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J-shaped association between 72-hour net fluid balance and 90-day mortality in critically ill patients with cirrhosis: a retrospective cohort study

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Abstract

Background

Critically ill patients with cirrhosis face competing fluid-management demands, with some indications requiring fluid restriction and others requiring aggressive resuscitation. Whether cumulative net fluid balance is related to mortality in a J-shaped fashion, and where any optimal range lies, is unknown.

Methods

We conducted a retrospective cohort study using the MIMIC-IV database (accessible upon data use agreement). We included adults (≥ 18 years) with cirrhosis admitted to the intensive care unit (ICU). The primary exposure was 72-hour cumulative net fluid balance (NFB72). The primary outcome was 90-day all-cause mortality. We modeled the dose-response relationship with restricted cubic spline (RCS) logistic regression adjusted for twelve prespecified covariates, and tested effect modification by vasopressor use.

Results

Among 3801 critically ill patients with cirrhosis (median age 60 years; 36.9% female), 781 (20.5%) died within 90 days. NFB72 exhibited a J-shaped association with 90-day mortality (nonlinearity $P < 0.0001$; ΔAIC − 21.0 versus linear; P for trend = 0.004). Compared with the second quartile (near-neutral balance), the adjusted odds ratio (OR) for 90-day mortality was 2.45 (95% CI 1.78–3.40) in the fourth quartile. The optimal balance point was − 231 mL, corresponding to a minimum predicted risk of 8.2%. The association was modified by vasopressor use (interaction P = 0.007): positive balance was associated with mortality among vasopressor-treated patients (OR 2.89, 95% CI 1.87–4.57) but not among vasopressor-free patients (OR 1.52, 95% CI 0.84–2.71).

Conclusions

In critically ill patients with cirrhosis, 72-hour net fluid balance showed a J-shaped association with 90-day mortality, with harm more pronounced among vasopressor-treated patients and an optimal balance near zero. These findings support individualized, hemodynamic-status-informed fluid management.

Introduction

Critically ill patients with cirrhosis have high mortality: although short-term survival has improved over recent decades [1], long-term outcomes remain poor [2]. Fluid management in these patients is difficult because different indications pull treatment in opposite directions. Ascites, the hepatorenal syndrome, and portal hypertension [3] are treated with sodium restriction, diuretics, and, in some patients, albumin

or vasoconstrictors [4, 5, 6]; sepsis, gastrointestinal bleeding, and shock, by contrast, require aggressive volume resuscitation [7, 8, 9, 10]. Current guidelines cover each of these situations separately but do not define an integrated fluid target [11].

The net effect of these competing demands on outcome remains poorly defined. Positive fluid balance has been associated with increased mortality in critically ill patients [12, 13, 14]. In cirrhosis, prior studies have reported similar associations, but they were largely restricted to acute-on-chronic liver failure (ACLF) populations, used conventional linear or binary exposure models, and did not identify a target net fluid balance at which risk is minimized [15]. Whether the relationship between cumulative fluid balance and mortality is monotonic or J-shaped, and where any optimal range lies, is unknown.

We sought to examine the dose-response relationship between 72-hour cumulative net fluid balance (NFB72) and 90-day all-cause mortality in a large cohort of critically ill patients with cirrhosis. We focused on the first 72 hours because this resuscitation window is when fluid accumulation is most modifiable, and on 90-day mortality as an outcome that captures both acute organ failure and its downstream consequences. We hypothesized a J-shaped association, reasoning that severely negative balance may reflect under-resuscitation with hypoperfusion and prerenal injury, whereas severely positive balance may represent fluid overload with capillary leak and organ congestion, such that risk is lowest at a near-neutral balance. We further tested whether this association was modified by hemodynamic status, as reflected by vasopressor use.

Materials and methods

Data source

This retrospective cohort study used the Medical Information Mart for Intensive Care (MIMIC-IV, version 2.2) [16], a single-center database of critically ill patients admitted to Beth Israel Deaconess Medical Center between 2008 and 2022. The database is accessible upon data use agreement.

Study population

We included adults (≥ 18 years) with a first ICU admission and a diagnosis of cirrhosis, defined by ICD-9 codes 571.2, 571.5, or 571.6, or ICD-10 codes K70.3, K71.7, or K74.1–K74.6. We excluded patients who underwent liver transplantation during the index hospitalization, patients with an ICU length of stay shorter than 24 hours, patients who died within 72 hours of ICU admission (to ensure a complete exposure window and avoid immortal time bias), and patients with no fluid intake or output records within the first 72 hours.

Exposure

The primary exposure was cumulative net fluid balance over the first 72 hours of ICU admission (NFB72), calculated as the sum of all fluid input minus the sum of all fluid output recorded in the inputevents and outputevents tables during the first 72 hours, restricted to records with a milliliter unit of measurement. Bladder irrigation input was subtracted to correct for its contribution to output volume. NFB72 was analyzed as a continuous variable and divided into quartiles for categorical analyses, with the second quartile (near-neutral balance) serving as reference.

Covariates

Covariates were selected a priori based on clinical knowledge: age, sex, ascites, mechanical ventilation, and vasopressor use, together with laboratory values collected within the first 24 hours of ICU admission using the worst value (total bilirubin, INR, creatinine, and albumin), the Sequential Organ Failure Assessment (SOFA) score, the Model for End-Stage Liver Disease (MELD) score [17] computed by the United Network for Organ Sharing formula, and the Charlson Comorbidity Index. Patients with missing covariate data were excluded from the fully adjusted model. Race data were obtained from electronic health record (EHR) registration data at the time of hospital admission (not self-reported) and were categorized as White, Black, or Other. Race was reported descriptively per STROBE recommendations but was not included in the regression models.

Outcomes

The primary outcome was 90-day all-cause mortality, calculated from ICU admission. Death within 28 days served as an alternative outcome in sensitivity analyses.

Ethical

This study used de-identified data from the MIMIC-IV database. Because of the retrospective design and use of de-identified data, the study was exempt from institutional review board approval, and the requirement for informed consent was waived. The research adhered to the Declaration of Helsinki, and the reporting followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

Statistical analysis

Baseline characteristics were summarized as median (interquartile range [IQR]) for continuous variables, given their non-normal distribution, and as number (percentage) for categorical variables. Differences across the four NFB72 quartiles were compared using the Kruskal–Wallis test for continuous variables and the chi-square test (or Fisher's exact test as appropriate) for categorical variables.

We modeled the association between NFB72 and 90-day mortality using restricted cubic spline (RCS) logistic regression [18, 19] with four knots at the 5th, 35th, 65th, and 95th percentiles, adjusted for the

twelve prespecified covariates. Nonlinearity was assessed by comparing the RCS model against a linear model using a likelihood-ratio test, with the change in Akaike information criterion (ΔAIC) reported. A P for trend was estimated by modeling quartile as an ordinal variable. Categorical odds ratios (ORs) with 95% confidence intervals (CIs) were estimated from the fully adjusted model, with the second quartile as reference. The optimal balance point was defined as the minimum of the fitted RCS curve. Multicollinearity was assessed using variance inflation factors (VIF); the maximum VIF was 3.66 (MELD score), with all VIF < 5, indicating acceptable collinearity (Additional file 1).

Prespecified subgroup analyses were conducted across eight strata (ascites, vasopressor use, renal replacement therapy, sepsis, chronic kidney disease, heart failure, MELD ≥ 20, and age ≥ 65), using the same quartile cutpoints as the primary analysis, and effect modification was tested with interaction terms. Sensitivity analyses excluded patients with hepatocellular carcinoma, renal replacement therapy (in whom fluid balance is managed by ultrafiltration [20]), vasopressor use, and hypoalbuminemia (< 2.5 g/dL), using the same quartile cutpoints as the primary analysis. The E-value was computed [21] for the primary contrast to quantify the strength of unmeasured confounding required to explain away the observed association. To assess whether missing covariate data (principally albumin, missing in 26.2% of patients) influenced the complete-case analysis, we performed multiple imputation by chained equations (MICE) [22] assuming missing at random, with 20 imputed datasets using predictive mean matching and re-estimated the categorical odds ratios. Analyses were performed in R (version 4.6.0). A two-sided P < 0.05 was considered statistically significant.

Results

Study cohort

After applying inclusion and exclusion criteria, 3801 critically ill patients with cirrhosis were included, of whom 781 (20.5%) died within 90 days (Fig. 1, Table 1). The median age was 60 years, 36.9% were female, and 45.4% required vasopressors. The median MELD score was 20.0, the median SOFA score was 2.0, and the median NFB72 was 1869 mL (IQR − 806 to 5488 mL). In the fully adjusted analysis (complete case), 2741 patients with 586 events were analyzed.

Table 1
Baseline characteristics of patients with cirrhosis by net fluid balance quartile

Characteristic	Overall N = 3801[1]	Q1 (< −806 mL) N = 951[1]	Q2 (−806 to 1869 mL) N = 950[1]	Q3 (1869 to 5488 mL) N = 950[1]	Q4 (> 5488 mL) N = 950[1]	p-value[2]
Age, years	60.0 (52.0–68.0)	62.0 (54.0–69.0)	60.0 (53.0–69.0)	59.0 (52.0–67.0)	58.0 (51.0–67.0)	< 0.001
Sex						0.09
Female	1404 (36.9%)	321 (33.8%)	352 (37.1%)	372 (39.2%)	359 (37.8%)	
Male	2397 (63.1%)	630 (66.2%)	598 (62.9%)	578 (60.8%)	591 (62.2%)	
Race						0.04
White	2566 (67.5%)	649 (68.2%)	652 (68.6%)	664 (69.9%)	601 (63.3%)	
Black	319 (8.4%)	68 (7.2%)	80 (8.4%)	78 (8.2%)	93 (9.8%)	
Other	916 (24.1%)	234 (24.6%)	218 (22.9%)	208 (21.9%)	256 (26.9%)	
SOFA score	2.0 (0.0–5.0)	2.0 (0.0–5.0)	1.0 (0.0–4.0)	2.0 (1.0–5.0)	3.0 (1.0–6.0)	< 0.001
MELD score	20.0 (13.0–27.0)	19.0 (13.0–26.0)	18.0 (12.0–25.0)	19.0 (13.0–26.0)	23.0 (16.0–32.0)	< 0.001
Charlson comorbidity index	6.0 (4.0–8.0)	6.0 (4.0–8.0)	6.0 (4.0–8.0)	6.0 (4.0–8.0)	6.0 (4.0–8.0)	< 0.01
Ascites	1078 (28.4%)	233 (24.5%)	259 (27.3%)	287 (30.2%)	299 (31.5%)	< 0.01
Hepatocellular carcinoma	260 (6.8%)	59 (6.2%)	77 (8.1%)	56 (5.9%)	68 (7.2%)	0.21
Sepsis	1169 (30.8%)	258 (27.1%)	190 (20.0%)	255 (26.8%)	466 (49.1%)	< 0.001
Heart failure	828 (21.8%)	298 (31.3%)	195 (20.5%)	168 (17.7%)	167 (17.6%)	< 0.001
Chronic kidney disease	892 (23.5%)	236 (24.8%)	227 (23.9%)	208 (21.9%)	221 (23.3%)	0.50

Characteristic	Overall N = 3801[1]	Q1 (< − 806 mL) N = 951[1]	Q2 (− 806 to 1869 mL) N = 950[1]	Q3 (1869 to 5488 mL) N = 950[1]	Q4 (> 5488 mL) N = 950[1]	p-value[2]
Total bilirubin, mg/dL	2.5 (1.2–6.1)	2.1 (1.0–5.2)	2.1 (1.0–5.1)	2.8 (1.3–5.9)	3.3 (1.5–8.8)	< 0.001
INR	1.7 (1.4–2.2)	1.7 (1.4–2.2)	1.6 (1.3–2.0)	1.7 (1.4–2.2)	1.9 (1.5–2.5)	< 0.001
Creatinine, mg/dL	1.3 (0.8–2.3)	1.3 (0.9–2.1)	1.1 (0.8–2.0)	1.2 (0.8–2.0)	1.6 (0.9–3.1)	< 0.001
Albumin, g/dL	2.9 (2.5–3.4)	3.0 (2.6–3.5)	3.0 (2.6–3.5)	2.8 (2.5–3.3)	2.7 (2.3–3.2)	< 0.001
Platelets, ×10⁹/L	90.0 (55.0–143.0)	102.0 (62.0–159.0)	92.0 (58.0–140.0)	85.0 (53.0–139.0)	81.0 (50.0–133.0)	< 0.001
Hemoglobin, g/dL	8.6 (7.2–10.2)	8.6 (7.3–10.3)	8.7 (7.4–10.4)	8.6 (7.2–10.1)	8.3 (7.2–9.9)	< 0.01
WBC, ×10⁹/L	10.8 (7.1–16.1)	10.3 (6.8–15.4)	9.1 (6.4–13.7)	10.7 (7.0–15.9)	13.5 (9.0–19.3)	< 0.001
BUN, mg/dL	28.0 (17.0–48.0)	29.0 (17.0–49.0)	27.0 (16.0–45.0)	27.0 (15.0–45.0)	29.0 (18.0–52.0)	< 0.001
Sodium, mEq/L	135.0 (131.0–139.0)	135.0 (131.0–139.0)	136.0 (132.0–139.0)	136.0 (131.0–139.0)	135.0 (131.0–139.0)	0.22
Mechanical ventilation	743 (19.5%)	91 (9.6%)	136 (14.3%)	195 (20.5%)	321 (33.8%)	< 0.001
Vasopressor use	1724 (45.4%)	216 (22.7%)	315 (33.2%)	462 (48.6%)	731 (76.9%)	< 0.001
Renal replacement therapy	259 (6.8%)	22 (2.3%)	42 (4.4%)	62 (6.5%)	133 (14.0%)	< 0.001
72-h net fluid balance, mL	1868.7 (-805.6–5487.8)	-2715.0 (-4615.7–-1637.9)	544.4 (-141.0–1229.7)	3431.1 (2539.0–4281.7)	9089.5 (6918.5–12794.0)	< 0.001
ICU length of stay, days	3.0 (1.8–5.8)	3.0 (1.9–5.5)	1.9 (1.3–3.3)	2.6 (1.7–4.7)	5.6 (3.3–10.1)	< 0.001
90-day mortality	781 (20.5%)	166 (17.5%)	111 (11.7%)	168 (17.7%)	336 (35.4%)	< 0.001

Characteristic	Overall N = 3801[1]	Q1 (< − 806 mL) N = 951[1]	Q2 (− 806 to 1869 mL) N = 950[1]	Q3 (1869 to 5488 mL) N = 950[1]	Q4 (> 5488 mL) N = 950[1]	p-value[2]
[1]Median (Q1–Q3); n (%)						
[2]Kruskal-Wallis rank sum test; Pearson's Chi-squared test						
Other includes Hispanic, Asian, American Indian, Alaska Native, Native Hawaiian, Pacific Islander, Multiple race categories, and Unknown.						

J-shaped dose-response relationship

Ninety-day mortality across NFB72 quartiles was 17.5%, 11.7%, 17.7%, and 35.4% for Q1 (< − 806 mL), Q2 (− 806 to 1869 mL), Q3 (1869 to 5488 mL), and Q4 (> 5488 mL), respectively. The RCS model showed a J-shaped relationship (nonlinearity P < 0.0001; ΔAIC − 21.0 versus linear) (Fig. 2). The P for trend was 0.004.

In the fully adjusted categorical model, compared with Q2, the adjusted ORs for 90-day mortality were 1.73 (95% CI 1.24–2.42) for Q1, 1.34 (95% CI 0.96–1.88) for Q3, and 2.45 (95% CI 1.78–3.40) for Q4 (Table 2). The optimal balance point was − 231 mL, corresponding to a minimum predicted risk of 8.2%. Segmented regression with an inflection point at − 231 mL supported the J-shaped pattern: each 1 L increase in NFB72 below − 231 mL was associated with lower odds of 90-day mortality (OR 0.92, 95% CI 0.88–0.96), whereas each 1 L increase at or above − 231 mL was associated with higher odds (OR 1.07, 95% CI 1.05–1.09); the two-segment model fit significantly better than a single linear model (likelihood ratio $\chi^2 = 26.20$, P < 0.001) (Table 3). The E-value for the Q4 versus Q2 contrast was 4.33 (lower CI 2.95).

Table 2
Association between 72-hour net fluid balance and 90-day mortality following intensive care unit admission

Variable	Non-adjusted	Model 1	Model 2
NFB72, per 1 L	1.08 (1.07, 1.10)	1.08 (1.07, 1.10)	1.04 (1.02, 1.06)
NFB72 quartile			
Q1 (< − 806 mL)	1.68 (1.24, 2.30) < 0.001	1.69 (1.24, 2.31) < 0.001	1.73 (1.24, 2.42) 0.001
Q2 (− 806 to 1869 mL)	Ref	Ref	Ref
Q3 (1869 to 5488 mL)	1.67 (1.23, 2.27) 0.001	1.68 (1.24, 2.29) < 0.001	1.34 (0.96, 1.88) 0.089
Q4 (> 5488 mL)	4.41 (3.34, 5.88) < 0.001	4.51 (3.41, 6.01) < 0.001	2.45 (1.78, 3.40) < 0.001
P for trend	< 0.001	< 0.001	0.004

Non-adjusted: crude model without adjustment. Model 1: adjusted for age and sex. Model 2: adjusted for age, sex, ascites, mechanical ventilation, vasopressor use, total bilirubin, INR, creatinine, albumin, SOFA score, MELD score, and Charlson comorbidity index.

Table 3
Threshold effect analysis of 72-hour net fluid balance on 90-day mortality

Model	OR (95% CI)	P value
Model I: Linear (per 1 L)	1.04 (1.02, 1.06)	< 0.001
Model II: Piecewise linear		
Inflection point of NFB72	−231 mL	
≤ −231 mL (per 1 L)	0.92 (0.88, 0.96)	< 0.001
> −231 mL (per 1 L)	1.07 (1.05, 1.09)	< 0.001
Log-likelihood ratio test	-	< 0.001

Model II was adjusted for age, sex, ascites, mechanical ventilation, vasopressor use, total bilirubin, INR, creatinine, albumin, SOFA score, MELD score, and Charlson comorbidity index.

Effect modification by vasopressor use

The association between NFB72 and mortality was modified by vasopressor use (interaction P = 0.007). Among patients receiving vasopressors, positive fluid balance was strongly associated with mortality (adjusted OR for Q4 vs Q2 2.89, 95% CI 1.87–4.57), whereas among patients not receiving vasopressors, no significant association was observed (adjusted OR 1.52, 95% CI 0.84–2.71) (Fig. 3).

Sensitivity analyses

The J-shaped relationship persisted across sensitivity analyses (Table 4). The adjusted Q4 versus Q2 ORs were 2.52 (95% CI 1.80–3.55) after excluding hepatocellular carcinoma, 2.42 (95% CI 1.72–3.41) after excluding renal replacement therapy, 1.52 (95% CI 0.84–2.71) after excluding vasopressor use, and 2.07 (95% CI 1.41–3.06) after excluding hypoalbuminemia. The results were consistent across multiple imputation: the Q4 versus Q2 OR was 2.25 (95% CI 1.71–2.96) using multiple imputation by chained equations, and the J-shaped nonlinearity persisted (P < 0.001), consistent with the complete-case estimate of 2.45 (95% CI 1.78–3.40). The association was also consistent with 28-day mortality (OR 2.18, 95% CI 1.57–3.07).

Table 4
Sensitivity analyses for 90-day mortality

Analysis	N	Events	Nonlinear P	Adjusted OR (95% CI)
Primary analysis (complete case)	2741	586	< 0.001	2.45 (1.78–3.40)
Exclude HCC	2544	535	< 0.001	2.52 (1.80–3.55)
Exclude RRT	2550	510	< 0.001	2.42 (1.72–3.41)
Exclude vasopressor use	1428	202	0.012	1.52 (0.84–2.71)
Exclude albumin < 2.5 g/dL	2069	385	< 0.001	2.07 (1.41–3.06)
Alternative outcome (28-day mortality)	2741	532	< 0.001	2.18 (1.57–3.07)

HCC, hepatocellular carcinoma; RRT, renal replacement therapy. All odds ratios are for the fourth (Q4) versus second (Q2) quartile of 72-hour net fluid balance. All sensitivity analyses used the same restricted cubic spline model (four knots) with adjustment for the 12 prespecified covariates as the primary analysis.

Discussion

In this cohort of 3801 critically ill patients with cirrhosis, 72-hour net fluid balance exhibited a J-shaped association with 90-day mortality, with the lowest mortality at a near-neutral balance and a steep increase at more positive balances. The association was not uniform: positive fluid balance was associated with mortality predominantly among patients requiring vasopressors, whereas no significant association was observed in hemodynamically stable patients.

The J-shaped pattern is biologically plausible. A near-neutral balance reflects adequate resuscitation with preserved renal clearance, whereas progressive positive balance in the absence of appropriate output signals an inability to excrete administered fluid. This accumulation is greatest in vasopressor-dependent patients: vasopressors maintain perfusion pressure in the face of systemic vasodilation, which is commonly accompanied by increased capillary permeability. Fluid that escapes the intravascular compartment under these conditions accumulates in the interstitium, producing edema of

the lung, gut, and kidney that further compromises the very organ function fluid administration was intended to support. In hemodynamically stable patients, the endothelial barrier is more likely intact, allowing a given positive balance to be accommodated without comparable tissue edema, which may explain why no significant association was observed in this subgroup.

Our findings extend prior work in ACLF populations [15, 23, 24], which reported harm from positive balance but did not estimate an optimal range. By modeling NFB72 as a continuous spline and testing effect modification, we identified an approximate optimal balance near zero and showed that the harm of positive balance is more pronounced in the hemodynamically unstable. The near-zero optimal point is consistent with emerging evidence favoring a restrictive, individualized fluid strategy in critically ill patients [25, 26, 27].

A potential alternative explanation is that positive fluid balance is a marker, rather than a driver, of illness severity, since sicker patients receive more fluid and are more likely to die. Several observations argue against this interpretation. The association was adjusted for illness severity, including SOFA and MELD scores, and remained strong; the E-value of 4.33 indicates that an unmeasured confounder would need to more than quadruple the odds of both positive balance and mortality to explain away the observed association; and the association persisted after excluding patients receiving renal replacement therapy (OR 2.42), in whom fluid balance is governed by ultrafiltration rather than hemodynamic status. These considerations support a genuine role for fluid accumulation rather than confounding by severity alone.

These findings indicate that fluid management in cirrhotic ICU patients should be guided by hemodynamic status rather than by a uniform liberal or restrictive target [28]. For vasopressor-dependent patients, aggressive de-resuscitation after initial stabilization may be particularly important; for hemodynamically stable patients, a near-neutral balance may be acceptable.

This study has several strengths, including a large sample, a precise cirrhosis definition spanning all etiological subtypes, rigorous exclusion of patients dying within the exposure window to avoid immortal time bias, worst-value laboratory covariates, and multiple sensitivity analyses with a favorable E-value of 4.33. Limitations include the single-center, retrospective design; residual confounding inherent to observational data, which the consistency across sensitivity analyses and the E-value analysis partially address; and possible measurement error in fluid balance from unrecorded insensible losses and oral intake, which is likely nondifferential and would therefore tend to attenuate rather than inflate the observed association. Although MELD is derived from bilirubin, INR, and creatinine, the maximum variance inflation factor (3.66) indicated acceptable collinearity. Race data were obtained from EHR registration records rather than self-report, and misclassification is possible; however, this should not bias the main results because race was not included in the regression models. The complete-case approach for the fully adjusted model was supported by a multiple-imputation sensitivity analysis that yielded consistent results. The vasopressor interaction, while prespecified, should be interpreted as hypothesis-generating, and external validation in independent cohorts is needed.

Prospective studies should validate these findings, ideally with protocolized fluid-balance recording and adjudicated hemodynamic status, and examine whether targeting near-zero balance in vasopressor-dependent patients improves outcomes.

Conclusions

Among critically ill patients with cirrhosis, positive 72-hour net fluid balance was associated with higher 90-day mortality, with the harm more pronounced in vasopressor-treated patients. These findings, from a single-center retrospective cohort, support hemodynamic-status-informed fluid management targeting a near-zero balance. Prospective, multicenter studies are needed to validate these results.

Abbreviations

ACLF
acute-on-chronic liver failure
CI
confidence interval
ICU
intensive care unit
MELD
Model for End-Stage Liver Disease
NFB72
72-hour net fluid balance
OR
odds ratio
RCS
restricted cubic spline
SOFA
Sequential Organ Failure Assessment
ΔAIC
change in Akaike information criterion.

Declarations

Authors' contributions

Yaqiang Li conceived and designed the study, performed the data extraction and statistical analysis, and drafted the manuscript. Zhigang Xu contributed to data extraction and statistical analysis and revised the manuscript. Dayu Kuai and Baohong Xu supervised the work and critically revised the manuscript for important intellectual content. All authors read and approved the final manuscript.

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Availability of data and materials

The MIMIC-IV database is accessible upon data use agreement from PhysioNet (https://physionet.org/content/mimiciv/).

Ethics approval and consent to participate

This study used de-identified data from the MIMIC-IV database and was exempt from institutional review board approval.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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Figures

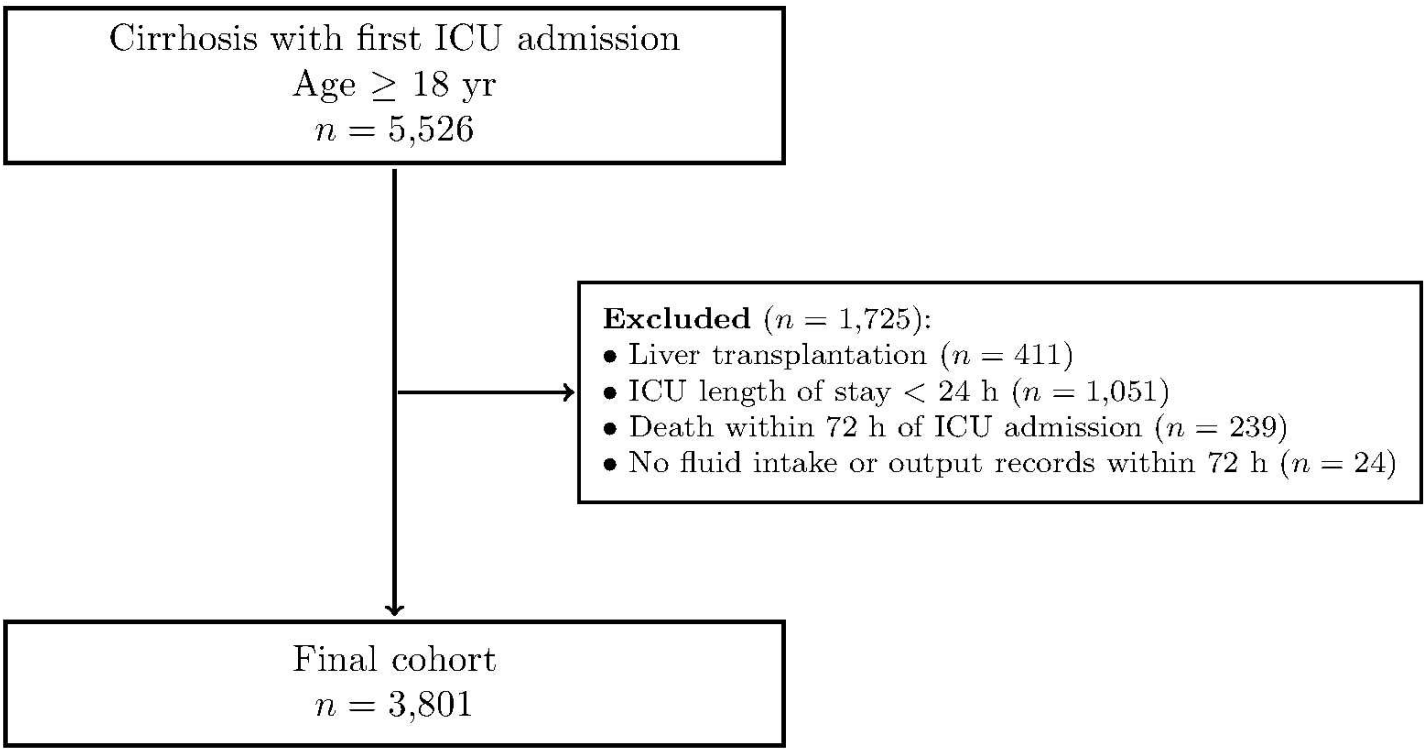


Figure 1

Patient selection flow diagram.

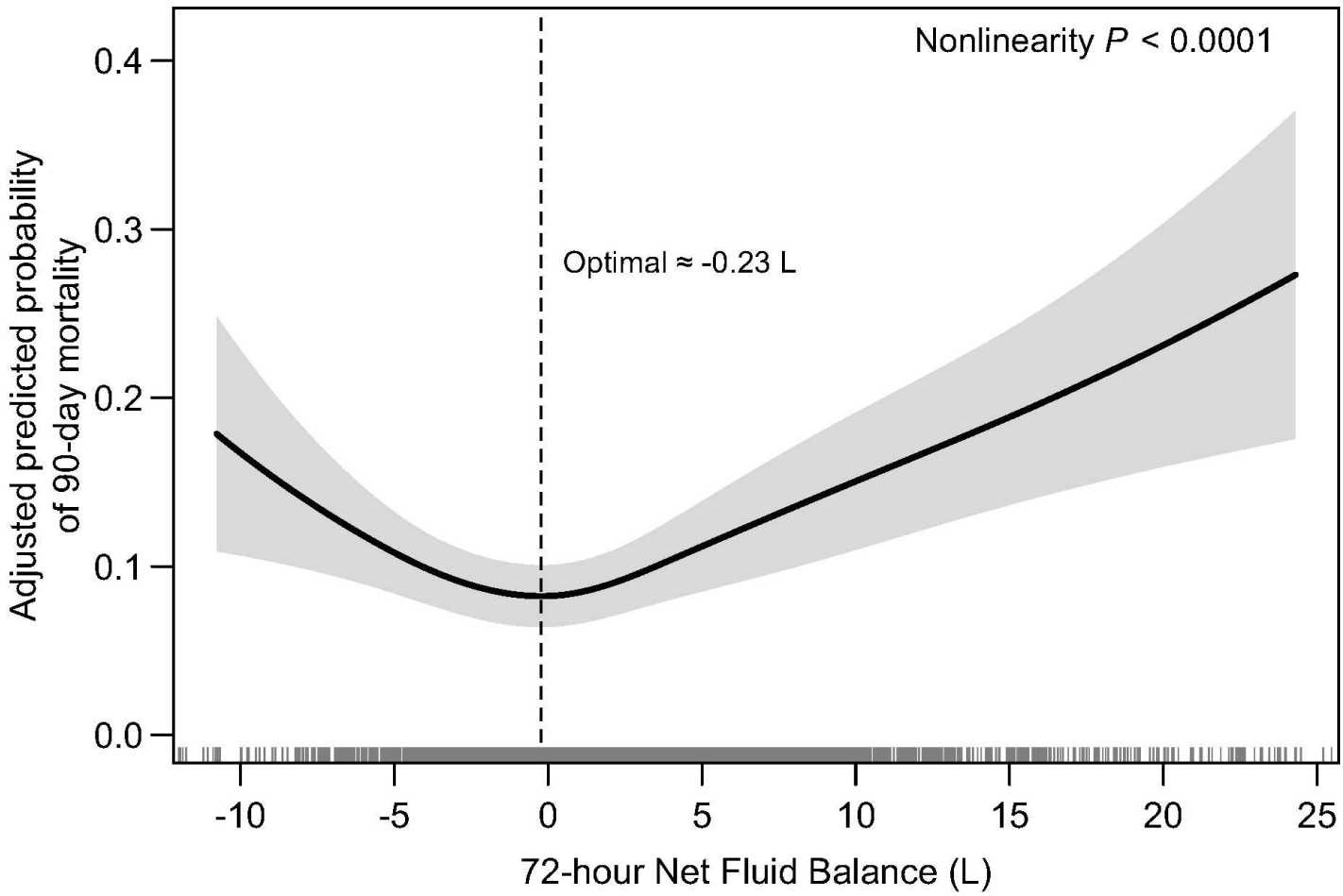


Figure 2

Restricted cubic spline for the association between 72-hour net fluid balance and 90-day mortality (nonlinearity P < 0.0001). The curve is adjusted for age, sex, ascites, mechanical ventilation, vasopressor use, total bilirubin, INR, creatinine, albumin, SOFA score, MELD score, and Charlson comorbidity index. Shading indicates the 95% confidence interval. The dashed vertical line marks the optimal balance point (−231 mL). The spline had four knots at the 5th, 35th, 65th, and 95th percentiles.

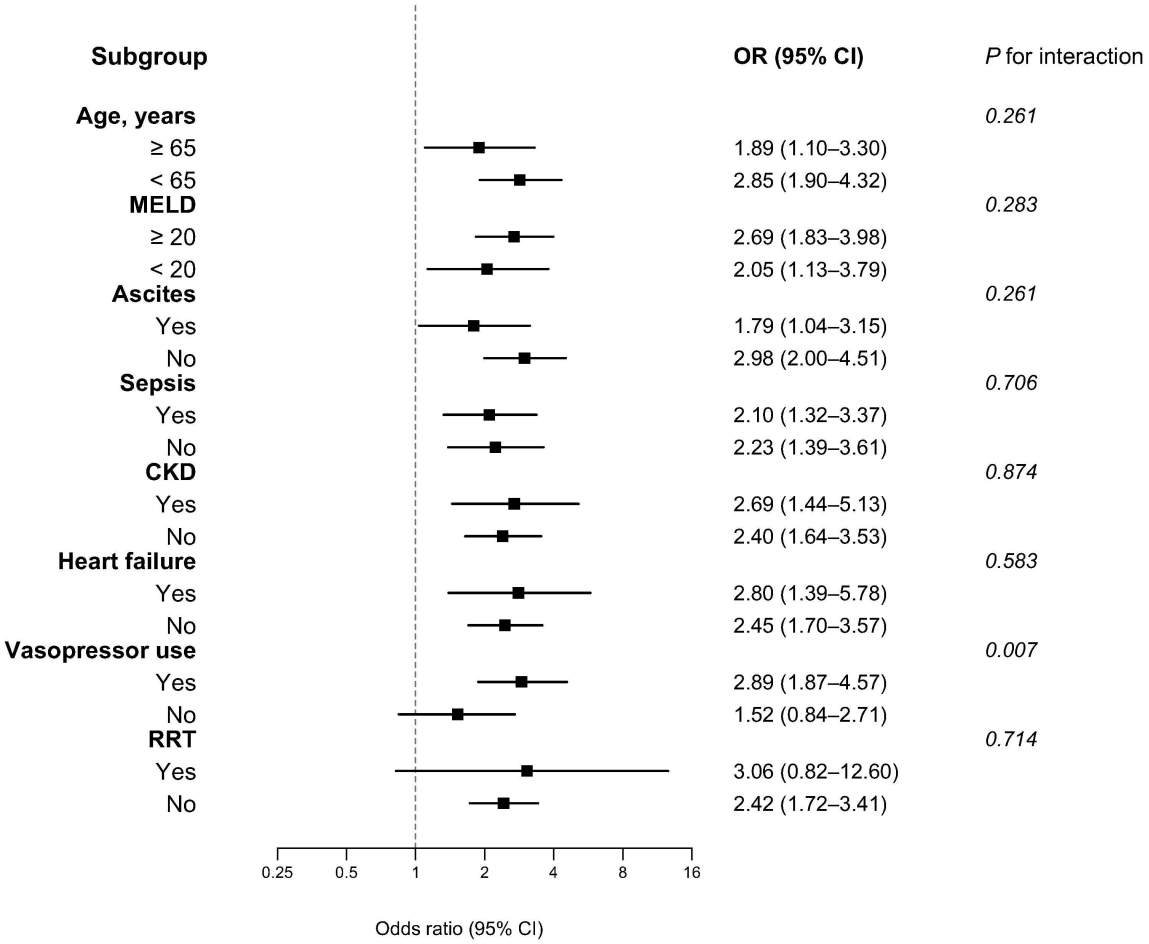


Figure 3

Subgroup analyses for 90-day mortality by net fluid balance quartile (Q4 vs Q2). Error bars indicate 95% confidence intervals. The P value for interaction was assessed by the likelihood ratio test.

Supplementary Files

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