

Comparison of the predictive value of four-dimensional speckle tracking imaging risk classification and the TIMI system after STEMI reperfusion therapy

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Abstract. The predictive value of four-dimensional speckle tracking imaging (4D-STI) risk classification and TIMI risk scores for the prognosis of patients with ST-segment elevation myocardial infarction (STEMI) after reperfusion therapy were investigated. One hundred and twenty patients with STEMI after reperfusion therapy were involved. At 12 h after reperfusion therapy, 2nd and 3rd day, the three-dimensional longitudinal strain (LS), circumferential strain (CS) and radial strain (RS), area strain (AS), as well as other 4D-STI detection indicators, were collected. The patients were followed up for one year, and were divided into good prognosis group and poor prognosis group. LS, CS, RS and AS indicators were analyzed between these two groups. The ROC curve was drawn to establish the 4D-STI risk classification and its predictive value for poor prognosis and mortality were compared with TIMI risk scores. AS, LS and RS at 12 h after reperfusion treatment, and AS and RS at 2nd and 3rd day had a certain degree of prediction accuracy in STEMI patients in the poor prognosis group. In the 4D-STI and TIMI risk scores, the risk of death and adverse prognosis significantly increased as the risk scores increased ($P < 0.01$). The 4D-STI risk score for predicting poor prognosis and mortality was greater than the TIMI risk score. 4D-STI risk scores are superior to TIMI risk scores in predicting poor prognosis and mortality in patients with STEMI after reperfusion therapy.

Introduction

Acute ST-segment elevation myocardial infarction (STEMI) is the most common type of coronary artery syndrome (ACS). At present, the preferred option to treat STEMI patients in clinic is the early implementation of myocardial reperfusion therapy, in order to save the dying heart muscle. However, due to the continuous occlusion of small blood vessels and difficulties in

reversing the prolonged lack of blood supply caused myocardial necrosis, the occurrence of heart failure, cardiac rupture, and other serious adverse events in patients after reperfusion treatment cannot be ignored. At present, TIMI, GRACE, CCP and other scoring systems have been used for STEMI risk assessment in clinic, and a number of studies have also shown that several risk scores can clearly indicate the prognosis of STEMI patients (1-3). However, this existing system needs to integrate the patient's body mass index, pathological condition, electrocardiogram analysis, cardiac function classification and other indicators, in order to prevent poor performance. Therefore, there is an important need to establish a STEMI reperfusion risk score system that has a high degree of accuracy and is easy to implement, in order to guide clinical treatment and prevent poor prognosis after reperfusion. Four-dimensional speckle tracking imaging (4D-STI) is the result of the latest development in the field of ultrasound medicine, in which four-dimensional trajectories of echo spots in the myocardium are employed to calculate the myocardial relaxation function. Due to its measurement accuracy, ease of use and high repeatability, its great potential for the clinical diagnosis and treatment of cardiovascular disease, it has become the focus of cardiovascular imaging research. To date, the application of 4D-STI for analyzing the prognosis of STEMI patients after reperfusion treatment remains unreported. In the present study, STEMI was determined by 4D-STI within 72 h after reperfusion treatment through the four-dimensional strain of the patient's heart. Data were collected after STEMI reperfusion treatment to establish a new risk stratification classification, and this was compared with the traditional TIMI risk score system to determine its predictive value, aiming to improve postoperative patient management and effectively prevent poor prognosis.

Materials and methods

General information. From March 2013 to November 2015, patients who attended the Department of Cardiology of Shanghai Jiading Center Hospital (Shanghai, China) due to the onset of acute myocardial infarction, and were diagnosed according to the 2010 edition of the acute STEMI diagnostic and treatment guidelines for STEMI in parallel with emergency percutaneous coronary intervention (PCI), were studied (4). Inclusion criteria were: i) Patients who were 20-75 years, with first occurrence of STEMI; ii) patients who were admitted (<12 h from onset),

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received reperfusion treatment, and underwent direct line PCI without thrombolysis. Exclusion criteria were: i) Patients with serious arrhythmias such as frequent premature beats, atrial fibrillation, acute heart failure, or cardiogenic shock detected by electrocardiogram and echocardiography; ii) patients suffering from severe emphysema, pulmonary fibrosis, or other ventilated dysfunction; iii) patients with obvious acidosis or uremia, or previously in a coma; iv) patients with a tendency to severe bleeding; and v) patients with poor acoustic conditions.

According to these criteria, a total of 120 patients were included in the present study. Among these patients, 81 were male and 39 patients were female; and the average age was 50.21 ± 11.66 years. This study was approved by the Ethics Committee of Shanghai Jiading Center Hospital. The patients and their families were informed of the details and possible risks of the study, and a signed consent form was obtained from the patients or guardians prior to enrollment into the study.

Instruments and ultrasound detection indicators. A Vivid E9 color ultrasound diagnostic apparatus (GE Healthcare, Milwaukee, WI, USA) with a 4D real-time three-dimensional phased array probe was used within 12 h after all patients underwent PCI. Then, four-dimensional echocardiography was performed on the 2nd and 3rd day after the operation. The subjects were asked to take the supine position and breathe normally during the probe scan: i) Conventional series of standard sections; ii) the three short axis views of the sternal left ventricular mitral valve level, papillary muscle level and apical level; iii) the three long axis sections of the apical four-chamber, two-chamber and long axis; and iv) the four-dimensional surface of the apical four-chamber view. The ECHO-PAC left ventricular quantitative software (GE Healthcare) was used to automatically analyze the segments of the myocardium (17 segment standard) in the three-dimensional longitudinal strain (LS), circumferential strain (CS), radial strain (RS) and area strain (AS).

Method. After the enrollment of each patient, their contact numbers and home address were kept to facilitate the follow-up. Age at admission, body weight, history of diabetes/hypertension/angina, clinical symptoms, records of the time of reperfusion therapy and surgery, detection of the three observation points within 72 h after the operation (12 h after PCI, 2nd and 3rd day after operation) in the myocardial four-dimensional strain, as well as the evaluation of systolic blood pressure at 3rd day after operation, and the heart rate and cardiac function Killip classification of patients, were collected. For the 1-year postoperative follow-up, the follow-up was first conducted one month after the end of treatment, and every three months thereafter. Follow-up was conducted on an outpatient basis, by telephone, or once through home visit, in order to collect patient outcomes. Patients were grouped according to the outcome of the follow-up period: Cured cases were assigned in the good prognosis group, while patients at postoperative one year after the occurrence of adverse cardiac events (myocardial infarction, heart failure or malignant arrhythmia) and mortality cases were assigned in the poor prognosis group.

In analyzing the LS, CS, RS and AS data of the two groups at PCI 12 h, 2nd and 3rd day after operation, the STEMI reperfusion criteria for risk assessment (4D-STI system) was

Table I. The TIMI system risk score criteria.

Risk factors	Score	Grade
65-74 years	2 points	
≥ 75 years	3 points	
Systolic blood pressure <100 mmHg	3 points	
Heart rate >100 beats/min	2 points	
Heart function (Killip classification) class II-IV	3 points	7-14 points high risk 4-6 points middle risk
Anterior wall ST segment elevation	1 points	0-3 points low risk
History of diabetes/hypertension/angina anterior wall ST-segment elevation	1 points	
Female	1 points	
Onset to reperfusion time >4 h	1 points	

established based on the myocardial dimensional strain from which the relevant parameters were screened out. Patient risk factors were summarized according to the respective statistical scores in the 4D-STI and TIMI risk score systems, and patients were classified according to their scores: Low-, middle- and high-risk groups. The TIMI system risk score criteria are presented in Table I.

Statistical analysis. SPSS 19.0 statistical software (SPSS, Inc., Chicago, IL, USA) was used for statistical analysis. Myocardial four-dimensional strain indicators (LS, CS, RS and AS) were expressed as ($x \pm SD$), and compared between the two groups by using t-test. The ROC curve analysis was drawn, and patient prognosis related to the myocardial four-dimensional strain for STEMI after reperfusion treatment was evaluated to determine the effects of poor prognosis and the cutoff points. In the 4D-STI and TIMI risk score system, the multiple group comparisons of the adverse cardiac events and incidence of death in the low-, middle- and high-risk groups were compared by using the χ^2 test or Fisher's exact test. The post hoc test was performed using χ^2 test or Fisher's exact test as well. The area under the ROC curve was used to evaluate the 4D-STI and TIMI system, and determine its effectiveness in predicting poor prognosis and mortality. $P < 0.05$ was considered to indicate a statistically significant difference.

Results

Comparison of myocardial four-dimensional strain indicators at 12 h, 2nd and 3rd day after operation between the good prognosis and poor prognosis groups. In the present study, the four-dimensional myocardial strain indicators (AS, LS, CS and RS) of the three observation points were detected in 120 patients with STEMI within 72 h after reperfusion through the successful application of 4D-STI (Figs. 1 and 2). The AS, LS, CS and RS absolute values in the poor prognosis group were significantly lower than those in the good prognosis group at 12 h, 2nd and 3rd day after reperfusion treatment, and the difference was statistically significant ($P < 0.05$; Tables II-IV).

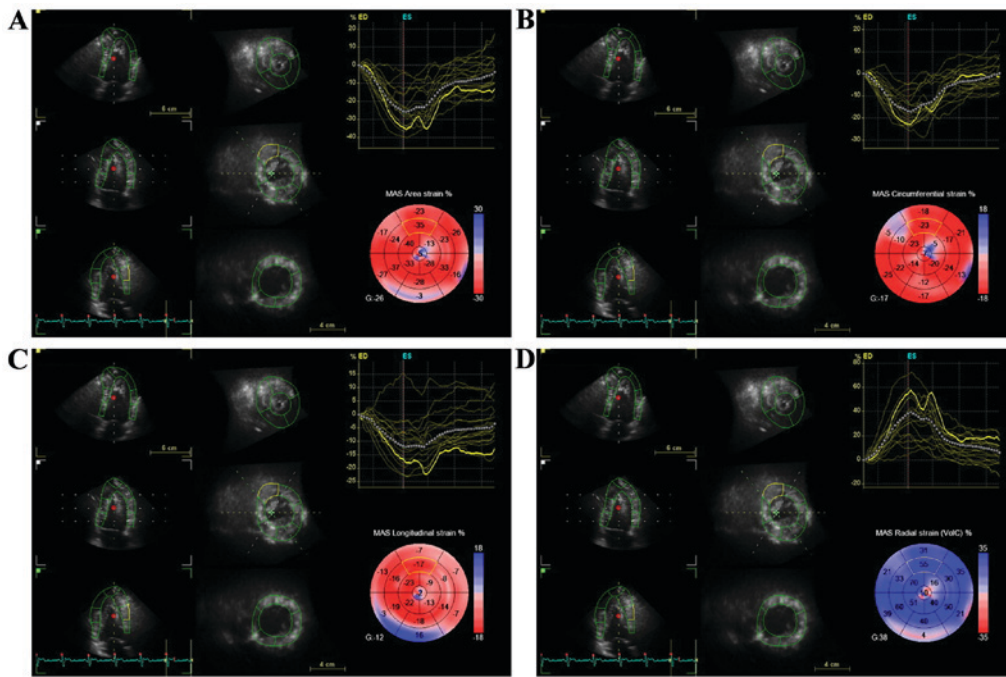


Figure 1. The myocardial strain curve and bull's eye diagram of a patient with good prognosis by 4D-STI technology. (A) The myocardial area strain curve and bull's eye diagram of a patient with good prognosis at postoperative 12 h. (B) The myocardial circumferential strain curve and bull's eye diagram of a patient with good prognosis at postoperative 12 h. (C) The myocardial longitudinal strain curve and bull's eye diagram of a patient with good prognosis at postoperative 12 h. (D) The myocardial radial strain curve and bull's eye diagram of a patient with good prognosis at postoperative 12 h. 4D-STI, four-dimensional speckle tracking imaging.

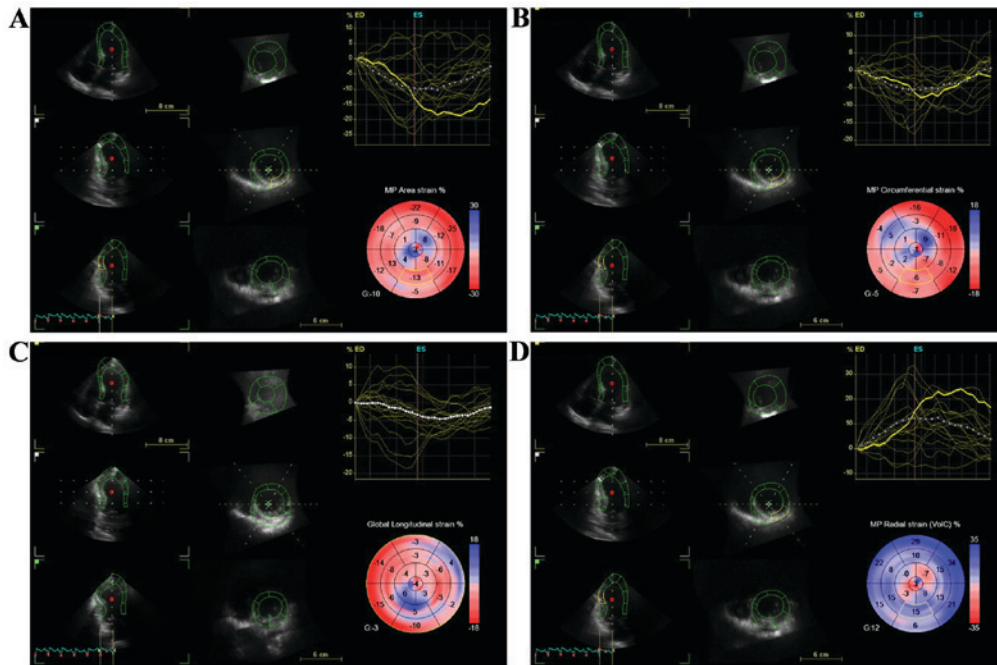


Figure 2. The myocardial area strain curve and bull's eye diagram of a patient with poor prognosis by 4D-STI. (A) The myocardial area strain curve and bull's eye diagram for the prognosis of death of a patient at postoperative 12 h. (B) The myocardial circumferential strain curve and bull's eye diagram for the prognosis of death of a patient at postoperative 12 h. (C) The myocardial longitudinal strain curve and bull's eye diagram for the prognosis of death of a patient at postoperative 12 h. (D) The myocardial radial strain curve and bull's eye diagram for the prognosis of death of a patient at postoperative 12 h. 4D-STI, four-dimensional speckle tracking imaging.

Comparison of the ability of the myocardial four-dimensional strain to evaluate the prognosis of patients at 12 h, 2nd and 3rd day after operation. The area under the ROC curve of AS, LS and RS within 12 h after reperfusion was 0.740, 0.735 and 0.781, respectively; the cutoff points were ≥ -20.716 , ≥ 11.285

and ≤ 30.902 , respectively; the sensitivity to predict poor prognosis was 74.3, 72.9 and 77.1%, respectively; the specificity to predict poor prognosis was 68.0, 70.0 and 70.0%, respectively. The area under the ROC curve of AS and RS on 2nd day was 0.785 and 0.765, respectively; the cutoff points were ≥ 18.060

Table II. Comparison of the four-dimensional myocardial strain indicators between the two groups at postoperative 12 h.

Groups	AS	LS	CS	RS
Good prognosis (n=50)	-22.451±5.443	-12.557±3.228	-13.009±4.072	33.806±7.001
Poor prognosis (n=70)	-17.677±5.372	-9.761±3.290	-11.498±4.036	26.525±7.619
P-value	<0.001	<0.001	0.046	<0.001
t-test	-4.773	-4.626	-2.014	5.336

AS, area strain; LS, longitudinal strain; CS, circumferential strain; RS, radial strain.

Table III. Comparison of the four-dimensional myocardial strain indicators between the two groups at 2nd day.

Groups	AS	LS	CS	RS
Good prognosis (n=50)	-21.985±4.370	-11.602±3.060	-12.825±2.962	33.679±8.177
Poor prognosis (n=70)	-16.102±6.070	-9.627±3.160	-11.024±3.877	25.299±9.340
P-value	<0.001	0.001	0.007	<0.001
t-test	-5.852	-3.420	-2.759	5.099

AS, area strain; LS, longitudinal strain; CS, circumferential strain; RS, radial strain.

Table IV. Comparison of the four-dimensional myocardial strain indicators between the two groups at 3rd day.

Groups	AS	LS	CS	RS
Good prognosis (n=50)	-23.593±5.756	-11.372±3.705	-12.963±3.642	36.379±9.901
Poor prognosis (n=70)	-18.479±5.719	-9.622±3.296	-11.134±3.617	27.475±9.511
P-value	<0.001	0.007	0.007	<0.001
t-test	-4.798	-2.722	-2.723	4.970

AS, area strain; LS, longitudinal strain; CS, circumferential strain; RS, radial strain.

and ≤ 28.420 , respectively; the sensitivity to predict poor prognosis was 68.6 and 71.4%, respectively; the specificity to predict poor prognosis was 80.0 and 80.0%, respectively. The area under the ROC curve of AS and RS on 3rd day was 0.742 and 0.743, respectively; the cutoff points were ≥ -21.298 and ≤ 32.236 , respectively; the sensitivity to predict poor prognosis was 68.6 and 72.9%, respectively; the specificity to predict poor prognosis was 76.0 and 66.0%, respectively (Figs. 3-5).

In the ROC analysis, the area under the ROC curve was between 0.735 and 0.785 for AS, LS and RS at postoperative 12 h, AS and RS at 2nd day, and AS and RS at 3rd day. The assessments of the prognosis of patients were similar. Hence, the set impact factor score was equal. With reference to the TIMI risk score, according to the cutoff points of these seven indicators and based on the myocardial four-dimensional strain, the risk scoring system for STEMI after reperfusion treatment was established (4D-STI system; Table V).

Comparison of patient groups under the 4D-STI and TIMI risk score system. All patients were divided into three groups according to 4D-STI and TIMI risk score system: Low-, medium- and high-risk groups. Under the 4D-STI risk score

Table V. 4D-STI system risk score criteria.

Risk factors	Score	Grade
AS (1 day) ≥ -20.716	2 points	
AS (1 day) < -20.716	0 point	
LS (1 day) ≥ -11.285	2 points	
LS (1 day) < -11.285	0 point	
RS (1 day) ≤ 30.902	2 points	
RS (1 day) > 30.902	0 point	0-4 points low-risk
AS (2 days) ≥ -18.060	2 points	6-8 points medium-risk
AS (2 days) < -18.060	0 point	10-14 points high-risk
RS (2 days) ≤ 28.420	2 points	
RS (2 days) > 28.420	0 point	
AS (3 days) ≥ -21.298	2 points	
AS (3 days) < -21.298	0 point	
RS (3 days) ≤ 32.236	2 points	
RS (3 days) > 32.236	0 point	

4D-STI, four-dimensional speckle tracking imaging.

Table VI. Comparison of poor prognosis and mortality among groups using the 4D-STI and TIMI risk score system.

Groups	4D-STI risk score system			TIMI risk score system		
	No. of cases	Mortality (n/%)	Poor prognosis (n/%)	No. of cases	Mortality (n/%)	Poor prognosis (n/%)
Low risk	41	0	8/19.51	37	0	11/29.73
Medium risk	54	1/1.85	37/68.52 ^a	60	2/3.33	40/66.67 ^a
High risk	25	6/24.00 ^{a,b}	25/100 ^{a,b}	23	5/21.74 ^{a,b}	19/82.61 ^{a,b}

Compared with the low risk group, ^aP<0.01; compared with the medium risk group, ^bP<0.01. 4D-STI, four-dimensional speckle tracking imaging.

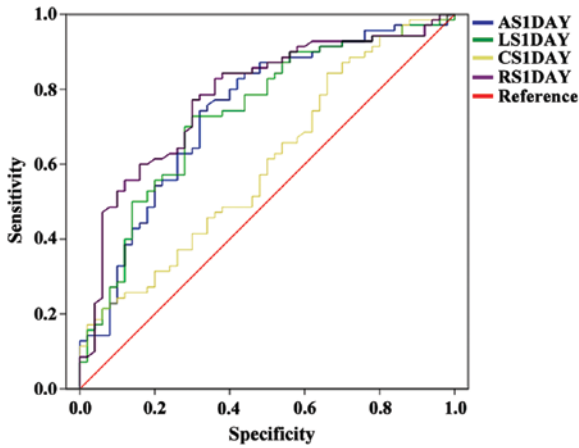


Figure 3. ROC curves of the myocardial four-dimensional strain indicators for predicting the prognosis of patients within 12 h after reperfusion treatment.

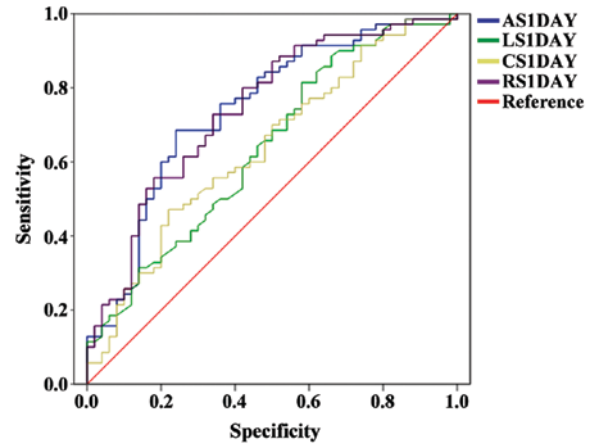


Figure 5. ROC curves of the myocardial four-dimensional strain indicators for predicting the prognosis of patients at three days after reperfusion treatment.

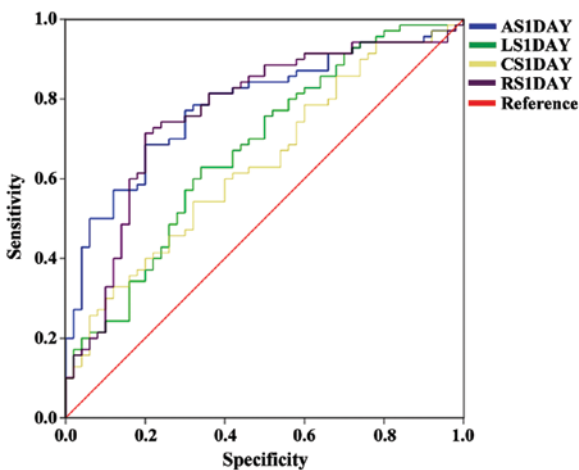


Figure 4. ROC curves of the myocardial four-dimensional strain indicators for predicting the prognosis of patients at two days after reperfusion treatment.

system and TIMI risk score system, the differences of the poor prognosis and mortality rates in the three groups were statistically significant (P<0.01). Under these two scoring systems, poor prognosis and mortality were significantly higher in the high- and medium-risk groups compared with the low-risk group. Compared to the medium-risk group, poor prognosis and mortality in the high-risk group also exhibited a significant increase. The differences were statistically significant (P<0.01) (Table VI).

Comparison of the efficacy of the 4D-STI and TIMI risk score system for predicting the poor prognosis and mortality of patients. The corresponding ROC curve for the poor prognosis and mortality of patients within one year after reperfusion treatment based on the 4D-STI and TIMI risk score system is shown in Figs. 6 and 7. Compared with the TIMI risk score system, the corresponding area under the ROC curve based on the 4D-STI risk score system was larger (0.848 vs. 0.720 and 0.901 vs. 0.883, respectively).

Discussion

According to survey statistics, new cases of acute ACS in China have reached nearly one million cases annually. Furthermore, morbidity and mortality have increased year by year, and long-term prognosis after treatment remains poor (5). Data indicate that mortality for ACS patients at one year after onset is 15%, and increases to 25% at three years after onset. At the same time, complications due to disability have caused the quality of life of some patients to rapidly decline (6). Although reperfusion therapy has been widely implemented in hospitals to significantly reduce patient mortality, the incidence of STEMI has rapidly increased due to profound changes in diet and lifestyle. However, clinical studies have shown that the possibility of incomplete myocardial reperfusion after coronary recanalization can reach as high as 37 to 43%. If not found in time, disease progression would lead to complete myocardial necrosis, expanded infarct size and ventricular remodeling,

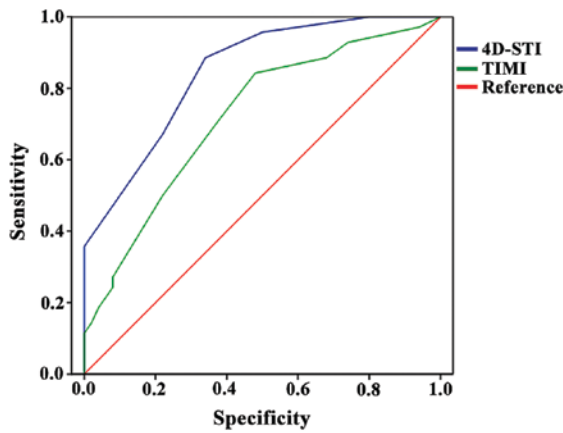


Figure 6. ROC curves of the 4D-STI and TIMI risk score system for predicting the poor prognosis of patients after reperfusion treatment. 4D-STI, four-dimensional speckle tracking imaging.

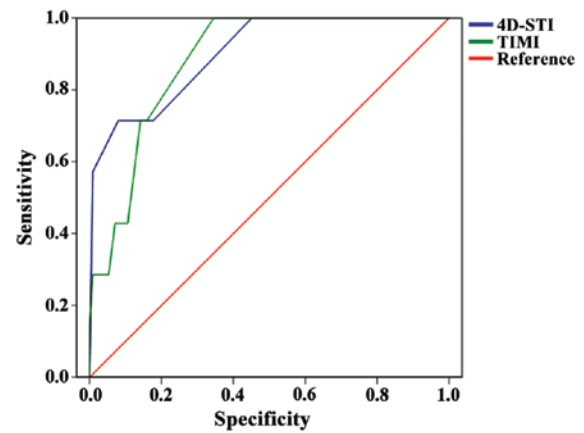


Figure 7. ROC curves of the 4D-STI and TIMI risk score system for predicting the mortality of patients after reperfusion treatment. 4D-STI, four-dimensional speckle tracking imaging.

leading to heart failure, increased risk of arrhythmia, and a 5-10 times increase in patient mortality (7,8). In order to improve the prognosis of patients, researchers have continuously worked to establish a score system that can objectively reflect the risk factors of malignant heart events after reperfusion treatment, which could assist physicians in determining a timely and accurate case-based reasonable and effective treatment program, and reduce the occurrence of poor prognosis.

Establishment of the myocardial four-dimensional strain 4D-STI risk score system using 4D-STI. The study conducted by Szymczyk *et al* (9) suggests that two-dimensional ultrasound speckle tracking imaging can effectively evaluate the degree of structural and functional repair of the damaged myocardium in STEMI cases. In addition, 4D-STI has become an emerging assessment method for wall motion abnormalities in recent years, and is the extended application of two-dimensional echocardiography. It overcomes the shortcoming of not being able to fully detect changes in myocardial motion in a single section, allows the overall analysis of the local myocardial strain and strain rate to be achieved, and provides a more objective and accurate evaluation of the myocardial systolic and diastolic function (10,11). In the present study, 4D-STI was applied to determine the four-dimensional myocardial strain indicators of the three observation points of STEMI patients within 72 h after reperfusion treatment, and it was found that the AS, CS, LS and RS absolute values of patients with poor prognosis were lower than those in patients with good prognosis. This is because STEMI causes the patient's heart blood supply to throttle, impairs heart muscle elasticity and reduces compliance, causing difficulties in cardiac wall motion performance, and resulting in decreased myocardial response (12,13). The difference in the four-dimensional echocardiographic data between the two groups can be presumed or applied to the relevant four-dimensional myocardial strain indicators to predict the prognosis of STEMI patients after reperfusion treatment. Further research revealed that AS, LS and RS within 12 h after reperfusion therapy, AS and RS at 2nd and 3rd day had a certain degree of prediction accuracy for STEMI patients with poor prognosis after surgery. Furthermore, the area under the ROC curve was between 0.735

and 0.785, suggesting that the seven indicators for evaluating the prognosis of patients were similar. Thus, the 4D-STI risk score system was established based on the myocardial four-dimensional strain to predict the prognosis of STEMI after reperfusion treatment.

Comparison of the prognostic values of the 4D-STI and TIMI risk score system. At present, the TIMI risk score is the most commonly used means to assess acute ACS prognosis in clinic, which is a summary of 15,000 cases of STEMI patients who underwent thrombolytic therapy, including historical data, hemodynamic parameters, electrocardiogram indicators, and clinical treatment and development. A number of studies have confirmed that TIMI scores are closely correlated with acute ACS cases, and have a good correlation with the long-term prognosis of the incidence of adverse events (14,15). In the present study, in the 4D-STI and TIMI risk score system, as the risk assessment score increased, the probability of occurrence of deaths and poor prognosis were substantially increased in the high- and low-risk groups. In the medium- and high-risk groups, mortality and poor prognosis were significantly different, clearly demonstrating that the indicative prognostic value of the 4D-STI and TIMI risk score system for STEMI patients was the same. Moreover, compared to the TIMI risk score, the 4D-STI system for patients with poor prognosis and mortality under the ROC curve area was greater, showing the application of the 4D-STI score and its stratification allows the determination of the prognosis of the outcome to have higher accuracy. Presumably, the reason may be as follows: i) The four-dimensional myocardial strain indicators can be measured by 17 segments of the myocardial dysplasia distribution, and the proportion of unfavorable areas of the microcirculation to the total myocardium is the most intuitive reflection of myocardial segment activity; and ii) the TIMI system provides a comprehensive reference for the clinical risk factors of patients. However, in the score of evaluation factors such as history of chronic diseases and other health concerns by patient awareness, the medical level of residence has a huge impact, and errors may exist in the information.

In the present study, the predictive effect of the four-dimensional myocardial strain indicators was only able to determine

the one year prognosis of patients within 72 h after reperfusion treatment, and the number of research samples was small. On this basis, it is expected to further expand the number of samples, increase the frequency of myocardial four-dimensional strain measurements, and conduct in-depth study on the prognostic significance of the various stages of AS, CS, LS and RS, while extending follow-up time, in order to further study the predictive value of four-dimensional echocardiography long-term prognosis.

In conclusion, four-dimensional echocardiography can better evaluate the prognosis of STEMI patients after reperfusion. AS, LS and RS at postoperative 12 h, AS and RS at 2nd and 3rd day has a certain predictive value for poor prognosis after reperfusion therapy. The predictive efficacy of the risk stratification of STEMI after reperfusion treatment based on the established myocardial four-dimensional strain on poor prognosis and mortality was superior to the TIMI risk score. The 4D-STI score is expected to be the most sensitive and easy to operate prognostic indicator to improve the prognosis of patients in clinical management.

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Availability of data and materials

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

Authors' contributions

YW and JZ conceived and designed the study, and finally approved the manuscript. RX and XY collected the patient data. JW and LF were responsible for the analysis and interpretation of the data. YW drafted and revised the manuscript critically for important intellectual content. All authors read and approved the final manuscript.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Shanghai Jiading Center Hospital (Shanghai, China). Signed informed consents were obtained from the patients or guardians.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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