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The value of sST2 in predicting the characteristics of vulnerable plaques in criminals with acute myocardial infarction: a prospective observational study

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Abstract

Background: Elevated soluble growth stimulation-expressed gene 2 (sST2) protein levels are associated with poor prognosis in patients with myocardial infarction or heart failure. However, few studies have investigated the association between sST2 expression and plaque stability. This study aimed to investigate the expression of sST2 in patients with acute myocardial infarction and its predictive value for vulnerable plaque characteristics in culprit lesions.

Methods: From October 2022 to December 2024, 230 patients with acute myocardial infarction who underwent coronary angiography and optical coherence tomography (OCT) in (emergency) outpatient and inpatient departments of Jining No.1 People's Hospital were selected as subjects of this prospective study. Based on the inclusion and exclusion criteria, 203 patients were included in this study. Clinical data were analyzed. Based on the characteristics of criminal plaques detected by OCT, 123 cases were divided into a thin-cap fibroatheroma (TCFA) group (60.6%) and a non–thin-cap fibroatheroma (NTCFA) group (80 cases). Serum sST2 levels were measured before surgery. Optical coherence tomography was used to observe the nature of the criminal lesions before interventional therapy. The relationship between serum sST2 levels and criminal plaque vulnerability was analyzed using a multivariable logistic regression model.

Results: Serum cardiac troponin, C-reactive protein, and sST2 levels were higher in the TCFA group than those in the NTCFA group. OCT observations showed that patients in the TCFA group had many characteristics of vulnerable plaques, including macrophage aggregation, larger lipid radians, and thinner minimum fibrous caps. sST2 independently predicted the presence of TCFA in patients with acute myocardial infarction, with enhanced predictive accuracy when combined with C-reactive protein (area under the curve 0.837 vs. 0.782 for sST2 alone, $P = 0.043$).

Conclusion: sST2 can independently predict the presence of thin cap atherosclerosis in patients with acute myocardial infarction, and when combined with C-reactive protein, its prediction accuracy is higher.

Keywords: Soluble growth stimulation expressed gene 2 protein, Acute myocardial infarction, Atherosclerotic plaque of thin fibrous cap, Culprit lesion

Introduction

Acute myocardial infarction (AMI) is a major cause of death in China.[1] The overall mortality rate of AMI in China has increased. From 2002 to 2020, the AMI mortality rates in urban and rural areas increased 5.5-fold and 2.7-fold, respectively.[2] The timely treatment of AMI has been incorporated into the "Healthy China 2030" cardiovascular disease prevention and control initiative. AMI is typically caused by the rupture or erosion of high-risk coronary atherosclerotic plaques (i.e., vulnerable plaques). Recent research confirmed[3] that approximately 60% of acute myocardial infarctions are caused by plaque rupture, 30% by plaque erosion, and 10% by calcification. Although traditional angiography is widely used, it has obvious limitations as it can only provide a two-dimensional representation of the complex three-dimensional vascular structure. This hinders the accurate assessment of plaque characteristics and the severity of stenosis[4] and has limitations in judging plaque stability, making it difficult to accurately evaluate whether a plaque is truly vulnerable. Moreover, recent studies have found that some vulnerable plaques do not rupture, whereas some ruptured plaques heal and remain stable without causing acute events in the short term.[5] Some studies[6] have shown that most of the culprit lesions responsible for major cardiovascular events are thin-cap fibroatheromas (TCFA) or are characterized by a large plaque burden, a small lumen area, or a combination of these features, which can be identified by intracoronary imaging. With advancements in intracoronary imaging technology, vulnerable coronary plaques responsible for future cardiovascular events can be identified. Identifying high-risk vulnerable plaques and implementing active interventions can help to reduce the occurrence of future cardiovascular events, which can serve as evidence for future local preventive treatments.[3] At

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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present, with the development of intracavitary imaging techniques, such as intravascular ultrasound and optical coherence tomography (OCT), the characteristics of vulnerable plaques can be accurately identified through plaque imaging, which can be used to evaluate vulnerable plaques in the culprit lesions of myocardial infarction. In particular, OCT has a high spatial resolution as a diagnostic tool. It can accurately identify the culprit lesions in ambiguous cases. Thin-fibrous-cap atherosclerotic plaques defined by OCT have a high degree of consistency with pathology. They are independent predictors of rapid plaque progression and serve as guides for optimizing percutaneous coronary intervention (PCI) procedures.[7,8] However, most evaluations using intracavitary imaging are invasive. Currently, few studies have evaluated the vulnerability of culprit plaques to acute myocardial infarction through noninvasive tests. Plaque vulnerability may not only depend on plaque morphological characteristics but also depend on the interactions among lumen stenosis, shear stress, inflammatory response, and ischemia are equally important.[9] In the process throughout the formation and progression of vulnerable plaques. Evaluation of the degree of plaque inflammation will contribute to the identification of vulnerable plaques.[10]

Soluble growth stimulation-expressing gene 2 (sST2) is a subtype of the growth stimulation-expressed gene 2 (ST2) protein. sST2 is a sensitive myocardial protein secreted by myocardial cells and fibroblasts in response to mechanical stress and load changes. The promotion of oxidative stress and inflammation leads to cardiac damage, and is a potential marker of mechanical cardiac overload.[11] Some studies have focused on the relationship between serum sST2 levels and the cardiovascular system. Previous studies have shown that elevated serum sST2 levels are associated with poor prognosis in patients with myocardial infarction or heart failure.[12,13] In recent years, sST2 has demonstrated the value of a novel biomarker in aspects, such as the inflammatory response, cardiac damage, cardiac stress, cardiac fibrosis, and prognosis of cardiovascular diseases,[14] and has become a new research hotspot in the field of cardiovascular diseases. This study aimed to explore the expression of sST2 in patients with AMI and assess its predictive value for vulnerability to culprit vessel plaques. The results were as follows:

Materials and methods

Study population

This study consecutively enrolled patients with acute myocardial infarction admitted to Jining No.1 People's Hospital between October 2022 and December 2024. Eligible participants underwent coronary angiography during (emergency) outpatient or inpatient hospitalization and OCT examination. Initially, 230 patients aged >18 years who provided informed consent for OCT examination and met the diagnostic criteria for type I myocardial infarction as defined in the Fourth Universal Definition of Myocardial Infarction were included.[15] Participants were excluded from the study if they met any of the following criteria:

(1) presence of severe bradyarrhythmia; (2) significant calcification, tortuosity, or coagulation in measured segments of the target coronary artery; (3) coexisting severe pericarditis; (4) severe heart failure, or marked impairment of liver, kidney, or respiratory function;(5) history of coronary artery bypass grafting; (6) active bleeding in the vital organs; the (7) presence of autoimmune diseases, hematological disorders, tumors, and acute or chronic infectious diseases; (8) severe lesions in the left main coronary artery or chronic total occlusive lesions; and (9) incomplete clinical data and poor patient compliance. A total of 203 patients were enrolled in this study. A flowchart of the sample selection is shown in Fig. 1.

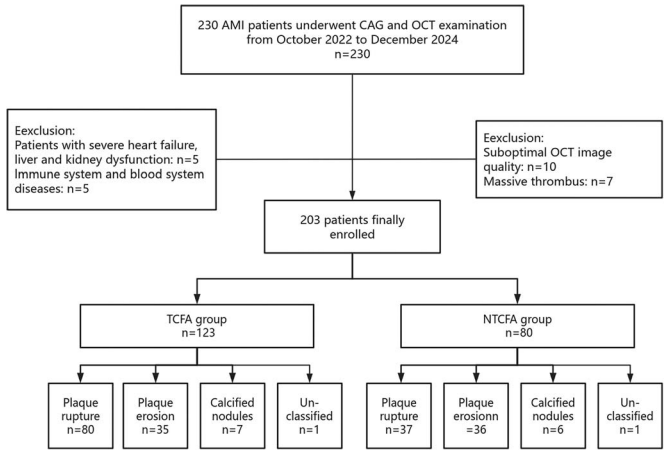

Figure 1. Process of selecting the study subjects. CAG, coronary angiography; NTCFA, non-thin-cap fibroatheroma; OCT, optical coherence tomography; TCFA, thin-cap fibroatheroma.

Sample size calculation

The sample size was calculated using the following formula to compare the means of the two independent groups:

$$n = \frac{2(Z_\alpha + Z_\beta)^2 \sigma^2}{(\mu_1 - \mu_0)^2}$$

We first used samples collected in October 2022 from 27 patients with TCFA and 18 patients with non–thin-cap fibroatheroma (NTCFA) to conduct a preliminary experiment. Based on pilot data, the mean ± standard deviation of the measured variable was: 51.04 ± 9.30 in case the group and 41.75 ± 7.78 in the control group with $\alpha = 0.05$ (two-tailed), power = 80%, and measured standard deviation σ of 9.61. The required sample size was[16] per group. To account for 20% attrition, a minimum sample size of 44 participants was required.

Data collection

A clinical database was established to record the ages of all study subjects. Baseline clinical data and laboratory test results of the enrolled patients were collected. All selected patients were followed up in the outpatient department or by telephone at 1 and 3 months postoperatively. The clinical database included information on sex, height, weight, body mass index (BMI), total ischemia time, baseline medication use (including antithrombotic drugs, statins, and antihypertensive medications), and relevant medical history, such as smoking history, hypertension, diabetes, hypercholesterolemia, and chronic kidney disease. Blood samples were collected from all study participants upon admission. Preoperative routine blood tests, C-reactive protein (CRP), serum creatinine, creatine kinase myocardial band, cardiac troponin I (cTnI), and N-terminal pro-B-type natriuretic peptide (NT-pro-BNP) were obtained. Additionally, total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), glycated hemoglobin, liver function, and serum sST2 levels were measured after fasting. The left ventricular ejection fraction (EF) was also determined. To measure serum sST2 levels, 2 mL of peripheral venous blood was collected. An automatic dry-type fluorescence immunoassay analyzer (A5000 PLUS, Boditech Med Inc., China) was used. This analyzer uses a semiconductor diode as the light source to irradiate the reaction plate with

the processed samples. When the laser irradiated the fluorescently labeled analytical substances that accumulated on the detection line of the reaction plate, these substances emitted fluorescence. The analyzer collects the fluorescence emitted by the analyte complex from the scattered lasers, filters out the pure fluorescence from the mixture, detects its intensity, and converts it into an electronic signal. The microprocessor on the mainboard calculates the concentration of the analyte in the test sample according to the calibration curve stored in the ID chip.

Coronary angiography and measurement of culprit vessels

Prior to coronary angiography, patients received a loading dose of dual-antiplatelet therapy (300 mg aspirin +180 mg ticagrelor/300 mg clopidogrel administered by chewing). Coronary angiography was performed using the radial artery approach to identify the coronary artery infarction-related culprit vessels. Thrombus aspiration was performed in patients with a heavy thrombus burden. The degree and quantity of coronary artery stenosis, the location and lesion length of the culprit vessels, and blood flow status were recorded.

Acquisition and analysis of OCT images

The frequency-domain OCT system used was the Wofuman intravascular tomography system F-1 (Nanjing Wofuman Medical Technology Co., Ltd., China). The OCT examinations were performed using the conventional approach. Specifically, intravascular OCT was performed at the segments of the culprit lesions to obtain OCT images of the fibrolipid plaques in the coronary culprit lesions. The acquired OCT images were analyzed after their quality was jointly approved by technicians and experienced physicians. The minimum lumen area (MLA) of the blood vessels at the location of the culprit plaque was measured. Additionally, relevant indicators of plaque vulnerability, including lipid-rich plaques, minimum fibrous cap thickness, lipid angle, macrophage aggregation, cholesterol crystals, and calcification, were identified and the lipid angle was measured in each 1-mm cross-section. Maximum and average lipid angles were calculated. A lipid-rich plaque was defined as a lipid plaque with a lipid angle >90° in any cross-section. The minimum fibrous cap thickness was measured at the thinnest part of the fibrous cap of the lipid plaque, and the measurement was repeated thrice to obtain an average value. Thin-cap fibroatheroma (TCFA) was defined as a lipid-rich plaque (lipid arc >90°) with a minimum fibrous cap thickness <65 μm at the culprit lesion. According to the OCT classification criteria for culprit plaque lesion types[7,16]: Plaque rupture was defined as the interruption of the continuity of the fibrous cap of the lipid plaque, accompanied by cavity formation. Plaque erosion was defined as fibrocap atherosclerosis with thrombus formation, where the plaque structure covered by the thrombus was identifiable, without thrombus but with an irregular plaque surface, or when the plaque structure covered by the thrombus was unidentifiable and there was no superficial calcification or lipid near the proximal or distal end of the thrombus. Calcified nodules were defined as nodular calcifications protruding into the lumen, accompanied by rupture of the surface fibrous cap, which could be associated with thrombus formation. Cholesterol crystals were thin linear regions with high signal intensity and weak attenuation, usually located in the fibrous cap or the necrotic core of the lipid plaque, and often accompanied by lipid deposits. Macrophages present as single or clustered strong-signal areas on the OCT image, followed by radial shadows with high signal intensity and strong attenuation of the fibrous cap. Vulnerable plaques were defined as being closely associated with a thin fibrous cap (thickness <65 μm), a large lipid core, and inflammatory cell infiltration around the fibrous cap.

Table 1

The Baseline Characteristics of Participants

Characteristics	TCFA (n = 123)	NTCFA (n = 80)	*P*
Male	79 (64.2)	44 (55.0)	0.096
Age, y	65.38 ± 3.71	64.34 ± 4.40	0.162
Smoking	25 (20.3)	13 (16.3)	0.467
Drinking	19 (9.4)	7 (8.8)	0.878
Hypertension	58 (47.75)	37 (46.2)	0.900
Diabetes	32 (26.0)	19 (23.8)	0.716
Hypercholesterolemia	30 (24.3)	19 (23.8)	0.917
BMI, kg/m^2	24.85 ± 4.18	24.75 ± 4.96	0.731
Total ischemic time, min	298 ± 32.75	309 ± 39.15	0.157
EF, %	54.3 ± 1.75	57.9 ± 1.92	0.102
Low-density lipoprotein cholesterol, mmol/L	2.93 ± 0.78	2.79 ± 0.79	0.089
TG, mmol/L	1.51 ± 0.91	1.44 ± 0.63	0.178
TC, mmol/L	4.32 ± 1.30	4.13 ± 1.07	0.097
cTnI, ng/mL	2.91 ± 2.73	2.27 + 2.45	0.002
Creatinine, μmol/L	73.81 ± 9.15	78.71 + 8.03	0.601
NT-proBNP, pg/mL	1521 ± 149.21	1345 ± 152.13	0.793
CK-MB, ng/mL	13.3 (8.1,25.4)	11.2 (6.9,22.3)	0.192
Target lesion vessel			
Left anterior descending	57 (46.3)	46 (56.3)	0.120
Left circumflex artery	20 (16.3)	13 (16.3)	0.998
Right coronary artery	46 (37.4)	24 (30.0)	0.279
sST2, ng/mL	55.61 ± 8.21	39.40 ± 7.49	<0.001
CRP, mg/L	18.25 ± 3.97	13.14 ± 4.25	<0.001

Continuous variables were presented as means ± standard deviation (SD) or median (P25, P75), while categorical variables were presented as frequency (%).

BMI, body mass index; CK-MB, creatine kinase myocardial band; CRP, C-reactive protein; cTnI, cardiac troponin I; EF, ejection fraction; NTCFA, non-thin-cap fibroatheroma; NT-proBNP, N-terminal pro-B- type natriuretic peptide; sST2, Soluble growth stimulation expressed gene 2 protein; TC, total cholesterol; TCFA, thin-cap fibroatheroma; TG, triglyceride.

Table 2

Comparison of OCT Imaging Characteristics between Two Groups of Patients

Characteristics	TCFA (n = 123)	NTCFA (n = 80)	*P*
Plaque rupture	80 (65.0)	37 (46.2)	
Plaque erosion	35 (28.5)	36 (45.0)	
Calcified nodules	7 (5.7)	6 (7.5)	
Unclassified	1 (0.8)	1 (1.3)	
			0.069*
Minimum lumen area, mm^2	2.08 ± 0.598	2.58 ± 0.41	0.09
Maximum lipid arc°	229.73 ± 35.92	159.41 ± 48.75	0.01
Minimum fiber cap thickness, μm	52.69 ± 8.82	75.08 ± 11.05	0.01
Cholesterol crystals	50 (40.7)	25 (31.3)	0.175
Macrophage aggregation	55 (44.7)	22 (27.5)	0.03

*Two cells had expected counts <5; thus, Fisher's exact test was applied; data are n (%) and mean ± standard deviation (SD).

MLA, minimal lumen area; NTCFA, non-thin-cap fibroatheroma; OCT, optical coherence tomography; TCFA, thin-cap fibroatheroma.

Statistical analysis

All statistical analyses were performed using SPSS software (version 27.0; SPSS Inc., Chicago, IL, USA). Continuous variables were presented as means ± standard or median (P25, P75) while categorical variables were presented as frequency (%). The differences between TCFA and NTCFA group were analyzed using *t* test or Mann-Whitney *U* test and chi-square test or Fisher's exact test. Variables with $P < 0.05$ in the univariate analysis along with clinically relevant indicators were incorporated into a backward stepwise multivariable logistic regression to identify the independent predictors of vulnerable plaques. The receiver operating characteristic (ROC) curve was analyzed, and the optimal cutoff value of the independent factors was determined using the maximum Youden index. The DeLong test was used to compare the area under the curve (AUC) under two or more ROC curves. A two-tailed P <0.05 was considered statistically significant.

Results

General characteristics of patients

In total, 203 participants were enrolled in this study. Among them, 123 (60.6%) were in the TCFA group and 80 (39.4%) were in the NTCFA group. Compared with the NTCFA group, patients in the TCFA group had significantly higher values of the CRP inflammatory response index and higher levels of sST2 and cTnI ($P < 0.05$). In the TCFA and NTCFA groups, there were no statistically significant differences in age, gender, BMI, smoking history, hypertension history, diabetes history, hypercholesterolemia, total ischemia time, blood lipid levels, EF, NT-proBNP, creatinine levels, or location of AMI culprit vessels between the two groups of patients ($P > 0.05$) (Table 1).

Comparison of OCT imaging characteristics between two groups of patients

A comparison between the two groups revealed that in the TCFA group, the culprit vessel lesions exhibited a thinner fibrous cap, larger lipid arc, and more macrophage aggregation. These differences were considered statistically significant ($P < 0.05$).

Regarding the plaque characteristics in the two groups of acute myocardial infarction patients with AMI, Fisher's exact test showed that although plaque rupture was more common in the TCFA group and plaque erosion was more prevalent in the NTCFA group, the difference between the two groups was not statistically significant ($P > 0.05$). The proportions of the MLA at the stenosis of the culprit vessel lesions, cholesterol crystals, and calcified nodules were similar between the two groups of acute myocardial infarction patients with AMI. Still, the differences were not statistically significant ($P > 0.05$) (Table 2).

Multivariable logistic regression analysis of factors associated with thin-cap fibroatheroma

Confounding factors were adjusted considering the occurrence of TCFA as the dependent variable and using single factors with differences in clinical data identified in the study (CRP, sST2, and cTnI) and clinically significant indicators (age and history of hypertension) as independent variables. Multivariate logistic regression analysis was performed and collinearity was examined to exclude factors with severe multicollinearity. The results of the collinearity diagnosis analysis showed that all of the variance inflation factors were <10, which showed that there was no collinearity between variables and that they were independent of each other. The final multivariate logistic regression analysis indicated that both CRP (odds ratio [OR]: 1.063; $P < 0.001$) and sST2 (OR: 1.025; $P = 0.003$) were associated with the occurrence of TCFA. Both are independent risk factors for vulnerable plaques (Table 3).

Results of ROC curve analysis of sST2 for predicting thin-cap fibroatheroma

The results of the ROC curve analysis showed that for sST2 in predicting TCFA, the AUC was 0.782 (95% confidence interval [CI]: 0.721–0.844; $P < 0.001$) (Fig. 2). Serum sST2 was an independent factor associated with the occurrence of TCFA, suggesting that serum sST2 levels have a good predictive value for TCFA. The optimal cutoff value calculated using the Youden index was 52.5 ng/mL. When the sST2 was 52.5 ng/mL, the sensitivity and specificity were 78.9% and 68%, respectively. The AUC for CRP in predicting TCFA was 0.779 (95% CI: 0.717–0.841; $P < 0.001$), indicating that the serum CRP level also had a good predictive value for TCFA. The optimal cutoff value calculated using the Youden index was 13.5 mg/L. When the CRP was 13.5 mg/L, the sensitivity and specificity were 66.7% and 84%, respectively, and the combined predictive value of sST2 and CRP was significantly higher than that of the

Table 3

Multivariable Logistic Regression Analysis of Factors Associated with Thin-Cap Fibroatheroma

Characteristics	B	SE	Wald χ^2	OR	95% CI	*P*	OR Per 1 SD Increase*	*P* Per 1 SD Increase
sST2	0.061	0.012	24.079	1.063	1.037–1.089	<0.001	1.31 (1.21–1.49)	<0.001
CRP	0.025	0.008	9.100	1.025	1.009–1.042	0.003	1.23 (1.12–1.41)	<0.001

* Relative change in risk when the variable increases by one standard deviation.

B, unstandardized regression coefficient; CI, confidence interval; CRP, C-reactive protein; OR, odds ratio; SD, standard deviation; SE, standard error; sST2, soluble growth stimulation-expressed gene 2 protein.

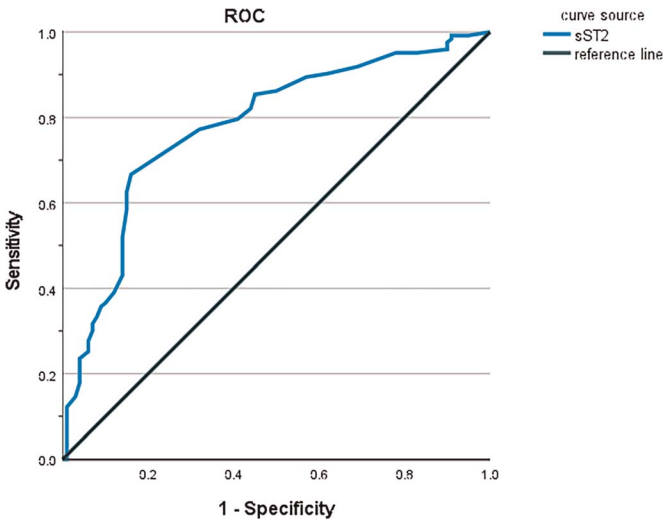

Figure 2. Receiver operating characteristic curve of serum sST2 Level for predicting thin-cap fibroatheroma. ROC, receiver operating characteristic; sST2, soluble growth stimulation expressed gene 2 protein.

individual indicators mentioned above (Fig. 3). The AUC for the combined prediction was 0.837 (95% CI: 0.785–0.889; $P < 0.001$) (Table 4). The statistical results of the Delong test showed that the combined prediction of sST2 and CPR had a higher predictive value for the occurrence of thin-cap atherosclerosis than sST2 (z = –1.547, P = 0.043) and CRP alone (z = –1.421, P = 0.048) (Table 5).

Discussion

This study found that sST2 is an independent risk factor for predicting the occurrence of TCFA. Compared to the NTCFA group, the TCFA group had a higher incidence of plaque rupture, a larger lipid arc at the culprit lesion, a thinner fibrous cap, and a

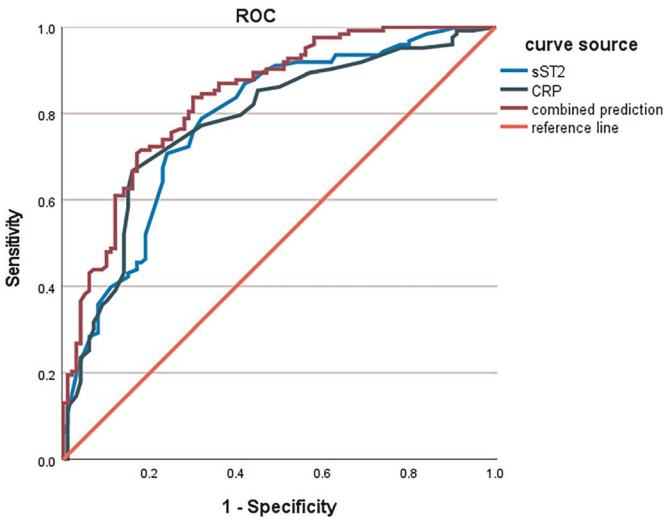

Figure 3. Receiver operating characteristic curve of sST2 alone, CRP alone, and their combination in predicting thin-cap fibroatheroma. CRP, C-reactive protein; ROC, receiver operating characteristic; sST2, soluble growth stimulation expressed gene 2 protein.

Table 4

ROC Curve

Index	AUC	Std. Error	Asymptotic Sig	Asymptotic 95% CI	
				Lower Bound	Upper Bound
sST2	0.782	0.031	<0.001	0.721	0.844
CRP	0.779	0.032	<0.001	0.717	0.841
combined prediction	0.837	0.027	<0.001	0.785	0.889

AUC, area under the curve; CI, confidence interval; CRP, C-reactive protein; ROC, receiver operating characteristic; sST2, soluble growth stimulation expressed gene 2 protein.

smaller lumen stenosis area, suggesting that the plaques in the TCFA group were at a higher risk of vulnerability. The sST2 expression was higher in the TCFA group. However, the specific underlying mechanisms remain unclear. Relatively few studies have been conducted in this area.[17] A recent study[18] first proposed that sST2 could be a new potential serological marker, potentially related to the stability of atherosclerotic plaques in acute coronary syndrome (ACS), helping to assess the vulnerability and complexity of atherosclerotic plaques. This is similar to the results of Demyan et al.[19] Culprit plaques exhibit more instability and vulnerability, with a higher incidence of plaque rupture and thrombosis. Shi et al.[20] measured serum sST2 levels in patients with coronary heart disease and found that serum sST2 levels were significantly elevated in patients with non–ST-segment elevation myocardial infarction, negatively correlated with the thickness of the fibrous cap of coronary lipid plaques, and had a very high predictive value for prognosis. Elevated serum soluble ST2 levels are associated with plaque vulnerability in patients with non–ST-elevation acute coronary syndrome.[21] Collectively, these findings suggest that the ST2L/IL-33 axis may play a role in the development of vulnerability and plaque rupture, consistent with the results of the present study. Inflammation plays a crucial role in plaque vulnerability pathogenesis.[10]

This study revealed a close relationship between sST2 and CRP levels and plaque vulnerability. sST2 is a strong predictor of TCFA. The term "vulnerable plaque" is used to designate high-risk plaques prone to rapid lumen stenosis or occlusive intraluminal thrombosis, which can lead to catastrophic cardiovascular events.[22–24] Intravascular OCT has high spatial resolution, precise plaque localization, and real-time image-processing capabilities. It can identify atherosclerotic changes in the coronary artery wall before and after the progression of luminal stenosis, recognize the nature of the culprit plaques in patients with AMI, and accurately assess plaque stability.[25] Thin-cap fibroatheroma (TCFA) is a plaque subtype that is prone to rupture.[26] As is well-known, inflammation plays a crucial role in the pathogenesis of plaque vulnerability.[10] sST2 is the soluble form of ST2. When secreted into circulation, it can regulate the inflammatory response and exert a proinflammatory effect.[27] Elevated serum sST2 levels have been observed in patients with various inflammatory and autoimmune diseases. sST2 is released from the fibroblasts and vascular structures. Based on the IL-33/ST2 signaling pathway, it competitively binds to IL-33,[28] thereby preventing the IL-33 from interacting with ST2L and exerting its protective effect on the myocardium, effectively acting as a receptor-blocking agent. When the myocardium is damaged and under stress, sST2 levels increase, participating in the homeostasis/pathogenesis of the disease, inhibiting the effect of IL-33 on other immune cells, and being triggered and expressed during fibrosis, tissue damage, inflammation, and remodeling.[29] Recent studies have shown that recombinant sST2 can promote mitochondrial fusion in human cardiac fibroblasts, increasing oxidative stress and the secretion of inflammatory cytokines[30]; however, the specific mechanism requires further investigation.

Table 5

Paired-Sample Area Difference under the ROC Curve

Test Result Pair(s)	Z	*P*	AUC Difference	Std. Error Difference	Asymptotic 95% CI	
					Lower Bound	Upper Bound
PRE_1 - PRE_2	0.069	0.945	0.003	0.251	–0.084	0.090
PRE_2 - PRE_3	–1.421	0.048	–0.043	0.259	–0.186	–0.004
PRE_1 - PRE_3	–1.547	0.043	–0.061	0.262	–0.126	–0.001

AUC, area under the curve; CI, confidence interval; PRE_1, sST2 predicted probability; PRE_2, C-reactive protein predicted probability; PRE_3, combined predicted probability; ROC, receiver operating characteristic.

CRP is synthesized by hepatocytes and is an acute-phase reactant induced by various acute injuries, infections, or other inflammatory stimuli. Smooth muscle cells within atherosclerotic plaques secrete CRP, which binds to lipoproteins, activates the complement system, releases many inflammatory mediators, damages the vascular intima, leads to plaque instability,[31] and promotes the development of atherosclerotic plaques. Multiple clinical studies[32,33] have confirmed the important role of the inflammatory response marked by the CRP level in atherosclerosis. It can also be used to assess coronary inflammation for the risk stratification of high-risk plaques.

Current screening and diagnostic methods are insufficient for identifying victims before the occurrence of events. Understanding the role of vulnerable plaques has opened new opportunities in the field of cardiovascular medicine. An expert consensus has proposed a classification system for the clinical and pathological assessment of vulnerable plaques. Substantial effort is required to quantify the risk of an individual experiencing an event according to each vulnerability component (plaque, blood, and myocardium). This comprehensive risk-stratification tool, which is capable of predicting acute coronary syndrome and sudden cardiac death, is of great value in preventive cardiology. It is crucial to determine whether the disruption of vulnerable plaques in patients leads to clinical events.[34] The aim is to identify vulnerable plaques and individuals susceptible to cardiovascular diseases, enabling more patients to receive standardized treatment or preventive stent implantation, providing better prevention for patients, and reducing the occurrence of recurrent cardiovascular events.[35] Incorporating sST2 into routine clinical practice can improve the management of AMI by the early identification of high-risk patients and guiding personalized treatment strategies.[36] Predicting the risk of vulnerable plaques using sST2 can provide a basis for future clinical PCI interventions, consistent with the currently proposed precision medicine approach for treating AMI.[37] That is, the treatment strategy for critical lumen stenosis lesions can be determined based on vulnerable plaques, or a basis can be provided for the local preventive PCI treatment of high-risk vulnerable plaques. The results of this study showed that the combined prediction of the occurrence of TCFA in patients with AMI using serum CRP and cTnI had an AUC of 0.837, indicating that the combined detection of CRP and cTnI has a high predictive value for the occurrence of TCFA in patients with AMI. Clinicians can assess the risk of TCFA, conduct a stratified management of patients with plaque vulnerability, reduce the occurrence of adverse cardiovascular events, and improve patient prognosis.

Limitations

Our study has some limitations. First, this was a single-center study with a relatively small sample size, which may have led to bias. The conclusions were based on an investigation of a single-center hospital, and whether they can be extended to a larger population remains to be determined. Further multicenter and large-sample studies are needed to explore this issue. Second, although patients with a heavy thrombus burden underwent sufficient and gentle thrombus aspiration before OCT, it is inevitable that the plaque morphology and structure might be altered during the thrombus aspiration process.

Conclusion

In the assessment of thin-cap fibroatheroma development in patients with acute myocardial infarction, sST2 demonstrated independent prognostic value. This study revealed that the combined predictive value of sST2 and CRP was significantly higher than either individual marker.

Conflict of interest

The authors declare no conflict of interest.

Author contributions

All authors contributed to the study's conceptualization and design, analysis and interpretation, and participated in drafting and critically revising the manuscript. The final manuscript was approved by all the authors.

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Ethical approval of studies and informed consent

The study followed the principles of the Declaration of Helsinki as revised in 2013. The study protocol was approved by the Ethics Committee of Jining No.1 People's Hospital (Ethics Research No. (12), 2022; April 4, 2022). The personal information of the patients was protected, and all patients signed an informed consent form.

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None.

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