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Low-dose dobutamine stress myocardial contrast echocardiography for evaluating myocardial microcirculation perfusion and predicting long-term prognosis in ST-segment elevation myocardial infarction after percutaneous coronary intervention

Li Li¹, Na Hu¹, Linzi Li² and Liangyi Li^{3*}

Abstract

Objective Percutaneous coronary intervention (PCI) can effectively restore myocardial perfusion in patients with ST-segment elevation myocardial infarction (STEMI). Nevertheless, STEMI patients may still experience a “no-reflow” phenomenon after PCI. Accordingly, this study focused on the clinical value of low-dose dobutamine stress myocardial contrast echocardiography (MCE) for evaluating myocardial microcirculation perfusion and long-term prognosis in STEMI patients after PCI.

Methods This study included 70 STEMI patients receiving PCI. Low-dose dobutamine stress MCE was performed to detect viable myocardium at 72 h after PCI and quantitatively analyze myocardial microcirculation perfusion at 72 h and 6 months after PCI. Patients were categorized into dobutamine stress echocardiography (DSE)-positive and DSE-negative groups, followed by comparisons of LVEF. The 3-year survival of STEMI patients after PCI was analyzed.

Results No adverse reactions occurred during low-dose dobutamine stress MCE. Low-dose dobutamine stress MCE effectively detected viable myocardium at 72 h after PCI (AUC: of 0.849). Under the basal or stress state, A, β , and $A \times \beta$ values of viable myocardium at 6 months after PCI were prominently higher than values at 72 h after PCI. A and $A \times \beta$ values of viable myocardium at 6 months after PCI were considerably higher in the stress state than in the basal state. LVEF and long-term survival rates after PCI were markedly higher in the DSE-positive group than in the DSE-negative group.

Conclusion Low-dose dobutamine stress MCE is an effective evaluation method for myocardial perfusion, left ventricular function recovery, and poor long-term prognosis in STEMI patients after PCI.

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Keywords ST-segment elevation myocardial infarction, Myocardial contrast echocardiography, Dobutamine stress, Percutaneous coronary intervention, Myocardial perfusion, Left ventricular function recovery, Long-term prognosis

Introduction

Acute myocardial infarction (AMI) is a cardiovascular disease resulting from irreversible myocardial damage evoked by insufficient oxygen [1, 2]. As a subtype of AMI, ST-segment elevation myocardial infarction (STEMI) typically manifests as typical ST-segment elevation on electrocardiogram (ECG) and is the dominating cause of morbidity and death of patients with coronary artery disease (CAD) [3]. Percutaneous coronary intervention (PCI) is recommended by guidelines for STEMI patients to effectively restore myocardial perfusion in the infarcted area since it can restore coronary perfusion through a stent [4–6]. However, even if revascularization is successful, STEMI patients still exhibit a “no-reflow” phenomenon in the infarct area and myocardial reperfusion injury after PCI [7, 8]. Moreover, the “no-reflow” phenomenon is associated with clinical adverse events after PCI, such as malignant arrhythmia, left ventricular (LV) dysfunction, recurrent MI, and even death [9]. Therefore, early and accurate evaluation of myocardial perfusion and ventricular function after PCI is key for improving the prognosis of STEMI patients.

Myocardial contrast echocardiography (MCE) is an ionizing radiation-free strategy that can timely evaluate the integrity of myocardial vasculature based on microbubbles and then rapidly acquire and interpret myocardial viability (MV) data for prognostic prediction [10]. MCE can be utilized in the assessment of infarct size and MV because it reflects myocardial microcirculation *via* myocardial perfusion [11]. MCE has been applied to predict prognosis and evaluate coronary microcirculation after PCI in MI patients, particularly STEMI patients [12, 13]. As a mature technology in adult cardiology, stress echocardiography is primarily applied to evaluate regional myocardial function in patients with suspected or diagnosed CAD as it can detect both ischemia and valve disease-induced hemodynamic changes [14]. In this procedure, dobutamine is a commonly used stressor [15], which is a relatively cardio-selective drug [16]. Dobutamine stress echocardiography (DSE) can evaluate MV in patients with chronic LV systolic dysfunction, where non-viable tissues with transmural or non-transmural infarction can be accurately differentiated from stunned or hibernating myocardium according to the presence or absence of contractile responses to dobutamine [17]. Additionally, low-dose dobutamine can increase coronary blood flow and then improve myocardial systolic function [18]. At present, most patients refuse positron emission tomography (PET) owing to its high price and radioactivity. In recent years, research on stress MCE

is limited [19, 20]. After long-term clinical practice and application, low-dose dobutamine is considered safe, and the safety of dobutamine stress MCE has been confirmed in studies [21, 22]. Prior studies have revealed that low-dose dobutamine stress MCE is effective in assessing post-PCI cardiac function in AMI patients and has a diagnostic effect on myocardial ischemia and damage in patients with coronary heart disease [23]. Nevertheless, there is no relevant research on the assessment of long-term prognosis in STEMI patients after PCI with low-dose dobutamine stress MCE. In the present study, low-dose dobutamine stress MCE was utilized to assess myocardial microcirculation perfusion in 70 STEMI patients receiving PCI and to predict the risk of 3-year dismal prognosis after PCI, which can provide data reference and effective guidance for the prediction and management of myocardial microcirculation and all-cause mortality in STEMI patients after PCI.

Materials and methods

Participants

This study included 70 STEMI patients who received PCI at the Fourth Hospital of Changsha from June 2018 to May 2020. In our study, the double-blind method was utilized to control the bias caused by grouping on the experiment, and the randomization method was used to avoid the bias induced by the predictability of treatment assignment when grouping. The inclusion criteria were as follows: (i) patients conforming to the definition of AMI in the 4th edition of the *Fourth Universal Definition of Myocardial Infarction* (2018) jointly formulated by ACC, AHA, ESC, and WHF and the diagnostic criteria of STEMI in the *Guidelines for the Diagnosis and Treatment of Acute ST-segment Elevation Myocardial Infarction* issued by the China Society of Cardiology of Chinese Medical Association in 2015: chest pain ≥ 30 min, a new left bundle branch block, ST-segment elevation (>0.1 mV) in consecutive ECG leads, and elevated levels of serum creatine kinase (CK) or troponin (myocardial damage biomarkers; CK >24 U/L and high-sensitivity cardiac troponin I [hs-cTnI] >0.4 ng/mL); (ii) patients with thrombolysis in myocardial infarction (TIMI) grade 0/1 (no thrombolytic therapy prior to PCI); (iii) patients with cardiopulmonary function of Killip classes I–III; (iv) patients receiving PCI within 24 h after the onset of chest pain and undergoing dobutamine stress MCE before PCI and at 72 h and 6 months after PCI (all patients discontinued β -blockers until 24 h before dobutamine stress MCE); (v) first-episode patients; (vi) patients aged ≥ 18 years; (vii) patients who met the indications for PET and

underwent PET. The exclusion criteria were as follows: (i) patients with left main CAD or severe triple vessel CAD; (ii) patients with persistent tachycardia; (iii) patients with allergy-like reactions to contrast media; (iv) patients with contraindications to antiplatelet or anticoagulant therapy, MCE, or PET; (v) patients combined with severe hepatic or renal impairment, aortic dissection, hemorrhagic cerebrovascular disease, or active hemorrhage in organs; (vi) patients who had undergone thrombolytic therapy; (vii) patients with cardiogenic shock. All experiments in this study were approved by the Ethics Committee of the Fourth Hospital of Changsha and complied with the *Declaration of Helsinki*.

Treatment of patients

Coronary angiography was performed with the Judkins method to determine the arterial stenosis degree. After the location of the infarcted vessel and the extent of stenosis or occlusion were determined with coronary angiography, the appropriate stent was selected based on the internal diameter of the vessel at the lesion. The catheter was withdrawn after PCI. The radial artery was punctured for 6 h of local compression hemostasis, and the femoral artery was punctured for 12–24 h of compression hemostasis. Criteria for surgical success were as follows: residual stenosis of the target vascular lumen <20% and TIMI grade III after stenting. In this study, stenting was successfully completed in all patients, with a surgical success rate of 100%.

Clinical data collection

Baseline data of all participants were obtained at the time of enrollment, encompassing age, gender, body mass index (BMI), smoking history, comorbidities (diabetes mellitus [DM], hypertension, and hyperlipidemia), Killip class, TIMI grade, infarct-related arteries (circumflex artery, anterior descending artery, and right coronary artery), CK-MB, and hs-cTnI.

PET

Indications for PET included staging, grading, and early diagnosis of tumors, localization of primary foci of metastatic tumors, assessment of efficacy and prognosis, cardiovascular diseases, and neurological diseases. PET, which is currently utilized as the gold standard for the detection of viable myocardium [24, 25], was performed at 72 h after PCI. Myocardial segments were categorized into normal myocardium (segments with normal perfusion and metabolism), viable myocardium (segments with reduced perfusion but normal metabolism), and non-viable myocardium (segments with impaired perfusion and metabolism) groups according to the PET results.

Routine echocardiography

Prior to MCE, routine echocardiography was performed using a Philips iE33 color Doppler ultrasound machine equipped with an S5-1 2D probe (frequency: 1–5 MHz). Patients were placed in a left-lateral position and connected with the electrocardiograph. Left ventricular ejection fraction (LVEF) was measured with the biplane Simpson method.

MCE

MCE was carried out with a Philips iE33 color Doppler ultrasound machine equipped with an X3-1 3D probe (frequency: 1–3 MHz) at 72 h and 6 months after PCI. Before MCE, a two-dimensional ECG was conducted, with SonoVue (Bracco Imaging SpA, Milan, Italy) as the contrast medium. Specifically, 59 mg of SonoVue diluted with normal saline (20 mL) was shaken for 20 s to harvest white microbubble suspensions, which were injected into patients *via* the anterior vein of the upper extremity at 1.5 mL/min. After 2–3 min of contrast medium stabilization in the myocardial image, the contrast microbubbles in the myocardium were destroyed by high-mechanical index ultrasound beam emission, and microbubble reperfusion was observed in the view of the heart apex with a mechanical index <0.2. β -blockers and drugs that may affect myocardial contractility were prohibited 24 h before MCE.

Low-dose dobutamine stress MCE

Patients were given low-dose dobutamine at an initial dose of 5 μ g/kg/min which were then elevated to 10 μ g/kg/min and then 20 μ g/kg/min every 3 min. Heart rate and blood pressure were measured, and MCE was performed again with the same settings when the stress dose was reached.

MCE analysis

MCE images were analyzed: myocardial segments with abnormal ventricular wall motion were selected for qualitative analysis. MCE results were scored with the following criteria: 1 score, enhanced uniform echoes suggested good myocardial perfusion; 2 scores, sparse or uneven echoes and subendocardial filling defects represented diminished myocardial perfusion; 3 scores, filling defects marked no myocardial perfusion. An MCE result score of ≤ 2 indicated viable myocardium, whereas myocardial filling defects signified no myocardial viability.

Semi-quantitative analysis of MCE was carried out: (1) uniform and adequate contrast medium display and favorable perfusion (1 score); (2) sparse contrast medium display and weak or partial flaky perfusion (0.5 scores); (3) contrast medium filling defects or no perfusion (0 scores). The semi-quantitative index was statistically analyzed with the contrast enhancement index (CSI), which

was calculated with the following method: the sum of the angiographic scores of the relevant segments was divided by the number of segments.

MCE results were also quantitatively analyzed. The region of interest (ROI) was positioned in the center of the wall of each segment (for the size of the ROI, 5 mm² was set as a standard) to analyze changes in the echo intensity of contrast medium microbubble signals in myocardial tissues over time. The endometrium, epicardium, and papillary muscles were not selected for analysis. QLAB version 10.5 software (Philips, Andover, MA) was utilized to automatically plot the time-perfusion intensity curve and fit the following function: $Y = A \times (1 - e^{-\beta t})$ (A , the peak intensity of the curve, indicating the myocardial blood volume; β , the slope of the curve, representing the myocardial blood flow [MBF] velocity; $A \times \beta$, reflecting MBF) [26–28].

Endpoints and follow-up

Patients were followed up for 3 years at an interval of 3 months. The endpoint event of this study was all-cause mortality within 3 years or until the end of follow-up. The hospital information system was used to collect data during hospitalization, and telephone follow-up was used after discharge to mainly inquire about the post-PCI survival status of patients.

Statistical analysis

Sample size estimation was performed with G*Power 3.1.9.7 (University of Düsseldorf, Düsseldorf, Germany) and a statistical efficiency-based method, and the sample size in this study met the sample size requirements for the independent samples t -test and the paired t -test (Figure S1A–B). Data were statistically analyzed and graphed with SPSS 21.0 statistical software (IBM, Armonk, NY, USA) and GraphPad Prism 8.01 software (GraphPad Software, San Diego, CA, USA). The Shapiro-Wilk test was utilized to test the normality of measurement data. Measurement data conforming to normal distribution were summarized as mean \pm standard deviation, with the independent samples t -test for intergroup comparisons. The paired t -test was utilized for comparisons of measurement data at 72 h and 6 months after PCI. Measurement data not matching normal distribution were presented as median [interquartile range], with the Wilcoxon test for intergroup comparisons. Count data were presented as the number of cases and percentages, and comparisons of count data between two groups were conducted with the chi-square test. Receiver-operating characteristic (ROC) curves were drawn to analyze the value of low-dose dobutamine stress MCE in detecting viable myocardium at 72 h after PCI. The quantitative analysis of MCE was carried out when low-dose dobutamine stress MCE was performed to evaluate myocardial

microcirculation perfusion at 72 h and 6 months after PCI. The semi-quantitative analysis of MCE was conducted when low-dose dobutamine stress MCE was conducted to assess the LV function of STEMI patients after PCI and when the value of low-dose dobutamine stress MCE in assessing long-term prognosis in STEMI patients after PCI was evaluated according to LV function results. Log-rank analysis was performed to assess the 3-year survival of STEMI patients after PCI in the DSE-positive and DSE-negative groups. The difference was considered statistically significant at $p < 0.05$.

Results

Baseline data of the participants

This study involved 70 STEMI patients who underwent PCI, comprising 41 males and 29 females. The patients were aged 45.3 to 79.6 years, with a mean age of 62.5 ± 10.4 years. Among these patients, patients with smoking history accounted for 44.29%, and patients complicated with DM, hypertension, and hyperlipidemia accounted for 41.43%, 25.71%, and 18.57%, respectively. Meanwhile, there were 9 patients with circumflex artery-related infarcts, 33 with anterior descending artery-related infarcts, and 28 with right coronary artery-related infarcts. Additional baseline data are specified in Table 1.

Value of low-dose dobutamine stress MCE in detecting viable myocardium of STEMI patients 72 h after PCI

In our study, PET was utilized for the detection of viable myocardium, and PET and low-dose dobutamine stress MCE were conducted at 72 h after PCI, respectively. According to the PET results, 321 myocardial segments were collected from the blood supply area of the infarcted coronary artery, including 205 segments of viable myocardium and 116 segments of non-viable myocardium. Adverse reactions such as abnormal heart rate, abnormal blood pressure, chest distress, belching, and dizziness were not observed during MCE. Myocardial segments in the blood supply area of the infarcted coronary artery 72 h after PCI were subsequently analyzed with low-dose dobutamine stress MCE, which revealed 190 segments of viable myocardium and 131 segments of non-viable myocardium. ROC was further utilized to analyze the value of low-dose dobutamine stress MCE in the detection of viable myocardium 72 h after PCI, which showed that the area under the ROC curve (AUC) was 0.849, with a sensitivity of 84.39% (173/205) and a specificity of 85.34% (99/116) (Fig. 1).

Value of low-dose dobutamine stress MCE in evaluating myocardial microcirculation perfusion of STEMI patients at 72 h and 6 months after PCI

Further, this study analyzed the value of low-dose dobutamine stress MCE in evaluating myocardial

Table 1 Baseline data of STEMI patients

Item	Values
Gender (n, %)	
Male	41 (58.57%)
Female	29 (41.43%)
Age (years, mean ± SD)	62.5 ± 10.4
BMI (kg/m ² , mean ± SD)	21.58 ± 1.34
Smoking history (n, %)	
Yes	31 (44.29%)
No	39 (55.71%)
Comorbidities (n, %)	
Diabetes mellitus	29 (41.43%)
Hypertension	18 (25.71%)
Hyperlipidemia	13 (18.57%)
Killip class (n, %)	
I	32 (45.71%)
II	27 (38.57%)
III	11 (15.71%)
TIMI grade (n, %)	
0	18 (25.71%)
1	52 (74.29%)
Infarct-related arteries (n, %)	
Circumflex artery	9 (12.86%)
Anterior descending	33 (47.14%)
Right coronary artery	28 (40.00%)
CK-MB (μg/mL, mean ± SD)	8.05 ± 1.06
Hs-cTnI (ng/mL, mean ± SD)	4.39 ± 0.87

Notes STEMI, ST-segment elevation myocardial infarction; SD, standard deviation; BMI, body mass index; TIMI, thrombolysis in myocardial infarction; CK-MB, creatine kinase-myocardial band; hs-cTnI, high-sensitivity cardiac troponin I

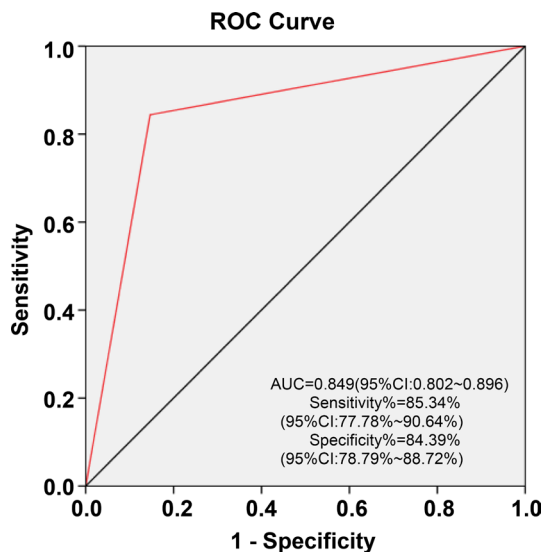


Fig. 1 ROC curve of low-dose dobutamine stress MCE for detecting viable myocardium 72 h after PCI. **Notes** The ROC curve was used to analyze the value of low-dose dobutamine stress MCE in the detection of viable myocardium 72 h after PCI

microcirculation of STEMI patients after PCI. In brief, 321 myocardial segments in the blood supply area of the infarcted coronary artery into viable myocardium ($N=205$ segments) and non-viable myocardium ($N=116$ segments) based on PET findings, and myocardial microcirculation perfusion in the basal or stress state (A , β , and $A \times \beta$ values) at 72 h and 6 months after PCI was quantified with MCE. The data showed that the A , β , and $A \times \beta$ values of viable myocardium at 6 months after PCI were notably higher than the values at 72 h after PCI under either the basal or stress condition (all $p < 0.05$, Fig. 2A-C). However, there were no remarkable differences in the A , β , and $A \times \beta$ values of non-viable myocardium at 72 h and 6 months after PCI (all $p > 0.05$, Fig. 2D-F), which indicated that myocardial microvascular perfusion was substantially restored at 6 months after PCI compared with that at 72 h after PCI. Additionally, this study analyzed microcirculation in different states (basal or stress state) at 72 h and 6 months after PCI. At 72 h after PCI, A , β , and $A \times \beta$ values of either viable or non-viable myocardium were insignificantly different between the basal and stress states (all $p > 0.05$, Fig. 2A-F). At 6 months after PCI, the A and $A \times \beta$ values of viable myocardium were greatly higher in the stress state than in the basal state ($p < 0.05$, Fig. 2A, C), with insignificant differences noted in β values ($p > 0.05$, Fig. 2B), whilst no obvious differences were observed in A , β , and $A \times \beta$ values of non-viable myocardium between the stress and basal states (all $p > 0.05$, Fig. 2D-F). Overall, low-dose dobutamine stress MCE could more accurately evaluate long-term myocardial microcirculation of STEMI patients after PCI.

Value of low-dose dobutamine stress MCE in evaluating LV function recovery of STEMI patients 6 months after PCI

Subsequently, we first compared changes in LVEF at 72 h and 6 months after PCI for analyzing LV functional recovery. The results displayed that LVEF at 6 months after PCI was substantially higher than that at 72 h after PCI ($p < 0.05$, Fig. 3A). To assess the value of dobutamine stress MCE in assessing cardiac function, 70 patients were classified into DSE-positive ($n=39$, an increase or decrease of ≥ 0.2 in CSI after the dobutamine stress test) and DSE-negative ($n=31$, an increase or decrease of < 0.2 in CSI after the dobutamine stress test) groups based on the change in CSI at 6 months after PCI. It was found that the DSE-positive group had remarkably higher LVEF as compared to the DSE-negative group ($57.33 \pm 4.25\%$ vs. $52.69 \pm 5.26\%$) ($p < 0.05$, Fig. 3B). To sum up, low-dose dobutamine stress MCE could effectively evaluate LV function recovery in STEMI patients after PCI.

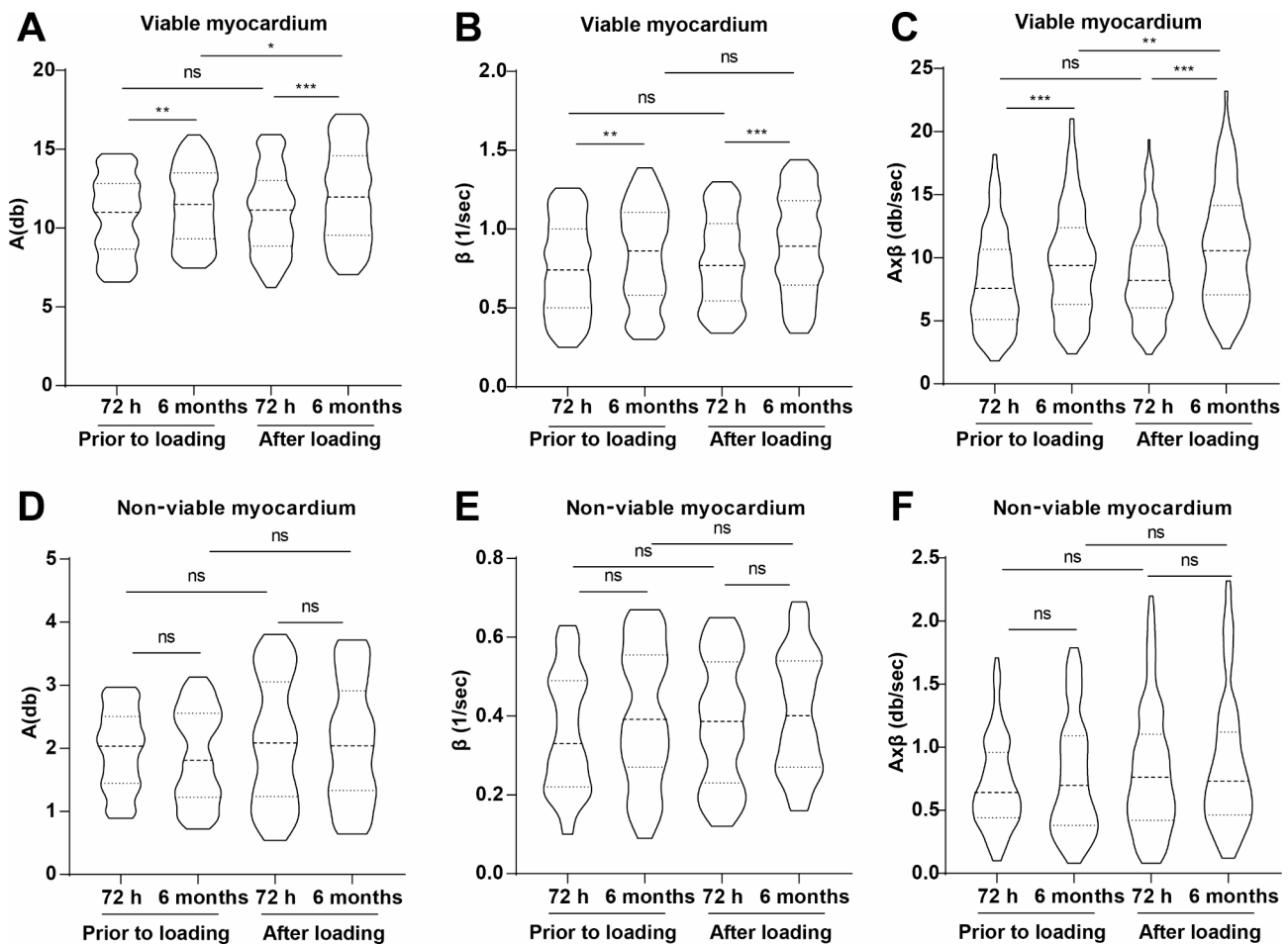


Fig. 2 Evaluation of myocardial microcirculation perfusion at 72 h and 6 months after PCI through low-dose dobutamine stress MCE. *Notes (A-F)* MCE quantitatively analyzed the microcirculation perfusion of viable myocardium (A-C) and non-viable myocardium (D-F) at 72 h and 6 months after PCI. “Prior to loading” refers to the basal state with neither MCE nor low-dose dobutamine stress MCE, and “after loading” refers to the state of low-dose dobutamine stress MCE. A signifies the peak intensity of the curve, indicating the myocardial blood volume. β denotes the slope of the curve, illustrating the myocardial blood flow velocity. $A \times \beta$ reflects the myocardial blood flow. Measurement data conforming to normal distribution were summarized as mean \pm standard deviation, with the independent samples *t*-test for intergroup comparisons. The paired *t*-test was utilized for comparisons of measurement data at 72 h and 6 months after PCI. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; ns, no significance

Predictive value of low-dose dobutamine stress MCE for long-term prognosis of STEMI patients after PCI

Lastly, to assess long-term prognosis, 70 STEMI patients were followed up for 3 years, and the occurrence of all-cause mortality was recorded. Among the patients, 7 and 5 patients were lost to follow-up in the DSE-positive and DSE-negative groups, respectively. Ultimately, 32 STEMI patients in the DSE-positive group and 26 STEMI patients in the DSE-negative group were subjected to the survival analysis. The results of the log-rank analysis demonstrated that long-term survival rates after PCI in the DSE-positive group prominently increased versus that in the DSE-negative group ($p = 0.016$, Fig. 4). Conclusively, low-dose dobutamine stress MCE could predict poor long-term prognosis after PCI in STEMI patients.

Discussion

Although PCI effectively opens infarct-related arteries and recovers TIMI-flow 3 in most STEMI patients, a small but significant population still shows decreased myocardial reperfusion in the successful opening of the obstructed epicardial artery after PCI, which is termed “no-reflow” [29]. The “no-reflow” phenomenon after PCI is linked to elevated myocardial damage and unfavorable prognosis in STEMI patients [30, 31]. Accordingly, it is of significance to promptly and accurately evaluate post-PCI myocardial perfusion in STEMI patients. Herein, this study probed the potential of low-dose dobutamine stress MCE to evaluate the myocardial perfusion, LV function, and long-term survival of STEMI patients. The results unraveled that low-dose dobutamine stress MCE effectively predicted myocardial perfusion, LV function

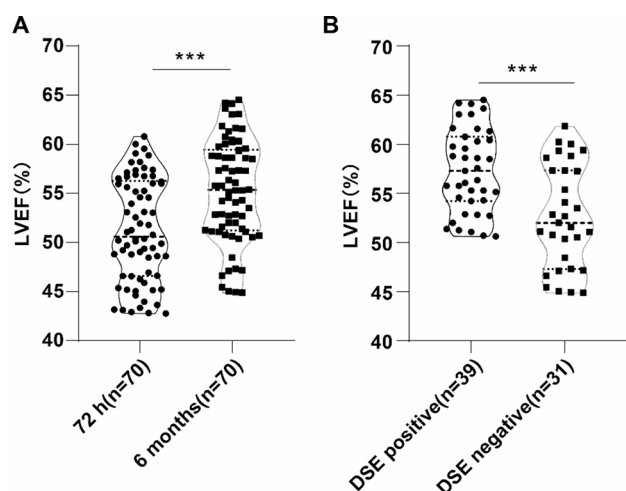


Fig. 3 Evaluation of left ventricular function recovery at 6 months after PCI through low-dose dobutamine stress MCE. Notes (A) Changes in LVEF in STEMI patients at 72 h and 6 months after PCI; (B) LVEF of patients in DSE-positive and DSE-negative groups that were classified according to MCE semi-quantitative analysis of CSI changes. Measurement data were expressed as mean \pm standard deviation. Data in panel A were compared with the paired *t*-test, and data in panel B were compared with the independent samples *t*-test (B). *** $p < 0.001$

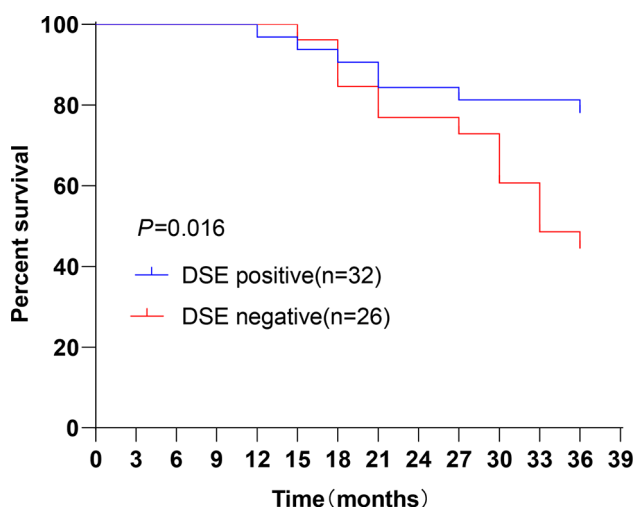


Fig. 4 Survival graph of low-dose dobutamine stress MCE for the prediction of long-term prognosis of STEMI patients after PCI. Notes The log-rank analysis was performed to analyze the 3-year survival of STEMI patients after PCI in the DSE-positive and DSE-negative groups

recovery, and adverse long-term prognosis in STEMI patients after PCI.

MCE can enable visualization of post-AMI myocardial perfusion abnormalities [32], which has the advantages of safety, inexpensiveness, and relatively high image resolution [33]. Additionally, DSE has shown high sensitivity and specificity in MV assessment [34]. Clinically, MCE and DSE are extensively used for detecting viable myocardium and therefore MI [10, 35, 36]. DSE has the disadvantages of subjective wall motion interpretation and

image quality dependence [37]. MCE may only evaluate myocardial microcirculation in the resting state, with a possibility of false positives [28]. Considering the respective disadvantages of these two techniques, our study focused on low-dose dobutamine stress MCE. Our results exhibited that MCE detected 190 segments of viable myocardium and 131 segments of non-viable myocardium and that low-dose dobutamine stress MCE possessed a high AUC in detecting viable myocardium 72 h after PCI with relatively high sensitivity and specificity.

Myocardial microcirculation dysfunction may occur in the majority of STEMI patients after PCI [38]. A recent study reported MCE as a safe and effective technique for the assessment of myocardial microcirculation dysfunction in STEMI patients [13]. Myocardial perfusion parameters, A , β , and $A \times \beta$ values, can reflect myocardial blood flow in AMI patients [39, 40]. With the use of A , β , and $A \times \beta$ values, MCE can accurately evaluate myocardial microcirculation and myocardial perfusion in patients with acute STEMI after PCI [39]. A similar finding was also obtained in our study. Specifically, our quantitative analysis of MCE demonstrated that the A , β , and $A \times \beta$ values of viable myocardium at 6 months after PCI were markedly elevated as compared to values at 72 h after PCI in either the basal or stress state, supporting the promising value of MCE in evaluating post-PCI myocardial microcirculation of STEMI patients. Moreover, Liu et al. observed that changes in MBF and myocardial perfusion scores under low-dose dobutamine stress MCE were highly accurate in predicting myocardial function recovery in CAD patients following revascularization [41]. The research by Lin et al. also revealed low-dose dobutamine stress MCE as an effective evaluation method for post-PCI myocardial microcirculation perfusion in AMI patients [28]. Consistently, our study indicated low-dose dobutamine stress MCE as a more accurate technique in evaluating post-PCI myocardial microcirculation of STEMI patients, as evidenced by substantially higher A and $A \times \beta$ values of viable myocardium at 6 months after PCI in the stress state than in the basal state.

LV dysfunction typically occurs in STEMI patients. LVEF is a marker of LV function, and LVEF can provide risk stratification and treatment guidance for STEMI patients [42, 43]. In our study, LVEF was remarkably elevated at 6 months after PCI compared to that at 72 h after PCI. CSI during low-dose dobutamine stress MCE was previously proposed as a semi-quantitative indicator to assess the LV function of AMI patients [28]. In the current study, patients were arranged into DSE-positive and DSE-negative groups according to changes in CSI after the dobutamine stress test. Greatly higher LVEF was found in the DSE-positive group than in the DSE-negative group, also illustrating low-dose dobutamine stress

MCE as an effective evaluation method for LV function recovery after PCI in STEMI patients. Innovatively, the included patients in this study were followed up for 3 years to evaluate their long-term prognosis. Further survival analysis results displayed substantially higher long-term survival rates of STEMI patients after PCI in the DSE-positive group than in the DSE-negative group. In addition, we observed no adverse reactions (abnormal heart rate and abnormal blood pressure) during low-dose dobutamine stress MCE.

Conclusively, our results unveiled the safe and effective evaluation of low-dose dobutamine stress MCE for myocardial microcirculation perfusion, LV function recovery, and long-term survival in STEMI patients after PCI, highlighting its application potential in assessing the long-term prognosis of CAD after PCI. Notably, this study, for the first time, analyzed the value of low-dose dobutamine stress MCE in assessing the long-term prognosis of AMI patients after PCI, providing useful references for the management of myocardial microcirculation and all-cause mortality in AMI patients after PCI. Of course, limitations existed in this study. First, the present study was a prospective study with an obvious small sample size. Accordingly, large-sample multi-center studies are needed to further validate our findings. Second, this study only included patients with single-vessel CAD. Further research is warranted to excavate the impact of the extent or size of MI on the recovery of coronary microcirculation. Third, although the semi-quantitative analysis of MCE has been confirmed to assess LV function in AMI patients, the method is still somewhat subjective and the results may vary across observers. Fourth, this study focused only on the evaluation of MCE for viable myocardium, myocardial microcirculation perfusion, and LV function and did not explore indicators other than viability indicators that can be provided by this method. Fifth, viable myocardium does not represent the absence of ischemia in this segment. Therefore, the classification of the viable group into ischemic and nonischemic subgroups may be more accurate in assessing the value of low-dose dobutamine stress MCE in assessing post-PCI myocardial microcirculation perfusion. Sixth, DSE is hazardous to patients with recent MI due to their irritable myocardium. As a consequence, the applicability and safety of DSE still needs to be further explored. Seventh, our extensive exclusion criteria may limit the generalizability of the findings to broader patient populations.

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s13019-024-03216-6>.

Supplementary Material 1: Fig. S1 Sample size estimation with G*Power **Notes (A)** Estimation of the sample size required for the

independent samples *t*-test; **(B)** Estimation of the sample size required for the paired *t*-test. Statistical parameters are two-tailed tests with α err prob = 0.05 and $1 - \beta$ err prob = 0.80

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Not applicable.

Author contributions

LL is the guarantors of integrity of the entire study and contributed to the study design; NH contributed to the study concepts, data acquisition, manuscript review; LZL contributed to the clinical studies, statistical analysis; LYL contributed to the literature research, manuscript editing; LL, LZL contributed to the data analysis, the definition of intellectual content; All authors read and approved the final manuscript.

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Data availability

The datasets generated during and analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

All experiments in this study were approved by the Ethics Committee of the Fourth Hospital of Changsha, and the experimentation procedures conformed to the *Declaration of Helsinki*.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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References

1. Reed GW, Rossi JE, Cannon CP. Acute myocardial infarction. *Lancet*. 2017;389(10065):197–210.
2. Reyes-Retana JA, Duque-Ossa LC. Acute myocardial infarction Biosensor: a review from bottom up. *Curr Probl Cardiol*. 2021;46(3):100739.
3. Vogel B, Claessen BE, Arnold SV, Chan D, Cohen DJ, Giannitsis E, et al. ST-segment elevation myocardial infarction. *Nat Rev Dis Primers*. 2019;5(1):39.
4. Konijnenberg LSF, Damman P, Duncker DJ, Kloner RA, Nijveldt R, van Geuns RM, et al. Pathophysiology and diagnosis of coronary microvascular dysfunction in ST-elevation myocardial infarction. *Cardiovasc Res*. 2020;116(4):787–805.
5. Banning AP, Baumbach A, Blackman D, Curzen N, Devadathan S, Fraser D, et al. Percutaneous coronary intervention in the UK: recommendations for good practice 2015. *Heart*. 2015;101(Suppl 3):1–13.
6. Serruys PW, Ono M, Garg S, Hara H, Kawashima H, Pompilio G, et al. Percutaneous coronary revascularization: JACC historical breakthroughs in perspective. *J Am Coll Cardiol*. 2021;78(4):384–407.
7. Qian G, Zhang Y, Dong W, Jiang ZC, Li T, Cheng LQ, et al. Effects of Nicorandil Administration on Infarct size in patients with ST-Segment-Elevation

- myocardial infarction undergoing primary percutaneous coronary intervention: the CHANGE trial. *J Am Heart Assoc.* 2022;11(18):e026232.
8. d'Entremont MA, Alazzoni A, Dzavik V, Sharma V, Overgaard CB, Lemaire-Paquette S, et al. No-reflow after primary percutaneous coronary intervention in patients with ST-elevation myocardial infarction: an angiographic core laboratory analysis of the TOTAL trial. *EuroIntervention.* 2023;19(5):e394–401.
 9. Ciofani JL, Allahwala UK, Scarsini R, Ekmejian A, Banning AP, Bhindi R, et al. No-reflow phenomenon in ST-segment elevation myocardial infarction: still the Achilles' heel of the interventionalist. *Future Cardiol.* 2021;17(2):383–97.
 10. Pradhan J, Senior R. Assessment of myocardial viability by myocardial contrast echocardiography: current perspectives. *Curr Opin Cardiol.* 2019;34(5):495–501.
 11. Wang J, Yang M, Yang Z, Ye L, Luo H, Guo Y. Long-term prognostic value of myocardial viability by myocardial contrast Echocardiography in patients after Acute myocardial infarction: a systematic review and Meta-analysis. *Med (Kaunas).* 2022;58(10).
 12. Hayat SA, Senior R. Myocardial contrast echocardiography in ST elevation myocardial infarction: ready for prime time? *Eur Heart J.* 2008;29(3):299–314.
 13. Wang L, Ma Y, Jin W, Zhu T, Wang J, Yu C, et al. Coronary microcirculation dysfunction evaluated by myocardial contrast echocardiography predicts poor prognosis in patients with ST-segment elevation myocardial infarction after percutaneous coronary intervention. *BMC Cardiovasc Disord.* 2022;22(1):572.
 14. Cifra B, Dragulescu A, Border WL, Mertens L. Stress echocardiography in paediatric cardiology. *Eur Heart J Cardiovasc Imaging.* 2015;16(10):1051–9.
 15. Plonska-Gosciniak E, Gackowski A, Kukulski T, Kasprzak JD, Szyzka A, Braksator W, et al. Stress echocardiography. Part I: stress echocardiography in coronary heart disease. *J Ultrason.* 2019;19(76):45–8.
 16. Mielgo V, Valls i Soler A, Rey-Santano C. Dobutamine in paediatric population: a systematic review in juvenile animal models. *PLoS ONE.* 2014;9(4):e95644.
 17. Khemka A, Sawada SG. Dobutamine echocardiography for assessment of viability in the current era. *Curr Opin Cardiol.* 2019;34(5):484–9.
 18. Tsigrikli L, Kleitsioti P, Dimitriadis F, Sidiropoulos G, Alkagiet S, Efstratiou D, et al. The utility of low-dose-dobutamine stress Echocardiography in patients with heart failure with reduced ejection fraction: an update. *Diagnostics (Basel).* 2023;13:18.
 19. Galiuto L, Locorotondo G, Paraggio L, De Caterina AR, Leone AM, Fedele E, et al. Characterization of microvascular and myocardial damage within perfusion defect area at myocardial contrast echocardiography in the subacute phase of myocardial infarction. *Eur Heart J Cardiovasc Imaging.* 2012;13(2):174–80.
 20. Taghizadeh Asl M, Mandegar MH, Roshanali F, Assadi M. Comparison of stress dobutamine echocardiography and stress dobutamine gated myocardial SPECT for the detection of viable myocardium. *Nucl Med Rev Cent East Eur.* 2014;17(1):18–25.
 21. Aggeli C, Giannopoulos G, Roussakis G, Christoforatos E, Marinou G, Toli C, et al. Safety of myocardial flash-contrast echocardiography in combination with dobutamine stress testing for the detection of ischaemia in 5250 studies. *Heart.* 2008;94(12):1571–7.
 22. Timperley J, Mitchell AR, Thibault H, Mirza IH, Becher H. Safety of contrast dobutamine stress echocardiography: a single center experience. *J Am Soc Echocardiogr.* 2005;18(2):163–7.
 23. Aggeli C, Polyarchou K, Felekos I, Zisimos K, Venieri E, Verveniatis A, et al. Effect of gender on the prognostic value of dobutamine stress myocardial contrast echocardiography. *Hellenic J Cardiol.* 2017;58(6):419–24.
 24. Benz DC, Nagao M, Grani C. Digital Positron emission tomography - making cardiac risk stratification fit for the future. *Int J Cardiol.* 2023;371:486–7.
 25. Treglia G, Piccardo A, Garibotto V. [(18)F]FDOPA positron emission tomography for cardiac innervation imaging: a new way or a dead-end street? *Clin Auton Res.* 2022;32(6):399–401.
 26. Wei K, Jayaweera AR, Firoozan S, Linka A, Skyba DM, Kaul S. Quantification of myocardial blood flow with ultrasound-induced destruction of microbubbles administered as a constant venous infusion. *Circulation.* 1998;97(5):473–83.
 27. Roldan P, Ravi S, Hodovan J, Belcik JT, Heitner SB, Masri A, et al. Myocardial contrast echocardiography assessment of perfusion abnormalities in hypertrophic cardiomyopathy. *Cardiovasc Ultrasound.* 2022;20(1):23.
 28. Lin Y, Guan X, Ren K, Zhu Y, Lu Y, Shang Y. Low-dose dobutamine stress myocardial contrast echocardiography for the evaluation of myocardial microcirculation and prediction of overall cardiac function recovery. *Exp Ther Med.* 2020;20(2):1315–20.
 29. Gupta S, Gupta MM. No reflow phenomenon in percutaneous coronary interventions in ST-segment elevation myocardial infarction. *Indian Heart J.* 2016;68(4):539–51.
 30. Sondergaard FT, Beske RP, Frydland M, Moller JE, Helgestad OKL, Jensen LO, et al. Soluble ST2 in plasma is associated with post-procedural no-or-slow reflow after primary percutaneous coronary intervention in ST-elevation myocardial infarction. *Eur Heart J Acute Cardiovasc Care.* 2023;12(1):48–52.
 31. Bayramoglu A, Hidayet S. Association between pan-immune-inflammation value and no-reflow in patients with ST elevation myocardial infarction undergoing percutaneous coronary intervention. *Scand J Clin Lab Invest.* 2023;83(6):384–9.
 32. Iwakura K, Ito H, Okamura A, Kurotobi T, Koyama Y, Date M, et al. Comparison of two- versus three-dimensional myocardial contrast echocardiography for assessing subendocardial perfusion abnormality after percutaneous coronary intervention in patients with acute myocardial infarction. *Am J Cardiol.* 2007;100(10):1502–10.
 33. Zhou X, Zhi G, Xu Y, Wang J, Yan GH. Estimation of coronary artery stenosis by low-dose adenosine stress real-time myocardial contrast echocardiography: a quantitative study. *Chin Med J (Engl).* 2012;125(10):1795–8.
 34. Valente FX, Gavaia J, Gutierrez L, Rios-Navarro C, Rello P, Maymi M et al. Predictive value of Cardiac magnetic resonance feature tracking after Acute myocardial infarction: a comparison with dobutamine stress Echocardiography. *J Clin Med.* 2021;10(22).
 35. Guo Y, Du GQ, Shen WQ, Du C, He PN, Siyu S. Automatic myocardial infarction detection in contrast echocardiography based on polar residual network. *Comput Methods Programs Biomed.* 2021;198:105791.
 36. Li DY, Hao J, Xia Y, Zhang H, Xu TD, Wang XP, et al. Clinical usefulness of low-dose dobutamine stress real-time myocardial contrast echocardiography for detection of viable myocardium. *J Clin Ultrasound.* 2012;40(5):272–9.
 37. Joyce E, Hoogslag GE, Al Amri I, Debonnaire P, Katsanos S, Bax JJ, et al. Quantitative dobutamine stress Echocardiography using speckle-tracking analysis versus conventional visual analysis for detection of significant coronary artery disease after ST-Segment Elevation myocardial infarction. *J Am Soc Echocardiogr.* 2015;28(12):1379–e891.
 38. Fukunaga M, Fujii K, Kawasaki D, Sawada H, Miki K, Tamaru H, et al. Thermo-dilution-derived coronary blood flow pattern immediately after coronary intervention as a predictor of microcirculatory damage and midterm clinical outcomes in patients with ST-segment-elevation myocardial infarction. *Circ Cardiovasc Interv.* 2014;7(2):149–55.
 39. Lyu WY, Qin CY, Wang XT, Shi SL, Liu HL, Wang JW. The application of myocardial contrast echocardiography in assessing microcirculation perfusion in patients with acute myocardial infarction after PCI. *BMC Cardiovasc Disord.* 2022;22(1):233.
 40. Zhang J, Guan L, Li X, Yang Y, Ma Y, Mu Y. Value of myocardial contrast Echocardiography in detecting Coronary Microcirculatory Dysfunction in Ischemia with non-obstructive coronary artery disease. *Ultrasound Med Biol.* 2023;49(9):2089–94.
 41. Liu C, Xiu C, Xiao X, Ni L, Liu Z, Wang B, et al. Microvascular damage after coronary artery bypass surgery: assessment using dobutamine stress myocardial contrast echocardiography. *Am J Med Sci.* 2014;347(5):387–92.
 42. Ezekowitz JA, Armstrong PW, Granger CB, Theroux P, Stebbins A, Kim RJ, et al. Predicting chronic left ventricular dysfunction 90 days after ST-segment elevation myocardial infarction: an Assessment of Pexelizumab in Acute myocardial infarction (APEX-AMI) Substudy. *Am Heart J.* 2010;160(2):272–8.
 43. Katsi V, Georgiopoulos G, Laina A, Koutli E, Parissis J, Tsioufis C, et al. Left ventricular ejection fraction as therapeutic target: is it the ideal marker? *Heart Fail Rev.* 2017;22(6):641–55.

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