Impact of albumin infusion on prognosis of intensive care unit patients with congestive heart failure-hypoalbuminemia overlap: a retrospective cohort study

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Background: Hypoalbuminemia is common in congestive heart failure (CHF) patients. Serum albumin is associated with the prognosis of CHF patients. Impact of albumin infusion on prognosis of patients with CHF-hypoalbuminemia overlap remains unclear. We retrospectively investigated the impact of albumin infusion on prognosis of intensive care unit (ICU) patients with CHF-hypoalbuminemia overlap.

Methods: We enrolled all patients whose diagnosis included CHF [ICD-9 (international classification of diseases 9) code =428.0] at first ICU admission from the MIMIC III (Medical Information Mart for Intensive Care III) database, and excluded those with missing serum albumin values, with serum albumin >3.4 g/dL or <18 years old. According to the exposure of albumin infusion during hospitalization, patients were stratified into non-albumin and albumin groups. Propensity-score matching (PSM) was performed (1:1 ratio) to control for baseline confounding. Outcome measures were in-hospital mortality as well as length of stay in the ICU (ICU LOS) and the hospital (hospital LOS).

Results: There were 3,190 eligible patients in the initial search. Patients with albumin infusion had markedly higher in-hospital mortality (36.42% *vs.* 21.81%, P<0.001), longer ICU LOS [median 6.93 (3.39–14.82) *vs.* 3.84 (1.96–8.00) days, P<0.001], and longer hospital LOS [median 17.46 (11.45–28.33) *vs.* 10.92 (6.81–18.00) days, P<0.001] than those without albumin infusion. The multivariate logistic regression analysis revealed that albumin infusion [odds ratio (OR), 1.509; 95% confidence interval (CI), 1.164–1.957; P=0.002] was significantly associated with increased risk of in-hospital mortality. After PSM, a cohort of 429 pairs of patients was included in the final analysis. Patients with albumin infusion had markedly higher in-hospital mortality (34.97% *vs.* 27.27%, P=0.015), longer ICU LOS [median 8.43 (4.33–16.28) *vs.* 6.43 (3.07–13.66) days, P<0.001], and longer hospital LOS [median 16.92 (11.27–28.06) *vs.* 13.33 (8.00–21.10) days, P<0.001] than those without albumin infusion. The multivariate logistic regression analysis revealed that albumin infusion (OR, 1.594; 95% CI, 1.143–2.223; P=0.006) was significantly associated with increased risk of in-hospital mortality.

Conclusions: Albumin infusion increased in-hospital mortality, ICU LOS, and hospital LOS in ICU patients with CHF-hypoalbuminemia overlap.

Keywords: Congestive heart failure (CHF); hypoalbuminemia; albumin infusion; in-hospital mortality; propensity score match

Introduction

Serum albumin accounts for more than 50% of plasma protein molecules in healthy individuals and its physiological level is 3.5–5.0 g/dL. Hypoalbuminemia is common in patients with cardiovascular diseases (1-3), and 20–50% of patients with heart failure (HF) have overlapping hypoalbuminemia (4-6). This proportion can be as high as 89% in frail, elderly patients with HF (7). Serum albumin has many physiological properties, including anti-inflammatory, anti-oxidant, anti-platelet aggregation, and anti-coagulant (8-11). More importantly, it provides 75% of plasma colloid oncotic pressure (12). Serum albumin deficiency is associated with the occurrence of HF (13,14), and is related to mortality, rehospitalization, and aggravation in HF patients (4-6).

As an important means of serum albumin supplementation, albumin infusion has been widely used in decompensated cirrhosis patients in clinical practice (15). However, the impact of albumin infusion remains controversial in critically ill patients. Albumin infusion improves organ function in critically ill patients with hypoalbuminemia (16). For the underlying disease, albumin infusion improves the prognosis in acute lung injury and severe sepsis patients (17,18). However, albumin infusion appears to increase mortality in patients with traumatic brain injury (19). For HF patients, albumin infusion could theoretically improve organ perfusion, but might also increase the load on the heart. In clinical practice, we prescribed albumin infusion for congestive heart failure (CHF) patients with severe hypoalbuminemia and edema. In some patients, edema was subsided and organ perfusion was improved. But some patients got worsen. Therefore, the impact of albumin infusion remains unclear. There is lack of research to investigate the impact of albumin infusion on the prognosis of CHF patients complicated with hypoalbuminemia. The purpose of this study was to investigate the impact of albumin infusion on prognosis of Intensive Care Unit (ICU) patients with CHF-hypoalbuminemia overlap. We present the following article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-648/rc).

Methods

Date source and variables

We performed a retrospective cohort study based on the Medical Information Mart for Intensive Care III (MIMIC-III) database version 1.4, which comprises the characteristics, laboratory outcomes, and medical records of more than 50,000 patients admitted to Beth Israel Deaconess Medical Center from 2001 to 2012 (20). We completed the National Institutes of Health's web-based course, passed the Protecting Human Research Participants module, and obtained database access (ID: 32540900). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

We used structure query language (SQL) to extract data from the MIMIC-III database, including demographics [age, gender, ethnicity, and body mass index (BMI)], comorbidities [diabetes mellitus, hypertension, acute myocardial infarction (AMI), cardiac arrhythmias, chronic pulmonary disease, renal failure, liver disease, stroke, and malignancy], vital signs [systolic blood pressure (SBP), diastolic blood pressure (DBP)], laboratory results [hemoglobin, glucose, potassium, sodium, serum creatine (SCr), alanine transaminase (ALT), aspartate transaminase (AST), lactate, serum albumin, and left ventricular ejection fraction (LVEF)], scoring system [SAPS-II (simplified acute physiology score II) scores (21) and SOFA (sequential organ failure assessment) scores (22)] and therapy [albumin infusion, beta-blockers (BBs), renin-angiotensin system inhibitors (RASIs), mineralcorticoid receptor antagonists (MRAs), diuretic, vasopressor, renal replacement therapy (RRT), and ventilation].

Inclusion and exclusion criteria

We enrolled all patients whose diagnosis included CHF [ICD-9 (international classification of diseases 9) code =428.0] at first ICU admission from the database. The exclusion criteria were as follows: (I) patients with missing

serum albumin values; (II) serum albumin >3.4 g/dL; and (III) patients <18 years old.

Patient stratification

We stratified the patients into two groups based on their exposure to albumin infusion: the albumin group included patients who received albumin infusion, and the non-albumin group comprised patients who did not receive albumin infusion during hospitalization.

Follow-up and outcomes

Patients were followed up from the date of admission to the date of discharge or death. Information on mortality was obtained from the Social Security Death Index records. This study's primary outcome was in-hospital mortality, and the secondary outcomes were the length of stay in the ICU (ICU LOS) and the hospital (hospital LOS).

Statistical analyses

To unbiasedly ascertain the impact of albumin infusion on in-hospital mortality, we performed a 1:1 propensity-score matching (PSM) between the albumin and non-albumin groups based on the estimated propensity scores, using the nearest neighbor method without replacement (23,24). A caliper width of 0.2 was used. The following variables were used to construct the propensity score model: age, liver disease, malignancy, lactate, albumin, LVEF, SAPS-II scores, SOFA scores, ventilator, RRT, vasopressor, BBs, RASIs, and diuretic.

Continuous variables were summarized using the median [interquartile range (IQR)], and categorical variables were summarized using counts (percentages). Differences in baseline variables between the albumin and non-albumin groups were evaluated using the Mann-Whitney U test for continuous variables and the chi-square test for categorical variables. Logistic regression analysis was used to examine the association between albumin infusion and in-hospital mortality. Odds ratios (ORs) and 95% confidence intervals (CIs) were presented. Variables with a P value <0.1 in the univariate logistic regression analysis model were entered into the multivariate models. A two-sided P value <0.05 was considered to indicate statistical significance in all analyses. Statistical analysis was performed by using STATA 12.0 (STATA Corporation, College Station, USA) and SPSS 22.0 (SPSS Inc, Chicago, IL, USA).

Results

Subject characteristics

Overall, 8,593 ICU patients met the inclusion criteria. Among them, 3,761 patients with missing serum albumin values, 1,641 patients with serum albumin >3.4 g/dL, and one patient younger than 18 years old were excluded. In total, 3,190 patients [median age 75.79 (64.50–83.34) years old, 52.41% males] satisfied the selection criteria (*Figure 1*). These patients were divided into albumin and non-albumin groups depending on whether they received albumin infusion during hospitalization. A comparison of the baseline clinical characteristics between the two groups is shown in *Table 1*. Patients in the albumin group tended to have a higher proportion of liver disease, malignancy, MRAs, BBs, diuretic, vasopressor, RRT, ventilation, and a lower proportion of AMI and RASIs. They also tended to be younger, with higher BMI, LVEF, SAPS-II scores, and SOFA scores, and lower SBP, DBP, hemoglobin, sodium, glucose, ALT, lactate, and serum albumin.

Subsequently, PSM was performed to control for measurable confounding factors. The mean propensity score of all patients was 0.142. The mean scores of the albumin and non-albumin groups were 0.206 and 0.122, with minimum and maximum scores ranging from 0.013–0.925 and 0.006–0.803, respectively. A graphical representation of the propensity score is displayed in *Figure 2*. After matching, 429 pairs of patients [median age 74.33 (63.07–82.12) years old, 53.61% male] were included in the final analysis (*Figure 1*). There were no statistically significant differences in the baseline characteristics between the two groups (*Table 1*).

Outcomes

Before PSM, there were 762 (23.89%) in-hospital deaths. The in-hospital mortality of the albumin group was markedly higher than that of the non-albumin group (36.42% *vs.* 21.81%, P<0.001). After matching, there were 267 (31.12%) deaths, and the in-hospital mortality was still higher in the albumin group compared to the non-albumin group (34.97% *vs.* 27.27%, P=0.015) (*Figure 3A*).

Before matching, the ICU LOS [median 6.93 (3.39–14.82) *vs.* 3.84 (1.96–8.00) days, P<0.001] and hospital LOS [median 17.46 (11.45–28.33) *vs.* 10.92 (6.81–18.00) days, P<0.001] were longer in the albumin group than the non-albumin group. After matching, the ICU LOS [median 8.43 (4.33–16.28) *vs.* 6.43 (3.07–13.66) days, P<0.001] and hospital LOS [median 16.92 (11.27–28.06)
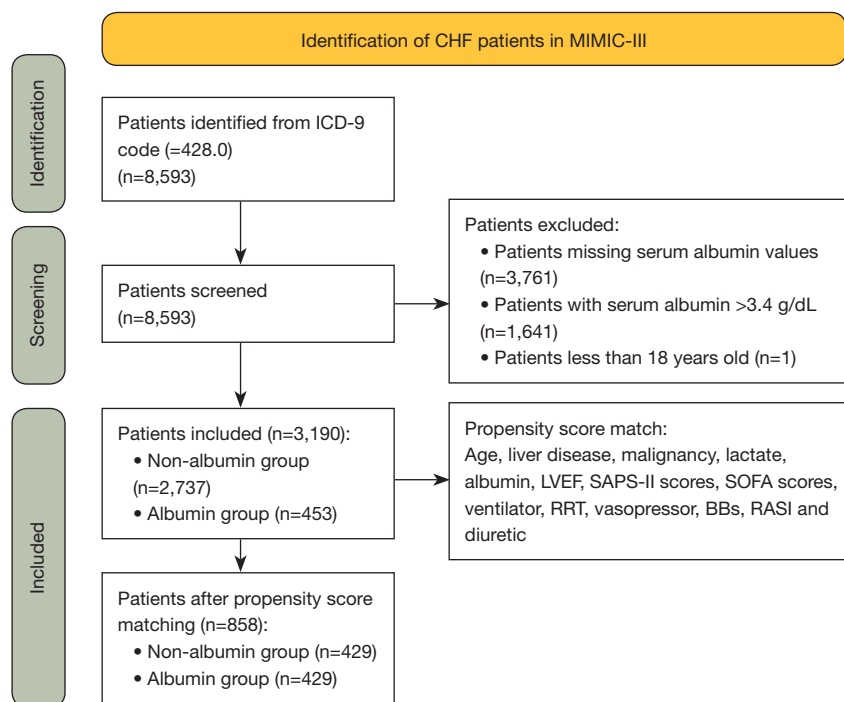
Figure 1 Patient selection flow chart. CHF, congestive heart failure; MIMIC-III, Medical Information Mart for Intensive Care III; LVEF, left ventricular ejection fraction; SAPS-II, simplified acute physiology score II; SOFA, sequential organ failure; RRT, renal replacement therapy; BBs, beta-blockers; RASIs, renin-angiotensin system inhibitors.

vs. 13.33 (8.00–21.10) days, P<0.001] remained longer in the albumin group than the non-albumin group (*Figure 3B,3C*).

Before matching, the serum albumin levels were similar between admission and discharge in the albumin group [median 2.7 (2.3–3.1) *vs.* 2.7 (2.3–3.1) g/dL, P=0.629]. In the non-albumin group, the serum albumin level was 2.9 (2.6–3.2) g/dL at admission and 2.8 (2.4–3.1) g/dL at discharge (P<0.0001 *vs.* admission). After matching, the serum albumin levels remained similar between admission and discharge in the albumin group [median 2.7 (2.4–3.1) *vs.* 2.7 (2.3–3.1) g/dL, P=0.838]. In the non-albumin group, the serum albumin level was 2.7 (2.3–3.1) g/dL at admission and 2.6 (2.3–3.0) g/dL at discharge (P=0.019 *vs.* admission) (*Figure 4*).

Albumin infusion and in-hospital mortality

Table 2 shows the results of the logistic regression analysis before PSM. In the univariate analysis, age, ethnicity (Other), cardiac arrhythmias, liver disease, stroke, potassium, SCr, ALT, AST, lactate, LVEF (<30%), SAPS-

II scores, SOFA scores, vasopressor, RRT, ventilation, and albumin infusion were associated with an increased risk of in-hospital mortality. Meanwhile, BMI, diabetes mellitus, SBP, DBP, hemoglobin, sodium, serum albumin, RASIs, BBs, and diuretic were associated with a decreased risk of in-hospital mortality.

In the multivariate analysis, albumin infusion (OR, 1.509; 95% CI: 1.164–1.957; P=0.002), age (OR, 1.020; 95% CI: 1.011–1.028; P<0.001), ethnicity (other; OR, 1.521; 95% CI: 1.205–1.921; P<0.001), cardiac arrhythmias (OR, 1.437; 95% CI: 1.174–1.759; P<0.001), liver disease (OR, 1.507; 95% CI: 1.020–2.227; P=0.040), stroke (OR, 1.915; 95% CI: 1.314–2.789; P=0.001), lactate (OR, 1.105; 95% CI: 1.053–1.160; P<0.001), LVEF (<30%; OR, 1.571; 95% CI: 1.227–2.012; P<0.001), SAPS-II scores (OR, 1.038; 95% CI: 1.031–1.046; P<0.010), vasopressor (OR, 1.358; 95% CI: 1.087–1.697; P=0.007), RRT (OR, 2.642; 95% CI: 1.813–3.852; P<0.001), and ventilation (OR, 1.619; 95% CI: 1.285–2.040; P<0.001) were independently associated with an increased risk of in-hospital mortality, while sodium (OR, 0.979; 95% CI: 0.962–0.996; P=0.017), serum albumin (OR, 0.682; 95% CI: 0.555–0.838; P<0.001), RASIs (OR, 0.514;

Table 1 Baseline characteristics before and after propensity-score matching

Characteristics	Before matching			After matching		
	Non-albumin group (n=2,737)	Albumin group (n=453)	P	Non-albumin group (n=429)	Albumin group (n=429)	P
Gender, n (%)			0.794			0.681
Male	1,432 (52.32)	240 (52.98)		233 (54.31)	227 (52.91)	
Female	1,305 (47.68)	213 (47.02)		196 (45.69)	202 (47.09)	
Age, years	76.22 (64.68–83.60)	72.98 (62.88–81.23)	<0.001	75.06 (62.78–82.81)	73.86 (63.16–81.53)	0.383
Ethnicity, n (%)			0.081			0.167
White	2,035 (74.35)	352 (77.70)		324 (75.52)	332 (77.39)	
Black	204 (7.45)	21 (4.64)		32 (7.46)	19 (4.43)	
Others	498 (18.20)	80 (17.66)		73 (17.02)	78 (18.18)	
BMI, kg/m^2	26.93 (23.19–31.59)	27.76 (24.61–32.57)	0.006			0.355
Comorbidities, n (%)						
Diabetes mellitus	910 (33.25)	166 (36.64)	0.157	135 (31.47)	160 (37.30)	0.072
Hypertension	511 (18.67)	93 (20.53)	0.349	70 (16.32)	88 (20.51)	0.113
AMI	647 (23.64)	88 (19.43)	0.049	95 (22.14)	85 (19.81)	0.402
Cardiac arrhythmias	907 (33.14)	156 (34.44)	0.587	150 (34.96)	147 (34.27)	0.830
Chronic pulmonary disease	674 (24.63)	116 (25.61)	0.654	122 (28.44)	110 (25.64)	0.356
Renal failure	627 (22.91)	115 (25.39)	0.248	93 (21.68)	108 (25.17)	0.227
Liver disease	126 (4.60)	66 (14.57)	<0.001	43 (10.02)	51 (11.89)	0.382
Stroke	152 (5.55)	25 (5.52)	0.976	26 (6.06)	25 (5.83)	0.885
Malignancy	532 (19.44)	119 (26.27)	0.001	113 (26.34)	114 (26.57)	0.938
Vital signs, mmHg						
SBP	119 (103–137)	113 (98–132)	<0.001	117 (100.5–134.5)	113 (98–133)	0.094
DBP	59 (49–71)	57 (48–67)	0.008	59 (50–69)	57 (49–66)	0.069
Laboratory results						
Hemoglobin, g/dL	10.7 (9.5–12)	10.4 (9.2–11.8)	0.001	10.4 (9.4–11.8)	10.5 (9.3–11.8)	0.832
Sodium, mEq/L	139 (136–142)	139 (135–141)	0.005	139 (136–141)	139 (135–141)	0.216
Potassium, mEq/L	4.1 (3.7–4.6)	4.2 (3.8–4.6)	0.175	4.2 (3.7–4.6)	4.2 (3.8–4.6)	0.741
Glucose, mg/dL	128 (103–170)	124 (99–159)	0.017	129 (101.5–175)	123 (100–157)	0.057
SCr, mg/dL	1.2 (0.9–2)	1.2 (0.9–2)	0.650	1.2 (0.8–2.1)	1.2 (0.9–1.9)	0.980
ALT, IU/L	31 (17–72)	26 (14–59)	0.005	30 (16–65)	26 (14–58)	0.096
AST, IU/L	41 (23–93)	41 (23–83)	0.961	44 (24–96.5)	41 (23–83)	0.282
Lactate, mmol/L	1.9 (1.3–2.5)	1.7 (1.2–2.5)	0.016	1.8 (1.3–2.5)	1.7 (1.2–2.4)	0.089
Serum albumin, g/dL	2.9 (2.6–3.2)	2.7 (2.3–3.1)	<0.001	2.7 (2.3–3.1)	2.7 (2.4–3.1)	0.414

Table 1 (*continued*)

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Table 1 *(continued)*

Characteristics	Before matching			After matching		
	Non-albumin group (n=2,737)	Albumin group (n=453)	P	Non-albumin group (n=429)	Albumin group (n=429)	P
LVEF, n (%)			0.017			0.166
>50%	1,226 (44.79)	233 (51.43)		236 (55.01)	216 (50.35)	
40–50%	418 (15.27)	68 (15.01)		56 (13.05)	65 (15.15)	
30–40%	490 (17.90)	79 (17.44)		57 (13.29)	77 (17.95)	
<30%	603 (22.03)	73 (16.11)		80 (18.65)	71 (16.55)	
Scoring system						
SAPS-II	41 (33–50)	46 (36–55)	<0.001	44 (36–56)	46 (36–55)	0.729
SOFA	5 (3–7)	6 (4–9)	<0.001	6 (4–9)	6 (4–9)	0.957
Therapy, n (%)						
RASIs	1,155 (42.02)	147 (32.45)	<0.001	136 (31.70)	147 (34.27)	0.424
MRAs	163 (5.96)	49 (10.82)	<0.001	32 (7.46)	42 (9.79)	0.224
BBs	1,935 (70.70)	374 (82.56)	<0.001	355 (82.75)	354 (82.52)	0.928
Diuretic	1,995 (72.89)	406 (89.62)	<0.001	378 (88.11)	383 (89.28)	0.590
Vasopressor	1,241 (45.34)	327 (72.19)	<0.001	310 (72.26)	303 (70.63)	0.597
RRT	96 (3.51)	69 (15.23)	<0.001	48 (11.19)	50 (11.66)	0.830
Ventilation	1,509 (55.13)	350 (77.26)	<0.001	334 (77.86)	328 (76.46)	0.626

For categorical variables, n (%) is presented. For continuous variables, median [interquartile range (IQR)] is presented. BMI, body mass index; AMI, acute myocardial infarction; SBP, systemic blood pressure; DBP, diastolic blood pressure; SCr, serum creatine; ALT, alanine transaminase; AST, aspartate transaminase; LVEF, left ventricular ejection fraction; SAPS-II, simplified acute physiology score II; SOFA, sequential organ failure assessment; RASIs, renin-angiotensin system inhibitors; MRAs, mineralcorticoid receptor antagonist; BBs, beta-blockers; RRT, renal replacement therapy.
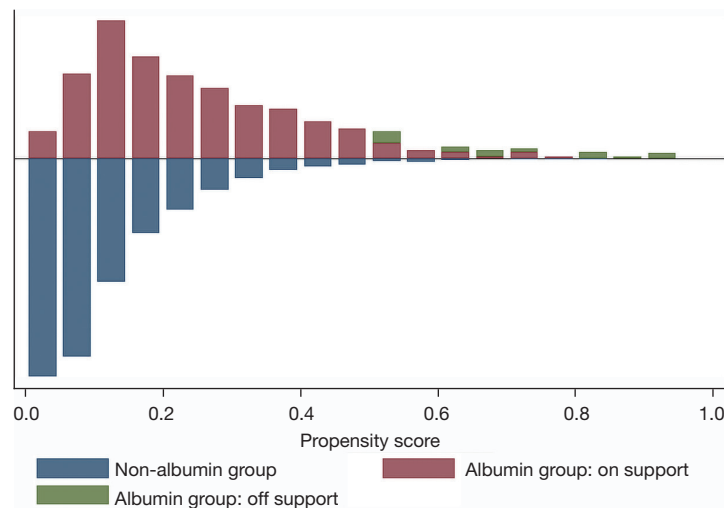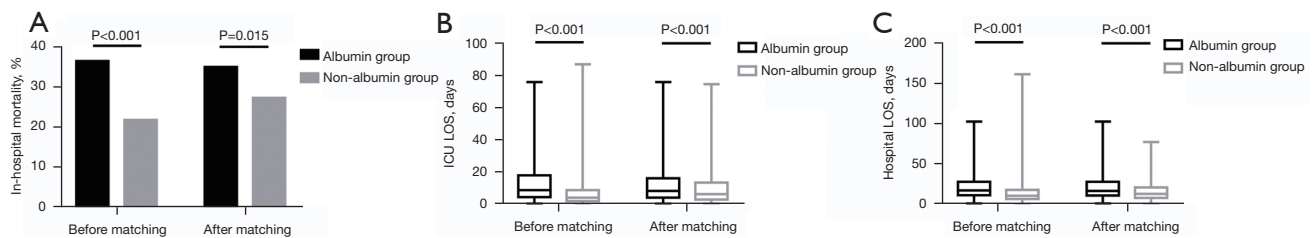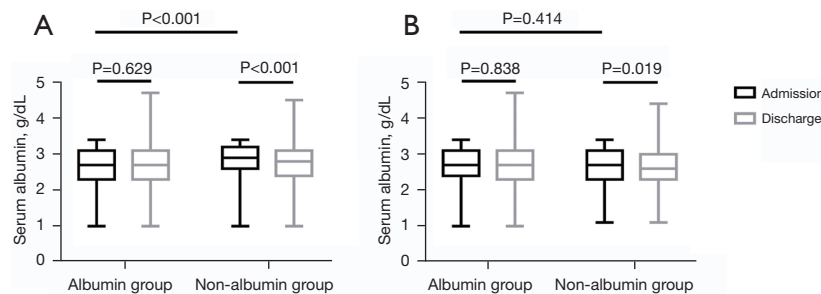

Figure 2 Distributions of patients in the albumin and non-albumin groups after propensity-score matching.

Figure 3 Comparison in outcomes between albumin and non-albumin group. (A) Histogram of in-hospital mortality; (B) boxplot of ICU LOS; (C) boxplot of hospital LOS. ICU, intensive care unit; LOS, length of stay.

Figure 4 Comparison in serum albumin levels between admission and discharge. (A) Boxplot of serum albumin before propensity-score matching; (B) boxplot of serum albumin after propensity-score matching.

95% CI: 0.412–0.640; P<0.001), and BBs (OR, 0.456; 95% CI: 0.368–0.566; P<0.001) were significantly associated with a decreased risk of in-hospital mortality (*Table 3*).

Table 4 shows the results of the logistic regression analysis after PSM. In the univariate analysis, age, liver disease, SCr, lactate, SAPS-II scores, SOFA scores, vasopressor, RRT, ventilation, and albumin infusion were associated with an increased risk of in-hospital mortality. Meanwhile, diabetes mellitus, SBP, DBP, hemoglobin, sodium, serum albumin, RASIs, BBs, and diuretic were associated with a decreased risk of in-hospital mortality.

In the multivariate analysis, albumin infusion (OR, 1.594; 95% CI: 1.143–2.223; P=0.006), age (OR, 1.024; 95% CI: 1.009–1.039; P=0.001), SAPS-II scores (OR, 1.022; 95% CI: 1.005–1.039; P=0.010), SOFA scores (OR, 1.082; 95% CI: 1.014–1.156; P=0.018), and RRT (OR, 3.196; 95% CI: 1.933–5.282; P<0.001) were independently associated with an increased risk of in-hospital mortality, while serum albumin (OR, 0.582; 95% CI: 0.418–0.812; P=0.001), RASIs (OR, 0.525; 95% CI: 0.357–0.773; P=0.001), BBs (OR, 0.331; 95% CI: 0.214–0.512; P<0.001), and diuretic (OR, 0.560; 95% CI: 0.333–0.942; P=0.029) were significantly associated with a decreased risk of in-hospital mortality (*Table 5*).

Discussion

Among the 4,832 patients with serum albumin values, the proportion of patients with overlapping hypoalbuminemia was as high as 66.04% (3,191/4,832), which is higher than that reported in previous studies (4-6). Among the 3,190 eligible patients, the proportion of patients receiving albumin infusion was only 14.20% (453/3,190). Hypoalbuminemia is widespread in ICU patients with CHF. However, due to the absence of evidence, clinicians are cautious about albumin infusion. Therefore, it is particularly important to investigate the impact of albumin infusion on prognosis of ICU patients with CHF-hypoalbuminemia overlap. ICU patients with CHF-hypoalbuminemia overlap. The present real-world PSM study is the first to verify that albumin infusion significantly increased the in-hospital mortality, ICU LOS, and hospital LOS of ICU patients with CHF-hypoalbuminemia overlap, after adjusting for multiple covariates, including age, diabetes mellitus, liver disease, SBP, DBP, hemoglobin, sodium, SCr, lactate, serum albumin, SAPS-II scores, SOFA scores, RASIs, BBs, diuretic, vasopressor, RRT, and ventilation.

HF is a complex clinical syndrome caused by structural or functional impairment of ventricular filling or ejection

Table 2 Univariate logistic regression analysis before propensity-score matching

Variables	P	OR	95% CIs	
			Lower	Upper
Age	<0.001	1.019	1.012	1.025
Ethnicity				
White	Ref.	Ref.	Ref.	Ref.
Black	0.098	0.741	0.520	1.057
Other	<0.001	1.588	1.301	1.940
BMI	0.082	0.990	0.980	1.001
Diabetes mellitus	0.008	0.789	0.662	0.941
Cardiac arrhythmias	0.001	1.325	1.119	1.570
Liver disease	0.002	1.648	1.206	2.250
Stroke	0.003	1.643	1.189	2.271
SBP	<0.001	0.994	0.991	0.997
DBP	<0.001	0.990	0.985	0.995
Hemoglobin	0.035	0.955	0.915	0.997
Sodium	0.092	0.987	0.971	1.002
Potassium	0.093	1.094	0.985	1.214
SCr	0.036	1.052	1.003	1.103
ALT	0.022	1.000	1.000	1.000
AST	0.018	1.000	1.000	1.000
Lactate	<0.001	1.225	1.174	1.278
Serum albumin	<0.001	0.446	0.374	0.531
LVEF				
>55	Ref.	Ref.	Ref.	Ref.
40–55	0.855	0.977	0.762	1.253
30–40	0.276	1.135	0.903	1.426
<30	<0.001	1.469	1.194	1.806
SAPS-II	<0.001	1.062	1.055	1.069
SOFA	<0.001	1.226	1.195	1.258
RASIs	<0.001	0.344	0.286	0.415
BBs	<0.001	0.402	0.339	0.478
Diuretic	<0.001	0.584	0.489	0.699
Vasopressor	<0.001	2.919	2.455	3.470
RRT	<0.001	5.492	3.972	7.592
Ventilation	<0.001	2.492	2.081	2.985

Table 2 (*continued*)

Table 2 (*continued*)

Variables	P	OR	95% CIs	
			Lower	Upper
Albumin infusion	<0.001	2.054	1.662	2.538

OR, odds ratio; CI, confidence interval; BMI, body mass index; SBP, systemic blood pressure; DBP, diastolic blood pressure; SCr, serum creatine; ALT, alanine transaminase; AST, aspartate transaminase; LVEF, left ventricular ejection fraction; SAPS-II, simplified acute physiology score II; SOFA, sequential organ failure assessment; RASIs, renin-angiotensin system inhibitors; BBs, beta-blockers; RRT, renal replacement therapy.

of blood and is characterized by pulmonary and peripheral circulation congestion (25). Chronic peripheral circulation congestion can impair liver and kidney function, which inhibits albumin synthesis and promotes albumin loss. Meanwhile, peripheral circulation congestion increases hydrostatic venous pressure, which in turn increases vascular endothelial permeability, leading to albumin escape to the extravascular space through the venous end of the microvasculature (26). In addition, intestinal congestion not only increases albumin enteric losses (27) but also reduces the absorption of nutrients and leads to malnutrition, which inhibits albumin synthesis (28). HF is a systemic inflammatory disease in which activated monocytes promote the release of IL (interleukin)-1, IL-6, and TNF (tumor necrosis factor)-α (29). These cytokines not only act against the hepatic synthesis of albumin but also increase vascular endothelial permeability and albumin escape (28,30). Low serum albumin is a downstream biomarker of HF syndrome severity but is not a determinant of poorer prognosis. Zhuang *et al.* found that serum albumin is inversely associated with the occurrence of HF; however, Mendelian randomization analyses did not show evidence of serum albumin in the etiology of HF (31). This partially supports our view, especially given the absence of etiological studies of low albumin and HF prognosis.

Human albumin is used to correct hypoalbuminemia, volume expansion, and resuscitation (18). In practice, clinicians are cautious about albumin infusion. Clinicians may prescribe albumin infusion for patients with severe hypoalbuminemia or severe edema. However, Margarson *et al.* found that a 20% albumin infusion in sepsis patients led to a significantly faster decrease in serum albumin compared with healthy controls (32). Lewis *et al.* reported that due to the increased vascular endothelial

Table 3 Multivariate logistic regression analysis before propensity-score matching

Variables	P	OR	95% CIs	
			Lower	Upper
Age	<0.001	1.020	1.011	1.028
Ethnicity				
White	Ref.	Ref.	Ref.	Ref.
Black	0.594	0.893	0.589	1.355
Other	0.000	1.521	1.205	1.921
Cardiac arrhythmias	<0.001	1.437	1.174	1.759
Liver disease	0.040	1.507	1.020	2.227
Stroke	0.001	1.915	1.314	2.789
Sodium	0.017	0.979	0.962	0.996
Lactate	<0.001	1.105	1.053	1.160
Serum albumin	<0.001	0.682	0.555	0.838
LVEF				
>55	Ref.	Ref.	Ref.	Ref.
40–55	0.694	0.945	0.711	1.255
30–40	0.164	1.206	0.926	1.571
<30	<0.001	1.571	1.227	2.012
SAPS-II	<0.001	1.038	1.031	1.046
RASIs	<0.001	0.514	0.412	0.640
BBs	<0.001	0.456	0.368	0.566
Vasopressor	0.007	1.358	1.087	1.697
RRT	<0.001	2.642	1.813	3.852
Ventilation	<0.001	1.619	1.285	2.040
Albumin infusion	0.002	1.509	1.164	1.957

OR, odds ratio; CI, confidence interval; LVEF, left ventricular ejection fraction; SAPS-II, simplified acute physiology score II; RASIs, renin-angiotensin system inhibitors; BBs, beta-blockers; RRT, renal replacement therapy.

Table 4 Univariate logistic regression analysis after propensity-score matching

Variables	P	OR	95% CIs	
			Lower	Upper
Age	0.011	1.015	1.003	1.026
Diabetes mellitus	0.033	0.711	0.520	0.972
Liver disease	0.069	1.507	0.969	2.344
SBP	0.006	0.992	0.986	0.998
DBP	0.004	0.986	0.977	0.996
Hemoglobin	0.006	0.896	0.829	0.969
Sodium	0.080	0.975	0.948	1.003
SCr	0.009	1.138	1.034	1.254
Lactate	<0.001	1.249	1.145	1.362
Serum albumin	<0.001	0.512	0.383	0.684
SAPS-II	<0.001	1.049	1.038	1.061
SOFA	<0.001	1.216	1.163	1.271
RASIs	<0.001	0.377	0.267	0.532
BBs	<0.001	0.234	0.162	0.338
Diuretic	<0.001	0.242	0.156	0.375
Vasopressor	<0.001	2.070	1.458	2.937
RRT	<0.001	4.015	2.599	6.201
Ventilation	0.009	1.634	1.131	2.360
Albumin infusion	0.015	1.434	1.072	1.917

OR, odds ratio; CI, confidence interval; SBP, systemic blood pressure; DBP, diastolic blood pressure; SCr, serum creatine; SAPS-II, simplified acute physiology score II; SOFA, sequential organ failure assessment; RASIs, renin-angiotensin system inhibitors; BBs, beta-blockers; RRT, renal replacement therapy.

permeability, the formation of edema was governed more by hydrostatic venous pressure than colloid oncotic pressure (33). Therefore, the impact of albumin infusion on hypoalbuminemia and edema is uncertain, but it will increase the workload of the heart, which may explain the results of our study.

For ICU patients with CHF-hypoalbuminemia overlap, treatment of upstream pathological processes such as congestion, inflammation, and malnutrition is crucial. Diuretics can alleviate congestion and reduce the transcapillary escape rate of albumin (26). RASIs, BBs, and omega-3 polyunsaturated acids may attenuate the inflammatory responses in HF patients (34-36). Exogenous amino acid supplementation may be a better option for correcting malnutrition (37).

Limitations

Our study also had shortcomings that should be noted. Firstly, this was a retrospective cohort study; we demonstrated a correlation between exposure and outcome, but not causation. Secondly, our study was based on the

Table 5 Multivariate logistic regression analysis after propensity-score matching

Variables	P	OR	95% CIs	
			Lower	Upper
Age	0.001	1.024	1.009	1.039
Serum albumin	0.001	0.582	0.418	0.812
SAPS-II	0.010	1.022	1.005	1.039
SOFA	0.018	1.082	1.014	1.156
RASIs	0.001	0.525	0.357	0.773
BBs	<0.001	0.331	0.214	0.512
Diuretic	0.029	0.560	0.333	0.942
RRT	<0.001	3.196	1.933	5.282
Albumin infusion	0.006	1.594	1.143	2.223

OR, odds ratio; CI, confidence interval; SAPS-II, simplified acute physiology score II; SOFA, sequential organ failure assessment; RASIs, renin-angiotensin system inhibitors; BBs, beta-blockers; RRT, renal replacement therapy.

MIMIC database, from which the opportunity and dose of albumin infusion were difficult to confirm. This affected our assessment of the impact of albumin infusion. Finally, BNP (brain natriuretic polypeptide) and pro-BNP were excluded from our analysis due to their missing values being more than 50%, which may have affected the reliability and accuracy of our results.

Conclusions

Low serum albumin is a downstream biomarker of HF syndrome severity but is not a determinant of poorer prognosis. Albumin infusion increased the in-hospital mortality, ICU LOS, and hospital LOS in ICU patients with CHF-hypoalbuminemia overlap.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-648/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-648/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

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