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Original Article

Myocardial recovery after percutaneous coronary intervention in coronary artery disease patients with impaired systolic function-predictive utility of global longitudinal strain

Sheeren Khaled [a, b, *], Ghada Shalaby [c, b]

[a] Banha University, Egypt
[b] King Abdullah Medical City, Muzdallfa Road, Makkah, Saudi Arabia
[c] Zagazig University, Egypt

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ABSTRACT

Objective: Coronary revascularization is associated with better outcomes in coronary artery disease patients. We aim to investigate the prevalence, and factors associated with left ventricular (LV) improvement following successful percutaneous coronary intervention (PCI) of patients with impaired systolic function with specific reference to the value of baseline GLS.
Methods: This retrospective study reviewed the records of coronary artery disease patients with impaired systolic function who were admitted and treated with PCI.
Result: Out of 420 consecutive acute coronary syndrome patients with an impaired systolic function who were admitted and treated with PCI during the period from January 2021 to December 2021, 147 patients (35%) showed no improvement in the Left ventricular ejection fraction (LVEF) post PCI and 273 patients (65%) showed improvement of the LVEF post PCI in their follow up echocardiogram. Larger myocardial injury dilated LV dimension at the acute phase showed a strong impact on further improving LV systolic function. Baseline GLS showed a higher statistical difference between the Non-improving LVEF and improving LVEF groups. Moreover, the early GLS and further LV systolic function improvement were strongly correlated ($P < 0.001$) with higher sensitivity and specificity. A receiver operating characteristic curve (ROC) analysis demonstrated that GLS values greater than 9% are a predictor of significant LVEF improvement in the follow-up stage.
Conclusion: Sizable proportion of patients with impaired systolic function following successful PCI show further LV systolic recovery. We demonstrated that the baseline GLS values of more than 9% are an accurate predictor of significant LVEF improvement.

1. Introduction

Left ventricular systolic function is the most crucial factor affecting morbidity and mortality in patients with coronary artery disease (CAD).[1] Percutaneous coronary intervention (PCI) is a known procedure of choice for symptom relief in patients with CAD.[2] However, the effect of PCI on systolic functions in patients with impaired baseline LV systolic function is still challenging.

Echocardiography has been the most popular and noninvasive technique that can provide all information on the structure and function of the heart. In clinical practice, Left ventricular ejection fraction (LVEF) is widely utilized as an index of myocardial systolic function.[3] Another modality as Tissue Doppler imaging (TDI) has emerged as a sensitive quantitative measure of both systolic and diastolic longitudinal myocardial functions.[4,5]

Measurement of myocardial deformation by strain has emerged as a promising tool to evaluate normal and ischemic myocardium to evaluate regional and LV global function. New measurements have been introduced for proper and early risk estimation after revascularization such as global LV strain parameters.[6,7] Data derived from meta-analysis denoting that Global Longitudinal Strain is a better predictor of all-cause mortality than LVEF.[8]

* Corresponding author. King Abdullah Medical City, Muzdallfa Road, Makkah, Saudi Arabia.
E-mail addresses: sheeren.khaled@gmail.com (S. Khaled), ghadashalaby10@gmail.com (G. Shalaby).

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The current study aims to investigate the effect of PCI on LVEF in coronary artery disease patients with impaired systolic function assessing the prevalence of improvement and associated predictors with a special focus on the predictive utility of early GLS.

2. Method

This retrospective study reviewed the records of acute coronary syndrome patients with impaired systolic function who were admitted and treated with PCI during the period from January 2021 to December 2021. LV systolic dysfunction was defined as LVEF <52% for men and <54% for women.[9] Successful PCI was defined as post-intervention residual stenosis <30% with thrombolysis in myocardial infarction flow grade III. This study is designed to be part of the standard of patient care and has received approval from the ethics committee/institutional review board of our institution.

Inclusion criteria: Patients presenting with acute coronary syndrome including:

- ❖ ST-elevation myocardial infarction (STEMI) is either treated with primary PCI or received thrombolytic therapy in the referral hospital and then referred for elective PCI
- ❖ Non- ST-elevation myocardial infarction (NSTEMI)
- ❖ Unstable angina

Those patients showed LV systolic dysfunction in their baseline echocardiography (as defined above) and were treated with PCI (within 7 days of hospital admission) in addition to the standard recommended medical therapy.

Exclusion criteria: Patients known to have old LV systolic dysfunction from before, those who had previous revascularization or those with unsuccessful angioplasty, and those who did not have post-procedure completed data.

2.1. Data collection

2.1.1. Clinical data

Baseline patient's demographics, characteristics, and cardiovascular risk factors. Electrocardiographic data included rhythm and ischemic changes including ST-elevation. Laboratory data included troponin levels. Angiographic data included the presence of left main (LM) disease and the number of significantly diseased coronary arteries; defined as stenosis >50% for the left main and >70% for the left anterior descending (LAD) arteries, left circumflex artery (LCX), and right coronary artery (RCA). Intervention procedures include PCI done to one or more of the affected coronaries and device therapy use.

Echocardiography: All patients underwent a baseline standard transthoracic Doppler echocardiography within 24–48 h of hospitalization before PCI and repeated within 3–6 months after the procedure. It was performed with a Vivid 7 ultrasound system assessing the slandered parameters. (a) Left ventricular ejection fractions (LVEF) are the fraction of chamber volume ejected in systole (stroke volume) concerning the volume of the blood in the ventricle at the end of diastole (end-diastolic volume). Stroke volume (SV) is calculated as the difference between end-diastolic volume (EDV) and end-systolic volume (ESV). LVEF is calculated from LVEF [SV/EDV] x 100. (b) The presence of significant mitral regurgitation (MR) was also assessed and recorded. (c) TDI was performed by activating the TDI function. Spectral waveforms from pulse wave tissue Doppler are used to measure peak myocardial velocities. To assess the LV systolic function by tissue Doppler, the mitral annular peak systolic myocardial velocities (Sm) were recorded at different LV sites (the septal, lateral, anterior, and inferior), and then an average value was used to assess the global systolic function. Normal reference values for (Sm) should be interpreted according to age and gender.[10] (d) Based on 2D-standard echocardiography, automated function imaging (AFI) is utilized to identify the systolic LV function by assessment of the LV global longitudinal strain (GLS). Gray-scale 2D ECG-triggered, apical 2-chamber, apical long axis, and apical 4- chamber cine-loops were recorded and digitally stored with high frame rates, and one cardiac cycle from each view was selected for offline analysis. AFI method using two points was applied on each side of the mitral valve and a third point at the apex of the LV followed by automated tracing of endocardial and epicardial borders defining a region of interest and occasionally using a manual modification for better alignment. The peak systolic strain values in a 17-segment LV model were used in our study. The segmental longitudinal strain was calculated as the percentage of lengthening or shortening, and the results for each plane were presented. The results for all three planes were then combined in a single bull's-eye summary. The sum of longitudinal strain averaged over the number of segments with interpretive scores gave the GLS. A computer algorithm calculated peak systolic strain values within each segment together with global peak systolic strain from each view, and finally, complete averaged global longitudinal peak systolic strain (a global peak systolic strain) of the apical 4- chamber, apical 2-chamber, and apical long axis views are calculated. Normal values for the GLS are in the range of −18% to −22%[11] and below this value, is considered to be abnormal.[9]

2.1.2. In-hospital outcomes

Data include the short-term in-hospital outcomes; pulmonary edema, cardiogenic shock, history of mechanical ventilation, cardiac arrest, left ventricular thrombus (LVT), and length of hospital stay.

2.2. Statistical analysis

Patients were divided into two groups based on improvement in LVEF value after 3–6 months. A 5% improvement was considered as the cut-point. Statistical analysis was performed by use of the SPSS software package (SPSS Inc.; Chicago, Ill), version 21.0. Continuous data were expressed as mean ± standard deviation and compared using the Student *t*-test. Categorical data were given as a percentage and compared with a chi-square test. Regression analysis was also used for the prediction of post PCI- LV recovery. Also, a receiver operating characteristic curve (ROC) analysis was carried out to figure out the predictive value of early GLS for the prediction of improving systolic function. For all analyses a p-value < 0.05 was considered significant and not significant if it is > 0.05).

3. Results

3.1. Patients and clinical characteristics

A total of 420 consecutive patients who met the criteria were included in the analysis. We classified our patients into two groups: Group I; patients with no improvement of the LVEF post PCI in their follow-up echocardiography: 147 patients (35%) and Group II: 273 patients (65%) with an improvement of the LVEF post-PCI Fig. 1. We compared the two groups of patients in all parameters. Neither age nor gender showed an impact on improving LV systolic function among our variable population after revascularization. Also, the prevalence of most cardiovascular risk factors showed no significant statistical difference between both groups. History of permanent or paroxysmal atrial fibrillation and presence of renal impairment was more prevalent among patients without LVEF improvement group compared to the other group of patients

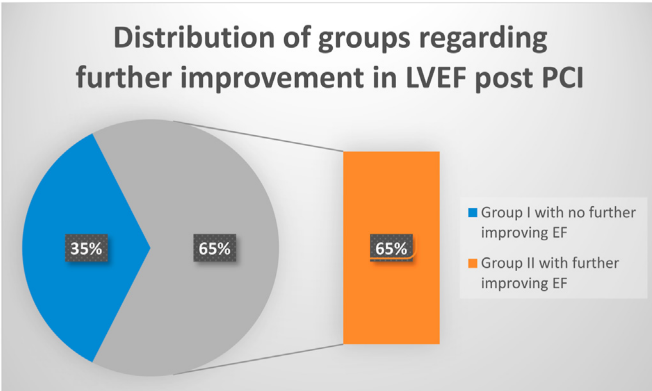

Fig. 1. Distribution of groups regarding further LVEF improvement post PCI.

($P = 0.08$ and 0.07 respectively). Larger myocardial injury (represented by a higher peak of troponin) and dilated LV dimension at the acute phase showed a strong impact on further improving LV systolic function after revascularization (95.6 ± 32.7 ng/mL VS 39.5 ± 24.5 ng/mL and 100.59 ± 38.7 mL VS 82.05 ± 21.6 mL for Non-improving LVEF and improving LVEF groups; $P = 0.029$ and 0.004 respectively) Table 1.

The mean baseline (early) GLS was 12% in patients with final LV recovery > 5% and about 7% in the rest of the patients ($P = 0.036$). Moreover, there was a highly significant statistical difference between the two groups regarding the mean LVEF after PCI by modified Simpson's methods ($P < 0.005$) Table 1. Neither presence of significant mitral regurgitation nor baseline systolic myocardial velocity (Sm by TDI) had an impact on further LV remolding or improvement in systolic function after revascularization in the current study Table 1. Also, there was no significant difference between both groups of patients regarding the distribution of diseased coronaries and severity including the presence of left main and multi-vessel disease Table 2. However, the patients of group II showed a relatively higher prevalence of PCI to RCA ($P = 0.07$) with a lower rate of device use ($P = 0.08$) compared to group I Table 2.

Regarding the in-hospital outcome parameters, the group of patients with further LV improvement after PCI showed a better prognosis reflected by the lesser indication for mechanical ventilation during hospitalization, lower rates of cardiogenic shock, cardiac arrest& left ventricular thrombus in their echocardiography, and shorter in-hospital length of stay ($P = 0.08$,0.08, 0.05.0.002 and 0.002 respectively) Table 3.

3.2. GLS and LV recovery

Early GLS values, larger myocardial injury (represented by a higher peak of troponin) and dilated LV dimension at the acute phase were found the independent predictors of LV recovery post PCI in the studied patients; however the baseline of both LVEF and systolic myocardial velocity (Sm by TDI) was not found to have a significant prediction of any further LV recovery Table 4.

Moreover, the early GLS and further LV systolic function improvement were strongly correlated ($P < 0.001$) Fig. 2. ROC analysis on the early GLS values indicated the values greater than 9% (with a sensitivity of 100% and specificity of 88%) to predict a>5% increase in LVEF (in the next 3–6 months after PCI). GLS values greater than 9% were significantly more prevalent in cases of non-anterior myocardial infarction and cases with PCI to RCA, and lower values were observed in cases of anterior STEMI and cases with PCI to LAD artery ($P < 0.001$)Table 5.

4. Discussion

Coronary revascularization with PCI is widely utilized and improves the outcome in patients with reduced LVEF.[1] Echocardiography including myocardial strain (GLS) has been validated to assess global cardiac function.[12,13] Our study provides beneficial insights into the prevalence of improvement post-PCI treated coronary artery disease patients with impaired systolic function, predictors, and outcomes, focusing on the practical use of early GLS as a predictor of risk estimation for further recovery. We observed the following: First, there is about two third of the population showed significant LV recovery and improvement post PCI which has a major concern on the prognosis and burden of the health care system. The second, degree of myocardial injury at the acute phase

Table 1
Comparing clinical characteristic of patients with and without improvement of LVEF post PCI treated ischemic cardiomyopathy.

Variable	Group I with no improving LVEF post PCI N = 147 (35%)	Group II with improving LVEF post PCI N = 273 (65%)	p value
Age (years) M ± SD	55.23 ± 12.9	58.83 ± 11.45	NS
Male n,%	113 (77%)	232 (85%)	NS
DM n,%	110 (75%)	193 (71%)	NS
HTN n,%	100 (68%)	180 (66%)	NS
Smoking n,%	43 (29%)	109 (40%)	NS
Dyslipidemia n,%	21 (14%)	46 (17%)	NS
AF/PAF n,%	20 (14%)	7 (2.5%)	0.08
CKD n,%	34 (23%)	14 (5%)	0.07
STEMI n,%	40 (27%)	65 (24%)	NS
NSTEMI/UA n,%	107 (73%)	208 (76%)	
History of thrombolytic therapy n,%	12 (8%)	16 (6%)	NS
Primary PCI n,%	28 (19%)	49 (18%)	
Troponin (ng/mL) Mean ± SD	95.6 ± 32.7	39.5 ± 24.5	0.029
LVEF% (Pre PCI) M ± SD	26.59 ± 6.9	35.29 ± 7.7	NS
Mitral regurgitation grade II/III n,%	7 (5%)	19 (7%)	NS
EDV (mL) Mean ± SD	100.59 ± 38.7	82.05 ± 21.6	0.004
Average Sm by TDI (cm/sec) Mean ± SD	5.8 ± 1.1	6.7 ± 1.2	NS
GLS% Mean ± SD	7.1 ± 1.8	11.9 ± 2.8	0.036
LVEF% (post PCI) at follow up Mean ± SD	24.68 ± 6.6	45.02 ± 7.2	0.005

AF: Atrial fibrillation; CKD: Chronic kidney disease; DM: Diabetes mellitus; EDV: End diastolic volume; GLS: Global longitudinal strain; HTN: Hypertension; LVEF: Left ventricular ejection fraction; NSTEMI: Non -ST elevation myocardial infarction; PAF: Paroxysmal atrial fibrillation; PCI: Percutaneous coronary intervention; STEMI: ST-elevation myocardial infarction; TDI: Tissue Doppler imaging; UA: Unstable angina.

Table 2
Comparing between the two groups regarding coronary angiography and intervention data.

Variable	Group I with no improving LVEF post PCI N = 147 (35%)	Group II with improving LVEF post PCI N = 273 (65%)	*p* value
LM disease n,%	7 (5%)	30 (11%)	NS
LAD disease n,%	126 (86%)	246 (90%)	NS
LCX disease n,%	53 (36%)	142 (52%)	NS
RCA disease n,%	74 (50%)	134 (49%)	NS
MVD n,%	87 (59%)	172 (63%)	NS
PCI to LM n,%	0	14 (5%)	NS
PCI to LAD n,%	117 (80%)	229 (84%)	NS
PCI to LCX n,%	24 (16%)	66 (24%)	NS
PCI to RCA n,%	16 (11%)	85 (31%)	0.07
Device use n,%	19 (13%)	8 (3%)	0.08

LAD: Left anterior descending artery; LCX: Left circumflex artery; LM: Left main; LVEF: Left ventricular ejection fraction; MVD: Multi-vessel disease; PCI: Percutaneous coronary intervention; RCA: Right coronary artery.

Table 3
Comparing between the two groups regarding in-hospital outcome data.

Variable	Group I with no improving LVEF post PCI N = 147 (35%)	Group II with improving LVEF post PCI N = 273 (65%)	*p* value
Mechanical ventilation n,%	19 (13%)	8 (3%)	0.08
Arrhythmias n,%	40 (27%)	49 (18%)	NS
Pulmonary edema n,%	26 (18%)	13 (5%)	NS
Cardiogenic shock n,%	19 (13%)	9 (3%)	0.08
Cardiac arrest n,%	13 (9%)	0	0.05
LVT n,%	60 (41%)	19 (7%)	0.002
LOS M ± SD	9.5 ± 11.8	4.07 ± 4.3	0.002

LOS: Length of stay; LVEF: Left ventricular ejection fraction; LVT: Left ventricular thrombus; PCI: Percutaneous coronary intervention.

Table 4
Binary regression analysis for prediction of LV recovery after PCI.

Variable	B	SE	EXP (B)	*p* value
Troponin (ng/mL)	0.897	0.545	0.406	0.048
LVEF% (Pre PCI)	0.575	0.379	1.77	NS
EDV (mL)	0.987	0.467	0.188	0.012
Average Sm by TDI (cm/sec)	0.428	0.359	0.652	NS
GLS%	1.719	0.436	0.179	<0.001

EDV: End diastolic volume; GLS: Global longitudinal strain; LVEF: Left ventricular ejection fraction; PCI: Percutaneous coronary intervention; TDI: Tissue Doppler imaging.

of ischemia and/or LV remolding was strongly predicting further LV recovery post-myocardial revascularization. Third, Early GLS values in the acute phase are a sensitive parameter for further myocardial recovery and are strongly correlated with following-up LVEF. Fourth, higher values of GLS in the current study are associated with non-anterior myocardial infarction cases and with RCA-related disease/intervention.

Interestingly, our study showed significant improvement in LV systolic function (65%) after PCI during the follow-up as shown by the significant improvement in LVEF. This supports that restoration of coronary patency of occluded coronary arteries by successful PCI strategy is associated with significant improvement in the global LV function and in-hospital clinical outcome. This finding is consistent with many other studies.[14–16] The overview of most of the literature investigating the LV recovery post PCI concerns STEMI, however, the unique value of our study is to evaluate myocardial recovery among all patients who presented with different types of ACS and had impaired LV systolic function. This also explains the relatively higher prevalence of LV improvement at the follow-up stage in the current study. Another factor that might explain the prevalence of LV recovery in our study is the nature of our population who had different backgrounds (including genetic variation, degree of atherosclerosis, different thrombotic activity, distribution of collateral circulation) and hence the effect of PCI and further LV recovery might be relatively different. This is due to the unique location of our tertiary cardiac center in the holy city of Makkah near Haram and holy sites, which receives huge numbers of different populations. This also reflects the proper outstanding of

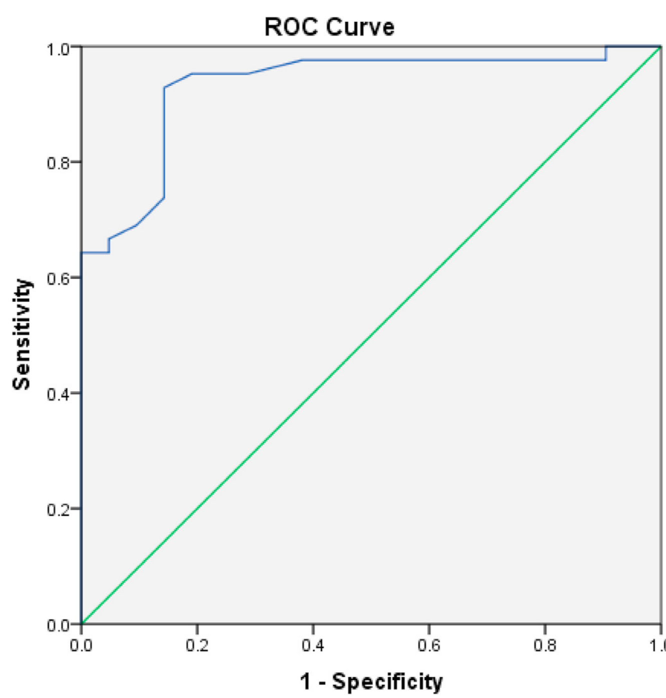

Fig. 2. The ROC curve of GLS to predict EF improvement. Sensitivity = 100%, Specificity = 88%, AUC = 0.931, *p*-value <0.001.

Table 5
The relation between GLS level, type of ACS and the occluded coronary artery intervention.

Variable	GLS ≤9%	GLS >9%	*p* value
Anterior STEMI (n = 75) n,%	59 (78%)	16 (22%)	<0.001
Non anterior STEMI (n = 30) n,%	2 (7%)	28 (93%)	<0.001
NSTEMI/UA (n = 315) n,%	149 (47%)	166 (53%)	NS
PCI to LM/LAD (n = 360) n,%	285 (79%)	75 (21%)	<0.001
PCI to LCX (n = 90) n,%	43 (48%)	47 (52%)	NS
PCI to RCA (n = 101) n,%	12 (12%)	89 (88%)	<0.001

ACS: Acute coronary syndrome; LAD: Left anterior descending artery; LCX: Left circumflex artery; LM: Left main; NSTEMI: Non ST elevation myocardial infarction; PCI: Percutaneous coronary intervention; RCA: Right coronary artery; STEMI: ST elevation myocardial infarction; UA: Unstable angina.

our center to guideline recommendations for early revascularization and optimal medical therapy.

Moreover, the present study demonstrated that elevated troponin level at the time of ACS was significantly associated with further impairment of LV recovery. This was consistent with other studies.[14,17,18] Also, there was a statistically significant difference between the study groups regarding baseline LV- EDV as the group improving LVEF post PCI had smaller values and this is similar to other studies.[14,19] This all could be explained by the severity/extension of myocardial injury (reflected by an elevated level of serum troponin) and the degree of LV remodeling (dilatation) during the acute ischemic phase both hindering LV improvement and further recovery even after successful revascularization.

It is worth mentioning that we primarily aimed to assess the short-term echo outcome to define different parameters regarding the prediction of myocardial functional recovery. GLS has been validated to assess the global cardiac function in the setting of different kinds of ACS and even in a general healthy population and this was utilized in our current study. We found that early GLS has been an excellent predictor of future LV improvement and this was in concordance with many other studies.[7,20–23] Moreover, it was even superior to LVEF and EDV for the prediction of LV recovery. This was also powered by the strong correlation between early GLS and further LV systolic function improvement. On the other hand, basal TDI [peak systolic myocardial velocity (Sm)] in this study was not found as a predictor of significant improvement in LV systolic function. This finding is dis concordant with other studies.[7,24,25] This might be explained by relative angle dependency and the frame-rate limitations of TDI, different ACS presentations selected in each study, and variable degrees of LV systolic impairment.

Of note, according to previous studies, a consensus has not yet been established on a cut-off GLS value that most accurately predicts further post-PCI-myocardial recovery. They mostly suggested a GLS lower than about 12%–15% to be a significant independent predictor of adverse outcomes.[14,26,27] Our results showed that a GLS- cut-off value of greater than 9%; predicts further LV recovery and this relatively differs from other reported values among similar studies. Many factors might be attributed to this finding; the mean age of our patients is slightly older compared to other studies, variable types of ACS presentation, lower mean LVEF at the acute insult, and a larger sample of the population with a variable background. Furthermore, our study supports previous data[21] that greater values of GLS were significantly more prevalent in cases of non-anterior infarction and RCA-related occlusion/intervention.

Finally, our results highlight the observed better in-hospital outcomes of the patient's group with improving LVEF post PCI including length of hospital stay, which reflects the contractile reserve of those patients associated with initial clinical recovery. Similarly, others demonstrated a significant association between the absence of left ventricular contractile reserve and an increased rate of cardiovascular events.[28]

5. Limitations

The number of patients included is due to the nature of the single center and the limited selected period. A known limitation of TDI (relative angle and the frame-rate dependency). Lack of investigating LV remodeling-associated parameters. Drugs and other treatments may synergize the effects of revascularization on LV function. Moreover, no long-term outcomes and that is because we are a tertiary center and refer most cases back to their primary hospitals after a certain follow-up period of revascularization. We hope to reduce the effect of these limitations by sharing with other hospitals in the region to conduct similar studies in the future including long-term follow-up data.

6. Conclusion

Our study demonstrated about two third of acute coronary syndrome patients with impaired systolic function and treated with PCI showed contractile recovery, while the remodeling of the LV has been observed in 35%. GLS could provide an important objective and quantitative evaluation of global LV systolic function and serve as a useful practical predictor of further myocardial recovery with a cut-off value greater than 9%. So, GLS might be considered a complementary approach in those patients as the early prediction of future LV function can guide both medical and device therapy. However, more comprehensive evidence on larger study populations and considering long-term prognostic outcomes are needed to support its application in future practice guidelines.

Key message

Patients with the acute coronary syndrome and who had LV dysfunction who are candidates for PCI should be revascularized because PCI in those patients showed significant improvement in the LV systolic function. Echocardiography should be considered for the assessment of its effect on LV systolic functions as well as during the follow-up (to identify the effect of myocardial revascularization with PCI in this function). Moreover, our study recommended the utilization of the GLS modality as a valuable and practical parameter for the prediction of LV systolic function recovery. This may serve as a tool, to allow the proper identification of those patients with and without future myocardial recovery, and hence it can be a useful method in our practice to guide medical and advanced heart failure therapy.

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None.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ihj.2022.11.004.

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