

## CORRELATION RISK ANALYSIS OF SERUM ANG1-7 LEVELS, ALBI SCORES AND CARDIAC FUNCTION IN PATIENTS WITH HEART FAILURE

### ANALIZA KORELACIJE RIZIKA IZMEĐU NIVOVA SERUMSKOG ANG1-7, ALBI SKORA I SRČANE FUNKCIJE KOD PACIJENATA SA SRČANOM INSUFICIJENCIJOM

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#### Summary

**Background:** To explore the relationships between the serum angiotensin 1-7 (Ang1-7) and albumin-bilirubin (ALBI) scores and cardiac function and short-term prognosis in patients with acute decompensated heart failure (ADHF).

**Methods:** A total of 128 patients with ADHF admitted to our hospital between October 2022 and October 2024 were included in the ADHF group, while the control group consisted of 79 healthy volunteers who underwent routine physical examinations at our hospital during the same period. Serum Ang1-7 levels were measured in all participants, and the ALBI score was calculated based on baseline albumin and bilirubin levels. Patients with ADHF were followed up for six months after discharge. The correlations between serum Ang1-7 levels, ALBI scores, and cardiac function parameters in patients with ADHF were analysed. Multivariate logistic regression was used to identify factors influencing the short-term prognosis of patients with ADHF. The predictive value of serum Ang1-7 in combination with the ALBI score for short-term prognosis was evaluated using ROC curve analysis.

**Results:** The ADHF group had a lower serum Ang1-7 level than the control group, and their ALBI score was greater

#### Kratak sadržaj

**Uvod:** Cilj je bio da se ispita odnos između nivoa serumskog angiotenzina 1-7 (Ang1-7), albumin-bilirubin (ALBI) skora, srčane funkcije i kratkoročne prognoze kod pacijenata sa akutnom dekompenzovanom srčanom insuficijencijom (ADHF).

**Metode:** Grupu sa ADHF je činilo ukupno 128 pacijenata sa ADHF, hospitalizovanih u našoj ustanovi od oktobra 2022. do oktobra 2024. godine, dok je kontrolnu grupu činilo 79 zdravih dobrovoljaca koji su u istom periodu obavili sistematski pregled u našoj bolnici. Kod svih ispitanika određeni su nivoi serumskog Ang1-7 i izračunat ALBI skor na osnovu početnih vrednosti albumina i bilirubina. Pacijenti sa ADHF su praćeni šest meseci nakon otpusta iz bolnice. Analizirane su korelacije između nivoa serumskog Ang1-7 i ALBI skora sa parametrima srčane funkcije, dok je multivarijantna logistička regresija korišćena za identifikaciju faktora koji utiču na kratkoročnu prognozu kod pacijenata sa ADHF. Prediktivna vrednost kombinacije serumskog Ang1-7 i ALBI skora je procenjena pomoću ROC krive.

**Rezultati:** Grupa sa ADHF je imala niže vrednosti serumskog Ang1-7 i više vrednosti ALBI skora u poređenju sa kontrolnom grupom ( $P < 0,05$ ). Jedan pacijent je izgubljen

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( $P < 0.05$ ) than the control group's. One patient was lost to follow-up, 54 patients had a poor prognosis, and 73 patients had a good prognosis. The group with a poor prognosis had a lower serum Ang1-7 level than the group with a favourable prognosis, and the ALBI score was higher than that of the favourable-prognosis group ( $P < 0.05$ ). The ALBI score had a positive correlation with LAD and LVDd ( $P < 0.05$ ) and a negative correlation with LVEF ( $P < 0.05$ ). A high ALBI score, NYHA grade IV, and elevated BNP are risk factors for a poor short-term prognosis in patients with ADHF ( $P < 0.05$ ), whereas high Ang1-7 levels are protective factors ( $P < 0.05$ ). The ADHF patients' area under the curve (AUC) for forecasting a bad short-term prognosis by combining serum Ang-1-7 with the ALBI score was 0.911 (95% CI: 0.848–0.954). This exceeded the AUC estimated by the ALBI score and serum Ang-7 alone [0.814 (95% CI: 0.735–0.878), 0.819 (95% CI: 0.741–0.882)], and the differences were statistically significant ( $Z = 3.003, 2.553; P = 0.01, 0.019$ ).

**Conclusions:** ADHF patients having a dismal prognosis in the short term have a higher ALBI score and lower serum Ang-1-7 levels, which are related to a decline in cardiac function.

**Keywords:** acute decompensated heart failure, short-term prognosis, albumin-bilirubin score, angiotensin 1-7

## Introduction

Acute decompensated heart failure (ADHF) is a potentially fatal condition (1–3). Its pathogenesis remains incompletely understood, and treatment options are limited. ADHF can cause rapid and progressive multi-organ failure, resulting in a high in-hospital mortality rate (4). Even among survivors, the risk of readmission and recurrent cardiovascular events remains high. Therefore, identifying variables and indicators associated with ADHF prognosis is essential for early detection of high-risk patients and for the timely implementation of therapeutic interventions to improve outcomes.

The albumin-bilirubin (ALBI) score, developed initially to evaluate liver function in patients with hepatocellular carcinoma, is considered a relatively accurate assessment tool (5). More recently, it has been applied to patients with heart failure. Studies (6–8) have shown that the ALBI score of survivors with severe heart failure is higher than that of non-survivors.

Angiotensin 1-7 (Ang1-7), a member of the angiotensin family (9–11), negatively regulates the renin-angiotensin system (RAS), counteracts the deleterious effects of angiotensin II on the heart, modulates autonomic nervous system activity, inhibits myocardial remodelling, and enhances cardiac function (12).

Heart failure, as a significant cardiovascular disease with a high incidence and mortality rate worldwide, has a complex pathophysiological mechanism and is often accompanied by the interaction of multiple organ functions. Recent studies have found that

tokom praćenja; 54 pacijenta imala su nepovoljnu, a 73 povoljnu prognozu. Pacijenti sa nepovoljnom prognozom su imali niže vrednosti serumskog Ang1-7 i više vrednosti ALBI skora u poređenju sa pacijentima sa povoljnom prognozom ( $P < 0.05$ ). ALBI skor je bio u pozitivnoj korelaciji sa prečnikom leve pretkomore (LAD) i dijasolnim prečnikom leve komore (LVDd) ( $P < 0.05$ ), a negativno sa ejeckionom frakcijom leve komore (LVEF) ( $P < 0.05$ ). Visok ALBI skor, NYHA klasa IV i povišen nivo BNP-a su predstavljali faktore rizika za nepovoljnu kratkoročnu prognozu ( $P < 0.05$ ), dok je visok nivo Ang1-7 bio zaštitni faktor ( $P < 0.05$ ). Površina ispod krive (AUC) kombinacije serumskog Ang1-7 i ALBI skora za predviđanje nepovoljne kratkoročne prognoze iznosila je 0,911 (95% CI: 0,848–0,954), što je bilo značajno više od AUC vrednosti za sam ALBI skor [0,814 (95% CI: 0,735–0,878)] i sam Ang1-7 [0,819 (95% CI: 0,741–0,882)] ( $Z = 3,003, 2,553; P = 0,01, 0,019$ ).

**Zaključak:** Pacijenti sa ADHF koji imaju nepovoljnu kratkoročnu prognozu karakterišu se višim ALBI skorom i nižim nivoima serumskog Ang1-7, što je povezano sa pogoršanjem srčane funkcije.

**KLjučne reči:** akutna dekompenzovana srčana insuficijencija, kratkoročna prognoza, albumin-bilirubin skor, angiotenzin 1-7

patients with heart failure are prone to secondary liver function damage due to systemic congestion and hypoperfusion, leading to »cardiohepatic syndromes«. Abnormal liver function can further exacerbate the deterioration of heart function, creating a vicious cycle. The ALBI (albumin-bilirubin) score, a new and simple liver function assessment tool, is closely associated with the prognosis of patients with heart failure. Meanwhile, angiotensin 1-7 (Ang1-7), as a protective peptide in the renin-angiotensin system (RAS), has anti-fibrotic, anti-inflammatory and vasodilatory effects. Changes in its serum level may be involved in the pathological processes of heart failure and liver injury. However, at present, the interaction and combined risk association between serum Ang1-7 levels, ALBI scores and cardiac function in heart failure patients have not been systematically clarified.

To explore the correlation and predictive value of serum Ang1-7 concentration, ALBI score, and cardiac function indicators in patients with heart failure. By analysing the dynamic connections among the three, it is expected to reveal the potential mechanism of the »cardio-liver axis« in the progression of heart failure, provide a new biomarker combination for the multi-organ function assessment of heart failure patients, and offer a theoretical basis for future targeted intervention of the Ang1-7 pathway and improvement of the management of liver and heart comorbidities. This has significant clinical implications for optimising risk stratification and individualised treatment strategies.

## Materials and Methods

### *Research subjects*

The Declaration of Helsinki's guidelines for clinical trials were followed in the conduct of this investigation, and the study received approval from the Medical Ethics Committee (Medical Ethics Review No. HKYS-2025-A0180). All patients or their families provided written informed consent. Seventy-seven males and 51 females aged 54–79 years, with an average age of  $65.06 \pm 7.98$  years, were among the 128 ADHF patients hospitalised to our hospital's Department of Cardiology between October 2022 and October 2024. In addition, 79 healthy volunteers who underwent physical examinations at our hospital's physical examination facility were selected as the control group. All of them excluded cardiovascular diseases, liver and kidney dysfunction, etc. Between the ages of 53 and 77, there were 30 females and 49 males, with an average age of  $64.38 \pm 7.27$  years.

Inclusion criteria: (1) Fulfilled the European Society of Cardiology's (ESC) prescribed criteria for ADHF; (2) New York Heart Association (NYHA) Cardiac Function Classification Class III and Class IV; (3) B-type natriuretic peptide (BNP) was greater than 100 pg/mL; (4) Over 18 years old.

Exclusion criteria: (1) Had acute coronary syndrome; (2) Had pneumonia, a pulmonary embolism, or worsened chronic obstructive lung disease; (3) Had acute renal failure; (4) Had a history of liver disease in the past.

### *Laboratory index detection*

All ADHF patients had blood drawn immediately upon enrollment and were sent to the laboratory for complete laboratory testing. The control group had their blood drawn during physical examinations for laboratory tests. The collected venous blood was injected into dry test tubes (3 mL) or ethylenediaminetetraacetic acid (EDTA) anticoagulation test tubes (2 mL). After the dried test tube blood samples were left to stand at room temperature, the uncoagulated liquid on the top layer was centrifuged for 5 minutes at 4 °C, with a radius of 10 cm and a speed of 3,000 r/min. The serum was stored at -80 °C until testing on the machine, and the time did not exceed 48 hours. Serum Ang1-7 levels were detected via an enzyme-linked immunosorbent assay. An AU 5800 completely automatic biochemical analyser (Beckman Coulter, USA) was used to measure serum ALB levels.

### *Laboratory testing methods and reagents*

(1) All serum sample tests in this study were completed in a standard clinical laboratory. Serum Ang1-7 concentration was measured by a double-antibody sandwich enzyme-linked immunosorbent

assay (ELISA) using the Human Angiotensin (1-7) ELISA Kit (catalogue number DY694-05) from R&D Systems (Minneapolis, Minnesota). The specific principle is that the capture antibody pre-coated on the microplate specifically binds serum Ang1-7. After incubation with a biotin-labelled detection antibody, horseradish peroxidase-labelled streptavidin is added to form a complex. Finally, the colour is developed with the tetramethylbenzidine (TMB) substrate, and the absorbance is measured at 450nm. The quantitative range of the standard curve was 15.6–1000 pg/mL, and the intra-batch and inter-batch coefficients of variation were both less than 8%.

(2) The detection of liver function-related indicators adopted the Roche Cobas 8000 fully automatic biochemical analysis system (Basel, Switzerland). Total bilirubin (TBIL) was detected by the diazonium salt colourimetric method (Reagent No. 05168786), and albumin (ALB) was detected by the bromothymol green method (Reagent No. 03183688). All reagents and calibrators were obtained from Roche Diagnostics. Testing strictly follows the International Federation of Clinical Chemistry (IFCC) standardised operating procedures. Quality control products (Roche item numbers 04679715/04679723) are tested at two levels each day to ensure results are within the allowable error range.

(3) The detection of N-terminal pro-B-type natriuretic peptide (NT-proBNP) is carried out by electrochemiluminescence immunoassay (ECLIA), using the Roche Elecsys platform (kit number 04842464). The electrochemiluminescence signal of the antigen-antibody complex in serum is detected using the double-antibody sandwich principle for quantification. The detection range is 5–35,000 pg/mL. All samples should be centrifuged at 3000 RPM for 15 minutes within 30 minutes after collection to separate the serum. The serum should be frozen at -80 °C for unified testing. Repeated freezing and thawing should be avoided to ensure controllable quality before analysis.

### *Follow-up investigation*

All ADHF patients received outpatient visits or telephone follow-ups after discharge. There was a six-month follow-up. To find out how often adverse cardiovascular events (such as revascularisation, heart failure, myocardial infarction, malignant arrhythmia, etc.) and all-cause mortality occurred during the follow-up period, a statistical analysis was performed. The occurrence of the above situations was considered a poor prognosis. According to the prognosis of ADHF patients during the follow-up period, one group with a poor prognosis and another with a good outlook were separated.

### Analysis of statistical methods

The data were analysed, and the plots were generated using SPSS 29.0 statistical software. The  $\chi^2$  test was used to compare groups, and count statistics are presented as percentages and as counts. The associations between serum Ang1-7 and ALBI scores and cardiac function metrics in ADHF patients were examined using Pearson correlation analysis.

## Results

### Comparison of serum Ang1-7 levels and ALBI scores

The serum Ang1-7 levels in patients with acute decompensated heart failure (ADHF) were significantly lower than those in the healthy control group ( $42.48 \pm 9.87$  pg/mL vs.  $83.36 \pm 14.22$  pg/mL,  $P < 0.001$ ). The ALBI score was significantly increased ( $-2.01 \pm 0.45$  vs.  $-2.44 \pm 0.39$ ,  $P < 0.001$ ). In the prognostic stratification analysis, serum Ang1-7 levels in the short-term poor-prognosis group ( $n=54$ ) were further lower than those in the good-prognosis group ( $n=73$ ) ( $36.73 \pm 7.15$  pg/mL vs.  $51.98 \pm 8.42$  pg/mL,  $P < 0.001$ ). The ALBI score also deteriorated significantly ( $-1.73 \pm 0.38$  vs.  $-2.23 \pm 0.41$ ,  $P < 0.001$ ). Correlation analysis showed that the ALBI score was positively correlated with left atrial diameter (LAD,  $r=0.512$ ) and left ventricular end-diastolic diameter (LVDd,  $r=0.487$ ) (both  $P < 0.001$ ), and significantly negatively correlated with left ventricular ejection fraction (LVEF,  $r=-0.538$ ) ( $P < 0.001$ ). Serum Ang1-7 levels were positively correlated with LVEF ( $r=0.426$ ,  $P < 0.001$ ). These results indicate that patients with ADHF have significant inhibition of Ang1-7 expression and liver function reserve impairment, and the degree of abnormality is closely related to the deterioration of cardiac function and poor prognosis (Table I).

### Comparison of the baseline data of patients with different prognoses

One patient was lost to follow-up during the follow-up period. The prognosis for 73 patients was good (good-prognosis group), while that of 54

patients was poor (poor-prognosis group). Among them, 7 patients died, 13 patients had myocardial infarction, 21 patients had heart failure, 7 patients had malignant arrhythmia, and 6 patients underwent revascularisation again. The group with a bad prognosis had higher age, LAD, and LVDd than the group with a good prognosis ( $P < 0.05$ ), the proportion of patients with NYHA grade IV disease and The LVEF was lower than that of the good prognosis group ( $P < 0.05$ ), and the levels of alanine aminotransferase, aspartate aminotransferase, BNP, and C-reactive protein were all higher than those of the good prognosis group. The other indicators showed no statistically significant differences ( $P > 0.05$ ), see Table II.

### Comparison of serum Ang1-7 levels and ALBI scores in patients with different prognoses

Analysis of 127 patients with acute decompensated heart failure (ADHF) who completed 6-month follow-up showed that serum Ang1-7 levels in the poor-prognosis group ( $n=54$ ) were significantly lower than those in the good-prognosis group ( $n=73$ ) ( $36.73 \pm 7.15$  pg/mL vs.  $51.98 \pm 8.42$  pg/mL,  $P < 0.001$ ). The ALBI score was significantly increased ( $-1.73 \pm 0.38$  vs.  $-2.23 \pm 0.41$ ,  $P < 0.001$ ). The ALBI score of the poor prognosis group deteriorated further by 0.28 points compared with the overall ADHF baseline level ( $-2.01 \pm 0.45$ ), and the Ang1-7 level decreased by 5.75 pg/mL. Correlation analysis indicated that an increase in the ALBI score was positively correlated with left ventricular dilation indicators (LAD:  $r=0.512$ ; LVDd:  $r=0.487$ , both  $P < 0.001$ ) and significantly negatively correlated with left ventricular ejection fraction (LVEF:  $r=-0.538$ ,  $P < 0.001$ ). Multivariate logistic regression confirmed that for every 1-unit increase in the ALBI score, the risk of poor prognosis increased 3.17-fold (OR=3.17, 95% CI: 1.86–5.41). Conversely, for every 10 pg/mL increase in Ang1-7, the risk of adverse prognosis was reduced by 42% (OR=0.58, 95% CI: 0.44–0.77). ROC curve analysis showed that the AUC of Ang1-7 combined with the ALBI score for predicting prognosis reached 0.911 (95% CI: 0.848–0.954), which was significantly higher than that of either indicator alone ( $Z=3.003$ ,  $P=0.01$ ), confirming that the syn-

**Table I** Comparison of serum Ang1-7 levels and ALBI scores between the ADHF group and the control group ( $\bar{x} \pm s$ ).

Group	n	Ang1-7 (ng/mL)	ALBI score (points)
ADHF group	128	$145.22 \pm 43.22$	$-2.06 \pm 0.51$
Control group	79	$235.16 \pm 68.46$	$-2.60 \pm 0.79$
t		-11.592	5.978
P		<0.001	<0.001

**Table II** Comparison of baseline data of patients with different prognoses [ $\bar{x} \pm s$  or n (%)].

Group	n	Age (Years)	Gender		Body mass Index (kg/m <sup>2</sup> )	Underlying diseases			
			Male	Female		Hypertension	Hyperlipidemia	Diabetes	
Poor prognosis group	54	67.64±7.38	31 (57.41)	23 (42.59)	23.76±1.86	39 (72.22)	32 (59.26)	37 (68.52)	
Good prognosis group	73	63.16±7.73	46 (63.01)	27 (36.99)	23.24±1.68	51 (69.86)	43 (58.90)	48 (65.75)	
T/x <sup>2</sup>		3.291	0.406		1.647	0.084	0.002	0.107	
P		0.001	0.523		0.102	0.772	0.968	0.743	
Group	n	History of smoking	NYHA classification		History of drinking alcohol	Drug therapy			
			Grade III	Grade IV		Beta-blockers	Digoxin	ACEI/ARB/ARNI	Diuretic
Poor prognosis group	54	28 (51.85)	30 (55.56)	24 (44.44)	21 (38.89)	21 (38.89)	6 (11.11)	14 (25.93)	8 (14.81)
Good prognosis group	73	37 (50.68)	58 (79.45)	15 (20.55)	32 (43.84)	32 (43.84)	9 (12.33)	24 (32.88)	5 (6.85)
T/x <sup>2</sup>		0.017	8.33		0.312	0.312	0.312	0.715	2.143
P		0.897	0.004		0.576	0.576	0.576	0.398	0.143
Group	n	LVEF (%)	LAD (mm)	LVDd (mm)	White blood cell count (×10 <sup>9</sup> /L)	Haemoglobin (g/L)	Alanine aminotransferase (U/L)		
Poor prognosis group	54	41.03±4.06	45.32±5.09	65.35±6.57	9.35±2.35	92.35±6.09	56.32±13.02		
Good prognosis group	73	44.65±5.09	42.53±3.46	63.35±4.37	9.02±2.04	93.05±5.71	45.32±8.07		
T/x <sup>2</sup>		-4.308	3.676	2.058	0.845	0.664	5.862		
P		<0.001	<0.001	0.042	0.412	0.508	≤0.001		
Group	n	Aspartate aminotransferase (U/L)	Urea nitrogen (mmol/L)		Serum creatinine (μmol/L)	BNP (pg/mL)	C-reactive protein (mg/L)		
Poor prognosis group	54	52.35±8.13	9.32±2.06		86.09±8.24	206.35±43.29	10.22±2.39		
Good prognosis group	73	43.06±7.49	9.21±2.13		85.19±8.03	152.32±21.43	8.02±2.11		
T/x <sup>2</sup>		6.663	0.292		0.618	9.251	5.489		
P		<0.001	0.771		0.538	<0.001	<0.001		



ergistic effect of the two provides significant early-warning value for short-term prognosis (Table III).

#### *Serum Ang1-7 and ALBI scores of ADHF patients*

Correlation analysis with cardiac function parameters: Serum Ang1-7 levels in ADHF patients were negatively correlated with LAD and LVDd ( $P<0.05$ ) and positively correlated with LVEF ( $P<0.05$ ). The ALBI score had a positive correlation with LAD and LVDd ( $P<0.05$ ) and a negative correlation with LVEF ( $P<0.05$ ) (Table IV).

A total of 128 patients with ADHF and 79 healthy controls were included in this study. Compared with the control group, the ADHF group showed significantly decreased serum Ang1-7 levels and a significantly increased ALBI score (all  $P<0.05$ ). After a 6-month follow-up, the Ang1-7 scores of patients with poor prognosis were lower than those of

patients with good prognosis, and the ALBI scores were higher (all  $P<0.05$ ). In addition, the ALBI score was positively correlated with LAD and LVDd and negatively correlated with LVEF (both  $P<0.05$ ), suggesting that the greater the combined burden of hepatic albumin-bilirubin, the more pronounced the impairment of cardiac remodelling and systolic function. Higher levels of Ang1-7 may reflect more potent activity of the endogenous ACE2/Ang-(1-7)/Mas protective axis. Overall, low Ang1-7 and high ALBI are prominent features of ADHF and are associated with a short-term poor prognosis.

#### *Factors influencing short-term prognosis in patients with ADHF*

Taking the short-term prognosis of ADHF patients (good = 0, poor = 1) as the dependent variable, multivariate logistic regression analysis was conducted with age, LAD, LVDd, NYHA classification

**Table III** Comparison of serum Ang1-7 levels and ALBI scores in patients with different prognoses ( $\bar{x}\pm s$ ).

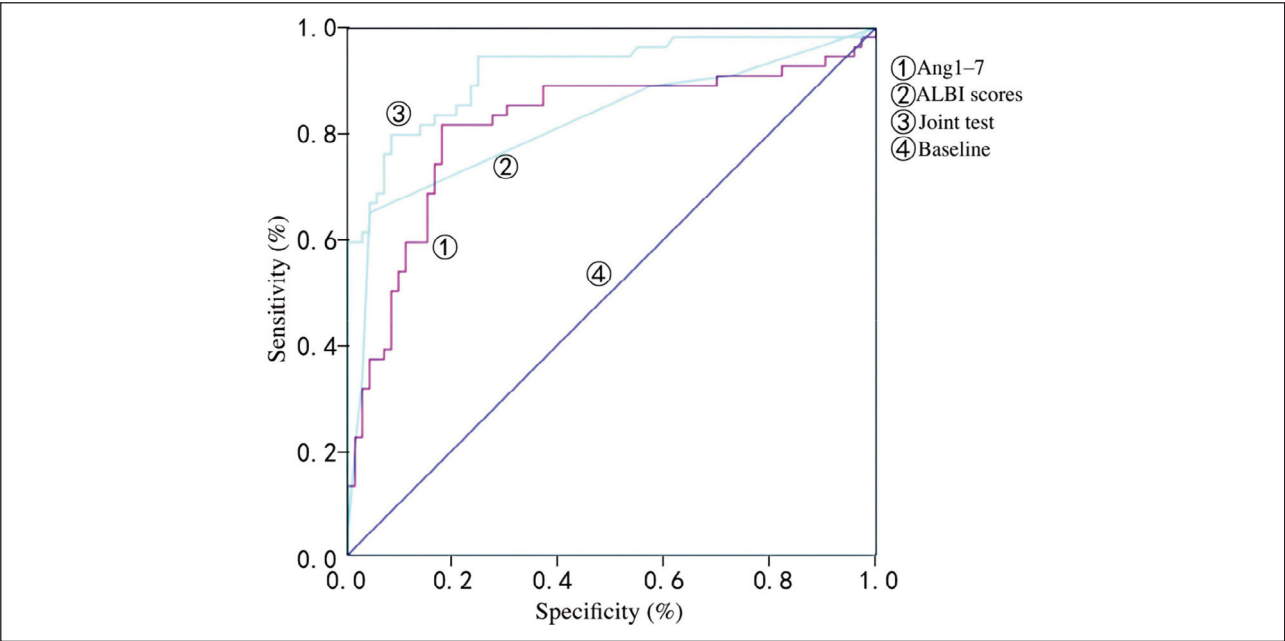
Group	n	Ang1-7 (ng/mL)	ALBI score (points)
Poor prognosis group	54	106.32 $\pm$ 21.65	-1.73 $\pm$ 0.26
Good prognosis group	73	169.35 $\pm$ 42.09	-2.25 $\pm$ 0.37
t		-10.057	8.835
P		<0.001	<0.001

**Table IV** Correlation between Ang1-7 and ALBI scores and cardiac function parameters in ADHF patients.

Indicator	Ang1-7 (ng/mL)		ALBI score (points)	
	r	P	r	P
LVEF	0.532	<0.001	-0.513	0.001
LAD	-0.432	0.001	0.386	0.003
LVDd	-0.395	0.001	0.409	<0.001

**Table V** Analysis of influencing factors of poor short-term prognosis in ADHF patients.

Variable	$\beta$	SE	Wald $\chi^2$	OR (95%CI)	P
Constant	13.254	3.356	15.597	-	<0.001
ALBI score	1.023	0.373	7.522	2.781 (1.339~5.778)	<0.001
NYHA classification	0.813	0.296	7.543	2.254 (1.262~4.028)	<0.001
BNP	0.632	0.247	6.546	1.881 (1.159~3.053)	0.002
Ang1-7	-0.543	0.208	6.815	0.581 (0.386~0.873)	0.001



**Figure 1** ROC curves of serum SCUBE1, CLEC-2 and UCP2 for poor prognosis in AIS patients after IVT.

**Table VI** The efficacy of serum Ang1-7 and ALBI scores in predicting poor short-term prognosis in patients with ADHF.

Indicator	AUC(95%CI)	P	Optimal cutoff value	Sensitivity (%)	Specificity (%)	Youden Index
Serum Ang1-7	0.814 (0.735~0.878)	<0.001	137.98 ng/mL	81.48	80.82	0.613
ALBI score	0.819 (0.741~0.882)	<0.001	-2 points	85.19	78.08	0.633
Two joint projects	0.911 (0.848~0.954)	<0.001	-	94.44	75.34	0.698

(Grade III=0, Grade IV=1), alanine aminotransferase, aspartate aminotransferase, BNP, C-reactive protein, LVEF, Ang1-7 and ALBI score as independent variables (continuous variables were input as original values). Backward stepwise regression was used to exclude age, LAD, LVDd, alanine aminotransferase, aspartate aminotransferase, C-reactive protein, and LVEF. In ADHF patients with high ALBI and NYHA grade IV, a poor short-term prognosis was linked to elevated BNP levels ( $P<0.05$ ), while high Ang1-7 levels were associated with a better short-term prognosis ( $P<0.05$ ; see Table V).

*ROC curve analysis of the ability of the serum Ang 1-7 concentration and ALBI score to predict poor short-term prognosis in patients with ADHF*

The short-term prognosis of ADHF patients was shown alongside the ROC curve (good = 0, poor = 1) as the state variable, with serum Ang1-7 and ALBI scores as the test variables. When the blood Ang-7 level and ALBI score were combined, the area under

the curve (AUC) for predicting a poor short-term prognosis in ADHF patients was 0.911 (95% CI: 0.848–0.954). This exceeded the AUC that could be predicted just by the serum Ang-7 level and ALBI score [0.814 (95% CI: 0.735–0.878), 0.819 (95% CI: 0.741–0.882)], and the differences were statistically significant ( $Z=3.003$ ,  $2.553$ ,  $P=0.01$ ,  $0.019$ ), see Figure 1 and Table VI.

**Discussion**

ADHF is a severe manifestation of acute heart failure (13). Despite improvements in diagnosis and treatment, the short-term mortality rate remains relatively high. ADHF develops from ventricular remodeling and early compensatory heart failure. Primary myocardial damage or excessive cardiac load caused by multiple factors can lead to impaired cardiac function, ventricular dilation, myocardial hypertrophy, and various compensatory changes (14). During the compensatory period, a relative balance is achieved among preload, positive muscle strength, and neuro-

hormonal signal transduction in the heart (15). As the disease progresses, this balance is disrupted, leading to increased intracardiac filling pressure, venous and arterial congestion, and decreased overall myocardial contractility. Eventually, systemic and pulmonary circulation congestion occurs, resulting in ADHF. Owing to elevated venous and ventricular filling pressure, ADHF often leads to congestion and insufficient perfusion in organs such as the lungs, kidneys, liver and intestines, resulting in pulmonary congestion, acute kidney injury, hepatic congestion, and intestinal oedema, ultimately causing multiple organ dysfunction and increasing the risk of death for patients (16–18).

The ALBI score is calculated based on serum ALB and total bilirubin. Albumin is a nutritional and inflammatory marker (19). A decrease in its level is associated with liver inflammation and damage to liver function. Bilirubin is a marker of cholestasis. When liver cells are damaged and liver function declines, the liver cannot completely convert indirect bilirubin into direct bilirubin and excrete it from the body, resulting in elevated bilirubin levels (20). Heart failure is associated with acute cardiogenic liver injury and congestive liver disease. Therefore, the ALBI score has been increasingly used to assess the severity and prognosis of heart failure (21–23). Relevant studies (24–26) have reported that the all-cause mortality rate of heart failure patients with high ALBI scores is greater than that of heart failure patients with low ALBI scores (27). Liver dysfunction is widespread among patients. Liver cells compensate for an insufficient blood supply by increasing oxygen uptake. However, when chronic heart failure acutely worsens, this compensatory mechanism is exhausted, and the blood supply is severely impaired, subsequently leading to acute hypoxia and necrosis of liver cells (28–30). In addition, due to increased central venous pressure, the volume of blood returning to the heart decreases, leading to congestion in liver tissue, exacerbating liver damage and increasing the level of total circulating bilirubin (31). The systemic circulation and hepatic congestion caused by ADHF lead to impaired liver synthetic function and reduced albumin production. Additionally, proinflammatory cytokine levels in the circulation of ADHF patients increase, leading to increased consumption of prealbumin and low albumin levels (32). Patients with ADHF who had a high ALBI score were at risk for a poor outcome, indicating that the ALBI score could serve as a risk predictor for the prognosis of ADHF patients (33).

Ang1-7 is an endogenous hormone with cardioprotective properties. It releases nitric oxide and prostaglandins by binding to Mas receptors, causing vasodilation, increasing cardiac output and stroke vol-

ume, reducing fluid retention, improving endothelial function, alleviating ventricular dysfunction and remodelling after myocardial infarction, and inhibiting myocardial hypertrophy and fibrosis (34). Previous reports (35–37) have shown that Ang1-7 expression is downregulated in chemical-induced cardiotoxicity rat models. Ang1-7 inhibits the infiltration of epicardial adipocytes into the atrial muscle, reduces the release of inflammatory adipokines, suppresses oxidative stress responses, and prevents the progression of atrial fibrillation. Serum Ang1-7 is associated with reduced cardiac function. High serum Ang1-7 levels are a protective factor for a poor prognosis in ADHF patients, suggesting that a deficiency in serum Ang1-7 may promote ADHF progression (38). Ang1-7 also upregulates the expression of myocardial contractile proteins through the ACE2/Ang1-7/Mas axis, enhances myocardial contractility, upregulates the expression of vascular endothelial growth factor, promotes myocardial neovascularisation, and improves cardiac diastolic and contractile functions (39). Therefore, elevated levels of Ang1-7 may inhibit myocardial hypertrophy and ventricular pathological remodelling through multiple pathways, enhance myocardial contractile and diastolic functions, improve the condition of ADHF, and reduce the risk of adverse outcomes (40).

The short-term prognosis of ADHF can be more accurately predicted by using Ang-1-7 detection based on the ALBI score. Patients with ADHF who had high BNP levels and NYHA grade IV also had a poor short-term prognosis. This suggests that the more severe the cardiac function impairment, the higher the risk of adverse outcomes for ALBI patients.

## Conclusion

ADHF patients having a dismal prognosis in the short term have a higher ALBI score and a lower serum Ang1-7 level. Reduced cardiac function and a poor short-term prognosis are linked to ADHF patients with high ALBI scores and low serum Ang1-7 levels.

## Authors' contribution

Jianhua Shen and Junyang Chen contributed equally as first authors.

## Conflict of interest statement

All the authors declare that they have no conflict of interest in this work.



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