ORIGINAL RESEARCH

Comparison of Diagnostic Value Between STE +LDDSE and CMR-FT for Evaluating Coronary Microvascular Obstruction in Post-PCI Patients for STEMI

Tao Liu*, Chaofan Wang*, Jie Yin, Lili Wang [ID], Haochen Xuan, Yan Yan, Junhong Chen, Jieli Bao, Dongye Li, Tongda Xu

Department of Cardiology, The Affiliated Hospital of Xuzhou Medical University, Xuzhou, People's Republic of China

*These authors contributed equally to this work

Correspondence: Tongda Xu; Dongye Li, Department of Cardiology, The Affiliated Hospital of Xuzhou Medical University, Xuzhou, People's Republic of China, Email xutongda3004@163.com; dongyeli@xzhmu.edu.cn

Background: Coronary microvascular obstruction (CMVO) is closely associated with poor prognosis of ST-segment elevation myocardial infarction (STEMI) patients. However, data showing the comparison between cardiac magnetic resonance feature tracking (CMR-FT) and speckle tracking echocardiography (STE) combined with low-dose dobutamine stress echocardiography (LDDSE) in evaluating CMVO was scarcely available. We aimed to explore and compare the predictive value between CMR-FT and STE+LDDSE in detecting CMVO.

Methods: Sixty-one STEMI patients were executed cardiac magnetic resonance and echocardiography within the first 5–7 days after primary percutaneous coronary intervention (PCI). The myocardial strain analysis was performed in STE, STE+LDDSE, and CMR-FT, and strain parameters included radial strain (RS), circumferential strain (CS), and longitudinal strain (LS). ROC curves were performed to predict infarcted myocardium segments with CMVO.

Results: Finally, 324 infarcted myocardium segments were analyzed, including 100 infarcted segments with CMVO and 224 segments without CMVO by the gold standard assessment of late gadolinium-enhancement cardiac magnetic resonance imaging (LGE-CMR). The results showed that CS was generally superior to RS and LS in identifying CMVO. CS in CMR-FT facilitated the detection of CMVO, with a sensitivity, specificity, and accuracy of 78.00%, 81.25%, and 80.25%, respectively. The sensitivity, specificity, and accuracy of CS in STE combined with LDDSE were better than STE alone (76.00% vs 60.00%, 79.91% vs 64.29%, and 78.70% vs 62.96%, $P < 0.05$). In addition, CMR-FT is not superior to STE+LDDSE for detection of CMVO ($P > 0.05$).

Conclusion: Low-dose dobutamine can improve the clinical value of STE for evaluating CMVO in STEMI patients. Compared with CMR-FT, STE+LDDSE might be a better choice for STEMI patients because of its safety, convenience, and low-cost.

Keywords: ST-segment elevation myocardial infarction, magnetic resonance feature tracking, speckle tracking echocardiography, low-dose dobutamine, coronary microvascular obstruction

Introduction

ST-segment elevation myocardial infarction (STEMI), as a severe type of acute myocardial infarction, is an important cause of death and disability in the world. Percutaneous coronary intervention (PCI) can reduce the mortality of STEMI patients, but approximately 50% of patients experience cardiac microvascular obstruction (CMVO) after primary PCI.[1] CMVO, especially the size of CMVO, is associated with poor prognosis, such as adverse ventricular remodeling, rehospitalization for heart failure, and death.[2] In addition, some studies have shown that the size of CMVO may be

improved significantly after early treatment.[3–5] Therefore, it is important for STEMI patients to formulate a treatment strategy and judge their clinical prognosis by early detection of CMVO.

Currently, there are two ways to detect CMVO, including invasive and non-invasive. The index of microvascular resistance (IMR) is a coronary angiography-based, reliable, quantitative technique for assessing CMVO, and IMR >25 is considered as CMVO.[6,7] However, IMR is difficult to promote clinically due to its invasiveness, time-consuming, high-cost, and potentially dangerous complications. In addition, non-invasive detection methods for CMVO mainly include single-photon emission computed tomography (SPECT) and cardiac magnetic resonance (CMR). Although SPECT is an emerging method to detect CMVO,[8] due to poor imaging sensitivity, temporal resolution, and limitation of radiation exposure and high cost, SPECT is still not widely used in clinical practice. Currently, CMR has become a preferred method for noninvasive diagnosis of CMVO.[9,10] However, the long operation time and the effect of gadolinium contrast agent on renal function might limit the clinical application of CMR. Therefore, a convenient, inexpensive, and clinically scalable method for the detection of CMVO needs to be investigated.

The association between CMVO and poor prognosis has been well established, but the relationship between CMVO and regional function possesses limited data. Wall thickening measured by CMR could assess regional function.[11] However, some documents have currently demonstrated that myocardial strain is superior to wall thickening in evaluating regional function.[12] In recent years, the study by Everaars et al also confirmed that strain analysis could be used to differentiate infarcted myocardium segments without or with CMVO by the methods of myocardial tissue tagging.[13] However, many shortcomings of myocardial tissue tagging, such as difficult image acquisition and complex post-processing images, may make it less clinically useful. Compared with myocardial tissue tagging, the advantages of cardiac magnetic resonance feature-tracking (CMR-FT), including low time consumption, low cost, high repeatability, and accuracy, make it more suitable for clinical application. As a result, CMR-FT is expected to be the new standard for diagnosing CMVO in clinic.

Speckle tracking echocardiography (STE) based on frame-to-frame tracking of ultrasonic speckles could be a promising technique to identify left ventricular (LV) regional function by quantifying the analysis of myocardial deformation.[14] Several studies showed that STE could effectively assess CMVO.[15,16] Bergerot confirms that LS >-13% in STE could differentiate the presence of CMVO.[17] Previous studies believe that low-dose dobutamine stress echo-cardiography (LDDSE) can improve the clinical application value of STE. The study by Li et al showed that low-dose dobutamine could improve the value of STE in detecting viable myocardium.[18] LDDSE can strengthen myocardial contractility and improve microcirculatory blood flow by stimulating β1 receptors in the heart.[19] However, little research on CMVO evaluated by STE combined with LDDSE was reported. Therefore, we assume that LDDSE enhances the diagnostic value of STE for assessing CMVO.

Myocardial deformation has been proven valuable for detecting CMVO. However, CMR-FT was not applicable for detecting CMVO in patients with pacemaker implantation, claustrophobia, or severe heart failure. STE+LDDSE might be a preferred substitute due to its safety, convenience, and low-cost. Whereas few studies have compared the values between CMR-FT and STE+LDDSE in assessing CMVO, and data showing the comparison of sensitivity, specificity, and accuracy of CMR-FT, STE, and STE+LDDSE in evaluating CMVO was scarcely available. Therefore, the study aimed to explore and compare the value between STE+LDDSE and CMR-FT in detecting CMVO.

Methods and Materials
Study Population
The study enrolled 61 consecutive patients with STEMI (the average age was 53.0 ± 13.4, and 90.2% were male) from September 2020 to September 2022. The present study was conducted according to the Declaration of Helsinki and was approved by the Medical Research Ethics Committee of the Affiliated Hospital of Xuzhou Medical University. Informed consent was provided by all patients to participate in this study, and questionnaires was provided in Supplementary Figure 1.

The criteria for inclusion were as follows: all STEMI patients had the first STEMI diagnosis, and revascularization by primary PCI within 12 h of ischemic symptoms was performed.[20]

The major exclusion criteria were as follows: 1) Patients younger than 18 years old; 2) Patients who are unable to perform cardiac magnetic resonance, STE and STE+LDDSE; 3) Patients who cannot obtain the satisfactory images. 4)

Based on safety, patients with a previous history of myocardial infarction, severe arrhythmia, coronary artery bypass grafting, shock, severe hypertension, congenital heart disease, malignant tumors, dilated cardiomyopathy, hypertrophic cardiomyopathy, and myocarditis would be excluded.

Cardiac Magnetic Resonance Imaging

All CMR image acquisitions were conducted on a 3.0 T scanner (Ingenia 3.0 T, Philips, the Netherlands) with a phased-array cardiac receiver coil within seven days after primary PCI, and short-axis images covering the left ventricle (10–12 slices) and long-axis images (the apical four-chamber, the apical two-chamber, and three-chamber) were obtained. Meanwhile, the short- and long-axis slice positions of a late gadolinium-enhancement cardiac magnetic resonance imaging (LGE-CMR), identical to the cine images, were acquired after 10–15 min of the administration of gadolinium-based contrast agent (0.1 mmol/kg) by Phase Sensitive Inversion Recovery (PSIR). In the CMR parameters, the slice thickness was set at 7 mm, the echo-time was set at 1.4 ms, the repetition time was set at 2.8 ms, the field of view was set at 300 × 300 mm, and the matrix size was set at 280 × 240.

LV myocardial strain analysis and LGE-CMR image post-processing were analyzed in an American Heart Association (AHA) 16-segment model by using CVI 42 software (Circle Cardiovascular Imaging 42, Calgary, Canada) version 5.13. The infarcted area in LGE-CRM was accurately measured by using a threshold technique of >5 standard deviations (SD) from the remote myocardium,[21] and CMVO was defined as the hypo-enhancement area within the infarcted area.[22,23] Subsequently, the myocardial infarcted segment with CMVO was qualitatively assessed (Figure 1Ai–Aiii). The endocardial (red line) and epicardial (green line) borders of the LV myocardium were delineated semi-automatically at end-diastole of long-axis images (the apical four-chamber, the apical two-chamber, and three-chamber) and short-axis images (10–12 slices), and the region of interest was manually adjusted to ensure accuracy. Finally, many different types of peak systolic strain parameters could be automatically tracked in cine-MRI, including longitudinal strain (LS), circumferential strain (CS), and radial strain (RS) (Figure 1Bi–Biii).

Echocardiography and STE-LDDSE

All patients underwent echocardiography within 7 days of reperfusion. Routine echocardiographic images were acquired by using cardiovascular ultrasound imaging equipment (Philips EPIQ 7C, The Netherlands), including long-axis images (the apical four-chamber, the apical two-chamber, and three-chamber) and short-axis images (basal segment, middle segment, and apex segment). After that, dobutamine (2mL; 20mg) was pumped intravenously at a dose of 10μg/(kg-min) for 5 minutes, and two-dimensional dynamic images of the above sections were stored again for subsequent analysis.

The acquisition of strain parameters was completed off-line by QLAB software (Version 10.8, The Netherlands). As with CMR, strain analysis between STE and STE+LDDSE was performed in the AHA 16-segment model by using QLAB software (Version 10.8, The Netherlands). The endocardial and epicardial borders of the LV myocardium during the movement of the myocardium were automatically tracked by the software, with manual adjustment to ensure accuracy if necessary. Then, peak systolic strain parameters were calculated for each direction, including LS, CS, and RS (Figure 1Ci–Ciii).

Statistical Analysis

Continuous variables were presented as mean ± standard deviation (MD ± SD), and categorical variables were expressed as percentages. Continuous variables or ratio between infarcted myocardium segments with CMVO and without CMVO was compared by t-tests or chi-square. The predictive value of strain parameters for infarcted myocardium segments with CMVO was based on logistic regression analyses. Receiver-operator characteristics (ROC) curves were performed to evaluate the ability of different strain parameters to predict infarcted myocardium segments with CMVO and identify the optimal cutoff point. A comparison of ROC curves was performed by using the method of DeLong.[24] In addition, to ensure the consistency of results, we randomly selected 6 patients. Strain value of each parameter obtained by two experienced examiners was used to calculate the intraclass correlation coefficient (ICC) for verifying reproducibility of experimental results. MedCalc (Version 20.0, https://www.medcalc.org/) and R Studio (Version 4.1.2, https://www.Rproject.org) were used to analyze the data. All statistical tests with a P-value <0.05 were significant.
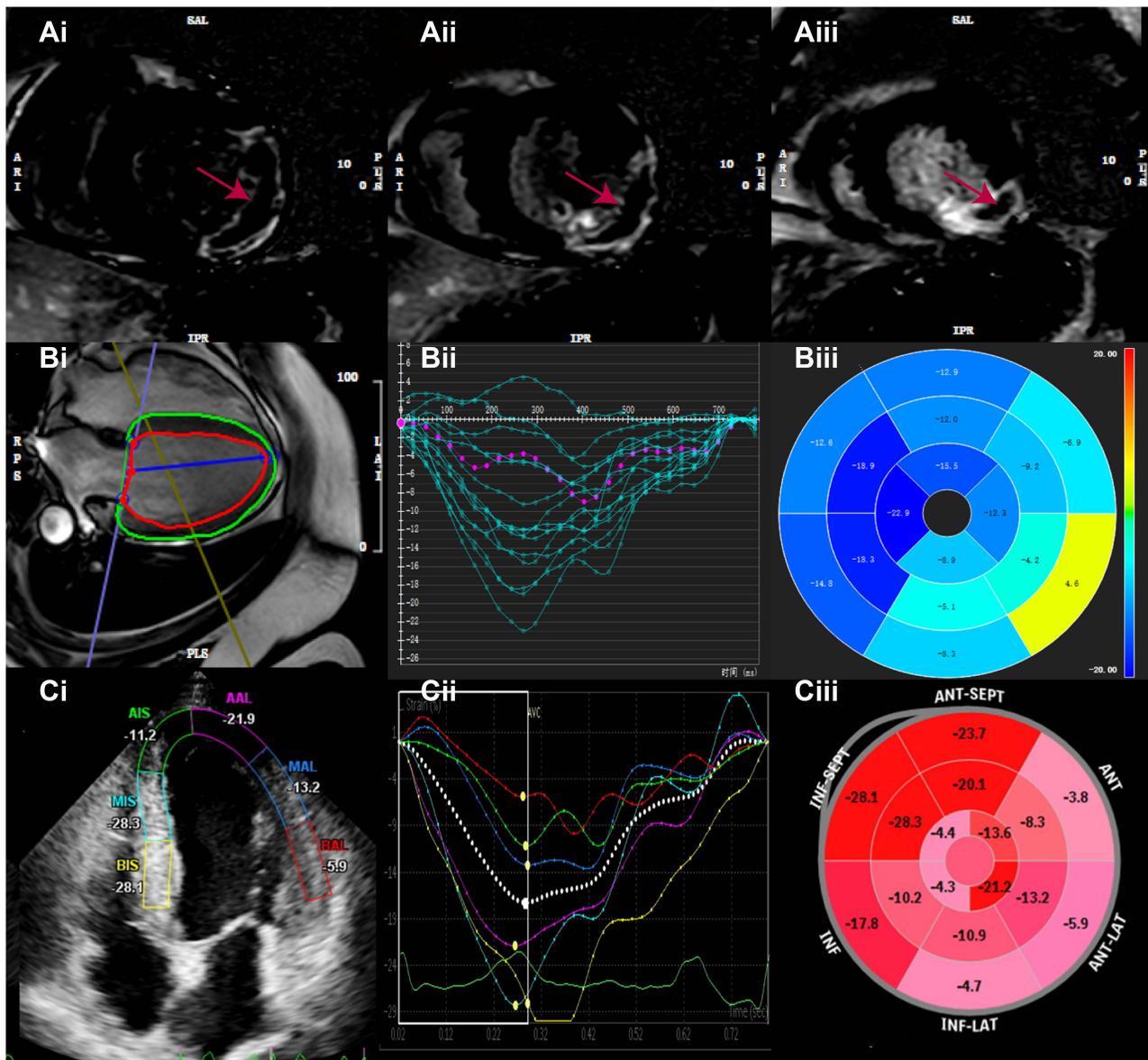
Figure 1 Typical CMVO appearance on LGE-CMR images (**A**) and measurement of myocardial longitudinal peak systolic strain using CMR-FT (**B**) and STE+LDDSE (**C**). Red arrow represents CMVO within infarcted myocardium segment (**Ai**: basis, **Aii**: middle, **Aiii**: apex), (**Bi** and **Ci**) represent longitudinal peak systolic strain measurements of CMR-FT and LDDSE, respectively. (**Bii** and **Cii**) represent longitudinal peak systolic strain–time curve of CMR-FT and LDDSE, respectively. (**Biii** and **Ciii**) represents bull's eye plot of CMR-FT and LDDSE, respectively.
Abbreviations: CMVO, coronary microvascular obstruction; LGE-CMR, late gadolinium-enhancement cardiac magnetic resonance imaging; CMR-FT, cardiac magnetic resonance feature tracking; STE, speckle tracking echocardiography; LDDSE, low-dose dobutamine stress echocardiography.

Results

The Study Populations

The detailed clinical characteristics of 61 STEMI patients are listed in Table 1. In addition, 61 STEMI patients contained 976 myocardial segments, of which 30 had poor image acquisition. Of the remaining 946 infarcted myocardium segments, 622 infarcted myocardium segments were excluded because of no delayed enhancement by CMR. Finally, 324 infarcted myocardium segments were included in the present study, including 100 infarcted segments with CMVO and 224 infarcted segments without CMVO, establishing a CMVO incidence of infarcted myocardium segments of 30.9% (Figure 2). The gold standard for infarcted myocardium segments with CMVO was based on LGE-CMR.

Table 1 Patient Characteristics

Variables	Total (N = 61)
Age (years)	53.0 ± 13.4
Male, n (%)	55 (90.2)
Hypertension, n (%)	20 (32.8)
Diabetes mellitus, n (%)	15 (24.6)
Hypercholesterolemia, n (%)	31 (50.8)
Smoking, n (%)	33 (54.1)
Symptom onset-to-balloon time, (h)	3.7 ± 2.4
Myocardial edema, n (%)	50.8
Intramyocardial hemorrhage, n (%)	39.3
Myocardial fibrosis, n (%)	88.5
Culprit vessel, n (%)	
LAD	31 (50.8)
LCX	11 (18.0)
RCA	19 (31.1)
Ejection fraction (%)	51.4 ± 5.5
CKMB (ng/mL)	168.3 ± 104.2
TnI (ng/mL)	18.0 ±17.3
Triglycerides, mmol/L	1.78 ±1.07
LDL-C, mmol/L	2.61 ± 0.66

Abbreviations: LAD, left anterior descending; LCX, left circumflex branch; RCA, right coronary artery; CKMB, creatine kinase-MB; TnI, troponin I; LDL-C, low-density lipoprotein cholesterol.

The Value of Strain for Evaluating Infarcted Segments with CMVO

Among the 324 segments of infarcted myocardium, compared with the infarcted segments without CMVO, RS, CS, and LS in CMR-FT, STE, and LDDSE+STE were impaired in the infarcted segments with CMVO (all $P<0.05$) (Table 2). In
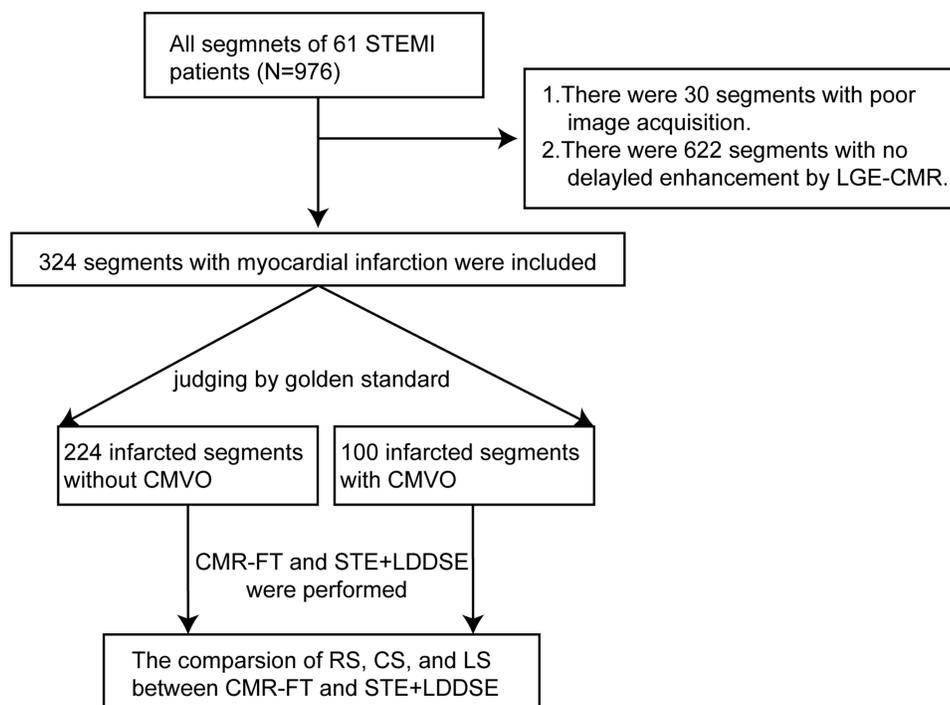
Figure 2 The flow chart.
Abbreviations: CMVO, coronary microvascular obstruction; LGE-CMR, late gadolinium-enhancement cardiac magnetic resonance imaging; CMR-FT, cardiac magnetic resonance feature tracking; STE, speckle tracking echocardiography; LDDSE, low-dose dobutamine stress echocardiography; RS, radial strain; CS, circumferential strain; LS, longitudinal strain.

Table 2 The Comparison of Myocardial Deformation Parameters Between CMR-FT, STE, and STE Combined with LDDSE in the Segments with CMVO and without CMVO

Variables	CMVO (-) (n = 224)	CMVO (+) (n = 100)	*P*-value
RS$_{CMR-FT}$ (%)	14.96 (5.27)	10.06 (3.83)	<0.001
CS$_{CMR-FT}$ (%)	−10.92 (3.88)	−6.58 (2.29)	<0.001
LS$_{CMR-FT}$ (%)	−13.53 (5.75)	−8.84 (6.64)	<0.001
RS$_{STE}$ (%)	18.84 (4.76)	16.77 (4.83)	<0.001
CS$_{STE}$ (%)	−16.65 (5.25)	−13.79 (4.98)	<0.001
LS$_{STE}$ (%)	−15.21 (4.46)	−12.86 (3.43)	<0.001
RS$_{LDDSE}$ (%)	21.00 (4.63)	16.53 (4.36)	<0.001
CS$_{LDDSE}$ (%)	−23.02 (5.00)	−17.76 (5.10)	<0.001
LS$_{LDDSE}$ (%)	−18.37 (3.31)	−14.64 (3.19)	<0.001

Abbreviations: CMVO, coronary microvascular obstruction; RS, radial strain; LS, longitudinal strain; CS, circumferential strain; CMR-FT, cardiac magnetic resonance feature tracking; STE, speckle tracking echocardiography; LDDSE, low-dose dobutamine stress echocardiography.

multivariate logistic regression, RS$_{CMR-FT}$, CS$_{CMR-FT}$, LS$_{CMR-FT}$, RS$_{LDDSE}$, and LS$_{LDDSE}$ emerged as independent predictors of infarcted segments with CMVO (Table 3).

Discriminating Between Infarcted Myocardium with and without CMVO

With ROC curve analysis (Table 4), the area under the curve (AUC) of RS$_{STE}$, CS$_{STE}$, and LS$_{STE}$ for discriminating infarcted segments with CMVO was 0.622, 0.652, and 0.648 (all *P*<0.001), respectively. The sensitivity, specificity, and accuracy of RS$_{STE}$, CS$_{STE}$, and LS$_{STE}$ were 64.00%, 59.38%, and 60.80%; 60.00%, 64.29%, and 62.96%; 67.00%, 59.38%, and 61.73%, respectively. The optimal cutoff points of RS$_{STE}$, CS$_{STE}$, and LS$_{STE}$ were 18.50%, −15.30%, and −13.80% (Figure 3Ai–Aiii).

When STE was combined with LDDSE, the AUC were 0.775, 0.798, and 0.806 (all *P*<0.001), respectively. The sensitivity, specificity, and accuracy of RS$_{LDDSE}$, CS$_{LDDSE}$ and LS$_{LDDSE}$ were 77.00%, 73.66%, and 74.69; 76.00% and 79.91%, and 78.70%; 81.00%, 78.57%, and 79.32%, respectively. The optimal cutoff points of RS$_{LDDSE}$, CS$_{LDDSE}$, and LS$_{LDDSE}$ were 20.10%, −21.1%, and −16.60% (Figure 3Bi–Biii).

The AUCs of RS$_{CMR-FT}$, CS$_{CMR-FT}$, and LS$_{CMR-FT}$ for identifying infarcted segments with CMVO were 0.781, 0.833, and 0.756 (all *P*<0.001), respectively. The sensitivity, specificity, and accuracy of RS$_{CMR-FT}$, CS$_{CMR-FT}$, and LS$_{CMR-FT}$

Table 3 Logistic Regression Analysis to Evaluate the Independent Predictive Accuracy of Different Myocardial Strain Measurements for Detecting CMVO

Variables	Unadjusted Logistic Analysis		Adjusted Logistic Analysis	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
RS$_{CMR-FT}$ (%)	0.79 (0.74;0.84)	<0.001	0.83 (0.74,0.91)	<0.001
CS$_{CMR-FT}$ (%)	1.54 (1.38;1.72)	<0.001	1.41 (1.23,1.65)	<0.001
LS$_{CMR-FT}$ (%)	1.14 (1.09;1.20)	<0.001	1.10 (1.03,1.18)	0.006
RS$_{STE}$ (%)	0.91 (0.87;0.96)	<0.001	1.10 (1.00,1.21)	0.057
CS$_{STE}$ (%)	1.11 (1.06;1.17)	<0.001	0.96 (0.89,1.04)	0.371
LS$_{STE}$ (%)	1.15 (1.08;1.23)	<0.001	0.94 (0.84,1.05)	0.245
RS$_{LDDSE}$ (%)	0.81 (0.76;0.86)	<0.001	0.85 (0.77,0.93)	0.001
CS$_{LDDSE}$ (%)	1.24 (1.17;1.32)	<0.001	1.08 (1.00,1.18)	0.077
LS$_{LDDSE}$ (%)	1.45 (1.32;1.60)	<0.001	1.32 (1.16,1.52)	<0.001

Abbreviations: CMVO, coronary microvascular obstruction; RS, radial strain; LS, longitudinal strain; CS, circumferential strain; CMR-FT, cardiac magnetic resonance feature tracking; STE, speckle tracking echocardiography; LDDSE, low-dose dobutamine stress echocardiography.

818

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Therapeutics and Clinical Risk Management 2022:18

Table 4 Optimal Cut-off Values and Diagnostic Performance of Myocardial Deformation Parameters for Detecting CMVO Within Infarcted Myocardium Segments

Variables	AUC	*P*-value	Cut-Off (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)
RS$_{STE}$ (%)	0.622	<0.001	18.50	64.00	59.38	60.80
RS$_{LDDSE}$ (%)	0.775	<0.001	20.10	77.00	73.66	74.69
RS$_{CMR-FT}$ (%)	0.781	<0.001	10.79	75.00	74.55	74.69
CS$_{STE}$ (%)	0.652	<0.001	−15.30	60.00	64.29	62.96
CS$_{LDDSE}$ (%)	0.798	<0.001	−21.1	76.00	79.91	78.70
CS$_{CMR-FT}$ (%)	0.833	<0.001	−7.12	78.00	81.25	80.25
LS$_{STE}$ (%)	0.648	<0.001	−13.80	67.00	59.38	61.73
LS$_{LDDSE}$ (%)	0.806	<0.001	−16.60	81.00	78.57	79.32
LS$_{CMR-FT}$ (%)	0.756	<0.001	−11.84	80.00	73.66	75.62

Abbreviations: CMVO, coronary microvascular obstruction; AUC, area under the curve; RS, radial strain; LS, longitudinal strain; CS, circumferential strain; CMR-FT, cardiac magnetic resonance feature tracking; STE, speckle tracking echocardiography; LDDSE, low-dose dobutamine stress echocardiography.

were 75.00%, 74.55%, and 74.69%; 78.00%, 81.25%, and 80.25%; 80.00%, 73.66%, and 75.62%, respectively. The optimal cutoff points of RS$_{CMR-FT}$, CS$_{CMR-FT}$, and LS$_{CMR-FT}$ were 10.79%, −7.12%, and −11.84% (Figure 3Ci–Ciii).

Comparison of Strain Measurements for Discriminating Between Infarcted Myocardium with and without CMVO

To reveal the strain with the highest discriminative power, we compared the AUC, sensitivity, specificity, and accuracy of STE, STE+LDDSE and CMR-FT in discriminating CMVO. The RS, CS, and LS at rest had a significantly lower AUC than both STE-LDDSE (all *P* < 0.05) and CMR-FT (all *P* < 0.05), and the comparison between STE-LDDSE and CMR-FT on RS, CS, and LS was not statistically significant (all *P* > 0.05). The sensitivity, specificity, and accuracy of RS, CS, and LS in CMR-FT were similar to STE+LDDSE (all *P* > 0.05), and the sensitivity, specificity, and accuracy of RS, CS, and LS at rest had lower diagnostic potential than in CMR-FT (all *P* < 0.05). When combined with LDDSE, the sensitivity, specificity, and accuracy of RS, CS, and LS at rest were significantly improved.

Reproducibility

For LS, 6 patients were selected randomly, and 33 infarcted segments were analyzed. The ICC was 0.887, 0.845, and 0.813 in CMR-FT, STE+LDDSE, and STE (all *P* < 0.05), and this indicated that the reproducibility was good. The ICC of RS and CS was provided in Supplementary Table 1.

Discussion

STEMI, one of the most severe types of coronary heart disease, is a common and frequently-occurring disease of the cardiovascular system and can lead to heart failure, and even sudden death. The primary PCI significantly reduced the mortality of STEMI patients, but some patients still have major adverse cardiovascular events after successful revascularization. CMVO is considered to be the primary cause of myocardial reperfusion failure after successful revascularization of epicardial coronary arteries.[25] CMVO was mainly induced by the blockage of distal small vessels due to spontaneous or mechanical rupture of atherosclerotic plaque in coronary arteries. In addition, reduction or elimination of blood flow in functional vessels might also lead to CMVO, as a result of the compression on the functional vessels resulting from severe myocardial edema.[26,27] Because it is important for STEMI patients' treatment and clinical prognosis to detect the occurrence of CMVO earlier. Therefore, how to choose CMVO detection methods was further discussed in the present study.

Currently, CMR has become a preferred method for noninvasive diagnosis of CMVO, due to its characteristics such as high spatial resolution, non-radiation, and one-stop evaluation of the heart function and anatomy, the blood flow perfusion, and histologic features.[9,10] CMVO is mainly identified by LGE-CMR in CMR. However, the operation time in
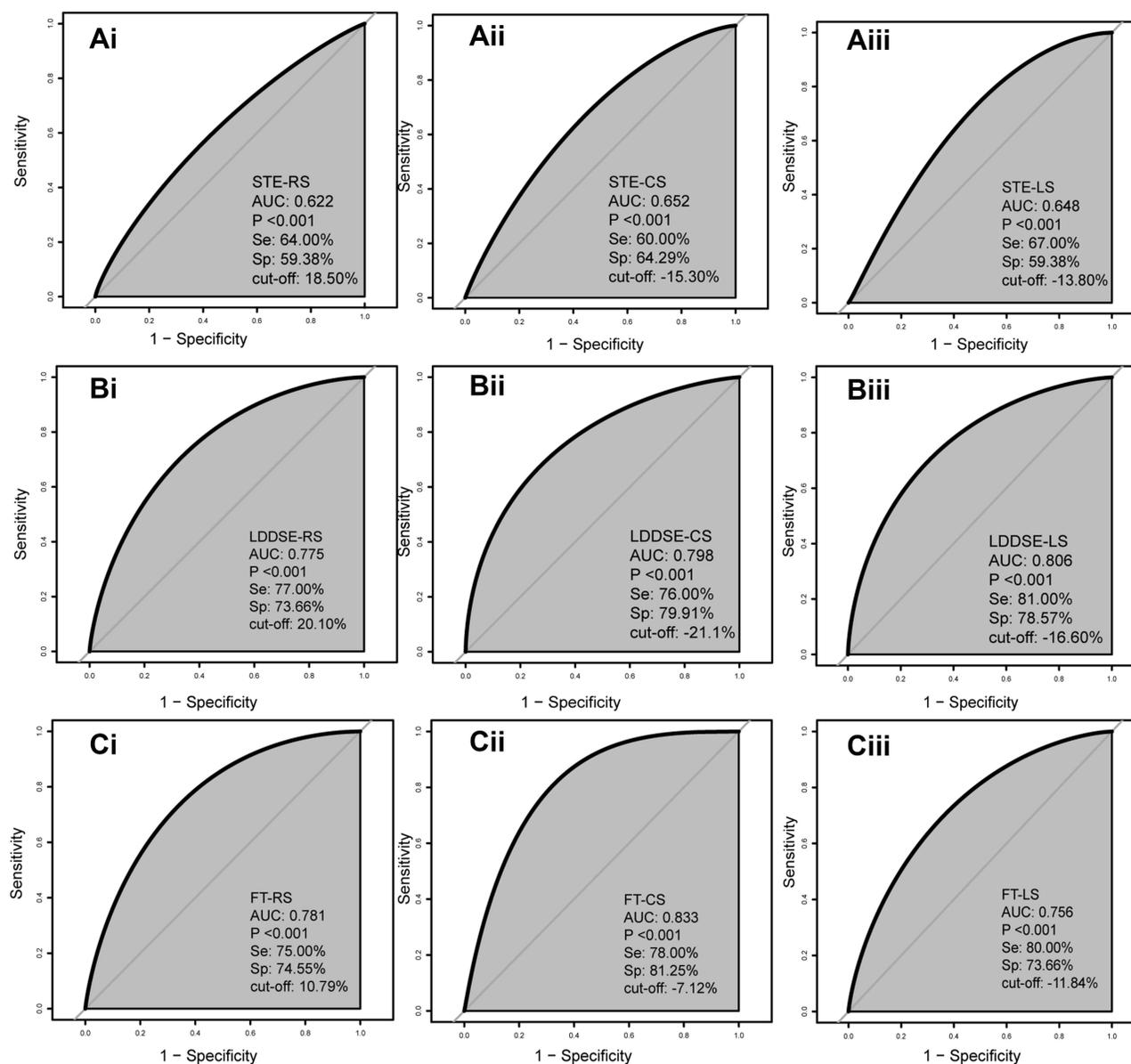
Figure 3 The ROC curves of myocardial deformation parameters in evaluating CMVO. (**Ai–Aiii**) represent ROC curves of RS, CS, and LS in STE, respectively; (**Bi–Biii**) represent ROC curves of RS, CS, and LS in STE+LDDSE, respectively; (**Ci–Ciii**) represent ROC curves of RS, CS, and LS in CMR-FT, respectively.
Abbreviations: ROC, receiver operating characteristic; CMVO, coronary microvascular obstruction; RS, radial strain; LS, longitudinal strain; CS, circumferential strain; STE, speckle tracking echocardiography; LDDSE, low-dose dobutamine stress echocardiography; CMR-FT, cardiac magnetic resonance feature tracking; Se, sensitivity; Sp, specificity.

LGE-CMR is too long for many patients to tolerate. Moreover, the gadolinium contrast agent is detrimental to renal function, and patients with poor heart function, pacemaker implantation and claustrophobia could not be used, which limits the clinical promotion of CMR to some extent. Myocardial strain technology could track the degree of myocardial deformation to reflect the systolic and diastolic functions of the myocardium by obtaining a continuous image sequence.[28] The prospective study by Zhao et al has confirmed that the occurrence of CMVO after successful reperfusion has an effect on cardiac mechanics.[29] Leung et al pointed out that the association between LV contractile reserve and index of microcirculatory resistance (IMR) was significant (correlation formula: $IMR^{-1} = (0.0014 \times CR + 0.05)$).[30] As we all know, the integrity of the structure and function of cardiac microcirculation is the foundation of myocardial survival after myocardial infarction. Therefore, myocardial deformation has a certain diagnostic value for differentiating CMVO. In the present study, we found that myocardial strain could discriminate the presence of CMVO in STEMI patients.

Therefore, in STEMI patients with renal dysfunction, poor heart function, pacemaker insertion, claustrophobia, and being allergic to gadolinium-contrast agents, the selectivity of myocardial deformation technology for discriminating CMVO might be superior to LGE-CMR.

For CMR-FT, myocardium contractile reserve was also evaluated by myocardial deformation calculated through the optical-flow method.[31] Previous studies suggested that CMR-FT provided important information for LV remodeling and incremental prognostic value for MACE prediction.[32,33] With the development of CMR-FT technology, CMR-FT has been used to detect CMVO. A study by Tamarappoo et al showed that CS of LV could predict CMVO.[34] This is consistent with our findings. Both CMR-FT and LGE-CMR have the advantages of high spatial resolution and no-radiation, but contrast agent injection is essential for LGE, compared to CMR-FT, this renders CMR-FT to be more applicable in clinic. However, CMR-FT might not be applicable for detecting CMVO in patients with pacemaker implantation, claustrophobia and severe heart failure. Our study showed that CMR-FT had a high value for CMVO detection, but it was not superior to STE+LDDSE. Therefore, STE+LDDSE might be a preferred substitute for these patients, due to its safety, convenience, and low-cost.

Currently, STE, as a quantitative technique to accurately assess the global or partial heart function,[35] has been used to evaluate CMVO.[17,36] In the present study, we found that the RS, CS, and LS at rest for identifying CMVO have some diagnostic value, which means that the results of our study are consistent with those of previous studies. In addition, the results of the present study showed that the detective value of STE for differentiating CMVO would be improved significantly when STE was combined with LDDSE. Dobutamine is a synthetic catecholamine and can improve myocardium contractile reserve by enhancing coronary blood flow at a low dose. Gong et al confirmed that low-dose dobutamine could improve the value of STE in detecting viable myocardium,[37] but there was little data on the effect of STE combined with LDDSE on assessing CMVO. In the present study, we found that LDDSE could improve the diagnostic value of STE for evaluating CMVO. Therefore, STE+LDDSE might be a new way to detect CMVO.

In a word, our study results showed that between STE+LDDSE and CMR-FT had a high value for CMVO detection, and value of CMR-FT for CMVO detection was not superior to STE+LDDSE. In addition, the benefits of STE+LDDSE from less costs, easier use, safety and convenience were better than those of CMR-FT. In brief, based on our study, STE+LDDSE might be a new way for STEMI patients to detect CMVO and a preferred alternative to CMR-FT for STEMI patients with pacemaker implantation, claustrophobia and severe heart failure.

Limitations

Firstly, this study is a small-sample study, so it is necessary to expand the sample size to further verify the experimental results of this study. Secondly, the layered strain parameters in CMR-FT cannot be analyzed at present. Therefore, layered strain studies will be needed in the future. Thirdly, since the object of this study is the myocardial infarction segment, the global strain is not studied. Finally, smoking, hyperlipidemia, diabetes mellitus, and other risk factors could lead to the emergence of CMVO. Due to the small sample size, no subgroup analysis was performed.

Conclusion

Low-dose dobutamine can improve the clinical value of STE for evaluating CMVO in STEMI patients. Compared with CMR-FT, STE+LDDSE might be a preferred method for STEMI patients to assess the occurrence of CMVO, regarding its characteristics of low cost, convenience, and safety.

Data Sharing Statement

The datasets are available by contacting the corresponding author (xutongda3004@163.com).

Ethics Statement

This study was conducted by the Declaration of Helsinki and was approved by the Medical Research Ethics Committee of the Affiliated Hospital of Xuzhou Medical University. Due to prospective studies, informed consent was provided by all patients, and questionnaires were provided in <u>Supplementary Figure 1</u> (Ethical Number: XYFY2018-KL043-01). Prior to analysis, confidential patient information was deleted from the entire data set prior to analysis.

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Disclosure

The authors report no conflicts of interest in this work.

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