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# Assessment of left ventricular function in ST-elevation myocardial infarction by global longitudinal strain: a comparison with ejection fraction, infarct size, and wall motion score index measured by non-invasive imaging modalities

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**Aims** We aimed to compare two-dimensional global longitudinal strain (GS) with different non-invasive imaging modalities for the assessment of left ventricular function in an ST-elevation myocardial infarction population.

**Methods and results** GS was compared with ejection fraction (EF) determined by magnetic resonance imaging (MRI), standard echocardiography (echo), contrast echo, and electrocardiography-gated single-photon emission computed tomography (SPECT), as well as with MRI-determined relative infarct size and echo-determined wall motion score index (WMSI), in 163 patients participating in the NORwegian Study on District Treatment of ST-Elevation Myocardial Infarction (NORDISTEMI). The linear relation between GS and standard echo ($r^2 = 0.43$, $P < 0.001$), contrast echo ($r^2 = 0.38$, $P < 0.001$), and SPECT-determined EF ($r^2 = 0.52$, $P < 0.001$) was almost identical as that between GS and the gold standard MRI-determined EF ($r^2 = 0.47$, $P < 0.001$). GS was best associated with WMSI by echo ($r^2 = 0.55$, $P < 0.001$), while the associations between GS and relative infarct size were weaker ($r = 0.43$, $P < 0.001$). Receiver operator characteristics curves, used to analyse the ability of GS to discriminate low EF ($\leq$40%) measured by the four different modalities, large myocardial infarction (MI $\geq$ 15.7%), and high WMSI ($\geq$1.5), were significant for all. GS was shown to be the best predictor of low EF measured by MRI [area under the curve (AUC) 0.965], while the lowest AUC was found between GS and large MI (0.814).

**Conclusion** Global strain is associated well with EF measured by all modalities. Global strain was found to be the best predictor of low EF measured by the gold standard MRI. Since global strain is an inexpensive test, these data may be of health economic interest.

**Keywords** Global strain • EF • Infarct size • Wall motion score index • Left ventricular function

## Introduction

The assessment of left ventricular (LV) function is important for decisions on medical treatment and for risk stratification in patients following ST-elevation myocardial infarction (STEMI).[1,2] Magnetic resonance imaging (MRI), standard echocardiography (echo), contrast echo, and electrocardiography (ECG)-gated single-photon emission computed tomography (SPECT) are all methods

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frequently used for the assessment of LV function such as ejection fraction (EF). However, these imaging modalities have several technical shortcomings;[3–9] in addition, EF measured by standard echo and contrast echo has intra- and inter-observer variability.

Global longitudinal strain (GS) by 2D speckle-tracking echocardiography is a relatively new method for evaluation of LV myocardial deformation, which reportedly has good temporal and spatial resolution. Moreover, GS has low intra- and inter-observer variability[10] and the lack of angle dependency is of great advantage.[11] MRI is considered to be the gold standard in assessing LV function in STEMI patients; however, GS is inexpensive and less time-consuming than MRI. In the present study, we aimed to compare GS with different non-invasive imaging modalities for the assessment of LV function in an STEMI population.

# Methods

## Study population

The patients included in this study were participants in the NORwegian Study on District treatment of ST-Elevation Myocardial Infarction (NORDISTEMI; NCT00161005),[12] which was, in brief, a prospective, randomized, multicentre controlled trial and included 266 patients with STEMI from five different community hospitals. The patients, aged 18–75 years, were treated with thrombolysis (tenecteplase) and randomized to either immediate transport to percutaneous coronary intervention (PCI) or a conservative, ischaemia-driven strategy with rescue or delayed PCI when indicated. The majority of the patients (93%) underwent angiography. After PCI treatment at Oslo University Hospital Ullevaal, the patients were transferred back to their local hospitals.

MRI, SPECT, standard echo, and contrast echo with the assessment of LV function was performed at Oslo University Hospital after 3 months. The primary clinical endpoint of the NORDISTEMI study was a composite of death, reinfarction, stroke, or new myocardial ischaemia within 12 months. The assessment of LV function by SPECT was prioritized over the other imaging modalities, since one of the secondary outcomes in the main study was infarct size determined by SPECT. The number of patients examined with the different imaging modalities was therefore unequal. The main reasons for not being included in this substudy were contraindications to gadolinium, implanted intracardiac device/pacemaker, reluctance to examination/travelling, claustrophobia, and logistic reasons due to a busy clinical practice.[13]

As there was no difference in EF between the two study groups,[13] we considered the 266 patients in NORDISTEMI as one group and extracted the patients who had been examined with GS as well as MRI, SPECT, standard echo, contrast echo, and wall motion score index (WMSI) 3 months following STEMI for further analysis. The readers were blinded to each technique. The study was approved by the Regional Committee for Ethics and complies with the Declaration of Helsinki. The patients were enrolled after written consent had been obtained.

## Cardiac magnetic resonance imaging

Cardiac MRI was performed in a 1.5 T whole-body scanner (Philips Intera, Best, The Netherlands), using a five-element synergy-cardiac coil and vector-based ECG. The LV was scanned in two- and four-chamber long-axis view using balanced fast-field echo sequences for functional analysis, and short-axis images were acquired for complete LV volume analysis. The late gadolinium enhancement (LGE) study was performed in short-axis view, using a 3D turbo-field-echo technique with inversion pre-pulses, covering the whole LV. For LGE imaging, a dose of 0.15 mmol/kg body weight of gadolinium-diethylenetriaminepentaacetic acid (Magnevist®, Schering AG, Germany) was injected 15 min before acquisition.

MRI analysis was performed offline on a View Forum workstation (Philips Medical Systems). EF was calculated by the assessment of the volumes of the endocardial contours in diastole and systole of the stacked short-axis images.[14] The size of the infarction was assessed in the LGE images, by drawing the contour of the infarcted area in all short-axis slices. The volume of the infarction is related to the total LV myocardial volume. An experienced MRI reader who was blinded to the clinical data analysed all MRI images. The intra-observer variation coefficients for EF and for total infarct volume were 3.8 and 10.2%, respectively.

## Standard echocardiography and contrast echocardiography

An experienced physician performed the echocardiography with a Vivid 7 scanner in second harmonic mode (GE Vingmed, Horten, Norway). Volumes and EF were calculated using the Simpson's biplane method. Contrast echocardiography was recorded in three consecutive cycles of apical four- and two-chamber views after given 0.5–1 mL Sonovue intravenously (Bracco, Milan, Italy). The intra-observer variation coefficients for EF and end-diastolic volume (EDV) measured with contrast echo were 9.6 and 8.9%, respectively. Intra-observer variation coefficients for EF and EDV measured with standard echo were 9.5 and 6.5%, respectively. Inter-observer variation coefficients for EF and EDV measured with standard echo were 10 and 12%, respectively.

Regional wall motion was evaluated using a 16-segment model recommended by the American and European Societies of Echocardiography.[15] The LV was divided into six basal segments (anterior, anterolateral, inferolateral, inferior, inferoseptal, and anteroseptal), six middle segments (same subgroups), and four apically located segments (anterior, septal, inferior, and posterior). By visual analysis of systolic wall thickening, segments were assigned a wall motion score (WMS) as follows: 1, normal or hyperkinetic (normal endocardial excursion and systolic wall thickening); 2, hypokinetic (reduced excursion and wall thickening); 3, akinetic (absent excursion and wall thickening); and 4, dyskinetic (paradoxic systolic outward wall motion). WMSI was calculated by dividing the sum of all WMS by the total number of segments analysed. The intra-observer variation coefficient for WMSI was 4.4%.

Two-dimensional speckle-tracking echocardiography was performed in the standard three apical image planes, using dedicated software (Echopac version 108.1.5 GE Vingmed). Longitudinal peak negative systolic strain was measured to assess myocardial function in a 16-segment model of the LV as described previously.[16,17] Global strain (GS) was defined as the average of segmental strain values and was calculated only for patients with acceptable image quality of the relevant myocardial segments in at least two out of three image planes. Segments with poor tracking quality due to suboptimal image quality (dropouts, reverberations, or artefacts) were excluded. The median frame rate (25th and 75th quartiles) was 38/s (35–44). In all, 79.6 % of total available segments were included in the analysis. The intra-observer variation coefficient for GS was 3.7%.

## Myocardial perfusion tomography (single-photon emission computed tomography)

After injection of $^{99m}$Tc-tetrofosmin (Myoview$^{TM}$, GE Healthcare, UK), perfusion imaging was performed as a standard SPECT to obtain infarct size, supplemented with ECG-gated SPECT. The injected dose was 400–500 mBq. Processing was achieved by the use of an interfaced, dedicated computer system (Siemens e.soft, Erlangen, Germany) equipped with the 4D-MSPECT Cardiac Package (University of Michigan, Ann Arbor, MI, USA) to produce short-axis, vertical, and horizontal long-axis tomographic slices as well as bull's eye plot of the LV. LV cavity volumes were obtained from the gated SPECT perfusion data throughout the cardiac cycles. The largest cavity volume was defined as EDV and the smallest cavity volume was defined as end-systolic volume. These measurements are geometry-independent. The intra-observer variation coefficients for EDV and EF were 7 and 5%, respectively, and the inter-observer variation coefficients were 6 and 5%, respectively.

## Statistics

Data were analysed using Epi Info (version 3.3.2). Continuous variables were expressed as medians with 25th and 75th percentiles and categorical data as frequencies with percentages. GS was compared with the other measures of LV function using linear regression. The associations between GS/EF/WMSI and relative infarct size were tested in a multivariate regression model, correcting for possible confounding factors (age, gender, diabetes mellitus, and hypertension).

Low EF was defined as $\leq$40%. The cut-off value for large MI ($\geq$15.7% of total LV mass) and high WMSI ($\geq$1.5) was defined as the $75^{th}$ percentile. Receiver operator characteristic (ROC) curves were used to analyse the ability of GS to discriminate low EF measured with the different modalities and to discriminate large MI as well as high WMSI.

# Results

GS was performed in 163 patients and 80% of the LV segments were accepted for GS analysis. A comparison between patients with a complete set of GS and standard echo ($n = 162$), GS and MRI ($n = 138$), GS and SPECT ($n = 160$), GS and WMSI ($n = 162$), and GS and contrast echo ($n = 154$) was performed. Patient characteristics and median values of LV function are shown in *Tables 1* and *2*, respectively.

## Associations between global strain and other measures of left ventricular function

GS showed moderately strong and significant associations between EF determined by standard echo ($r^2 = 0.43$, $P < 0.001$), as were the associations between GS and the gold standard MRI-determined EF ($r^2 = 0.47$, $P < 0.001$) (*Figure 1*). The linear associations between GS and SPECT-determined EF was the highest ($r^2 = 0.52$, $P < 0.001$), while the associations between GS and EF measured by contrast echo was the lowest ($r^2 = 0.38$, $P < 0.001$) when comparing the modalities measuring EF (*Figure 1*).

Of all methods used to measure LV function, the associations were found to be highest between GS and WMSI ($r^2 = 0.55$, $P < 0.001$), while the associations between GS and relative infarct size were weaker ($r^2 = 0.43$, $P < 0.001$).

## Multivariate regression analysis

Multivariate regression analysis adjusted for several potential confounders revealed that the association between WMSI and relative infarct size was the strongest ($r^2 = 0.61$), while the lowest association was found between standard echo-determined EF and relative infarct size ($r^2 = 0.33$). The associations between SPECT-EF, MR-EF, GS, and contrast-EF vs. relative infarct size was in a descending order 0.59, 0.56 0.47, and 0.40, respectively.

Diabetes mellitus was the only significant confounder for MRI, standard echo, and GS in the multivariate analysis, while for SPECT-EF and contrast-EF, gender was the only significant confounder. When adding only significant variables in the analysis, the associations between EF/WMSI/GS and relative infarct size

**Table 1** **Patient characteristics**

| | **Global strain (*n* = 163)** |
|---|---|
| Age (years) | 60 (52–66) |
| Male gender, *n* (%) | 148 (82) |
| Weight (kg) | 80 (74–90) |
| Current and previous smokers, *n* (%) | 140 (77) |
| Heart rate, beats/min, (%) | 65 (58–75) |
| Hypertension, *n* (%) | 50 (28) |
| Diabetes, *n* (%) | 10 (6) |
| Previous myocardial infarction, *n* (%) | 21 (12) |
| Hypercholesterolaemia, *n* (%) | 29 (16) |
| Infarct location on ECG, *n* (%) | |
| Anterior infarction | 79 (44) |
| New left bundle branch block | 2 (1) |
| Non-anterior infarction | 100 (55) |
| Time intervals (min) | |
| Symptom onset to thrombolysis | 109 (75–168) |
| Medication at discharge, *n* (%) | |
| β-Blockers | 167 (92) |
| ACE-inhibitors or ARBs | 93 (52) |
| Diuretics | 12 (7) |

Values are given as medians with 25th and 75th percentiles or numbers (%). ECG, electrocardiography; ARBs, angiotensin II receptor blockers.

**Table 2** **Median (25th and 75th percentile) values of the different measures of left ventricular function**

| | **Median (25th and 75th percentile)** |
|---|---|
| Global strain (%) | −18.03 (−19.48– −16.12) |
| EF (%) | |
| MRI | 57 (50–63) |
| Standard echo | 55 (49–62) |
| Contrast echo | 57 (49–65) |
| SPECT | 64 (54–70) |
| Relative infarct size by MRI (%) | 8.73 (3.63–15.93) |
| WMSI by echocardiography | 1.25 (1.13–1.50) |

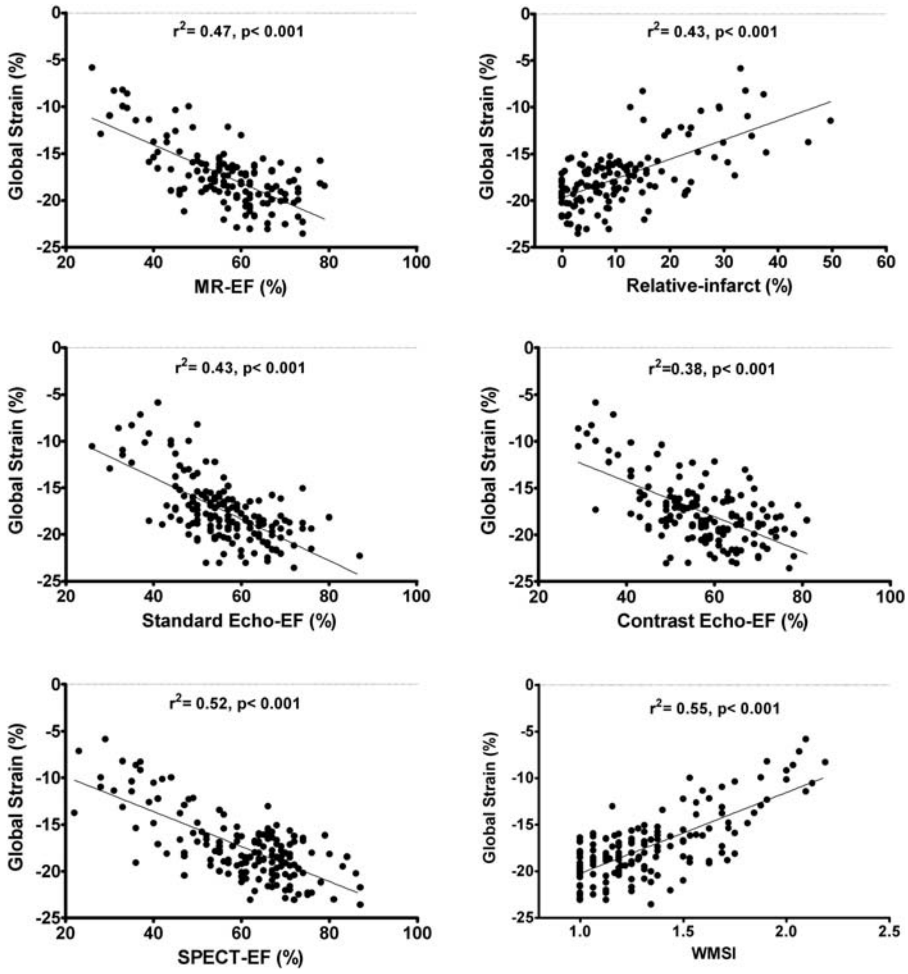

**Figure 1** Linear regression between global longitudinal strain and magnetic resonance-ejection fraction, magnetic resonance-relative infarct size, standard echo-ejection fraction, contrast echo-ejection fraction, single-photon emission computed tomography-ejection fraction, and wall motion score index.

remained almost identical ($r^2$ for WMSI = 0.60; for standard echo-EF, $r^2$= 0.33; for SPECT-EF, $r^2$= 0.58; for MR-EF, $r^2$= 0.55; for GS, $r^2$= 0.44; and for contrast echo-EF, $r^2$= 0.36).

## Receiver operator characteristics curves

ROC curves, used to analyse the ability of GS to discriminate low EF (≤40%) measured by the four different modalities, large MI (≥15.7% of total LV volume), and high WMSI (≥1.5), were significant for all (*Table 3*). GS was shown to be the best predictor of low EF measured by MRI with an area under the curve (AUC) of 0.965 ($P < 0.001$), where GS > −15.96% discriminated low MR-EF with 100% sensitivity and 86.3% specificity. The ability of GS to discriminate low EF measured by standard echo was also significant ($P <$ 0.001, AUC = 0.883), where GS > −13.0% discriminated low EF with 85.7% sensitivity and 92.4% specificity. The lowest AUC, which was still high, was found between GS and large MI (AUC = 0.814, $P < 0.001$), where GS > −15.9% discriminated large MI with 68.8% sensitivity and 91.5% specificity.

# Discussion

This study demonstrated that the associations between GS and EF measured by standard echo and SPECT were almost equally high as between GS and the often-considered gold standard MRI. The associations were found to be even higher between GS and WMSI. The lowest relation was found between GS and contrast echo, which was somewhat unexpected; however, it may be explained by the relatively high number of patients with normal EF. When adjusted for several potential confounders, WMSI was found to be the most accurate modality for assessing LV function, while for the echo modalities, GS was found to be the most accurate modality. However, the differences between the modalities were only small. Furthermore, ROC curve analysis of the ability of GS to discriminate low EF (≤40%), large MI (≥15.7%), and high WMSI (≥1.5) was significant and effective with all methods.

Our findings were in accordance with other smaller studies. Reisner *et al.*[18] demonstrated good correlations ($r = 0.68$, $P <$ 0.001) between GS and WMSI in 27 post-MI patients, as did

**Table 3** The ability of global strain to discriminate low ejection fraction, large myocardial infarction, and high wall motion score index

| | AUC | Std. error | 95% CI | *P*-value |
|---|---|---|---|---|
| Low EF (<40%) | | | | |
| MRI ($n = 14$) | 0.965 | 0.016 | 0.934–0.995 | <0.001 |
| Standard echo ($n = 7$) | 0.883 | 0.077 | 0.733–1.034 | <0.001 |
| Contrast echo ($n = 9$) | 0.949 | 0.041 | 0.870–1.028 | <0.001 |
| SPECT ($n = 15$) | 0.932 | 0.044 | 0.847–1.018 | <0.001 |
| Large MI (>15.7%) ($n = 32$) | 0.814 | 0.048 | 0.720–0.907 | <0.001 |
| High WMSI (>1.5) ($n = 35$) | 0.889 | 0.034 | 0.822–0.956 | <0.001 |

Std., standard; echo, echocardiography; MRI, magnetic resonance imaging; large MI, large myocardial infarction; WMSI, wall motion score index; AUC, area under the curve; CI, confidence interval.

Palmieri *et al.*[19] in ($r^2 = 0.90$) in 40 patients with a variety of clinical conditions. Sjøli *et al.*[20] compared GS and EF measured by standard echo in 39 patients with STEMI and demonstrated that GS was a more precise predictor of large infarct size measured by MRI.

Furthermore, Brown *et al.*[21] compared two-dimensional (2D) GS with MRI-derived EF in 62 patients with previous MI. Their findings were similar to ours ($r = 0.69$, $P < 0.001$) and they concluded that GS is an effective method for quantifying global LV function. Eek *et al.*[22] found both GS and WMSI ($n = 61$) to be good parameters to identify patients with substantial MI who might benefit from urgent reperfusion therapy. Good correlations were also found in a study comparing GS by automated functional imaging and SPECT ($r^2 = 0.55$) in 60 MI patients.[23]

GS has, in other studies, been validated against WMSI, relative infarct size, and EF determined by different modalities. However, to our knowledge, this is the largest study to compare GS with six different methods of assessing LV function in the same STEMI population.

ROC curve analysis of GS to discriminate low EF with the different modalities was high and significant for all; however, the largest AUC was obtained for low EF measured by the gold standard MRI and contrast echo. Although the number of patients with EF ≤ 40% was low, AUC obtained in our study was in accordance with other studies.

Standard echo, contrast echo, SPECT, and MRI are frequently used for the assessment of LV function; however, technical challenges often limit the examination, and except for SPECT and MRI, the imaging modalities have high intra- and inter-observer variability. MRI is often considered the gold standard in the assessment of LV function, and it is non-invasive, does not include ionizing radiation, and has a high spatial resolution;[24] however, MRI has low temporal resolution, it cannot be performed bed-side, and it is a time-consuming and costly examination.

Two-dimensional GS is an inexpensive examination, with good temporal and spatial resolution, and reportedly relative high reproducibility. The speckles are tracked in 2D, along the wall of the LV, and not along the ultrasound beam, and GS is thus angle-independent.[10] Moreover, estimation of GS can be performed even in patients with poor tracking quality;[18] however, the necessity of having high-resolution imaging with a high frame rate is a major limitation.[25] Our study was not primarily designed to measure GS; hence, frame rates were low in some patients (median 38/s, 25 and 75% quartiles 35–44/s), yet the associations between GS and the gold standard MRI were good, demonstrating the nobility of GS.

The linear associations between GS vs. standard and contrast echo were almost equally good as between GS and MRI. However, in an STEMI population, one must assume that the LV is dysfunctional and therefore asymmetric.[20] The assessment of EF with both standard and contrast echo was performed using Simpson's biplane method which is based on an assumption of symmetric LV geometry.[15] Among the methods described in this study, MRI, SPECT, GS, and WMSI are all geometrically independent. SPECT, however, has the disadvantage that it exposes the patients to a radiation dose and that it has a tendency to overestimate EF.[6,9] MRI, on the other hand, is not available in everyday clinical practice while WMSI is observer-dependent. GS is therefore a method that can readily be used for the assessment of LV function in an STEMI population.

## Limitations

Our study was initiated before speckle tracking became an option, and the focus was thus on image quality rather than on high frame rates as advised for 2D strain analysis. Thus, the median frame rate in our study is lower than the frame rates used in validation studies. Patients were included consecutively and not selected on the basis of ultrasound image quality, which therefore varied and led to exclusion of 20.4% of segments in the analyses. In addition, 11 examinations had to be excluded due to poor image quality. In addition, only few patients had large MI with low EF, thus the range of LV dysfunction was limited which might have contributed to the lower associations than expected. Though exploratory statistics were done looking at the NORDISTEMI primary cardiovascular endpoint[12] with the Kaplan–Meier curves and Cox's analyses in patients with low vs. high EF, large vs. low infarct size, high vs. low WMSI, and high vs. low GS measured by the different imaging modalities, these data did not give meaningful results because of a statistical power of <50%. The main reason for the low power with respect to the clinical endpoint was that only patients assessed by GS as well as MRI, SPECT, standard echo, and contrast echo at 3 months were included in this substudy.

# Conclusion

GS by echo is well associated with standard echo-determined WMSI, MRI-determined relative infarct size, and EF measured by MRI, SPECT, standard echo, and contrast echo. GS was also a good determinant of large MI, high WMSI by echo, and low EF measured by the different modalities. GS was found to be the best predictor of low EF measured by the gold standard MRI. Since GS is inexpensive and less time-consuming than MRI, these findings may be of health economic interest.

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