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ST2 AS A MARKER FOR HEART FAILURE: A COMPARATIVE CROSS-SECTIONAL STUDY WITH 2D ECHO, AND NT-PROBNP

General Medicine

Dr Manish Kumar Third-Year Junior Resident, Department of Medicine, Subharti Medical Collage Meerut, Uttar Pradesh, India.

Dr Amit Kumar Professor, Department of Medicine, Subharti Medical Collage Meerut, Uttar Pradesh, India.

Dr Narendra Dev Yadav Senior Resident, Department of Medicine, Subharti Medical Collage Meerut, Uttar Pradesh, India.

Dr Shobhit Tomar Associate Professor, Department of Cardiology, Subharti Medical Collage Meerut, Uttar Pradesh, India.

Dr Saurabh Singhal Professor and Head, Department of Medicine, Subharti Medical Collage Meerut, Uttar Pradesh, India.

ABSTRACT

Background: Heart failure (HF) is a major cardiovascular disorder associated with significant morbidity and mortality. Although NT-proBNP and echocardiography are widely used for diagnosis and risk stratification, soluble suppression of tumorigenicity-2 (sST2) has emerged as a novel biomarker reflecting myocardial stress, fibrosis, and remodeling. The present study evaluated the diagnostic and prognostic utility of sST2 in comparison with NT-proBNP and two-dimensional (2D) echocardiography in patients with HF. **Objectives:** To assess the diagnostic accuracy and prognostic value of sST2 in heart failure, compare its performance with NT-proBNP and 2D echocardiography, and evaluate its correlation with echocardiographic parameters and clinical outcomes. **Materials and Methods:** A hospital-based case-control study of 60 participants (30 heart failure cases and 30 controls) was conducted. Serum levels of sST2 and NT-proBNP was measured by ELISA and all the participants underwent comprehensive 2D echocardiographic evaluation. Appropriate statistical methods were used to determine diagnostic accuracy parameters, correlation analysis and prognostic evaluation. **Results:** Cases had significantly higher sST2 (130.93 ± 42.77 ng/mL) and NT-proBNP (3493.33 ± 1896.49 pg/mL) levels than controls ($p<0.001$). Echocardiographic parameters showed significantly lower LVEF and higher LVEDD, LVESD, E/e′ ratio, and PASP among cases ($p<0.001$). All diagnostic modalities had 100% sensitivity while echocardiography had the highest specificity and accuracy (100%) sST2 had higher specificity (83.3%) and accuracy (91.7%) than NT-proBNP. Raised sST2 was significantly associated with adverse outcomes and showed strong correlations with NT-proBNP and echocardiographic indices ($p<0.001$). **Conclusion:** sST2 is a promising biomarker with significant diagnostic and prognostic value in heart failure. Its strong association with echocardiographic indices and clinical outcomes supports its use as a complementary tool to NT-proBNP and 2D echocardiography for improved diagnosis, risk stratification, and prognostic assessment of HF patients.

KEYWORDS

Heart Failure; Soluble ST2; NT-proBNP; Echocardiography; Biomarkers; Prognosis; Risk Stratification.

INTRODUCTION

Heart failure (HF) is a complex cardiovascular syndrome characterized by impaired cardiac structure or function resulting in inadequate ventricular filling or ejection. Progressive myocardial stress promotes inflammation, fibrosis, and ventricular remodeling, which contribute to deterioration of cardiac performance and adverse clinical outcomes. Biomarkers reflecting these pathological processes have gained considerable importance in contemporary HF evaluation.[1] HF is classified into heart failure with reduced ejection fraction (HFrEF), mildly reduced ejection fraction (HFmrEF), and preserved ejection fraction (HFpEF). Despite advances in diagnostic strategies, HFpEF remains particularly challenging because conventional clinical and imaging findings may not adequately reflect underlying myocardial dysfunction. A systematic review demonstrated that biomarker-based assessment can improve diagnostic evaluation in HFpEF.[2] Myocardial fibrosis and diastolic dysfunction are recognized as major contributors to HF progression and symptom burden. In an Indian study, serum ST2 levels showed significant correlations with echocardiographic and cardiac magnetic resonance indicators of diastolic dysfunction and myocardial fibrosis.[3]

Echocardiography remains a cornerstone in the assessment of patients with suspected HF, providing information regarding ventricular structure and function. Stress echocardiography combined with biomarker assessment has been shown to improve the evaluation of symptomatic patients with preserved ejection fraction.[4] NT-proBNP continues to be one of the most widely utilized biomarkers for diagnosis and prognostic assessment because it reflects myocardial wall stress and neurohormonal activation.[5]

However, reliance on a single biomarker may not fully capture the diverse mechanisms involved in HF progression. Contemporary multimodal approaches integrating imaging and biomarkers have therefore been advocated to improve risk stratification and disease characterization.[6] Soluble suppression of tumorigenicity-2 (sST2), a biomarker associated with myocardial stress and remodeling, has emerged as a promising adjunctive marker, with studies demonstrating dynamic changes in response to HF therapy.[7] Combined biomarker models incorporating sST2 have also shown superior prognostic performance in HF populations.[8] Biomarkers reflecting cardiac remodeling, fibrosis, and inflammation have further been associated with disease severity in chronic HF.[9]

Current HF assessment increasingly relies on integrated evaluation using echocardiography and circulating biomarkers.[10] Recent studies have demonstrated the prognostic utility of sST2 in patients with HF and reduced ejection fraction, while predictive models combining serological markers with echocardiographic parameters have enhanced risk assessment.[11] [12] Therefore, the present study was undertaken to evaluate the diagnostic accuracy and prognostic value of sST2 in heart failure and compare its performance with 2D echocardiography and NT-proBNP.

MATERIAL AND METHODS

Study Design: This hospital-based case-control study was conducted to evaluate the diagnostic accuracy and prognostic value of soluble suppression of tumorigenicity-2 (sST2) in patients with heart failure (HF) and to compare its performance with two-dimensional (2D) echocardiography and N-terminal pro-brain natriuretic peptide (NT-proBNP).

Study Setting: The study was carried out in the Department of Cardiology and the Department of Medicine, CSSH.

Study Population: Adult patients presenting with clinical features suggestive of heart failure like dyspnea, fatigue and peripheral edema were enrolled and assessed.

Sample Size: Sixty subjects (30 cases of heart failure and 30 controls) were studied.

Inclusion Criteria

- Adult patients aged ≥18 years.
- Patients presenting with symptoms suggestive of heart failure.

- Patients willing to provide written informed consent.

Exclusion Criteria

- Significant valvular heart disease requiring intervention.
- Patients unable to undergo echocardiographic evaluation.
- Severe renal impairment (estimated glomerular filtration rate <30 mL/min/1.73 m²).

Data Collection and Investigations: Baseline demographic and clinical data were collected. Serum levels of sST2 and NT-proBNP were quantified by ELISA. All patients underwent 2D echo-cardiography to evaluate the left ventricular systolic and diastolic function, valvular morphology, and pulmonary artery systolic pressure. Data on hospitalization and mortality were collected for prognostic evaluation.

Ethical Consideration: Institutional Ethics Committee approval was obtained and written informed consent was secured from all participants prior to enrolment.

Statistical Analysis: Data were analyzed using appropriate statistical software. Descriptive statistics were used to summarize baseline characteristics. Diagnostic accuracy parameters (sensitivity, specificity, PPV, NPV and AUC) were calculated. Correlation analysis was used to analyze the associations between sST2, NT-proBNP and echocardiographic parameters. Prognostic evaluation was performed using Kaplan-Meier survival analysis and Cox regression. A p-value <0.05 was considered statistically significant.

RESULTS

Table 1. Comparison of Laboratory Parameters Between Cases and Controls (N = 60).

Parameter	Cases (Mean ± SD)	Controls (Mean ± SD)	p-value
sST2 (ng/mL)	130.93 ± 42.77	0.00 ± 0.00	<0.001
NT-proBNP (pg/mL)	3493.33 ± 1896.49	149.17 ± 85.00	<0.001
Serum creatinine (mg/dL)	1.63 ± 0.49	1.05 ± 0.23	<0.001
eGFR (mL/min/1.73m²)	54.43 ± 17.54	79.07 ± 14.00	<0.001
Hemoglobin (g/dL)	10.78 ± 1.35	12.59 ± 0.93	<0.001

Statistical Test: Independent samples t-test (Welch).

Table 1 compares laboratory parameters between cases and controls. The cases had significantly higher mean levels of sST2, NT-proBNP and serum creatinine and significantly lower levels of eGFR and hemoglobin compared with controls (p<0.001) suggesting greater degree of cardiac dysfunction and systemic impairment among cases.

Table 2. Comparison of Continuous Echocardiographic Parameters Between Cases and Controls (N = 60).

Parameter	Cases (Mean ± SD)	Controls (Mean ± SD)	p-value
LVEF (%)	37.60 ± 7.70	60.30 ± 3.45	<0.001
LVEDD (mm)	63.27 ± 5.28	48.73 ± 2.30	<0.001
LVESD (mm)	48.93 ± 5.77	32.13 ± 2.62	<0.001
E/e′ ratio	17.58 ± 4.45	10.07 ± 2.50	<0.001
PASP (mmHg)	51.97 ± 12.30	27.10 ± 3.63	<0.001

Statistical test: Independent samples t-test (Welch).

Table 2 compares continuous echocardiographic parameters between cases and controls. The cases had significantly lower LVEF and significantly higher LVEDD, LVESD, E/e' ratio and PASP compared to controls. These findings suggest significant systolic dysfunction, ventricular dilatation, impaired diastolic function and increased pulmonary pressures among heart failure patients (p<0.001 for all).

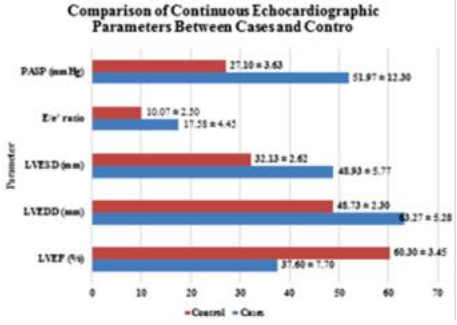


Table 3. Diagnostic Positivity of sST2, NT-proBNP, and 2D Echocardiography Among Cases and Controls (N = 60).

Diagnostic variable	Cases positive n (%)	Controls positive n (%)	p-value
sST2 positive	30 (100.0)	5 (16.7)	<0.001
NT-proBNP positive	30 (100.0)	9 (30.0)	<0.001
Echo suggestive of HF	30 (100.0)	0 (0.0)	<0.001

Statistical test: Fisher's exact test

Table 3 presents the diagnostic positivity of sST2, NT-proBNP, and 2D echocardiography among cases and controls. All cases tested positive for sST2, NT-proBNP, and echocardiographic evidence of heart failure. Positivity rates were significantly lower in controls suggesting high discriminatory power of such diagnostic modalities (p<0.001).

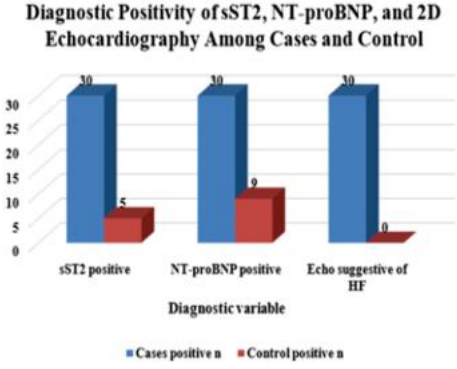


Table 4. Diagnostic Accuracy of sST2, NT-proBNP, and 2D Echocardiography Against Gold Standard HF Diagnosis

Modality	T P	F N	F P	T N	Sensitivit y (%)	Specificit y (%)	PPV (%)	NPV (%)	Accurac y (%)
sST2 positivity	30	0	5	25	100.0	83.3	85.7	100.0	91.7
NT- proBNP positivity	30	0	9	21	100.0	70.0	76.9	100.0	85.0
Echo suggestiv e of HF	30	0	0	30	100.0	100.0	100.0	100.0	100.0

Statistical test: 2×2 contingency table analysis

Table 4 presents the diagnostic accuracy of sST2, NT-proBNP, and 2D echocardiography against the gold standard diagnosis of heart failure. All modalities had 100% sensitivity, but the highest specificity, positive predictive value, negative predictive value, and total accuracy were obtained with 2D echocardiography (100%) than with sST2 and NT-proBNP.

Table 5. Comparison of Biomarker, Renal, Hematological, and Echocardiographic Parameters According to Event Occurrence Among Cases (N= 60).

Parameter	Event occurred (n=20) Mean ± SD / n (%)	No event (n=10) Mean ± SD / n (%)	p-value
sST2 (ng/mL)	155.05 ± 26.78	82.70 ± 22.41	<0.001
NT-proBNP (pg/mL)	4485.00 ± 1454.67	1510.00 ± 752.33	<0.001
Serum creatinine (mg/dL)	1.90 ± 0.36	1.10 ± 0.19	<0.001
eGFR (mL/min/1.73m²)	44.50 ± 10.87	74.30 ± 9.20	<0.001
Hemoglobin (g/dL)	10.02 ± 0.83	12.30 ± 0.78	<0.001
LVEF (%)	33.20 ± 5.05	46.40 ± 2.88	<0.001
E/e′ ratio	19.98 ± 3.28	12.80 ± 1.69	<0.001
PASP (mmHg)	58.95 ± 8.15	38.00 ± 4.71	<0.001
Hospital stay (days)	9.80 ± 2.02	5.30 ± 0.95	<0.001
RWMA present	13 (65.0)	0 (0.0)	0.001
Acute decompensation present	20 (100.0)	0 (0.0)	<0.001

Statistical test: Independent samples t-test (Welch) / Fisher's exact test

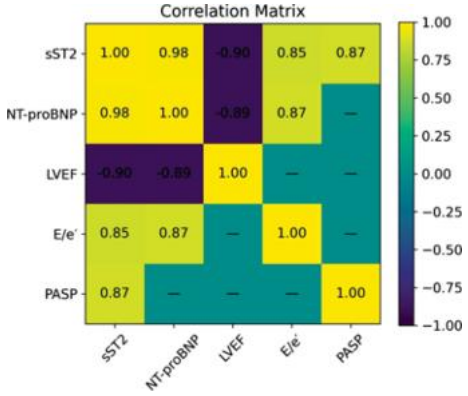
Table 5 compares biomarker, renal, hematological, and echocardio-graphic parameters according to event occurrence among cases. Patients with adverse events had significantly higher sST2 and NT-proBNP levels, worse renal function, lower hemoglobin and LVEF, higher E/e′ ratio and PASP, longer hospital stay, and greater prevalence of RWMA and acute decompensation (p<0.05).

Table 6. Correlation of sST2 and NT-proBNP with Key Echocardiographic Parameters Among Cases (N = 60).

Correlation pair	Pearson's r	p-value
sST2 vs NT-proBNP	0.982	<0.001
sST2 vs LVEF	-0.895	<0.001
sST2 vs E/e′ ratio	0.853	<0.001
sST2 vs PASP	0.869	<0.001
NT-proBNP vs LVEF	-0.894	<0.001
NT-proBNP vs E/e′ ratio	0.869	<0.001

Statistical test: Pearson correlation

Table 6 presents the correlation of sST2 and NT-proBNP with key echocardiographic parameters among cases. sST2 showed a very strong positive correlation with NT-proBNP and significant correlations with LVEF, E/e′ ratio, and PASP. Similar associations were observed for NT-proBNP, indicating that higher biomarker levels were associated with greater heart failure severity (p<0.001).



DISCUSSION

Laboratory evaluation showed significantly increased levels of sST2 (130.93 ± 42.77 ng/mL) and NT-proBNP (3493.33 ± 1896.49 pg/mL) in cases compared to controls (p< 0.001). Similar results were reported by Li et al. 1 (2025) with higher levels of sST2 and NT-proBNP in HFpEF Subjects. Chogle et al (2023)11 also reported elevated levels of sST2 in HFrEF patients which were also associated with adverse outcomes. Cases also had considerably greater serum creatinine, decreased eGFR and hemoglobin levels. Similar relationships between biomarker increase, renal dysfunction and worsening heart failure severity were observed by Andreasová et al. (2020)[9] and Dsouza and Sharma (2024)[5]. In contrast, Chen et al. (2021)[3] demonstrated a reduced diagnostic value of ST2 compared with natriuretic peptides.

Echocardiographic assessment showed significantly decreased LVEF and increased LVEDD, LVESD, E/e' ratio and PASP in patients than controls (p<0.001) suggesting significant structural and functional damage of heart. Yu et al. (2024)[6] also reported similar results with increased LVEDD and LVESD with decreased LVEF in all NYHA classes. Agrawal et al. (2022)[2] also demonstrated considerable relationships between levels of ST2 and the E/e′ ratio demonstrating increasing diastolic dysfunction. Aimo et al. 2022 [12] described unfavorable remodeling as ventricular dilatation with reduced systolic function, while Ilie iu et al. 2022 [10] highlighted the prognostic relevance of greater filling pressures and congestion. This is in contrast to the study by Kubicius et al. (2022)[4] who studied individuals with preserved LVEF and reported less echocardiographic abnormalities.

All cases were positive in sST2, NT-proBNP and echocardiographic indications of heart failure while the controls showed 16.7%, 30% and 0% positivity correspondingly (p<0.001). Li et al. (2025)[1] showed similar findings where sST2 and NT-proBNP had good diagnostic performance in HFpEF. Dsouza and Sharma (2024)[5] mentioned the well-known function of NT-proBNP in heart failure diagnosis while Ilieşiu et al. (2022)[10] proposed integrating biomarkers with imaging as ideal for diagnostic accuracy. The absence of echocardiographic positivity in controls also revealed the imaging discriminating value. However, the studies of Chen et al. (2021)[3] and Kubicius et al. (2022)[4] have shown a higher diagnostic usefulness of natriuretic peptides than ST2

All three modalities demonstrated 100% sensitivity for heart failure diagnosis, with no false-negative cases. Similar findings were reported by Li et al. (2025)[1], who observed good diagnostic performance of sST2 and NT-proBNP in HFpEF patients. Dsouza and Sharma (2024)[5] and Ilie iu et al. (2022)[10] also emphasized the value of combining biomarkers with imaging for accurate diagnosis. A notable observation was the superior performance of echocardiography, which achieved 100% specificity, PPV, NPV, and accuracy, compared with sST2 (91.7% accuracy) and NT-proBNP (85.0% accuracy). In contrast, Chen et al. (2021)[3] and Kubicius et al. (2022)[4] reported greater diagnostic utility for natriuretic peptides than ST2.

Patients experiencing adverse events had significantly increased levels of sST2 and NT-proBNP, poorer renal function, decreased hemoglobin levels, decreased LVEF, increased E/e′ ratio and increased PASP compared to patients without events (p<0.001). Similar findings were reported by Chogle et al. (2023)[11] sST2 levels were increased in patients with worse prognosis. ST2 and NT-proBNP were independent predictors of adverse events (2023)[8] .Yu et al. (2024)[6] sST2 was also high with impaired ventricle function and mortality risk. A unique finding was the presence of acute decompensation in 100% of patients with events and RWMA in 65.0%. Comparable prognostic associations were described by Andreasová et al. (2020)[9].

A very strong positive correlation was found between sST2 and NT-proBNP (r=0.982, p<0.001), and both biomarkers correlated strongly negatively with LVEF and positively with E/e′ ratio and PASP. Li et al. (2025)[1] and Yu et al. (2024)[6] described increasing levels of biomarkers with the worsening cardiac function and severity of disease. Similar relations of biomarker elevation with cardiac dysfunction were described by Andreasová et al. (2020)[9]. However, limited diagnostic utility of ST2 was suggested by Kubicius et al. (2022)[4] However despite strong correlation of ST2 with echocardiographic abnormalities as seen in the present study.

CONCLUSION

This study shows that soluble suppression of tumorigenicity-2 (sST2) is a useful biomarker in the evaluation of heart failure, with significant diagnostic and prognostic value when used in conjunction with NT-proBNP and two-dimensional echocardiography. Heart failure patients had significantly higher sST2 and NT-proBNP levels, significant alterations in echocardiographic parameters, and more severe clinical and hemodynamic impairment compared with controls. The strong correlations between sST2, NT-proBNP, left ventricular ejection fraction, E/e′ ratio, and pulmonary artery systolic pressure indicate that increasing levels of the biomarkers reflect the worsening cardiac structure and function. Echocardiography had the best overall diagnostic performance and sST2 had higher specificity and accuracy than NT-proBNP, supporting the hypothesis that sST2 can be used as a reliable adjunct biomarker. High sST2 was also significantly associated with adverse clinical outcomes such as readmission, mortality, prolonged hospitalization, renal failure and severe cardiac dysfunction, confirming its prognostic value. The combination of sST2 with conventional biomarkers and echocardiography may improve risk stratification, facilitate early detection of high-risk patients, and improve clinical decision-making in heart failure management.

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