The association between serum albumia and length of stay of intensive care units in patients with heart failure

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Abstract

Objective: To assess the relationship between serum albumia and length of stay (LOS) of the intensive care units (ICUs).

Design and Participants: we retrospectively analyze 2843 patients from the medical information mart for intensive care III (the MIMIC-III) database.

Materials and Methods: The exposure variable of the present study was serum albumia, which was defined as serum albumia level at the time of admission to ICUs. The outcome variable was LOS of ICUs. The final models were established by multivariate linear regression, and trend test and smooth fitting curves were used to evaluate the association between serum albumia level and LOS of ICUs. The subgroups were conducted based on age, sex and body mass index (BMI).

Results: Higher serum albumia level can reduce LOS of ICUs in patients with heart failure (HF) than lower serum albumia level (β: -1.18; 95%CI: -1.50, -0.86; *P* <0.001). Trend test and smooth curve fittings suggested that LOS of ICUs was gradually shorten when serum albumia level was gradually increased. The subgroups based on age, sex and BMI demonstrated similar results between serum albumia level and LOS of ICUs.

Conclusion: The negative correlation between serum albumia level and LOS of ICUs among patients with HF was found. High serum albumia level might reduce LOS of ICUs in patients with HF, and the conclusion might guide clinical treatments and judge prognosis.

1. Introduction

As a common and growing medical problem, heart failure(HF) is one of the most frequent causes of admission and hospital mortality. The limitation of options for the management of patients with HF lead to long hospital length of stays (LOS). Especially, some patients with HF in the intensive care units(ICUs) might have many underlying diseases, which might lead to longer hospital staying time. As a major problem of cardiovascular disease, HF not only seriously affects the quality of life of patients, but also weighs their economic burden. Therefore, it is essential for us to pay more attention to hospital LOS.

As an inexpensive and powerful indicator, serum albumia is an essential protein in the human body produced by the liver, and often used to evaluate the prognosis of a variety of diseases, such as HF, acute pulmonary embolism, diabetic nephropath and patients with severe illness in ICUs. Previous studies had shown that serum albumia was powerful indicators to short-term and long-term prognosis of patients with HF. Whether chronic heart failure (CHF) or acute heart failure (AHF) patients, high albumin levels would significantly reduce their hospital mortality and rehospitalization. However, there were few studies on whether serum albumia level affects the hospital LOS in patients with HF. Hypoalbuminemia often occurs in ICUs, and it is closely related to the longer LOS. Although high albumia level might reduce LOS of patients in ICUs, a specific association was not revealed between albumia level and the hospital

LOS of patients with HF in ICUs, and previous studies were not analyzed at the subgroup. Thus, it is difficult to apply albumia level as a predictive indicator for LOS of patients with HF in ICUs to clinical practice.

Therefore, it is necessary to reassess the relationship between serum albumia and the hospital LOS in patients with HF, especially patients with HF in ICUs. In the present study, we analyzed the association between serum albumia level and LOS of ICUs in patients with HF from the medical information mart for intensive care III (the MIMIC-III) database, and we conducted a subgroup analysis of the relationship between serum albumia levels and LOS of ICUs under different age, genders and body mass index((BMI). In particular, the trend relationship between albumia level and LOS of ICUs was explained.

2. Materials And Methods

2.1 Database introduction and data sources

As a large, single-center database containing 53423 patients from 2001 to 2012 and 7870 neonates admitted from 2001 to 2008, The MIMIC-III database was maintained by the laboratory for computational physiology at the Massachusetts Institute of Technology. The institutional review boards of the Massachusetts Institute of Technology and Beth Israel Deaconess Medical Center approved the establishment of the database, and Requirement for individual patient consent was waived because the database establishment did not impact clinical care and all protected health information was deidentified . All methods were conducted in accordance with the relevant guidelines and regulations. The data provided by the above database was the original data. Thus, data used for this study was retrieved from MIMIC-III by author Liu (ID: 9008147), who had completed the online training course of the National Institutes (the CITI certificate had be uploaded to the supplementary file). The baseline data of this article was from 2001 to 2012 MIMIC-III database for patients with acute heart failure or chronic decompensated heart failure who are older than 18 years old.

2.2 Populations

We collected 9263 patients with HF in MIMIC-III, and these patients all had been diagnosed with acute heart failure and chronic decompensated heart failure during ICUs, of which 4342 were excluded because albumia levels were not measured during ICUs stay, 2078 of the remaining 4921 were excluded because of insufficient data. Patients who were pregnant or younger than 18 years old and stayed in ICUs less than 24 hours were also excluded. Finally, 2843 admissions were included in the present study.

2.3 Variables

The exposure variable of the present study was serum albumia, which was defined as serum albumia level at the time of admission to ICUs. The outcome variable was LOS of ICUs. Categorical variables [including gender, ethnicity, first care unit, admission type, diabete, hypertnsion, coronary artery atherosclerosis, chronic obstructive pulmonary disease(COPD), atrial fibrillation(AF), myocardial infarction(MI), pneumonia, liver disease, respiratory failure, stroke and chronic renal disease] and continuous covariates [including age, BMI and sequential organ failure assessmen(SOFA) socre] were analyzed in the present study.

2.4 Statistical analysis

Continuous variables were represented by mean ± standard deviation or median (25th quartile, 75th quartile) in the table. If the test of normality and the homogeneity test of variance are performed, the T test is appropriate, otherwise, the Kruskal Wallis test is appropriate. Categorical variables are presented as a percentage in the tables and compared using the X^2 test. Multivariate linear regression with significant difference of 0.05 was used to build the final models. The subgroup analysis was performed by stratified multivariate linear regression analysis under different age, sex and BMI. Trend test and smooth fitting curves were used to evaluate the association between serum albumia level and LOS of ICUs. All statistical analyses were performed using the software Stata15. All P value < 0.05 was significant.

3 Results

3.1 Baseline characteristics

The mean age of 2843 patients were 70.95 ± 13.51, and men made up 57.58% of the total. All patients were grouped by the interquartile range of average serum albumia levels($1.1 \le Q1 < 3.1$; $3.1 \le Q2 < 3.5$; $3.5 \le Q3 < 3.9$; $3.9 \le Q4 \le 5.1$) during the ICUs (Table 1). Except BMI and stroke ($P > 0.05$), all variables were significant ($P < 0.05$).

Table 1
Clinical characteristics

Variables	Total	Q1(1.1≤,<3.1)	Q2(3.1≤,<3.5)	Q3(3.5≤,<3.9)	Q4(3.9≤,≤5.1)	*P* value
age	70.95 ± 13.51	70.51 ± 13.88	71.54 ± 14.40	71.93 ± 12.80	70.01 ± 13.14	0.010
gender						0.008
female	1206 (42.42%)	294 (46.67%)	266 (44.04%)	318 (42.51%)	328 (38.10%)	
male	1637 (57.58%)	336 (53.33%)	338 (55.96%)	430 (57.49%)	533 (61.90%)	
ethnicity						0.009
white	2048 (72.04%)	424 (67.30%)	436 (72.19%)	531 (70.99%)	657 (76.31%)	
black	186 (6.54%)	53 (8.41%)	40 (6.62%)	41 (5.48%)	52 (6.04%)	
asian	45 (1.58%)	8 (1.27%)	8 (1.32%)	17 (2.27%)	12 (1.39%)	
other	564 (19.84%)	145 (23.02%)	120 (19.87%)	159 (21.26%)	140 (16.26%)	
BMI	27.91 ± 5.73	27.92 ± 5.98	27.47 ± 5.70	28.16 ± 5.68	28.00 ± 5.59	0.090
first care unit						< 0.001
CSRU	1089 (38.30%)	96 (15.24%)	168 (27.81%)	306 (40.91%)	519 (60.28%)	
CCU	763 (26.84%)	138 (21.90%)	199 (32.95%)	246 (32.89%)	180 (20.91%)	
SICU	169 (5.94%)	69 (10.95%)	36 (5.96%)	33 (4.41%)	31 (3.60%)	
MICU	719 (25.29%)	293 (46.51%)	179 (29.64%)	140 (18.72%)	107 (12.43%)	
TSICU	103 (3.62%)	34 (5.40%)	22 (3.64%)	23 (3.07%)	24 (2.79%)	
admission type						< 0.001
emergency	2195 (77.21%)	546 (86.67%)	540 (89.40%)	597 (79.81%)	512 (59.47%)	

Variables	Total	Q1(1.1≤, <3.1)	Q2(3.1≤, <3.5)	Q3(3.5≤, <3.9)	Q4(3.9≤,≤5.1)	*P* value
elective	529 (18.61%)	44 (6.98%)	43 (7.12%)	112 (14.97%)	330 (38.33%)	
urgent	119 (4.19%)	40 (6.35%)	21 (3.48%)	39 (5.21%)	19 (2.21%)	
diabete						0.010
No	1815 (63.84%)	417 (66.19%)	372 (61.59%)	449 (60.03%)	577 (67.02%)	
Yes	1028 (36.16%)	213 (33.81%)	232 (38.41%)	299 (39.97%)	284 (32.98%)	
hypertension						< 0.001
No	1664 (58.53%)	432 (68.57%)	375 (62.09%)	442 (59.09%)	415 (48.20%)	
Yes	1179 (41.47%)	198 (31.43%)	229 (37.91%)	306 (40.91%)	446 (51.80%)	
coronary artery atherosclerosis						< 0.001
No	1444 (50.79%)	428 (67.94%)	313 (51.82%)	312 (41.71%)	391 (45.41%)	
Yes	1399 (49.21%)	202 (32.06%)	291 (48.18%)	436 (58.29%)	470 (54.59%)	
COPD						0.041
No	2758 (97.01%)	606 (96.19%)	579 (95.86%)	728 (97.33%)	845 (98.14%)	
Yes	85 (2.99%)	24 (3.81%)	25 (4.14%)	20 (2.67%)	16 (1.86%)	
atrial fibrillation						< 0.001
No	1495 (52.59%)	374 (59.37%)	327 (54.14%)	389 (52.01%)	405 (47.04%)	
Yes	1348 (47.41%)	256 (40.63%)	277 (45.86%)	359 (47.99%)	456 (52.96%)	
myocardial infarction						< 0.001
No	2599 (91.42%)	582 (92.38%)	536 (88.74%)	670 (89.57%)	811 (94.19%)	

Variables	Total	Q1(1.1≤, <3.1)	Q2(3.1≤, <3.5)	Q3(3.5≤, <3.9)	Q4(3.9≤,≤5.1)	*P* value
Yes	244 (8.58%)	48 (7.62%)	68 (11.26%)	78 (10.43%)	50 (5.81%)	
pneumonia						< 0.001
No	2286 (80.41%)	440 (69.84%)	460 (76.16%)	625 (83.56%)	761 (88.39%)	
Yes	557 (19.59%)	190 (30.16%)	144 (23.84%)	123 (16.44%)	100 (11.61%)	
liver disease						0.013
No	2824 (99.33%)	621 (98.57%)	598 (99.01%)	746 (99.73%)	859 (99.77%)	
Yes	19 (0.67%)	9 (1.43%)	6 (0.99%)	2 (0.27%)	2 (0.23%)	
respiratory failure						< 0.001
No	2200 (77.38%)	375 (59.52%)	434 (71.85%)	622 (83.16%)	769 (89.31%)	
Yes	643 (22.62%)	255 (40.48%)	170 (28.15%)	126 (16.84%)	92 (10.69%)	
stroke						0.201
No	2672 (93.99%)	588 (93.33%)	561 (92.88%)	714 (95.45%)	809 (93.96%)	
Yes	171 (6.01%)	42 (6.67%)	43 (7.12%)	34 (4.55%)	52 (6.04%)	
Chronic renal disease						0.010
No	2221 (78.12%)	472 (74.92%)	460 (76.16%)	586 (78.34%)	703 (81.65%)	
Yes	622 (21.88%)	158 (25.08%)	144 (23.84%)	162 (21.66%)	158 (18.35%)	
SOFA score	5.70 ± 3.17	6.65 ± 3.63	5.49 ± 3.24	5.39 ± 2.97	5.43 ± 2.76	< 0.001
LOS of ICUs	4.13 (2.20–7.05)	6.07 (3.07–9.75)	4.69 (2.70–7.26)	4.07 (2.15–6.15)	3.15 (1.97–5.01)	< 0.001

Variables	Total	Q1(1.1≤, <3.1)	Q2(3.1≤, <3.5)	Q3(3.5≤, <3.9)	Q4(3.9≤,≤5.1)	*P* value

Mean ± standard deviation or median(25th quartile, 75th quartile) for continuous variables.

Percent for categorical variables.

LOS of ICUs, length of stay of the intensive care units; BMI, body mass index; CSRU, cardiac surgical intensive care unit; CCU, coronary care unit; SICU, surgical intensive care unit; MICU, medical intensive care unit; TSICU, traumatic surgical Intensive care unit; COPD, chronic obstructive pulmonary disease; SOFA score, sequential organ failure assessment score.

3.2 Analysis of association between serum albumia and LOS of ICUs

In unadjusted linear regression model, higher serum albumia level can reduce LOS of ICUs in patients with HF than lower serum albumia level (β: -2.11; 95%CI: -2.41, -1.81; $P < 0.001$). After adjusting for age, gender and ethnicity (Model I), the above association was also significant(β: -2.12; 95%CI: -2.42, -1.81; $P < 0.001$). After adjusting all the variables (Model II), the value of serum albumia was still significant (β: -1.18; 95%CI: -1.50, -0.86; $P < 0.001$). Finally, trend test based on the interquartile of serum albumia level showed LOS of ICUs of patient with HF was gradually shortened when serum albumia level was gradually increased (P for trend < 0.001) (Table 2 and **Fig. 1**).

Table 2
Association of serum albumia level with length of stay of the intensive care units.

Exposure	unadjusted model	Model I	Model II
	β (95%CI) *P* value	β (95%CI) *P* value	β (95%CI) *P* value
albumia	-2.11 (-2.41, -1.81) < 0.001	-2.12 (-2.42, -1.81) < 0.001	-1.18 (-1.50, -0.86) < 0.001
albumia			
Q1	1.0	1.0	1.0
Q2	-1.67 (-2.25, -1.09) < 0.001	-1.66 (-2.24, -1.08) < 0.001	-0.98 (-1.53, -0.44) < 0.001
Q3	-2.56 (-3.11, -2.01) < 0.001	-2.56 (-3.11, -2.01) < 0.001	-1.37 (-1.90, -0.83) < 0.001
Q4	-3.44 (-3.97, -2.90) < 0.001	-3.44 (-3.97, -2.91) < 0.001	-1.83 (-2.38, -1.28) < 0.001
P for trend	< 0.001	< 0.001	< 0.001

CI, confidence interval

unadjusted model: None was adjusted.

Model I: age, gender and ethnicity were adjusted.

Model II: Age, gender, ethnicity, body mass index, first care unit, admission type,

diabete, hypertension, coronary artery atherosclerosis, chronic obstructive pulmonary disease, atrial fibrillation, myocardial infarction, pneumonia, liver disease, respiratory failure, stroke and chronic renal disease and sequential organ failure assessment score were adjusted.

3.3 Subgroup analysis of association between serum albumia and LOS of ICUs

The present study based on subgroup analysis of age, gender and BMI showed that the relationship between serum albumia level and LOS of ICUs was still significant. By comparing the correlation between serum albumia level and LOS of ICUs, different subgroups for age < 60 years old(β: -1.53; 95%CI: -2.19, -0.88; $P < 0.001$) and age ≥ 60 years old groups (β: -1.07; 95%CI: -1.43, -0.71; $P < 0.001$), female (β: -1.25; 95%CI: -1.72, -0.77; $P < 0.001$) and male groups (β: -1.13; 95%CI: -1.57, -0.70; $P < 0.001$), BMI < 30kg/m^2 (β: -1.23; 95%CI: -1.62, -0.85; $P < 0.001$) and BMI ≥ 30kg/m^2 groups (β: -1.12; 95%CI: -1.70, -0.54; $P < 0.001$) were all negative correlation (Table 3). Smooth curve fittings based on subgroup of age, sex and BMI showed linear relationship between serum albumia level and LOS of ICUs. When serum albumia level was gradually increased, LOS of ICUs was gradually shorten (**Fig. 2**).

Table 3
Association between serum albumia level with length of stay of the intensive care units in the subgroup analysis stratified by age, gender and BMI.

Exposure	Unadjusted model	Model I	Model II
	β (95%CI) *P* value	β (95%CI) *P* value	β (95%CI) *P* value
Age			
< 60	-2.69 (-3.29, -2.09) < 0.001	-2.68 (-3.28, -2.08) < 0.001	-1.53 (-2.19, -0.88) < 0.001
≥ 60	-1.93 (-2.28, -1.58) < 0.001	-1.94 (-2.29, -1.59) < 0.001	-1.07 (-1.43, -0.71) < 0.001
Gender			
female	-2.16 (-2.62, -1.70) < 0.001	-2.15 (-2.61, -1.69) < 0.001	-1.25 (-1.72, -0.77) < 0.001
male	-2.09 (-2.49, -1.68) < 0.001	-2.08 (-2.48, -1.67) < 0.001	-1.13 (-1.57, -0.70) < 0.001
BMI			
< 30 kg/m2	-2.03 (-2.40, -1.67) < 0.001	-2.06 (-2.42, -1.69) < 0.001	-1.23 (-1.62, -0.85) < 0.001
≥ 30 kg/m2	-2.28 (-2.82, -1.74) < 0.001	-2.28 (-2.82, -1.74) < 0.001	-1.12 (-1.70, -0.54) < 0.001

CI, confidence interval

unadjusted model: None was adjusted.

Model I: age, gender and ethnicity were adjusted.

Model II: Age, gender, ethnicity, body mass index, first care unit, admission

type, diabete, hypertension, coronary artery atherosclerosis, chronic obstructive pulmonary disease, atrial fibrillation, myocardial infarction, pneumonia, liver disease, respiratort failure, stroke and chronic renal disease and sequential organ failure assessment score were adjusted.

4. Discussion

In the present study, multivariate linear regression analysis showed that serum albumia level was closely related to LOS of ICUs. Trend test and smooth curve fittings suggested that LOS of ICUs was gradually shorten when serum albumia level was gradually increased. The above relationships was also found in subgroup of age, sex and BMI.

The nutritional status of patients with HF in ICUs significantly affects their prognosis and LOS of ICUs. Albumia not only maintains the colloidal osmotic pressure, but also plays an important role in their nutritional status. Hypoalbuminemia, occurred commonly in patients with HF in ICUs, might be related to their poorer heart function and more underlying diseases, and it could result in serious adverse events. Previous studies showed that hypoalbuminemia significantly affected prognosis and LOS of various diseases, such as patients for acute decompensated HF with preserved ejection fraction, acute decompensated chronic obstructive pulmonary disease and requiring surgery.[□□□□] In the present study, linear relationships between serum albumia level and LOS of ICUs of patients with HF was found, and elevation of serum albumia level could reduce the LOS of ICUs.

Currently, several studies had suggested that serum albumia level < 3.5g/dL was an independent risk factor for prolonged LOS of ICUs,[13][14] but the present study found that LOS of ICUs was gradually shorten when serum albumia level was gradually increased, and the above relationship was also showed in subgroup based on age, sex and BMI. In the past studies, age not only was an independent risk factor for mortality of various diseases, but also determined the length of their hospital stay, and with age increasing, the length of hospital stay was prolonged. The elderly often had multiple organ failure, which lead to poor prognosis and long length of hospital stay. Especially some patients with HF in ICUs, not only having poor heart function, but also presenting other serious underlying diseases. Similar to age, sex difference had also different influence on patients with HF in ICUs. Systolic blood pressure could increase the heart load of patients who had severe diseases, especially patients with HF, which could have an adverse influence on their prognosis and prolong the length of hospital stay. Compared with men, female had higher systolic blood pressure, and as patients grew older, female could have heavier arteriosclerosis. Severe coronary arteriosclerosis reduced blood supply of heart, and made prognosis of patients with HF worse. Unlike gender and age, high BMI might be protective factor for patients in ICUs. Although the above opinion has been controversial, most current studies supported this opinion. Mukhopadhyay, et al. analyzed 273 patients in ICUs that high BMI was associated with low mortality and long LOS of ICUs. It could be seen from the above that age, gender and BMI could affect the length of hospital stay to a certain degree. In order to further analyze whether the above three variables had an impact on the relationship between serum albumin level and LOS of ICUs, we conducted subgroup analysis based on the above three variables in the present study, and found that associations of serum albumia level for LOS of ICUs were all negative correlation in subgroups.

Patients with HF in ICUs might had poor prognosis and long LOS of ICUs because of poor nutritional status and high inflammatory status. Indeed, albumia were association with malnutrition and inflammatory factors, this might be an explanation for association between LOS of ICUs and serum albumia level. The present study found that high serum albumia level was protective factor for patients with HF in ICUs, and the result could guide clinicians to reduce LOS of ICUs by changing albumin levels. However, our study also have some limitations. Firstly, the study was a single-center retrospective design, the numbers of patients included are not large, and the selected population is relatively limited, therefore, it might has selection bias, and a multicenter study needs to be conducted to confirm these findings. Secondly, we excluded populations who were younger than 18 years, because big differences were seen in serum albumin levels between adults and minors. Finally, we might not adjust other potential confounding factors.

5. Conclusion

The negative correlation between serum albumia level and LOS of ICUs among patients with HF was found. High serum albumia level might reduce LOS of ICUs in patients with HF, and the conclusion might guide clinical treatments and judge prognosis.

Declarations

Contributors: TL was mainly responsible for extraction of data and writing of the manuscript, LLW, XQL, ZHL, ZXT, HCX and CFW was responsible for data processing and collection; JHC was responsible for reviewing the literature; TDX and DYL contributed to their support and guidance in article design and writing.

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Competing interests: None declared.

Ethics approval: The institutional review boards of the Massachusetts Institute of Technology and Beth Israel Deaconess Medical Center approved the establishment of the database and Requirement for individual patient consent was waived because the database establishment did not impact clinical care and all protected health information was deidentified.

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Figures

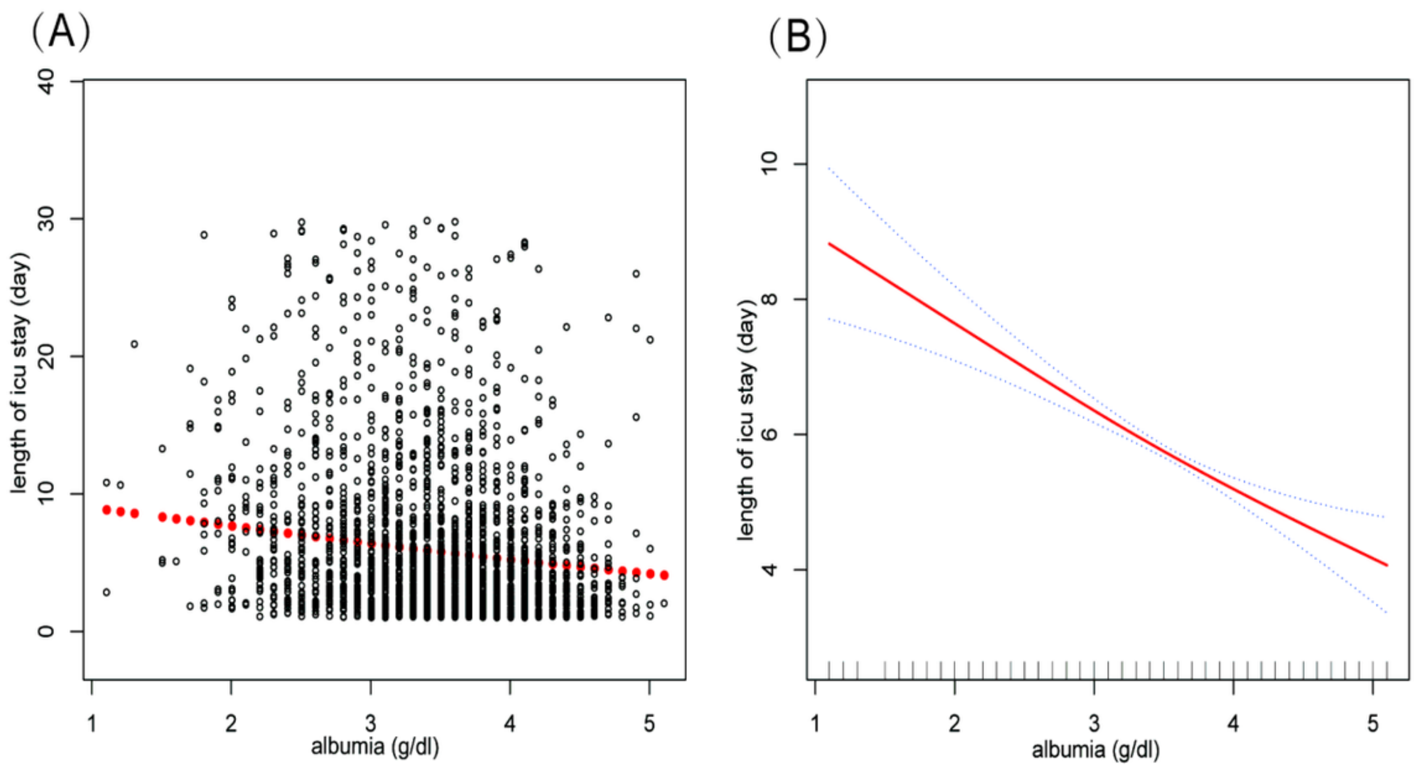

Figure 1

The association between serum albumia level with length of stay of the intensive care units. (A):Each black point represents a patient with heart failure in the intensive care units. (B)The upper and lower blue dashed lines represent 95% CI of serum albumia level. A continuous red line indicates the level of serum albumia. Age, gender, ethnicity, body mass index, first care unit, admission type, diabete, hypertension, coronary artery atherosclerosis, chronic obstructive pulmonary disease, atrial fibrillation, myocardial infarction, pneumonia, liver disease, respiratort failure, stroke and chronic renal disease and sequential organ failure assessment score were adjusted.

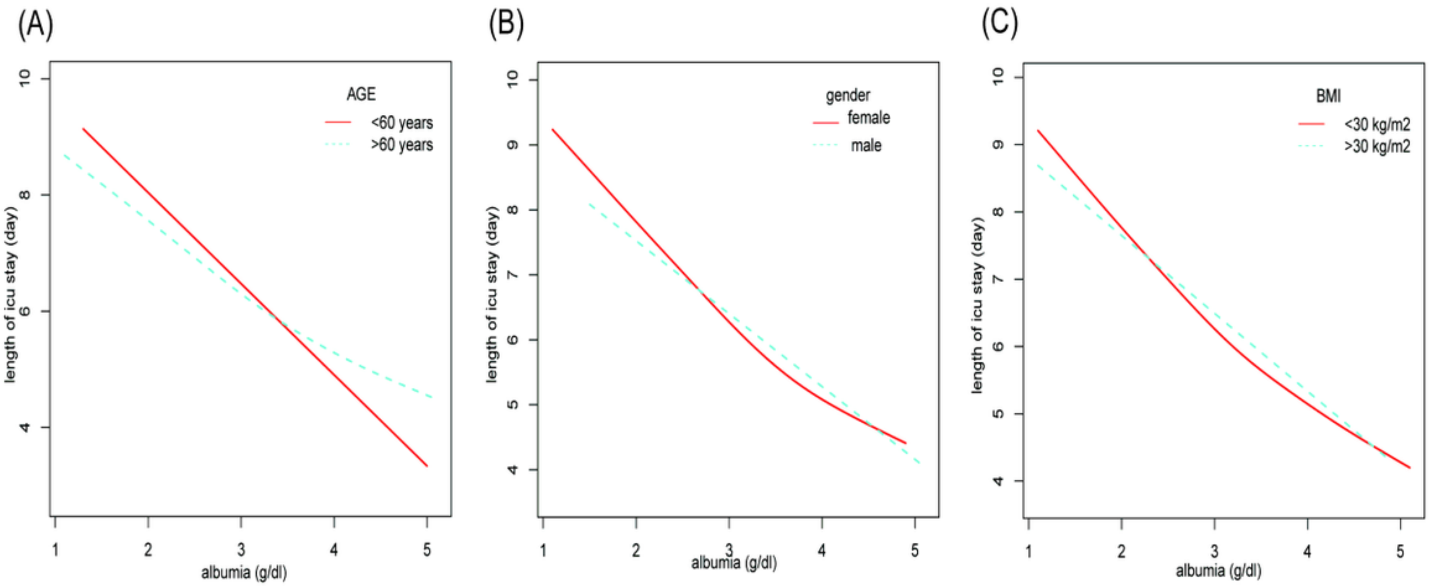

Figure 2

The association between serum albumia levle and length of stay of the intensive care units stratified by age gender and body mass index. Age, gender, ethnicity, body mass index, first care unit, admission type, diabete, hypertension, coronary artery atherosclerosis, chronic obstructive pulmonary disease, atrial fibrillation, myocardial infarction, pneumonia, liver disease, respiratort failure, stroke and chronic renal disease and sequential organ failure assessment score were adjusted.

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