BMC Cardiovascular Disorders

RESEARCH

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Soluble suppression of tumorigenicity 2 associated with left ventricular thrombosis in patients with ST-segment elevation myocardial infarction

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Abstract

Background Left ventricular thrombosis (LVT) after acute ST-segment elevation myocardial infarction (STEMI) is closely related to inflammation. Soluble Suppression of Tumorigenicity 2 (sST2) expressed as a novel inflammatory marker, has received much attention in recent years. However, the relationship between sST2 and LVT is unclear. This study aimed to investigate the correlation between sST2 and LVT formation after emergency PCI (pPCI) in STEMI patients.

Methods 293 patients with STEMI who were tested for sST2 at admission within 24 h at the Affiliated Hospital of Xuzhou Medical University from June 2018 to August 2023 were consecutively enrolled and evaluated for myocardial infarction characteristics and the presence of LVT by cardiac magnetic resonance imaging (CMR). The diagnosis of LVT was defined as a left ventricular cavity in the late gadolinium enhancement (LGE) of CMR with a low signal intensity mass.

Results A total of 38 patients developed LVT after STEMI, multivariable logistic regression analysis showed that sST2 [$P=0.002$, OR = 1.01 (1.01 ~ 1.02)] an independent predictor of LVT formation. The results of the net reclassification index (NRI) and Integrated Discrimination Improvement Index (IDI) suggested that sST2 could improve the conventional model of LVT. A linear relationship between sST2 and LVT was fitted using a restricted cubic spline (RCS).

Conclusion sST2 was independently associated with LVT formation after pPCI in STEMI patients, and sST2 improved the risk modeling of LVT.

Clinical trial number Not applicable.

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Keywords Left ventricular thrombosis, Soluble suppression of tumorigenicity 2, Cardiovascular magnetic resonance, Myocardial infarction, Prognosis

Introduction

Acute ST-segment elevation myocardial infarction (STEMI) is the type of acute coronary syndrome with the highest mortality rate and is usually associated with severe complications [1]. Although percutaneous coronary intervention (PCI) can greatly improve the prognosis of STEMI patients by opening the offender vessel promptly, patients with STEMI still face a poorer prognosis, with potential causes including irreversible myocardial necrosis and related complications [2]. Among them, ventricular appendage thrombosis (LVT), one of the serious complications of myocardial infarction, has an incidence of up to 12% [3]. Mechanistically, the formation of LVT is associated with ventricular wall dyskinesia after myocardial infarction leading to blood stasis, endothelial injury, and hypercoagulability, in which inflammatory response plays a key role [4]. Previous studies have shown that LVT is associated with major adverse cardiac events (MACE) and worse prognosis in STEMI patients [5]. Therefore, the discovery of more risk markers related to LVT formation will help us to identify high-risk patients early, intervene early, and optimize risk stratification, thus improving the prognosis of STEMI patients.

With a specificity of nearly 100% and a sensitivity of 82–88%, cardiac magnetic resonance imaging (CMR) is currently the best imaging technique for the diagnosis and assessment of LVT [6]. In recent years, Soluble Suppression of Tumorigenicity 2 (sST2) is strongly associated with cardiovascular disease as a novel and promising inflammatory marker [7, 8]. The European Cardiovascular Society states that sST2 can be used in the diagnosis, prognosis, and treatment of heart failure (HF) [9]. In addition, sST2 is strongly associated with myocardial fibrosis, ventricular remodeling, HF, new-onset atrial fibrillation (NOAF), and the development of MACE after pPCI in STEMI patients [7, 10–12]. Although LVT is associated with inflammation [4], the relationship between sST2 and LVT formation in STEMI patients is unclear. This study aimed to investigate the predictive value of sST2 for LVT formation after PCI in patients with acute STEMI.

Materials and methods

Study population

This was a single-center retrospective study that included patients with STEMI [13] who underwent emergency PCI (pPCI) from June 2018 to August 2023 at the Affiliated Hospital of Xuzhou Medical University. Each patient received a load of aspirin and P2Y12 antagonists before PCI. Inclusion criteria: Age > 18 years, successful pPCI within 12 h of symptom onset (postoperative TIMI ≥ 2), complete CMR during hospitalization, and completion of sST2 test during hospitalization. Exclusion criteria: glomerular filtration rate (eGFR) < 30 ml/min/1.73 m^2, history of inflammatory disease, history of malignancy, history of previous heart attack, poor quality of CMR, history of previous heart failure (HF). The study was approved by the Ethics Committee of Xuzhou Medical University Hospital. Ethical approval number: XYFY2024-KL512. According to the relevant Ethics Review Board (IRB) regulatory guidelines, the requirement for signed written consent was waived as the study posed no risk to patients. The inclusion and exclusion criteria are shown in Fig. 1.

Clinical data collection

The patient's gender, age and related clinical indicators are collected through the hospital's medical record system. Such as total cholesterol (TC), triglycerides (TG), low density lipoprotein (LDL), high density lipoprotein (HDL), fasting blood glucose (FBG), peak hypersensitive cardiac troponin T (peak hs-TnT), peak amino-terminal Pro brain natriuretic peptide (peak NTproBNP), peak high sensitivity c-reactive protein (peak hs-CRP), left ventricular ejection fraction (LVEF), Killip grade, TIMI blood flow grade, treatment status and medication information of patients. All patients completed sST2 detection at admission within 24 h and sST2 was evaluated utilizing an immunoassay kit (provided by Spring bio, Guangzhou, China) according to the protocol.

Cardiac MRI-related parameters

Each patient underwent CMR at a median time of 5 (IQR 4,6) after admission. Long-axis images (two, three, and four-chamber) and short-axis images (fiber-optic digital coil, two-dimensional multilayer scanning) of the left atrium and left ventricle were obtained using a 3.0T scanner (Philips, The Netherlands). A balanced turbo field echo (BTFE) sequence was used. Scanning parameters: layer thickness = 7 mm, echo time (TE) = 1.47 ms, repetition time (TR) = 2.94 ms, flip angle = 60°, field of view (FOV) = 300 mm × 300 mm, matrix = 280 mm × 240 mm, voxel size = 1.22 mm × 1.22 mm × 8.0 mm. Scanning parameters for the LGE sequence: layer thickness = 7 mm. echo time = 6.1ms, repetition time = 3.0ms, field of view = 350 × 350 mm. Left ventricular mass (LV-mass), left ventricular ejection fraction (LVEF), infarction area size (LGE), and microvascular Obstruction(MVO). On LGE-CMR images, endocardial and epicardial contours were manually traced, and areas with signal

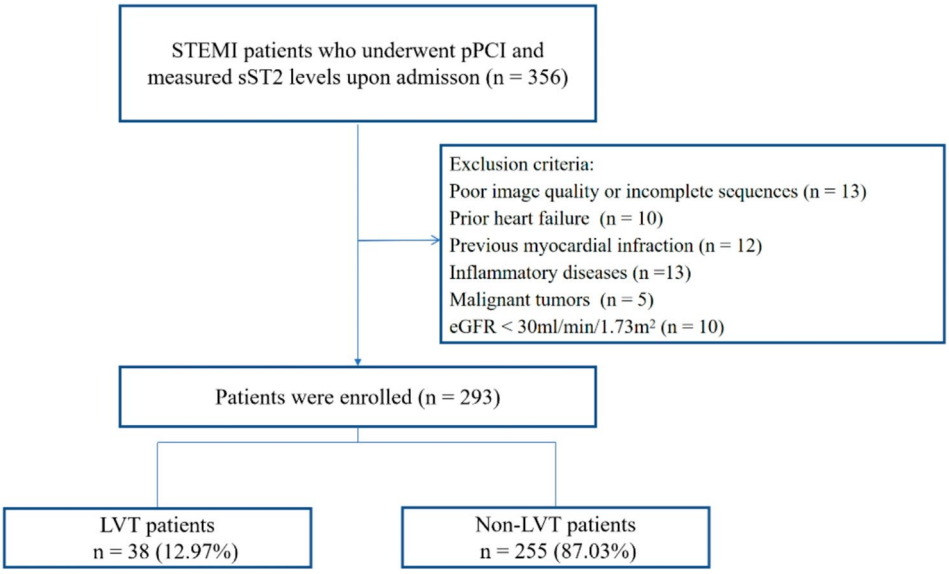

Fig. 1 Study Flowchart

intensity more than 5 standard deviations above normal myocardium on LGE short-axis images were defined as infarcted areas, and LGE was defined as infarcted area mass (g) as a percentage of left ventricular mass (LV-mass). MVO mass (MVO%) was defined as low-signal area mass within the infarcted myocardium as a percentage of total LV mass. Signal region mass as a percentage of total left ventricular mass (LV- mass). The diagnosis of LVT was defined as a low-signal-intensity mass within the left ventricular cavity in a delayed imaging sequence of CMR (LGE-CMR) that has a distinct margin from the ventricular endocardium, is differentiated from papillary muscle, tendon cords, trabeculae, or artifacts, and can be distinguished from nearby high-intensity structures such as intramyocardial hemorrhage and myocardial scarring) can be distinguished.

Statistical analysis

The Kolmogorov-Smirnov test was used to assess the normality of the data. Normally distributed continuous variables expressed as mean ± standard deviation was analyzed using Student's t-test. Non-normally distributed continuous variables expressed as median (Q1, Q3) were analyzed using the Mann-Whitney U test. Categorical variables were expressed as frequencies (n, %) and analyzed using the chi-square test. Correlations with variables related to sST2 and LVT formation were analyzed using Spearman regression analysis. All variables were analyzed using one-way logistic regression analysis, and variables with $P < 0.1$ in the one-way regression analysis were analyzed using the stepwise forward method for multivariable logistic regression analysis, and stepwise forward analysis for predictors of LVT formation. Receiver Operating Characteristic (ROC) curves were used to evaluate the sensitivity and specificity of sST2 for predicting LVT, and the optimal cutoff value of sST2 for predicting LVT was also obtained. Subsequently, the combination of independent risk factors was used as a new prediction model, and risk factors other than sST2 were used as a traditional model, and the net reclassification index (NRI) and the integrated discrimination improvement index (IDI) of the two models were calculated. The improvement effect of sST2 on risk prediction was obtained. The statistical analysis of this paper was performed using SPSS 26.0 (Inc, Chicago, IL, USA) and R 4.1.2 (https://cran.r-project.org).

Results

Baseline data comparison between groups

As shown in Table 1, among the laboratory indices, the differences between Non-LVT and LVT groups in peak hs-CRP ($p < 0.001$), Peak hsTnT ($p < 0.001$), and sST2 ($p < 0.001$) were statistically significant ($p < 0.05$). Among the cardiac angiography-related indices, IRA-LAD ($p = 0.025$) showed a significant difference, while the other indices showed no statistically significant difference. For cardiac magnetic resonance indices, infarct area (LGE, %) left ventricular ejection fraction (LVEF,%) and microcirculatory obstruction (MVO,%) showed significant differences, while the rest were not statistically significant.

Comparison of baseline data of different sST2 groups

Table S1 summarizes the baseline characteristics of the study population stratified by sST2 levels into four groups: Q1 (< 29.16 ng/mL), Q2 (29.16–44.43 ng/mL),

Table 1 Baseline data comparison between groups

Variables	Non LVT (*n* = 255)	LVT (*n* = 38)	*P*
Age, (years)	57.22 ± 11.90	59.95 ± 10.64	0.184
Male, n(%)	220 (86.27)	29 (76.32)	0.109
BMI, (kg/m^2)	26.40 ± 3.66	26.65 ± 3.39	0.685
Systolic blood pressure, (mm/Hg)	127.44 ± 19.12	129.79 ± 22.39	0.490
Diastolic blood pressure, (mm/Hg)	80.20 ± 12.63	79.47 ± 14.21	0.745
Heart rate, (times/min)	78.57 ± 12.67	79.76 ± 12.95	0.589
Peak hsTnT, (ng/L)	3116.00 (1406.50, 6370.35)	6981.00 (3691.25, 10000.00)	<0.001
Peak NTproBNP, (pg/mL)	1171.00 (701.84, 1980.97)	2280.65 (1357.75, 3046.00)	<0.001
Peak hs-crp, (mg/L)	37.56 ± 34.45	70.02 ± 52.28	<0.001
TC, (mmol/L)	1.70 ± 1.26	1.98 ± 1.83	0.235
TG, (mmol/L)	4.32 ± 1.08	4.18 ± 0.98	0.434
LDL-C, (mmol/L)	2.81 ± 1.11	2.62 ± 0.74	0.311
HDL-C, (mmol/L)	0.96 ± 0.26	0.99 ± 0.28	0.513
eGFR, (mL/min/1.73 m^2)	107.01 ± 15.74	110.39 ± 11.71	0.205
LVEF, (%)	52.93 ± 6.60	48.75 ± 6.23	<0.001
sST2,(ng/ml)	43.18 (27.56, 70.89)	107.30 (39.94, 161.14)	<0.001
Smoking, n(%)	142 (55.69)	21 (55.26)	0.961
Different sST2 groups, n(%)			<0.001
Q1 (< 29.16 ng/ml)	71 (27.84)	2 (5.26)	
Q2 (29.16-44.43ng/ml)	64 (25.10)	9 (23.68)	
Q3 (44.43-97.87ng/ml)	68 (26.67)	6 (15.79)	
Q4 (> 97.87 ng/ml)	52 (20.39)	21 (55.26)	
Hypertension, n(%)	121 (47.45)	18 (47.37)	0.992
Diabetes, n(%)	62 (24.31)	12 (31.58)	0.336
Stroke, n(%)	29 (11.37)	2 (5.26)	0.390
Killip class ≥ 2, n(%)	25 (9.80)	8 (21.05)	0.077
IRA-LCX, n(%)	34 (13.33)	5 (13.16)	0.976
IRA-LAD, n(%)	105 (41.18)	24 (63.16)	0.011
IRA-RCA, n(%)	112 (43.92)	13 (34.21)	0.259
D-to-B, (min)	50.00 (32.00, 120.00)	53.50 (37.00, 149.25)	0.662
S-to-B, (min)	270.00 (158.50, 415.00)	262.50 (171.25, 495.50)	0.517
Thrombolysis, n(%)	2 (0.78)	1 (2.63)	0.342
GP2b3a inhibitors, n(%)	9 (3.53)	0 (0.00)	0.501
Thrombectomy, n(%)	22 (8.63)	4 (10.53)	0.938
Pre-TIMI ≤ 1, n(%)	199 (78.04)	34 (89.47)	0.103
LV-mass, (g)	107.36 ± 29.31	114.98 ± 31.82	0.141
LGE, (%)	27.99 ± 16.69	44.20 ± 17.38	<0.001
MVO, (%)	1.60 ± 3.51	3.86 ± 4.03	0.002
Sacubitril Sodium Tablets/ACEI/ARB, n(%)	139 (54.51)	22 (57.89)	0.696
β-blockers, n(%)	226 (88.63)	36 (94.74)	0.390
Spirolactone, n(%)	9 (3.53)	2 (5.26)	0.964
Anticoagulant medications, n(%)	0 (0.00)	1 (2.63)	0.130

BMI = body mass index; LAD = left atrium dimension; LVEF = left ventricular ejection fraction; TC = Serum total cholesterol; TG = Serum triglyceride; LDL-C = low-density lipoprotein cholesterol; HDL-C = high-density lipoprotein cholesterol; NT-proBNP = N-terminal pro B-type natriuretic peptide; hsTnT = high-sensitivity troponin T; peak hs-crp = peak high sensitivity c-reactive protein; eGFR = estimated glomerular filtration rate; hs-CRP, highly sensitive C-reactive protein; LCX = left circumflex branch; LAD = left anterior descending branch; RCA = right coronary artery; D-to-B = Door-to-Balloon Time; S-to-B = Symptom-to-Balloon Time; TIMI = thrombolysis in myocardial infarction; LGE = late gadolinium enhancement; LV-mass = left ventricular mass; sST2 = soluble growth stimulator gene 2 protein; ARB = angiotensin II receptor antagonist; ACEI = angiotensin-converting enzyme inhibitors

Q3 (44.43–97.87 ng/mL) and Q4 (> 97.87 ng/mL). Patients with higher sST2 levels had a higher incidence of LVT than those with lower sST2 level(28.77% vs. 2.74%). Patients with higher sST2 levels also had higher LGE mean LGE 38.94 ± 16.84 vs. 21.88 ± 14.03%, p<<0.001) and MVO mean MVO 3.57 ± 3.78 vs. 0.79 ± 1.92%, p<<0.001 than those with lower sST2 levels. These results suggest that higher sST2 levels are associated with greater MVO, increased LGE, and the occurrence of LVT.

Correlation between sST2 and other indicators

As shown in Table 2, sST2 was significantly associated with a variety of metrics that have been shown to predict LVT formation, including peak hsTnT ($r = 0.373$, $p < 0.001$), peak NT-proBNP ($r = 0.225$, $p < 0.001$), LVEF (r=-0.225, $p < 0.001$), peak hs-CRP ($r = 0.240$, $p < 0.001$), LGE ($r = 0.303$, $p < 0.001$).

Logistic regression analysis results

As shown in Tables 3 and 4, univariate logistic regression analysis showed that sST2 (OR = 1.01, 95% CI:1.01 ~ 1.02, $p < 0.001$), Killip classification ≥ 2 (OR = 2.45, 95% CI:1.02 ~ 5.93, $p = 0.046$), Peak hs-CRP (OR = 1.02, 95% CI:1.01 ~ 1.03, $p < 0.001$), Peak hsTnT (OR = 2.30, 95% CI:1.43 ~ 3.69, $p < 0.001$), PeakNT-proBNP (OR = 2.12, 95% CI:1.37 ~ 3.72, $p < 0.001$), LVEF (OR = 0.91, 95% CI:0.86 ~ 0.96, $p < 0.001$), IRA-LAD (OR = 2.45, 95% CI:1.21 ~ 4.96, $p = 0.013$), LGE (OR = 1.05, 95% CI:1.03 ~ 1.07, $p < 0.001$) and MVO (OR = 1.13, 95% CI:1.04 ~ 1.22, $p = 0.003$) were correlated. Subsequently, we divided sST2 into quartile categorical variables for logistic regression. As shown in Table 4, higher sST2 has independent predictive value for ventricular thrombosis. Subsequently, variables with $p < 0.1$ were included in stepwise forward multivariable logistic regression analysis, which showed that Peak hs-CRP (OR = 1.01, 95% CI:1.01 ~ 1.02, $p = 0.002$), IRA-LAD (OR = 4.42, 95% CI:1.88 ~ 10.39, $p < 0.001$), sST2 (OR = 1.01, 95% CI:1.01 ~ 1.02, $p = 0.002$), and LGE (OR = 1.04, 95%

Table 2 Correlation between sST2 and predictive indicators of LVT

Parameter	Correlation Coefficient (*r*)	*p*-value
peak hsTnT, (ng/L)	0.378	< 0.001
Peak NT-proBNP, (pg/mL)	0.204	< 0.001
LVEF, (%)	-0.174	0.003
hs-CRP, (mg/L)	0.211	< 0.001
LGE, (%)	0.381	< 0.001

hsTnT = high-sensitivity troponin T; NT-proBNP = N-terminal pro B-type natriuretic peptide; LVEF = left ventricular ejection fraction; peak hs-crp = peak high sensitivity c-reactive protein; LGE = late gadolinium enhancement

CI:1.01 ~ 1.06, $p = 0.001$) were independent predictors of LVT ($p < 0.05$). As shown in Fig. 2, restricted cubic spline (RCS) was used to fit the nonlinear relationship between sST2 and LVT, and there was a linear relationship between sST2 and LVT (p for overall < 0.001, p for non-linear = 0.294). A 19-cross-validation was conducted to evaluate the performance of the logistic regression model in predicting ventricular thrombosis. The accuracy across different folds ranged from 81.2 to 93.8%, with an average

Table 3 Association of patient characteristics with LVT:: univariate logistic regression analysis

Variables	Univariate Logistic Regression Analysis	
	P	OR (95%CI)
Age, (years)	0.184	1.02(0.99 ~ 1.05)
BMI, (kg/m^2)	0.683	1.02 (0.93 ~ 1.12)
Systolic blood pressure, (mm/Hg)	0.488	1.01 (0.99 ~ 1.02)
Diastolic blood pressure, (mm/Hg)	0.744	1.00 (0.97 ~ 1.02)
Heartrate, (Times/min)	0.588	1.01 (0.98 ~ 1.03)
PeakhsTnT, (ng/L)	< 0.001	2.30 (1.43 ~ 3.69)
PeakNTproBNP, (pg/mL)	< 0.001	2.12 (1.37 ~ 3.27)
TC, (mmol/L)	0.242	1.14 (0.92 ~ 1.40)
TG, (mmol/L)	0.431	0.88 (0.63 ~ 1.22)
LDL-C, (mmol/L)	0.305	0.82 (0.57 ~ 1.19)
HDL-C, (mmol/L)	0.512	1.51 (0.44 ~ 5.14)
Fasting blood glucose, (mmol/L)	0.860	0.98 (0.79 ~ 1.22)
Peakhs-CRP, (mg/L)	< 0.001	1.02 (1.01 ~ 1.03)
eGFR, (mL/min/1.73 m^2)	0.206	1.02 (0.99 ~ 1.04)
LVEF, (%)	< 0.001	0.91 (0.86 ~ 0.96)
IRA-LAD, n (%)	0.013	2.45 (1.21 ~ 4.96)
Pre-TIMI ≤ 1, n (%)	0.113	2.39 (0.81 ~ 7.03)
S-to-B, (min)	0.238	1.00 (1.00 ~ 1.00)
D-to-B, (min)	0.288	1.00 (1.00 ~ 1.00)
Thrombolysis, n (%)	0.320	3.42(0.30 ~ 38.65)
GP2b3ainhibitors, n (%)	0.985	0.00 (0.00 ~ Inf)
Thrombectomy, n (%)	0.701	1.25 (0.40 ~ 3.84)
Stroke, n (%)	0.266	0.43 (0.10 ~ 1.89)
Male, n (%)	0.114	0.51 (0.22 ~ 1.17)
Hypertension, n (%)	0.922	1.00 (0.50 ~ 1.97)
Smoking, n (%)	0.961	0.98 (0.50 ~ 1.95)
Diabetes, n (%)	0.338	1.44 (0.68 ~ 3.02)
Killip class ≥ 2, n (%)	0.046	2.45 (1.02 ~ 5.93)
sST2, (ng/ml)	< 0.001	1.01(1.01 ~ 1.02)
Different sST2 groups, n(%)		
Q1 (< 29.16 ng/ml)		1.00 (Reference)
Q2 (29.16-44.43ng/ml)	0.079	4.86(0.83 ~ 26.87)
Q3(44.43-97.87ng/ml)	0.171	3.13(0.61 ~ 16.06)
Q4 (> 97.87 ng/ml)	< 0.001	14.43 (3.22 ~ 63.86)
LV-mass, (g)	0.140	1.01(1.00 ~ 1.02)
LGE, (%)	< 0.001	1.05(1.03 ~ 1.07)
MVO, (%)	0.003	1.13(1.04 ~ 1.22)

BMI = body mass index; LAD = left atrium dimension; LVEF = left ventricular ejection fraction; TC = Serum total cholesterol; TG = Serum triglyceride; LDL-C = low-density lipoprotein cholesterol; HDL-C = high-density lipoprotein cholesterol; NT-proBNP = N-terminal pro B-type natriuretic peptide; hsTnT = high-sensitivity troponin T; peak-hsCRP = peak high sensitivity c-reactive protein; eGFR = estimated glomerular filtration rate; LCX = left circumflex branch; LAD = left anterior descending branch; D-to-B = Door-to-Balloon Time; S-to-B = Symptom-to-Balloon Time; TIMI = thrombolysis in myocardial infarction; LV-mass = left ventricular mass; sST2 = soluble growth stimulator gene 2 protein; MVO = microvascular obstruction; hs-CRP; LGE = late gadolinium enhancement

Table 4 Association of patient characteristics with LVT: multivariable logistic regression analysis

Variables	Multivariable logistic regression analysis			
	Model 1		Model 2	
	OR (95%CI)	*P*	OR (95%CI)	*P*
sST2	1.01(1.01 ~ 1.02)	0.002	Not in model	
sST2-Q4	Not in model		13.10 (2.19 ~ 78.19)	0.005
LGE	1.04 (1.01 ~ 1.06)	0.001	1.04 (1.01 ~ 1.06)	0.010
$Peak^{hs-CRP}$	1.01 (1.01 ~ 1.02)	0.002	1.02 (1.01 ~ 1.02)	0.002
$IRA\text{-}^{LAD}$	4.42 (1.88 ~ 10.39)	< 0.001	4.65 (1.95 ~ 11.1)	< 0.001

Peak-hsCRP = peak high sensitivity c-reactive protein; LAD = left atrium dimension; sST2 = soluble growth stimulator gene 2 protein; LGE = late gadolinium enhancement; OR = Odds Ratio; CI = Confidence Interval. Model 1 contains all variables with $p < 0.05$ in uni-variable logistic regression analysis except sST2-Q4; Model 2 contains all variables with $p < 0.05$ in uni-variable logistic regression analysis except sST2

accuracy of 88.7%. These results suggest that the model demonstrates reliable classification performance.

ROC curve analysis

Subsequent ROC curves based on the results of multivariable logistic regression analysis showed that sST2, IRA-LAD, LGE%, and Peak hs-CRP had significant predictive value for LVT (as shown in Fig. 3; Table 5). The sensitivity and specificity of sST2 in predicting LVT were 0.553 and 0.796. The sensitivity and specificity of Peak hs-CRP were 0.474 and 0.847. The sensitivity and specificity of LGE% were 0.526 and 0.886. The

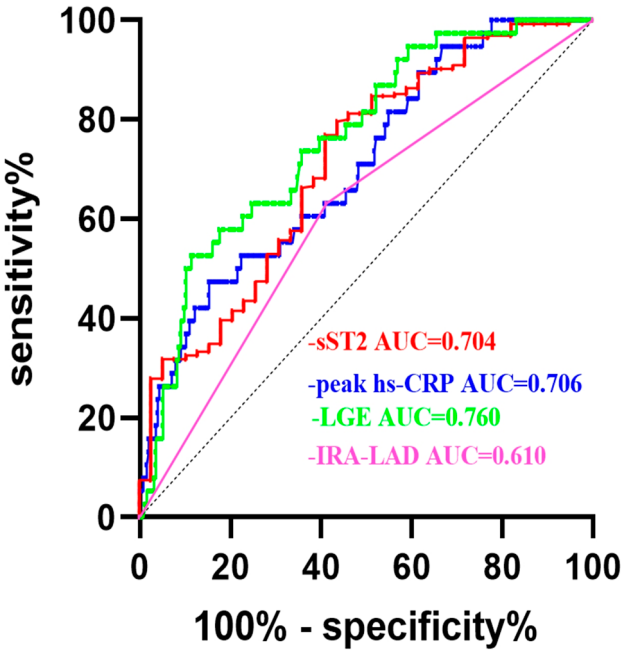

Fig. 3 Receiver operating characteristic analysis (ROC) for identifying LVT. sST2 = Soluble Suppression of Tumorigenicity 2; peak hs-CRP = peak high sensitivity c-reactive protein; LVT = Left ventricular thrombosis; LGE = late gadolinium enhancement; LAD = left anterior descending branch

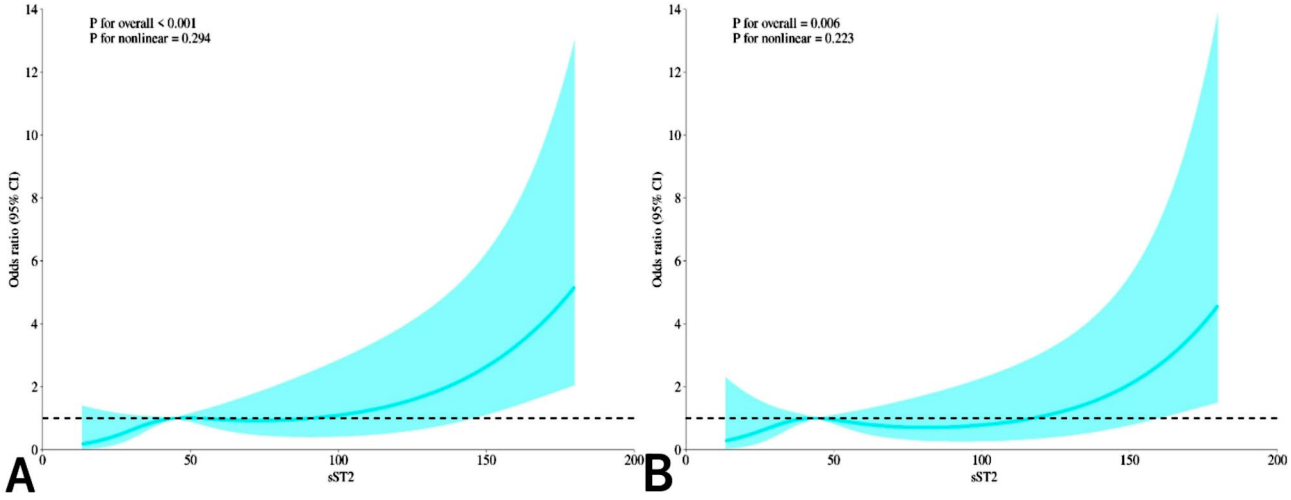

Fig. 2 Dose-response relationship between sST2 and LVT in patients with STEMI. (**A**) unadjusted dose-response relationship between sST2 and LVT; (**B**) adjusted dose-response relationship between sST2 and LVT

Table 5 ROC curve analysis

	AUC	95% CI	*P*	Cut-off	Sensitivity	Specificity
sST2	0.704	0.614–0.795	< 0.001	97.87	0.553	0.796
IRA-LAD	0.610	0.514–0.705	0.029	—	0.632	0.588
LGE	0.760	0.684–0.873	< 0.001	45.70	0.526	0.886
Peak hs- crp	0.706	0.620–0.792	< 0.001	78	0.474	0.847

sST2 = soluble growth gene 2 protein; hsTnT = high-sensitivity troponin T; peak hs-crp = peak high sensitivity c-reactive protein; ROC = receiver operating characteristic; LAD = left anterior descending branch; AUC = area under the curve; CI = confidence interval; LGE = late gadolinium enhancement

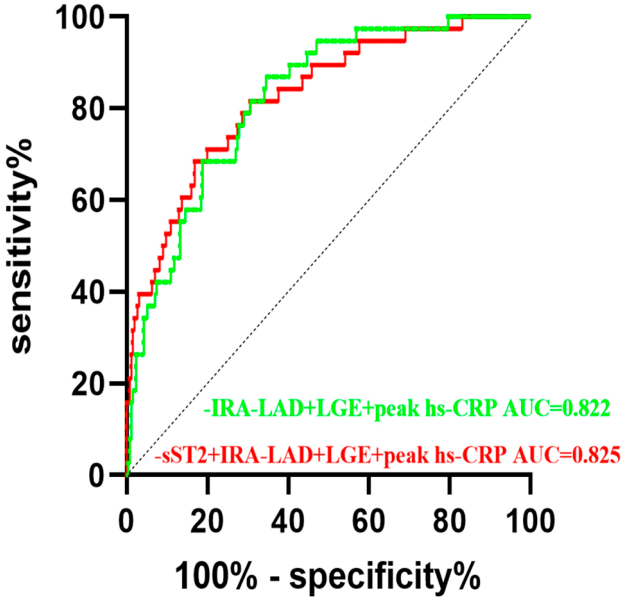

Fig. 4 Receiver operating characteristic analysis (ROC) of combined parameters for identifying LVT. sST2 = Soluble Suppression of Tumorigenicity 2; peak hs-CRP = peak high sensitivity c-reactive protein; LVT = Left ventricular thrombosis; LGE = late gadolinium enhancement; LAD = left anterior descending branch

Table 6 ROC curve analysis of combined parameters

	AUC	95% CI	*P*	Sensitivity	Specificity
IRA-LAD + LGE%+peak hs-CRP	0.822	0.758–0.886	< 0.001	0.868	0.655
IRA-LAD + LGE%+peak hs-CRP + sST2	0.825	0.754–0.896	< 0.001	0.684	0.831

IRA = Infarct-related arteries; LAD = Left anterior descending branch; LGE = Late gadolinium enhanced; LAD = left atrium dimension; ROC = receiver operating characteristic; sST2 = soluble growth stimulator gene 2 protein; hs-CRP = highly sensitive C-reactive protein; AUC = area under the curve; CI = confidence interval

Table 7 Discrimination accuracy and reclassification of sST2 for MVO

	NRI		IDI	
	Estimate (95% CI)	*P* value	Estimate (95% CI)	*P* value
Conventional model	Reference	-	Reference	-
Conventional model + sST2	0.600(0.261–0.929)	< 0.001	0.061 (0.022-0.100)	0.0021

sensitivity and specificity of IRA-LAD were 0.632 and 0.588. As shown in Fig. 4; Table 6, the addition of sST2 to the traditional model (peak hs-CRP + IRA-LAD + LGE) (AUC = 0.822) improved the predictive value of the traditional model, with the new model having an AUC of 0.825, and a sensitivity and specificity of 0.684 and 0.831, respectively. Subsequently, the IDI and the NRI were computed, and the results showed that the NRI = 0.600(0.261–0.929), $p < 0.001$, IDI = 0.061(0.022-0.100), $p = 0.0021$, indicating that the predictive ability of the new model was improved over the traditional model and that the new model was improved by 6.1% over the traditional model with $p < 0.05$, suggesting that the difference was statistically significant and that the new model had a higher ability to predict LVT than the traditional model (as shown in Table 7).

Discussion

To the best of our knowledge, this study is the first to investigate the relationship between LVT formation and sST2 after pPCI in STEMI patients. The main findings of this study are as follows. Firstly, elevated sST2 levels were independently associated with LVT formation after pPCI in STEMI patients. Secondly, the integration of sST2 significantly improved the risk modeling of LVT.

STEMI is one of the leading causes of death in the population, and although the prognosis of STEMI patients has improved significantly in recent decades due to the popularization of early PCI [1], LVT remains a common and serious complication of STEMI [14]. Previous studies have shown that LVT is associated with the development of MACE in STEMI patients [14]. Clinically, although there are more methods to diagnose LVT, there is still a risk of missed diagnosis. Therefore, choosing a simple and easily accessible risk marker can help us identify high-risk patients and optimize risk stratification, thus improving the prognosis of STEMI patients.

In recent years, CMR has been considered the noninvasive gold standard for diagnosing LVT by determining the presence of a thrombus based on histologic characteristics [15]. In a study that included 265 patients with STEMI, all patients were examined by CMR, which showed a 12.8% incidence of LVT [16]. Similarly, the incidence of LVT detected after PCI in STEMI patients in this study was 12.97%. The correlation between inflammation and LVT has been confirmed by numerous studies [5, 17]. Recently, sST2, as a new and valuable biomarker of inflammation, has emerged as a useful tool for predicting various cardiovascular disease outcomes and guiding therapeutic decisions [7, 10, 11, 20]. In a previous study, sST2 was shown to be an independent predictor of the occurrence of MACE events in the short and long term after PCI in STEMI patients [18]. In addition, sST2 was shown to be associated with new-onset AF in STEMI patients undergoing emergency hemodialysis [19]. In the present study, we innovatively identified sST2 as an independent risk marker for LVT formation after PCI treatment in STEMI patients. RCS demonstrated a nonlinear relationship between sST2 and LVT. Although the specific pathophysiological mechanism by which sST2 leads to LVT formation is not yet clear to us, it may

be closely related to Virchow's triad, which is blood stasis, vascular endothelial injury, and hypercoagulable state of blood, and is the core mechanism of LVT development after acute myocardial infarction [21]. Some studies have shown that inflammatory factors are involved in the process of Virchow's triad [21]. Studies have shown that inflammatory responses are involved in various processes after acute myocardial infarction [5, 6]. sST2, as a member of the interleukin-1 (IL-1) receptor family, may activate interleukin 6 (IL-6) to promote inflammatory responses, leading to elevated levels of tumor necrosis factor-alpha (TNF-α) and hs-CRP, and this inflammatory response may lead to endothelial damage of the vasculature, exposing subendothelial tissue and collagen, which continues to trigger inflammation, which in turn promotes a hypercoagulable state of the blood, further contributing to the development of LVT [7]. Finally, sST2 is a decoy receptor for interleukin-33 (IL-33). sST2 levels in the blood increase during acute myocardial infarction when the myocardium is subjected to mechanical strain, which will competitively bind to IL-33 and impede the binding of IL-33 to ST2L, thus inhibiting the cardioprotective functions of the IL-33/sST2 pathway, which include myocardial fibrosis, hypertrophy, apoptosis, and positive effects on myocardial function, leading to myocardial dysfunction and myocardial fibrosis, which in turn leads to blood stasis, which may partially explain sST2 contributing to the formation of LVT after PCI in STEMI patients [11, 22]. Moreover, in this study, sST2 was associated with known LVT risk markers, such as peak hs-CRP, peak NT-proBNP, LVEF, peak hsTnT, and LGE, which explains the results of the present study from another perspective [5, 17, 23] (As shown in Table 3).

Peak hs-CRP, IRA-LAD, and LGE as correlates of LVT have been confirmed by previous studies [5, 17, 23], and in line with this, the present study also found Peak hs-CRP, IRA-LAD, and LGE to be independent factors in LVT formation. A conventional model containing Peak hs-CRP, IRA-LAD, and LGE was established immediately after this study, and ROC analysis suggested that the new model after combining sST2 had a better ability to discriminate LVT (AUC = 0.825). The IDI and NRI results suggested that the integration of sST2 could significantly improve the risk prediction model of LVT. The RCS demonstrated that a nonlinear relationship between sST2 and LVT existed a nonlinear relationship. We found no statistical difference in thrombus aspiration, thrombolysis, and other antithrombotic treatments between the thrombotic and non-thrombotic groups (As shown in Table 3). Study by Călburean, Paul-Adrian et al. has shown that a more intensive regimen of antithrombotic Therapy, other than effective Dual Antiplatelet Therapy (DAPT), has not Improve the risk of MACEs [24]. This study demonstrated that sST2, as a clinically simple and easily accessible indicator, can predict LVT formation after PCI in STEMI patients with better sST2 biostability. sST2 may therefore become a potentially useful marker for identifying LVT formation after pPCI in the clinic, helping us to identify high-risk patients as early as possible, thus optimizing risk stratification and improving the long-term prognosis of patients.

Limitations

First, this study is a single-center retrospective study, which may have some unavoidable bias. Second, the study population consisted of STEMI patients, and the conclusions may not be directly applicable to other populations. Third, the specific pathological mechanism of sST2 leading to LVT is not fully understood, and further basic studies are still needed to elucidate it. Fourth, in this study, the CMR examination was performed during admission, which may have resulted in some, LVT not being detected. The ideal time point for the highest LVT detection rate has not been clarified. Fifth, We did not repeat the measurement of sST2 in our article, so it may not be possible to study the relationship between the dynamic changes of sST2 and thrombus more accurately. Therefore, a multicenter, larger sample size, and longer follow-up time are needed for further validation.

Conclusion

sST2 is strongly associated with the formation of LVT after pPCI in STEMI patients, and the addition of sST2 improves the conventional model of LVT.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12872-025-04667-y.

Supplementary Material 1

Supplementary Material 2

Author contributions

Xinjia Du: Writing -original draft. Perkash Kumar: Data curation.Chen Liu: Data curation. Jiahua Liu: Data curation. Lei Chen: Writing-revie & editing. Zhuoqi zhang: Writing–review & editing. Yuan Lu: Writing–review & editing.

Funding

This work was partly supported by China Postdoctoral Science Foundation funded project, the 68th batch of surface projects (No. M681738) and Jiangsu Provincial Health Commission Medical Research Project (No. M2021046).

Data availability

The datasets and materials generated during and/or analyzed during the current study are available by request from the corresponding author (drluyuan329@163.com).

Declarations

Ethical approval

As this study is retrospective, it does not infringe on the rights of the included patients. Therefore, informed consent was waived. This study was approved

by the Ethics Committee of Xuzhou Medical University Affiliated Hospital. The ethics approval number is XYFY2024-KL512.

Competing interests
The authors declare no competing interests.

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Received: 6 February 2025 / Accepted: 13 March 2025
Published online: 20 March 2025

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