Relationship Between Fluid Therapy Strategies and Mortality Among Sepsis Patients in ICU with high CVP: A Retrospective Analysis of the eICU Database

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Abstract

Objective: It is still debated whether sepsis patients with high CVP (central venous pressure) benefit from it. We performed a retrospective study of sepsis patients with CVP ≥ 12 mmHg to analyze mortality resulting from the different amounts of fluid administered in the fluid therapy at the first 6, 24, and 48 h of the course.

Methods: This study included sepsis patients from the eICU database who met the sepsis-3 diagnostic criteria and showed CVP ≥ 12 mmHg on admission. We analyzed the differences between the survivors and the non-survivors at baseline and the difference in fluid balance at 6, 24, and 48 h. Restricted cubic spline (RCS) and logistic regression model were used to identify the association between fluid balance and mortality.

Results: Out of the 1150 sepsis patients that showed a high CVP obtained from the eICU database, 847 were survivors and 303 were non-survivors. Compared to survivors, non-survivors had a larger positive fluid balance at 6, 24, and 48 h. The fluid balance and mortality in sepsis patients with high CVP showed an inverted U-type relationship. At 6 h, lower mortality was found in patients who required less than -5 ml/kg fluid therapy. At 24 h, mortality was the lowest at -40~-20 ml/kg. At 48 h, low mortality was observed in patients with < -40 ml/kg fluid balance. In septic shock patients with high CVP, positive balance decrease mortality. In sepsis patients with high CVP without a history of chronic heart failure, and with a history of heart failure negative fluid balance can decrease mortality.

Conclusion: In the sepsis group without shock, achieving negative fluid balance possible may significantly improve the prognosis of patients with high CVP, and patients with no history of chronic heart failure and patients with history of chronic heart failure should limit fluid infusion. In patients with septic shock whose CVP ≥ 12 mmHg, positive fluid balance may decrease mortality.

Introduction

Sepsis is a life-threatening organ dysfunction caused by an abnormal host response to infection [1]. Peripheral vasodilation leads to blood redistribution, leading to insufficient perfusion in organs and tissues, leading to sepsis. Fluid therapy is an important treatment for sepsis. The guidelines of the Surviving Sepsis Campaign recommend that fluid resuscitation should be started early with a 30-ml/kg fluid balance [2]. However, recent reports suggested that superfluous fluid may increase mortality in sepsis patients [3–10]. A few studies reported that appropriate restriction in 24-h fluid therapy may reduce mortality [7–10], and excessive fluid therapy can aggravate tissue and organ edema and increase the incidence of AKI (acute kidney injury) and other complications [5]. It is important to adjust the fluid therapy regime according to the patients' volume status for sepsis patients. CVP (central venous pressure), a standard index to evaluate patient volume status and right ventricular function, plays an important role in fluid therapy. However, a follow-up study reported that CVP does not correctly reflect the volume status of patients and is poorly correlated with volumetric reactivity. Patients with high CVP may have insufficient fluid or a volume overload [11]. Other studies showed that a CVP ≥ 12 mmHg had a better correlation with insufficient cardiac volume and volume overload. Although it is difficult to administer fluid therapy for sepsis patients with CVP ≥ 12 mmHg, there is a lack of literature on administering early fluid therapy for sepsis patients with a CVP ≥ 12 mmHg. In the current study, patients who met the sepsis-3 criteria, had an initial CVP ≥ 12 mmHg, and did not receive large volumes of fluids within 24 h before ICU admission, were extracted from the eICU database. We analyzed the association between mortality and fluid therapy in these patients.

Methods

Database

eICU database is a structured database jointly established by Philips healthcare and MIT computational physiology laboratory. The database contains information on more than 200,000 patients from 208 hospitals in the United States admitted in 2014 and 2015. The database contains demographic and clinical data of the admitted patients, including length of stay, vital signs, laboratory tests, prescription and administration of drugs, and medical history. The database is continuously updated and in the current study, we used the latest database version (v2.0, May 2018) and PostgreSQL v11.2 to query and manage the data (http://www.postgresql.org/).

Sample Selection

Inclusion criteria - The following patients were considered for the analysis:

1. Sepsis was diagnosed within 24 h before admission to the ICU and the SOFA (Sequential Organ Failure Assessment) score at admission to the ICU was ≥ 2.
2. The patient's first CVP measured in ICU was ≥ 12 mmHg.
3. The patient was ≥ 18 years of age.

Exclusion criteria - The following patients were excluded:

1. Patients with positive fluid balance within 24 h before admission to the ICU.
2. Patients whose data on the amount of fluids used in therapy could not be extracted.

Data extraction

Age, gender, height, weight, BMI, amount of fluids used in therapy, CVP, SOFA score, Apache IV (Acute Physiology and Chronic Health Evaluation), score, MAP (mean arterial pressure), RR (respiratory rate), HR (heart rate), creatinine levels, bilirubin levels, lactic acid levels, Hb (Hemoglobin), WBC (white blood cell) count, use of vasoactive drugs, use of cardiotonic drugs, tracheal intubation, and history of chronic heart failure of the patients were extracted. CVP was the first measurement after ICU admission. SOFA score was the worst within 24 h before and after being admitted. Apache IV, MAP, RR, HR, creatinine levels, bilirubin levels, lactic acid levels, Hb, and WBC count were the worst within 24 h of ICU admission. The use of vasoactive drugs and cardiotonics after ICU admission was noted. Septic shock was defined as maintenance of blood pressure with vasoactive drugs, according to sepsis-3. We considered septic shock patients that were diagnosed only within 48 h of being admitted to the ICU [12].

Statistical analysis

We transformed outliers into missing values and removed variables with missing values > 10%. We used the multiple imputation method to fill in and analyze the data. The differences in age, gender, height, weight, BMI, amount of fluids used in therapy, CVP, SOFA score, Apache IV score, MAP, RR, HR, creatinine levels, bilirubin levels, lactic acid levels, Hb, WBC count, septic shock, cardiotonic drug use, tracheal intubation, and history of chronic heart failure between the two groups were analyzed. The patients were divided into septic shock and non-shock groups, according to sepsis-3. According to the history of chronic heart failure, the patients were divided into chronic heart failure and non-chronic heart failure groups. The restricted cubic spline (RCS) function was drawn according to the OR (odds ratio). The logistic regression model was used to calculate the adjusted OR of fluid balance and mortality and the differences in each segment [13]. RCS and logistic regression models were adjusted using age, BMI, WBC, MBP, and APACHE IV score.

Results

A total of 1150 patients conformed to sepsis-3 and the first measurement of CVP after admission to the ICU being greater than 12 mmHg, and the data on these patients were extracted from the database (Fig. 1). Patients included in the analysis comprised 847 survivors and 303 non-survivors. Figure 2 shows the amounts of fluids used in the treatment (Fig. 2). Non-survivors had higher age, CVP, SOFA score, Apache IV score, respiratory rate, heart rate, creatinine, tracheal intubation rate, and vasoactive drug usage rate than the survivors ($P < 0.05$). Non-survivors had lower blood pressure and BMI than the survivors ($P < 0.05$). There were no significant differences in gender, history of chronic heart failure, Hb, cardiotonic drug use, and WBC count between the two groups (Table 1).

Table 1
Differences in the baseline characteristics between survivors and non-survivors.

Baseline characteristics	**Survivor (n = 847)**	**Non-survivor (n = 303)**	**P**
Age (years)	65 (54, 74)	71 (58, 79)	< 0.001
Male % (n)	52.25% (451)	53.14% (161)	0.973
BMI (kg/m^2)	29.45 (24.80, 36.58)	27.51 (23.02, 33.85)	< 0.001
CVP (mmHg)	15 (13, 19)	16 (14, 20)	0.002
SOFA	7(5, 10)	11 (8, 13)	< 0.001
APACHE IV	71.12 (57, 91)	98 (78, 121)	< 0.001
MAP (mmHg)	54 (46, 118)	50 (42, 127)	< 0.001
RR (beats per minute)	29 (24, 34)	30 (26, 35)	0.002
HR (bpm)	112.57 (98, 127)	121 (105, 135)	< 0.001
WBC (10^9/L)	14.4 (10.16, 20.9)	16.06 (10.8, 23)	0.056
Hb (g/dL)	9.2 (10.5, 12)	9.2 (10.6, 12.2)	0.261
Cre (mg/dl)	1.6 (1.02, 2.66)	2.2 (1.40, 3.24)	< 0.001
CHF (n/%)	18.06% (153)	22.44% (68)	0.097
Venti (N = 1128) (%)	53.67% (446)	79.80% (177)	< 0.001
Shock (N = 1128) (%)	32.80% (254)	48.18% (146)	< 0.001
Cardiac agents (N = 1128) (%)	4.01% (34)	5.94% (18)	0.166

Abbreviations: BMI, Body Mass Index; CVP, Central Venous Pressure; SOFA, Sequential Organ Failure Assessment; MAP, Mean Arterial Pressure; RR, Respiratory Rate; HR, Heart Rate; WBC, White blood cell count; Hb, Hemoglobin; Cre, creatinine; CHF, Chronic Heart Failure; Venti, ventilation.

Fluid balance and mortality in sepsis patients and different subgroup

The fluid balances at 6, 24, and 48 h in survivors were significantly less than those in the non-survivors (Fig. 3, Table 2). In the sepsis subgroup without shock, we found that the fluid balances of the survivors at 24 and 48 h were significantly less than those of non-survivors ($P < 0.05$), but there were no significant differences at 6 h (Fig. 4, Table 2). In patients with septic shock, there were no significant differences in the fluid volume between survivors and non-survivors at 6, 24, and 48 h ($P > 0.05$) (Fig. 4, Table 2). In patients without chronic heart failure, we found that survivors had significantly lower fluid balance than non-survivors ($P < 0.05$) (Fig. 4, Table 2). In patients with chronic heart failure, we found that there were no significant differences at 6, 24, and 48 h (Fig. 4, Table 2).

Table 2
Fluid balance in survivors and non-survivors.

Time points	Survivors	Non-survivors	P
6 h	2.56 ± 10.78	4.42 ± 11.25	0.008
24 h	5.08 ± 33.72	15.25 ± 36.54	< 0.001
48 h	2.91 ± 52.16	20.47 ± 53.53	< 0.001
subgroup analysis			
Non-shock			
6 h	1.18 ± 10.24	1.89 ± 8.91	0.425
24 h	-0.87 ± 30.64	5.49 ± 30.12	0.021
48 h	-6.63 ± 47.55	6.51 ± 45.45	0.002
septic shock			
6 h	5.80 ± 11.39	7.16 ± 12.84	0.272
24 h	18.97 ± 36.43	25.76 ± 39.87	0.084
48 h	25.12 ± 55.28	33.99 ± 59.69	0.079
Non-CHF			
6 h	2.65 ± 10.93	5.10 ± 12.13	0.004
24 h	5.67 ± 34.43	17.36 ± 39.13	< 0.001
48 h	3.72 ± 53.16	23.36 ± 56.43	< 0.001
CHF			
6 h	2.16 ± 10.22	2.11 ± 7.18	0.976
24 h	2.41 ± 30.25	7.97 ± 24.51	0.184
48 h	-0.76 ± 47.34	10.50 ± 40.80	0.09

CHF, Chronic Heart Failure.

Fluid Balance And Mortality In Sepsis Patients

It was found that fluid balance and mortality in patients with sepsis showed an inverted U-shaped relationship, and the highest mortality was at 0 ml/kg fluid balance. With the increase of negative balance, mortality decreased gradually. At 6 h, mortality was significantly lower at < -5 ml/kg fluid balance compared to the other time intervals. At 24 h, mortality was significantly lower when the fluid balance was at -40 ~ 0 ml/kg compared to other fluid balance intervals. At 48 h, significantly lower mortality was observed in patients with < -40 ml/kg fluid balance compared to the other fluid balance intervals (Fig. 5, Fig. 6).

Fluid Balance And Mortality In Sepsis Patients Without Shock

Similar results were obtained in the subgroup analysis of sepsis patients without shock. The fluid balance and mortality in septic patients at 6, 24, and 48 h showed an inverted U-shaped relationship, and the highest mortality was observed at 0 ml/kg fluid balance. Mortality was significantly lower at < -5 ml/kg at 6 h compared to the other intervals. At 24 h, mortality was significantly lower at -40~-20 ml/kg compared to the other intervals. At 48 h, mortality was significantly lower in patients with − 60~-40 ml/kg compared to the other intervals (Fig. 7, Fig. 8A).

Fluid Balance And Mortality In Septic Shock Patients

Subgroup analysis of patients with septic shock showed that there was an L-shaped relationship between fluid balance and mortality at 6 h. With an increase in the fluid volume, mortality risk gradually decreased. However, at 6 h, the OR of mortality in patients with fluid balances of < -5 ml/kg, ~-5 ~ 0 ml kg, 0 ~ 5 ml/kg, 5 ~ 10 ml/kg, 10 ~ 20 ml/kg, and ≥ 20 ml/kg were not statistically different. At 24 and 48 h, fluid balance and mortality showed an inverted U-shaped relationship. At 24 h, significantly lower mortality was observed at 30 ~ 50 ml/kg compared to other intervals. At 48 h, significantly lower mortality was observed at ≥ 80 ml/kg compared to other intervals. (Fig. 8B, Fig. 9).

Fluid balance and mortality in sepsis patients without heart failure

Fluid balance and mortality showed an inverted U-shaped relationship in the subgroup of sepsis patients without heart failure at 6, 24, and 48 h but there were no significant differences in the fluid balances at -10~-5 ml/kg, ~-5 ~ 0 ml/kg, 0 ~ 5 ml/kg, 5 ~ 10 ml/kg, 10 ~ 20 ml/kg, 20 ~ 30 ml/kg, and ≥ 30 ml/kg at 6 h. At 24 h, significantly lower mortality was observed at -40~-20 ml/kg compared to the other intervals. At 48 h, significantly lower mortality was observed at -60~-40 ml/kg compared to other intervals (Fig. 8C, Figure S1).

Fluid balance and mortality in sepsis patients with heart failure

Subgroup analysis of sepsis patients with heart failure showed that there was significantly lower mortality at < -5 ml/kg at 6 h compared to the other intervals. At 24 h, there were no significant differences in the fluid balance between the < -20 ml/kg, -20~-10 ml/kg, -10 ~ 0 ml/kg, 0 ~ 10 ml/kg, 10 ~ 30 ml/kg, and ≥ 30 ml/kg groups. Mortality was significantly lower with the fluid balance of < -40 ml/kg at 48 h compared to the other intervals (Fig. 8D, Figure S2).

Discussion

The results from the current study showed that in the patients with CVP ≥ 12 mmHg, non-survivors showed more positive fluid balance at 6, 24, and 48 h than survivors. Also, fluid balance and mortality showed an inverted U-shaped relationship. We retrospectively studied patients with sepsis and found that patients with negative fluid balance at 6, 24, and 48 h showed decreased mortality compared to other patients, including those without shock and with and without CHF. However, septic shock patients whose fluid balance at 24 h was 30 ~ 50 ml/kg and that at 48 h was ≥ 80 ml/kg showed lower mortality.

Sepsis is an immune disorder characterized by a systemic inflammatory response involving changes in the functions of multiple organs in the body [14]. Current Surviving Sepsis Guidelines recommend early administration of 30 ml/kg of intravenous fluids for septic shock or sepsis-induced hypoperfusion, which may lead to an "acute organ dysfunction and/or decreased blood pressure and increased serum lactate" [2]. Some sepsis patients show fluid overload. Potential mechanisms of the deleterious effects of excessive fluid therapy include soft tissue and organ edema, worsened by the endovascular leak, which may lead to respiratory, cardiac, and renal failure [15–17]. Additionally, crystalloid resuscitation may directly injure the glycocalyx, which could contribute to organ failure [18]. A growing number of studies advocate limited fluid resuscitation and fluid therapy. Patients with high CVP are more prone to volume overload, and a suitable volume of fluid resuscitation for fluid therapy is not known.

For sepsis patients with initial CVP ≥ 12 mmHg, the fluid balance of non-survivors was significantly higher at 48 h than that of the survivors. A restricted cubic spline curve was plotted according to the patient's adjusted OR, and we found that the fluid balance and mortality presented an inverted U-shaped relationship. For sepsis patients with high CVP, the fluid balances of < -10 ml/kg, -40~-20 ml/kg, and –60~-40 ml/kg at 6, 24, and 48 h were associated with lower mortality. Negative fluid balance improved the prognosis of non-septic shock patients with high CVP, probably because these patients did not need so much fluid, and their cardiac output, organ perfusion, and oxygen delivery were sufficient. Here, high CVP indicated that there was too much fluid in the patient's body and the heart was overloaded. Reducing the amount of fluid may be beneficial to the patient. We believe that some patients with a CVP > 12 mmHg may have overload, and these patients should be treated early on to maintain a negative fluid balance.

In septic shock patients, at 6 h, mortality decreased as the fluid balance increased, and mortality was the highest in patients with a negative balance. Patients with a 24-h fluid balance of 30 ~ 50 ml/kg and a 48-h fluid balance of ≥ 80 ml/kg showed lower mortality. In septic shock patients with high CVP, maintaining a positive fluid balance for 48 h decreased the mortality. It indicated that some septic shock patients with high CVP had an insufficient capacity and fluid responsiveness to fluid therapy. In this study, we did not conduct stratified analysis according to whether there was fluid responsiveness. In future studies, we aim to distinguish whether there was fluid responsiveness in patients with high CVP after fluid treatment.

For sepsis patients with no history of heart failure, the CVP was not high, and a high CVP during fluid therapy indicated that the patients may have an acute myocardial injury or fluid overload, so negative fluid balance may be beneficial to the patients. In the current study, patients with a history of heart failure were not stratified according to whether their heart function was compensated or decompensated, nor were they stratified according to their normal heart function grades. A high CVP in these patients indicated that the heart function may be decompensated, a large amount of fluid may have aggravated the patient's load, and the patients may not have tolerated the volume. A low CVP indicated that the patient's heart function was compensated. Although CVP was high during the course of the disease, the heart was not overloaded and could continue to accept fluid therapy.

In recent years, an increasing number of studies have reported that early large-volume fluid therapy may increase mortality in patients [1, 4, 5, 19]. Sadaka *et al.* reported that mortality in patients with septic shock with fluid volumes < 6 L at 24 h was significantly lower than that in patients with fluid volumes of 6 L [11]. Anparasan *et al.* found that although the amount of fluid used in therapy at 72 h and mortality decreased gradually over time after the year 2000, the condition of the patients did not change significantly. The authors believed that restrictive fluid therapy could decrease mortality [3]. Our current study included patients with CVP ≥ 12 mmHg. Also, in our study, the amount of fluid used in therapy administered to patients with septic shock was markedly less than that in other studies [3, 11, 20].

For sepsis patients with high CVP, the guidelines for fluid therapy are debated [21]. Boyd *et al.* reported that large amounts of fluids during the early stages of sepsis significantly increased mortality in patients with a CVP ≥ 8 mmHg at 12 h [22]. In the guidelines for the diagnosis and treatment of sepsis, it was recommended that sepsis patients with a CVP ≥ 8 mmHg should be treated with caution [14]. Nevertheless, an increased number of reports suggested that CVP should not be used as the lone indicator to determine fluid therapy in sepsis patients [23–25]. As early as 2013, Marik *et al.* reported that CVP predicted volume responsiveness AUC = 0.56 and believed that CVP could not serve as a guide for fluid therapy [26]. Further research by Vieillard-Baron *et al.* found that CVP was not associated with the RV size of sepsis patients, and it did not reflect the volume status of patients [27]. The results from the current study showed that sepsis patients with a CVP ≥ 12 mmHg may have had volume overload. We believe that CVP cannot be used as the lone indicator to guide fluid therapy in sepsis patients. However, a high CVP indicated that our patients were at risk of volume overload, requiring further judgment in combination with other indicators for administering fluid therapy.

Limitations

1. Sepsis patients with a high CVP may have had volume overload. Due to missing values and since cardiac function data could not be extracted, it was not possible to distinguish between the reasons for a high CVP. Identifying the causes of high CVP is conducive to differentiating patients with volume overload or insufficient volume. 2. Retrospective research may have added a selective bias. 3. Among the patients included in the study, a few were administered a delayed fluid therapy. They had been diagnosed with sepsis in the inpatient ward or the emergency department but they did not receive fluid therapy in time and the fluid therapy was administered only after admission to the ICU. These patients may have contributed to the increased mortality.

Prospects

In future studies, it is important to distinguish between the different causes of an increase in the CVP and take into consideration their influence on fluid therapy.

Conclusion

In sepsis patients with an initial CVP ≥ 12 mmHg, the patients without shock and patients without heart failure and patients with heart failure may have volume overload. Treatment of negative fluid balance for these sepsis patients may decrease mortality. In patients with septic shock whose CVP ≥ 12 mmHg, positive fluid balance at 24 h and 48 h may decrease mortality. In future studies, it is important to distinguish between the different causes of an increase in CVP and take into consideration their influence on fluid therapy.

Abbreviations

CVP
central venous pressure; ICU:Intensive Care Unit; RCS:Restricted cubic spline; AKI:acute kidney injury; SOFA:Sequential Organ Failure Assessment; Apache IV:Acute Physiology and Chronic Health Evaluation Score; MAP:Mean Arterial Pressure; RR:Respiratory Rate; HR:Heart Rate; Hb:Hemoglobin; WBC:White Blood Cell; Cre:Creatinine; CHF:Chronic Heart Failure; Venti:Ventilation; BMI, Body Mass Index.

Declarations

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None.

Authors' Contribution

PY and RT designed the study and drafted the manuscript; JY contributed to conception, manuscript revision for controversial intellectual content and decided to submit the report. RZ finished the results and write some discussion. XL and XL helped to collect the data and prepared the figures. JS and JY performed statistical analysis. HC and JW contributed to data interpretation and modified the article language. All authors read and approved the final manuscript.

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Availability of data and materials

Data are available upon reasonable request and with the approval from the Massachusetts Institute of Technology Affiliates.

Ethics approval and consent to participate

An approval by an ethics committee was not applicable.

Consent for publication

All authors have agreed to the publication of this manuscript.

Competing interests

There was no conflicts of interests in this review.

Publisher's Note

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Figures

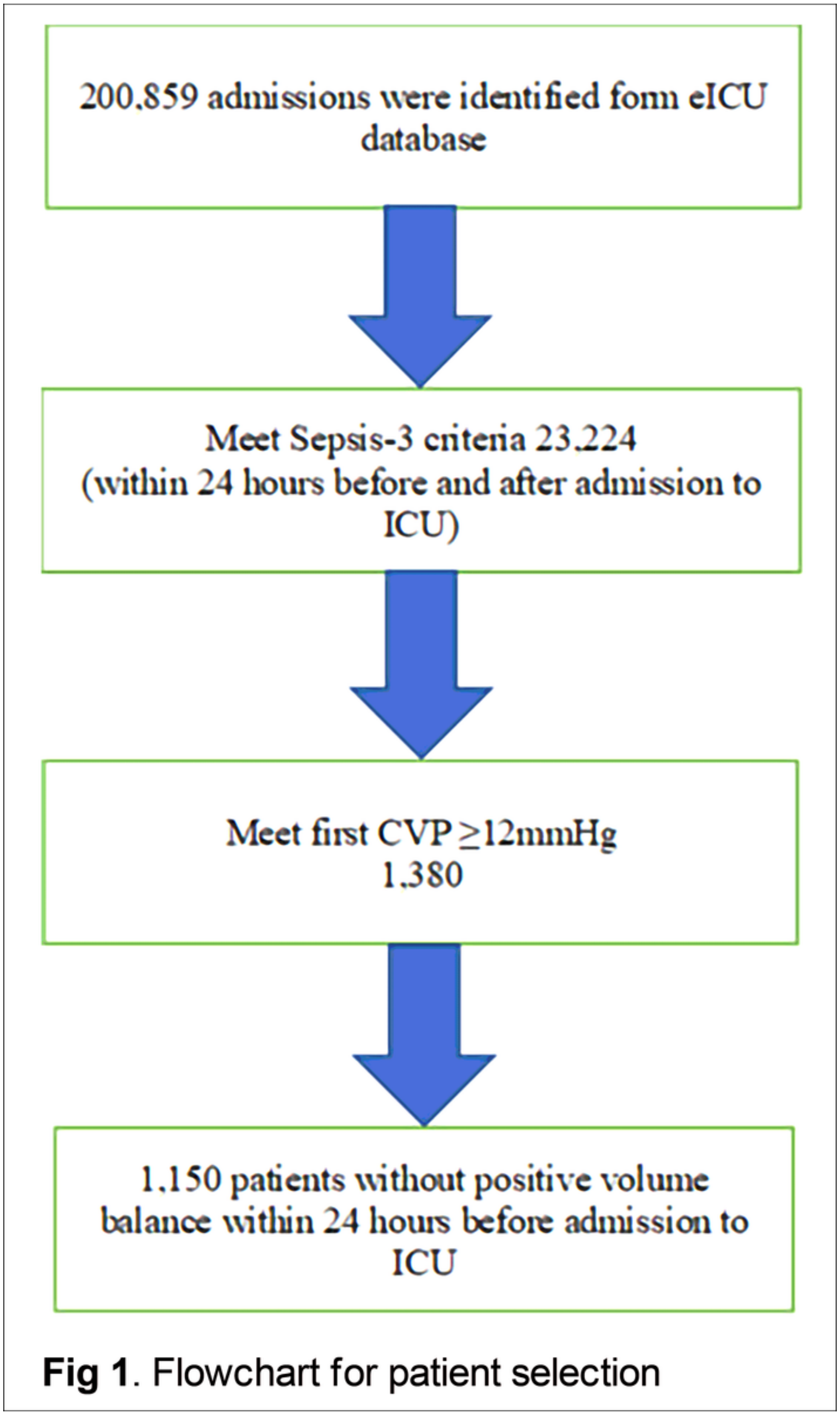

Figure 1

Flowchart for patient selection.

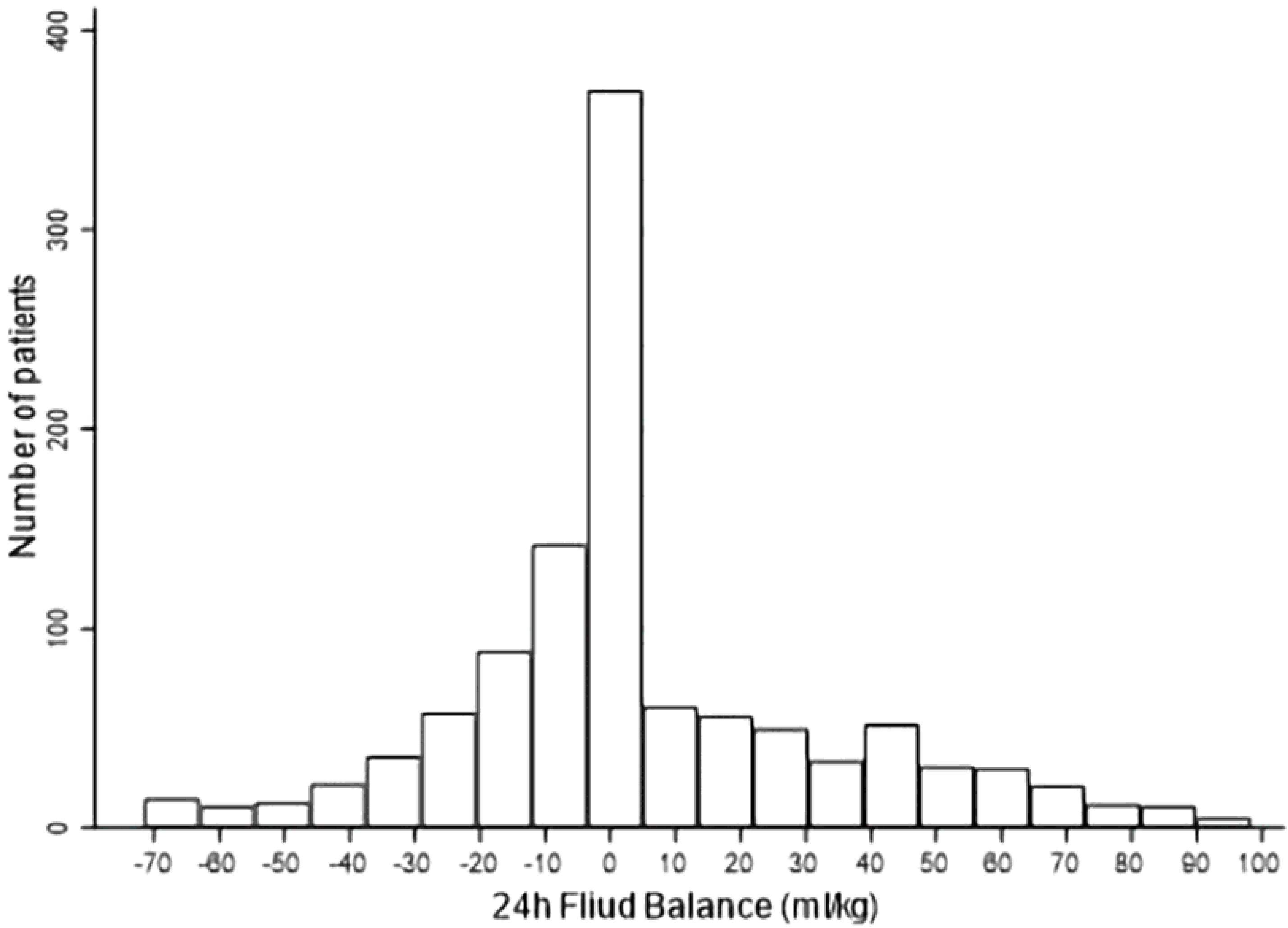

Fig.2 A histogram of 24-hour fluid balance distribution.

Figure 2

A histogram of 24-hour fluid balance distribution.

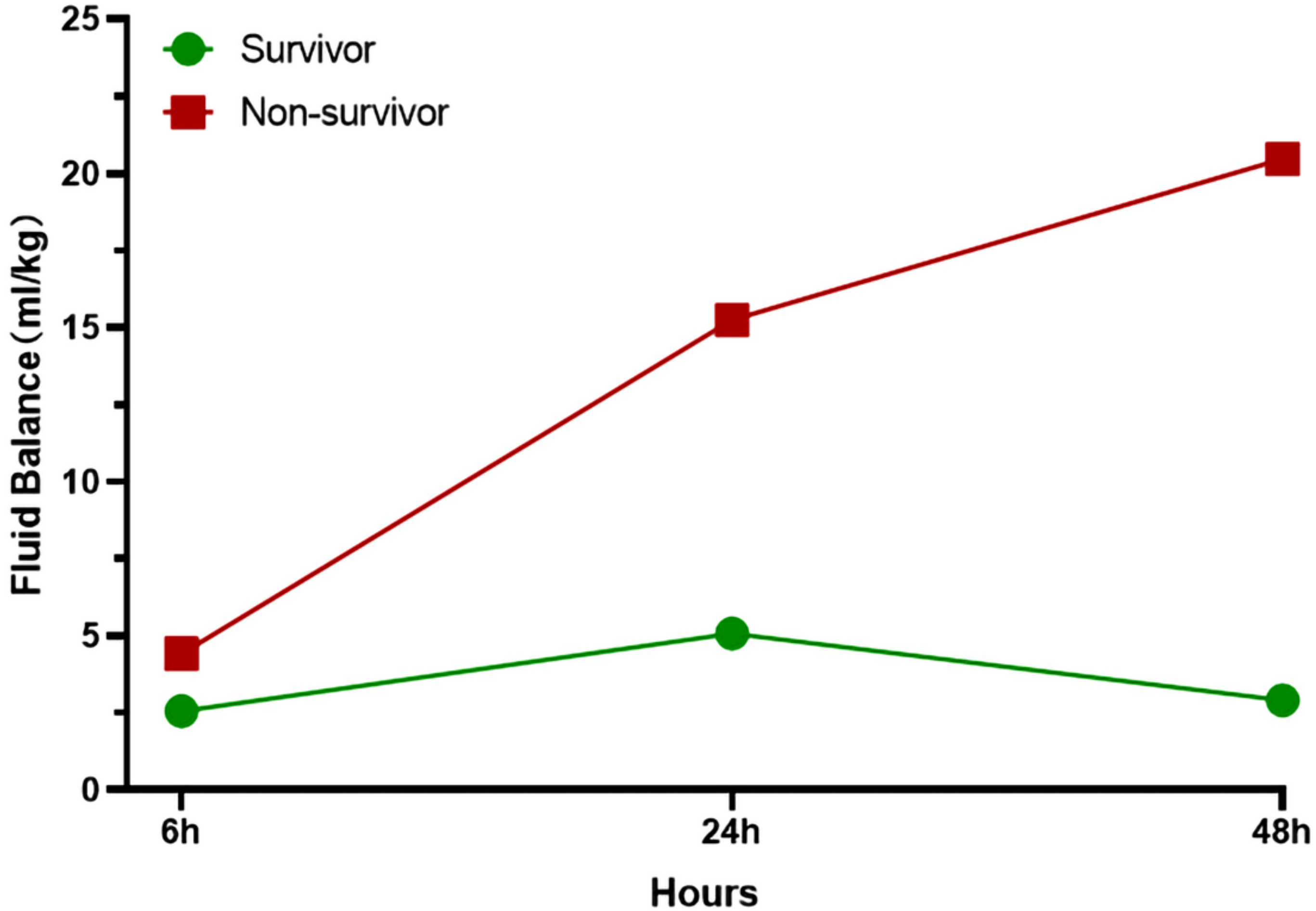

Fig 3. Fluid balance between survivors and non-survivors with high CVP.The fluid balance between survivors and non-survivors was significantly different at 6, 24, and 48 h ($P < 0.05$).

Figure 3

Fluid balance between survivors and non-survivors with high CVP. The fluid balance between survivors and non-survivors was significantly different at 6, 24, and 48 h ($P < 0.05$).

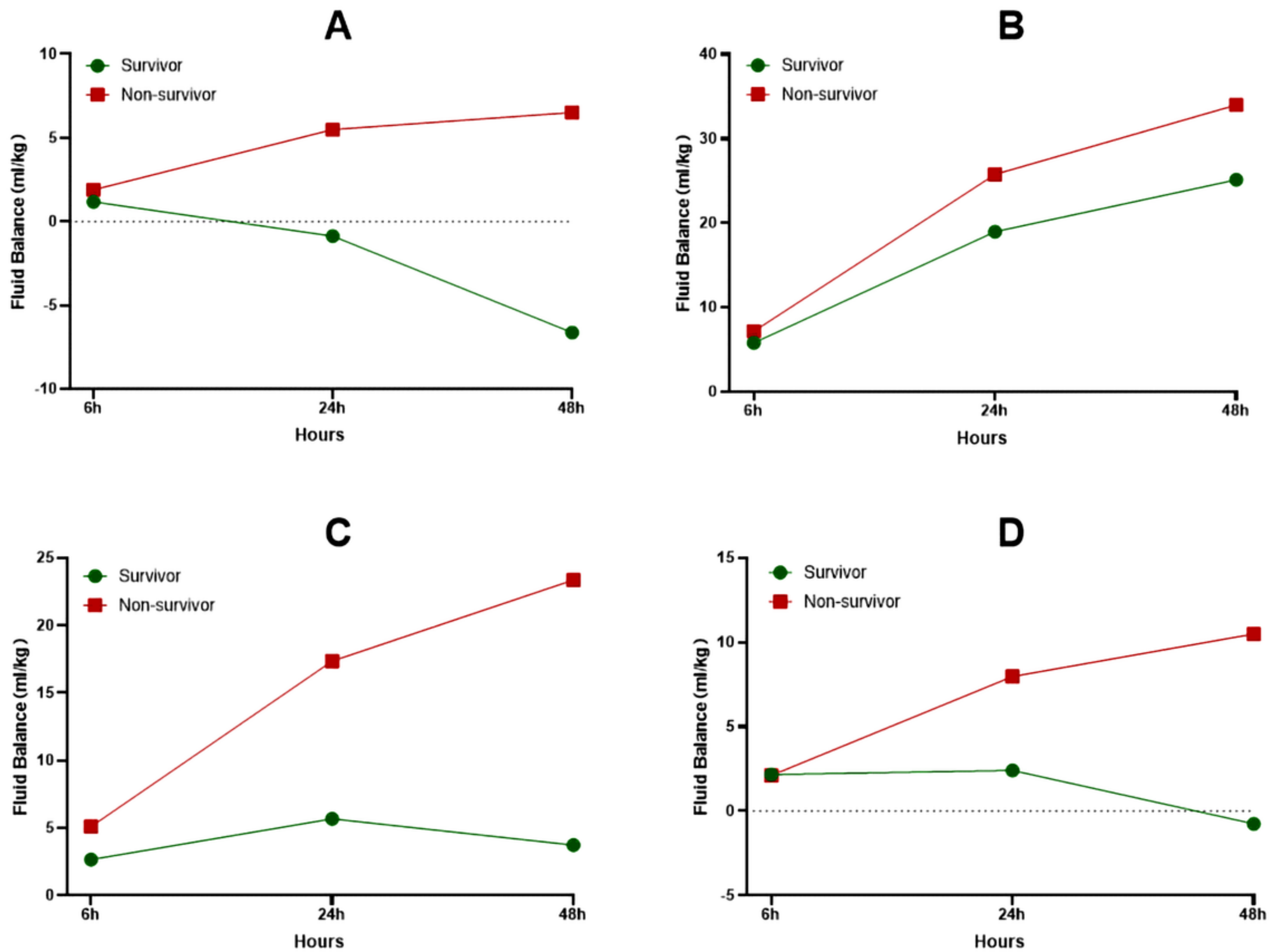

Fig.4 Fluid balance and mortality in the different subgroups. **A.** Sepsis (non-shock): The fluid balance between survivors and non-survivors was significantly different at 24 and 48 h ($p < 0.05$). **B.** Septic shock: The fluid balance between survivors and non-survivors was not significantly different at 6, 24, and 48 h ($p > 0.05$).**C.**Non-chronic heart failure: The fluid balance between survivors and non-survivors was significantly different at 6, 24, and 48 h ($p < 0.05$). **D.** Chronic heart failure: The fluid balance between survivors and non-survivors was not significantly different at 6, 24, and 48 h ($p > 0.05$).

Figure 4

Fluid balance and mortality in the different subgroups. A. Sepsis (non-shock): The fluid balance between survivors and non-survivors was significantly different at 24 and 48 h ($P < 0.05$). B. Septic shock: The fluid balance between survivors and non-survivors was not significantly different at 6, 24, and 48 h ($P > 0.05$). C. Non-chronic heart failure: The fluid balance between survivors and non-survivors was significantly different at 6, 24, and 48 h ($P < 0.05$). D. Chronic heart failure: The fluid balance between survivors and non-survivors was not significantly different at 6, 24, and 48 h ($P > 0.05$).

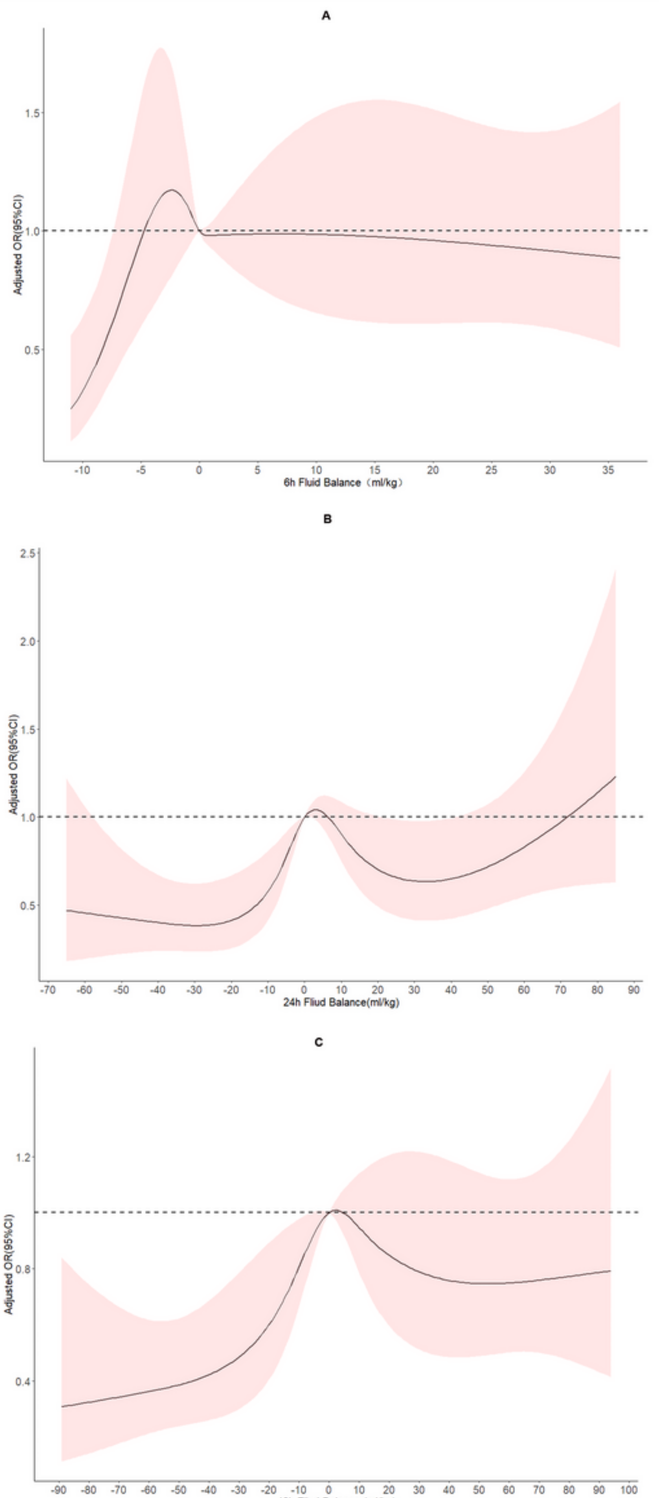

Fig 5. Fluid balance and OR of mortality in sepsis patients with high CVP. A. At 6 h; B. At 24 h; C. At 48 h

Figure 5

Fluid balance and OR of mortality in sepsis patients with high CVP. A. At 6 h; B. At 24 h; C. At 48 h.

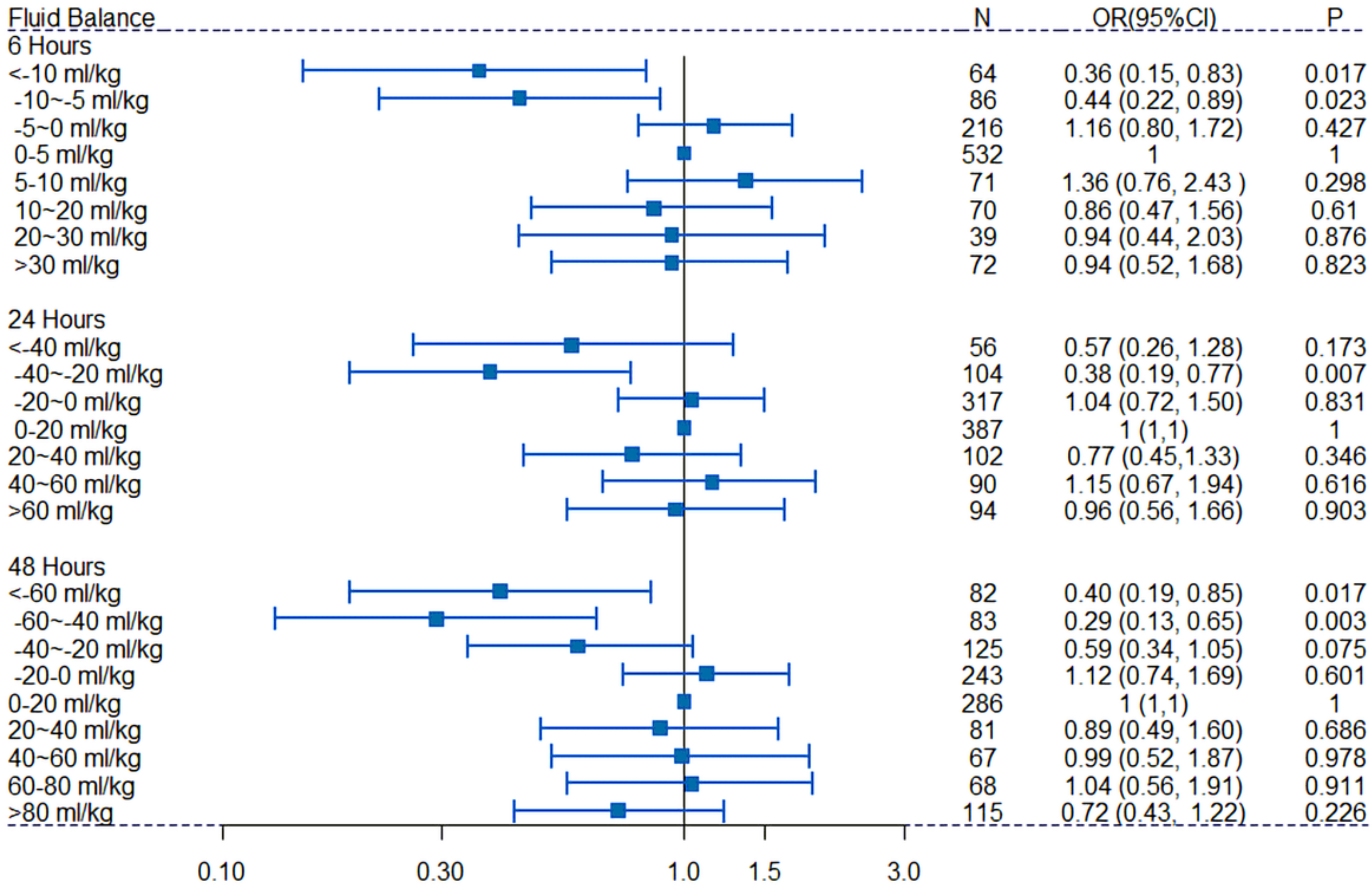

Fig 6. Fluid balance and adjusted OR of mortality in sepsis patients with high CVP.

Figure 6

Fluid balance and adjusted OR of mortality in sepsis patients with high CVP.

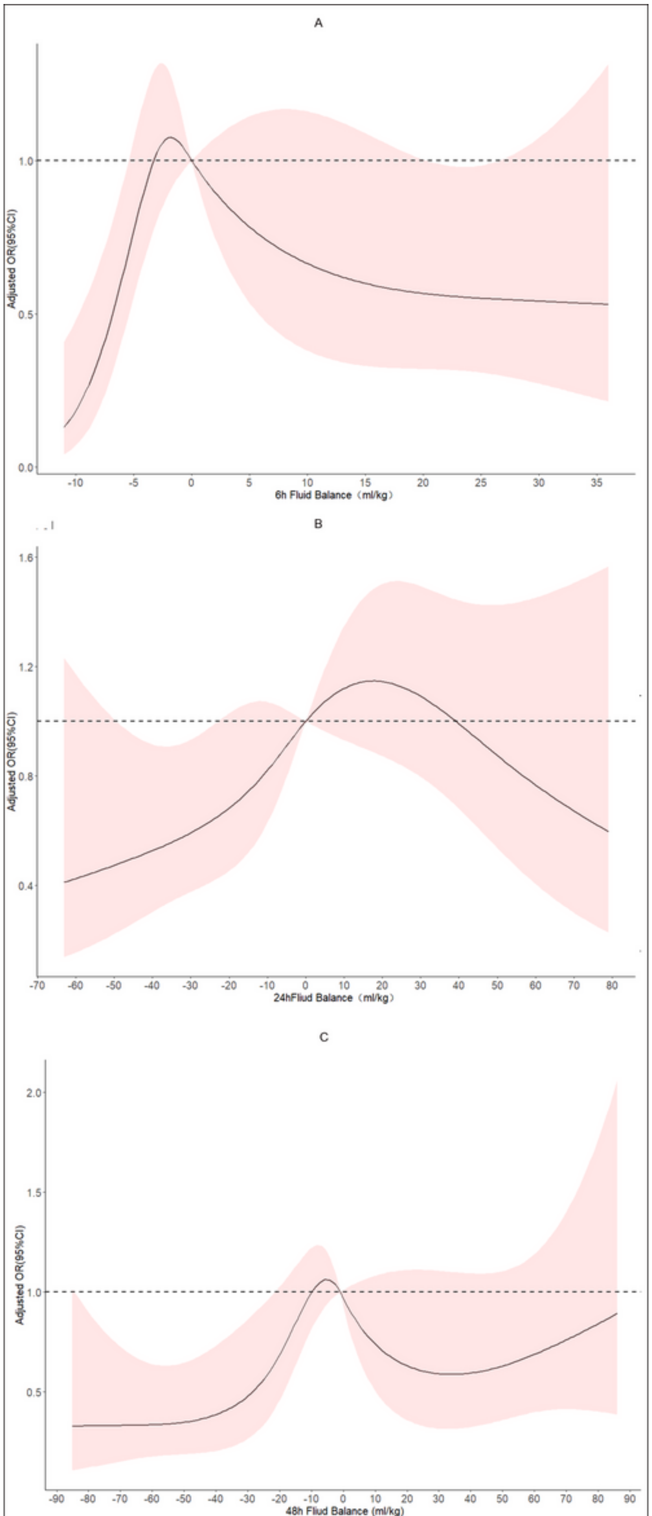

Fig 7. Fluid balance and mortality in sepsis patients with high CVP without shock. **A.** At 6 h; **B.** At 24 h; **C.** At 48 h.

Figure 7

Fluid balance and mortality in sepsis patients with high CVP without shock. A. At 6 h; B. At 24 h; C. At 48 h.

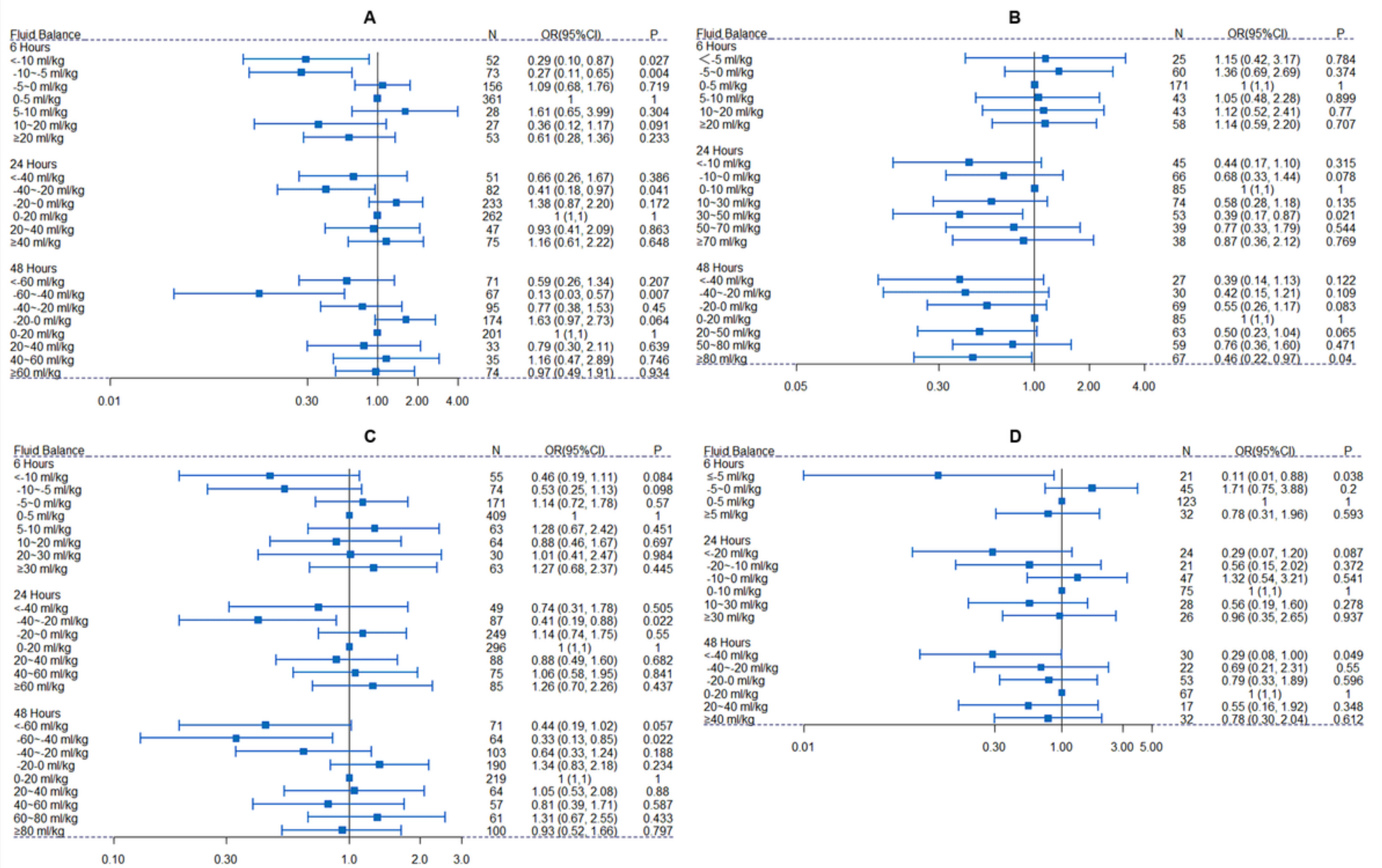

Fig 8. Fluid balance and adjusted OR of mortality in different subgroups. A. Sepsis (non-shock); B. Septic shock; C. Non-chronic heart failure; D. Chronic heart failure.

Figure 8

Fluid balance and adjusted OR of mortality in different subgroups. A. Sepsis (non-shock); B. Septic shock; C. Non-chronic heart failure; D. Chronic heart failure.

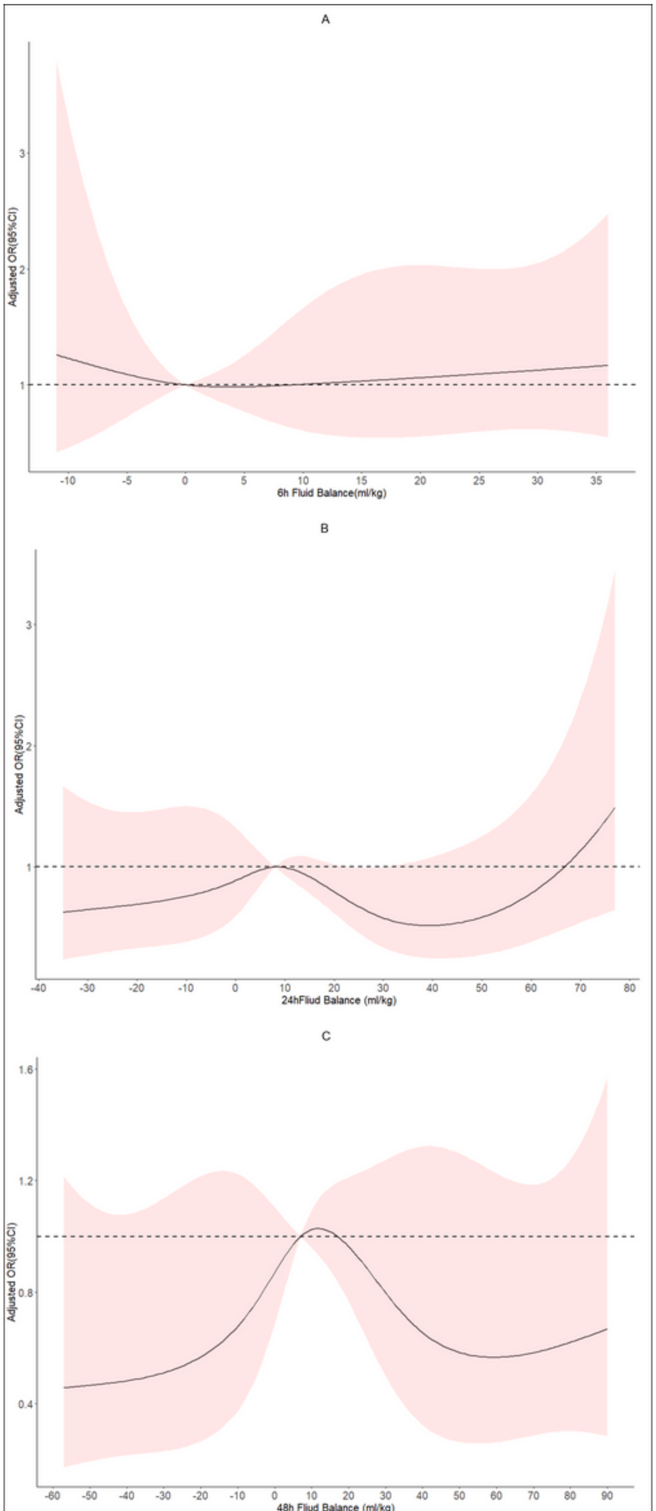

Fig 9. Fluid balance and mortality in septic shock patients with high CVP. **A.** At 6 h; **B.** At 24 h; **C.** At 48 h.

Figure 9

Fluid balance and mortality in septic shock patients with high CVP. A. At 6 h; B. At 24 h; C. At 48 h.

Supplementary Files

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