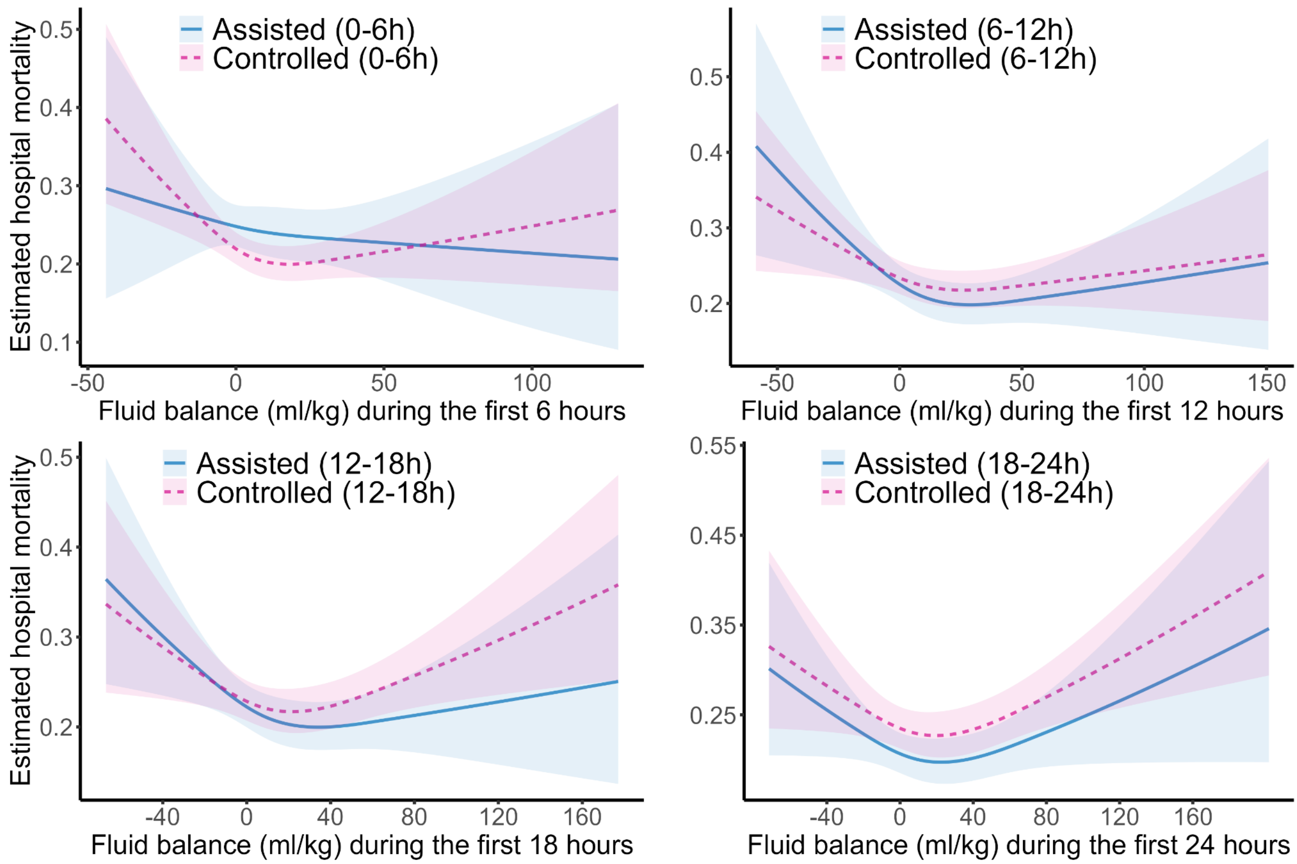

Fig. 5 The relationship between fluid balance during the first 6 h, 12 h, 18 h, and 24 h and hospital mortality for patients with assisted and controlled mechanical ventilation, respectively. Multivariable regression models were used and interaction effect of ventilation mode on relationship between fluid balance and hospital mortality were separately explored. The confounders included age, sex, Charlson comorbidity index, SOFA score, mode of mechanical ventilation, PEEP, and use of CRRT (Supplemental Table 3). CRRT, continuous renal replacement treatment, PEEP positive end-expiratory pressure, SOFA, sequential organ failure assessment

sepsis and septic shock patients [30]. However, during the fluid de-escalation phase of sepsis management, daily negative fluid balance was associated with lower mortality [31]. In the first 6 h, negative fluid balance was associated higher mortality; while in the first 24 h, higher positive fluid balance had higher mortality. Although the phases of treatment in the present study were not recorded, the trajectory of relationship of fluid balance and outcome was similar. The window of salvage phase is quite short. More attention should be paid to fluid overload after the salvage phase [32].

The mode of assisted ventilation can allow patients breathing spontaneously. However, vigorous inspiratory efforts during assisted ventilation could impair hemodynamic, increase transpulmonary pressures, and increase lung perfusion [33–35]. In experimental acute lung injury model, conservative fluid strategy compared with liberal fluid strategy combined with PSV yielded less lung epithelial cell damage; however, regardless of the mode of MV, liberal fluid strategy resulted in less kidney injury markers [36]. It has been demonstrated that superior vena cava transmural pressure decreased during inspiration in volume control ventilation, which could be protective with a liberal fluid management [37]. The results of the present study suggested relationship of fluid balance and mortality did not differ between assisted or controlled modes. Whether modes of MV modify the relationship of fluid strategy and outcomes still needs investigation.

The amount of fluid and PEEP level may interact leading to poor outcomes. Changes in thoracic pressure could have great effect on hemodynamics [38]. In the present study, patients with low PEEP and less fluid had higher mortality in the early phase and patients with high PEEP and more fluid had higher mortality in the late phase, which suggested the modification effect of PEEP level. The PEEP level should be taken into account when considering the fluid strategy. In experimental endotoxin-induced ARDS model, the combination of a liberal fluid strategy and high PEEP level led to more lung damage [39]. In addition, the combination of abrupt PEEP decrease and high fluid administration worsened diffuse

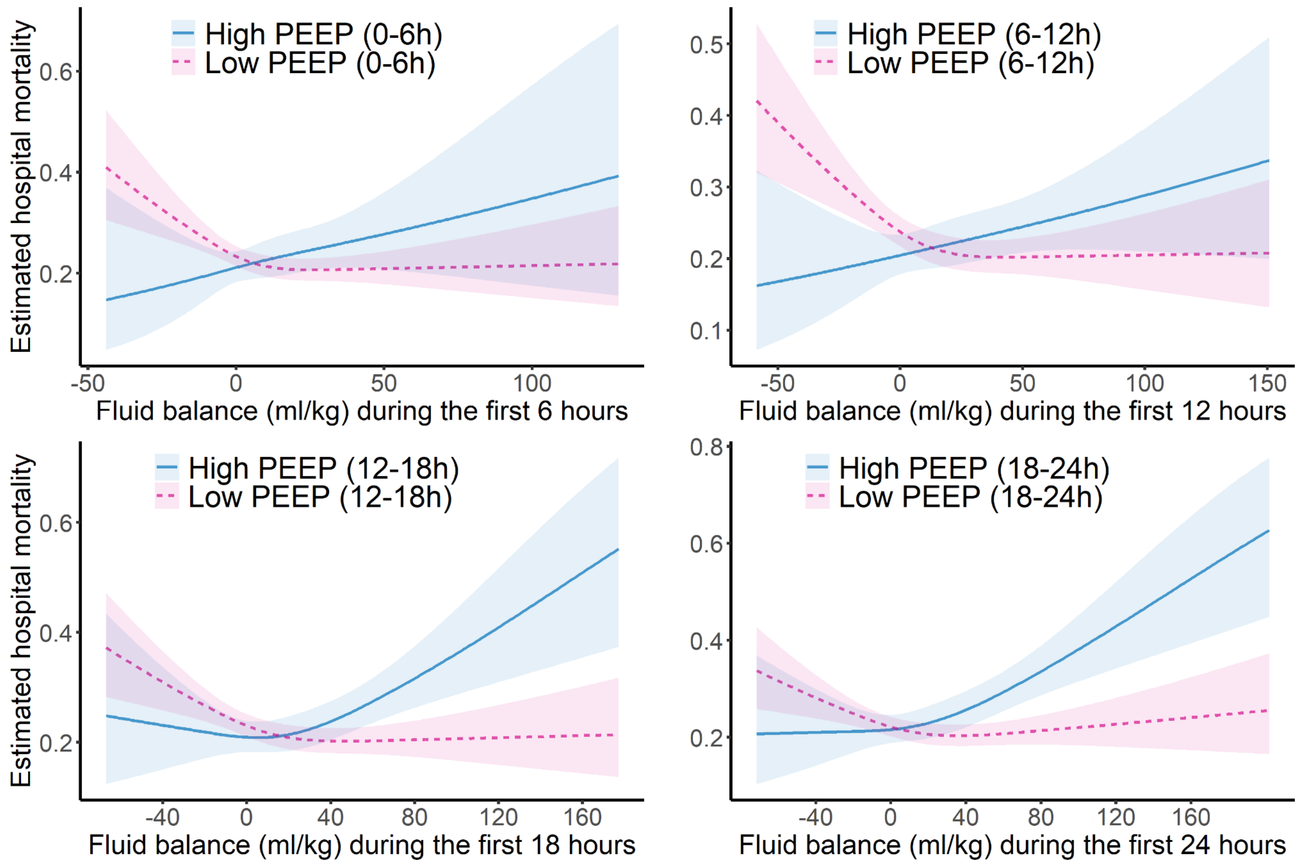

Fig. 6 The relationship between fluid balance during the first 6 h, 12 h, 18 h, and 24 h and hospital mortality for patients with high and low PEEP, respectively. Multivariable regression models were used and interaction effect of PEEP on relationship between fluid balance and hospital mortality were separately explored. The confounders included age, sex, Charlson comorbidity index, score, mode of mechanical ventilation, PEEP, and use of (Supplemental Table 4). CRRT, continuous renal replacement treatment, PEEP positive end-expiratory pressure, SOFA, sequential organ failure assessment

alveolar damage and increased the levels of inflammatory and endothelial cell damage biomarkers, which led to greater lung and kidney damage [40]. The interaction of low PEEP and negative fluid balance in early phase was weird. Whether this combination aggravated the distal organ damage needs further exploration.

With the large database, we explored the modified effect of ventilator setting on the relationship between fluid balance and hospital mortality. The results suggested that the setting of mechanical ventilation may have interaction effect on fluid therapy. However, several obvious limitations should be considered to this study. First, the study was retrospectively designed and unmeasured confounders could be present. Data of MV were collected every 6 h, not hours of duration of MV modes. In addition, whether patients whose total rate equals the set rate have spontaneous breathing was uncertain. Second, the potential for patient-ventilator asynchrony as well as inspiratory effort were not assessed, which were very important for the heart lung interaction. Third, the controlled mode of MV included pressure or volume control ventilation, which was not recorded in the present study. Fourth, the definition of high or low PEEP level was arbitrary. Fifth, the fluid balance was calculated during the first 24 h, which was quite short. Fluid balance for long duration may further explore the relationship. In addition, the fluid balance before admitting to ICU was unknown. Based on these limitations, the extrapolation of the present study should be cautious.

Conclusions

For sepsis patients admitted to ICU with invasive MV, the PEEP level, but not the mode of MV, appeared to modify the relationship of fluid balance and hospital mortality. The setting of mechanical ventilation may be an important consideration for fluid therapy.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12871-025-02954-x.

Supplementary Material 1

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None.

Author contributions
DW Z and C W conceived this study. DW Z and D L designed and performed the statistical analyses. DW Z and Y L wrote the first draft of the manuscript. DW Z and C W reviewed and modified the final manuscript.

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None.

Data availability
Data analyzed during the present study are currently stored in the MIMIC-IV database (https://mimic.mit.edu/). No additional datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
The MIMC-IV database was established in collaboration with Privacert (Cambridge, MA), who certified the re-identification risk as meeting safe harbor standards (HIPAA Certification no. 1031219-2). Due to the HIPAA standards in this database and in accordance with the Declaration of Helsinki, the Institutional Review Boards requirement was waived. The data used in the study is publicly available.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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