Impact of global longitudinal strain on left ventricular remodeling and clinical outcome in patients with ST-segment elevation myocardial infarction (STEMI)

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Abstract
Background: Predicting left ventricle (LV) remodeling is important for outcome prediction in patients with ST-segment elevation myocardial infarction (STEMI). Novel echocardiographic techniques may be beneficial for those patients.
Objectives: We hypothesized that the semiautomated calculation of baseline global longitudinal strain (GLS) can predict LV remodeling and 6-month clinical outcomes in these patients.
Methods: During the period from March to December 2018, 130 patients with successful reperfusion of STEMI were prospectively included. Within 48 hours, patients underwent a baseline GLS study with follow-up study at 6 months. Patients were divided into two groups: group I: patients who showed adverse LV remodeling and group II: patients who did not. The endpoint was a composite of cardiovascular mortality, readmission due to heart failure, and urgent revascularization.
Results: The mean baseline GLS changed from −13.1 ± 3.5% for group I and −16.8 ± 3.1% for group II, to −10.2 ± 4.7% and −12.6 ± 3.1%, respectively, at 6-month follow-up. ROC analysis demonstrated a cutoff value of baseline GLS > −12.5% predicted LV remodeling with 64.5% sensitivity and 89% specificity (AUC 0.797, 95% CI 0.690-0.904). Multivariate logistic regression analysis model using 6-month MACEs occurrence as a dependent factor showed baseline GLS value > −12.5% to be the only significant independent predictor MACEs occurrence (OR 0.704, 95% CI 0.597-0.829, P < .001). Linear regression analysis showed that for every point estimate deterioration of baseline GLS, there was a significant corresponding 2.55 mL increase in LVEDV at 6-month follow-up (CI −4.501 to −0.612, P = .01).
Conclusion: GLS measurement can predict remodeling and adverse clinical events in STEMI patients.

Keywords
6-month outcome, GLS, remodeling, STEMI
1 | INTRODUCTION

ST-elevation myocardial infarction (STEMI) is a common disease that has dangerous complications. It represents a major healthcare problem, and, if untreated, it can lead to the development of severe medical complications.1 Myocardial damage that shortly follows STEMI leads to many chemical and mechanical alternations in the left ventricular (LV) structure that may end in changes in LV volume and shape, which ultimately culminates in heart failure. These changes are known as “LV remodeling.”1 Left ventricular remodeling is defined as the process by which ventricular shape, size, and function are regulated by mechanical, neuro-hormonal, and genetic factors.2 It takes place, even after proper and efficient reperfusion, whether the primary percutaneous coronary intervention (PPCI) or fibrinolytic therapy. The incidence ranges from 30% to 35%.3 Many echocardiographic parameters have been used to diagnose LV remodeling,4 involving LV end-systolic (ESV) and end-diastolic volumes (EDV) and ejection fraction (EF) by conventional echocardiography,5 and global longitudinal strain (GLS) by two-dimensional speckle tracking echocardiography (2D-STE).6 Myocardial strain and strain rate assessed by 2D-STE can be used in evaluating myocardial performance and is considered a better tool to assess changes in LV function. Many studies used the 2D-STE to predict left ventricle remodeling after STEMI.7 In this study, we tested the predictive value of GLS on LV remodeling and clinical outcomes in patients with STEMI who had successful reperfusion.

2 | METHODS

2.1 | Study design

This single-center, prospective, cohort study included 104 consecutive patients admitted with STEMI to Coronary Care Unit at Benha University Hospital, Egypt, in the period from March to December 2018. STEMI was defined as chest pain typical for myocardial infarction of at least 30 minutes duration and <6 hours, and new ST-segment elevation in two contiguous leads with the cutoff points ≥ 0.2 mV in men or ≥0.15 mV in women in leads V2-V3 and/or ≥0.1 mV in other leads on the 12-lead ECG. According to the local protocol, all patients were candidates for reperfusion therapy (PPCI or fibrinolysis). Included patients were required to have successful reperfusion, which was defined as disappearance or improvement of chest pain with resolution of ST-segment elevation by more than 50% in the lead with maximum elevation on baseline ECG 90 minutes of starting of fibrinolysis or shortly after PPCI (culprit-only) that restores TIMI-II to III flow without major intraprocedural complications (defined as absence of no-reflow, dissections, perforations, or thrombus formation). The study was approved by the local ethics committee at our institution, and patients were required to provide informed consent before the echocardiographic examination. Key exclusion criteria were as follows: patients with late presentation after symptom onset (more than 12 hours from onset of chest pain), patients with failed reperfusion, patients with noncardiac diseases that limit life expectancy, patients with atrial fibrillation, paced rhythms or more than mild aortic stenosis, or other conditions that may hamper the quality of obtained echocardiographic data.

2.2 | Study protocol and endpoints

During hospital stay, after proper clinical examination and collection of all necessary data, all patients were observed for the occurrence of in-hospital mortality, heart failure, reinfarction, revascularization, major bleeding, and stroke. Baseline echocardiographic examination including evaluation of ESV, EDV, biplane EF using Simpson’s method in addition to GLS measurement using speckle tracking. Six months later, every patient was contacted to arrange a follow-up visit to assess clinical endpoints and to perform a follow-up echocardiographic study.

Patients were divided into two groups:

- Group I: Patients showed adverse LV remodeling (defined as a ≥20% increase in biplane LV EDV from the initial presentation to the 6-month follow-up)3
- Group II: Patients did not show LV remodeling.

We used a primary outcome of composite three-point major adverse cardiac events (MACEs) at 6 months (mortality due to cardiovascular causes, readmission due to heart failure (HF), and urgent revascularization). Adjudication of individual components of the endpoint was done by an independent review committee blinded to echocardiographic data related to index MI. Data on mortality were obtained from hospital records and classified as cardiovascular and noncardiovascular. Readmission for HF was defined as hospitalization due to dyspnea with objective signs of pulmonary congestion together with treatment with intravenous diuretics. Urgent revascularization was defined as any urgent PCI or coronary artery bypass grafting (CABG) performed within 72 hours of hospital readmission.

2.3 | Echocardiographic measurements

Echocardiographic examination was performed using a commercially available ultrasound system (Philips EPIC 7 Ultrasound System) equipped with a 3.5 MHz phased array transducer. Patients underwent echocardiographic study at baseline (within 48 hours of admission) and repeated during follow-up (at 6 months after discharge). All examinations were performed by two experienced operators blinded to follow-up data. Before the execution of the study and for reproducibility of measurements, these 2 experienced operators repeated 10 measurements of ESV, EDV, LVEF, WMSI, and GLS. Differences in measurements by the 2 observers were obtained for estimation of interobserver variability. The image was obtained at held end-expiration. LVEF was calculated using Simpson’s biplane method by the European Association of Echocardiography and the American Society of Echocardiography.
recommendations. Wall-motion score index (WMSI) was assessed using the 17-segment model. For the two-dimensional speckle tracking echocardiography (2D-STE) image technique, sector depth and size were optimized to achieve perfect visualization of all LV myocardium in the three standard apical views (4-, 2-, and long-axis view) with a frame rate between 60 and 100 fps. End-systole was defined by the aortic valve closure in the apical long-axis view. The regions of interest were manually outlined at end-systole by outlining the endocardial borders in the apical views. Peak systolic longitudinal myocardial strain was automatically calculated throughout the myocardium for each LV apical view and reported spatially from base to apex and circumferentially in a polar plot map using a color-coded parametric representation. The global longitudinal strain (GLS) was calculated by taking an average of all peak systolic segmental strain values from the three standard apical views. Longitudinal peak strain values were averaged over three consecutive cardiac cycles.

LV remodeling was defined as by an increase of at least 20% of LVEDV from the first postinfarction imaging; this definition is also being used in large studies such as the AMICI trial.

2.4 | Statistical analysis

The sample size was calculated using epi-info software (v.7.2.2) based on the results of the study by Munk et al which reported 79% accuracy of GLS in predicting MACE. The precision level was adjusted to 0.08, and the confidence level was adjusted to 95%. The calculated sample size was 100 patients. Data management and statistical analysis were done using SPSS vs.25 (IBM). Numerical data were summarized as means and standard deviations. Categorical data were summarized as numbers and percentages. Comparisons between two groups were done using independent t-test for numerical data. Categorical data were compared using the chi-square test or Fisher’s exact test if appropriate. ROC analysis was done for GLS in the prediction of remodeling. The area under curve with 95% confidence interval, the best cutoff point, and diagnostic indices were calculated. Logistic regression analysis was done for the prediction of remodeling. Odds ratios with 95% confidence intervals were calculated. Linear regression analysis was used for prediction of 6-month EDV using GLS as a predictor. Kaplan–Meier curves were drawn for time to MACE in patients with complete and partial resolution and patients above and below the GLS cutoff point. Kaplan–Meier curves were compared using log-rank test. All P values were two-sided. P values < .05 were considered significant.

3 | RESULTS

3.1 | Study population

A total of 130 patients with successful reperfusion after STEMI were prospectively included. Eighteen patients were excluded because of AF (n = 10), ventricular paced rhythm (n = 3), and more than mild aortic stenosis (n = 5). Of the remaining 112 patients, eight patients were excluded due to poor image quality, leaving 104 patients for the final analysis. The mean age was 58 ± 14, 55.8% were male, 26.9% had diabetes, 33.7% were hypertensives, 39.4% were smokers, 21.1% were obese, 19.2% had known dyslipidemia, 13.5% had positive family history of coronary artery disease, 18.3% with past history of ischemic heart disease, and 10.6% had past history of coronary interventions. Between groups, the analysis did not show any statistically significant differences (Table 1).

3.2 | STEMI

3.2.1 | Location of STEMI as suggested by ECG

Anterior STEMI was the target in 52.9% (64.5% vs 47.9%, in group I and II, respectively), inferior STEMI in 36.5% (29.0% vs 39.7%, in group I and II, respectively), and lateral STEMI in 10.6% (6.5% vs 12.3%, in group I and II, respectively). There were no statistically significant differences between the groups regarding STEMI location (P = .283).

3.2.2 | ST-segment resolution

ST-segment resolution was complete in 51% (41.9% vs 54.8%, in group I and II, respectively) and not complete in 49% (58.1% vs 45.2%, in group I and II, respectively) There were no statistically significant differences between the groups (P = .23).

3.2.3 | Reperfusion strategies and total ischemic time

Streptokinase was used in 78.8% (80.6% vs 78.1%, in group I and II, respectively), while primary PCI in 21.1% (19.4% vs 21.9%, in group I and II, respectively). The mean total ischemic time was 202 ± 46 minutes (205 ± 61 vs 201 ± 38 in group I and II, respectively). There were no statistically significant differences between the groups regarding reperfusion strategies or total ischemic time (P = .77 and .682, respectively) (Table 1).

There was no statistically significant difference regarding the location of STEMI, ST-segment resolution, reperfusion strategy (SK vs PPCI), or total ischemic time.

3.3 | Six-month outcome

MACEs were more predominant in group I (35.5% vs 15.1%, P = .02), derived mainly from rehospitalization for heart failure (22.6% vs 6.8% in group I and II, respectively, P = .022). Cardiovascular mortality in 4.8% (6.5% vs 4.1% in group I and II, respectively, P = .633) and target vessel urgent revascularization in 4.8% (6.5% vs 4.1% in group I and II, respectively, P = .633) (Table 2).
The mean follow-up time was 179 ± 6.5 days. At baseline, interobserver variabilities were 5.5 ± 3.0% for LVEF, 4.15 ± 2.2% for WMSI, and 6.8 ± 3.6 for GLS. Intra-observer variabilities were 4.6 ± 2.4% for LVEF, 5.7 ± 3.2% for WMSI, and 5.8 ± 3.4% for GLS. At 6-month follow-up, interobserver variabilities were 5.1 ± 2.8% for LVEF, 4.8 ± 3.4% for WMSI, and 5.8 ± 3.2 for GLS. Intra-observer variabilities were 4.7 ± 3.1% for LVEF, 4.7 ± 2.9% for WMSI, and 5.1 ± 2.9% for GLS. The test-retest variability of GLS was 5.1 ± 2.2% (maximum 81.1, minimum −111.3).
The mean baseline LVEF was 55.6 ± 7.5% (55.5 ± 6.1% vs 55.7 ± 8% in group I and II, respectively, $P = .904$), mean 6-month LVEF 47.4 ± 13.4% (40.6 ± 16.8% vs 50.4 ± 10.6% in group I and II, respectively, $P = .005$). The mean baseline WMSI was 1.3 ± 0.4 (1.3 ± 0.4 vs 1.3 ± 0.3% in group I and II, respectively, $P = .588$), mean 6-month WMSI 1.3 ± 0.3 (1.3 ± 0.3 vs 1.3 ± 0.3 in group I and II, respectively, $P = .165$). The mean baseline GLS was −15.7 ± 3.6% (−13.1 ± 3.5% vs −16.8 ± 3.1% in group I and II, respectively, $P < .001$), mean 6-month GLS 11.9 ± 3.8% (−10.2 ± 4.7% vs −12.6 ± 3.1% in group I and II, respectively, $P = .003$). The mean baseline ESV was 47.4 ± 18.7 mL (54 ± 25.8 vs 44.6 ± 14.1 mL in group I and II, respectively, $P = .018$), mean 6-month ESV 54.3 ± 17.4 mL (57.2 ± 24.6 vs 53.1 ± 13.2 mL in group I and II, respectively, $P = .393$). The mean baseline EDV was 107.4 ± 32.9 mL (111.8 ± 41.4 vs 105.5 ± 28.7 mL in group I and II, respectively, $P = .378$), mean 6-month EDV 115.4 ± 37.2 mL (137.1 ± 49.1 vs 106.1 ± 26.2 mL in group I and II, respectively, $P = .002$) (Table 3).

### Predictors of LV remodeling

ROC analysis showed that a cutoff value of baseline GLS $>-12.5\%$ predicted LV remodeling with a sensitivity and specificity of 64.5% and 89%, respectively (AUC 0.797, 95% CI 0.690-0.904) (Figure 1).

Moreover, a multivariate logistic regression analysis model using the occurrence of 6-month MACEs as a dependent factor showed baseline GLS value $>-12.5\%$ to be the only significant independent predictor for the occurrence of MACEs (OR 0.704, 95% CI 0.597-0.829, $P < .001$) (Table 4).

Linear regression analysis showed that for every point estimate deterioration of baseline GLS, there was a significant corresponding 2.55 mL increase in LVEDV at 6-month follow-up (CI $-4.501$ to $-0.612$, $P = .01$).

Assessment the probability of MACE at 6-month stratified by the best cutoff level of baseline GLS for prediction of LV remodeling, showed that baseline GLS $<-12.5\%$ was significantly associated with lower rates of MACE compared to GLS $\geq -12.5\%$ ($P = .046$) proving GLS to be a strong predictor of 6-month outcome (Figure 2).

### Table 3

Baseline and 6-mo echocardiographic parameters

<table>
<thead>
<tr>
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<th>All Patients (n = 104)</th>
<th>Group I (n = 31)</th>
<th>Group II (n = 73)</th>
<th>P value</th>
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<tr>
<td></td>
<td>Mean ±SD</td>
<td>Mean ±SD</td>
<td>Mean ±SD</td>
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<td>ESV (mL)</td>
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<tr>
<td>EDV (mL)</td>
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<td>Baseline</td>
<td>107.4 ± 32.9</td>
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<td>.378</td>
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<td>137.1 ± 49.1</td>
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<tr>
<td>EF (%)</td>
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<tr>
<td>6 mo</td>
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<tr>
<td>Baseline</td>
<td>1.3 ± 0.4</td>
<td>1.3 ± 0.4</td>
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Abbreviations: EDV = end-diastolic volume; EF = ejection fraction; ESV = end-systolic volume; GLS = global longitudinal strain; WMSI = wall-motion score index.
Changes in the left ventricle (LV) shape and geometry following STEMI are a complex phenomenon characterized by many phases. Remodeling is defined by changes in LV end-diastolic volume (LVEDV) and/or end-systolic volume (LVESV) between time of STEMI and late follow-up measuring. Adverse remodeling is defined as a clinically significant increase in LVEDV; however, reverse remodeling is defined as a clinically significant decrease in LVESV. This has an important clinical application as it may provide a tool for early identification for reaching better clinical outcomes. This study showed that GLS analysis at the initial presentation of baseline GLS > −12.5% (OR 0.704, 95% CI 0.597-0.829, \(P < .001\)) was an independent predictor of risk stratification in the acute phase. The best cutoff value for the GLS was −9.55% (sensitivity: 83.3%, specificity: 83.5%).

This is partially similar to ours, as we found that best cutoff value of baseline GLS > −12.5% (OR 0.704, 95% CI 0.597-0.829, \(P < .001\)) was more associated with MACEs (specificity of 64.5% and 89%, respectively) which also applies for 6-month EF, while that was not evident for baseline EF (OR 1.007, 95% CI 0.945-1.074, \(P = .82\)).

This was similar to Reindl et al who studied prognostic implications of global longitudinal strain by feature-tracking cardiac magnetic resonance in STE elevation myocardial infarction and found that there was association between GLS derived by CMR and MACE (\(P < .001\) after adjustment for global radial strain, global circumferential strain, and LVEF as well as for infarct size and microvascular obstruction.

This is not similar to Lacalzada et al who studied left ventricular global longitudinal systolic strain predicts adverse remodeling and subsequent cardiac events in patients with acute myocardial infarction treated with primary percutaneous coronary intervention as they did not consider myocardial recanalization as an event during follow-up, as at the discharge, complete recanalization.
was often already planned so they could not be considered to be a spontaneous event; however, they have found that best cutoff value of baseline GLS > -9.27% (HR = 3.4, 95% CI = 1.7-6.8, P < .001) so strain proved to be a better predictor of adverse LV remodeling than did WMSI or LVEF which is similar to ours.

4.1 | Study limitations

We did not evaluate other strain data such as lengthening strain, postsystolic shortening, radial strain, and circumferential strain. However, this study was intended for evaluation of LV function by more convenient and quantitative parameters such as GLS, not by sophisticated strain parameters.

5 | CONCLUSION

Baseline GLS is an independent predictor of future adverse events and LV remodeling in patients with STEMI who had successful reperfusion therapy.

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CONFLICTS OF INTEREST

None declared.

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