ORIGINAL RESEARCH

Expression and Clinical Significance of Serum sST2, BDNF, CTnI, and BUN/Cr in Patients With Heart Failure

Cui Xie, MS; Yu Zhan, MS; You Wu, MS; Zhixin Zhang, MS; Yang Xiang, MS; Lin Wang, BS; Dan Chen, MS

ABSTRACT

Context • Of the 26-million people suffering from heart failure worldwide, 80% require hospitalization for treatment every year. Biomarkers for clinical diagnosis and prognostic evaluation of heart failure may include: (1) growth-stimulating expression gene 2 protein (sST2), (2) blood urea nitrogen (BUN) and creatinine (Cr), (3) cardiac troponin I (CTnI), and (4) brain-derived neurotrophic factor (BDNP). At present, few studies have occurred on the expression of those biomarkers in patients with heart failure.

Objective • The study intended to investigate the expression and clinical significance of serum- soluble sST2, BDNF, CTnI, and BUN/Cr in patients with heart failure.

Design • The research team designed a prospective controlled study.

Setting • The study took place at Renmin Hospital at the Hubei University of Medicine in Shiyan, Hubei, China.

Participants • Participants were 108 patients with heart failure who had been admitted to the hospital between March 2020 and March 2021 and 115 healthy individuals who received physical examinations during the same period.

Intervention • The intervention group included the 108 participants with heart failure, and the control group included the healthy individuals. The research team further divided the intervention group into stage II, III, and IV groups, with 23, 65, and 20 patients, respectively.

Outcome Measures • The research team collected and compared the serum levels of sST2, BDNF, CTnI, BUN/Cr, and left ventricular ejection fraction (LVEF) between the groups. The team used the Pearson correlation analysis to analyze the correlation between each parameter and participants' cardiac function and multivariate logistic regression analysis to analyze the factors influencing heart failure.

Results • No significant differences existed in age, gender, or disease course between the combined intervention groups and the control group at baseline ($P > .05$). The sST2, CTnI, and BUN/Cr levels of the combined intervention groups were significantly higher than those of the control group postintervention. In addition, the sST2, CTnI, and BUN/Cr levels significantly increased as the disease stage progressed (all $P < .05$). The levels of BDNF and LVEF in the combined intervention group were significantly lower than those in the control group postintervention, with the two parameters having significantly decreased in the intervention groups as the disease stage progressed (all $P < .05$). The Pearson correlation analysis found that the sST2, CTnI, and BUN/Cr were positively correlated with cardiac function, with $r = 0.483$, $P = .017$; $r = .521$, $P = .011$; $r = 0.321$, $P = .021$; $r = 0.271$, $P = .032$; and $r = 0.632$, $P = .007$, respectively. The BDNF and LVEF were negatively correlated with cardiac function, with $r = -0.43$, $P < .001$ and $r = -0.39$, $P < .001$, respectively. With heart failure as the dependent variable, the logistic regression analysis showed that the sST2, CTnI, BUN, Cr, and BUN/Cr were the risk factors for heart failure, and the BDNF and LVEF were the protective factors against heart failure.

Conclusions • The serum sST2, CTnI, and BUN/Cr were highly expressed in patients with heart failure, while the expression of BDNF was low. Medical practitioners should pay attention to the risk factors sST2, CTnI, and BUN/Cr, and a higher BNDF indicates a better condition in patients with heart failure. (*Altern Ther Health Med.* 2023;29(1):176-181).

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Heart failure has become a global public-health problem. It's the end-stage manifestation of a variety of cardiovascular diseases with different clinical symptoms; for example, symptoms of patients: (1) with right heart failure include swelling of the limbs, obvious upper abdominal pain, nervousness, somnolence, nausea, and vomiting; (2) with left heart failure include insomnia, oliguria, dyspnea, hemoptysis,

and coughing; and (3) with total heart failure include reduced blood output and dyspnea.[1,2]

About 26-million people worldwide suffer from heart failure, and 80% of those patients require hospitalization for treatment every year. At least one-third of patients need to be hospitalized repeatedly, which brings heavy economic burdens to patients and society.[3,4]

Despite the continuous advancement of medical technology, heart failure is still the leading cause of death in hospitalized patients worldwide. Therefore, early detection, early diagnosis, accurate assessment of patients' prognoses, early intervention, and active development of reasonable treatment plans can improve patients' clinical outcome and reduce the mortality rate, which is of great clinical significance.

Adamo et al[5] have confirmed that ventricular remodeling, as the basis for the occurrence and development of chronic heart failure, allows the body to promote the progression of heart failure through seven pathways: myocardial stretch, muscle-cell damage, neuro-hormonal activation, matrix remodeling, inflammatory responses, oxidative stress, and renal insufficiency. A variety of biomarkers in these pathways can be indicators for clinical diagnosis and prognostic evaluation. They include: (1) growth-stimulating expression gene 2 protein (sST2), (2) blood urea nitrogen (BUN) and creatinine (Cr), (3) cardiac troponin I (CTnI), and (4) brain-derived neurotrophic factor (BDNP).

sST2

Among the biomarkers, the serum-soluble sST2 is an emerging marker that has been associated with an increased risk of adverse cardiovascular events.[6] ST2 is a member of the interleukin-1 (IL-1) receptor family, which exists in three forms: a trans-membrane receptor (ST2L), a variant STV, and a soluble decoy receptor (sST2). The American College of Cardiology (ACC) and American Heart Association (AHA) guidelines pointed out in 2017 that sST2 was a good marker for myocardial fibrosis, which can predict the risk of hospitalization and death in patients with heart failure.[7]

ST2L can combine with IL-33; can inhibit the activation of angiotensin II and nuclear factor-KB (NF-kB), which has a protective effect on cardiomyocytes; and can protect cells from the influence of apoptosis, adaptive hypertrophy, and fibrosis, thereby reducing the incidence of cardiac dysfunction.[8] When cardiomyocytes are injured, the body secretes a large amount of sST2 to competitively inhibit the cardioprotective function of ST2L/IL-33, leading to ventricular remodeling, myocardial fibrosis and loss of function.[9]

In in-vivo and in-vitro models, Januzzi found that ST2L can transduce the effects of interleukin-33, while excess sST2 can lead to cardiac hypertrophy, fibrosis, and ventricular dysfunction.[10] Jirak et al analyzed the prognostic effect of sST2 and heart failure for patients with acute or chronic heart failure.[11] Those researchers found a correlation between an increase in sST2 and severe vascular death and adverse cardiovascular events, making it an independent risk factor for predicting hospitalization and death.

Zhu et al pointed out that sST2 was significantly related to the mortality and rehospitalization rate of patients with heart failure.[12] In addition, Emdin et al pointed out that sST2 has an independent prognostic value in chronic heart failure.[13]

BUN and Cr

The heart and the kidneys have a close, two-way connection. Five types of clinically defined cardiorenal syndromes exist, of which the type I cardiorenal syndrome reflects the sudden deterioration of heart function that causes acute kidney injury. Therefore, changes in renal-function indicators of patients with heart failure may be related to the prognosis of patients.

BUN and Cr are recognized indicators of renal function and are related to the prognosis of acute heart failure.[14] The dysfunction of ventricular contraction and diastole in patients with heart failure can cause insufficient renal perfusion, induce kidney damage, reduce the glomerular filtration rate, increase water and sodium reabsorption, and reduce urea excretion. The renal tubules don't reabsorb creatinine but can reabsorb part of the urea nitrogen. The renin-angiotensin-aldosterone system (RASS) and the sympathetic nervous system (SNS) regulate the reabsorption, so BUN/Cr can be an effective indicator of neurohormonal activity, which may have a certain predictive value for heart failure.[15]

Since many factors can affect the results when using urea nitrogen and serum creatinine alone to predict the prognosis of patients with acute heart failure, those different factors can form the basis of a hypothesis that BUN/Cr may be more stable and more capable than urea nitrogen and serum creatinine alone to accurately assess the prognosis of patients with acute heart failure.[16]

Matsue et al confirmed that BUN/Cr or urinary nitrogen can be an independent predictor of patients with heart failure.[17] Takaya et al[18] found that BUN/Cr can better predict the prognosis of patients with heart failure than urea nitrogen and serum creatinine alone. Brisco et al demonstrated that BUN/Cr and renal function can have a strong correlation with the prognosis of patients with acute heart failure.[19]

CTnI

CTnI is a protein that regulates myocardial muscle contractions and can reflect the occurrence of myocardial diseases to a certain extent.[20] CTnI is a complex subunit of cardiac troponin, which is mainly stored in cardiomyocytes. When heart failure occurs, cardiomyocytes can cause ventricular-muscle remodeling, endothelial-cell dysfunction, ventricular-cavity enlargement, cardiomyocyte apoptosis, and increased cell-membrane permeability under the condition of ischemia and hypoxia.

After CTnI has entered the blood, its level increase.[21] The CTnI levels tend to increase within 3-4 hours after myocardial injury and reach a peak within 10-24 hours. Its peak value can be as high as 50 times the maximum reference value, which reflects the specific serological markers of myocardial acid and

necrosis in the body. The more serious the myocardial ischemia, hypoxia, and damage, the higher are patients' CTnI levels.

Biancardi et al,[22] Zhang,[23] and Bao et al[24] found that the CTnI levels of patients with heart failure were significantly higher than those of healthy people and were closely related to heart failure. This may be due to the fact that the more serious the hypoxia and ischemia of myocardial cells, the more severe the damage to the cell membranes, which provides good conditions for the penetration of CTnI into the intercellular substance. This penetration is conducive to the entry of CTnI into blood vessels and increases in the levels of plasma CTnI.

Huang et al[25] confirmed that the serum CTnI levels of patients with heart failure were significantly higher than those of healthy people, and the elevation of CTnI was related to the classification of patients' cardiac function.

BDNP

BDNP is a member of the neurotrophic-factor family, and it: (1) helps regulate nerve regeneration, neuroprotection, and synaptic plasticity; (2) plays an important role in the nervous system; (3) can help endothelial cells survive during cardiovascular development; (4) participates in cell proliferation and apoptosis by activating its tropomyosin-related kinase receptor B (TrkB), and (5) has an obvious myocardial protective effect, helping avoid the effects of ventricular remodeling after myocardial infarction.[15,26,27]

Two other studies have confirmed that the BDNF levels in patients with coronary heart disease were significantly reduced and were closely related to the occurrence of adverse cardiovascular reactions in patients, suggesting that BDNF also can play an important role in the cardiovascular system.[28,29]

Kadowaki[30] showed that BDNF was related to the severity of illness of and prognosis for older adults with heart failure and that it can play an important role in the development of heart failure, which may be due to skeletal muscle's secretion of BDNF. When heart failure occurs, the blood flow of the patient's skeletal muscle decreases, and the secretion of BDNF declines, resulting in the decrease of BDNF levels in patients with heart failure.

In addition, BDNF can promote the excitement of sympathetic nerves of patients with cardiovascular diseases, and the sympathetic-nerve activation was associated with poor prognosis. Moreover, those researchers found that it can lead to increased levels of glucocorticoids, which can reduce the secretion of BDNF. It is found that a decrease of BDNF in patients with heart failure can affect the patient's condition and prognosis.[13]

Current Study

At present, few studies have occurred on the expression of serum sST2, BDNF, CTnI, and BUN/Cr in patients with heart failure.[31-34] Zhang[23] found that the levels of sST2, NT-proBNP and hs-cTnI can be used to assess the prognosis of heart failure.

Therefore, the current study intended to investigate the expression and clinical significance of serum-soluble sST2, BDNF, CTnI, BUN/Cr in patients with heart failure.

METHODS

Participants

The research team designed a prospective controlled study. The study took place at Renmin Hospital at the Hubei University of Medicine in Shiyan, Hubei, China. Potential participants were patients with heart failure who had been admitted to the hospital between March 2020 and March 2021 and 115 healthy individuals who had received physical examinations during the same period.

Potential participants were included in the study if they: (1) had received a diagnosis of heart failure according to the relevant diagnostic criteria in *The 2018 Guidelines for the Diagnosis and Treatment of Heart Failure in China,*[20] with their heart ultrasounds having shown incomplete, left heart function, an LVEF of ≤50%, and a BNP of ≥200 ng/L; (2) were patients with cardiac-function classification from the New York Heart Association (NYHA) being a grade of stage II-IV, with a higher grade indicating higher levels of illness; (3) were patients with good compliance and normal mental abilities: the unity and integrity of the mental and environmental activities and the relative stability of character; and (4) had a normal blood-coagulation function: activated partial thromboplastin time (aPTT) of 32-43 s, plasma fibrinogen of 2-4 g/L, prothrombin time (PT) of 11-13 s, and plasma coagulase time of 18 s.

Potential participants were excluded from the study if they: (1) had incomplete clinical data or lost to follow-up; (2) had severe liver or kidney dysfunction: obvious or lasting liver-disease symptoms, such as fatigue, loss of appetite, abdominal distention, or yellow urine; continuous or repeated increase of glutamic-pyruvic transaminase and glutamic-oxaloacetic transaminase; or decreased serum albumin; (3) had severe anemia; (4) had had an acute myocardial infarction or had congenital heart disease, myocarditis, constriction pericarditis or pulmonary embolism; (5) were pregnant or lactating women; (6) had malignant tumors; (7) had severe infectious diseases; (8) had a reduced immune function; (9) had rheumatic immune diseases; or (10) were in cardiogenic shock.

The research team enrolled participants with normal electrocardiograms and without a history of cardiovascular disease as the healthy controls.

Participants received information about the study's protocols and intent and signed a written informed consent.

Procedures

Data collection. The research team collected participant's demographic and clinical data: ages, genders, blood pressures, heart rates, blood lipids, risk of diabetes, hypertension, and other common risk factors for heart failure.

Having had an empty stomach for more than eight hours, all participants provided 5 ml of cubital venous blood

in the morning of the day after admission to the hospital. After the blood's centrifugation, the research team stored the samples in a refrigerator at -40°C for use.

Outcome measures. At baseline and postintervention, the research team compared the levels of serum sST2, BDNF, CTnI, BUN/Cr, and LVEF between the groups. The research team detected the serum sST2 and BDNF using an enzyme-linked immunosorbent assay (ELISA). The team purchased the kits from Wuhan Elite Biotech and strictly followed the manufacturer's instructions. The team measured the CTnI using a double-site enzyme-linked immunoassay, an ELISA, purchasing the kits from Beijing Biolab Technology and strictly following the manufacturer's instructions. The hospital's laboratory measured biochemical indicators, such as urea and creatinine, using an AU 5800 automatic biochemical analyzer.

Luo Yao et al[35] found that the left ventricular ejection fraction (LVEF) can play a role in diagnosing cardiac function in patients with heart failure. Therefore, the study used the LVEF to evaluate the index of cardiac function in patients with heart failure. The study used the German Siemens Sonoline G50 Doppler ultrasonic detector to measure all participants' LVEF values.

Correlations between variables as well as the factors influencing heart failure Postintervention, the research team analyzed the to investigate the relationships between participants' demographic and clinical data and indicators with significant differences in between-groups comparisons and cardiac function as well as the factors influencing heart failure.

Statistical Analysis

The research team used SPSS 23.0 software for statistical analysis of data. They tested all data for normality and homogeneity of variance, using means ± standard deviations (SDs) to represent measurement data, the *t* test for measurement data between groups, and a one-way analysis of variance (ANOVA) and the Fishers least significant difference (LSD)-t test for comparisons between groups.

The team conducted a Pearson correlation analysis to investigate the relationships between participants' demographic and clinical data and indicators with significant differences in between-groups' comparisons and cardiac function as well as the factors influencing heart failure.

The analysis used heart failure as the dependent variable, and parameters with significant differences between groups, including the sST2, BDNF, CTnI, BUN, Cr, BUN/Cr, and LVEF as independent variables. The team used univariate and multivariate logistic regression to analyze the factors related to the curative effects of gene polymorphic membranous nephropathy. $P < .05$ was considered to be a statistically significant difference.

RESULTS

The study included and analyzed the data of 108 patients with heart failure and 115 healthy individuals. The stage II, III, and IV groups included 23, 65, and 20 participants, respectively.

Demographics and Clinical Data

Table 1 shows that no statistically significant differences in age, gender, or disease course existed between the combined intervention groups and the control group at baseline ($P > .05$). The differences in the disease course, primary disease, and medications in the stage II, III, and IV intervention groups weren't statistically significant at baseline ($P > .05$).

At baseline, the combined intervention groups' BUN and Cr levels were significantly higher than those of the control group. The stage II group had significantly lower levels than those in the stage III and IV intervention groups, and the stage III group's levels were significantly lower than those of the stage IV group ($P < .05$).

Serum sST2, BDNF, CTnI, BUN/C, and LVEF

Table 2 shows that the combined intervention groups' levels of sST2, CTnI, and BUN/Cr were significantly higher than those of the control group postintervention. The stage III and IV groups postintervention had significantly higher levels than those of the stage II group, and the stage IV group had significantly higher levels than those of the stage III group ($P < .05$). The combined intervention groups' levels of BDNF and LVEF were significantly lower than those in the control group ($P < .05$).

Correlation of Serum Variables and Cardiac Function

The combined intervention groups' ST2, CTnI, BUN, Cr, and BUN/Cr were positively correlated with cardiac function, with $r = 0.483$, 0.521, 0.321, 0.271, and 0.632, respectively, and $P = .017$, .011, .021, .032, and .007, respectively (data not shown). The intervention groups' BDNF and LVEF were negatively correlated with cardiac function, with $r = -0.43$, $P < .001$ and $r = -0.39$, $P < .001$, respectively (data not shown).

Factors Affecting Heart Failure

As Table 3 shows, the sST2, CTnI, BUN, Cr, and BUN/Cr were the risk factors for heart failure, and the BDNF and LVEF were the protective factors against heart failure.

DISCUSSION

The current study showed that the serum sST2, CTnI, and BUN/Cr levels of the combined intervention group were significantly higher than those of the control group; those in the stage III and IV groups were significantly higher than those in the stage II group; and those in the stage IV group were significantly higher than those in the stage III group. The BDNF and LVEF levels of the combined intervention group were significantly lower than those in the control group; those in the stage III and IV groups were significantly lower than those in the stage II group; and those in the stage IV group were significantly lower than those in the stage III group, suggesting that sST2, CTnI, and BUN/Cr levels increased for

Table 1. Comparison of Demographics and Clinical Data at Baseline

	Stage II Group n = 23 Mean ± SD n (%)	Stage III Group n = 65 Mean ± SD n (%)	Stage IV Group n = 20 Mean ± SD n (%)	Control Group n = 115 Mean ± SD n (%)	t/χ^2	*P* Value All Intervention Groups to Control Group	*P* Value
Age, y	52.87 ± 9.98	53.67 ± 9.92	54.58 ± 9.83	53.06 ± 9.39	0.132	.895	
Gender							
Males	14 (60.87)	39 (60.00)	13 (65.00)	62 (53.91)			
Females	9 (39.13)	26 (40.00)	7 (35.00)	53 (46.09)			
Disease course, mos	14.68 ± 4.01	14.99 ± 4.27	15.73 ± 4.31		0.666	.506	
BMI, kg/m^2	23.01 ± 3.56	23.67 ± 3.47	24.73 ± 3.48	23.24 ± 3.29	-6.609	<.001[a]	
BUN, mmol/L	67.98 ± 12.08[b]	78.87 ± 15.87[c]	89.08 ± 19.67	42.32 ± 12.02	9.439	<.001[a]	
Cr, μmol/L	60.02 ± 5.09[b]	65.81 ± 5.87[c]	71.92 ± 5.01	51.69 ± 5.09	146.591	<.001[a]	
Primary disease					-4.287		<.001[a]
Ischemic cardiomyopathy	19 (82.61)	51 (78.46)	13 (65.00)		-1.570		.118
Dilated cardiomyopathy	3 (13.04)	9 (13.85)	5 (25.00)		-1.643		.102
Hypertensive heart disease	1 (4.35)	5 (7.69)	2 (10.00)		0.291		.590
Medication[d]							
ACEI/ARB	15 (65.22)	45 (69.23)	16 (80.00)		0.003		.956
ARNI	1 (4.35)	10 (15.39)	6 (30.00)		0.062		.803
β-blocker	12 (52.17)	42 (64.62)	16 (80.00)		0.024		.877
MRA	6 (26.09)	22 (33.85)	11 (55.00)		13.538		.001[#]

[a]*P* < .05, indicating that the combined intervention group had significantly higher levels for BMI, BUN, and CR at baseline than did the control group
[b]*P* < .05, indicating that the stage II intervention group had significantly lower levels of BUN and CR at baseline than did the stage III and IV intervention groups
[c]*P* < .05, indicating that the stage III intervention group's levels of BUN and CR at baseline were significantly lower than those of the stage IV intervention group
[d]Some participants were taking more than one medication.

Abbreviations: ACEI/ARB, angiotensin converting enzyme inhibitor/angiotensin receptor blocker; ARNI, angiotensin receptor-enkephalinase inhibitor; BMI, body mass index; BUN, blood urea nitrogen; Cr, creatinine; MRA, aldosterone receptor antagonist.

Table 2. Comparison of Serum sST2, BDNF, CTnI, BUN/Cr and LVEF Levels

	Stage II Group n = 23 Mean ± SD	Stage III Group n = 65 Mean ± SD	Stage IV Group n = 20 Mean ± SD	Control Group n = 115 Mean ± SD	t/χ^2	*P* Value All Intervention Groups to Control Group
sST2, pg/mL	28.93 ± 4.39[a]	109.83 ± 6.39[b]	184.39 ± 9.32	16.83 ± 4.01	-7.386	<.001[c]
BDNF, ng/mL	21.02 ± 2.01[a]	18.23 ± 1.78[b]	14.02 ± 1.47	32.01 ± 2.23	-7.927	<.001[c]
CTnI, ng/L	23.03 ± 4.41[a]	31.93 ± 4.23[b]	34.93 ± 4.57	6.83 ± 2.01	98.721	<.001[c]
BUN/Cr, %	113.08 ± 2.27[a]	119.69 ± 2.36[b]	125.11 ± 2.67	81.33 ± 3.02	-1.587	<.001[c]
LVEF, %	53.28 ± 4.39	41.29 ± 4.63	33.29 ± 4.21	65.39 ± 4.09	0.399	.690

[a]*P* < .05, indicating that the stage II intervention group had significantly lower levels for sST2, CTnI, and BUN/CR and significantly higher levels for BDNF postintervention than did the stage III and IV intervention groups
[b]*P* < .05, indicating that the stage III intervention group had significantly lower levels for sST2, CTnI, and BUN/CR and significantly higher levels for BDNF postintervention than those of the stage IV intervention group
[c]*P* < .05, indicating that the combined intervention group had significantly higher levels for sST2, CTnI, and BUN/CR and significantly lower levels for BDNF and LVEF postintervention than did the control group

Abbreviations: BDNF, brain-derived neurotrophic factor; BUN/Cr, blood urea nitrogen/creatinine; CTnI, cardiac troponin I; LVEF, left ventricular ejection fraction; sST2, serum soluble growth-stimulating expression gene 2 protein.

Table 3. Multivariate Logistic Regression Analysis of the Factors Affecting Heart Failure. The sST2, CTnI, BUN, Cr, and BUN/Cr were the risk factors for heart failure, and the BDNF and LVEF were the protective factors against heart failure.

Variables	β value	s	Wald χ^2	*P* Value	OR (95%CI)
sST2	0.006	0.003	5.762	.015	1.006 (0.763-1.827)
BDNF	-0.626	0.031	11.528	.001	1.22 (1.068-1.301)
BUN	0.372	0.015	4.021	.019	0.132 (1.045-1.298)
Cr	0.622	0.177	12.583	.000	1.812 (1.356-2.432)
BUN/Cr	0.336	0.213	4.653	.009	1.389 (1.188-1.636)
LVEF	0.251	0.004	3.456	.042	1.632 (0.981-2.829)
CTnI	0.342	0.158	3.651	.019	1.412 (1.221-1.659)

Abbreviations: 95%CI, 95% confidence interval; BDNF, brain-derived neurotrophic factor; BUN, blood urea nitrogen; Cr, creatinine; LVEF, left ventricular ejection fraction; CTnI, cardiac troponin I; OR, odds ratio; sST2, serum soluble growth-stimulating expression gene 2 protein.

patients with heart failure. The BDNF and LVEF levels showed a downward trend, and the higher the NYHA cardiac function classification, the lower the levels were.

The current study showed that the sST2, CTnI, BUN, Cr, BUN/Cr were positively correlated with cardiac function in patients with heart failure, and BDNF and LVEF were negatively correlated with cardiac function. Further multivariate logistic regression analysis showed that the risk factors for heart failure were sST2, CTnI, BUN, Cr, BUN/Cr, and the protective factors were BDNF and LVEF.

The current study had the following limitations: (1) as a single-center study, it may have regional limitations and not be representative of all patients with heart failure; (2) the study was observational, and multivariate analysis can't exclude the influence of other confounding factors; and (3) it included only the data for serum sST2, BDNF, CTnI, and BUN/Cr of patients at the time of admission, and repeated testing wasn't performed during a long-term follow-up, which may bias the study's results.

CONCLUSIONS

The serum sST2, BDNF, CTnI, and BUN/Cr have a certain correlation with the severity of and prognosis for heart failure, can be used as effective serum markers for the diagnosis and evaluation of patients with heart failure, and may be used as new targets for the treatment of patients with heart failure.

AUTHOR CONTRIBUTIONS

Cui Xie and Yu Zhan contributed equally to this paper.

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