Original Article

Dynamic Right Ventricular Changes in Heart Failure: Insights From Serum sST2 and Strain Imaging

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ABSTRACT

Background: Suppression of tumorigenicity 2 (ST2) is a biomarker of myocardial fibrosis and remodeling proven to predict outcomes in patients with acute decompensated heart failure (ADHF), especially when measured serially. We aimed to evaluate right ventricular (RV) dynamic changes in ADHF patients using serum soluble ST2 (sST2) and speckle-tracking echocardiography imaging (STE).

Methods: We enrolled 61 ADHF patients with left ventricular ejection fractions below 50% and serum NT-proBNP levels exceeding 900 pg/mL. Serum sST2 levels were measured on hospital admission and discharge. The patients underwent serial conventional and STE examinations on admission, at 48 hours, and on discharge. RV STE analysis was done using 2D cardiac performance analysis.

Results: Serum sST2 had a significant positive correlation with serum NT-proBNP on admission (r = 0.84, P < 0.0001) and showed a significant reduction from 2.47 (1.27–4.05) ng/mL on admission to 1.86 (1.06–3.24) ng/mL at discharge (P < 0.0001), denoting successful decongestion. Significant decreases were observed in the inferior vena cava diameter (P < 0.0001) and the estimated pulmonary artery systolic pressure (P = 0.002); however, the changes were not associated with a significant change in RV dimensions (P > 0.05) or contractility assessed by trans-annular plane systolic excursion (P = 0.09) and tricuspid S-wave velocity (P = 0.9). There was a significant improvement in RV free wall strain (RVFWS) (P = 0.005) assessed by STE, primarily noticed after the first 48 hours until discharge, but the RV 4-chamber strain did not change significantly (P = 0.06).

Conclusions: RVFWS assessed by STE can detect improvements in RV systolic function not detected by conventional echocardiographic parameters in ADHF patients. Together with declines in serum sST2 levels, it can be used as a marker of improved cardiac mechanics and successful decongestion. ***(Iranian Heart Journal 2023; 24(4): 42-53)***

KEYWORDS: sST2, Acute decompensated heart failure, Speckle-tracking echocardiography, Right ventricular strain

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Acute heart failure (AHF) is a major medical and socioeconomic health concern and one of the most common causes of hospitalization in the world. AHF is a clinical syndrome characterized by the rapid onset of new or worsening symptoms and signs of HF due to abnormal cardiac function, often leading to hospitalization or a visit to the emergency department. [1] The clinical trajectory during AHF hospitalization is determined by responsiveness to therapy concerning clinical HF symptoms and signs and laboratory and diagnostic tests. This trajectory is crucial to define the next steps for management, health outcomes, risks, and prognosis. [2]

Suppression of tumorigenicity 2 (ST2) is a newly emerging biomarker for patient stratification in various clinical settings of HF. [3,4] ST2 is a member of the Toll interleukin 1 (IL-1) receptor superfamily including 2 unique proteins: truncated circulating soluble ST2 (sST2) and a membrane-bound form (lST2). Research has shown that sST2 competes with lST2 to bind with IL-33, which is involved in ameliorating myocardial hypertrophy and fibrosis in response to myocardial stretch. [5,6] Originally, elevated levels of sST2 were reported to be associated with the severity of adverse cardiac remodeling and tissue fibrosis in patients with HF. Further, higher levels of sST2 are correlated with more severe clinical symptoms and with other objective measures of HF severity, such as higher C-reactive protein levels, higher natriuretic peptide levels, lower left ventricular ejection fractions (LVEFs), and higher diastolic filling pressure. [7]

In addition to changes in biomarkers, cardiac structural and functional changes during HF hospitalization can also affect management and prognosis. One of the notable changes in this regard is right ventricular (RV) mechanics. [8]

To date, few studies have assessed the effects of congestion and decongestive therapy on cardiac mechanics. The current study aimed to evaluate the dynamic RV structural and functional changes in patients with AHF. Furthermore, the relationship between changes in RV function and serum sST2 changes was assessed.

METHODS

Study Design

Our study is a single-center, prospective, observational trial that enrolled 61 patients with AHF who presented to Kasr Al-Ainy Hospital between March 2018 and January 2020. Comprehensive clinical, laboratory, and echocardiographic data were obtained on admission, after 48 hours, and on hospital discharge. Standard transthoracic echocardiography was done using a commercially available machine in our facility (Philips Epiq 7C, equipped with the X5-1 transducer), where 2D, M-mode, and Doppler images were obtained. All echocardiographic parameters were measured according to the guidelines of the American Society of Echocardiography. [9] The study complied with the Declaration of Helsinki, and the locally appointed ethics committee approved the research protocol. Written informed consent was obtained from every patient before enrollment in the study.

Study Population

Patients were eligible if they were at least 18 years of age and presented with AHF, defined in accordance with guidelines from the 2013 American College of Cardiology/American Heart Association consensus statement and established by the European Society of Cardiology guidelines 2016 based on typical symptoms and signs of HF and elevated levels of natriuretic peptides. [10, 11] Additional inclusion criteria were LV systolic dysfunction using transthoracic echocardiography (LVEF ≤

50%) and New York Heart Association (NYHA) functional class III-IV. The exclusion criteria consisted of non-sinus rhythm/very frequent extrasystoles, insufficient imaging quality to allow adequate speckle-tracking echocardiography (STE), acute coronary syndromes, percutaneous coronary intervention, coronary artery bypass graft surgery within the preceding 1 month, the use of intravenous vasopressors or inotropes at any time during hospitalization, and inability to complete the hospital stay (eg, mortality or patient discharge against medical advice).

sST2 Sampling

Non-fasting blood samples were obtained within 24 hours of admission and on the day of discharge by venipuncture and transported to the chemical pathology laboratory for further processing according to a standardized protocol. The collected material was allowed to clot for 10 to 20 minutes before centrifugation at 2000 to 3000 rpm for 20 minutes, and then blood serum was separated. All blood aliquots were subsequently stored at a temperature of -20 °C within 2 hours after venipuncture. The concentrations of sST2 were determined in the serum by using the sandwich-Elisa method (Human Soluble ST2/IL-33 Receptor [sST2] Elisa Kit, SinoGeneClon Biotech Co, Ltd). Analysts were blinded to patients' characteristics and endpoints.

STE

Image acquisition and storage

High-quality 2D-gated images were obtained during end-expiratory breath holding with stable electrocardiographic traces, avoiding the foreshortening of the LV and the proper visualization of the endocardial border. The optimal frame rate was 50 to 100 frames per second. Sector widths and depths were kept minimal to focus on the structure of interest. Three consecutive cardiac cycles were obtained, and the values were averaged for the final processing. Images were stored and transferred to DICOM (Digital Imaging and Communications in Medicine) for offline analysis using 2D Cardiac Performance Analysis, version 4.6 (TOMTEC Imaging Systems, Unterschleißheim, Germany).

Assessment of conventional echocardiographic parameters

LV end-diastolic volume and end-systolic volume were calculated using the Simpson biplane methods of disks. LVEF was calculated and expressed as a percentage. Left atrial (LA) maximum volume (at the end of ventricular systole) was measured using the A-L rule and indexed to body surface area (LA volume index [LAVI]). Basal, mid, and longitudinal RV linear dimensions were measured in the RV-focused view, with the LV apex at the center of the scanning sector, while displaying the largest basal RV diameter and thus avoiding foreshortening. The maximum diameter of the inferior vena cava (IVC) was measured in the subcostal view 1.0 to 2.0 cm from the junction with the right atrium. The tricuspid regurgitation pressure gradient was derived from the peak tricuspid regurgitation jet velocity and then added to an estimate of right atrial pressure derived from the measurement of the IVC dimensions and the response to inspiration to obtain the estimated pulmonary artery systolic pressure (EPASP). Tricuspid annular plane systolic excursion (TAPSE) was measured at the RV free wall sight using M-mode.

Assessment of right ventricular mechanics and STE analysis

The region of interest was automatically selected by the software. The region of interest was then adjusted further to ensure that all myocardial regions were included. Thereafter, the software captured the myocardium, automatically tracking its

motion and thickening on the subsequent frames. Finally, the myocardium was divided into 6 segments. For the assessment of RV strain, the average value of the longitudinal peak systolic strain was evaluated only from the free wall (RVFWS) and from all the segments of the free wall and the septal wall of the RV (RV4CS) in the apical 4-chamber view focused in the RV (Fig. 1). The interobserver variability of RV speckle-tracking parameters showed excellent agreement (intraclass correlation coefficient > 0.9 for strain measurements).

Hospital Course

We followed up on the patients at 48 hours and on discharge regarding body weight, NYHA functional class, and conventional and RV STE. Any patient who developed an exclusion criterion during the hospital stay was excluded.

Statistical Analysis

Categorical data were expressed as numbers and proportions. Continuous variables were expressed as the mean ± standard deviation (SD) if normally distributed or the median (the interquartile range) if not. Normality was assessed using the Kolmogorov-Smirnov test and histograms. Repeated measurements were compared using the repeated measure ANOVA test for normally distributed variables. To account for between-subject differences and adjust for covariates (in-subject differences), we constructed an analysis of the covariance model assessing changes in between-subject factors and within-subject factors. Additionally, Δ sST2 was calculated by subtracting the serum sST2 level at discharge from its level on admission. Statistical significance was set at a 2-tailed probability level of less than 0.05. The statistical analyses were performed using SPSS, version 26 (IBM SPSS Statistics, IBM Corporation, Armonk, New York).

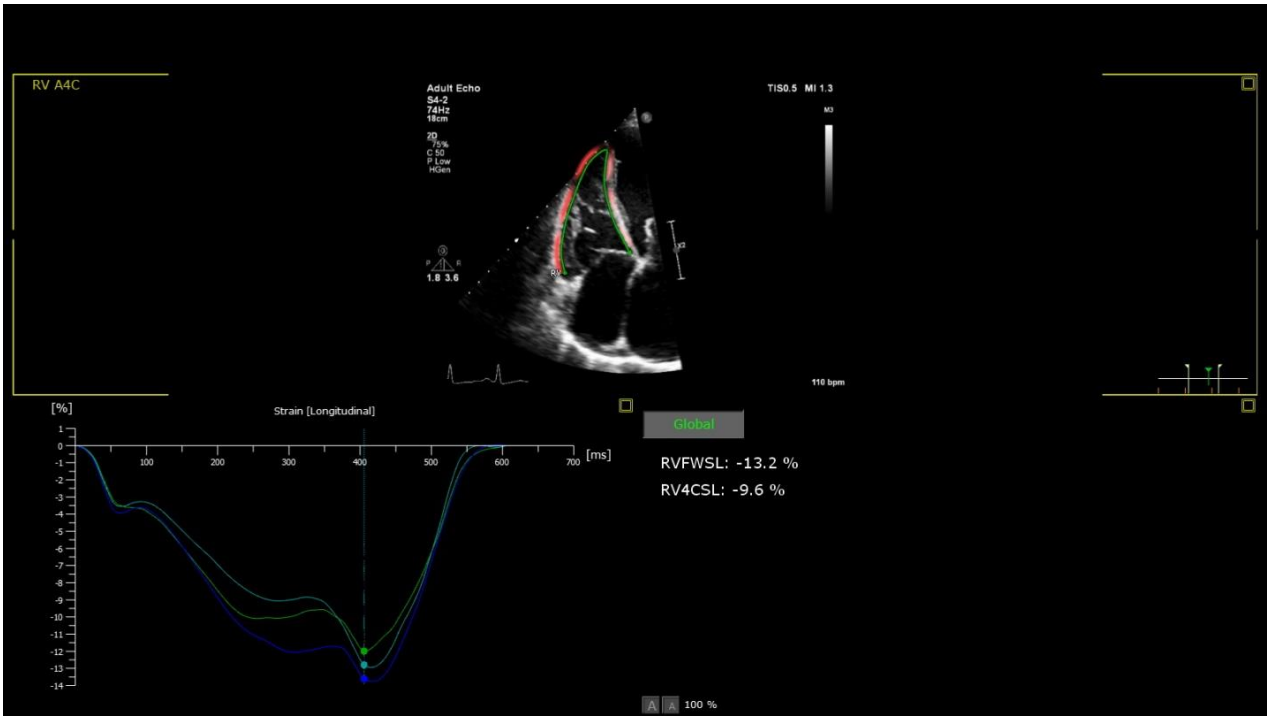

Figure 1: The image presents the right ventricular speckle-tracking analysis.

RESULTS

Study Population

Among 143 HF patients screened between March 2018 and January 2020, 75 patients met eligibility for our study. Fourteen patients were further excluded during the hospital stay due to various causes. As a result, analysis was conducted on 61 patients who were successfully discharged from the hospital with a mean hospital stay of 10.1 ± 7.7 (range= 4-50) days.

The baseline characteristics of the patient population are summarized in Table 1. Most of the studied patients were male (72.1%), with a median age of 57 years old. Approximately, 73% of the patients presented with acute on top of chronic HF, with more than half of them having no prior HF hospitalization. About half the patients had non-ischemic cardiomyopathy, primarily idiopathic dilated cardiomyopathy (39.4%). Non-compliance to medical treatment was the most common precipitating factor, with most patients falling into the NYHA functional class IV. Eighty percent of the patients were receiving diuretics before admission, and approximately 55% of the patients were receiving renin-angiotensin-aldosterone system blockers and β-blockers. None of the patients was receiving angiotensin receptor-neprilysin inhibitors. Laboratory findings on admission showed normal kidney function and electrolytes with normal liver transaminases. Serum N-terminal-pro B-type natriuretic peptide (NT-proBNP) levels on admission were elevated (median = 4317 (3512-6290.8) pg/mL).

Regarding baseline echocardiography data, both LV end-diastolic and systolic volume indices (LVESVI and LVESVI, respectively) were increased, and most of the patients had an LVEF below 40%, with only 18% of the patients having an LVEF from 40% to 50%. Twenty-eight patients (45.9%) had impaired RV systolic function (TAPSE < 17 mm). Forty-eight patients (78.7%) had elevated transmitral E/e` (> 14), denoting elevated LV filling pressure with dilated IVC and volume overload. The mean RVFWS and RV4CS were −12.6 ± 5.7% and −9.2 ± 4.6%, respectively, with 54 patients (88.5%) having an RVFWS below -20%.

In-Hospital Data and Treatment

Upon admission, 53 patients (86.9%) received intravenous furosemide shots, while 8 patients (13.1%) received an intravenous furosemide infusion, with a mean total daily furosemide dose of 116 ± 49.8 mg on the first day. No patient received intravenous inotropes or vasopressors during the hospital stay. None of the patients required ultrafiltration.

Serial Changes in Clinical Parameters

Serial changes in clinical parameters are presented in Table 2. There was a significant reduction in body weight from baseline to discharge ($P < 0.0001$), which was achieved mostly after the first 48 hours until discharge ($P= 0.001$). No significant reduction was observed from admission to the first 48 hours of hospital admission ($P = 0.2$) (Fig. 2A). NYHA functional class did not improve significantly during the first 48 hours; however, there was a significant improvement from admission to discharge ($P < 0.0001$) (Fig. 2B).

Serial Changes in Serum sST2 Levels

A significant decrease was noted in serum sST2 levels from 2.47 (1.27-4.05) ng/mL on admission to 1.86 (1.06-3.24) ng/mL at discharge ($P < 0.0001$), with a percentage reduction of 24.7%. Twenty patients (32.8%) showed a reduction above 25% in serum sST2 levels from admission to discharge, while 12 patients (19.7%) showed increased serum sST2 levels.

Serial Changes in Echocardiographic Parameters

Serial changes in echocardiographic parameters are presented in Table 2. Regarding LV volumes and function, there was a significant reduction in LVESVI (P = 0.002), mainly from admission to the first 48 hours of hospital admission (P = 0.004), with no significant change from the first 48 hours until discharge (P = 0.9). On the other hand, LVEDVI did not change significantly (P = 0.09). As a result, LVEF increased significantly (P = 0.004), with a major increase between admission and discharge (P = 0.01). There was a significant reduction in LAVI (P = 0.03), which was more prominent from admission to discharge. Nonetheless, no significant change was observed from admission to the first 48 hours (P = 0.1) or from the first 48 hours to discharge (P = 0.9).

There was a significant decrease in the IVC diameter throughout all the phases of the hospital stay (P < 0.0001) (Fig. 2C). Moreover, EPASP decreased significantly (P = 0.002), primarily from admission to discharge (P = 0.004), with no significant change between baseline and the first 48 hours (P = 0.2) and from the first 48 hours to discharge (P = 0.2) (Fig. 2D). Whereas the IVC diameter and EPASP decreased significantly, RV dimensions, TAPSE, and S-wave velocity at the lateral tricuspid annulus did not change significantly throughout the hospital stay (P > 0.05).

Regarding RV STE parameters, there was a significant improvement in RVFWS (P = 0.005), which was mainly noticed after the first 48 hours until discharge (P = 0.03) (Fig. 2E). Still, RV4CS did not change significantly throughout the hospital stay (P = 0.06).

Correlations Between Serum sST2 Levels and Clinical and Echocardiographic Parameters on Admission

There was a significant strong positive linear correlation between sST2 and serum NT-ProBNP levels (r = 0.84, P <0.0001) on admission (Fig. 3). There was also a significant weak positive linear correlation between sST2 levels and NYHA functional class (r = 0.31, P = 0.02).

Regarding the conventional echocardiography parameters of the left-sided chambers, there was a significant weak positive linear correlation between sST2 levels and LVEDVI (r = 0.3, P = 0.02) and LVESVI (r = 0.31, P = 0.01) and a significant moderate positive linear correlation with LAVI (r = 0.41, P = 0.001). However, sST2 levels showed a nonsignificant correlation with LVEF (r = −0.23, P = 0.08) and transmitral E/e` (r = 0.19, P = 0.1). In contrast, sST2 levels were nonsignificantly correlated with the parameters of the right-sided chambers, including the RV basal diameter (r = −0.008, P = 0.9), TAPSE (r = 0.03, P = 0.8), S-wave velocity at the lateral tricuspid annulus (r = 0.02, P = 0.8), the IVC (r = 0.1, P = 0.4), EPASP (r = 0.2, P = 0.1), RVFWS (r = 0.14, P = 0.3), and RV4CS (r = 0.05, P = 0.7). RVFWS showed a nonsignificant correlation with TAPSE (r = 0.1, P = 0.4) and S-wave velocity at the lateral tricuspid annulus (r = 0.2, P = 0.1).

Association Between Serial Changes in Serum sST2 Levels and Clinical and Echocardiographic Parameters

There was a significant moderate positive linear correlation between Δ sST2 and Δ NYHA functional class (r = 0.42, P = 0.001) and Δ body weight (r = 0.38, P = 0.003) from admission to discharge.

Further, a significant moderate positive linear correlation was observed between Δ sST2 and the Δ IVC diameter (r = 0.52, P < 0.0001) (Fig. 3A) and Δ transmitral E/e` (r = 0.49, P < 0.0001) (Fig. 3B), denoting improved LV filling pressures with decongestive drug therapy.

Table 1: Baseline demographics, comorbidities, and laboratory data

Variable	
Demographics and Comorbidities	
Age, y	57 (48.5 - 61.5)
Male sex	44 (72.1%)
Duration of HF, mon	12 (3 - 30)
Ischemic cardiomyopathy	32 (52.5%)
Systemic hypertension	29 (47.5%)
Type 2 diabetes mellitus	34 (55.7%)
Coronary artery disease	32 (52.5%)
History of myocardial infarction	27 (44.3%)
Clinical Data	
▪ Systolic blood pressure, mm Hg	120 (110 - 130)
▪ Diastolic blood pressure, mm Hg	80 (70 - 82.5)
▪ Heart rate, beat/min	95 (90 - 109.5)
▪ Body weight, kg	81.1 ± 16.1 *
▪ Body mass index, kg/m^2	28.6 ± 5.0 *
▪ NYHA functional class	
III	6 (9.8%)
IV	55 (90.2%)
Laboratory Data	
Haemoglobin, g/dL	12.5 ± 1.8
Serum Urea, mg/dL	39 (29.5 – 58.5) *
Serum creatinine, mg/dL	1.11 (0.9 – 1.41) *
Serum sodium, mmol/L	135.5 ± 5.7
Serum potassium, mmol/L	4.4 ± 0.6
Serum alanine aminotransferase, units/L	42.7 ± 51.8
Serum aspartate aminotransferase, units/L	42.3 ± 50.4
Serum albumin, g/dL	3.6 ± 0.4
Serum NT-ProBNP, pg/mL	4317 (3512 – 6290.8) *
Serum sST2, ng/mL	2.47 (1.27 – 4.05) *

Data are presented as mean ± SD*, medians (interquartile ranges), and numbers (%).
HF: heart failure; PCI: percutaneous coronary intervention; CABG: coronary artery bypass graft; COPD: chronic obstructive pulmonary disease; NYHA: New York Heart Association; NT-proBNP: N-terminal-pro B-type natriuretic peptide

Table 2: Changes in clinical and echocardiographic parameters from admission until hospital discharge

Variable	Admission	48 Hours	Discharge	*P* value
Clinical Parameters				
Body weight, kg	81.1 ± 16.1	80.5 ± 16	77 ± 15.8	<0.0001
NYHA class *	4 (4 – 4)	4 (3 – 4)	2 (2 – 3)	<0.0001
Echocardiographic Parameters				
LAVI, mL/m^2	55 ± 15.4	53 ± 16.7	52.5 ± 14.6	0.03
LVEDVI, mL/m^2	96.8 ± 30.1	94.2 ± 30.1	94.9 ± 30	0.09
LVESVI, mL/m^2	65.8 ± 24.3	63.1 ± 24.7	62.7 ± 24.6	0.002
LVEF, %	33.1 ± 7.0	34.6 ± 8.3	35.5 ± 9.0	0.004
Transmitral E/e`	17.8 ± 5.8	17.6 ± 6.1	16.6 ± 5.6	0.1
RV basal diameter, cm	4.2 ± 0.8	4.1 ± 0.8	4.1 ± 0.8	0.4
RV mid diameter, cm	3.1 ± 0.6	3.1 ± 0.6	3.0 ± 0.6	0.2
RV longitudinal diameter, cm	6.4 ± 0.9	6.5 ± 0.8	6.4 ± 0.8	0.4
TAPSE, mm	16.8 ± 5.2	17.4 ± 4.5	17.8 ± 4.6	0.09
S-wave at the lateral tricuspid annulus, cm/s	10.3 ± 2.7	10.2 ± 2.9	10.2 ± 2.8	0.9
IVC diameter, cm	2.4 ± 0.5	2.2 ± 0.5	2.0 ± 0.6	<0.0001
EPASP, mm Hg	50 ± 12.1	47 ± 12	44.4 ± 12.2	0.002
RVFWS,%	-12.6 ± 5.7	-12.9 ± 5.4	-14.4 ± 6.5	0.005
RV4CS,%	-9.2 ± 4.6	-9.3 ± 4.3	-10.1 ± 5.5	0.06

Data are presented as mean ± SD and medians (interquartile ranges).*

LA: left atrium; LAVI: left atrial volume index; LVEDVI: left ventricular end-diastolic volume index; LVESVI: left ventricular end-systolic volume index; LVEF: left ventricular ejection fraction; RV: right ventricle; TAPSE: transannular plane systolic excursion; IVC: inferior vena cava; EPASP: estimated pulmonary artery systolic pressure; RVFWS: right ventricular free wall strain; RV4CS: right ventricular 4-chamber strain

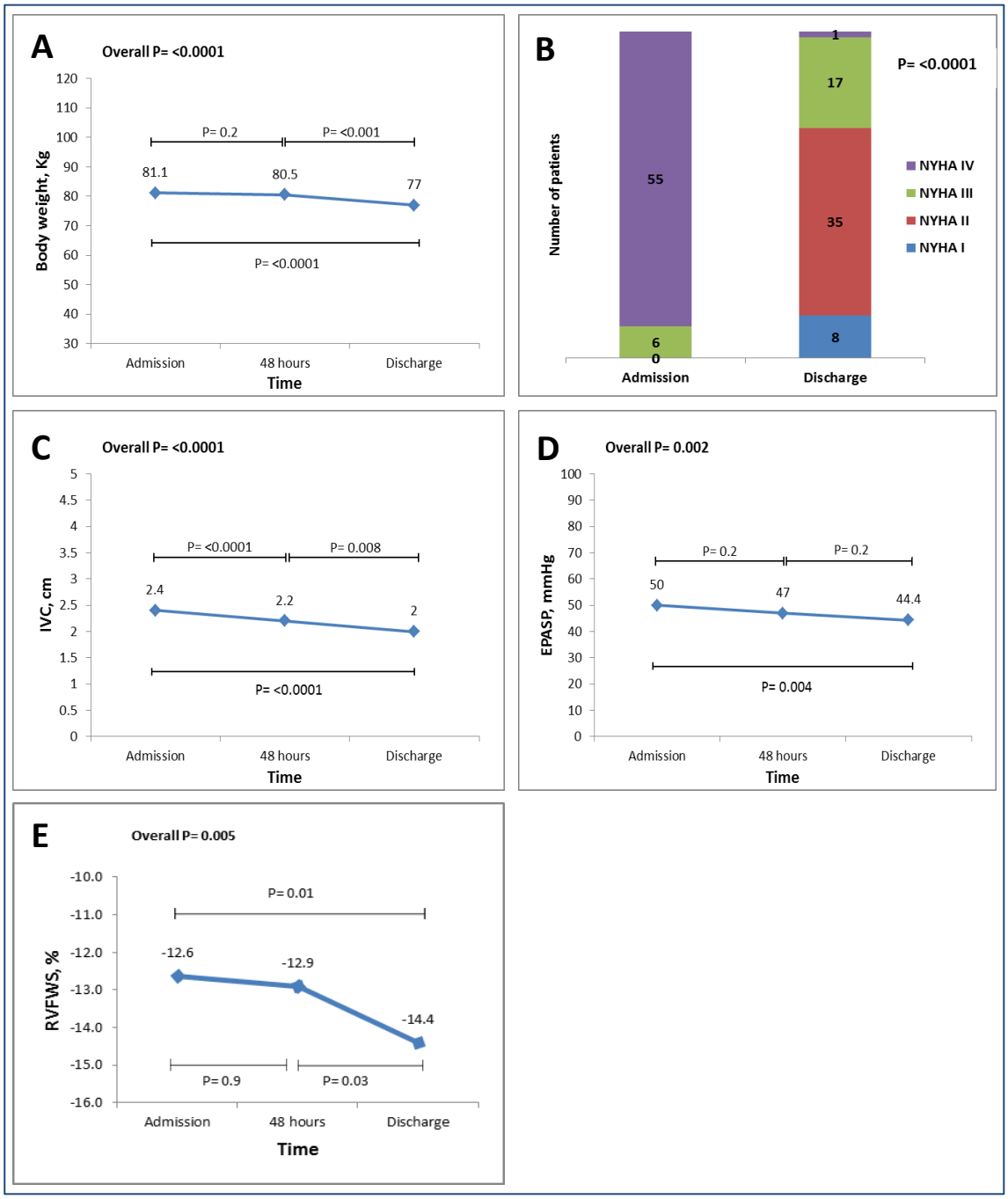

Figure 2: The image illustrates changes in clinical and echocardiographic parameters from admission until hospital discharge: (A) body weight, (B) NYHA functional class, (C) IVC diameter, (D) EPASP, and (E) RVFWS.

NYHA: New York Heart Association; IVC: inferior vena cava; EPASP: estimated pulmonary artery systolic pressure; RVFWS: right ventricular free wall strain

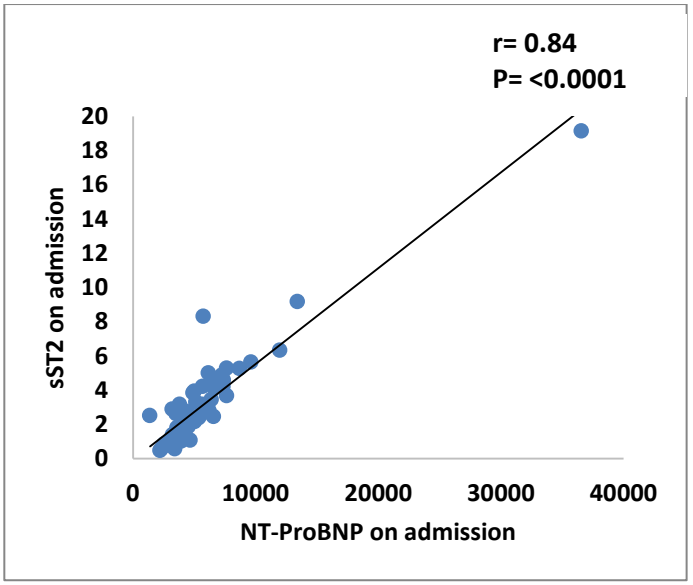

Figure 3: The scatter plot chart shows the correlation between serum sST2 and NT-proBNP.

DISCUSSION

sST2, a marker of myocardial fibrosis and remodeling, is a promising tool that has been successfully added to the conventional management of patients with HF. The biological variation and the low index of variation of sST2 make it a perfect candidate for monitoring and possibly guiding treatment in AHF. Although baseline sST2 values at AHF admission have been shown to predict outcomes, serial measurements may be of even greater benefit. [12] STI is a noninvasive ultrasound technique that allows an objective and quantitative evaluation of global and regional myocardial function. Changes in RV function in ADHF can be too small to be detected by conventional echocardiographic parameters, hence the need for more sensitive techniques to detect these subtle changes and correlate with changes in sST2 levels.

Our study showed a significant reduction in sST2 levels from admission to discharge, accompanied by a significant improvement in RVFWS in patients hospitalized with AHF. To the best of our knowledge, this is the first study to assess the relationship between changes in sST2 and changes in RV STE parameters during the hospital course in AHF patients.

Serum sST2 and NT-ProBNP on Admission

In our study, serum sST2 on admission strongly correlated with serum NT-ProBNP (r = 0.84, P <0.0001) as both sST2 and NT-ProBNP are markers of myocardial stretch, and they are thought to be elevated in a similar fashion in patients with ADHF. This finding is consistent with a sub-analysis of the PRIDE Study, which included 346 patients with a diagnosis of HF and concluded that sST2 concentrations at admission moderately correlated with NT-ProBNP (r = 0.41). [13] Moreover, Manzano-Fernández et al [14] showed a moderate correlation between sST2 and NT-ProBNP on admission in ADHF patients (r = 0.41, P = 0.001).

Serial Changes in Serum sST2 Levels

It should be noted that sST2 is a dynamic biomarker that could fall or remain elevated throughout the hospital course and beyond, depending on the volume status of the patient and the degree of myocardial stretch.

Repeated sST2 measurements appeared to be a strong predictor of the outcome in patients with AHF, independent of repeatedly measured NT-proBNP. [4] In our study, serum sST2 levels decreased significantly from 2.47 (1.27 – 4.05) ng/ml on admission to 1.86 (1.06 – 3.24) ng/ml at discharge ($P < 0.0001$), with a percentage reduction of 24.7%. Twenty patients (32.8%) showed a reduction above 25% in sST2 levels from admission to hospital discharge.

In a study on 150 patients hospitalized with AHF, Boisot et al [15] demonstrated that the percentage change in serum sST2 concentrations between admission (0.177 (0.086-0.344) ng/mL) to discharge (0.103 (0.043-0.219) ng/mL) was predictive of 90-day mortality. Patients whose serum sST2 levels decreased by 15.5% or more had a 7% 90-day mortality, whereas patients whose sST2 levels failed to decrease by at least 15.5% had a 33% 90-day mortality.

Breidthardt et al [16] measured serum sST2 levels on admission and at 48 hours among 207 patients with AHF and made similar observations. Patients were stratified according to their early sST2 response (responders: sST2 decrease > 25% vs non-responders: sST2 decrease < 25%). Patients who died within 1 year were noted to achieve a lesser sST2 decrease during hospitalization than survivors (median = −25% among the deceased vs −42% among survivors; $P < 0.01$). In a multivariate Cox regression analysis, changes in sST2 during hospitalization independently predicted mortality at 1 year.

In the TRIUMPH clinical cohort study, [4] 496 patients admitted with AHF were followed with serial measurements of serum sST2 after hospital discharge for 1 year. The authors demonstrated a significant association between a rising sST2 during follow-up after AHF hospitalization and a composite outcome of mortality and HF rehospitalization. Furthermore, sST2 levels appeared to rise several weeks before the time of the primary endpoint.

Serial Changes in RV STE Parameters

Our results revealed a significant improvement in RV systolic function assessed by STE (RVFWS [$P = 0.005$]), mainly noticed after the first 48 hours until discharge. Still, RV4CS, TAPSE, and S-wave velocity did not change significantly ($P = 0.06$, $P = 0.09$, and $P = 0.9$, respectively). This finding is consistent with that reported by Morris et al, [17] who recruited 208 patients with heart failure with reduced ejection fraction (HFrEF) and showed that RVFWS and RV4CS were more accurate in the detection of subtle RV functional abnormalities in patients with HFrEF than in those with heart failure with preserved ejection fraction (HFpEF). RV strain successfully showed RV functional changes despite preserved TAPSE, or S-wave velocity at the lateral tricuspid annulus by pulsed tissue Doppler imaging and RV fractional area change. Interestingly, RVFWS and RV4CS were significantly associated with the symptomatic status of patients.

Mateli et al [18] simultaneously performed echocardiography and right heart catheterization on 47 patients with HFrEF referred for cardiac transplantation assessment. They found no correlation between RV stroke volume and TAPSE or S-wave velocity at the lateral tricuspid annulus, but they reported a significant negative correlation between RVFWS and the RV stroke work index. Additionally, RVFWS showed good sensitivity and specificity (95% and 91%, respectively) to predict a reduced RV stroke work index, with a cutoff value below 11.8%. The predictive value of RVFWS was higher than that of RV4CS, TAPSE, and S-wave velocity at the lateral tricuspid annulus.

Correlation Between Serial Changes in Serum sST2 Levels and STE Parameters

We observed a significant decrease in sST2 levels from admission to discharge, reflecting the decongestion and decreased stretch of the myocardium, together with improvements in clinical parameters, including the NYHA functional class and body weight, and some echocardiographic parameters, including LVESVI, LVEF, LAVI, and RVFWS. However, this finding was not accompanied by improvements in RV systolic function measured by conventional parameters, namely TAPSE and S-wave velocity at the lateral tricuspid annulus, which means that patients with more successful decongestion reflected by a more pronounced decrease in sST2 levels from admission to discharge had more marked improvements in RV systolic function assessed by RVFWS. Therefore, combining changes in both sST2 levels and RVFWS can help direct more intensive medical treatment for those with inadequate improvements in both parameters to improve the outcome of patients.

The present study has some limitations. Firstly, we measured NT-ProBNP levels on admission only. Secondly, an accurate STE analysis relies on obtaining good acoustic images of the heart, which seems difficult to achieve, especially during the first few days after admission while the patient is still distressed and overloaded. Thirdly, we excluded patients with prosthetic heart valves and atrial fibrillation, constituting a considerable number of patients suffering from ADHF. Finally, we recruited a small number of patients.

CONCLUSIONS

RVFWS assessed by STE can detect improvements in RV systolic function not detected by other conventional echocardiographic parameters in ADHF patients. Improvements in RVFWS, together with declines in serum ST2 levels, can be used as a marker of improved cardiac mechanics and successful decongestion.

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