

The value of STE-LDDSE to detect viable myocardium

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Abstract

Objective To explore the value of speckle tracking echocardiography (STE) with low dose dobutamine stress echocardiography (LDDSE) for evaluation of viable myocardium (VM) in the acute ST-elevation myocardial infarction (STEMI) patients with or without type 2 diabetes mellitus (DM). **Methods** Eighty-five hospitalized patients with regional wall motion abnormalities (RWMA) according to routine echocardiography in STEMI, thirty patients with type 2 DM. All of them were underwent STE associated with LDDSE (STE-LDDSE) prior to coronary angiography and percutaneous coronary intervention (PCI). Every segment image was acquired and evaluated by wall-motion analysis. The images of STE-LDDSE were analyzed quantitatively for peak-systolic strain (S) and strain rate (Sr), the short axis of radial strain (RS), radial strain rate (RSr), circumferential strain (CS), circumferential strain rate (CSr) and the long axis of longitudinal strain (LS), longitudinal strain rate (LSr) by using the QLAB software. All patients underwent PCI within one week after completing STE-LDDSE examination, and echocardiograms were reviewed at 1, 3, and 6 months after surgery. **Results** A total of 183 regional wall motion abnormalities (RWMA) were detected in the DM group, of which 117 (63.93%) segments were viable myocardium; 357 RWMA were detected in non DM patients, of which 248 (69.47%) segments of viable myocardium were detected by echocardiography. The sensitivity, accuracy, and specificity of STE-LDDSE in detecting viable myocardium in DM group were 70.94%、77.45%、87.88% ; 92.31%、72.73% and 85.25% for LS and LSr. In the non DM group, the sensitivity, specificity, and accuracy of LS and LSr were 68.95%、92.66%、76.19% ; 77.42%、88.07% and 80.67%, respectively. Further parallel diagnostic tests were conducted on LS and LSr parameters. The sensitivity, specificity, and accuracy of detecting viable myocardium in the DM and non DM groups were 84.62%、45.45%、70.49%, 66.53%、63.30% and 65.55%, respectively, at rest; They were 84.62%、45.45%、70.49%, 66.53%、63.30% and 65.55%, respectively, during low dose dobutamine stress. **Conclusion** STE-LDDSE has a high value of detecting VM. Parallel diagnostic test for LS and LSr is the best choice in detecting VM in the patients with STEMI and is more sensitive for the patients with type 2 DM. It will be more effectively to guide the further treatment and to evaluate the prognosis of the STEMI patients.

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Abstract

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Methods

Eighty-five hospitalized patients with regional wall motion abnormalities (RWMA) according to routine echocardiography in STEMI, thirty patients with type 2 DM. All of them were underwent STE associated with LDDSE (STE-LDDSE) prior to coronary angiography and percutaneous coronary intervention (PCI). Every segment image was acquired and evaluated by wall-motion analysis. The images of STE-LDDSE were analyzed quantitatively for peak-systolic strain (S) and strain rate (Sr), the short axis of radial strain (RS), radial strain rate (RSr), circumferential strain (CS), circumferential strain rate (CSr) and the long axis of longitudinal strain (LS), longitudinal strain rate (LSr) by using the QLAB software. All patients underwent PCI within one week after completing STE-LDDSE examination, and echocardiograms were reviewed at 1, 3, and 6 months after surgery.

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A total of 183 regional wall motion abnormalities (RWMA) were detected in the DM group, of which 117 (63.93%) segments were viable myocardium; 357 RWMA were detected in non DM patients, of which 248 (69.47%) segments of viable myocardium were detected by echocardiography. The sensitivity, accuracy, and specificity of STE-LDDSE in detecting viable myocardium in DM group were 70.94%、77.45%、87.88% ; 92.31%、72.73% and 85.25% for LS and LSr. In the non DM group, the sensitivity, specificity, and accuracy of LS and LSr were 68.95%、92.66%、76.19% ; 77.42%、88.07% and 80.67%, respectively.

Further parallel diagnostic tests were conducted on LS and LSr parameters. The sensitivity, specificity, and accuracy of detecting viable myocardium in the DM and non DM groups were 84.62%、45.45%、70.49%, 66.53%、63.30% and 65.55%, respectively, at rest; They were 84.62%、45.45%、70.49%, 66.53%、63.30% and 65.55%, respectively, during low dose dobutamine stress.

Conclusion

STE-LDDSE has a high value of detecting VM. Parallel diagnostic test for LS and LSr is the best choice in detecting VM in the patients with STEMI and is more sensitive for the patients with type 2 DM. It will be more effectively to guide the further treatment and to evaluate the prognosis of the STEMI patients.

Key words speckle tracking echocardiography; low dose dobutamine stress echocardiography; ST-elevation myocardial infarction; diabetes mellitus; viable myocardium

Introduction

DM is a systemic metabolic disorder, and more than 70% of diabetic patients develop coronary heart disease (CHD), which exhibits a wider range and faster progression of coronary artery disease compared to non-diabetic individuals. The main lesions in CHD occur in the epicardium, whereas in DM, the primary lesions involve the myocardium and microvasculature. When both conditions coexist, the aforementioned lesions may be more extensive and severe. Clinical observations have shown that DM patients with concomitant CHD have a higher prevalence and severity of multi-vessel and diffuse coronary lesions compared to non-diabetic patients^[1-2]

Studies have confirmed that after acute myocardial infarction (AMI), the region of RWMA comprises not only necrotic myocardium but also viable myocardium, including stunned myocardium and hibernating myocardium^[3-4]. So far, there are three main approaches used to identify viable myocardium^[4]: (1) Assessment of myocardial cellular metabolism, including oxidative metabolism, glucose metabolism, and fatty acid metabolism; (2) Evaluation of myocardial perfusion; (3) Monitoring of myocardial contractile reserve. Among these, dobutamine stress echocardiography (DSE) is internationally recognized as the standard method for monitoring myocardial contractile reserve and is widely employed.

At present, STE-LDDSE offers significant advantages over traditional methods for assessing viable myocardium^[5-8]. It mainly tracks the speckles of high-frame-rate two-dimensional images frame by frame, allowing for the calculation and delineation of myocardial motion velocity and deformation. By observing

myocardial motion trajectories, it accurately measures myocardial fiber motion strain, strain rate, and rotation angles. Due to its angle-independent nature, STE can provide more accurate assessments of local and global myocardial function, making it highly valuable for detecting viable myocardium. The combination of STE and LDDSE further enhances the sensitivity and specificity, maximizing the detection of viable myocardium^[9-12].

Results

Basic Clinical Characteristics of Patients

A total of 85 patients were included in the study, including 30 patients in the DM group and 55 patients in the non-DM group. All patients successfully completed the examinations, and satisfactory cardiac ultrasound images were obtained (Fig. 1A and B). No malignant arrhythmias or cardiovascular events occurred during the entire examination process.

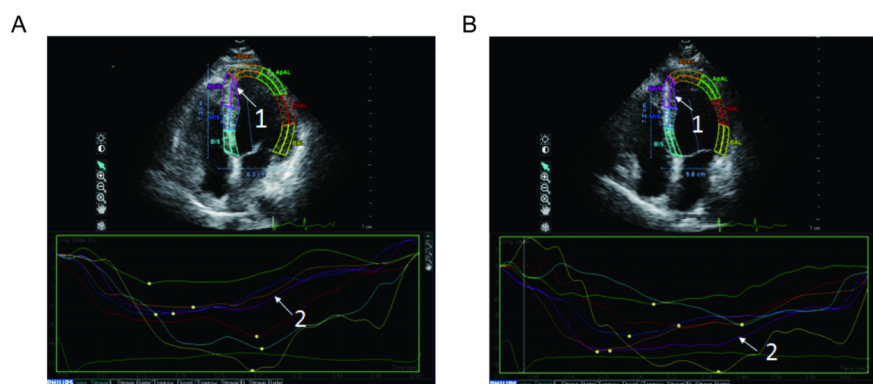


Figure 1 STE method for measuring LSr

(A) represents the pre-LDDSE condition, while (B) shows the post-LDDSE condition. Arrow 1 indicates the apical region of the interventricular septum, and arrow 2 represents the time curve of peak LS during systole in the apical region of the interventricular septum

Changes in Hemodynamic Parameters pre/post LDDSE

The comparison of heart rate and blood pressure pre/post LDDSE in the 85 patients (Table S1). The results showed an increase in heart rate after medication, while blood pressure did not show significant changes.

Analysis of Echocardiographic Wall Motion

A total of 1,445 segments from the 85 patients were included in the study, including 540 segments with RWMA. After LDDSE in the DM group, 119 segments were classified as viable myocardium, and 64 segments were classified as non-viable myocardium. In the non-DM group, 189 segments were classified as viable myocardium, and 168 segments were classified as non-viable myocardium (Table S2).

Follow-up echocardiography was performed at 1, 3, and 6 months after PCI. Based on the "gold standard", 540 segments were followed up, which 365 segments classified as viable myocardium and 175 segments classified as non-viable myocardium. Among the 183 segments followed up in the DM group, which 117 segments were classified as viable myocardium and 66 segments were classified as non-viable myocardium. In the non-DM group, 357 segments were followed up, which 248 segments classified as viable myocardium and 109 segments classified as non-viable myocardium (Table S3).

Comparison with the "gold standard" showed that the sensitivity, specificity, and accuracy of LDDSE semi-quantitative visual assessment for evaluating viable myocardium in the DM group were 70.09%, 43.94%, and 60.66%, respectively. In the non-DM group, the sensitivity, specificity, and accuracy were 55.65%, 53.21%,

and 54.90%, respectively. The DM group had higher sensitivity and accuracy compared to the non-DM group, with statistically significant differences ($P < 0.05$). However, the specificity was lower in the DM group compared to the non-DM group, with statistically significant differences ($P < 0.05$).

The Value of STE-LDDSE in Evaluating Viable Myocardium

It involves quantitative analysis of S and Sr parameters in 540 segments with RWMA by QLAB 8.1 software. Binary logistic regression analysis was performed to evaluate the value of different S and Sr parameters at rest for detecting viable myocardium. The results showed that CS, LS, and LSr had significant value ($P < 0.05$) in detecting viable myocardium (Table 1).

factor				B				P value			
RSr _{rest}	CS _{rest}	LS _{rest}	LSr _{rest}	-1.310	0.223	0.155	0.941	0.001	0.001	0.009	0.022

Table 1: The value of using binary logistic stepwise regression analysis to detect viable myocardium using different S and Sr parameters in the resting state.

Subsequently, LS, LSr and ROC curves were plotted to determine the optimal cutoff points for detecting viable myocardium using STE. Accordingly, sensitivity, specificity, and accuracy were calculated (Fig. 2A-D, Table 2 and 3).

In the DM group, the cutoff point for LS_{rest} was determined to be -13.27, with 46 out of 117 segments classified as viable myocardium (LS_{rest} [?] -13.27) and 71 segments as non-viable myocardium (LS_{rest} > -13.27) according to the gold standard. Similarly, for LS_{LDDSE} in the DM group, the cutoff point was -13.81, with 83 segments classified as viable myocardium (LS_{LDDSE} [?] -13.81) and 34 segments as non-viable myocardium (LS_{LDDSE} > -13.81). In terms of LSr_{rest}, the cutoff point was -0.875, resulting in 98 segments classified as viable myocardium (LSr_{rest} [?] -0.875) and 19 segments as non-viable myocardium (LSr_{rest} > -0.875) according to the gold standard. In the DM group, LSr_{LDDSE} had a cutoff point of -1.12, with 108 segments classified as viable myocardium (LSr_{LDDSE} [?] -1.12) and 9 segments as non-viable myocardium (LSr_{LDDSE} > -1.12).

In the non-DM group, the cutoff point for LS_{rest} was -12.33, with 123 out of 248 segments classified as viable myocardium (LS_{rest} [?] -12.33) and 125 segments as non-viable myocardium (LS_{rest} > -12.33) according to the gold standard. Similarly, for LS_{LDDSE} in the non-DM group, the cutoff point was -14.075, with 171 segments classified as viable myocardium (LS_{LDDSE} [?] -14.075) and 77 segments as non-viable myocardium (LS_{LDDSE} > -14.075). Regarding LSr_{rest}, the cutoff point was -1.075, resulting in 156 segments classified as viable myocardium (LSr_{rest} [?] -1.075) and 92 segments as non-viable myocardium (LSr_{rest} > -1.075) according to the gold standard. In the non-DM group, LSr_{LDDSE} had a cutoff point of -1.305, with 192 segments classified as viable myocardium (LSr_{LDDSE} [?] -1.305) and 56 segments as non-viable myocardium (LSr_{LDDSE} > -1.305) according to the gold standard.

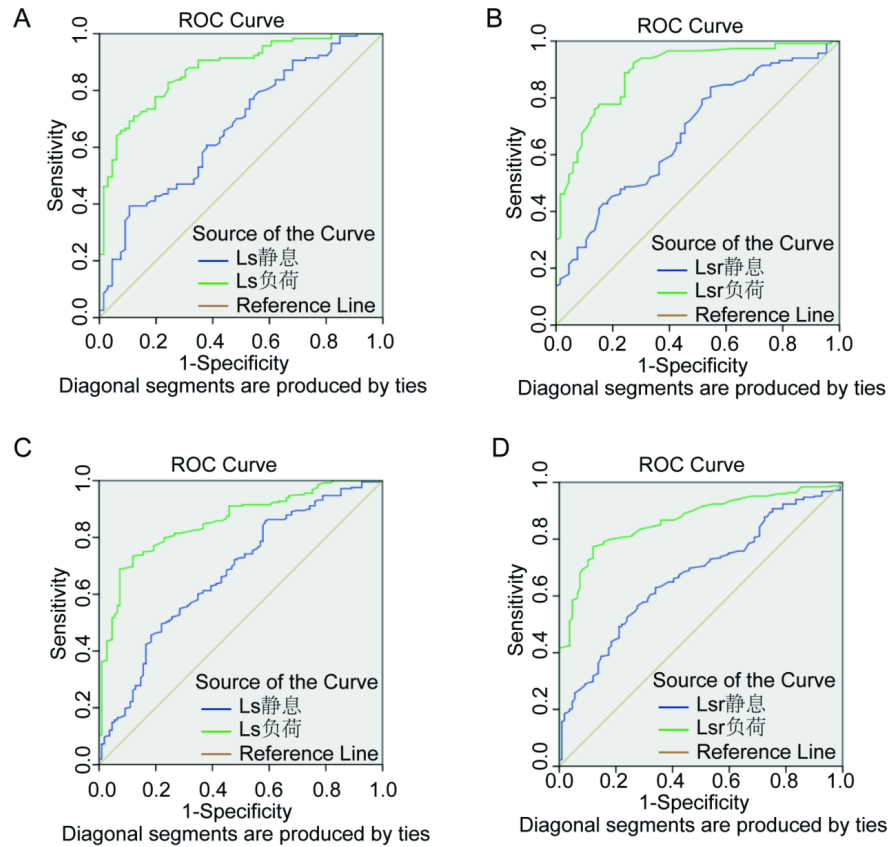


Figure 2 ROC curve for detecting viable myocardium

and (B) display the ROC curves of LS and LSr in the DM group for detecting viable myocardium during resting and LDDSE. (C) and (D) show the ROC curves of LS and LSr in the non-DM group for detecting viable myocardium during resting and LDDSE.

status	sensibility (%)	sensibility (%)	specificity (%)	specificity (%)	accuracy (%)	accuracy (%)
	DM	non-DM	DM	non-DM	DM	non-DM
LS _{rest}	39.32 [§]	49.60	89.39 [§]	77.98	57.38 ^Δ	58.26
LS _{LDDSE}	70.94 ^Δ	68.95	87.88 [§]	92.66	77.45 ^Δ	76.19
McNemar's ²	28.8	30.681	0	14.062	26.327	10.92
P	8.025e-08	3.042e-08	1	0.0001768	2.882e-07	0.0009511

[§]DM compared with non-DM, $P < 0.05$, ^Δ Compare with resting, $P > 0.05$

Table 2: The value of detecting LS parameters in STE for diagnosing viable myocardium.

status	sensibility (%)	sensibility (%)	specificity (%)	specificity (%)	accuracy (%)	accuracy (%)
	DM	non-DM	DM	non-DM	DM	non-DM
LSr _{rest}	83.76 [§]	62.90	45.45 [§]	66.06	69.95 [§]	63.87
LSr _{LDDSE}	92.31 [§]	77.42	72.73 [§]	88.07	85.25 [§]	80.67
McNemar's ²	22.042	16.118	12.042	22.042	1.0652	1.21
P	2.668e-06	5.95e-05	0.0005202	2.668e-06	0.302	0.2713

[§]DM compared with non-DM, $P < 0.05$, ^Δ Compare with resting, $P > 0.05$

Table 3: The value of detecting LSR parameters in STE for diagnosing viable myocardium.

Further parallel diagnostic testing was performed on the LS and LSR parameters at rest. In the DM group, the sensitivity, specificity, and accuracy were found to be 84.62%, 45.45%, and 70.49%, respectively. In the non-DM group, the sensitivity, specificity, and accuracy were 66.53%, 63.30%, and 65.55%, respectively. The DM group showed higher sensitivity and accuracy compared to the non-DM group, with statistically significant differences. However, the DM group had lower specificity compared to the non-DM group, also with statistically significant differences (Table 4 and 6). Parallel diagnostic testing was also conducted on the LS and LSR parameters under stress conditions. In the DM group, the sensitivity, specificity, and accuracy were 92.31%, 60.70%, and 84.15%, respectively. In the non-DM group, the sensitivity, specificity, and accuracy were 84.27%, 81.65%, and 83.47%, respectively (Table 5 and 6). The DM group exhibited higher sensitivity and accuracy compared to the non-DM group, with statistically significant differences. However, the DM group had lower specificity compared to the non-DM group, also with statistically significant differences. The accuracy was higher in the DM group, but the difference was not statistically significant.

In the DM group, STE demonstrated higher sensitivity, specificity, and accuracy for detecting viable myocardium under stress conditions compared to rest. Additionally, STE at rest showed higher sensitivity and accuracy compared to the semi-quantitative visual assessment of LDDSE, with statistically significant differences. The specificity of STE at rest was higher than that of LDDSE, but the difference was not statistically significant. In the non-DM group, STE at stress showed higher sensitivity, specificity, and accuracy for detecting viable myocardium compared to rest, with statistically significant differences. STE at rest also exhibited higher sensitivity, specificity, and accuracy compared to LDDSE, with statistically significant differences (Table 6).

LS _{rest} + LSR _{rest}	gold standard viable myocardium	gold standard Non-viable myocardium	total	total
viable myocardium ^a	99	36	36	135
viable myocardium ^b	165	40	40	205
Non-viable myocardium ^a	18	30	30	48
Non-viable myocardium ^b	83	69	69	152
total ^a	117	66	66	183
total ^b	248	109	109	357

^a DM, ^b non-DM

Table 4: Conducting parallel diagnostic trials using LS_{rest} and LSR_{rest} in combination to detect viable myocardium.

LS _{LDDSE} + LSR _{LDDSE}	gold standard viable myocardium	gold standard viable myocardium	gold standard Non-viable myocardium	total
viable myocardium ^a	108	20	20	128
viable myocardium ^b	209	20	20	229
Non-viable myocardium ^a	9	46	46	55
Non-viable myocardium ^b	39	89	89	128
total ^a	117	66	66	183
total ^b	248	109	109	357

^aDM, ^b non-DM

Table 5: Conducting parallel diagnostic trials using LS_{LDDSE} and LSR_{LDDSE} in combination to

detect viable myocardium.

status	sensibility (%)	specificity (%)	accuracy (%)
LDDSE semi-quantitative ^a LDDSE semi-quantitative ^b	70.09 ^{\$} 55.69	43.94 ^{\$} 53.21	60.66 54.90
Resting STE ^a Resting STE ^b	84.62 ^{*\$} 66.53 [*]	45.45 [#] 63.30 [*]	70.49 [*] 65.55 [*]
STE+LDDSE ^a STE+LDDSE ^b	92.31 ^{*Δ} 84.27 ^{*Δ}	60.70 ^{*Δ} 81.65 ^{*Δ}	84.15 ^{*Δ} 83.47 ^{*Δ}

^a DM, ^{*} compared with LDDSE semi-quantitative, $P < 0.05$, [#] compared with LDDSE semi-quantitative, $P > 0.05$, ^Δ $P < 0.05$ compared to resting time; ^b non-DM, ^{*} compared with LDDSE semi-quantitative, $P < 0.05$, ^Δ $P < 0.05$ compared to resting time

^{\$}DM compared with non-DM, $P < 0.05$

Table 6: The value of different diagnostic methods in diagnosing viable myocardium

Reproducibility Test

To assess inter-observer variability, two experienced ultrasound examiners analyzed S and Sr parameters for 39 RWMA segments in 6 randomly selected subjects, resulting in an inter-observer variability of 5.3%. Intra-observer variability was assessed by having the same ultrasound examiner analyze S and Sr parameters for 50 RWMA segments in 8 randomly selected subjects, resulting in an intra-observer variability of 4.9%. These findings indicate good reproducibility of the STE measurements.

Discussion

Recent studies have highlighted the presence of viable myocardium, including stunned and hibernating myocardium, within areas of RWMA after AMI. Viable myocardium refers to myocardial tissue that can recover its function, either partially or completely, upon restoration of blood supply. Effective revascularization can lead to functional recovery of viable myocardium, improving clinical symptoms and prognosis. On the other hand, non-viable myocardium does not regain its function even with successful revascularization. Therefore, the assessment of myocardial viability is crucial for guiding treatment decisions in patients with STEMI. The improvement of RWMA contraction function after PCI is widely regarded as the "gold standard" for determining viable myocardium^[13].

It is important to note that this study had a small sample size and focused solely on RWMA, which may have limited the detection of viable myocardium in segments with normal wall motion. To enhance the study's validity and generalizability, it is recommended to expand the sample size in future research. Additionally, the follow-up echocardiography assessed improvement in wall motion compared to baseline, considering an improvement of [?]1 grade as indicative of viable myocardium. However, further analysis comparing improvements of [?]1 grade to improvements of [?]2 grades or more was not conducted due to the limited number of eligible segments.

Future studies should consider including segments with normal wall motion to avoid potential underdiagnosis of viable myocardium. Additionally, exploring more comprehensive criteria for assessing viable myocardium, such as improvements of [?]2 grades or more, could provide further insights into the extent of functional recovery. These considerations would contribute to a more comprehensive understanding of myocardial viability assessment and its implications for clinical decision-making.

STE can track the movement of the myocardium by recognizing the echo-speckle signal of the myocardium in the image. This technology can evaluate the myocardial segmental strain from multiple directions without angle dependence, and can evaluate the local or global myocardial function changes. The research showed that longitudinal peak strain decreased during the acute phase and LS increased after contraction in patients with ST segment elevation myocardial infarction. It was concluded that the best indexes for evaluating transmural infarction in cardiac myotameric segments were longitudinal peak strain and post-systolic LS, with truncation values of -13% (AUC=0.86) and 8% (AUC=0.84), respectively, and these two indexes could

well predict the improvement of myocardial function 6 months later^[14]. Meanwhile, some scholars have applied three-dimensional speckle tracking imaging to evaluate the viable myocardium of myocardial infarction patients, and found that the cutoff value, sensitivity, and specificity of segmental radial strain detection for survival myocardium were 11.1%, 0.951, and 0.534, respectively. The cutoff value, sensitivity, and specificity of LS were 14.3%, 0.652, and 0.657, respectively. The cutoff value, sensitivity, and specificity of area strain were 23.2%, 0.915, and 0.828, respectively. Among them, the sensitivity and specificity of area strain were higher^[15]. However, the current frame rate of 3D strain imaging is still not high enough, and some useful information may be lost.

LDDSE is currently internationally recognized as the standard method for detecting the reserve of viable myocardial contractile function. The improvement of RWMA segments in resting echocardiography after LDDSE indicates the presence of viable myocardium in that segment. Dobutamine (dobu) is a synthetic catecholamine, which has a relative excitatory effect on β_1 receptor, but a weak excitatory effect on β_2 receptor and α receptor. Small dose of dobu([?]10 ug/kg/min) mainly excites β_1 receptor, has little effect on blood pressure and heart rate, enhances myocardial contractility and induces myocardial ischemia, which has important value in evaluating myocardial survival. In 1997, the using of LDDSE to detect myocardial viability in patients with acute myocardial infarction has been reported to have objective sensitivity and accuracy^[16].

The development of imaging technology has provided an important method for evaluating the viable myocardium of myocardial infarction patients. Currently, there are many methods available, and combined with clinical research, a single method has limited diagnostic value. Therefore, clinical practice is gradually inclined towards joint diagnostic evaluation. Both of these methods are non-invasive and highly feasible methods for detecting viable myocardial muscle. The sensitivity, specificity and accuracy of SET-LDDSE were significantly improved compared with the resting state. Studies have demonstrated that STE is accurate, reliable, and reproducible, with little intra-observer and inter-observer variation. Compare the diagnostic results with the "gold standard", the study results showed that STE-LDDSE had great value in the diagnostic accuracy, specificity and sensitivity of viable myocardium in patients with myocardial infarction, suggesting that STE-LDDSE should be the first choice in the evaluation of viable myocardium in patients with myocardial infarction.

In summary, compared to traditional and single examination methods, STE-LDDSE has higher sensitivity, specificity, and accuracy, which is more helpful in guiding patients to effectively evaluate viable myocardium before PCI, and has a certain guiding role in blood vessel reconstruction and prognosis.

Conclusion

STE-LDDSE detection has certain clinical value in assessing the viability of myocardium in STEMI patients, superior to semi-quantitative visual estimation of LDDSE and resting STE.

STE-LDDSE detection is more sensitive in assessing the viability of myocardium in DM patients with concurrent STEMI compared to non-DM patients.

3. Preoperative STE-LDDSE detection in STEMI patients is safe and feasible for assessing the viability of myocardium before coronary revascularization, providing certain guidance for reestablishing blood flow.

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Materials and Methods

Reagents

Dobutamine: Shanghai First Biochemical Pharmaceutical Co., Ltd., 20mg:2ml*10 vials, National Drug Approval Number H3102190.

Statistical Analysis

SPSS 16.0 statistical analysis software was used for statistical analysis. All continuous data were expressed as mean $\pm$ standard deviation ($\pm$ S). Paired data following a normal distribution were analyzed using t-tests, while independent samples were analyzed using independent sample t-tests. Binary logistic regression analysis was performed to select valuable S and Sr parameters for detecting viable myocardium. Receiver operating characteristic (ROC) curves were used to calculate the area under the curve (AUC) and determine

the optimal cutoff points, sensitivity, specificity, and accuracy for diagnosing viable myocardium. Chi-square test was used for intergroup comparison of rates. A p-value $[?]0.05$ was considered statistically significant, with a significance level of $\alpha=0.05$.

Additional methods can be found in SI Appendix, SI Materials and Methods.

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AUTHOR CONTRIBUTIONS

Author contributions: W.Q., and Y.M. designed research; W.Q., R.Z., T.C. and Y.M.; provided samples; X.Z., and Y.M.; performed research; W.Q., and Y.M. analyzed data; W.Q., and Y.M. wrote the paper.

COMPETING INTERESTS

The authors declare no competing interests.