Identification of High-Risk Patients with Non-ST Segment Elevation Myocardial Infarction using Strain Doppler Echocardiography: Correlation with Cardiac Magnetic Resonance Imaging

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ABSTRACT

Assessment of left ventricular (LV) function is important for decision-making and risk stratification in patients with acute coronary syndrome. Many patients with non-ST segment elevation myocardial infarction (NSTEMI) have substantial infarction, but these patients often do not reveal clinical signs of instability, and they rarely fulfill criteria for acute revascularization therapy.

AIM: This study evaluated the potential of strain Doppler echocardiography analysis for the assessment of LV infarct size when compared with standard two-dimensional echo and cardiac magnetic resonance (CMR) data.

METHODS: Thirty patients with NSTEMI were examined using echocardiography after hospitalization for 1.8 ± 1.1 days for the assessment of left ventricular ejection fraction, wall motion score index (WMSI), and LV global longitudinal strain (GLS). Infarct size was assessed using delayed enhancement CMR 6.97 ± 3.2 days after admission as a percentage of total myocardial volume.

RESULTS: GLS was performed in 30 patients, and 82.9% of the LV segments were accepted for GLS analysis. Comparisons between patients with a complete set of GLS and standard echo, GLS and CMR were performed. The linear relationship demonstrated moderately strong and significant associations between GLS and ejection fraction (EF) as determined using standard echo ($r = 0.452$, $P = 0.012$), WMSI ($r = 0.462$, $P = 0.010$), and the gold standard CMR-determined EF ($r = 0.57$, $P < 0.001$). Receiver operating characteristic curves were used to analyze the ability of GLS to evaluate infarct size. GLS was the best predictor of infarct size in a multivariate linear regression analysis ($\beta = 1.51$, $P = 0.027$). WMSI >1.125 and a GLS cutoff value of –11.29% identified patients with substantial infarction (≥12% of total myocardial volume measured using CMR) with accuracies of 76.7% and 80%, respectively. However, GLS remained the only independent predictor in a multivariate logistic regression analysis to identify an infarct size ≥12%.

CONCLUSION: GLS is a good predictor of infarct size in NSTEMI, and it may serve as a tool in conjunction with risk stratification scores for the selection of high-risk NSTEMI patients.

KEYWORDS: strain rate, infarct size, MRI, NSTEMI

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Introduction

Coronary artery disease (CAD) is the most prevalent manifestation of cardiovascular diseases, and it is associated with high mortality and morbidity.[1] Registry data consistently demonstrated that the incidence of non-ST segment elevation myocardial infarction (NSTEMI) has increased, and it is more frequent than ST elevation myocardial infarction (STEMI).[2]

Infarct size is a strong prognostic indicator of mortality and major adverse cardiovascular events after myocardial infarction (MI), and the transmural extent of MI is related to the probability of functional recovery after acute revascularization.[3–6] Revascularization limits infarct size and salvages viable myocardium, which has dramatically improved the prognosis of patients presenting with acute coronary syndromes.[7–9] Many patients with NSTEMI exhibit substantial infarction,[3,10] but these patients often do not develop ST segment elevation or reveal clinical signs of instability, and the criteria for acute reperfusion therapy are rarely fulfilled.

Techniques based on echocardiography, nuclear imaging, and magnetic resonance are used in current clinical practice to estimate infarct size and identify viable myocardial segments that may benefit from coronary revascularization.[4,11,12] However, the routine use of these advanced imaging technologies in daily clinical practice is constrained by availability, costs, and logistics. Acute coronary occlusion induces left ventricular (LV) systolic dysfunction, which is quantified using echocardiography and correlates with infarct size, and this method may be applicable during the very early development phase of MI. Strain echocardiography is an accurate and validated measure of regional systolic LV function that

exhibits an excellent ability to differentiate between different levels of infarct size.[12–14] Strain echocardiography is a validated and accurate measure of regional LV systolic function in correlation with the standard assessment of final infarct size using contrast-enhanced magnetic resonance imaging (CE-MRI).[15–18] Strain echocardiography was recently validated as a prognostic indicator.[19,20]

Objectives

The present study evaluated the potential of strain Doppler echocardiography analysis for the assessment of LV infarct size in NSTEMI patients when compared with standard two-dimensional (2D) echo and cardiac magnetic resonance (CMR) data.

Methods

Patients. The study enrolled 30 patients who presented with recent NSTEMI. All patients were clinically and hemodynamically stable during index admission, and none of the patients were referred for urgent coronary intervention. All patients received optimal medical therapy based on current guidelines.[21]

Exclusion criteria.

- Patients with ST segment elevation >0.1 mV (0.2 mV in precordial leads V1–V3) in two or more contiguous leads on any electrocardiogram (ECG) during index admission.
- Prior MI.
- Bundle branch block with a QRS duration >120 milliseconds.
- Severe valvular heart disease.
- Atrial fibrillation.
- Previous coronary artery bypass graft (CABG).
- Patients with any contraindication to MRI.

Clinical and laboratory evaluations. An independent physician who was blinded to all data performed baseline clinical and laboratory evaluations, including risk factors, Killip class assessment, and ECG. GRACE risk score for NSTEMI was calculated during admission to predict mortality and reinfarction in hospital and at six months. According to GRACE risk score, patients were categorized as low (≤108), intermediate (109–140), and high risk (>140).[22] Cardiac markers (eg, troponin I, creatinine kinase enzyme [CK-MB]) were measured in serial samples with at least three samples with six hours in-between.

Echocardiography. All patients underwent standard echocardiographic examinations within 48 hours from NSTEMI using standard commercially available equipment (HD11 XE PHILIPS) with a phased array transducer. Left ventricular ejection fraction (LVEF) was calculated from apical four-chamber images using the modified Simpson's method. Wall motion score was assessed in a 16-segment model, and segmental wall motion was judged on the basis of the observed wall thickening and endocardial motion of the myocardial segment as normal = 1, hypokinetic (reduced thickening) = 2, akinetic (absent or negligible thickening) = 3, and dyskinetic (systolic thinning or stretching) = 4. Wall motion score index (WMSI) was measured as the average of the scores of all segments visualized.[23]

Strain analysis. Three consecutive cycles in three apical planes (four-chamber, two-chamber, and long-axis planes) were obtained using color tissue Doppler echocardiography while holding the breath at the end of expiration to minimize translational movement of the heart, and loops were digitally stored and analyzed offline using Q_lab. Aliasing in the velocity mode longitudinal strain was measured using tissue Doppler echocardiography in a 16-segment LV model. Peak negative strain and strain rate, which represent maximum longitudinal shortening, were measured for each segment and obtained from one of the three consecutive cardiac cycles, not as an average of the three cycles. Values of all segments were averaged to obtain global longitudinal strain (GLS). Infarct zone strain was measured as an averaged strain value from the infarcted segments that were detected using contrast-enhanced cardiac magnetic resonance (CE-CMR).

Cardiac magnetic resonance imaging. CMR was performed for all patients 6.97 ± 3.2 days from admission using 1.5 T scanners equipped with master gradients and a dedicated cardiac software package (Philips Medical Systems). Cine steady-state free precession (SSFP) sequences in different planes (two-chamber, four-chamber, and ventricular short-axis planes) were used primarily for quantitative ventricular measurements. Slice thickness was ~8 mm with no gap in-between. Images were obtained while holding the breath at the end of expiration to minimize variations in the position of the diaphragm and the heart. Quantitative evaluation of ventricular function was achieved by obtaining a series of contiguous SSFP cine MRI slices that covered the ventricles in short-axis views. Myocardial delayed enhancement sequences were performed 10–20 minutes after the administration of 0.15 mmol/kg gadolinium-based contrast. MDE was first performed using several inversion times (TI scout) to select the one that best nulls the myocardium. MDE was performed in short- and long-axis planes using this inversion time. Total myocardial area was measured on each short-axis image by manually drawing the endocardium and epicardium in end-diastolic frames, and the area of infarcted myocardium was manually traced. Final infarct size was calculated as a percentage of infarct volume/total myocardial volume. Short- and long-term mortality rates are increased in patients with infarct size ≥12%.[3,4] Therefore, we classified the patients into two groups with infarct sizes <12% and ≥12%.

Segmental transmurality was calculated in a 17-segment model of the LV myocardium (the basal and mid-ventricular short-axis slices were divided into six segments, the apical short-axis slices were divided into four segments, and infarcts

at the apical cap were detected in two-chamber slices) as the infarct volume divided by myocardial volume per segment, and segments with ≥50% contrast enhancement were judged transmurally infarcted.[15]

Statistical analysis. Data were analyzed using IBM SPSS software package version 20.0. Qualitative data are described using numbers and percents. Quantitative data are described using means and standard deviation, medians, and minimum and maximum. Comparisons between different groups of categorical variables were performed using the chi-square test. The distributions of quantitative variables were tested for normality using the Kolmogorov–Smirnov test, Shapiro–Wilk test, and D'Agostino test, and histograms and QQ plots were used for vision tests. Parametric tests were applied for normally distributed data. Nonparametric tests were used for abnormally distributed data. Comparisons between two independent populations for normally distributed data were performed using independent *t*-tests. Comparisons between two independent populations for abnormally distributed data were performed using Mann–Whitney tests, and the Kruskal–Wallis test was used to compare different groups. Correlations between two quantitative variables were assessed using the Spearman coefficient. We used intraclass correlation coefficients in 10 randomly selected patients for reproducibility (interobserver variability and intraobserver variability), and two independent observers analyzed the strain in each segment. Agreement of different predictive factors with the outcome was used and expressed in sensitivity, specificity, positive predictive value, negative predictive value, and accuracy. Receiver operating characteristic (ROC) curve was plotted to analyze a recommended cutoff, and the area under the ROC curve denoted the diagnostic performance of the test. An area >50% denotes acceptable performance, and an area ~100% is the best performance for the test. Multivariate linear regression was assessed. Univariate and multivariate logistic regressions were assessed. Significant test results are quoted as two-tailed probabilities. Significance of the obtained results was judged at the 5% level.[24,25]

Ethics statement. The review board of the Faculty of Medicine, Alexandria University, reviewed and approved this study. All patients were informed about the technique, and we obtained informed consent from all participants. Our research complied with the principles of the Declaration of Helsinki.

Results

Patients' characteristics. Table 1 provides an overview of demographic and clinical characteristics of the study population.

Echocardiography and strain analysis. Echocardiographic evaluations were performed in all patients within 33.17 ± 14.03 hours of admission (range 5–48 hours). Standard echocardiography for evaluations of LVEF, LV volumes, and WMSI was performed for all patients. LVEF% was 56.82 ± 6.19% (range 42.6%–71.6%). A total of 480 segments were examined for wall motion abnormalities, and 86 of these segments (18%) were hypokinetic. The mean WMSI was 1.18 ± 0.14 (range 1.0–1.44).

Table 1. Demographic and clinical characteristics of the study population ($n = 30$).

VARIABLE	
Age (years) (mean ± SD)	52.73 ± 9.73
Male sex, n (%)	28 (93.3)
Risk factors	
Hypertension, n (%)	7 (23.3)
Diabetes mellitus, n (%)	6 (20)
Dyslipidaemia, n (%)	22 (73.3)
Smoking, n (%)	26 (86.7)
Family history of CAD, n (%)	1 (3.3)
Body surface area (m^2)	1.82 ± 0.14
HR (b/m)	72.7 ± 14.3
SBP (mmHg)	127.8 ± 21.6
DBP (mmHg)	86.7 ± 12.9
Pharmacological therapy	
ACEI/ARBs (%)	77.6
Beta-blockers (%)	72.6
Statins (%)	90.3
Aspirin (%)	100
Clopidogrel (%)	100

Notes: Dyslipidemia was defined as the use of statins or cholesterol >240 mg/dL. Hypertension was defined as the use of antihypertensive medication.
Abbreviations: ACEI, angiotensin-converting enzyme inhibitors; ARBs, angiotensin receptor blockers.

A total of 398 segments (82.9%) were accepted for GLS, and loops of color tissue Doppler were analyzed with a mean frame rate of 116.4 ± 16.79 Hz. GLS was −11.77 ± 2.54 (range −17.47 to −6.88). Intraclass correlation coefficients for interobserver and intraobserver variabilities of GLS were 0.948 and 0.967, respectively.

Infarct size and transmurality using CE-CMR. CMR was performed for all patients within 5.3 ± 1.03 days of admission (range three to seven days). The distribution of infarct size in patients is illustrated in Figure 1. The infarct size percentage was 10.93% ± 8.5% of the total myocardial volume (range 0%–24%). Four patients (13.3%) had no visible late enhancement on CE-MRI (infarct size, 0%). A total of 510 segments were assessed for transmurality: 367 segments (71.96%) exhibited no delayed enhancement, 100 segments (19.6%) had nontransmural infarction (1% to <50%), and 43 segments (8.43%) had transmural infarction (50%–100%).

Infarct transmurality and strain analysis. There were significant positive correlations between segmental peak negative strain and segmental transmurality ($r = 0.587$, $P < 0.001$) and strain rate and the corresponding segmental transmurality ($r = 0.377$, $P < 0.001$; Fig. 2).

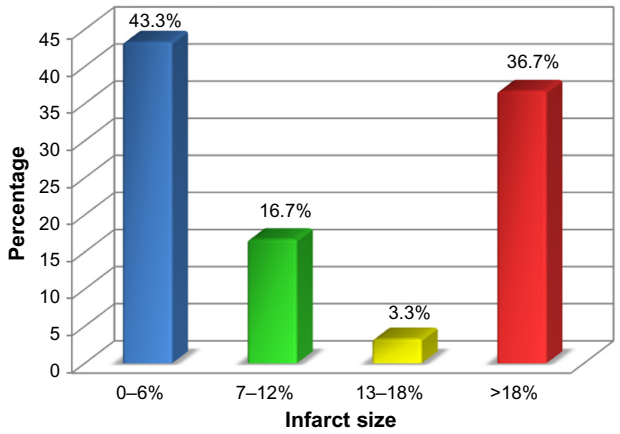

Figure 1. Infarct size in the study population using CE-CMR.

Segmental peak negative stain and strain rate significantly separated remote segments without infarction from segments with nontransmural or transmural infarction ($P < 0.001$ for all). However, these factors did not differentiate between nontransmural and transmural infarctions ($P = 0.227$ and $P = 0.075$, respectively). Segmental strain >−9.1 had a specificity of 72.42% and a sensitivity of 71.79% to detect transmural infarctions (ie, transmurality ≥50%).

Cardiac biomarkers and echocardiography versus infarct size. There were significant correlations between infarct size and the peak levels of cardiac biomarkers ($R^2 = 0.178$, $P = 0.02$), WMSI ($R^2 = 0.381$, $P < 0.001$), and GLS ($R^2 = 0.377$, $P < 0.001$; Fig. 3).

Linear regression model predicting the infarct size percent (without cutoff point) revealed that only GLS significantly predicted the infarct size percent ($P = 0.027$) after adjusting the other factors (troponin, CK-MB, 2D ejection fraction [EF], and WMSI; Table 2).

Patient characteristics, risk factors, ECG, and cardiac biomarkers with respect to infarct size. There were no significant differences between patients with infarct size <12% and patients with infarct size ≥12% in baseline characteristics, risk factors, clinical presentation, baseline ECG changes (88.9% vs. 100%, $P = 0.503$), peak troponin level ($P = 0.026$), and peak CK-MB ($P = 0.012$).

Echocardiography with respect to infarct size. LVEF, WMSI, and GLS discriminated between patients with infarct size <12% and ≥12% with significant differences between the groups (Table 3 and Table 4).

ROC analysis (Fig. 4) demonstrated that GLS exhibited a good ability to identify the patients with infarct size ≥12%, and it was superior to WMSI, EF, and cardiac biomarkers. Figure 5–6 are illustrations of CE-CMR and strain values from 2 patients.

Angiographic findings. Twenty-seven patients underwent coronary angiography during the index hospitalization, 10 patients had single-vessel CAD, 5 patients had two-vessel CAD, and 12 patients had multivessel CAD. Sixteen of these patients underwent PCI for the culprit artery during the index procedure, six patients were referred for surgical revascularization, and five patients were advised to receive medical treatment.

Discussion

The results of the present study confirm the usefulness of noninvasive imaging to identify high-risk patients presenting with acute NSTEMI. We found a significant correlation between tissue Doppler-derived GLS and infarct size.

The current guidelines recommend acute reperfusion therapy only in clinically unstable NSTEMI patients.[21] This strategy may be inadequate in the subgroup of NSTEMI patients who have substantial infarction. Our findings indicate that GLS evaluation provides an accurate assessment of the global myocardial function and the presence of segments with a transmural extent of necrosis. These results provide important clinical implications because these data may provide

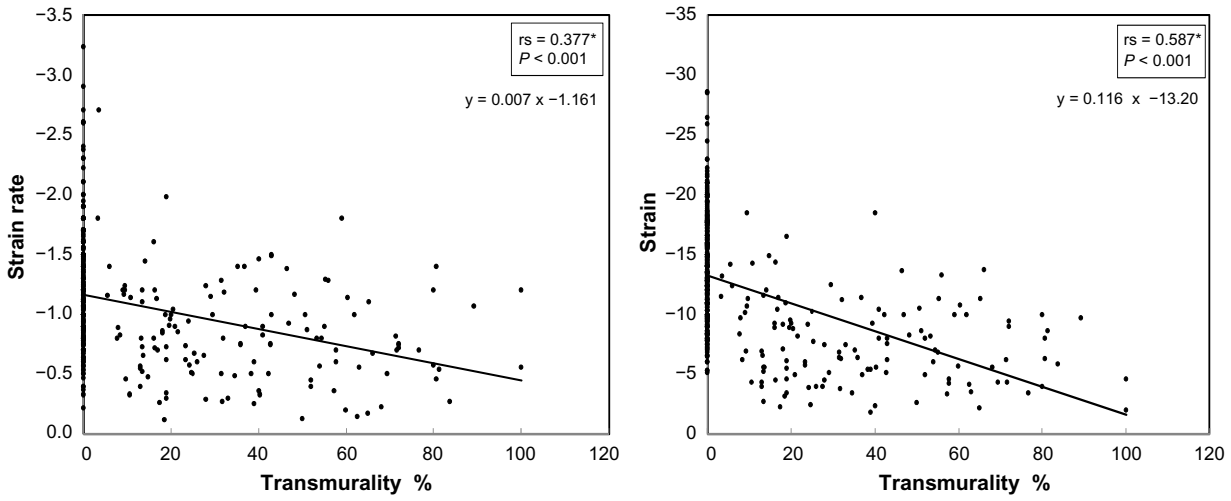

Figure 2. Scatterplots of the correlations between transmurality by segmental longitudinal strain and strain rate.

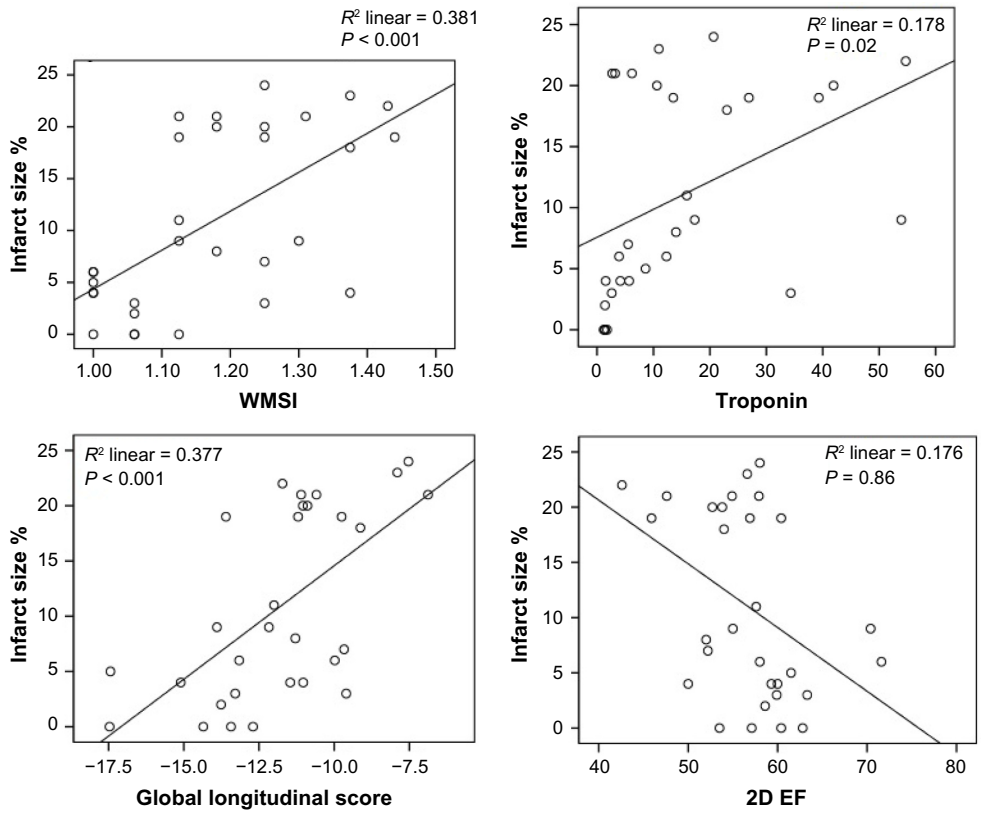

Figure 3. Scatterplots of infarct size using CE-MRI, echocardiographic parameters of LV systolic function, and cardiac enzymes.
Abbreviations: WMSI, wall motion score index; LVEF, left ventricular ejection fraction.

a means for the early identification of patients who have large and significant infarction and are at high risk. Echocardiography is the only bedside, noninvasive method to identify these patients.

The difference between STEMI and NSTEMI in the emergency room by definition is electrophysiological not pathophysiological. A subgroup of NSTEMI patients has substantial infarction, and there is a significant overlap in final infarct size between STEMI and NSTEMI patients. Even patients with a normal ECG may develop large infarctions.[10,26]

Infarct size is a strong predictor of mortality and major adverse cardiovascular events.[5] The current reperfusion therapy is highly effective in reducing infarct size. The relative reduction of infarct size achieved is typically 40% by using thrombolysis and 60% by using primary PCI.[27] These procedures salvage viable myocardium and favorably influence infarct healing.[28,29] Mortality rate is markedly reduced in the era of reperfusion therapy, and this benefit is largely attributed to a reduction of infarct size.[5,6]

The association of infarct size with increased mortality rate was demonstrated in previous studies,[3,4] which found that an infarct size ≥12% was associated with increased mortality. One of these studies was a large trial that found 12% to be the median infarct size in STEMI patients treated using acute reperfusion, and an IS <12% of the LV was associated with

Table 2. Linear regression model predicting the infarct size percent.

	B	SE	BETA	t	*P* VALUE
Troponin	0.101	0.128	0.186	0.789	0.438
CK-MB	0.020	0.037	0.135	0.560	0.581
Echo 2D EF	0.053	0.279	0.038	0.192	0.850
WMSI	11.499	16.43	0.189	0.700	0.491
GLS	1.510	0.640	0.451	2.361*	0.027*

Abbreviations: CK-MB, creatinine kinase enzyme; WMSI, wall motion score index; GLS, global longitudinal strain.

Table 3. Correlation between infarct size using CE-MRI and echocardiographic parameters.

	INFARCT SIZE <12 (n = 18)	INFARCT SIZE ≥12 (n = 12)	*P* VALUE
ESV (cm^3)	33.44 ± 13.92	37.17 ± 9.72	0.429
EDV (cm^3)	79.39 ± 26.27	80.0 ± 20.75	0.947
EF%	59.11 ± 5.74	53.58 ± 5.28	0.013*
WMSI	1.11 ± 0.12	1.27 ± 0.11	0.001*
GLS	–12.88 ± 2.30	–10.11 ± 1.95	0.002*

Note: Data are presented as the mean ± SD.
Abbreviations: ESV, end-systolic volume; EDV, end-diastolic volume; EF, ejection fraction; WMSI, wall motion score index; GLS, global longitudinal strain.

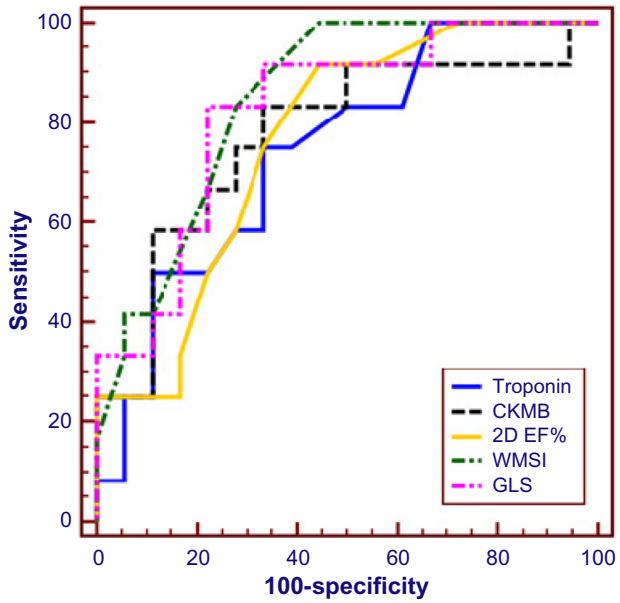

Figure 4. ROC analysis to identify infarct size ≥12% of the total LV myocardial volume.

low mortality. Therefore, we used 12% as the cutoff to identify patients who were at high risk. There were 12 patients with infarct size ≥12% in our study, which accounted for ~40% of the total number of patients. This fraction may have occurred because our patients were from a tertiary referral hospital that serves a wide area. Therefore, the patients referred to this hospital were relatively at high risk.

Diagnostic tools for the early assessment of infarct size. The time window for myocardial salvage after acute occlusion of a coronary artery is narrow. Therefore, a tool to predict infarct size should be based on information that can be obtained from the emergency department. Patients' characteristics, risk factors, and ECG changes did not correlate with infarct size in the present study and could not identify patients with substantial infarction.

Cardiac biomarkers, including CK-MB and troponin, correlated well with infarct size and identified patients with substantial infarction. The amount of enzymes depleted from the heart is proportional to the size of the infarction. However, only a small percentage of the amount depleted reaches the circulation in the absence of coronary revascularization. The remainder is hydrolyzed locally or in lymph tissue.[30] Serial samples permit a mathematical modeling of the amount of enzymes depleted, and therefore, an estimate of infarct size as long as a predictable relationship exists between the amount depleted and the amount that reaches the circulation.

Previous studies found that different parameters of cardiac enzyme measurements correlated with infarct size, except for admission and early (<12 hours) after the onset of chest pain measurements.[31–37] This correlation is primarily the result of the slow release of these biomarkers.

Prediction of infarct size using echocardiography. Myocardial systolic function is dependent on a continuous blood supply and deteriorates within seconds of acute coronary occlusion,[38] even before the onset of necrosis. Therefore, one important advantage of echocardiography is that it can identify patients with developing substantial infarction at a time point when the intervention may achieve a significant myocardial salvage.

LVEF using echocardiography is a well-established tool to describe LV function, and it has traditionally been used to assess the degree of myocardial damage, as a predictor of outcome and a marker of early and late complications after AMI. However, the assessment of LV damage using echocardiography shortly after revascularization provides less precise infarct size estimates as a result of stunning and the inability of resting myocardial dynamics to convincingly distinguish reversible from irreversible dysfunctional myocardium.[38–40] LVEF measured using echocardiography correlated well with LVEF measured using CMR in our study, and both correlated moderately with infarct size. However, the correlation was stronger with EF measured using CMR, which identified patients with

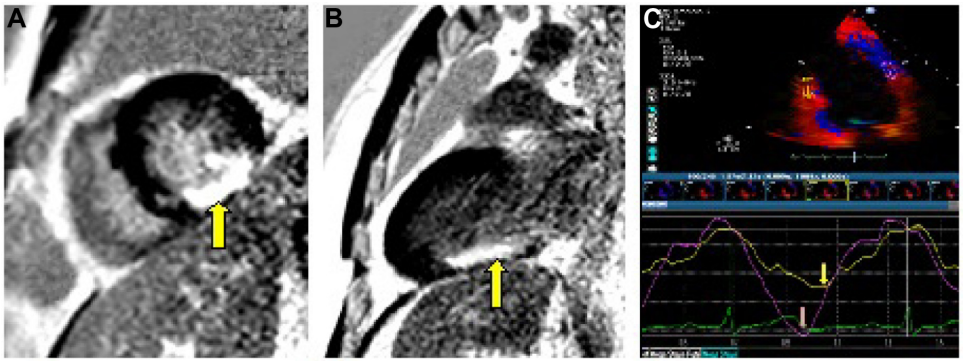

Figure 5. A 50-year-old male patient. ECG showed ST segment depression in leads V3–6 and inverted T waves in leads II, III, and aVF. CE-CMR images obtained in short axis (**A**) at the basal and midsegments and vertical long-axis (**B**) orientations show transmural infarction involving the basal and midsegments of the inferior wall (yellow arrows). Total infarct size was 19%. Myocardial strain (**C**) of the infarcted area in the midsegment of the inferior wall (the yellow curve) is diminished (–8%; $n = 17.3 \pm 3.7$) and the peak is delayed (the small yellow arrow), while the violet curve represents normal strain from normal midanterior wall (–18.5%; $n = -17.4 \pm 3.6$). GLS was –11.2 ($n = -15.8 \pm 2.2$).

Table 4. ROC analysis of troponin, CK-MB, and echocardiographic parameters for the identification of infarct size ≥12%.

	CUTOFF	SENSITIVITY	SPECIFICITY	AUC	*P* VALUE	PPV	NPV	ACCURACY
Troponin	9	75.0	66.67	0.743 (0.565–0.921)	0.013*	60.0	80.0	70.0
CK-MB	28	83.33	66.67	0.773 (0.592–0.955)	0.026*	62.5	85.7	73.33
2D EF%	55	58.33	72.22	0.764 (0.066–0.406)	0.016*	58.3	72.2	66.67
WMSI	1.125	83.33	72.22	0.847 (0.712–0.983)	0.001*	66.6	86.6	76.67
GLS	–11.29	83.33	77.78	0.824 (0.673–0.975)	0.003*	71.4	87.5	80.0

Note: The AUC is reported with 95% CIs.
Abbreviations: NPV, negative predictive value; PPV, positive predictive value.

substantial infarction, but at a low sensitivity and specificity. One possible reason is that LVEF describes the global LV function, but the infarcted area and reduced function are regional, and a decrease in LVEF supposes that several LV segments are involved. LVEF is primarily a measurement of the radial contraction of the wall plus some longitudinal contraction, which is reflected by the mitral plane movement.

WMSI is another established parameter of LV systolic function that is a validated prognostic indicator after MI.[41] Previous studies consistently demonstrated that evaluations of wall motion abnormalities perform better than volume-based LV indices in early risk assessment for MI patients.[41,42] However, this technique is semiquantitative, experience dependent, and based on the subjective interpretation of myocardial motion. Our study found a strong correlation between WMSI and infarct size measured using CE-CMR (R^2 = 0.381, $P < 0.001$). We also found that WMSI at a cutoff of 1.3 identified the patients with an infarct size ≥12% with a sensitivity of 77% and specificity of 92%.

Strain Doppler echocardiography for the prediction of infarct size. All functional indices based on myocardial deformation (including direct visual assessment, wall thickening, and strain measurements) are load-dependent. This load or local stress dependence is even more complex in the ischemic or infarcted part of the LV, where the mechanical behavior of infarcted subendocardial myocardium is largely dictated by the preserved subepicardial layers.[43,44] Similarly, the function of preserved myocardium adjacent to the infarct border is heavily dependent on the mechanical behavior of remote noninfarcted regions.[45,46]

Longitudinal strain echocardiography is a relatively new parameter that is not widely used in clinical practice. This technique quantifies contraction only in the longitudinal direction. This longitudinal vector of the LV three-dimensional contraction pattern primarily represents subendocardial contraction, and it is likely more sensitive to ischemia when compared with the radial contraction caused by the deformation of the circumferential midmyocardial and subepicardial layers.[47] Therefore, global strain may be a better indicator of myocardial damage due to ischemia.

Global strain reflects the averaged segmental myocardial long-axis relative shortening, and it is a global functional measurement that may provide information beyond what is available from WMSI and LVEF.[48]

GLS was –11.77% ± 2.54% (range –17.47% to –6.88%) in our study. The estimated values of GLS in our study were much lower than those of previously reported studies on healthy individuals.[49,50] GLS was also strongly correlated with infarct size ($r = 0.601$, $P < 0.001$).

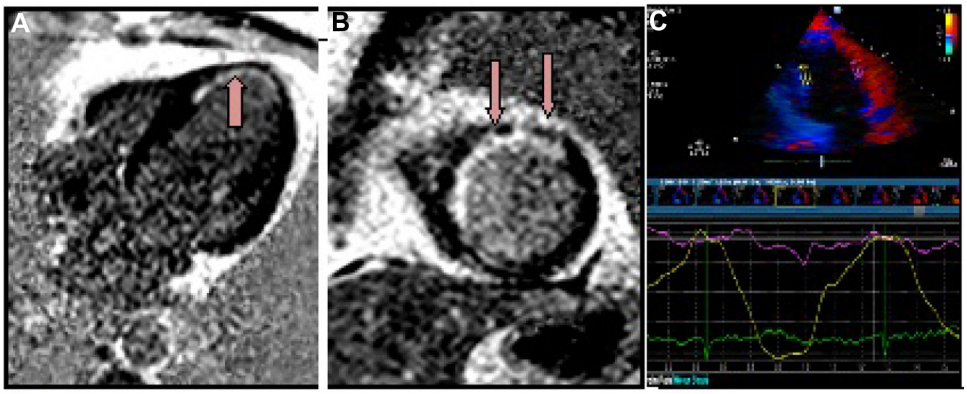

Figure 6. A 48-year-old male patient. ECG showed ST segment depressions in leads II, III, aVF, and V3–6. CE-CMR images obtained in horizontal long-axis (**A**) and short-axis (**B**) orientations at midlevels show predominantly transmural infarction involving the midsegments of the anterior and septal walls (violet arrows). Total infarct size was 21%. Strain (**C**) of the infarcted area in the midanterior wall (violet curve) is diminished (–6.2%; $n = –17.4 \pm 3.6$) and delayed (the small white arrow). The (yellow curve) represents normal strain from normal inferior wall (–19.3%; $n = –17.3 \pm 3.7$). GLS was –6.88 ($n = –15.8 \pm 2.2$).

The estimated values of averaged strain from infarct zone (–7.93% ± 2.27) were lower when compared with the values obtained from remote areas (–13.97 ± 2.59). However, strain of the infarcted zone was not significantly correlated with infarct size.

GLS was the only independent predictor of infarct size ($P = 0.027$) when entered as a covariate with other measures of LV systolic function and cardiac biomarkers in a linear regression analysis. GLS at –11.29% could identify patients with infarct size ≥12% with a sensitivity of 83.33% and specificity of 77.78% (area under the curve [AUC] = 0.824). GLS remained a significant and an independent predictor to identify patients with infarct size ≥12% when entered as a covariate in a logistic regression model, along with troponin, CK-MB, EF, and WMSI.

Transmurality. The evaluation of transmural myocardial infarct extension (≥50%) is predictive of myocardial viability.[51] We found a significant correlation between infarct transmurality and segmental peak negative strain and strain rate in corresponding segments ($r = 0.587$ and $r = 0.377$, respectively, $P < 0.001$ for both). However, the relationship was not as strong as between global strain and total infarct size ($r = 0.601$). One important reason for this finding is that the size and position of each myocardial segment using MRI and echocardiography are not identical. The effect of measurement variability of the two techniques is also reduced by calculating the total infarct size and global strain.

Peak negative segmental longitudinal strain also discriminated normal from necrotic myocardium ($P < 0.001$), but it did not differentiate between nontransmurally and transmurally infarcted segments ($P = 0.227$).

The infarction in NSTEMI is predominantly subendocardial, and 70% of infarcted segments in our study were subendocardial. The subendocardial layer of the myocardium contains predominantly longitudinal fibers, and the resolution is optimal because longitudinal strain tracks motions parallel to the ultrasound beam, which contrasts the motion beyond the subendocardial layer where circumferential fibers are predominantly found. This factor explains why the deterioration of longitudinal strain is not more pronounced in segments with transmural necrosis.

Conclusions

GLS is a good predictor of infarct size in NSTEMI, and it may serve as a tool in conjunction with risk stratification scores for the selection of high-risk NSTEMI patients who may benefit from urgent revascularization. These findings may be of health economic interest and possess several potential clinical implications.

Study Limitations

A technical limitation is that poor echocardiographic quality in some patients interfered with tissue Doppler-derived strain. A total of 17.1% of the total number of segments were not feasible for strain measurement in our study. Infarct expansion and edema developing during the first hours may be accompanied by alterations in systolic function, and CMR examination was performed one to two days after echocardiographic evaluation. In our study protocol, we chose to select a subgroup of clinically and hemodynamically stable patients with recent NSTEMI, undergoing PCI as a second therapeutic option for recurrent angina. This is a very common typology of ischemic patients in the clinical practice of our hospital, considering the limited availability of early intervention in patients with NSTEMI in our country. The sample size was relatively small, resulting in the lack of clinical end points, and larger studies are needed to validate these results.

Author Contributions

Conceived and designed the experiments: ML, EE, SA, SE. Analyzed the data: ML, EE, SE, KE. Wrote the first draft of the manuscript: ML, EE, KE. Contributed to the writing of the manuscript:ML, EE, KE. Agree with manuscript results and conclusions: ML, EE, SA. Jointly developed the structure and arguments for the paper: ML, EE, SA. Made critical revisions and approved final version: ML, EE, SA. All authors reviewed and approved of the final manuscript.

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