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Original Article

Early prediction of ventricular functional recovery after myocardial infarction by longitudinal strain study

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Abstract: Background: There are some suggestions that global myocardial strain (GLS) early after ST-elevation myocardial infarction (STEMI) is a predictor of improvement in left ventricular ejection fraction (LVEF). The goal of this study was to evaluate LV recovery after STEMI intervention based on GLS values. Methods: The study population consists of 43 patients with acute STEMI and no history of prior coronary intervention treated with primary percutaneous coronary intervention. LVEF and myocardial strain indices were measured 48 hours and two months after STEMI by transthoracic echocardiography and speckle tracking method. More than 5% improvement in LVEF was considered significant. Results: GLS values were significantly higher in patients with >5% improvement in LVEF 2 months after the STEMI (GLS=15.76% in patients with >5% improvement vs. 11.54% in the other group, P<0.05). ROC analysis suggested GLS values more than 13.5 to be a predictor of significant LVEF improvement 2 months after STEMI. Higher GLS was observed in patients with inferior, posterior and inferoseptal STEMI versus anterior, extensive or anteroseptal STEMI and in patients with right coronary occlusion versus occlusion of the left anterior descending or circumflex arteries. Conclusion: We have observed that early longitudinal LV strain after STEMI is a predictor of recovery after STEMI. This is a useful method to predict early LV recovery after STEMI. GLS values of more than 13.5% are a significant predictor of significant LVEF improvement.

Keywords: Echocardiography, acute myocardial infarction, strain rate imaging, myocardial strain, tissue and strain Doppler echocardiography, percutaneous intervention

Introduction

The severity of myocardial damage in the setting of acute ST elevation myocardial infarction (STEMI) is affected by many factors [1-5] and is usually measured using left ventricular ejection fraction (LVEF). Despite its wide utility, LVEF cannot report detailed regional differences in contractility and subtle myocardial damage in patients with normal LVEF [5-7]. New measurements have been introduced for accurate and early risk estimation after STEMI such as global LV strain parameters [4]. The latter determines the 30-day risk of major adverse cardiac events (MACE) after STEMI in patients with preserved post-MI LVEF [8]. Many patients with normal LVEF after STEMI seem to have impaired myocardial strain [5, 7, 9] confirming the limited value of LVEF alone in assessment of LV function. The superiority of myocardial strain values in predicting adverse long-term outcomes in patients with reduced LVEF is unclear. However, according to a meta-analysis of available data in patients with heart failure, Global Longitudinal Strain (GLS) is a better predictor of all-cause mortality than LVEF [10] after STEMI [11, 12]. It is also a better predictor of long-term cardiovascular morbidity and mortality in low risk general population [7, 13]. It seems that there is a significant correlation between the direction and extent of change in the LV strain parameters and LVEF in the first few months after STEMI in patients with reduced initial LVEF [5]. To investigate the predictive value of GLS and its relative factors, we studied echocardiographic markers of LV function including GLS and LVEF in a group

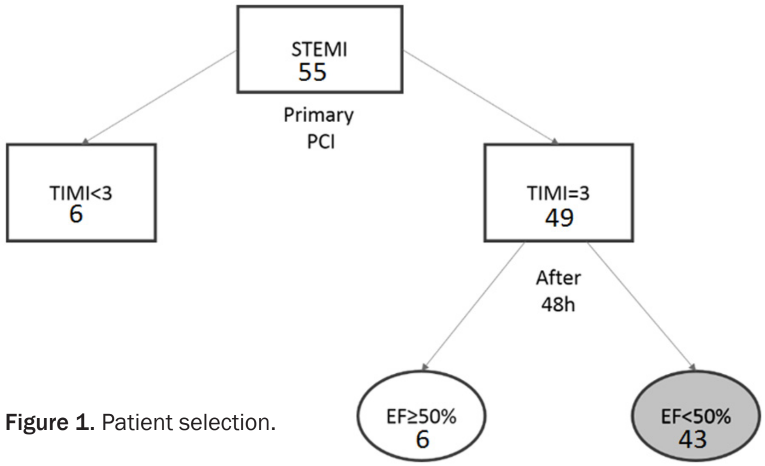

Figure 1. Patient selection.

of patients undergoing primary percutaneous coronary intervention (PCI) for acute STEMI in 48 hours and 2 months thereafter.

Materials and methods

Patient selection

The study population consisted of 43 patients who presented with acute STEMI and admitted to Sh. Modarres hospital for primary PCI. Patients that were included in this study had undergone a successful primary PCI on the culprit lesion with a post procedure Thrombolysis In Myocardial Infarction (TIMI) score of 3 [14] and estimated LVEF of less than 50% within forty-eight hours after performing PCI (**Figure 1**). Excluded were patients with a history of prior myocardial infarction, coronary artery bypass grafting (CABG) or previous revascularization. Patient with significant valvular heart disease or suboptimal echocardiographic views and patients who experienced any cardiovascular events including an episode of significant arrhythmia, early hospitalization or mortality in our 2 months follow-up were also excluded. All patients signed informed consent before performing the first echocardiographic study.

Echocardiographic assessment

All the study patients underwent an echocardiographic assessment 48 hours after STEMI. Those with measured LVEF of less than 50% in the first study had another assessment two months thereafter. All the studies were performed by a single echo trained cardiologist who was blinded to the angiography results. The patients had sinus rhythm during the study and their electrocardiogram was constantly recorded. Patients were in left lateral decubitus position during the study, based on the American Society of Echocardiography guidelines.

The echocardiographic study was done by conventional and speckle tracking methods. Conventional two dimensional and Doppler images were obtained in standard echocardiographic views, using Philips iE33 xMATRIX. LV EF was calculated by the biplane Simpson's method. Speckle tracking echocardiography (STE) images were recorded in 3 cardiac cycles with frame rate about 40-60 by Philip iE33 xMATRIX and analyzed by QLAB CMQ9.0 software. LV endocardium and epicardium were traced both manually and automatically to assess LV strain and strain rate. Strain analysis was done in apical four-chamber, two-chamber and long-axis views and the time interval between R wave and aortic valve closure was used as a reference for longitudinal strain. Mitral annulus and apex were defined by three index points at the end-systolic frame in every three apical views. LV was divided in 17 segments and the software calculated the average peaked systolic longitudinal strain of all 17 segments as GLS value. Five percent accepted as a threshold for improvement of LV systolic function [26].

Data analysis

All patients were divided to two groups based on improvement in EF value after 2 months. 5% improvement was considered as the cut-point. Data analysis was done by SPSS version 23.0 software. Independent-Samples-T test was performed. Also, a receiver operating characteristic curve (ROC) analysis was carried out to figure out the predictive value of early GLS for prediction of long-term EF. P values less than 0.05 were considered significant. This study was approved by institutional review board.

Results

Baseline characteristics

The mean age was 56.7±1.2 years, 86% of 43 patients were male. 44.2% were diabetic, 32.6% were hypertensive and 27.9% of 43 patients had abnormal lipid profile. Known fam-

Table 1. Study group characteristics

Demographic determinants		N (%)
Age	<60	22 (51.2)
	>60	21 (48.8)
Gender	Male	37 (86.0)
	Female	6 (14.0)
Diabetes	Pos	19 (44.2)
	Neg	24 (55.8)
Hypertension	Pos	14 (32.6)
	Neg	29 (67.4)
Hyperlipidemia	Pos	12 (27.9)
	Neg	31 (72.1)
Family history	Pos	11 (25.6)
	Neg	32 (74.4)
Smoking	Pos	23 (53.5)
	Neg	20 (46.5)
MI type		
Anterior		18 (41.9)
Anteroseptal		1 (2.3)
Inferior		17 (39.5)
Posterior		2 (4.7)
Inferoseptal		1 (2.3)
Extensive		4 (9.3)
Culprit vessel		
RCA		17 (39.5)
LAD		23 (53.5)
LCX		2 (4.7)
OM		1 (2.3)
Echocardiographic study parameters		
Mean EF at 48 hours after MI		42±5%
Mean EF at 2 months after MI		44±6%
Mean GLS at 48 hours after MI		12.5±1.8
Mean EF at 2 months after MI		12.9±2.1
EF recovery >5%		8 (18.6)
LV Diastoloc Dysfunction After 48 Hours		
Mild		24 (56)
Moderate		13 (30)
Severe		3 (7)
LV Diastoloc Dysfunction After 2 Months		
Mild		23 (53)
Moderate		13 (30)
Severe		4 (9)
RV dysfunction After 48 Hours		5 (11.6)
RV dysfunction After 2 Months		4 (9)

ily history of coronary artery disease (CAD) was reported in 25.6% of 43 patients and 53.5% of patients were smokers.

Table 2. The relationship between GLS after 48 hours and >5% increase in EF after two months

Significant (>5%) increase in EF after two months	Mean GLS after 48 hours (%)	*P*-value
Pos	15.56±1.01	<0.05
Neg	11.74±0.83	

Coronary involvement and baseline EF and GLS data

Myocardial infarction involved the anterior territory in 18 cases (41.9%), anteroseptal territory in one patient, inferior territory in 17 cases (39.5%), posterior territory in two cases, inferoseptal territory in one patient. Four cases (9.3%) had extensive Myocardial infarction (MI). The culprit vessel was right coronary artery (RCA) in 17 cases (39.5%), left anterior descending artery (LAD) in 23 cases (53.5%) and left circumflex artery (LCX) in two cases; obtuse marginal (OM) was occluded in one patient.

Mean EF and GLS values were 42% and 12.5 respectively at 48 hours after MI, and 44 and 12.9 at 2 months after MI. After dividing the cases in two groups with more than 5% improvement in the EF measurements after 2 months and the patients who had less or no improvement, the first group of patients consisted of 8 patients and the latter was including the resting 36 patients. The former group was consisting of 5 males and 3 females with a mean age of 52.1±0.9 years old, 4 patients were hypertensive, 5 patients had diabetes mellitus and 3 of them had hyperlipidemia and two of these patients were suffering all of the mentioned conditions simultaneously. 4 patients in this group were smokers and 2 of them had appositive family history of known CAD. The culprit lesion was RCA in 6 patients and LAD in two of them. Six patients had inferior MI while another two had extensive and anteroseptal MI.

The demographic properties of the study population are summarized in **Table 1**.

GLS correlation with EF recovery

The early GLS value and early EF were correlated with Pearson's r=0.32 and *P*-value =0.037. The late GLS value and late EF were also correlated with Pearson's r=0.48, *P*-value =0.001.

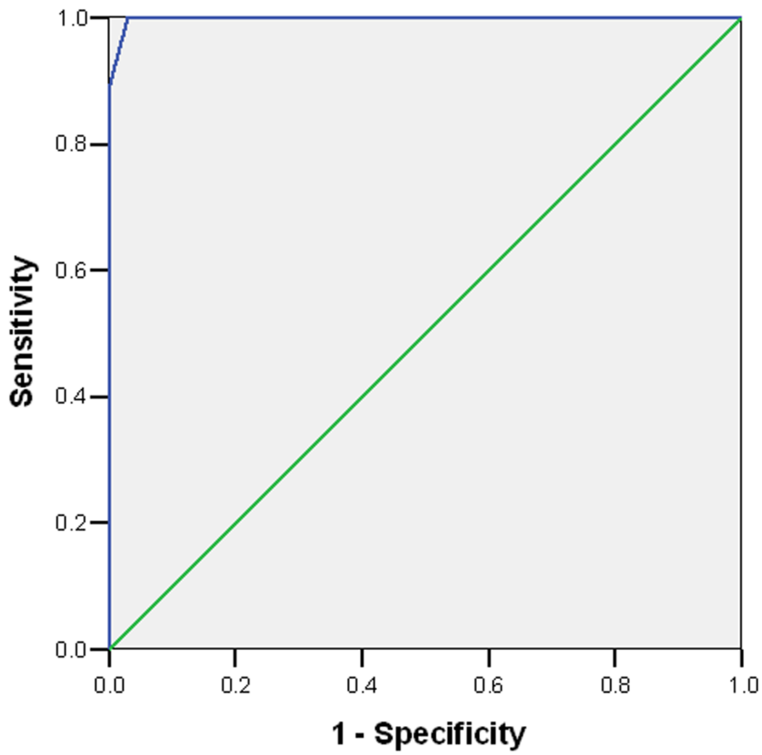

Figure 2. The ROC curve of GLS after 48 hours to predict EF improvement. Sensitivity =100%, Specificity =97%, AUC =0.998, *P*-value <0.0001.

Mean early EF was about 45% in patients with final EF recovery >5% and about 41% in the rest (*P*-value =0.069). Mean late EF was about 50% in patients with final EF recovery >5% and about 42% in the rest (*P*-value =0.002). Mean early GLS value was about 16% in patients with final EF recovery >5% and about 12% in the rest (*P*-value <0.0001). Mean late GLs value was the same as the early GLS values (*P*-value <0.0001). EF recovery >5% was not correlated with GLS recovery >5% (*P*-value =0.25).

The mean GLS value was 15.56 in the group of patients with >5% increase in EF after 2 months and 11.74 in the other group (**Table 2**). ROC analysis on the GLS values after 48 hours indicated the values greater than 13.5 to predict >5% increase in LVEF after 2 months (**Figure 2**).

GLS values greater than 13% were significantly more prevalent in cases of Inferior, Posterior and Inferoseptal MI 48 h after symptoms onset, and lower values were observed in cases of Anterior, Anteroseptal, and extensive MI (22.2% for anterior MI, 0% for anteroseptal MI and 25% for extensive MI versus 94.1% for inferior MI, 100% for posterior and inferoseptal MI, *P*-value <0.05).

GLS values greater than 13% were significantly more prevalent in cases with RCA occlusion and lower values were observed in cases with occlusion of LAD branch (100% for RCA occlusion versus 21.7% for LAD occlusion and 100% for LCX occlusion, *P*-value <0.05) (**Table 3**).

For decrease and validation of inter and intra observer variability, all Echocardiographic evaluations were performed only by two Echocardiographers separately who interpreted all images and data together for better agreement of the results.

Discussion

Myocardial strain is an echocardiographic determinant of regional and global myocardial function [15-18]. GLS has been validated to assess the global cardiac function in the setting of STEMI, stable chronic coronary artery disease, and general healthy population, as discussed in the following lines.

According to the study by Munk et al., on estimating the infarct size one day after STEMI, GLS was superior to LVEF and end-systolic volume index (ESVI), but comparable to WMSI. Then 30 days after STEMI, it was inferior to WMSI and comparable to LVEF and LVSD [21]. A previous study by Gjesdal et al. suggested a GLS greater than 15% as an excellent predictor of infarct size, 9 months after STEMI [22]. In patient with stable coronary artery disease GLS has been also useful. Ternacle et al., in a study on 20 patients with coronary artery disease who were candidate for PCI, measured the LVEF and LV GLS during coronary occlusion. They reported a significant decrease in GLS of ischemic regions, despite no change in LVEF and wall motion [9]. In a recent study on a similar population, Magdy et al. observed an improvement in baseline GLS 3 months after performing PCI [23].

Table 3. The relation between LGS level, type of MI and the culprit occluded coronary artery

		EF recovery >5%	LGS after 48 h		*P*-value
			≤13%	>13%	
Type of MI	Anterior	1	14 (77.8%)	4 (22.2%)	<0.005%
	Anteroseptal	0	1 (100%)	0	
	Inferior	6	1 (5.9%)	16 (94.1%)	
	Posterior	0	0	2 (100%)	
	Inferoseptal	0	0	1 (100%)	
	Extensive	1	3 (75%)	1 (25%)	
Culprit vessel	RCA	6	0	17 (100%)	<0.005%
	LAD	2	18 (78.3%)	5 (21.7%)	
	LCX	0	0	2 (100%)	
	OM	0	1 (100%)	0	

GLS in patients with revascularization is also promising. Song et al. studied the longitudinal, circumferential, and radial LV strains in a group of patients undergoing PCI after inferior STEMI. They reported a lower LV strain (in all three dimensions) compared to healthy controls and a 60% improvement in global longitudinal and circumferential LV strains after performing PCI. LV regional strain was impaired in 87% of patients with inferior MI and improved in 60% of patients after performing PCI [24]. A recent study by Yang et al. reported a significant improvement in GLS in a group of anterior STEMI, 3 days and 6 months after MI, though the global circumferential strain was only improved 6 months after Mic [25]. As mentioned above, Magdy et al. recently confirmed these findings in a group of patients with stable coronary artery disease who were candidate for PCI [23].

GLS has been a predictor of future cardiovascular events in the normal population. Russo et al. [7] designed a community-based study to define the prevalence and predictive value of LV GLS in the general population. Of the 708 subjects in the study population, about 96% had normal LVEF, among whom 16% had abnormal LV GLS. They followed vascular events in the population for 5 years and observed that both the abnormal GLS and abnormal LVEF were significantly associated with adverse events. Again, those participants with abnormal GLS and normal EF had also a significant increased risk for vascular events. This study confirmed the value of GLS measurement in patients with normal EF after ischemic events. In a more recent prospective study, Biering et al. [13] followed a population of 1296 participants for 11 years to determine the incidence of heart failure, acute myocardial infarction, or cardiovascular death and the predictive factors. They observed that lower GLS values are significantly associated with increased risk of adverse cardiovascular events. Note that, this association was not observed in women, when adjusted for sex alone.

According to previous studies, a consensus has not yet been established on a cut-off GLS value that most accurately predicts mortality and morbidity. Studies mostly suggested a GLS lower than about 12 to 15%; Bendary et al. recently suggested the baseline GLS values lower than 12.65% to be the only significant independent predictor of 30-days MACE, with a sensitivity of 77.8% and specificity of 83.7% [8]. Goedemans et al. suggested the cut-off value of 14.4%, or less to be significantly correlated with all-cause mortality in chronic obstructive lung disease (COPD) patients after STEMI [11].

Limitations

Due to small number of patients, our study is hypothesis generating and needs to be validated in larger studies.

Conclusion

Reduced GLS values to lower than 18% has been detected in all of our patientspost STEMI and reduced LVEF compatible with previously observed association between reduced LVEF and impaired LV strain [3]. We observed significantly greater early GLS values in those patients who had more than 5% improvement in early post-MI LVEF after 2 months. GLS cut off value that was a predictor of long-term improvement in LV function was 13.5%. Our study suggest that early GLS is a widely available and practical parameter in predicting future left ventricular recovery with minimal changes across the time after the acute coronary event. As the early prediction of future LV function can guide both the medical therapy and the indications for defibrillator implantation in first days after STEMI, GLS should be considered as a complementary approach in all patients with borderline or reduced ejection fraction early after MI, though more comprehensive evidence on larger study populations and with considering long-term prognostic outcomes are needed to support its application in the future practice guidelines.

Disclosure of conflict of interest

None.

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