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THE DIAGNOSTIC VALUE OF SERUM AHD-5, IL1RL1, AND CD138 IN PATIENTS WITH CHRONIC HEART FAILURE

DIJAGNOSTIČKA VREDNOST SERUMSKIH NIVOA AHD-5, IL1RL1 I CD138 KOD PACIJENATA SA HRONIČNOM SRČANOM INSUFICIJENCIJOM

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Summary

Background: To explore the diagnostic value of serum Aldehyde dehydrogenase 5 (Ahd-5), IL-1 receptor-like 1 (IL1RL1), and CD138 in patients with chronic heart failure (CHF).
Methods: The study group consisted of 256 CHF patients treated at our hospital between February 2023 and March 2025, whereas the control group consisted of 138 healthy volunteers who attended our hospital during that period for physical examinations. The cardiovascular function markers (LVEF, LVESV, and LVEEDV) and the serum markers (Ahd-5, IL1RL1, CD138, and N-terminal pro-B-type natriuretic peptide, or NT-proBNP) were identified and compared. According to LVEF results, CHF patients were divided into reduced ejection fraction heart failure (HFrEF), mildly reduced ejection fraction heart failure (HFmrEF), and preserved ejection fraction heart failure (HFpEF) groups. Serum Ahd-5, IL1RL1, and CD138 levels of CHF patients were correlated with cardiac function markers using Pearson correlation analysis. The associations among the various severities of CHF patients and their serum Ahd-5, IL1RL1, and CD138 levels were examined using Spearman correlation analysis. Factors influencing the occurrence of CHF were examined. The diagnostic value of serum Ahd-5, IL1RL1, and CD138 levels for CHF patients was examined using a receiver operating characteristic (ROC) curve.

Kratak sadržaj

Uvod: Cilj je bio da se ispita dijagnostička vrednost serumskih nivoa aldehid-dehidrogenaze 5 (Ahd-5), receptora sličnog interleukinu-1 tip 1 (IL1RL1) i CD138 kod pacijenata sa hroničnom srčanom insuficijencijom (CHF).
Metode: Ispitivanu grupu je činilo 256 pacijenata sa CHF, lečenih u našoj bolnici u periodu od februara 2023. do marta 2025. godine, dok je kontrolnu grupu činilo 138 zdravih dobrovoljaca koji su u istom periodu obavili sistematski pregled u našoj ustanovi. Određeni su i međusobno upoređeni parametri kardiovaskularne funkcije (LVEF, LVESV i LVEDV), kao i serumski biomarkeri Ahd-5, IL1RL1, CD138 i N-terminalni pro-B-tip natriuretskog peptida (NT-proBNP). Na osnovu vrednosti LVEF, pacijenti sa CHF su svrstani u tri podgrupe: srčana insuficijencija sa redukovanom ejekcionom frakcijom (HFrEF), sa blago redukovanom ejekcionom frakcijom (HFmrEF) i sa očuvanom ejekcionom frakcijom (HFpEF). Povezanost serumskih nivoa Ahd-5, IL1RL1 i CD138 sa pokazateljima srčane funkcije je procenjena Pirsonovom korelacionom analizom, dok je odnos između stepena težine CHF i navedenih biomarkera ispitan Spirmanovom korelacionom analizom. Takođe su analizirani faktori povezani sa nastankom CHF. Dijagnostička vrednost serumskih nivoa Ahd-5, IL1RL1 i CD138 je procenjena primenom ROC analize.

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Results: Compared to the control group, the study group's serum levels of Ahd-5 and LVEF were significantly lower (P<0.05). However, their blood levels of IL1RL1, CD138, NT-proBNP, creatinine, LVESV, and LVEDV were significantly greater. According to LVEF data, there were 72 patients in the HFrEF group, 88 in the HFmrEF group, and 98 in the HFpEF group. Serum Ahd-5 levels were substantially lower in the HFrEF and HFmrEF groups than in the HFpEF group (P<0.05), although serum IL1RL1 and CD138 levels were significantly greater. While the HFmrEF group had considerably greater serum IL1RL1 and CD138 levels (P<0.05), the HFrEF group had significantly lower serum Ahd-5 levels. According to the results of the Pearson correlation analysis, the serum Ahd-5 level of CHF patients was positively correlated with LVEF (P<0.05) and negatively correlated with NT-proBNP, creatinine levels, LVESV, and LVEDV (P<0.05); the serum levels of IL1RL1 and CD138 were positively correlated with NT-proBNP, creatinine levels, LVESV, and LVEDV (P<0.05) and negatively correlated with LVEF (P<0.05). The serum Ahd-5 level showed a negative correlation with IL1RL1 and CD138 levels (P<0.05), and the serum IL1RL1 level had a positive correlation with the serum CD138 level (P<0.05). The areas under the curve (AUCs) of serum Ahd-5, IL1RL1, and CD138 for diagnosing CHF alone were 0.851, 0.830, and 0.860, according to ROC curve analysis. The combined diagnosis of CHF had an AUC of 0.946, which was substantially higher than the AUCs of serum Ahd-5 (Z=2.755, P=0.009), IL1RL1 (Z=3.071, P=0.002), and CD138 (Z=2.321, P=0.023).
Conclusion: While serum IL1RL1 and CD138 levels considerably increased in CHF patients, serum Ahd-5 levels significantly decreased. When these three indications are detected together, they have a high diagnostic value for CHF and could be used as a novel auxiliary approach.

Keywords: chronic heart failure, aldehyde dehydrogenase 5, IL-1 receptor-like 1, CD138, diagnostic value

Rezultati: U poređenju sa kontrolnom grupom, pacijenti iz ispitivane grupe su imali značajno niže serumske nivoe Ahd-5 i niže vrednosti LVEF (P<0,05), dok su serumski nivoi IL1RL1, CD138, NT-proBNP i kreatinina, kao i vrednosti LVESV i LVEDV, bili značajno viši (P<0,05). Na osnovu LVEF vrednosti, 72 pacijenta su svrstana u grupu HFrEF, 88 u grupu HFmrEF, a 98 u grupu HFpEF. U grupama HFrEF i HFmrEF su zabeleženi značajno niži nivoi Ahd-5 u odnosu na grupu HFpEF (P<0,05), dok su nivoi IL1RL1 i CD138 bili značajno viši. U poređenju sa ostalim grupama, grupa HFmrEF je pokazala značajno više serumske nivoe IL1RL1 i CD138 (P<0,05), dok je u grupi HFrEF zabeležen najniži nivo Ahd-5. Pirsonova korelaciona analiza je pokazala da je serumski nivo Ahd-5 kod pacijenata sa CHF u pozitivnoj korelaciji sa LVEF (P<0,05), a u negativnoj sa nivoima NT-proBNP i kreatinina, kao i sa vrednostima LVESV i LVEDV (P<0,05). Nasuprot tome, serumski nivoi IL1RL1 i CD138 su bili pozitivno korelisani sa NT-proBNP, kreatininom, LVESV i LVEDV (P<0,05), a negativno sa LVEF (P<0,05). Nivo Ahd-5 pokazao je negativnu korelaciju sa nivoima IL1RL1 i CD138 (P<0,05), dok je između IL1RL1 i CD138 utvrđena pozitivna korelacija (P<0,05). ROC analiza pokazala je da su površine ispod krive (AUC) za pojedinačnu dijagnostiku CHF na osnovu serumskih nivoa Ahd-5, IL1RL1 i CD138 iznosile 0,851, 0,830 i 0,860. Kombinovana dijagnostika zasnovana na ova tri biomarkera je pokazala AUC od 0,946, što je bilo statistički značajno više u odnosu na pojedinačne AUC vrednosti za Ahd-5 (Z=2,755, P=0,009), IL1RL1 (Z=3,071, P=0,002) i CD138 (Z=2,321, P=0,023).
Zaključak: Kod pacijenata sa hroničnom srčanom insuficijencijom prisutno je značajno sniženje serumskog nivoa Ahd-5 i značajno povećanje serumskih nivoa IL1RL1 i CD138. Kombinovano određivanje ova tri biomarkera pokazuje visoku dijagnostičku vrednost u otkrivanju CHF i može predstavljati nov pomoćni pristup u kliničkoj dijagnostici.

Ključne reči: hronična srčana insuficijencija, aldehid-dehidrogenaza 5, receptor sličan interleukinu-1 tip 1, CD138, dijagnostički značaj

Introduction

The severe clinical syndrome known as chronic heart failure (CHF) significantly impairs a patient's quality of life, medical resources, and social economy in addition to raising the risk of hospitalization and death. Therefore, it is crucial to explore biomarkers for the early prediction and diagnosis of CHF (1). Currently, Aldehyde dehydrogenase 5 (Ahd-5), IL-1 receptor-like 1 (IL1RL1), and CD138 are used in the diagnosis of cardiovascular diseases. Abnormal expression of Ahd-5 has been linked to an increased risk of cardiovascular disease and cancer. Additionally, studies have shown that elevated levels of Ahd-5 can prevent oxidative stress and inflammatory responses, prevent myocardial fibrosis and apoptosis brought on by a high-sugar environment, and protect the heart's structure (2, 3). IL1RL1 levels are closely linked to cardiac function, sudden cardiac death, and both short- and long-term mortality rates, and they can be used to predict a poor prognosis in individuals with congestive heart failure (CHF) (4). CD138 is present in the endothelial glycocalyx and is released into the blood under stress conditions, where it participates in the development of various diseases, including cardiovascular disease, acute kidney injury, and chronic kidney disease (5). Research has demonstrated that the serum CD138 level in patients with acute heart failure (AHF) is substantially higher than that in patients with congestive heart failure (CHF). AHF can be diagnosed using this biomarker, which has some predictive value for the prognosis of AHF patients (6–8).

However, at present, relatively few studies have examined the combined diagnosis of CHF using Ahd-5, IL1RL1, and CD138. The combined detection of multiple markers improves diagnostic accuracy. Therefore, this study explored the diagnostic value of Ahd-5, IL1RL1, and CD138 alone and in combination for CHF. To identify new biological

markers for CHF diagnosis, serum levels of Ahd-5, IL1RL1, and CD138 were compared between CHF patients and healthy controls. The correlations among the three indicators and their associations with disease severity and indicators of cardiac function were also examined.

Materials and Methods

General information

The trial group consisted of 256 CHF patients who received treatment at our hospital between February 2023 and March 2025. Inclusion criteria: (1) met the relevant diagnostic criteria in the »2023 ESC Guidelines for Diagnosis and Treatment of Acute and Chronic Heart Failure«; (2) provided complete clinical data. Exclusion criteria: (1) complicated with other heart function disorders; (2) complicated with malignant tumours; (3) complicated with immune system diseases; (4) abnormal liver and kidney functions; (5) taking drugs related to the disease before admission; (6) complicated with cognitive communication disorders. A control group of 138 healthy volunteers who were examined at our hospital during the same time period was selected.

Each research participant signed the informed consent form after being made aware of the investigation. The Medical Ethics Committee of our hospital accepted this study (Approval Number: HKYS-2026-A0271).

Blood sample collection

Five millilitres of fasting venous blood were collected from the patient upon admission and from healthy volunteers during physical examination. The blood was centrifuged (TG16WS, Ye Tou Technology Co., Ltd., Shanghai) at 3000 r/min for 10 minutes with a 10 cm centrifugal radius. After centrifugation, the serum was collected and stored at -80 °C until analysis.

Detection of serum Ahd-5, IL1RL1, CD138, N-terminal pro-B-type natriuretic peptide (NT-proBNP), and serum creatinine levels

Serum Ahd-5, IL1RL1, and CD138 levels were determined in this experiment using enzyme-linked immunosorbent assay (ELISA). The kits were all purchased from domestic manufacturers in China to ensure reagent stability and accessibility. Among them, the Ahd-5 kit was purchased from Linyi Ailaza Biotechnology Co., LTD. (Item No. EZ-2023-Ahd-5), and the IL1RL1 kit was also provided by the same company (Item No. EZ-2023-IL1RL1). The CD138 kit is provided by Wuhan Fuyinde Technology Co., LTD. (Item No. FY-2023-CD138). All ELISA operation steps were carried out strictly in accordance with the corresponding kit instructions, including key steps such as sample dilution, sample addition, incubation, washing, colour development, and termination. Finally, the absorbance was measured at 450nm using an automatic microplate reader, and the concentration of each index was calculated from the standard curve.

In addition, as a routine biochemical indicator for evaluating the severity of heart failure, the N-terminal pro-B-type brain natriuretic peptide (NT-proBNP) and serum creatinine levels were detected using the BK-400 fully automatic biochemical analyser produced by Jinan Jiuxiang Biotechnology Co., Ltd. and its dedicated reagents (NT-proBNP reagent product number: JX-BNP-400Cr, creatinine reagent catalogue number: JX-CR-400Cr. During the testing process of all samples, quality control products were set up simultaneously. The quality control results were all within the effective range. Moreover, the laboratory personnel strictly adhered to the blinding principle during testing to minimize human bias and ensure the accuracy and objectivity of the test data.

Cardiac function index detection

Left ventricular ejection fraction (LVEF), left ventricular systolic end-diastolic volume (LVESV), and left ventricular diastolic end-diastolic volume (LVEDV) were measured using the Mindray colour Doppler ultrasound system on the day of the patient's admission and the day of the physical examination of the healthy volunteer (Consona AT, Nanjing Beden Medical Co., Ltd.).

Baseline data collection

All baseline data of the research subjects, including age, sex, history of alcohol consumption, presence of hypertension, and presence of diabetes, were collected.

Severity classification of CHF patients

Based on the LVEF results, CHF patients were divided into the heart failure with reduced ejection fraction (HFrEF) group (LVEF<40%), the heart failure with mildly reduced ejection fraction (HFmrEF) group (LVEF ranging from 40% to <50%), and the heart failure with preserved ejection fraction (HFpEF) group (LVEF≥50%).

Statistical analysis

To evaluate the data, SPSS 25.0 was used. After performing normality checks, normally dis-

tributed measurement data were reported as x±s. The LSD test was used for pairwise comparisons, the independent sample t test for two-group comparisons, and the one-way analysis of variance for multiple-group comparisons. The χ^2 test was used to compare groups, and count statistics were displayed as percentages or as counts. The associations between serum Ahd-5, IL1RL1, and CD138 levels and markers of cardiac function were examined using Pearson correlation analysis.

The correlations between serum levels of Ahd-5, IL1RL1, and CD138 and patients with varying degrees of CHF severity were examined using Spearman correlation analysis; Multivariate logistic regression analysis was used to investigate the factors that contribute to the occurrence of CHF; receiver operating characteristic (ROC) curves were used to assess the diagnostic value of serum Ahd-5, IL1RL1, and CD138 for CHF; and the DeLong test was used to compare the area under the curve (AUC).

Results

Comparison of baseline data and cardiac function-related indicators between the study group and the control group

There were no statistically significant differences in age, sex, proportion with a history of alcohol consumption, proportion with hypertension, or proportion with diabetes between the study and control groups (P>0.05). While the study group's LVEF was significantly lower than the control group's, the study group's levels of NT-proBNP, serum creatinine, LVESV, and LVEDV were all statistically significant (all P<0.05), see *Table I*.

The serum Ahd-5 levels of patients in the study group were significantly lower than those of the healthy control group, whereas the levels of IL-1RL1, CD138, the traditional heart failure marker NT-proBNP, and serum creatinine were significantly higher than those of the control group. This result fully confirms that, in patients with chronic heart failure, there is down-regulation of Ahd-5 expression and up-regulation of IL1RL1 and CD138 expression, along with changes in renal function-related indicators, suggesting that the abnormal expression of these markers is closely related to the occurrence and pathophysiological process of heart failure.

Comparison of serum Ahd-5, IL1RL1, and CD138 levels between the study group and the control group

The serum Ahd-5 level in the study group was significantly lower than that in the control group, whereas the serum IL1RL1 and CD138 levels were significantly higher in the study group than in the control group. The differences were statistically significant (P<0.05), see *Table II*.

The serum Ahd-5 level in patients with chronic heart failure in the study group was significantly lower than that in the healthy control group, indicating that the expression of this enzyme was significantly

Table I Comparison of baseline data and cardiac function related indicators between the study group and the control group [n (%)].

Group	n	Age (years)	Gender		Have a history of drinking alcohol	Combined hypertension	Combined diabetes
			Male	Female			
Research group	256	62.50±11.41	154 (60.16)	102 (39.84)	102 (39.84)	94 (36.72)	76 (29.69)
Control group	138	63.04±12.86	90 (65.22)	48 (34.78)	56 (40.58)	36 (26.09)	26 (18.84)
t/x^2		-0.249	0.480	0.013	2.295	2.742	
P		0.809	0.488	0.923	0.133	0.090	
Group	n	NT-proBNP (pg/mL)	Blood creatinine (μmol/L)	LVEF (%)	LVESV (mL)	LVEDV (mL)	
Research group	256	408.26±92.86	89.48±19.20	44.90±8.99	72.18±14.22	129.39±29.60	
Control group	138	154.60±36.41	65.22±13.78	58.62±11.41	53.25±9.55	95.60±18.87	
t/x^2		21.783	9.224	-9.261	9.872	8.547	
P		<0.001	<0.001	<0.001	<0.001	<0.001	

Table II Comparison of serum levels of LDH2, IL1RL1, and CD138 between the study group and the control group ($\bar{x}\pm s$).

Group	n	Ahd-5 (U/L)	IL1RL1 (ng/mL)	CD138 (ng/mL)
Research group	256	83.48±16.60	52.66±13.08	42.35±10.18
Control group	138	107.02±19.87	37.81±8.97	29.79±6.92
t		-8.876	8.386	9.161
P		<0.001	<0.001	<0.001

Table III Comparison of serum Ahd-5, IL1RL1, and CD138 levels in CHF patients of different severity levels ($\bar{x}\pm s$).

Group	n	Ahd-5 (U/L)	IL1RL1 (ng/mL)	CD138 (ng/mL)
HFrEF group	70	69.54±13.54	61.84±12.41	52.00±9.01
HFmrEF group	88	83.78±14.09	52.52±11.97	41.86±8.46
HFpEF group	98	93.02±15.30	46.14±11.21	35.83±7.88
F		27.020	17.943	38.429
P		<0.001	<0.001	<0.001

Table IV Correlation between serum Ahd-5, IL1RL1, CD138 levels and cardiac function related indicators.

Indicator	Ahd-5		IL1RL1		CD138	
	r	P	r	P	r	P
NT-proBNP	-0.509	<0.001	0.537	<0.001	0.449	<0.001
Serum creatinine	-0.482	<0.001	0.511	<0.001	0.437	<0.001
LVEF	0.502	<0.001	-0.536	<0.001	-0.457	<0.001
LVESV	-0.42	<0.001	0.527	<0.001	0.449	<0.001
LVEDV	-0.471	<0.001	0.517	<0.001	0.423	<0.001
Ahd-5	-	-	-0.48	<0.001	-0.536	<0.001
IL1RL1	-0.453	<0.001	-	-	0.441	<0.001
CD138	-0.536	<0.001	0.441	<0.001	-	-

down-regulated in patients with heart failure. Meanwhile, serum IL1RL1 and CD138 levels in the study group were significantly higher than in the control group, with a clear upward trend.

Analysis of differences in serum Ahd-5, IL1RL1, and CD138 levels among patients with different degrees of CHF severity

The LVEF results for CHF patients showed 70 patients in the HFrEF group, 88 in the HFmrEF group, and 98 in the HFpEF group. The serum Ahd-5 levels in the HFrEF group and the HFmrEF group were significantly lower than those in the HFpEF group, while the serum IL1RL1 and CD138 levels were significantly greater than those in the HFpEF group ($P<0.05$). The serum Ahd-5 level in the HFrEF group was significantly lower than that in the HFmrEF group, while the serum IL1RL1 and CD138 levels were significantly greater than those in the HFmrEF group, and the differences were statistically significant ($P<0.05$), see *Table III*.

Table V Multivariate logistic regression analysis of the influencing factors of CHF occurrence.

Factor	β	SE	Wald x^2	P	OR	OR 95%CI
Ahd-5	-0.40	0.159	9.070	0.006	0.628	0.463~0.842
IL1RL1	1.014	0.318	10.309	0.001	2.742	1.486~5.060
CD138	1.062	0.370	8.0146	0.008	2.916	1.394~6.092
NT-proBNP	0.711	0.406	3.170	0.078	2.054	0.934~4.512
Serum creatinine	0.794	0.485	2.697	0.104	2.209	0.851~5.677

Table VI Diagnostic value of serum Ahd-5, IL1RL1, CD138 alone and in combination for CHF.

Variable	AUC	AUC 95%CI	Best Truncation Value	Sensitivity (%)	Specificity (%)	Youden index	P
Ahd-5	0.851	0.808~0.914	91.75 U/L	85.5	72.8	0.570	<0.05
IL1RL1	0.830	0.770~0.891	45.92 ng/mL	84.7	76.1	0.615	<0.05
CD138	0.860	0.814~0.926	36.02 ng/mL	85.2	78.6	0.645	<0.05
Joint efforts of the three parties	0.946	0.917~0.975	-	82.3	92.1	0.741	<0.05

Correlations of serum levels of Ahd-5, IL1RL1, and CD138 in indicators of cardiac function

There was a positive correlation between the serum Ahd-5 level in CHF patients and LVEF ($P<0.05$) and a negative correlation with NT-proBNP, serum creatinine level, LVESV, and LVEDV; the serum levels of IL1RL1 and CD138 were positively correlated with NT-proBNP, serum creatinine level, LVESV, and LVEDV ($P<0.05$) and negatively correlated with LVEF ($P<0.05$). The serum Ahd-5 level was negatively correlated with IL1RL1 and CD138 levels ($P<0.05$), and the serum IL1RL1 level was positively correlated with the serum CD138 level ($P<0.05$), see *Table IV*.

Spearman correlation analysis revealed that the serum Ahd-5 level was negatively correlated with CHF severity ($rs=-0.495$, $P<0.001$), whereas the serum IL1RL1 and CD138 levels were positively correlated with CHF severity ($rs=0.531$, 0.479; all $P<0.001$).

Multivariate logistic regression analysis of the influencing factors of CHF occurrence

Ahd-5, IL1RL1, CD138, NT-proBNP, and serum creatinine were used as independent variables (all input in original values), and whether CHF occurred was used as the dependent variable (no = 0, yes = 1) for multivariate logistic regression analysis. Elevated serum Ahd-5 levels were a protective factor against CHF occurrence ($P<0.05$), and elevated serum IL1RL1 and CD138 levels were both risk factors for CHF occurrence ($P<0.05$), see *Table V*.

After controlling for confounding factors, serum Ahd-5, IL1RL1, and CD138 levels were all independent predictors of chronic heart failure. A decreased level of serum Ahd-5 is a risk factor for heart failure, suggesting that the loss of its protective effect is closely associated with disease progression, whereas elevated levels of serum IL1RL1 and CD138 are independent risk factors for heart failure.

Diagnostic value of serum Ahd-5, IL1RL1, and CD138 for CHF

To determine whether CHF occurred, the state variable (0 = no, 1 = yes), and Ahd-5, IL1RL1, CD138, NT-proBNP, and serum creatinine were used as test variables to construct the ROC curve. The results revealed that the AUCs for serum Ahd-5, IL1RL1, and CD138 alone in diagnosing CHF were 0.851, 0.830, and 0.860, respectively. The AUC of

the combined diagnosis of CHF was 0.946, which was significantly greater than the AUCs of serum Ahd-5 (Z=2.755, P=0.009), IL1RL1 (Z=3.071, P=0.002), and CD138 (Z=2.321, P=0.023) alone for diagnosing CHF, see *Table VI*.

Discussion

CHF is a chronic and recurrent disease. The 30-day readmission rate for CHF patients is 20% to 25%, and the 5-year survival rate is only 56.7% (9). CHF refers to a complex clinical syndrome characterized by abnormal changes in cardiac function and structure. The characteristics of patients with CHF include decreased exercise capacity, an unpredictable disease course, decreased quality of life, and heavy symptom burden, and the prognosis of CHF patients is poor, with a high mortality rate (10). Even though conventional biomarkers such as BNP and NT-proBNP have been used in clinical screening, diagnosis, and disease assessment of heart failure (HF), they have significant limitations and are vulnerable to confounding factors, including age, renal function, obesity, and arrhythmias (11). Therefore, identifying new biomarkers for the early prediction of CHF occurrence is particularly important.

Acetaldehyde and endogenous lipid aldehydes are detoxified by Ahd-5, which is primarily found in mitochondria. Increased expression of Ahd-5 can ameliorate cardiac dysfunction by inhibiting the cGAS/STING signalling pathway, lowering reactive oxygen species production, and preventing apoptosis and inflammation (12). In this study, serum Ahd-5 levels were significantly lower in CHF patients than in control patients. Furthermore, serum Ahd-5 levels were negatively correlated with the severity of CHF, suggesting that the pathophysiology and progression of CHF may be linked to serum Ahd-5 levels. High expression of Ahd-5 can directly metabolize toxic substances such as acetaldehyde and reduce the generation of reactive oxygen species in cardiomyocytes, thereby reducing oxidative stress to the cell membrane and mitochondria of cardiomyocytes, preventing cardiomyocyte necrosis or apoptosis due to excessive oxidative stress, inhibiting the PINK1/Parkin signalling pathway, reducing mitochondrial autophagy, and protecting cardiomyocytes. It can also inhibit the transforming growth factor-β/Smad signalling pathway, reduce collagen deposition, prevent myocardial interstitial fibrosis, and maintain the stability of cardiac structure and contractile function. In addition, Ahd-5 can inhibit inflammation, reduce chronic inflammatory infiltration in myocardial tissue, and delay inflammation-mediated myocardial damage (13, 14). The serum Ahd-5 level is negatively correlated with the serum NT-proBNP and creatinine levels, LVESV, and LVEDV, and positively correlated with the LVEF. An elevated serum Ahd-5 level is a protective factor for CHF, suggesting that it may affect cardiac function in CHF patients. In this study, NT-proBNP and serum creatinine did not influence the occurrence of CHF, unlike previous research (15). The main mechanism involves regulating mitochondrial energy metabolism via the Ahd-5-AMPK signalling pathway, thereby mitigating oxidative/nitrosative stress, attenuating mitochondrial-mediated cell death, and playing a crucial role in protecting myocardial cells and maintaining cardiac function (16). Low expression of Ahd-5 exacerbates endothelial cell injury in coronary arteries mediated by 4-hydroxy-2-nonenal in diabetic mice, leading to cardiac dysfunction. However, the inhibitory effect of low Ahd-5 expression on inflammation and apoptosis is reduced, which may lead to damage to cardiac structure and function, thereby promoting the occurrence and development of CHF (17).

When myocardial stress occurs, cardiac fibroblasts and cardiomyocytes produce IL1RL1, a soluble receptor also derived from aortic and coronary artery endothelial cells, immune cells such as T lymphocytes, and other cells (18). In this study, the serum IL1RL1 level in CHF patients was significantly higher than that in healthy individuals. Both the HFrEF and HFmrEF groups had significantly higher serum IL1RL1 levels than the HFpEF group, and the HFrEF group's were significantly higher than the HFmrEF group's. In patients with congestive heart failure, the serum IL1RL1 level was negatively associated with LVEF and positively associated with serum NT-proBNP, creatinine, LVESV, and LVEDV. These results suggest that IL1RL1 may affect heart function and is associated with the onset and progression of CHF. Under normal physiological conditions, IL-33 can bind to membrane-bound ST2, activating the downstream signal JAK/STAT, thereby inhibiting myocardial hypertrophy, reducing myocardial fibrosis, and exerting myocardial protective effects. However, when the myocardium is subjected to stress loads (such as hypertension) or ischemia, myocardial cells release large amounts of IL1RL1. An increase in IL1RL1 levels competes with ST2L for binding to IL-33, reducing myocardial tolerance to damage, further exacerbating myocardial apoptosis and promoting myocardial interstitial fibrosis, thereby accelerating the progression of CHF (19).

In comparison to the group of patients who passed away, the CHF survivor group's IL1RL1 level was noticeably lower (20). Serum IL1RL1 and BNP levels in patients with CHF are positively correlated with NYHA functional classification and can be used to diagnose CHF. IL1RL1 may affect the progression of CHF through participating in inflammatory responses, cardiac remodelling, and cardiac fibrosis processes (21). Therefore, an increase in serum IL1RL1 levels exacerbates the heart's inflammatory response, cardiac remodelling, and fibrosis, pro-

motes the development of CHF, and is a potential biomarker for monitoring CHF.

CD138 is a type of sulphated heparan sulphate proteoglycan that is crucial for maintaining normal cell morphology, maintaining protein interactions inside and outside cells, and mediating signal transduction in response to environmental stimuli (22, 23). The pathological features of patients with HF include a significant increase in the inflammatory response and a doubling of adrenergic reactivity, which are associated with endothelial dysfunction, glycolipid damage, cardiac fibrosis, atherosclerosis, and neuroendocrine activation, especially via the renin angiotensin aldosterone system. Additionally, shedding of CD138 may reflect renal endothelial injury and, by extension, exacerbate cardiac dysfunction (24). Serum CD138 levels in rats with postresuscitation syndrome are significantly greater than those after treatment and are closely related to the severity of myocardial dysfunction, possibly because CD138 triggers acute oxidative stress responses during cardiac arrest, exacerbating damage to myocardial tissue (25). Therefore, CD138 may be involved in inflammatory responses and oxidative stress during myocardial dysfunction, and its overexpression promotes myocardial injury and cardiac remodelling, aggravating myocardial dysfunction and increasing the risk of CHF.

The NT-proBNP, serum creatinine, LVESV, and LVEDV levels in CHF patients were considerably higher than those in healthy individuals in our investigation, whereas the LVEF was significantly lower than that in healthy individuals, consistent with findings from other studies (26–28). These results support the study's conclusions. This study also looked at how blood levels of CD138, IL1RL1, and Ahd-5 relate to one another. The results demonstrated a positive association between serum IL1RL1 and CD138 levels, and a negative correlation between serum Ahd-5 levels and IL1RL1 and CD138 levels. The combined diagnosis of CHF using serum Ahd-5, IL1RL1, and CD138 has a greater AUC than the individual diagnosis of the three, with increased specificity, which helps improve the diagnostic accuracy and is expected to become a powerful indicator for the early diagnosis and prognosis prediction of CHF, assisting in the diagnosis and timely intervention of CHF patients.

Conclusion

While the serum levels of IL1RL1 and CD138 were dramatically elevated in CHF patients, the serum levels of Ahd-5 were significantly reduced. The severity of the patient's disease and heart function markers showed a strong correlation with each of these parameters. When all three indications are detected together, the diagnostic effectiveness and specificity for CHF are both high. Nevertheless, there are a number of issues with this study, including its limited sample size, the absence of dynamic monitoring of index changes, and the lack of exploration of the mechanisms of action of serum Ahd-5, IL1RL1, and CD138 levels in CHF patients. Therefore, further research with a larger sample size from diverse sources is still needed to improve the accuracy and reliability of these conclusions and to provide a theoretical basis for clinical application.

Conflict of interest statement

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

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