Association Between Albumin-Bilirubin Score at Admission and In-Hospital Mortality in Patients with Acute Heart Failure

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Summary

Liver dysfunction is one of the most recognized complications in patients with acute heart failure (HF) and therefore a liver function score may be useful for risk-stratification in those patients. Recently, the albumin-bilirubin (ALBI) score was developed as a new model to assess liver function in liver disease. We explored the association between the ALBI score at admission and in-hospital mortality in patients with acute HF.

We enrolled 262 patients (median age, 86 years, 137 males) who were admitted to our hospital for treatment of acute HF. The following data were recorded: vital signs, laboratory data including B-type natriuretic peptide (BNP) level, echocardiographic data at admission, demographic and clinical characteristics, and treatment and prognostic information. The Get With the Guidelines-Heart Failure (GWTG-HF) risk score was calculated as an established risk model for each patient. The primary outcome was all-cause in-hospital mortality.

During hospitalization, 37 patients (14.1%) died. The in-hospital mortality rate was significantly higher in patients with ALBI scores > -2.25 compared with patients with ALBI scores ≤ -2.25 (21.1% versus 4.5%, respectively; $P = 0.0001$). Multivariate analysis revealed that the GWTG-HF score (odds ratio [OR] 1.16, 95% confidence interval [CI] 1.08-1.25, $P < 0.0001$), BNP level (OR 1.0007, 95% CI 1.0003-1.001, $P = 0.0003$) and ALBI score (OR 6.0, 95% CI 1.8-19.6, $P = 0.0017$) were independently associated with in-hospital mortality.

Our results indicated that the ALBI score was independently associated with in-hospital mortality in patients hospitalized for acute HF.

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Key words: Liver function marker, Prognosis

Heart failure (HF) is a major cause of death among elderly individuals in many countries. Since Japan and many Western countries have entered an era of an ultra-aging society, HF has become a significant public health problem. It has been reported that each episode of acute HF may lead to dysfunction or injury of end-organs other than the heart, such as the liver, kidneys, brain, or lungs, which interact with each other, leading to subsequent detrimental consequences.¹⁻³⁾ Acute HF is therefore not a simple failure of a single organ. In particular, liver dysfunction is a well-known major complication in patients with acute HF, and interactions between the heart and the liver have been increasingly recognized.

Recently, the albumin-bilirubin (ALBI) score was developed as a new parameter to assess liver function in patients with liver disease.⁴⁾ The ALBI score incorporates two variables, serum albumin and total bilirubin, and was developed in 2015 in patients with hepatocellular carcinoma⁴⁾ in response to problems encountered with the Child-Pugh score. These problems were that some factors were subjective (i.e., ascites and encephalopathy), while other factors such as serum albumin and ascites were in-

terrelated. Some studies of the usefulness of the ALBI score have reported its ability to predict prognosis and assist in decision making regarding treatment choices for patients with hepatocellular carcinoma, as it is a suitable tool for evaluation of hepatic reserve function.^{5,6)}

On the other hand, in the area of heart disease, previous reports have shown that both albumin⁷⁻⁹⁾ and bilirubin^{10,11)} alone, are prognostic factors in patients with HF. Moreover, albumin is also a major component of nutritional indicators such as the prognostic nutritional index, geriatric nutritional risk index, and controlled nutritional status. These indicators have attracted attention in recent years as prognostic factors for HF.^{12,13)} Therefore, the ALBI score, as a combined measurement of albumin and total bilirubin, may become a more attractive prognostic index in patients with HF, and not only in patients with hepatocellular carcinoma. However, to date, a study¹⁴⁾ which showed an association between ALBI score and one-year mortality after discharge in patients hospitalized for acute HF, remains the only report of ALBI score and HF. In the present study, we hypothesized that the ALBI score at admission is associated with in-hospital mortality in patients hospitalized for acute HF.

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Methods

Study subjects and protocol: The present study was a single-center, retrospective observational study. Records of patients who were admitted to our hospital for the treatment of acute HF between January 2017 and August 2020 were reviewed, and patients who had appropriate clinical data for analysis were enrolled. Acute HF was defined as rapid-onset HF or a change in the signs and symptoms of HF requiring urgent therapy and hospitalization, based on the Framingham criteria.¹⁵⁾ Based on these criteria, the clinical diagnosis of acute HF was made by individual cardiologists at our institution. Patients with acute coronary syndrome, acute myocarditis, infective endocarditis, obvious infectious disease, such as respiratory or urinary tract infections, and patients receiving chronic hemodialysis were not included in this study. Vital signs (e.g. blood pressure), laboratory data including B-type natriuretic peptide (BNP) level and echocardiographic data at admission, as well as demographic and clinical characteristics, treatment and prognostic information, were obtained from medical records. The primary outcome was all-cause in-hospital mortality. The study protocol was approved by our institutional ethics committee. All study procedures were performed in compliance with the principles outlined in the Declaration of Helsinki.

Comorbidities: The diagnoses of atrial fibrillation, coronary artery disease, valvular heart disease, cardiomyopathy, chronic obstructive pulmonary disease and cerebrovascular accident were assessed by the treating cardiologists. Hypertension was defined as already receiving medical treatment in the present study, since the patients included often received intravenous vasodilator therapy after admission. The following comorbidities were defined at steady state conditions during admission: diabetes was defined as recent use of insulin or antidiabetic drugs, a fasting blood glucose value ≥ 126 mg/dL and/or a glycosylated hemoglobin value $\geq 6.5\%$; dyslipidemia was defined as low-density lipoprotein cholesterol ≥ 140 mg/dL or high-density lipoprotein cholesterol < 40 mg/dL or triglycerides ≥ 150 mg/dL or already receiving medical treatment.

Calculation of the ALBI score: Venous blood samples were collected from all patients at admission. The ALBI score was calculated based on the serum albumin and total bilirubin levels using the following formula, as shown in the original report: $(\log_{10} \text{total bilirubin [mmol/L]} \times 0.66) + (\text{albumin [g/L]} \times -0.085)$.⁴⁾ The subjects were divided into two groups (ALBI score ≤ -2.25 and > -2.25) based on the mean ALBI score of a previous study that reported the characteristics of the enrolled patients.¹⁴⁾ In addition, to investigate the relationship between ALBI grade and in-hospital mortality, patients were classified 3 ALBI grades (≤ -2.60 = grade 1, > -2.60 to ≤ -1.39 = grade 2, > -1.39 = grade 3) based on the original report.⁴⁾

GWTG-HF risk model: The GWTG-HF risk model that was derived from a very large data set in the United States¹⁶⁾ is a useful tool for predicting in-hospital mortality in patients with acute HF. Since the discrimination and calibration of this risk score have also been well validated

in Japanese patients with acute HF,¹⁷⁾ this score was also calculated as an established prognosticator in the present study for each patient, as originally described. The GWTG-HF risk score is based on race, age, systolic blood pressure, heart rate, blood urea nitrogen, sodium level, and the presence of chronic obstructive pulmonary disease.

Echocardiography: Cardiac chamber quantification by 2D echocardiography was performed according to established guidelines.¹⁸⁾ Left ventricular (LV) mass was calculated using diastolic measurement of LV diameter and wall thickness according to the cube formula.¹⁸⁾ LV ejection fraction was calculated using the biplane method of disks (modified Simpson's rule). Both mitral inflow velocities and mitral annular motion velocities were recorded in the apical 4-chamber view, and the ratio of peak early diastolic trans-mitral flow velocity to annular velocity (E/e') was calculated as a parameter of LV diastolic function.¹⁹⁾ Tricuspid regurgitation velocity and maximal diameter of the inferior vena cava were measured as hemodynamic assessments of the right heart. Our echocardiographic machines and laboratory are maintained under the guidelines of the Japanese Society of Echocardiography.²⁰⁾

Statistical analysis: All data are expressed as the mean $\pm$ standard deviation (SD) for normally distributed variables and as the median with interquartile range (IQR) for non-normally distributed data. Categorical data are expressed as the number (%). Group differences were evaluated using the Student *t* test or Mann-Whitney *U* test for continuous variables and the chi-square test or Fisher exact test for categorical variables. A correlation analysis was also performed to calculate the Pearson coefficients between the ALBI score and liver function tests. The association of selected variables with in-hospital mortality was assessed by univariate logistic regression analysis, and the variables that were significant in the univariate model were then entered into a multivariate logistic regression analysis. We also calculated the areas under the receiver operating curve to assess the ability of each model to estimate in-hospital mortality (Model 1, model based on the GWTG-HF risk score; Model 2, model 1 + BNP level; Model 3, model 2 + ALBI score). Calculation of continuous net reclassification improvement (NRI) was used to evaluate the differences between the 3 models. A probability value of < 0.05 was considered significant. All data were analyzed statistically with JMP version 13.0 (SAS Institute, Cary, NC, USA) and R version 4.0.3 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Patient characteristics: Between January 2017 and August 2020, 289 patients with acute HF were admitted to our hospital, 27 of whom had inadequate clinical data (i.e., lack of BNP level or blood pressure at admission). Therefore, 262 patients were enrolled in the present study.

Table I presents the general characteristics, hemodynamic data at admission, comorbidities, treatment information and mortality data in all patients and patients stratified according to the ALBI score (≤ -2.25 and

Table I. Patient Baseline Characteristics

Variable	All <i>n</i> = 262	ALBI ≤ −2.25 <i>n</i> = 110	ALBI > −2.25 <i>n</i> = 152	<i>P</i>
Age, years	86 (79-91)	84 (75-91)	87 (82-91)	0.046
Male	137 (52.3)	57 (51.8)	80 (52.6)	0.90
Height, m	1.55 ± 0.11	1.56 ± 0.11	1.55 ± 0.11	0.71
Weight, kg	49.1 (41.8-58.4)	51.8 (44.2-60.7)	46.4 (40.7-56.0)	0.0051
BMI, kg/m ²	20.2 (17.8-23.2)	21.1 (18.9-23.7)	19.5 (17.5-22.5)	0.0024
NYHA III or IV at admission	233 (88.9)	95 (86.4)	138 (90.8)	0.32
History of HF hospitalization	67 (25.6)	24 (21.8)	43 (28.3)	0.25
Hemodynamic data				
Systolic BP, mmHg	136 (120-157)	142 (130-160)	130 (116-152)	0.0014
Diastolic BP, mmHg	82 (69-96)	84 (70-99)	78 (66-94)	0.053
Heart rate, bpm	90 (75-111)	91 (76-114)	90 (73-110)	0.52
Clinical diagnosis				
Atrial fibrillation	136 (51.9)	53 (48.2)	83 (54.6)	0.32
Hypertension	151 (57.6)	70 (63.6)	81 (53.3)	0.10
Diabetes	47 (17.9)	21 (19.1)	26 (17.1)	0.74
Dyslipidemia	58 (22.1)	30 (27.3)	28 (18.4)	0.099
Coronary artery disease	64 (24.4)	26 (23.6)	38 (25.0)	0.88
Valvular heart disease	48 (18.3)	21 (19.1)	27 (17.8)	0.87
Cardiomyopathy	34 (13.0)	13 (11.8)	21 (13.8)	0.71
Cerebrovascular disease	32 (12.2)	14 (12.7)	18 (11.8)	0.85
COPD	26 (9.9)	12 (10.9)	14 (9.2)	0.68
Medication at admission				
Loop diuretic	142 (54.2)	57 (51.8)	85 (55.9)	0.53
β Blocker	95 (36.3)	39 (35.5)	56 (36.8)	0.89
ACEi/ARB	109 (41.6)	48 (43.6)	61 (40.1)	0.61
MRB	61 (23.3)	21 (19.1)	40 (26.3)	0.19
Intravenous treatment				
Inotrope	60 (22.9)	18 (16.4)	42 (27.6)	0.037
Vasodilator	94 (35.9)	41 (37.3)	53 (34.9)	0.70
Diuretic	242 (92.3)	97 (88.2)	145 (95.4)	0.035
Respiratory management				
NPPV/intubation	18 (6.9)	10 (9.1)	8 (5.3)	0.32
Length of stay, days	17 (10-24)	15 (10-22)	18 (11-26)	0.062
In-hospital death	37 (14.1)	5 (4.5)	32 (21.1)	0.0001

Data are presented as the number (%) or mean ± SD or median (IQR). BMI indicates body mass index; NYHA, New York Heart Association; BP, blood pressure; COPD, chronic obstructive pulmonary disease; ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin-receptor blocker; MRB, mineralocorticoid blocker; and NPPV, noninvasive positive pressure ventilation.

> −2.25). The median (IQR) age of all patients was 86 (79-91) years. Compared with patients with ALBI scores ≤ −2.25, patients with ALBI scores > −2.25 were significantly older (87 versus 84 years, respectively) and weighed less (46.4 versus 51.8 kg, respectively), and consequently had a lower BMI (19.5 versus 21.1 kg/m², respectively). Vital status at admission, percentage of comorbidities, medication at admission, and treatment after admission were similar in both groups, except for systolic blood pressure, intravenous inotrope, and diuretic use. Median (IQR) length of stay was 17 (10-24) days, with no difference between groups. No patients required percutaneous coronary or valve intervention or cardiac surgery to treat or manage HF. During the index hospitalization, 37 patients (14.1%) died. The in-hospital mortality rate was significantly higher in patients with ALBI scores > −2.25 compared with patients with ALBI scores ≤ −2.25 (21.1% vs. 4.5%, respectively; *P* = 0.0001, Figure 1). The number of patients stratified according to ALBI grade were as follows: grade 1, *n* = 33; grade 2, *n* = 220;

grade 3, *n* = 9. Most of our subjects were classified in ALBI grade 2. Patients who died during hospitalization in each ALBI grade were 0, 32, and 5 patients, respectively. Therefore, in-hospital mortality increased with higher ALBI grades (Figure 1).

Echocardiography and laboratory data: Echocardiographic parameters, laboratory data, and the GWTG-HF risk score at admission are summarized in Table II. The median (IQR) LV ejection fraction of all patients was 45 (35-61) %. Maximal inferior vena cava diameter was significantly greater in patients with an ALBI score > −2.25 than in those with a score ≤ −2.25. The other echocardiographic parameters were comparable between the two groups. Regarding laboratory data, in patients with ALBI scores > −2.25, hemoglobin and albumin levels were significantly lower, and total bilirubin and BNP levels were significantly higher compared with those of patients with ALBI scores ≤ −2.25. Liver function tests such as aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were similar in both groups. The

GWTG-HF risk score was significantly higher in patients with an ALBI score > -2.25 (45 versus 42, respectively; $P = 0.0045$). There was no significant correlation between the ALBI score and AST ($r = -0.012$, $P = 0.85$) or ALT ($r = 0.0091$, $P = 0.88$), although a weak but significant positive correlation was observed between the ALBI score and total bilirubin ($r = 0.19$, $P = 0.0016$).

Factors associated with in-hospital mortality: Table III shows the results of the univariate logistic regression analysis of factors associated with in-hospital mortality. Since the GWTG-HF risk score includes age, blood pressure and heart rate, renal function, sodium, and presence

of chronic obstructive pulmonary disease, these parameters were excluded from this analysis. None of the echocardiographic parameters was associated with outcome except for LV ejection fraction. The higher the LV ejection fraction, the lower the risk of in-hospital death (odds ratio [OR] 0.97, 95% confidence interval [CI] 0.94-0.99, $P = 0.0069$). In addition, a history of HF hospitalization (OR 2.60, 95% CI 1.26-5.35, $P = 0.0094$), serum BNP level (OR 1.0008, 95% CI 1.0005-1.001, $P < 0.0001$), GWTG-HF risk score (OR 1.20, 95% CI 1.13-1.28, $P < 0.0001$) and ALBI score (OR 11.6, 95% CI 4.3-31.2, $P < 0.0001$) were significantly associated with patient outcomes.

Based on the results of the univariate analysis, a history of HF hospitalization, LV ejection fraction, BNP level, GWTG-HF risk score, and ALBI score were selected as variables for the multivariate analysis. This analysis showed that the BNP level (OR 1.0007, 95% CI 1.0003-1.001, $P = 0.0003$), GWTG-HF risk score (OR 1.16, 95% CI 1.08-1.25, $P < 0.0001$), and ALBI score (OR 6.0, 95% CI 1.8-19.6, $P = 0.0017$) were independently associated with in-hospital mortality (Table IV). Figure 2 and Table V show the receiver operating curve analysis of each model that estimated in-hospital mortality based on the results of the multivariate analysis. Compared with Model 1, a significant NRI occurred with the addition of the BNP level (Model 2). Compared with Model 2, there was a further significant increase in NRI with the addition of the ALBI score (Model 3).

Figure 1. A high ALBI score was associated with a higher mortality. In-hospital mortality was significantly higher in patients with ALBI scores > -2.25 compared with that in patients with ALBI scores ≤ -2.25 (21.1% vs. 4.5%, respectively; $P = 0.0001$). In-hospital mortality increased with higher ALBI grades.

Discussion

The key finding of the present study was that a high ALBI score on admission was independently associated with a high in-hospital mortality in patients hospitalized

Table II. Echocardiographic Data, Laboratory Data, GWTG-HF Risk Score and ALBI Score at Admission

Variable	All <i>n</i> = 262	ALBI ≤ -2.25 <i>n</i> = 110	ALBI > -2.25 <i>n</i> = 152	<i>P</i>
Echocardiography				
LV mass index, g/m ²	121.9 $\pm$ 38.3	120.4 $\pm$ 36.1	123.1 $\pm$ 39.8	0.29
LV ejection fraction, %	45 (35-61)	46 (37-61)	45 (33-61)	0.28
E/e'	21 (17-30)	22 (17-29)	21 (16-31)	0.84
TR velocity, m/second	2.9 $\pm$ 0.6	2.9 $\pm$ 0.6	2.9 $\pm$ 0.6	0.32
Maximal IVC diameter, mm	18.8 $\pm$ 4.4	18.0 $\pm$ 4.3	19.3 $\pm$ 4.3	0.021
Laboratory data				
Hemoglobin, g/dL	11.9 $\pm$ 2.4	12.2 $\pm$ 2.2	11.6 $\pm$ 2.5	0.034
Albumin, g/dL	3.5 (3.2-3.8)	3.8 (3.6-3.9)	3.2 (2.9-3.4)	< 0.0001
Sodium, mEq/L	139 (137-142)	139 (136-142)	139 (137-142)	0.33
Creatinine, mg/dL	1.01 (0.77-1.41)	1.00 (0.77-1.35)	1.03 (0.77-1.52)	0.58
eGFR, mL/minute/1.73 m ²	46 (32-64)	48 (34-62)	45 (31-67)	0.54
BUN, mg/dL	24.5 (17.9-38.0)	23.5 (16.6-34.8)	25.1 (18.2-41.1)	0.24
Total bilirubin, mg/dL	0.86 (0.63-1.24)	0.74 (0.59-1.12)	0.95 (0.68-1.33)	0.0013
AST, IU/L	31 (23-46)	30 (22-46)	32 (23-48)	0.47
ALT, IU/L	21 (13-40)	20 (13-39)	22 (13-42)	0.78
BNP, pg/mL	732 (453-1271)	659 (358-926)	841 (509-1561)	0.0012
GWTG-HF risk score	44 $\pm$ 8	42 $\pm$ 8	45 $\pm$ 8	0.0045
ALBI score	-2.15 $\pm$ 0.40	-2.50 $\pm$ 0.20	-1.89 $\pm$ 0.30	< 0.0001

Data are presented as the mean $\pm$ SD or median (IQR). LV indicates left ventricular; E/e', the ratio of peak early diastolic trans-mitral flow velocity to annular velocity; TR, tricuspid regurgitation; IVC, inferior vena cava; eGFR, estimated glomerular filtration rate; BUN, blood urea nitrogen; AST, aspartate aminotransferase; ALT, alanine aminotransferase; BNP, B-type natriuretic peptide; GWTG-HF, Get With the Guidelines-Heart Failure; and ALBI, albumin-bilirubin.

Table III. Univariate Logistic Regression Analysis of Factors Associated with Outcome

Variable	Odds ratio (95% CI)	P
Male	0.74 (0.37-1.49)	0.41
BMI	0.96 (0.87-1.05)	0.33
NYHA III or IV at admission	5.1 (0.67-38.8)	0.11
History of HF hospitalization	2.60 (1.26-5.35)	0.0094
Atrial fibrillation	0.86 (0.43-1.72)	0.67
Hypertension	1.24 (0.61-2.54)	0.55
Diabetes	1.32 (0.56-3.09)	0.53
Dyslipidemia	0.80 (0.33-1.92)	0.61
Coronary artery disease	1.85 (0.88-3.89)	0.11
Valvular heart disease	1.82 (0.81-4.08)	0.16
Cardiomyopathy	0.79 (0.26-2.38)	0.67
LV mass index	1.00 (0.99-1.01)	0.80
LV ejection fraction	0.97 (0.94-0.99)	0.0069
E/e'	1.03 (0.99-1.06)	0.072
TR velocity	1.002 (0.57-1.78)	0.99
Maximal IVC diameter	1.06 (0.97-1.15)	0.21
Hemoglobin	0.90 (0.77-1.04)	0.15
AST	1.001 (0.99-1.004)	0.19
ALT	1.002 (0.99-1.006)	0.22
BNP	1.0008 (1.0005-1.001)	< 0.0001
GWTG-HF risk score	1.20 (1.13-1.28)	< 0.0001
ALBI score	11.6 (4.3-31.2)	< 0.0001

Abbreviations as in Tables I and II.

Table IV. Multivariate Logistic Regression Analysis of Factors Associated with Outcome

Variable	Odds ratio (95% CI)	P
History of HF hospitalization	1.0008 (0.36-2.77)	0.99
LV ejection fraction	0.99 (0.96-1.03)	0.84
BNP	1.0007 (1.0003-1.001)	0.0003
GWTG-HF risk score	1.16 (1.08-1.25)	< 0.0001
ALBI score	6.0 (1.8-19.6)	0.0017

Abbreviations as in Tables I and II.

for acute HF. Moreover, we confirmed that the GWTG-HF risk score and BNP level, established as prognostic indicators, were strongly associated with in-hospital mortality even in very elderly patients.

Albumin is a hepatic protein and its plasma concentration is controlled by several factors, including the rate of albumin synthesis, albumin distribution, catabolic rate, and exogenous albumin loss.^{21,22)} Synthesis of albumin is affected by nutritional intake, variations in colloid oncotic pressure, and the presence of systemic inflammation.^{21,23)} Plasma albumin levels are known to be decreased in inflammatory conditions, including infection, trauma, and surgery.²⁴⁾ Previous clinical trials demonstrated that the HF syndrome is characterized by activation of inflammatory factors, including C-reactive protein and circulating cytokines and chemokines.^{25,26)} Bonilla-Palomas, *et al.*²⁷⁾ showed in their detailed study that both malnutrition and inflammatory activation were the most important etiological factors associated with hypoalbuminemia in patients with acute HF. Therefore, we presume that hypoalbuminemia is common in patients with HF, and to date, this condition is a well-established predictor for short-term prognosis in patients with acute HF.^{7,27)} In recent years, there

has been increasing evidence that 3 nutritional indices, the prognostic nutritional index, geriatric nutritional risk index, and controlled nutritional status are all associated with the short- and long-term prognosis of patients with acute HF,^{12,13)} with the main component of each nutritional index being albumin. These findings indicate that albumin is an important indicator of malnutrition and inflammation in patients with HF. In addition, the mechanism that causes hypoalbuminemia due to liver dysfunction associated with acute HF is also possible. Liver dysfunction is one of the most recognized complications in patients with acute HF, with the most common cause being liver congestion indicated by the finding of an elevated central venous pressure (CVP) due to right HF. Drazner, *et al.*²⁸⁾ examined invasive hemodynamic data in detail from 4,079 patients with HF and found that CVP and pulmonary capillary wedge pressure remained concordant in most patients. Therefore, the most common and typical phenomenon in HF is systemic congestion. Several studies have reported that albumin levels may be associated with systemic congestion in patients with acute HF. Bonilla-Palomas, *et al* also reported that a low albumin level was associated with a CVP > 15 mmHg estimated by echocardiography.²⁷⁾ Uthamalingam, *et al.* showed that the presence of severe tricuspid regurgitation is independently associated with low serum albumin.²⁹⁾ A report from 1976³⁰⁾ showed that increased microvascular protein escape is present in HF with increased CVP. It is possible that intestinal congestion favors albumin enteric losses.³¹⁾ Hypoalbuminemia may therefore also be a surrogate marker of liver dysfunction that reflects an elevated CVP. In fact, the present study showed that the maximal inferior vena cava diameter was significantly greater in patients with an ALBI score > -2.25 despite them having a smaller body size.

Figure 2. Area under the receiver operating curves for estimating in-hospital mortality in the study patients ($n = 262$). See also Table V.

Table V. Area Under the Curve Analysis of Each Model and Associated Net Reclassification Improvement

Variable	AUC (95% CI)	NRI (95% CI)	<i>P</i>
Model 1 (GWTG-HF risk score)	0.81 (0.73-0.88)		
Model 2 (model 1 + BNP level)	0.85 (0.77-0.92)	0.55 (0.21-0.89) *	0.0017
Model 3 (model 2 + ALBI score)	0.88 (0.82-0.94)	0.46 (0.12-0.80) **	0.0085

AUC indicates area under the curve; and NRI, net reclassification improvement; other abbreviations as in Tables I and II. *versus Model 1. **versus Model 2.

This result suggests that patients with an ALBI score > -2.25 may have a higher CVP, although this difference is small and invasive data on this association are lacking.

Regarding bilirubin, low hepatic blood flow due to decreased cardiac output and high CVP may induce atrophy of liver cells and edema of the peripheral area, changes that both lead to hypoxic hepatocellular injury.³²⁻³⁴ Hypoxic hepatocellular injury, in turn, causes impaired uptake of indirect bilirubin from blood and secretion of bilirubin directly into bile, leading to an increase in serum bilirubin level. A high CVP also leads to biliary occlusion and subsequently to an increase in serum bilirubin level. In fact, several studies have shown that serum bilirubin correlated positively with CVP and pulmonary artery wedge pressure, and inversely correlated with the cardiac index, though a rise in total bilirubin was not noticeable.^{32,35} Vishram-Nielsen, *et al.*³⁶ also reported that CVP obtained by an invasive method was associated with both markers of biliary excretion (alkaline phosphatase and bilirubin) and liver synthesis function (international normalization ratio) in hospitalized or out-patients with acute HF. An elevated total bilirubin level was independently associated with worse clinical outcomes in both the CHARM program¹⁰ and the ASCEND-HF study.¹¹ More recently, in patients with myocardial infarction complicated with HF and/or systolic dysfunction, the total bilirubin concentration was shown to be an independent predictor of mortality and may improve risk stratification.³⁷ Therefore, the ALBI score, a combined measurement of both albumin and total bilirubin, might reflect, at least in

part, liver congestion due to HF and subsequent liver dysfunction.

Although the ALBI score was developed originally using data of patients with hepatocellular carcinoma to estimate the degree of liver dysfunction,⁴ the utility of this score can be generalized to patients with cirrhosis irrespective of the etiology of the underlying liver disease (i.e., without hepatocellular carcinoma).³⁸ Therefore, the ALBI score may become a marker of liver dysfunction even in patients without hepatocellular carcinoma. In clinical practice, calculation of the ALBI score, measurement of the BNP level, as well as all of the variables used to obtain the GWTG-HF risk score, are available within the first 1-2 hours of patient evaluation, and these variables are objective indicators not subject to inter-observer errors. Our results showed that not only the GWTG-HF risk score and the BNP level, but also the ALBI score, can provide useful information for patient triage and treatment decisions in patients hospitalized for acute HF.

Limitations: The present study has several important limitations. First, although the treatment of acute HF was based on the guidelines, it was left to the discretion of each attending cardiologist. This may have had some impact on patient outcomes. In addition, an effect due to the decision of the attending physician may also exist regarding the diagnosis of the etiology of HF. Second, this study was conducted at a single center, and consequently included a limited number of patients. Moreover, this study was a retrospective observational study. Since our hospital is located in the suburbs of metropolitan Tokyo, the pa-

tient population of our hospital may reflect the patient population of general hospitals in Japan. However, prospective, large-scale studies are necessary to confirm our findings.

Conclusion

The ALBI score was independently associated with in-hospital mortality in patients hospitalized for acute HF. Moreover, as with previous reports, the GWTG-HF risk score and the BNP level also strongly provided short-term prognostic information in patients hospitalized for acute HF.

Disclosure

Conflicts of interest: The authors declare that there are no relationships to report with any industry.

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