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Published in:
Echo Research and Practice

DOI (link to publication from Publisher):
10.1530/ERP-19-0026

Publication date:
2019

Document Version
Publisher's PDF, also known as Version of record

RESEARCH

Echocardiographic global longitudinal strain is associated with infarct size assessed by cardiac magnetic resonance in acute myocardial infarction

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Abstract

The aim of this study was to investigate if there was an association between infarct size (IS) measured by cardiac magnetic resonance (CMR) and echocardiographic global longitudinal strain (GLS) in the early stage of acute myocardial infarction in patients with preserved left ventricular ejection fraction (LVEF). Patients with ST-segment elevation myocardial infarction who underwent primary percutaneous coronary intervention were assessed with CMR and transthoracic echocardiogram within 1 week of hospital admission. Two-dimensional speckle tracking was performed using a semi-automatic algorithm (EchoPac, GE Healthcare). Longitudinal strain curves were generated in a 17-segment model covering the entire left ventricular myocardium. GLS was calculated automatically. LVEF was measured by auto-LVEF in EchoPac. IS was measured by late gadolinium enhancement CMR in short-axis views covering the left ventricle. The study population consisted of 49 patients (age 60.4 ± 9.7 years; 92% male). The study population had preserved echocardiographic LVEF with a mean of 45.8 ± 8.7%. For each percent increase of IS, we found an impairment in GLS by 1.59% (95% CI 0.57–2.61), $P = 0.02$, after adjustment for sex, age and LVEF. No significant association between IS and echocardiographic LVEF was found: −0.25 (95% CI: −0.61 to 0.11), $P = 0.51$. At the segmental level, the strongest association between IS and longitudinal strain was found in the apical part of the LV: impairment of 1.69% (95% CI: 1.14–2.23), $P < 0.001$, for each percent increase in IS. In conclusion, GLS was significantly associated with IS in the early stage of acute myocardial infarction in patients with preserved LVEF, and this association was strongest in the apical part of the LV. No association between IS and LVEF was found.

Key Words

- global longitudinal strain
- infarct size
- 2D speckle tracking echocardiography
- acute myocardial infarction
- cardiac magnetic resonance imaging

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https://doi.org/10.1530/ERP-19-0026

Introduction

Clinical outcomes after an acute myocardial infarction (AMI) are determined by the initial morphological and functional alterations resulting from myocardial necrosis (1, 2, 3). Infarct size (IS) is a strong predictor of both cardiovascular morbidity and mortality (4, 5). Cardiac magnetic resonance (CMR) is a non-invasive imaging modality and the golden standard in the accurate quantification of IS (6, 7). Compared to other imaging modalities, CMR offers multiparametric high-resolution assessment of myocardial structure, function and viability, including detection of small infarcts (8, 9, 10, 11).

Although recommended in a broad spectrum of clinical entities as an examination with a high impact on patient management (10), CMR remains a relatively expensive examination, often with limited access, especially outside daytime. Meanwhile, echocardiography is usually the first-line imaging modality that is readily available in the acute clinical setting. Left ventricular ejection fraction (LVEF) by echocardiography is a widely used parameter to describe myocardial performance after an AMI. The risk stratification after AMI is recommended 6–12 weeks after the admission and LVEF <35% is currently the major indication for an implantable cardiac defibrillator (ICD) implantation (12). However, a significant rate of sudden cardiac deaths (SCD) following AMI occurs in patients with LVEF >35% and within the first 30 days after discharge from hospital (13, 14). This underscores the importance of studying the anatomical and physiological changes of the left ventricle in patients with preserved LVEF in the early phase of AMI.

Global longitudinal strain (GLS) is reproducible and easy to measure on a 2D echocardiogram (15). GLS is a myocardial deformation analysis that predominantly reflects the function of sub-endocardial longitudinally oriented fibers, which are most prone to ischemic damage and wall stress. Therefore, they can exhibit abnormal contraction patterns in the setting of apparently normal LVEF (16).

Recently, it was described how GLS assessed by speckle tracking echocardiography was associated with IS (17). GLS has also been established as a predictor of cardiovascular outcome (18, 19, 20).

The aim of this study was to investigate the association between IS measured by CMR and echocardiographic GLS in patients with ST-segment elevation myocardial infarction (STEMI) and preserved LVEF. Further, we aimed to compare this with the association between IS and echocardiographic LVEF. LVEF and GLS in this article refers to measures by 2D echocardiography. IS was measured by CMR.

Methods

From 2012 to 2015, patients admitted with STEMI, who underwent primary percutaneous coronary intervention (PCI) at Aalborg University Hospital, Denmark, were considered eligible for the study. The diagnosis of STEMI was defined by typical chest pain and at least 0.2 mV ST-segment elevation in at least two adjacent leads on electrocardiogram (ECG) at admission. The inclusion criteria for this study were (1) successful reperfusion of the infarct-related artery within 12 h from symptom onset; (2) no previous history of AMI or coronary artery bypass surgery; (3) CMR performed within the first week after the index event and (4) transthoracic echocardiogram performed within the first week after the primary PCI.

Information on hypertension, hypercholesterolemia and diabetes was collected from patient records. Family history of ischemic heart disease, smoking status and previous medical history were collected from patient medical records or reported by the patient. Patients with previous AMI, known heart failure, significant valvular heart disease and left bundle branch block were excluded.

All patients gave their informed consent to participate and The National Committee on Health Research Ethics approved the study protocol.

Primary PCI

Primary PCI was performed according to standard clinical practice and current guidelines from European Society of Cardiology. All patients received 300 mg aspirin, 10,000 IU unfractionated heparin and either 180 mg ticagrelor or 600 mg clopidogrel as loading doses. Thrombus aspiration, pre-dilatation before stenting, and the use of glycoprotein IIb/IIIa inhibitors were left to the operators' discretion.

Echocardiography

Experienced echocardiographers performed echocardiography using Vivid e9, GE Health Care. Two-dimensional speckle tracking at a framerate of 60–80 frames/s was performed on three apical views (long-axis, four-chamber and two-chamber) using a semi-automatic algorithm (EchoPac, GE Healthcare). Aortic valve closure was identified on 2D image. The region of interest was adjusted to cover the thickness of the myocardium. The LV was subsequently divided into 17 segments covering the entire left ventricular myocardium, and GLS was calculated automatically as the mean of the global peak systolic strain from each of the three views (Fig. 1).

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Careful inspection of tracking and manual correction, if needed, were performed. LVEF was measured by auto-EF in EchoPac. All patients had sinus rhythm and QRS width <120 ms during the echocardiography. The method has been described and validated in previous studies (19, 21, 22).

CMR

CMR was performed on whole-body 1.5 T MR scanner (GE Discovery 450; GE Healthcare) in a supine position with ECG-gated image acquisition. Approximately 5 min after an IV injection of 0.2 mmol/kg of a gadolinium-based contrast agent, contrast-enhanced steady-state free precession (CE-SSFP) short-axis cine images covering the entire LV as well as two-, three- and four-chamber long-axis cine images (image resolution 8 × 1.5 × 1.5 mm) were acquired. Approximately 15 min after injection of the contrast agent, late gadolinium-enhanced (LGE) images (image resolution 8 × 1.5 × 1.5 mm, no slice gap) were acquired in the corresponding imaging planes as for the CE-SSFP images using an inversion-recovery gradient echo sequence. Inversion time was manually adjusted to null the signal from remote myocardium (23).

IS was measured by LGE in short-axis views covering the LV using automated quantification algorithm in Segment software (Medviso AB, Lund, Sweden) (Fig. 2) (24, 25). The infarct quantification algorithm weights the infarct by signal intensity to compensate for partial

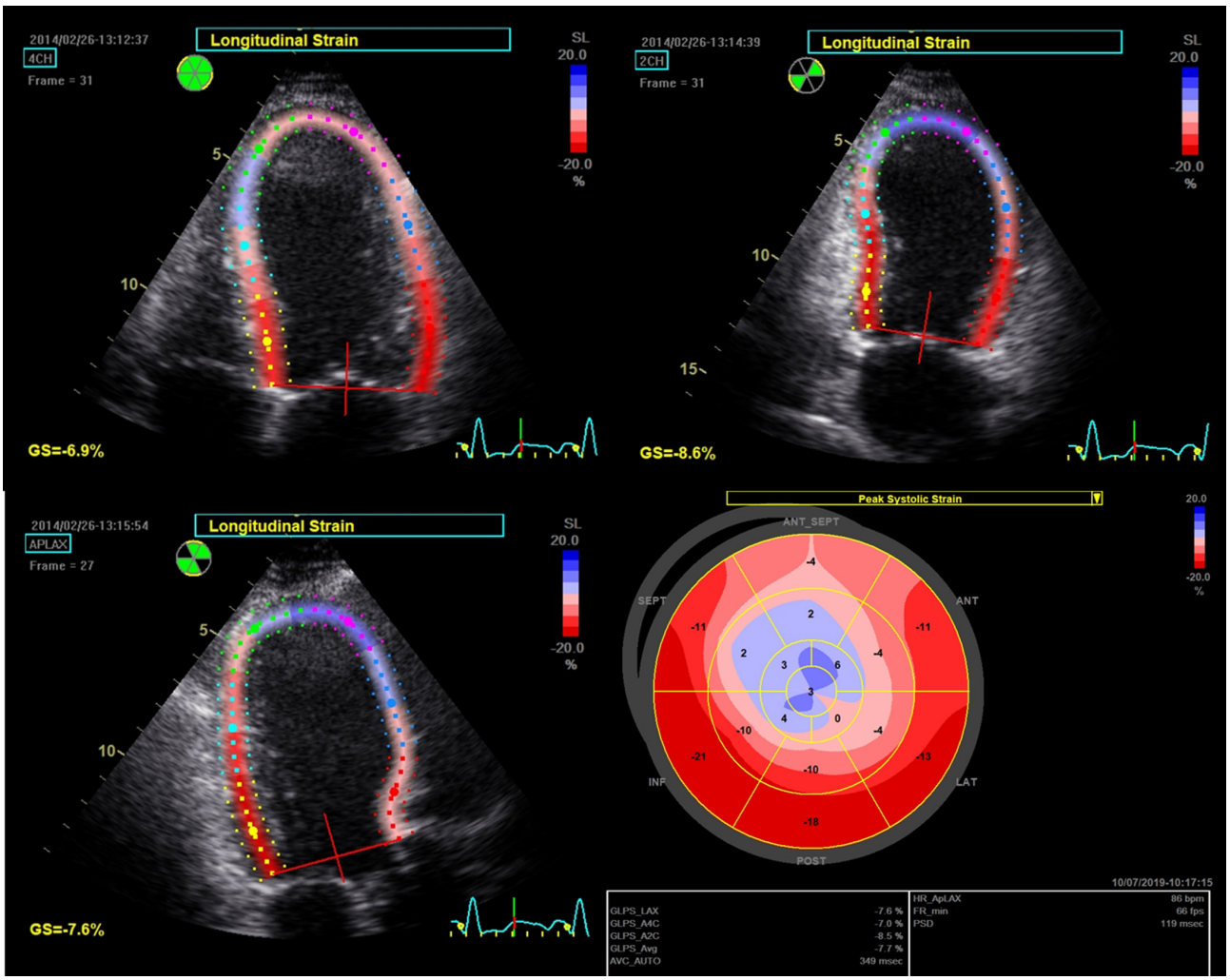

Figure 1
Measurement of GLS is performed in the three apical long-axis views. Region of interest is manually corrected. The peak systolic strain is given in the Bull's eye: Red colour illustrates normal systolic shortening. Normal value for GLS is −20%. The absolute value of GLS is decreased in impaired systolic deformation. Positive value of GLS is present when the segment-shortening is absent for example in LV aneurysm (blue colour). GLS, global longitudinal strain; LV, left ventricle.

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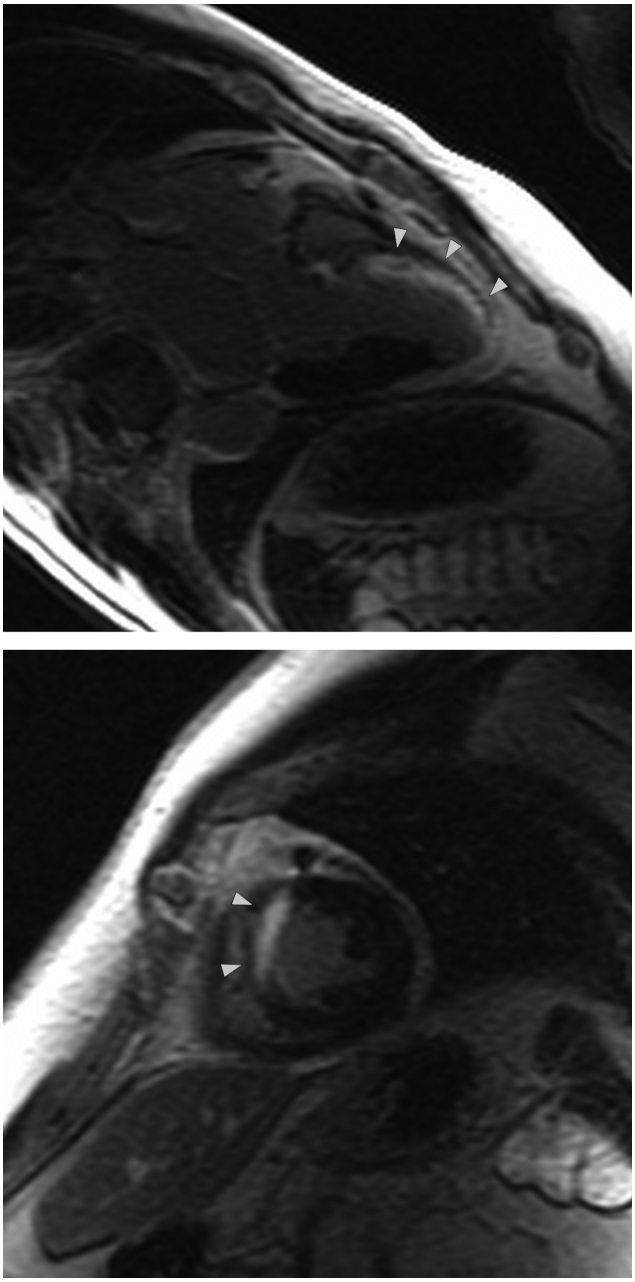

Figure 2
Cardiovascular magnetic resonance in a patient with ST-segment elevation myocardial infarction. Late gadolinium enhancement (arrows) is quantified for calculating the infarct size.

volume effects and has been carefully validated against computer phantoms, experimental setting and in patients by expert contours. LV mass was quantified in the corresponding short-axis views using cine steady-state free precession images. LV mass and IS were divided into the standard 17-segment model. The MR imaging technique for assessment of IS have previously been described and validated in detail (21, 23, 25).

The comparison of the 17-segments model in 2D-speckle tracking echocardiography and CMR is illustrated in Fig. 3.

Statistics

Continuous data are described as mean (standard deviation) or median (interquartile ranges (IQRs)). Categorical data are illustrated as percentages.

The associations between GLS and LVEF as predictors of IS were assessed using linear regression models. We considered univariable models with each echocardiographic parameter as the only predictor and a multivariable model with both parameters as potential predictors. The strength of associations was expressed as the regression coefficients with corresponding CI and *P* values. The predictive values of the models were assessed using R^2 and root mean squared error (RMSE) to determine which model had the higher predictive accuracy.

Both apparent and optimism-corrected model validation measure was calculated. The optimism in predictive performance was estimated using a bootstrap approach with 1000 bootstrap samples. Values in parentheses are 95% CI, unless specified otherwise.

Statistical analyses were performed in Stata version 15 and *P* values <0.05 were considered statistically significant.

Results

Characteristics of the population are given in Table 1. The majority of the population was male. No patients had a history of diabetes. Few (6.1%) were treated with medication for hypercholesterolemia, and 22.4% took antihypertensive medication.

IS and GLS

GLS was significantly associated with IS (Fig. 4). For each percent the IS increased, we saw an impairment in GLS by 1.27% (0.51–2.03), *P*=0.002. The results showed same pattern when adjusted for age and sex: 1.33% (0.54–2.12), *P*=0.01. After additional adjustment for LVEF, GLS worsened by 1.59% (0.57–2.61), *P*=0.02, for each percent increase in IS.

IS and LVEF

In the linear regression analysis (Fig. 5), we did not find any significant association between IS and LVEF (−0.25 (−0.59 to 0.09), *P*=0.15) The pattern remained

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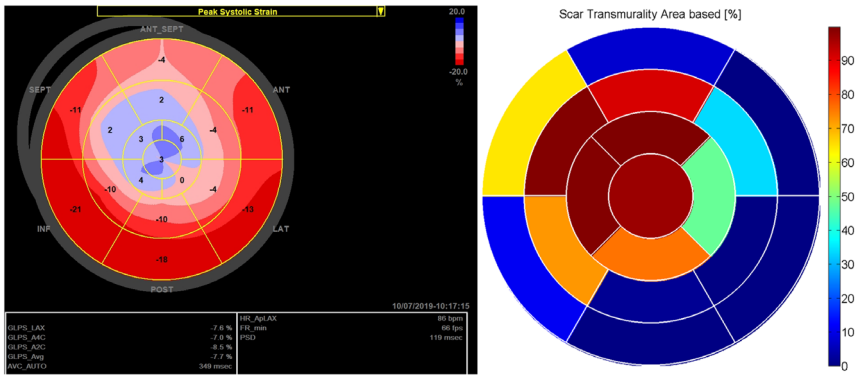

Figure 3
Both panels are from the same patient with ST-segment elevation myocardial infarction with occlusion of LAD. (Left) Bulls eye for the LV divided in 17 segments. Normal value for GLS is −20%. Positive value of GLS is present when the segment-shortening is absent for example in LV aneurysm (blue colour). (Right) Scar transmurality area (infarcted myocardium) in 17 segments assessed by CMR. The dark red/maroon colour areas have the highest transmurality. The dark blue colour represents the non-infarcted myocardium. CMR, cardiac magnetic resonance; GLS, global longitudinal strain; LAD, left anterior descendent coronary artery; LV, left ventricle.

unchanged when adjusted for sex and age (–0.25 (–0.61 to 0.11), P=0.51)

IS and GLS at the segmental plans

We studied the association between IS and GLS at the three segmental levels in the LV: basal, mid, apical. We found that the association between IS and GLS was strongest in the apical level, where we found an impairment in GLS by 1.69% (1.14–2.24) for each percent of higher IS, P<0.001. For the mid-LV the value was 0.86% (0.00–1.71), P=0.05 and for the basal LV: 0.38% (–0.45 to 1.25) (Fig. 6).

Discussion

In this study, we investigated the association between GLS and IS in the early phase of AMI in patients with preserved LVEF. We included patients with definite AMI so comparison between the two cardiac imaging modalities could be reliable.

The standard measure of myocardial performance (LVEF by echocardiography) after AMI was not associated with IS. We found that IS was significantly associated with echocardiographic GLS. This association was mainly driven by the strong association between GLS and IS in the apical part and mid-part of the LV.

LVEF is a generally accepted measure for left ventricular performance after AMI and considered an important factor in determining further medical treatment and in the risk stratification for SCD. According to current guidelines, an ICD is indicated in patients with LVEF ≤35% and symptomatic congestive heart failure at least 6–12 weeks after an AMI (12). The majority of patients dying suddenly after AMI have LVEF >35%, reflecting the poor sensitivity of LVEF as a risk-stratifying parameter (13). Furthermore, a significant rate of SCD following AMI occurs after hospital discharge and within the first 30 days after AMI (14), which underscores the importance of risk stratification before the recommended 6–12 weeks. Thus, there is a need for more sensitive parameters than LVEF in the early risk assessment in patients with AMI already by hospital admission.

Table 1 Population characteristics.

	Total, *n* = 49
Age, years	60.4 ± 9.7
Male, %	91.8
IHD in biological relatives, %	44.9
Smoking, %	
Never smoked	22
Current smoker	45
Former smoker	27
Diabetes	None
Medication for hypercholesterolemia, %	6.1
Medication for hypertension, %	22.4
Previous PCI, %	2.0
LVEF by echocardiography, %	45.8 ± 8.7
LVEF by CMR, %	50.4 ± 1.08
Time from admission and PCI to echocardiography, days	2.1 ± 1.3
Time from admission and PCI to CMR, days	4.0 ± 0.9
GLS, %	13.7 ± 3.4
Infarct size, %	15.4 ± 9.6
BMI, kg/m^2	27.3 (IQR 25.0–29.8)
Creatinine, µmol/L	84 ± 15
Peak TnT, ng/L	4179 (IQR 2017–6794)
Peak CKMB, µg/L	212.8 (IQR 143–323)
Infarcted coronary artery	
LAD	45% (*n* = 22)
RCA	35% (*n* = 17)
CX	20% (*n* = 10)

Mean and standard deviations are given, unless stated otherwise.
BMI, body mass index; CKMB, creatinine kinase-MB; CMR, cardiac magnetic resonance; CX, Ramus circumflexus; GLS, global longitudinal strain; IHD, ischemic heart disease; IQR, interquartile range; LAD, left anterior descendent coronary artery; PCI, percutaneous coronary intervention; RCA, right coronary artery; SD, standard deviation; TnT, high-sensitive Troponin T.

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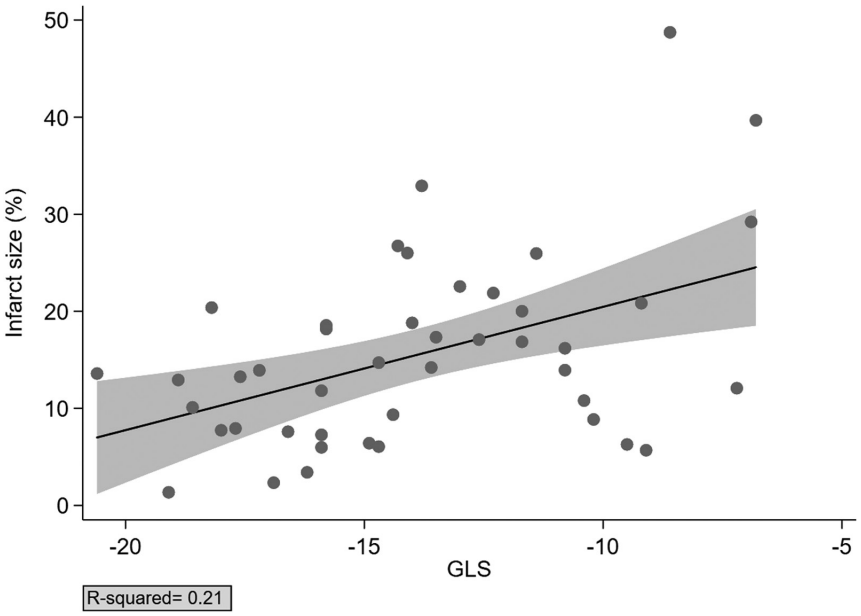

Figure 4
GLS was significantly associated with IS, $P = 0.002$. Regression equation ($P = 0.002$): IS = Intercept + 1.27 (0.51–2.03) × GLS. GLS, global longitudinal strain; IS, infarct size.

Previous studies have questioned the role of LVEF as a measure of myocardial performance after AMI. These investigations described GLS as a more sensitive predictor of ventricular arrhythmias and prognosis after AMI (26, 27).

Ersbøll *et al*. studied whether GLS was associated with the prognosis of patients with AMI and LVEF ≥40% (28). They found that GLS added prognostic information on risk assessment in AMI. Early measures of GLS were an independent predictor of SCD and ventricular tachyarrhythmia. Adding GLS to known risk factors provided significantly improved risk reclassification. The same group described that GLS has a prognostic value in patients with preserved LVEF after AMI (28).

Haugaa *et al*. demonstrated how LVEF was associated with arrhythmic events but failed as a predictor in those with relatively preserved function after AMI (26). GLS was a more sensitive predictor of arrhythmic events compared with LVEF and was useful, especially in patients with LVEF >35%.

Gjesdal *et al*. described how GLS could identify small, medium and large myocardial IS. They performed a study including 40 patients with STEMI treated with primary PCI (29). The patients underwent echocardiography and CMR 8.5±5.4 months after the index AMI. They found that circumferential and longitudinal strains correlated with myocardial infarct mass.

Roes *et al*. performed a similar study comparing findings on CMR and echocardiographic 2D speckle tracking GLS in patients with chronic ischemic heart disease (30). In their study, global and regional longitudinal strain measured by 2D speckle tracking was associated with the global and regional extent of scar tissue on CMR. In this study, patients with recent AMI (<3 months) were excluded.

Both Roes *et al*. and Gjesdal *et al*. studied patients who survived for long enough to go through the examinations several months after the index AMI. This might be a selected survivor group of patients and may not represent the unselected patients who are admitted to hospital with their first AMI. Patients who survived more than 3–6 months after their index AMI might have another mortality risk than those who suffered an AMI recently.

Meanwhile, studying the patients already during admission clarifies the immediate damage to the

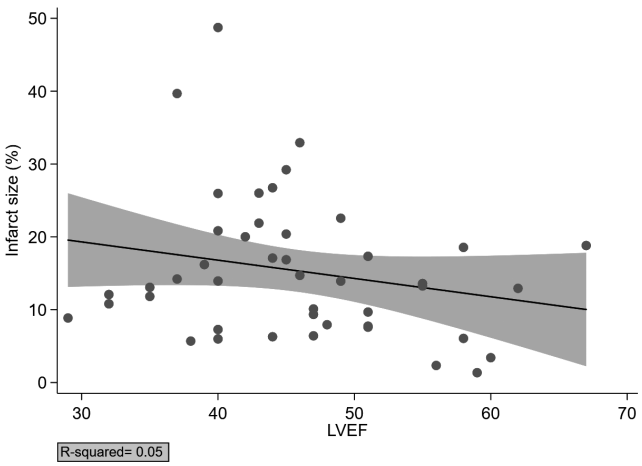

Figure 5
There was no significant association between IS and LVEF, $P = 0.15$. Regression equation ($P = 0.15$): IS = Intercept – 0.25 (–0.59 to 0.09) × LVEF. IS, infarct size; LVEF, left ventricular ejection fraction.

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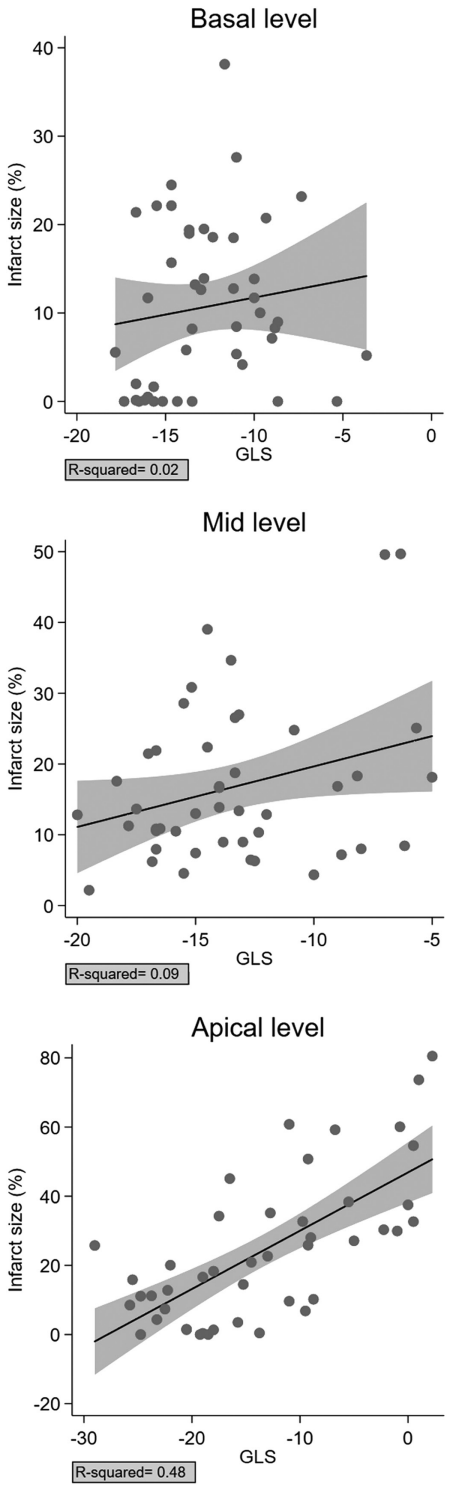

Figure 6
The association between GLS and IS was significant in mid-LV ($P = 0.05$) and apical LV ($P < 0.001$). In basal LV, there was no significant association ($P = 0.38$). Regression equation for basal LV ($P = 0.38$): IS = Intercept + 0.38 (–0.48 to 1.25) × GLS. Regression equation for mid-LV ($P = 0.05$): IS = Intercept + 0.86 (0.00–1.71) × GLS. Regression equation for apical LV ($P < 0.001$): IS = Intercept + 1.69 (1.14–2.23) × GLS. GLS, global longitudinal strain; IS, infarct size; LV, left ventricle.

myocardium, which may be an important player in the short-term outcome. Further, it is crucial to study patients with preserved LVEF, since this group is usually not considered as a high-risk population.

In the present study, the strongest association between IS and GLS was found in the LV apex, suggesting that strain in the apex is more sensitive to infarction than the basal segments of the LV. From a physiological point of view, this might be explained by the fact that the infarcted basal and mid-ventricular segments are easily pushed and pulled by adjacent segments with preserved systolic shortening, which is not the case for the apex. Consequently, infarction in basal and mid-ventricular segments will not be detected accurately by strain, since the systolic shortening might occur despite infarction because of transmission of the systolic movements in the adjacent segments. Strain in the apex is, in contrast, independent of movements from neighboring segments, and infarctions in the apical segments are very sensitive to changes in systolic shortening and longitudinal strain. Thus, GLS might be a good prognostic marker globally in LV, but regionally, it does not provide diagnostic information on presence of AMI except in the LV apex in patients with preserved LVEF. However, it is important to underscore, that we in this only had 49 patients which might also explain the weak association we found between IS and GLS in basal- and mid-LV. Both larger infarcts and larger number of patients would probably give a more significant association in the proximal parts of the LV.

Importantly, we show an association between GLS and IS in a population having preserved systolic function with a mean LVEF of 45.8%. Infarcts of small size do not affect LVEF significantly. The fact that GLS is affected by small infarcts that do not reduce LVEF supports the notion that GLS is a more sensitive marker than LVEF in predicting the presence of AMI. This fact should also be considered when evaluating the risk of SCD for patients with recent AMI and preserved LVEF.

Sjøli *et al*. analyzed longitudinal and circumferential strain in 36 patients within 3 h of thrombolysis and at hospital discharge (31). They compared these findings with IS measured by a later CMR and found that GLS was correlated with IS. Vartdal *et al*. found an association between echocardiographic GLS and total IS on CMR, and described an inverse relationship between segmental strain and the transmural extent of infarction (32). In both studies, echocardiography and GLS measurements were performed in an early phase after revascularization, and their findings partially support our results. Nevertheless, both study groups performed CMR several months after

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the index AMI. Because of the large time gap between echocardiography and CMR, the findings on the two imaging modalities might not be comparable since changes in LV function and anatomy over time as a result of LV remodeling might affect the IS and scar measured by CMR months later (33).

Usually, echocardiographic LVEF is considered as a measure of left ventricular performance in the early stage of AMI (12). GLS assessed by echocardiography, and not LVEF, was correlated with IS in the present study. Since IS is a predictor of prognosis after MI, we might consider GLS to be a more accurate measure of LV myocardial performance giving valuable information on IS and thus prognosis in patients with preserved LVEF.

A study performed by Cimino *et al.* investigated the association between GLS and transmural extent of myocardial scar in 20 patients in the early stage of STEMI and preserved LVEF (16). They found results comparable to ours, thus supporting our findings. Still, longitudinal studies are needed to clarify whether GLS provides better information on prognosis than LVEF.

Our study has some limitations. Most of the patients were male and only four patients were female. Besides, we have only 49 patients in the study. We suggest that our findings should be confirmed in a bigger study with more patients and equal proportion of both genders among the study population.

Our study has an important clinical impact since we assessed the patients in the early phase of AMI and during their hospital stay. GLS should be considered complementary to other information, such as patients' previous medical history, clinical condition and so forth. Time has an important role to play, both in assessing the patient's risk for major cardiovascular events in the early phase, but also on information provided on cardiac imaging techniques, because late CMR and echocardiography weeks or even months after AMI will illustrate scarring after LV remodeling and not the initial affection on the myocardium by the infarct.

Conclusion

In the present study, we describe how GLS measured by echocardiography has a better association with IS assessed by CMR than echocardiographic LVEF within the first week after revascularization in patients with preserved LVEF. We suggest studies exploring GLS as a tool in the early risk assessment in patients with AMI.

Declaration of interest

Einar Heiberg is founder of Medviso AB, manufacturer of Cardiac Image Analysis software Segment. Henrik Engblom is consultant at Imacor AB, core laboratory for cardiac image analysis. Peter Sogaard has received GE Health Care research grant. The other authors have nothing to disclose.

Funding

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Received in final form 29 July 2019
Accepted 7 August 2019
Accepted Manuscript published online 8 August 2019

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https://doi.org/10.1530/ERP-19-0026