

# Value of three-dimensional strain parameters for predicting left ventricular remodeling after ST-elevation myocardial infarction

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**Abstract** This study was to evaluate the value of multi-directional strain parameters derived from three-dimensional (3D) speckle tracking echocardiography (STE) for predicting left ventricular (LV) remodeling after ST-elevation myocardial infarction (STEMI) treated with primary percutaneous coronary intervention (PCI) compared with that of two-dimensional (2D) global longitudinal strain (GLS). A total of 110 patients (mean age,  $54 \pm 9$  years) after STEMI treated with primary PCI were enrolled in our study. At baseline (within 24 h after PCI), standard 2D echocardiography, 2D STE and 3D STE were performed to acquire the conventional echocardiographic parameters and strain parameters. At 3-month follow-up, standard 2D echocardiography was repeated to all the patients to determine LV remodeling, which was defined as a 20% increase in LV end-diastolic volume. At 3-month follow-up, LV remodeling occurred in 26 patients (24%). Compared with patients without LV remodeling, patients with remodeling had significantly reduced 2D GLS ( $-12.5 \pm 3.2\%$  vs  $-15.0 \pm 3.1\%$ ,

$p < 0.001$ ), 3D GLS ( $-9.9 \pm 2.2\%$  vs  $-13.1 \pm 2.7\%$ ,  $p < 0.001$ ), 3D global area strain (GAS) ( $-20.3 \pm 3.9\%$  vs  $-23.3 \pm 4.8\%$ ,  $p = 0.005$ ) and 3D global radial strain (GRS) ( $29.0 \pm 7.4\%$  vs  $34.3 \pm 8.5\%$ ,  $p = 0.007$ ) at baseline, but there is no significant difference in 3D global circumferential strain (GCS) ( $-12.7 \pm 2.9\%$  vs  $-13.0 \pm 3.2\%$ ,  $p = 0.822$ ). Separated multivariate analysis shows that 2D GLS, 3D GLS, 3D GAS and 3D GRS all can be independent predictors of LV remodeling. However, receiver-operating characteristic curve analysis showed that the area under the curve of 3D GLS (0.82) for predicting LV remodeling was significantly higher than that of 2D GLS (0.72,  $p = 0.034$ ), 3D GAS (0.68,  $p < 0.001$ ) and 3D GRS (0.68,  $p < 0.001$ ). In patients after STEMI, 2D GLS, 3D GLS, 3D GAS and 3D GRS but not 3D GCS measured after primary PCI are independent predictors of LV remodeling and 3D GLS is the most powerful predictor among them.

**Keywords** Three-dimensional speckle tracking echocardiography · Two-dimensional speckle tracking echocardiography · Left ventricular remodeling · ST-elevation myocardial infarction

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## Introduction

Due to the widespread use of percutaneous coronary intervention (PCI) treatment, the life quality of acute myocardial infarction (AMI) patients has been significantly improved [1]. However, despite successful early reperfusion therapy and secondary prevention therapy, patients still face a high risk of left ventricular (LV) remodeling after myocardial infarction (MI) [2]. LV remodeling after MI is a complex process, including expansion in infarct region, hypertrophy and progressive ventricular dilation in non-infarct region

[3]. It is a precursor for the development of heart failure (HF) and an important prognostic indicator of mortality [4]. Therefore, LV remodeling had been considered a primary target for treatment after AMI. Previous studies had shown that cardiac rehabilitation and pharmacological treatment could attenuated the LV remodeling after AMI, and they had been also recommended as effective interventions in the guideline [5]. However, it is the precondition of clinical intervention to identify the patients who are more likely to experience LV remodeling so that we can optimize risk stratification and implementation of individualized treatment plan at follow-up.

Because the speckle tracking echocardiography (STE) technique is one noninvasive, economical and practical method over other imaging technologies [6], it has been used to evaluate the LV remodeling. Previous studies had proved the ability of global longitudinal strain (GLS) measured by two-dimensional (2D) STE to predict LV remodeling [7, 8]. However, 2D STE has the limitation of plane-dependency, which may result in noise and reduced accuracy [9]. Recent experimental and clinical studies had shown that the newly developed STE, three-dimensional (3D) STE, is superior to 2D STE in the evaluations of myocardial deformation [10–12]. 3D STE can track global and regional strain parameters in a 3D full-volume LV data, which may overcome the limitation of 2D STE. By 3D STE, global and regional circumferential strain (CS) and radial strain (RS) can be simultaneously acquired with longitudinal strain (LS). Moreover, 3D STE also provide a new strain parameter named area strain (AS), which combines the analysis of both longitudinal and circumferential deformation and reflects the myocardial area change ratio [13]. However, whether GLS assessed by 3D STE is superior to that assessed by 2D STE for predicting LV remodeling is not clear. In addition, few studies explore the ability of global strain parameters derived from 3D STE in predicting LV remodeling.

Therefore, the aims of this study were to evaluate the value of multi-directional strain parameters derived from 3D STE and 2D GLS in predicting LV remodeling after STEMI and determine which strain is more powerful in this purpose.

## Methodology

### Study populations

This prospective cohort study was conducted at the Cardiology Department in the General Hospital of Guangzhou Military Command of People's Liberation Army (PLA) in Guangzhou, Guangdong Province, China, between June 2015 and December 2015. Patients with first STEMI after

primary PCI were enrolled. The inclusion criteria were as follows: (1) age 20 to 70 years, (2) established STEMI based on recent guidelines [5], (3) received revascularization of infarct-related artery (IRA) with primary PCI within 24 h of chest pain onset. The exclusion criteria were: previous myocardial infarction, previous PCI or coronary artery bypass, thrombolytic therapies before PCI, dilated cardiomyopathy, significant valvular heart disease, atrial fibrillation, malignant arrhythmia, cardiac shock, chronic lung disease, or neoplastic disease.

131 patients initially satisfied the eligibility criteria in our study. 21 patients were further excluded: 11 patients were excluded due to inadequate myocardial tracking (define as >2 non-visualized segments) (n=7 both in 2D and 3D mode; n=4 only in the 3D mode), 9 patients did not agree to participate, and 1 patient died during follow-up. As a result, the final study population consisted in 110 patients.

### Study protocol

At baseline (within 24 h after PCI), standard two-dimensional echocardiography, 2D STE and 3D STE were performed to acquire the conventional echocardiographic parameters and strain parameters. At 3-month follow-up, standard two-dimensional echocardiography was repeated. We defined the LV remodeling at three months as an increase in LV end-diastolic volumes (LVEDV) of greater than 20%. Previous studies have demonstrated that this criterion would be sufficient to confirm LV remodeling [14–16].

All the patients received the optimized therapy according to the recent guidelines [5]. The study protocol was reviewed and approved by Ethics Committee of General Hospital of Guangzhou Military Command of PLA and we had obtained the informed consent of the patients.

### Clinical data

After admission, clinical data were prospectively recorded and included: (1) demographics: age, gender; (2) cardiovascular risk factors: hypertension, diabetes, smoke; (3) clinical and laboratory evaluation: weight, height, time to perfusion, peak cardiac troponin I (cTnI), serum creatinine (Scr); (4) medication during the follow-up period. Then, body mass index (BMI), estimated glomerular filtration rate (eGFR), and body surface area (BSA) were calculated by these formulas:  $BMI (kg/m^2) = weight/height^2$ ,  $BSA (m^2) = 0.0061 \times height (cm) + 0.0124 \times weight(kg) - 0.0099$ , and  $eGFR (ml/min/1.73 m^2) = 86 \times [Scr(\mu mol/L) \times 0.0113]^{-1.154} \times age^{-0.203} \times (0.742 \text{ if female}) \times (1.233 \text{ if Chinese})$ .

## Angiographic assessment

Coronary angiography (CAG) was performed to detect the coronary lesions with a digital subtraction angiography machine (Allura Xper FD20, Philips Medical Systems Nederland B.V.). The IRA was confirmed by doctors based on the result of CAG and electrocardiography. Subsequent PCI was performed to restore blood flow in the IRA. During PCI, final thrombolysis in myocardial infarction (TIMI) flow grades were assessed.

## Echocardiography

All of echocardiography examination was performed using a Vivid E9 ultrasound machine (GE Healthcare, Horten, Norway). Two-dimensional echocardiography data was acquired by using a M5S-D probe and three-dimensional echocardiography data was acquired by using a 4D volume probe (4 V-D). All datasets were stored and analyzed by a background processing workstation EchoPAC 112 (GE Medical System, Horten, Norway). Image acquisition was performed with patients connected to the ECG at the left lateral decubitus position.

### Standard two-dimensional echocardiography

Standard two-dimensional echocardiography was performed to obtain morphological and conventional parameters in parasternal long axis, short axis, and apical four-chamber views. LV internal dimension in diastole (LVIDd), ventricular septal thickness in diastole (VSTd), and LV posterior wall thickness (LVPWd) were measured according to the recommendations of the American Society of Echocardiography. LV mass (LVM) was calculated by Devereux formula [17]:  $LVM(g) = 0.80 \times 1.04 \times [(VSTd + LVIDd + PWTd)^3 - (LVIDd)^3] + 0.6$ . After that, LV mass index (LVMI) was calculated by dividing LVM by BSA. LV end-systolic volumes (LVESV), LV end-diastolic volumes (LVEDV) and LV ejection fraction (LVEF) were measured using the 2D Simpson biplane method. A 16-segment LV model as recommended by the American Society of Echocardiography was used to calculate the wall motion score index (WMSI) [18]. Every segment was evaluated and scored (normokinetic = 1; hypokinetic = 2; akinetic = 3; dyskinetic = 4). WMSI was calculated by averaging all the regional scores.

### Two-dimensional speckle tracking echocardiography

2D STE images were performed by using 3 consecutive cardiac cycle images in apical four-chamber, two-chamber and apical long-axis view with frame rate of 50 to 70 frames/sec. A commercially available software “2DE Auto

LVQ” of EchoPAC 112 was used for 2D STE analysis. After the LV endocardial border was manually traced in three apical views, the 2D GLS were calculated by averaging all the values of the regional peak longitudinal strain [19].

### Three-dimensional speckle tracking echocardiography

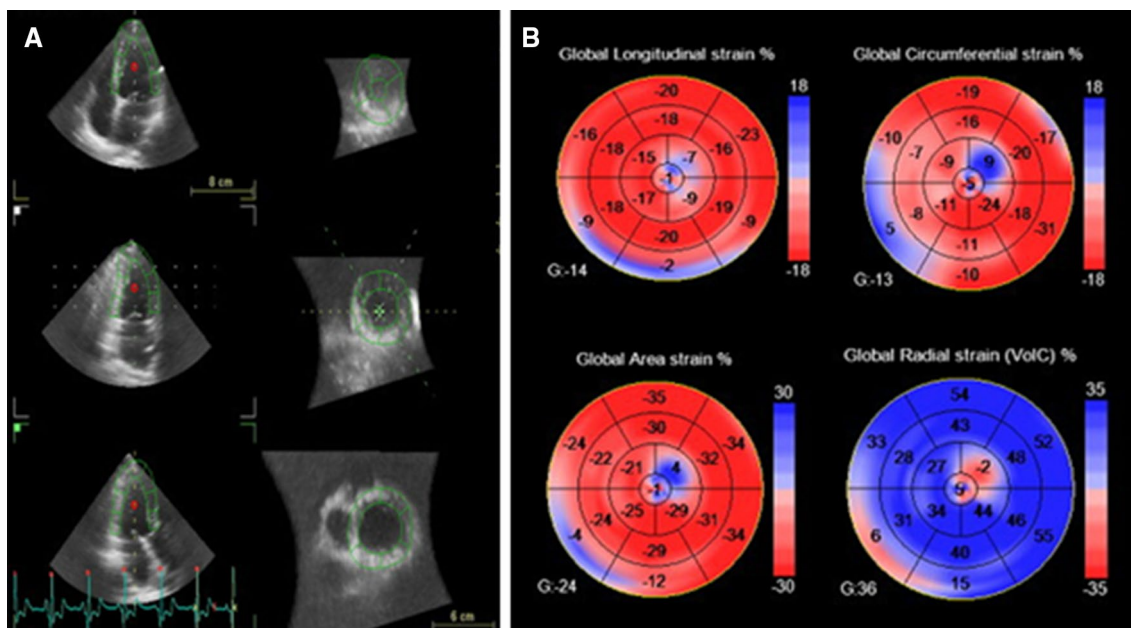
In the 3D mode, a full-volume dataset of LV with 4 to 6 consecutive cardiac cycles was obtained and stored from an apical four-chamber view. The frame rate was higher than 30 frames/sec. Then the dataset was analyzed by the “4D auto LVQ” software of EchoPAC 112. The software automatically identified the LV endocardial and epicardial border in the four-, two-, three-apical views and short-axis views. After that, a region of interest (ROI) including the entire myocardial wall was created. Myocardial deformation was therefore analyzed by speckle tracking within the ROI [20]. Subsequently, LV 3D global longitudinal strain (GLS), global circumferential strain (GCS), and global area strain (GAS), and global radial strain (GRS) were calculated as the weighted average of the regional peak strain values from the 17 myocardial segment (Fig. 1).

## Reproducibility

Inter-observer and intra-observer reproducibility of strain parameters were assessed in 10 randomly selected patients. To test intra-observer reproducibility, the selected datasets were analyzed twice by the same experienced observer at 2 two weeks apart. To test inter-observer reproducibility, the selected datasets were analyzed again by a second experienced observer.

## Statistical analysis

Continuous variables were expressed as mean  $\pm$  standard deviation or median and interquartile range depending on whether the variables were normally distributed. Normal distribution of variables was verified with Kolmogorov–Smirnov test. Categorical data were presented as absolute numbers and percentages. To compare patients with and without LV remodeling, independent-samples t test or Mann–Whitney U test was used for continuous variables, while Chi square test or Fisher’s exact test was used for categorical variables. The paired-samples t test was applied to evaluate changes in continuous variables between baseline and 3-month follow-up. Linear correlation was tested between 2D and 3D global longitudinal strain, and the Bland–Altman method was used to assess the agreement between them. Univariate logistic regression analysis identified several possible determinants of LV remodeling (those with P values < 0.10). These parameters were



**Fig. 1** Demonstration of three-dimensional speckle tracking echocardiography (3DSTE) analysis in EchoPAC workstation: **a** the software shows the entire myocardial wall tracking in the 4-, 2-, 3-chamber

apical views, and 3 short-axis views (apical, mid, and basal); **b** GLS, GCS, GAS and GRS were automatically obtained by the software

therefore included in a multivariate analysis, which were used to confirm the independent correlates of LV remodeling. To avoid the collinearity problems, strain parameters were evaluated in separate models. Receiver-operating characteristic curve (ROC) analysis was performed to determine the best cut off values and the area under the ROC curve (AUC) of strain parameters for predicting LV remodeling. Inter-observer and intra-observer reproducibility of strain parameters were assessed in 10 randomly selected patients, using intraclass correlation coefficient (ICC). A P-value < 0.05 was considered statistically significant. Statistical analysis was performed using SPSS (IBM Company, USA).

## Result

### Subject characteristics

Clinical and echocardiographic characteristics of the patients are summarized in Tables 1 and 2. Mean  $\pm$  SD age was  $54 \pm 9$  years, and 90.9% were males. At 3-month follow-up, LV remodeling (defined as a 20% increase in LV end-diastolic volume) appeared in 26 patients (24%). At baseline, there were no significant differences between groups in terms of gender distribution and coronary risk factors. Compared with patients without LV remodeling, patients with LV remodeling more frequently had left anterior descending artery (LAD) as the IRA and higher peak

cTnI level. Regarding conventional echocardiographic parameters, no significant differences in baseline were found between two groups. Although 3D GCS were similar between two groups, 2D GLS, 3D GLS, 3D GAS and 3D GRS demonstrated a lower absolute values in patients with LV remodeling. During follow-up, administration of antiplatelets, beta-blockers, angiotensin-converting enzyme inhibitors, angiotensin II receptor blockage and statins was also not significantly different between two groups.

At 3-month follow-up, patients with LV remodeling exhibited significant increase of LVEDV, LVESV and LVMI when compare to baseline values, while LVESV showed a significant decrease in patients without LV remodeling. And WMSI and LVEF remain unchanged in the 2 subgroups of patients (Table 2).

### Comparison between 2D and 3D global longitudinal strain values and their correlations

The comparison of GLS value in 2D and 3D modes is illustrated in Fig. 2. A good correlation was demonstrated between 2D and 3D GLS ( $r=0.79$ ,  $P<0.01$ ), with a mean error of measurement of  $-2.24 \pm 3.90\%$ .

### Prediction of left ventricular remodeling

Univariate logistic regression analysis identified several possible determinants of LV remodeling (those with P values < 0.10), including age, LAD as the IRA, time to

**Table 1** Clinical characteristics of patients with vs without left ventricular remodeling

Variable	All patients (n = 110)	Patients with remodeling (n = 26)	Patients without remodeling (n = 84)	p-value
Age (years)	54 ± 9	57 ± 11	53 ± 8	0.139
Male gender (%)	100 (90.9%)	24 (92.3%)	76 (90.5%)	0.777
Hypertension (%)	52 (47.3%)	12 (46.2%)	40 (47.6%)	0.896
Diabetes mellitus (%)	38 (34.5%)	10 (38.5%)	28 (33.3%)	0.631
Smoker (%)	97 (88.2%)	22 (84.6%)	75 (89.3%)	0.519
Body mass index (kg/m <sup>2</sup> )	25.1 ± 2.6	25.6 ± 2.6	24.9 ± 2.6	0.234
eGFR Level(ml/min/1.73 m <sup>2</sup> )	111 ± 29	106 ± 30	113 ± 29	0.252
LAD as the IRA (%)	60 (54.5%)	19 (73.1%)	41 (48.8%)	0.030
Multi-vessel coronary disease (%)	45 (40.9%)	10 (38.5%)	35 (41.7%)	0.771
TIMI flow grade <3 (%)	11 (10%)	1 (3.8%)	10 (11.9%)	0.233
Time to reperfusion (h)	11.5 ± 5.7	13.4 ± 5.5	10.9 ± 5.7	0.052
Peak cTnI level (ng/ml)	9.07 ± 5.76	11.11 ± 6.75	8.43 ± 5.31	0.038
Medication during follow-up(%)				
Antiplatelets	110 (100%)	26 (100%)	84 (100%)	1
ACEI(s) /ARB(s)	107 (97.3%)	26 (100%)	81 (96.4%)	0.331
Beta-blockers	109 (99.1%)	26 (100%)	83 (98.8%)	0.578
Statin	110 (100%)	26(100%)	84 (100%)	1

Value are presented as mean ± standard deviation or percentage (%)

eGFR estimated glomerular filtration rate, TIMI thrombolysis in myocardial infarction, LAD left anterior descending artery, IRA infarct-related artery, cTnI cardiac troponin I, ACEI angiotensin-converting enzyme inhibitors, ARB angiotensin II receptor blockage

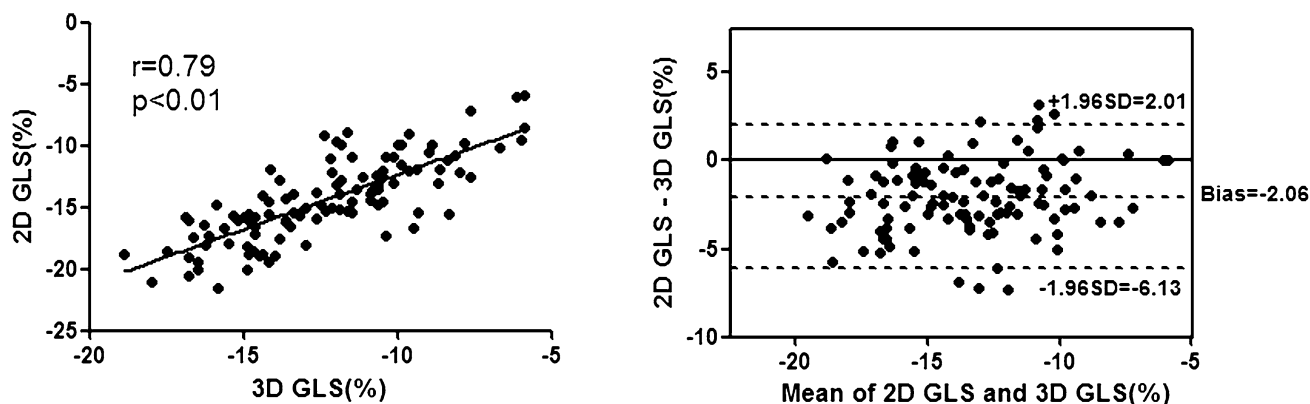
**Table 2** Echocardiographic characteristics of patients with vs without left ventricular remodeling

Variable	All patients (n = 110)	Patients with remodeling (n = 26)	Patients without remodeling (n = 84)	p-value
WMSI (baseline)	1.49 ± 0.34	1.55 ± 0.41	1.47 ± 0.31	0.288
WMSI (follow-up)	1.48 ± 0.34*	1.54 ± 0.40	1.46 ± 0.31	0.307
LVEDV (ml) (baseline)	105.6 ± 20.8	100.8 ± 14.9	107.1 ± 22.2	0.180
LVEDV (ml) (follow-up)	110.6 ± 24.1*	128.0 ± 18.2*	105.3 ± 23.2	<0.001
LVESV(ml) (baseline)	49.1 ± 14.4	48.1 ± 9.5	49.4 ± 15.6	0.606
LVESV (ml) (follow-up)	50.5 ± 17.5	61.7 ± 15.1*	47.0 ± 16.8*	<0.001
LVEF (%) (baseline)	53.9 ± 7.4	52.0 ± 5.8	54.6 ± 7.7	0.077
LVEF (%) (follow-up)	55.3 ± 8.5	52.6 ± 7.8	56.1 ± 8.6	0.060
LVMI (g/m <sup>2</sup> ) (baseline)	81.7 ± 8.9	79.0 ± 10.1	82.5 ± 8.4	0.083
LVMI (g/m <sup>2</sup> ) (follow-up)	82.2 ± 8.6	81.9 ± 10.0*	82.3 ± 8.1	0.843
2D GLS (%)	-14.4 ± 3.3	-12.5 ± 3.2	-15.0 ± 3.1	<0.001
3D GLS (%)	-12.4 ± 3.0	-9.9 ± 2.2	-13.1 ± 2.7	<0.001
3D GCS (%)	-12.9 ± 3.1	-12.7 ± 2.9	-13.0 ± 3.2	0.822
3D GAS (%)	-22.6 ± 4.8	-20.3 ± 3.9	-23.3 ± 4.8	0.005
3D GRS (%)	33.0 ± 8.5	29.0 ± 7.4	34.3 ± 8.5	0.007

Value are presented as mean ± standard deviation or percentage (%)

WMSI wall motion score index, LVESV left ventricular end-systolic volumes, LVEDV left ventricular end-diastolic volumes, LVEF left ventricular ejection fraction, LVMI left ventricular mass index, 2D two-dimensional, 3D three-dimensional, GLS global longitudinal strain, GCS global circumferential strain, GAS global area strain, GRS global radial strain

\*p < 0.05, compared with baseline values



**Fig. 2** Linear correlation and Bland–Altman analyses for two-dimensional global longitudinal strain and three-dimensional global longitudinal strain

reperfusion, peak cTnI level, 2D GLS, 3D GLS, 3D GAS and 3D GRS. The independent predictors of LV remodeling were analyzed using four separate multivariate logistic regression analysis. Age, and LAD as the IRA were the strong predictors in every model, and the LVMI was not significant in every model. In addition, time to reperfusion was significant in model 1, while peak cTnI level was significant in model 3 and model 4. Four separated models also exhibited that 2D GLS, 3D GLS, 3D GAS and 3D GRS were independent predictors of LV remodeling at 3 months follow-up (Table 3).

In ROC analysis, the optimal cutoff value of strain parameters at baseline for predicting LV remodeling was showed in Table 4. ROC also showed that the area under the curve (AUC) of 3D GLS (0.82) for predicting LV remodeling was significantly higher than that of 2D GLS (0.72,  $p=0.034$ ), 3D GAS (0.68,  $p<0.001$ ) and 3D GRS (0.68,  $p<0.001$ ). In addition, the AUC of 2D GLS, 3D GAS and 3D GRS for predicting LV remodeling were similar with each other ( $p>0.05$ ) (Fig. 3).

### Reproducibility analysis

The inter-observer and intra-observer ICC is presented in Table 5. The ICC values show that inter-observer and intra-observer reproducibility was good for all strain parameters and reproducibility for GLS was improved by 3D STE when compared with 2D STE. GCS had the lowest intra-observer and inter-observer reproducibility in all 3D parameters.

### Discussion

The results of this study demonstrated that: (1) the impaired 2D GLS, 3D GLS, 3D GAS, 3D GRS after STEMI was

able to predict LV remodeling after the adjustment of some variables related to prognosis; (2) 3D GLS was the most powerful parameter for predicting LV remodeling after STEMI.

### LV remodeling after AMI

As global LV dilation is the main form of LV remodeling, we had defined LV remodeling as at least 20% increase in LVEDV after 3-month follow-up. Previous studies have demonstrated that this criteria would be sufficient to confirm LV remodeling and indicates a poor prognosis [14–16]. In our study, 24% subjects reached the LV remodeling criteria, despite successful early reperfusion therapy and secondary prevention therapy. Even if this proportion is lower than 30 and 33% observed in previous studies [8, 14], the result is still striking since our sample represents a relatively low-risk population with a high rate of PCI and secondary prevention therapy. As we known, LV remodeling after AMI is a reparative process triggered by the acute damage of myocardium and an abrupt increase in load. It initially can repair the poor heart pump function after AMI. However, as time goes on, LV remodeling may leads to fatal events, such as heart failure and malignant arrhythmias [3]. Thus, early identification of patients at high risk of LV remodeling has important prognostic implications and affects clinical invention making.

### Strain parameters in LV remodeling prediction

At present, it has been suggested that myocardial strain assessed by 3D STE are more appropriate index of myocardial dysfunction and more powerful prognostic indicators of cardiovascular disease [20, 21]. However, data regarding the predictive value of 3D STE in post-MI remodeling is rare. A study involving patients with non-STEMI treated

**Table 3** Univariate and multivariate analyses of predictors of left ventricular remodeling

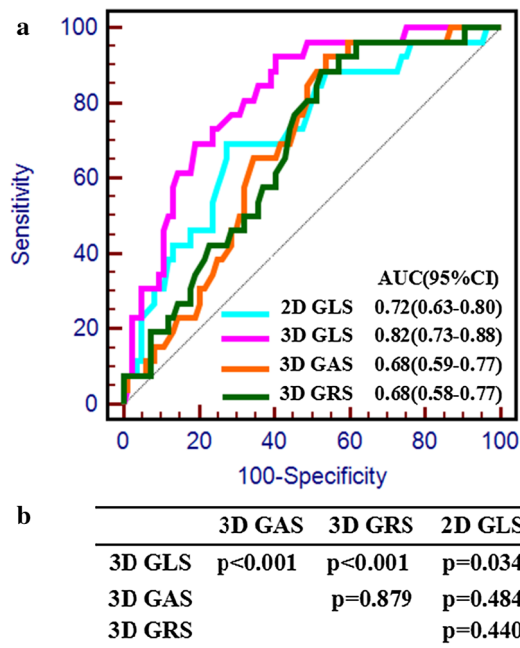
	Multivariate analyses														
	Univariate analyses			Model 1			Model 2			Model 3			Model 4		
	Crude OR	95% CI	p-Value	Crude OR	95% CI	p-Value	Logistic OR	95% CI	p-Value	Logistic OR	95% CI	p-Value	Logistic OR	95% CI	p-Value
Age	1.05	1.00–1.10	0.076	1.11	1.03–1.18	0.004	1.11	1.03–1.20	0.007	1.09	1.02–1.16	0.008	1.10	1.03–1.17	0.006
LAD as the IRA (%)	2.85	1.08–7.48	0.034	3.62	1.08–12.10	0.037	5.42	1.38–21.33	0.016	3.43	1.09–10.81	0.036	3.56	1.11–11.37	0.032
Time to reperfusion (hour)	1.081	1.00–1.17	0.055	1.10	1.00–1.22	0.048	1.07	0.96–1.19	0.193	1.08	0.98–1.18	0.129	1.08	0.99–1.19	0.091
Peak cTnI level (ng/ml)	1.09	1.00–1.18	0.042	1.09	0.98–1.22	0.120	1.08	0.95–1.22	0.247	1.14	1.03–1.27	0.016	1.14	1.03–1.27	0.014
LVMI	0.96	0.91–1.00	0.085	0.98	0.92–1.04	0.472	0.98	0.91–1.04	0.461	0.97	0.91–1.03	0.319	0.97	0.91–1.03	0.288
2D GLS	1.28	1.10–1.49	0.001	1.37	1.12–1.67	0.002									
3D GLS	1.58	1.28–1.95	<0.001				1.82	1.34–2.46	<0.001						
3D GAS	1.15	1.03–1.27	0.008							1.18	1.04–1.33	0.010			
3D GRS	0.93	0.87–0.98	0.009										0.90	0.84–0.97	0.007

OR odds ratio, CI confidence interval, LAD left anterior descending artery, IRA infarct-related artery, cTnI cardiac troponin I, LVMI left ventricular mass index, 2D two-dimensional, 3D three-dimensional, GLS global longitudinal strain, GAS global area strain, GRS global radial strain

**Table 4** Optimal cutoff values of strain parameters at baseline for predicting left ventricular remodeling

Strain parameter	Cutoff value (%)	Sensitivity	Specificity
2D GLS	>−13.6	69.2	72.6
3D GLS	>−12.6	92.3	59.5
3D GAS	>−24.2	92.3	46.4
3D GRS	≤34.6	88.5	47.6

2D two-dimensional, 3D three-dimensional, GLS global longitudinal strain, GAS global area strain, GRS global radial strain



**Fig. 3** Receiver-operating characteristic curve analyses of strain parameters at baseline for the prediction of left ventricular remodeling. **a** Comparison of the area under the curve (AUC) of strain parameters. **b** Statistical analysis of comparison of the AUC between each two strain parameters. 2D two-dimensional, 3D three-dimensional, GLS global longitudinal strain, GAS global area strain, GRS global radial strain

**Table 5** Intra- and inter-observer intraclass correlation coefficient of strain parameters

	Intra-observer	Inter-observer
2D GLS	0.91 (0.68–0.98)	0.89 (0.58–0.97)
3D GLS	0.97 (0.87–0.99)	0.95 (0.81–0.99)
3D GCS	0.90 (0.58–0.97)	0.91 (0.66–0.98)
3D GAS	0.95 (0.73–0.99)	0.94 (0.77–0.99)
3D GRS	0.98 (0.92–0.99)	0.96 (0.82–0.99)

2D two-dimensional, 3D three-dimensional, GLS global longitudinal strain, GAS global area strain, GRS global radial strain

with PCI show that 3D GAS measured after PCI could predict LV remodeling at 6-month follow-up [22]. However, the author only investigate the value of 3D GAS and it showed the lack of information on whether other components of strain should be taken into account as a predictor in LV remodeling after AMI. Moreover, the study mentioned above had applied the Artida system (Toshiba Medical Systems, Tochigi, Japan) to acquire the strain parameter. As we know, our study is one of the first studies to use the Vivid system to evaluate association between multi-directional components of 3D strain and LV remodeling. This is important because strain measurement is significant different on different vendors [23].

Analyses of multi-directional components of 3D STE showed that 3D GLS, 3D GAS and 3D GRS but not 3D GCS could be an alternative parameter to predict LV remodeling. In addition, 3D GLS would be the most robust parameter among them. A potential explanation for this discrepancy is that LS mainly represents the contractility of subendocardial fibers. Compare with fibers of middle layer and subepicardial layer, subendocardial fibers is more vulnerable to myocardial hypoperfusion and hypoxia [24]. Therefore, the reduced GLS can sensitively reflect myocardial ischemia and necrosis and provide an excellent prognostic value in risk stratification of cardiovascular disease. Furthermore, a recent study by Wang et al. reported that 3D GLS had a higher diagnostic value to evaluate LV global myocardial infarction size compared to other components of strain derive from 3D STE [25]. In a population with severe aortic stenosis and preserved LVEF, Nagata et al. found that 3D GLS was the most robust predictor for future major adverse cardiac events among multi-directional strain parameters derived from 3D STE and 2D STE [26]. That is to say, the decrease of LS may more accurately reflect the poor heart pump function and 3D GLS would be an excellent parameter with potential to be evaluated in future studies to determine prognostic implications. In contrast, CS mainly described the contraction of the mid-myocardial and subepicardial layers, and RS mainly represents the complex process of rearrangement of three myocardial layers of fibers [27]. As these layers are less likely to be injured in the early phase of AMI, CS and RS may remain normal or improve (to compensate for the reduced longitudinal strain) in segments without necrosis or with subendocardial necrosis [28]. Hence, GCS and GRS may not correctly reflect the magnitude of myocardial damage and have a low predictive value of LV remodeling.

3D GAS is known as a relatively new 3D strain parameter reflects the myocardial area change ratio. It has been considered as a sensitive marker to detect early and subtle LV systolic dysfunction. Wen et al. applied 3D STE to evaluate myocardial deformation in 160 patients with risk factors for heart failure, and had found that GAS is more sensitive



to identify patients with different stage of HF than other conventional strain parameters [29]. In our study, we had found that GAS was able to identify patients at high risk of remodeling, which has been confirmed in non-STEMI patients in previous study [22]. However, its accuracy for predicting LV remodeling was lower than that of 3D GLS. This is mainly because that 3D GAS combines the component of CS, which may reduce its sensibility on myocardial infarction.

Compared with 2DSTE, 3D STE have the advantage of a simultaneous acquisition of full LV segmental data from the cardiac apex and tracking the speckles in three dimensions, avoiding the speckles disappears in two dimensions. Using 3D STE technology for measurement of GLS may improve the precision of the measurement [30]. Although 3D GLS was correlated well with 2D GLS, ROC analysis had revealed that 3D GLS was superior to 2D GLS in predicting LV remodeling. In addition, our study also found that 3D STE improved the reproducibility for GLS when compared with 2D STE. These data suggested that 3D GLS may be more practical than 2D GLS in future prognosis evaluation. We abstained from acquiring 2D GCS and 2D GRS in our study, because short-axis views at the apical, mid, and basal level were not feasible in many subjects. In addition, 2D GCS and 2D GRS are measured at only one short-views level. Hence, they may be not sufficient to reflect the global circumferential or radial deformation in AMI patients. Similar problem has been reported in previous study [31].

### Conventional echocardiographic parameters and clinical data in LV remodeling prediction

LVEF and WMSI are the main echocardiographic parameter measured in the routine prognosis evaluation of patients after AMI. LVEF is a marker reflecting global LV systolic function, whereas WMSI allows evaluation of segmental LV systolic function. However, both of them in our study were similar between patients with remodeling and without remodeling and were unable to identify patients at high risk of LV remodeling. That is mainly because these two parameters have several drawbacks for risk stratification after AMI. After AMI, regional wall motion abnormalities may occur. However, compensatory regional hyperkinesis in non-infarcted region likely contributed to the preservation of LVEF [32]. And WMSI is a semi-quantitative motion score with inherent inter-observer variations and dependence on observer expertise level [31]. Moreover, these two parameters also could not detect the viable myocardium in infarcted area and subclinical myocardial dysfunction in the non-infarcted area due to technology limitations. Thus, they may be not sufficient to reflect the poor heart pump function and LV contractile reserve after AMI. Our result

is also in accordance with previous data [33]. That is to say, the predictive value of LVEF and WMSI for LV remodeling may not be accurate.

In our study, the increase of age is also a risk factor for LV remodeling, which may be ascribed to the decreased cardiomyocyte renewal capacity and the increased cardiomyocyte apoptosis in the elderly [34, 35]. The results of our study also revealed that left anterior descending artery as the infarct-related coronary artery, high peak cTnI level and a long time to reperfusion were independent predictors of LV remodeling. Similar results were already reported in many previous studies [8, 36, 37].

### Clinical implication

Our study confirmed that 2D GLS, 3D GLS, 3D GAS and 3D GRS can predict LV remodeling independently, however 3D GLS was superior to other strain parameters. Our finding may also provide a reference to select optimal strain parameters to predict LV remodeling. It makes sense of early risk stratification, medical, or specific interventions against LV remodeling.

### Study limitations

Some limitations in our study must be considered. First of all, this study is limited to patients after STEMI treated by PCI and included a relatively small sample from a single medical center. Consequently, our results may not be well extrapolated to the general patients after AMI. Second, the requirement of high-quality image window and good cooperation of patients in 3D STE analysis result in some people that could not be enrolled in this study. That may introduce a potential selection bias. Third, because the follow-up period was only three months, further study with longer follow-up was required to detect the long-term predictive value of strain. Nevertheless, the collection of clinical variables and the follow-up of patients was prospectively planned and our result is reliable. We believed that our findings added important information about strain parameters and LV remodeling after STEMI.

### Conclusions

We demonstrated that 2D GLS, 3D GLS, 3D GAS and 3D GRS were predictive of future LV remodeling after AMI, and 3D GLS was an excellent predictor with a highest predictive value among them. This study also suggested that 3D STE is a more practical tool that is a potential alternative to 2D STE in prognosis evaluation in AMI patients.

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#### Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

**Informed consent** Informed consent was obtained from all individual participants included in the study.

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