Original Article

The sST2 level is an independent influencing factor associated with atrial fibrillation in heart failure patients: a case-control study

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Background: Most heart failure (HF) patients were complicated with atrial fibrillation (AF). Previous study has reported a correlation between soluble suppression of tumorigenicity 2 (sST2) and HF. While the association between sST2 and AF in HF patients remains elusive, which will strengthen our understanding of sST2 in HF patients.

Methods: In the study, a case-control study was conducted with 306 HF patients enrolled from June 2019 to June 2020 at Beijing Anzhen Hospital. All the patients were divided into the following two groups, based on whether they AF complications prior to admission: (I) the HF group (patients with HF alone) and the HF-AF group (HF patients complicated with AF). Baseline data and sST2 levels were assessed and compared between the two groups, and the influencing factors associated with AF in HF patients were screened.

Results: The sST2 level in the HF-AF group was 40.6 (25.9–53.6) ng/mL, which was significantly higher than that in the HF group [23.7 (16.3–35.9) ng/mL] (P<0.001). Correlation analysis showed that sST2 level in the HF-AF group was positively correlated with age (r=0.287, P=0.001), New York Heart Association (NYHA) grade (r=0.470, P<0.0001), left ventricular diameter (LVD) (r=0.311, P=0.001), serum creatinine (r=0.320, P<0.0001), NT-pro-brain natriuretic peptide (r=0.540, P<0.0001), and D-dimer (r=0.322, P<0.0001), and negatively correlated with left ventricular ejection fraction (LVEF) (r=–0.259, P=0.004), hemoglobin (r=–0.188, P=0.039), and glomerular filtration rate (r=–0.283, P=0.002). Logistic regression analysis results indicated that history of coronary heart disease [odds ratio (OR): 0.176, 95% confidence interval (CI): 0.081–0.380, P<0.0001], LVEF (OR: 0.956, 95% CI: 0.915–0.998, P=0.039), LVD (OR: 1.156, 95% CI: 1.059–1.261, P=0.001), left arterial diameter (OR: 0.761, 95% CI: 0.695–0.833, P<0.0001), and sST2 (OR: 0.942, 95% CI: 0.917–0.967, P<0.0001) were independent influencing factors associated with AF in HF patients.

Conclusions: The sST2 level is an independent influencing factor associated with AF in HF patients, which may favor to optimize the clinical strategies in the management of HF patients complicated with AF.

Keywords: Soluble suppression of tumorigenicity 2 (sST2); heart failure (HF); atrial fibrillation (AF)

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Introduction

People over 65 years accounts for about 16.7% of the total population, and this figure is expected to reach 25% by 2050 (1). Organ aging and functional decline caused by aging leads to a variety of cardiovascular diseases among the elderly, such as heart failure (HF), atrial fibrillation (AF), and coronary heart disease. HF is the final stage of most cardiovascular diseases with a high mortality ranging from 5–50% (2,3).

Statistically, HF was often complicated with arrhythmias, of which AF is the most common complication. And AF can lead to chronic HF, increasing HF-related mortality. It was reported that AF can increase the risk of all-cause death and readmission in patients with chronic HF (4) and lead to a poorer prognosis in HF patients (5,6). Soluble suppression of tumorigenicity 2 (sST2) is a member of the interleukin (IL)-1 receptor family. It can inhibit the protective effect of the IL-33/trans-membrane ST2 (ST2L) signaling pathway on cardiomyocytes by binding to its ligand IL-33, resulting in myocardial hypertrophy, fibrosis, and cardiac dysfunction (7). sST2 is closely related to myocardial dysfunction, myocardial fibrosis, and ventricular remodeling. More and more studies have shown that sST2 has higher diagnostic value than other HF markers, and its level is not affected by sex, age, obesity, body mass index, hypertension, and renal function (7-9). A previous study has shown that there is a significant correlation between sST2 levels and all-cause mortality in HF patients (10). A follow-up study found that sST2 levels can be used to predict the incidence of HF and sudden death in healthy people (11). Two meta-analyses by Aimo *et al.* support the predictive value of sST2 in acute or chronic HF (12,13). The findings of these studies indicate that there is a correlation between sST2 and HF. Thus far, there are few reports on the changes of sST2 levels in HF patients complicated with AF, and the relevant clinical significance remains elusive.

In the present study, we conducted a case-control study to analysis the expression level and clinical significance of sST2 in elderly HF patients complicated with AF, which will strengthen our understanding of sST2 in HF patients, and help to optimize the clinical strategies in the management of HF patients complicated with AF. We present the following article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-470/rc).

Methods

Patients

The present study was a case-control study. A total of 306 patients hospitalized at Beijing Anzhen Hospital from June 2019 to June 2020 were included in this study, including 164 males and 142 females, with an average age of 74.21±6.85 years. The inclusion criteria were as follows: (I) the diagnostic criteria of HF were in accordance with the Chinese Guidelines for The Diagnosis and Treatment of Heart Failure 2018 (14); (II) the diagnostic criteria of AF were in accordance with the AF: Current Awareness and Treatment Recommendations-2018 (15); and (III) patients' aged ≥65 years. Exclusion criteria were as follows: (I) organic fibromypathy (e.g., liver fibrosis, renal fibrosis, pulmonary fibrosis); (II) severe infection; (III) autoimmune diseases and malignant tumors; (IV) previous history of AF with no recurrence of sinus rhythm after treatment; and (V) previous cardiac surgery within 6 months of admission (including percutaneous coronary intervention, valve replacement, cardiac pacemaker implantation). HF patients were divided into the HF group and the HF-AF group (HF patient complicated with AF group). According to the Heart Failure Guidelines of the European Society of Cardiology (16), HF patients were classified into the following three subgroups: HF with reduced ejection fraction (HFrEF), HF with preserved ejection fraction (HFpEF), and HF with mid-range ejection fraction (HFmrEF), based on the left ventricular injection fraction (LVEF) of HF patients. Heart function was graded according to the New York Heart Association (NYHA) classification (17).

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Beijing Anzhen Hospital (No. 2020-047II). All participants were informed of the research plan and provided signed informed consent.

Basic data collection

Demographic information, including sex and age, were collected, as well as clinical history and symptoms, physical examination, and previous medical records. The collection of laboratory examination data included hemoglobin (Hb), serum creatinine (Scr), NT-pro-brain natriuretic peptide(NT-proBNP), and sST2. The collection of heart

ultrasound data included LVEF, left ventricular diameter (LVD), and left atrial diameter (LAD).

All the data were collected and recorded by two recorders independently.

Statistical analysis

SPSS 19.0 software (IBM, Armonk, NY, USA) was used for data processing. After normality test, the normal distribution data were expressed as mean ± standard deviation. Differences between the HF and HF-AF group were compared by independent samples *t*-test, and differences among HFrEF, HFpEF and HFmrEF groups were compared by ANOVA. Skewness distribution metrological data were described by median and interquartile range (IQR; Q25–Q75). The significance of intergroup data was analyzed using non-parametric rank-sum test (Kruskal-Wallis test). Counting data were analyzed χ^2-test. Person analysis was used to analyze the correlation of continuous data, and spearman analysis was used to analyze the correlation of non-continuous data Multivariate regression analysis was used to identify the independent influencing factors associated with HF patients complicated with AF. A two-tailed P<0.05 was considered statistically significant.

Results

Baseline patient characteristics

A total of 306 HF patients were enrolled in the present study, including 186 patients in the HF group and 120 patients in the HF-AF group. The findings indicated that there was no significant difference in body mass index, systolic blood pressure, diastolic blood pressure, diabetes, cardiomyopathy, valvular disease, alanine aminotransferase (ALT), erythrocytes, leukocytes, Hb, platelets, D-dimer, and glomerular filtration rate between the HF and HF-AF groups. There were significant differences in sex, age, smoking, drinking, history of hypertension, history of coronary heart disease, NYHA classification, LVEF, LAD, LVD, platelets, NT-proBNP, and sST2 between the HF and HF-AF groups (P<0.05) (*Table 1*). The sST2 level of patients in the HF-AF group was higher than that in the HF group, and the difference was statistically significant.

Baseline data of the HFrEF, HFmrEF, and HFpEF subgroups

There were significant differences in body mass index, systolic blood pressure, cardiomyopathy, NYHA grade, LVEF, LVD, LAD, Scr, sST2, NT-proBNP, glomerular filtration rate in the HFrEF (LVEF <40%), HFmrEF (LVEF 41–49%), and HFpEF (LVEF ≥50%) groups (P<0.05) (*Table 2*).

Correlation analysis between sST2 and other indicators

Spearman correlation analysis indicated that sST2 level in the HF group was positively correlated with age, smoking history, coronary heart disease, NYHA grade, LVD, LAD, platelets, Scr, NT-proBNP, and D-dimer (r>0, P<0.05), and negatively correlated with cardiomyopathy, valvular disease, LVEF, and glomerular filtration rate (r<0, P<0.05). In the HF-AF group, sST2 level was positively correlated with age, NYHA grade, LVD, Scr, NT-proBNP, and D dimer, and negatively correlated with LVEF, Hb, and glomerular filtration rate (r<0, P<0.05) (*Table 3*).

Multivariate logistic regression analysis of AF in patients with HF

Statistically significant variables in the baseline data comparison between the HF group and the HF-AF group were taken as independent variables, and the occurrence of AF was included in the logistic regression model as a dependent variable. Logistic regression analysis showed that the history of coronary heart disease [odds ratio (OR): 0.176, 95% confidence interval (CI): 0.081–0.380, P<0.0001], LVEF (OR: 0.956, 95% CI: 0.915–0.998, P=0.039), LVD (OR: 1.156, 95% CI: 1.059–1.261, P=0.001), LAD (OR: 0.761, 95% CI: 0.695–0.833, P<0.0001), and sSt2 (OR: 0.942, 95% CI: 0.917–0.967, P<0.0001) were independent influencing factors for AF in HF patients (*Table 4*).

Discussion

AF is a common complication in patients with HF. Therefore, it is important to study the value of markers, particularly in elderly patients with HF complicated with AF. sST2 is a clinical biomarker reflecting the pathophysiological process, which is related to myocardial

Table 1 Comparison of baseline data between the HF group and HF-AF group

Variables	HF group (N=186)	HF-AF group (N=120)	P value
Age (years)	72 [68–78]	75 [68–81]	0.035
Male, n (%)	112 (60.2)	52 (43.3)	0.004
Body mass index (kg/m^2)	24.1 (21.7–26.6)	24.6 (22.3–27.0)	0.243
Systolic blood pressure (mmHg)	128 [118–140]	130 (122–144)	0.149
Diastolic blood pressure (mmHg)	74 [70–80]	80 [70–81]	0.058
Smoker, n (%)	83 (44.6)	26 (21.7)	<0.001
Drinker, n (%)	51 (27.4)	11 (9.2)	<0.001
Hypertension, n (%)			0.016
None	78 (41.9)	63 (52.5)	
Grade I	9 (4.8)	5 (4.2)	
Grade II	36 (19.3)	8 (6.7)	
Grade III	63 (33.9)	44 (36.7)	
Diabetes, n (%)	61 (32.8)	29 (24.2)	0.106
Cardiomyopathy, n (%)	12 (6.5)	2 (1.7)	0.050
Coronary heart disease, n (%)	160 (86.0)	43 (35.8)	<0.001
Valvular disease, n (%)	6 (3.2)	6 (5.0)	0.435
NYHA, n (%)			0.016
Grade II	112 (60.2)	58 (48.3)	
Grade III	58 (31.2)	39 (32.5)	
Grade IV	16 (8.6)	23 (19.2)	
LVEF, n (%)			0.004
<40%	44 (23.7)	20 (16.7)	
41–49%	36 (19.4)	10 (8.3)	
≥50%	106 (57.0)	90 (75.0)	
LVD (mm)	49 [46–56]	48 [45–53]	0.022
LAD (mm)	38 [35–41]	43 [40–47]	<0.001
ALT (U/L)	19 [13–26]	16 [12–28]	0.226
WBC (×10^9/L)	6.2 (5.1–7.6)	5.9 (5.0–6.8)	0.123
RBC (×10^{12}/L)	4.2 (3.8–4.6)	4.2 (3.9–4.5)	0.675
Hemoglobin (g/L)	131 [119–142]	131 [120–141]	0.977
Platelets (×10^9/L)	176 [147–210]	155 [125–187]	0.001
Serum creatinine (μmol/L)	73.4 (60.8–87.4)	74.2 (62.8–90.5)	0.710
NT-proBNP (pg/mL)	677 (202–2,035)	1,511 (996–4,169)	<0.001
sST2 (ng/mL)	23.7 (16.3–35.9)	40.6 (25.9–53.6)	<0.001
D-dimer (ng/mL)	447.3 (317.0–771.5)	463.8 (318.1–872.1)	0.787
Glomerular filtration rate (mL/min/1.73 m^2)	73.8 (59.0–85.8)	68.1 (52.1–82.8)	0.053

Data is presented as mean ± standard deviation or numbers and percentages. HF, heart failure; AF, atrial fibrillation; NYHA, New York Heart Association; LVEF, left ventricular ejection fraction; LVD, left ventricular end-diastolic diameter; LAD, left atrial diameter; ALT, alanine aminotransferase; WBC, white blood cell; RBC, red blood cell; NT-proBNP, NT-pro-brain natriuretic peptide; sST2, soluble suppression of tumorigenicity 2.

Table 2 Comparison of basic data of HFrEF, HFmrEF, and HFpEF patients

Variables	HFrEF (N=64)	HFmrEF (N=46)	HFpEF (N=196)	P value
Age (years)	73.5 (68.0–78.0)	72.5 (67.0–80.0)	74.0 (68.0–80.0)	0.532
Male, n (%)	40 (62.5)	26 (56.5)	97 (49.5)	0.187
Body mass index (kg/m^2)	23.5 (21.1–25.1)	24.0 (21.5–26.3)	24.6 (22.4–27.2)	0.021
Systolic blood pressure (mmHg)	126 [118–134]	128 [120–139]	130 [120–144]	0.035
Diastolic blood pressure (mmHg)	76 [72–81]	72 [69–80]	76 [70–81]	0.234
Smoker, n (%)	27 (42.2)	18 (39.1)	64 (32.7)	0.348
Drinker, n (%)	15 (23.4)	14 (30.4)	33 (16.8)	0.096
Hypertension, n (%)				0.139
None	37 (57.8)	21 (45.7)	82 (41.8)	
Grade I	2 (3.1)	4 (8.7)	10 (5.1)	
Grade II	8 (12.5)	10 (21.7)	26 (13.3)	
Grade III	17 (26.6)	11 (23.9)	78 (39.8)	
Diabetes, n (%)	19 (29.7)	18 (39.1)	53 (27.0)	0.278
Cardiomyopathy, n (%)	9 (14.0)	1 (2.2)	4 (2.0)	<0.001
Coronary heart disease, n (%)	42 (65.6)	36 (78.2)	125 (63.8)	0.184
Valvular disease, n (%)	3 (4.6)	2 (4.3)	7 (3.6)	0.915
NYHA, n (%)				<0.001
Grade II	17 (26.6)	26 (56.5)	126 (64.3)	
Grade III	22 (34.4)	16 (34.8)	59 (30.1)	
Grade IV	25 (39.1)	4 (8.7)	11 (5.6)	
LVD (mm)	58.0 (54.2–64.0)	52.0 (49.0–57.0)	47.0 (44.0–49.0)	<0.001
LAD (mm)	43.0 (38.2–46.0)	40.0 (38.0–44.0)	39.0 (35.0–43.0)	<0.001
ALT (U/L)	21.9 (13.8–28.5)	19.35 (12.2–23.7)	17.0 (13.0–27.1)	0.314
WBC (×10^9/L)	6.4 (5.3–7.5)	6.1 (4.9–7.6)	6.0 (5.2–7.4)	0.746
RBC (×10^{12}/L)	4.3 (3.8–4.5)	4.2 (3.9–4.6)	4.1 (3.8–4.5)	0.390
Hemoglobin (g/L)	130.0 (121.2–143.0)	132.5 (120.7–147.0)	131.0 (120.0–140.0)	0.436
Platelets (×10^9/L)	171.5 (117.0–209.0)	160.0 (141.7–200.5)	168.0 (138.0–208.0)	0.959
Serum creatinine (μmol/L)	84.4 (71.6–101.1)	73.6 (58.7–89.9)	72.5 (59.6–82.7)	<0.001
NT-proBNP (pg/mL)	2,400 (1,277–5,701)	1,084 (606–2,776)	785 (198–1,941)	<0.001
sST2 (ng/mL)	47.3 (24.5–53.6)	30.6 (20.7–39.3)	25.8 (16.5–38.9)	<0.001
D-dimer (ng/mL)	560.8 (355.0–1,071.0)	523.6 (321.14–953.7)	436.0 (302.0–703.0)	0.055
Glomerular filtration rate (mL/min/1.73 m^2)	61.9 (47.9–78.3)	70.5 (56.2–88.2)	72.3 (59.3–86.0)	0.014

Data is presented as mean ± standard deviation or numbers and percentages. HFrEF, heart failure with reduced ejection fraction; HFmrEF, heart failure with mid-range ejection fraction; HFpEF, heart failure with preserved ejection fraction; NYHA, New York Heart Association; LVD, left ventricular end-diastolic diameter; LAD, left atrial diameter; ALT, alanine aminotransferase; WBC, white blood cell; RBC, red blood cell; NT-proBNP, NT-pro-brain natriuretic peptide; sST2, soluble suppression of tumorigenicity 2.

Table 3 Correlation analysis between sST2 and clinical detection indexes

Variables	HF group (n=186)		HF-AF group (n=120)	
	r value	P value	r value	P value
Sex	0.045	0.539	–0.068	0.462
Age	0.169*	0.021	0.287**	0.001
Systolic blood pressure	0.041	0.578	0.008	0.932
Diastolic blood pressure	0.094	0.203	0.043	0.642
Smoking	0.204**	0.005	0.077	0.406
Drinking	0.125	0.090	0.051	0.578
Hypertension	–0.017	0.820	0.150	0.101
Diabetes	–0.023	0.754	–0.143	0.118
Cardiomyopathy	–0.210**	0.004	0.019	0.839
Coronary heart disease	0.158*	0.031	–0.026	0.777
Valvular disease	–0.156*	0.034	–0.026	0.779
NYHA	0.147*	0.045	0.470**	<0.0001
LVEF	–0.345**	<0.0001	–0.259**	0.004
LVD	0.200**	0.006	0.311**	0.001
LAD	0.231**	0.001	0.107	0.249
ALT	0.100	0.174	–0.021	0.819
WBC	0.136	0.064	0.145	0.114
RBC	–0.073	0.320	–0.090	0.330
Hemoglobin	–0.107	0.148	–0.188*	0.039
Platelets	0.145*	0.049	–0.037	0.688
Serum creatinine	0.195**	0.008	0.320**	<0.0001
NT-proBNP	0.474**	<0.0001	0.540**	<0.0001
D-dimer	0.336**	<0.0001	0.322**	<0.0001
Glomerular filtration rate	–0.213**	0.003	–0.283**	0.002
Body mass index	–0.093	0.209	–0.065	0.484

*, P<0.05; **, P<0.01. sST2, soluble suppression of tumorigenicity 2; HF, heart failure; AF, atrial fibrillation; NYHA, New York Heart Association; LVEF, left ventricular ejection fraction; LVD, left ventricular end-diastolic diameter; LAD, left atrial diameter; ALT, alanine aminotransferase; WBC, white blood cell; RBC, red blood cell; NT-proBNP, NT-pro-brain natriuretic peptide.

fibrosis and ventricular remodeling. It has good clinical value for the diagnosis and prognosis of HF and other cardiovascular diseases (18). At present, there are few published studies on sST2 in HF-AF patients. The present study was conducted to investigate the changes of sST2 in elderly HF patients with AF, and to evaluate the value of sST2 in these patients.

The findings of the present study indicated that sST2 and NT-ProBNP levels in the HF-AF group were higher than those in the HF group, and the LVD and LAD were statistically different between the two groups. ST2L binds to IL-33, a specific ligand, and activates the IL-33/ST2L signaling pathway, which is considered to be a mechanical activation system. When cardiomyocytes are stimulated by mechanical stretch, IL-33 molecules are released and form a receptor complex with ST2L on the cardiomyocyte

Table 4 Logistic regression analysis of atrial fibrillation in patients with HF

Variables	Regression coefficient	Standard error	Wald λ^2	P value	Odds ratio	95% confidence interval	
						Lower	Upper
Coronary heart disease	–1.738	0.393	19.565	<0.0001	0.176	0.081	0.380
LVEF	–0.045	0.022	4.279	0.039	0.956	0.915	0.998
LVD (mm)	0.145	0.045	10.494	0.001	1.156	1.059	1.261
LAD (mm)	–0.273	0.046	34.886	<0.0001	0.761	0.695	0.833
sST2	–0.060	0.014	19.815	<0.0001	0.942	0.917	0.967

Statistically significant variables in the baseline data comparison between the HF group and the HF-AF group were taken as independent variables, and the variables with no statistical difference are not included in the table. HF, heart failure; LVEF, left ventricular ejection fraction; LVD, left ventricular end-diastolic diameter; LAD, left atrial diameter; sST2, soluble suppression of tumorigenicity 2; AF, atrial fibrillation.

membrane to activate downstream pathway signals through paracrine action and the signals then play a protective role in the heart. When myocardial cells are damaged by mechanical stress, such as excessive sST2 in the serum, myocardial tissue will suffer from myocardial remodeling and cardiac dysfunction due to lack of adequate IL-33 protection, which will exacerbate HF (19). Therefore, sST2 is regarded as a marker of cardiomyocyte hypertrophy and myocardial fibrosis (20), and suggests that the sST2 level could be related to the damage and remodeling of the ventricle and atrium.

Epidemiological studies have shown that HFpEF has gradually become the main manifestation of HF worldwide, accounting for 52–71% cases (21,22). However, the pathogenesis of HFpEF is not clear. Some studies have suggested that HFpEF is related to diastolic filling disorder and increased end-diastolic pressure caused by impaired left ventricular systolic function and myocardial compliance (23,24). Other study suggests that there is a relationship between age, ex, diabetes, obesity, hypertension, cardiomyopathy, and HFpEF (25). In the present study, systolic blood pressure and body mass index in HFpEF group were higher than those in HFrEF and HFmrEF groups, and the difference was statistically significant. Although there was no significant difference for females, advanced age, and hypertension among the HFpEF, HFrEF, and HFmrEF groups, the proportion of females, elderly patients, and patients with hypertension in HFpEF group was higher than that in the HFrEF and HFmrEF groups. Increased cardiovascular stiffness is one of the important pathophysiological mechanisms in the progression of HFpEF. Females with hypertension are more likely to develop left ventricular hypertrophy; however, due to cardiomyocyte hypertrophy, apoptosis, and collagen deposition, the heart will have morphological and structural changes with age, and females are more likely to have increased ventricular stiffness and decreased compliance and diastolic function (26). Elevated body mass index increases the risk of hypertension, cardiomyopathy, coronary heart disease, and AF, all of which are associated with HFpEF. It is not clear whether obesity can independently cause ejection fraction retention of HF. Sun *et al.* reported that body mass index is positively correlated with left ventricular end-diastolic volume, left ventricular posterior wall thickness, left ventricular mass, and mitral annulus velocity (mitral annulus velocity) (27). In their study, Yuksel *et al.* selected 30 obese patients (body mass index >30 kg/m^2) for echocardiographic examination before and 3 months after weight loss (28). Echocardiography showed that after weight loss, peak early diastolic filling velocity increased, late diastolic peak filling velocity decreased, the ratio of the two groups increased, deceleration time and isovolumic relaxation time shortened, and mitral annulus motion velocity increased . Therefore, weight control could reverse the changes of left ventricular structure and diastolic dysfunction in obese patients. We reported that the sST2 and NT-proBNP levels in the HFpEF group were significantly lower than those in the HFrEF and HFmrEF groups. IL-33 is the functional ligand of ST2. The IL-33/ST2L signaling pathway plays a role in anti-myocardial fibrosis and cardiomyocyte hypertrophy. However, when cardiomyocytes induced by biomechanical stress produce a large amount of sST2, the endogenous myocardial protection of IL-33/ST2L is blocked, resulting in myocardial remodeling and ventricular dysfunction, which ultimately leads to an increased risk of death. This implies

that sST2 could be a new marker of myocardial fibrosis and ventricular remodeling (29). The higher the NT-proBNP level, the lower the ejection fraction and the worse the cardiac function. The findings of the present study indicate that sST2 and NT-proBNP levels are important indicators to reflect the severity of HF.

In the present study, correlation analysis showed that the sST2 level in the HF-AF group was positively correlated with NT-proBNP, but negatively correlated with LVEF. A study has found that hemodynamic disorders in AF patients aggravate atrial structural remodeling, and result in atrial irregular contraction, excessive energy consumption leading to ventricular dysfunction, as well as the release of ventricular BNP in the blood (30). The increase of NT-proBNP concentration in AF patients could be related to pathological changes, such as atrial enlargement, fibrosis, and lipid degeneration, which suggest that changes in sST2 and NT-ProBNP levels could be used to determine myocardial fibrosis and abnormal systolic function.

In the present study, logistic regression analysis showed that coronary heart disease history, LVD, and sST2 were independent influencing factors for HF complicated with AF. Kim *et al.* found that sST2 was not only associated with left atrial fibrosis but also the only independent risk factor for AF after correcting traditional risk factors, which was consistent with the results of this study (31). Tan *et al.* also found that increased sST2 can be used as a marker of recurrence after radiofrequency ablation in persistent AF patients, and that the patients with sST2 ≥39.25 ng/mL are more likely to develop recurrence within a year (32). Atrial structural remodeling is the basis of AF. LAD has been found to be closely related to the occurrence and persistence of AF, and it has been reported that LAD is an independent risk factor for the development of AF (33). Related study has shown that the internal diameter of the left atrium is one of the determinants of the number of re-entrant wavelets in the atrium at the same time. The larger the internal diameter of the left atrium, the more re-entrant wavelets, and the easier it is to trigger AF. When inflammation occurs in atrial muscle tissue, the electrophysiology of cardiomyocytes changes, promoting the formation of re-entrant wavelets and inducing AF (34).

The findings of the present study indicated that sST2 provides a reference index for HF complicated with AF, demonstrating the clinical value and significance of sST2, and provides a certain basis for clinical diagnosis and prediction. However, the study has some limitations. First, this study was affected by the time of the study, and the patients were only followed up for no longer than 1 year. Second, the present study was a retrospective study, so only a single plasma sST2 level of patients was analyzed. Long-term and continuous monitoring of SST2 level of patients might provide more clinical value. Further studies are warranted.

Conclusions

The sST2 level is an independent influencing factor associated with AF in HF patients, which may favor to optimize the clinical strategies in the management of HF patients complicated with AF.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-470/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-470/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Beijing Anzhen Hospital (No. 2020-047II). All participants were informed of the research plan and provided signed informed consent.

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