Difference in the Prognostic Impact of Left Ventricular Global Longitudinal Strain between Anterior and Nonanterior Myocardial Infarction

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Background: Speckle tracking–derived global longitudinal strain (GLS) of left ventricle is a potent prognostic marker for patients with ST-segment elevation myocardial infarction (STEMI). The purpose of this study was to investigate the difference of prognostic impact of GLS between anterior and nonanterior myocardial infarction. Methods: This study included 686 patients who underwent primary percutaneous coronary intervention for their first STEMI between November 2007 and April 2012. Differences in the prognostic impact of GLS between anterior MI group and nonanterior MI group were evaluated. The composite of all-cause mortality and hospitalization for heart failure in 2 years was investigated for outcome. Results: During the follow-up period, 77 (11.2%) adverse events occurred. The anterior and nonanterior MI groups included 339 and 347 patients, respectively. Among patients with anterior MI, GLS significantly predicted 2-year outcome in an adjusted model (adjusted hazard ratio [HR] 1.186; 95% confidence interval [CI] 1.071–1.314, P = 0.001), whereas the association between GLS and mortality was weaker in the nonanterior MI group (adjusted HR 0.977; 95% CI 0.884–1.081, P = 0.657). The interaction between the infarction territory and GLS was significant (P for interaction = 0.018), indicating that GLS was a more sensitive predictor of mortality in patients with anterior MI than that in those with nonanterior MI. Conclusions: Speckle tracking–derived GLS of left ventricle more sensitively predicted clinical outcome in patients with anterior MI than in those with nonanterior MI. (Echocardiography 2016;00:1–7)

Key words: myocardial strain, acute myocardial infarction

Left ventricular function is an effective prognostic indicator in patients with acute myocardial infarction (MI). Among the many echocardiographic parameters assessing left ventricular function, the left ventricular ejection fraction (LVEF) is one of the simplest, widely used, and reliable methods. Over the past years, speckle tracking–derived global longitudinal strain (GLS) has been validated for assessing left ventricular systolic function. GLS has been also demonstrated to be a reliable prognostic marker in patients with ST-segment elevation MI (STEMI). Unlike the volumetric LVEF measurement, GLS can represent longitudinal deformation of left ventricle. However, left ventricular myocardium is a nonhomogenous structure that contains myocardial helix and multilayered fibers. Thus, observed left ventricular segmental GLS is not homogenous throughout all myocardial segments. Longitudinal deformations more vigorously take place in apical segments than that of basal segments in normal subjects. Thus, we hypothesized that GLS should more sensitively decrease in anterior MI, which mainly involves the apical segments, than nonanterior MI when compared to LVEF. Furthermore, such difference might affect the prognostic impact of GLS between anterior and nonanterior MI. Therefore, the purpose of this study was to investigate the difference of the GLS value itself and difference of prognostic impact of GLS between anterior MI and nonanterior MI in patients who underwent primary percutaneous coronary intervention (PCI).

Methods:
We retrospectively enrolled patients who presented to the emergency department with STEMI in the author’s hospital between November 2007 and December 2012. Patients included in this study were those who underwent primary percutaneous coronary intervention.
taneous PCI and routine echocardiographic examinations. Patients with at least one of the following conditions were excluded: delayed PCI or no PCI, thrombolytic therapy before PCI, symptom-to-balloon time > 24 hours, prior MI, prior coronary bypass surgery, atrial fibrillation, poor echocardiographic images (including low frame rate), and missing data. Patients with mechanical complications of MI (i.e. myocardial perforation, interventricular septal shunt, and severe valvulopathy) were also excluded because of exceptional high mortality regardless of the left ventricular function. Among 933 patients diagnosed as STEMI during the index period, a total of 686 patients entered the final analysis after excluding the patients who met the exclusion criteria. Details of patient exclusion were depicted in Figure S1. Outcome of the patients were accessed by the composite of all-cause mortality and hospitalization for heart failure during 2-year follow-up.

Collection of Patient Data:
Patient demographic data were collected from medical charts. Laboratory data, including serum creatinine, N-terminal pro-brain natriuretic peptide (NT-proBNP) levels, and peak cardiac troponin I level, were also collected. The estimated glomerular filtration rate (eGFR) was calculated using the Modification of Diet in Renal Disease Study equation. All patients were calculated using the Modiﬁcation of Diet in Renal Disease Study equation. All patients were diagnosed as STEMI during the index period, a total of 686 patients entered the final analysis after excluding the patients who met the exclusion criteria. Details of patient exclusion were depicted in Figure S1. Outcome of the patients were accessed by the composite of all-cause mortality and hospitalization for heart failure during 2-year follow-up.

Statistical Analysis:
Statistical analyses were performed using SPSS version 20.0 for Windows (SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as the mean ± standard deviation, unless otherwise specified. Categorical variables were expressed as numbers and percentages. Q-Q plots were used to check the normality of continuous variables. Student’s t-tests were used to compare continuous variables, and chi-square tests were used for categorical variables. Kaplan–Meier survival analysis was used to compare the overall prognosis between anterior and nonanterior MI group. Pearson's correlation coefficient was used to analyze correlations between LVEF and GLS. Receiver operating characteristic (ROC) curve analysis was used to investigate the difference between GLS and LVEF in predicting 2-year outcome. Comparisons between ROC curves were performed using the method of Delong. Analysis of covariance was performed using a general linear model to assess difference in the GLS between the anterior and nonanterior MI groups after controlling for LVEF. Univariate and multivariate Cox models were used to assess relationships between potential risk factor and outcome. For adjusted association between GLS (or LVEF) and outcome, two adjusted models were built using multiple Cox regression with the addition of GLS (or LVEF) to clinical confounders as forced entry variables. The interaction between the infarction territory and GLS (or LVEF) was assessed by entering the presence of anterior MI, GLS (or LVEF), and an anterior MI-by-GLS (or anterior MI-by-LVEF) interaction term in each crude and adjusted Cox regression model. For all analyses, P-value < 0.05 was considered as significant.
Results:
Study Population and Outcome:
During the 2-year follow-up period (mean follow-up 20.0 ± 7.9 months) of the 686 patients (mean age, 61.9 ± 12.3; 524 men), 77 events (11.2%) occurred. Among study cohort, 339 and 347 patients were assigned to anterior and nonanterior MI groups, and 45 (13.3%) and 32 (9.2%) composite events occurred in each group, respectively (Table I). There was no significant difference in event rate between anterior and nonanterior MI group in Kaplan–Meier survival analysis (anterior MI vs. nonanterior MI group; 13.3 versus 9.2%; log rank \( P = 0.085 \)). The incidence of respective adverse events was not significantly different between the two groups (Table I). The time delay from patient admission to echocardiographic examination was 2.0 ± 1.7 days. There was no difference in the time lag from admission to echocardiographic examination between the anterior MI and nonanterior MI groups (1.9 ± 1.7 vs. 2.1 ± 1.6 days, \( P = 0.325 \)). Table I shows the baseline characteristics of the anterior and nonanterior MI groups. The anterior MI group showed higher systolic blood pressure (135.5 ± 29.7 vs. 124.6 ± 31.3 mmHg, \( P < 0.001 \)) and higher heart rate (83.9 ± 17.4 vs. 72.5 ± 20.1 beats/min, \( P < 0.001 \)) at admission, and higher NT-proBNP level (log NT-proBNP; 5.37 ± 1.97 vs. 5.03 ± 1.70, \( P = 0.017 \)) than the nonanterior MI group.

GLS and LVEF:
ROC curve analysis showed that there was no significant difference between GLS and LVEF in predicting 2-year outcome (area under curve; 0.709 [0.673–0.742] vs. 0.723 [0.688–0.756], \( P = 0.547 \)). GLS was significantly worse (–12.4 ± 3.8 vs. –15.7 ± 3.8%, \( P < 0.001 \)) and LVEF was significantly lower (46.0 ± 10.5 vs. 52.1 ± 9.5%, \( P < 0.001 \)) in the anterior MI group, which indicated worse left ventricular functioning in the anterior MI group than that in nonanterior MI group (Table I). A strong negative correlation between GLS and LVEF was noted in the overall study patient population (\( r = -0.718, P < 0.001 \); Fig. 2). Figure 1 also displays the results of separate analyses of the correlation between GLS and LVEF in the anterior and nonanterior MI groups. The correlations line between GLS and LVEF were exhibiting a tendency toward poor GLS values in the anterior MI group compared to those in the nonanterior MI group, even in the setting of similar LVEF (upward-shifted solid line of anterior MI)

### TABLE I
Baseline Characteristics of Anterior MI and Nonanterior MI and Adverse Events during 2-Year Follow-Up

<table>
<thead>
<tr>
<th>Baseline characteristics</th>
<th>Total (n = 686)</th>
<th>Anterior MI (n = 339)</th>
<th>Nonanterior MI (n = 347)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>61.9 ± 12.3</td>
<td>60.1 ± 12.4</td>
<td>62.7 ± 12.1</td>
<td>0.055</td>
</tr>
<tr>
<td>Male (n, %)</td>
<td>524 (76.4)</td>
<td>262 (77.3)</td>
<td>262 (75.5)</td>
<td>0.583</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>23.6 ± 3.1</td>
<td>23.6 ± 3.1</td>
<td>23.7 ± 3.2</td>
<td>0.506</td>
</tr>
<tr>
<td>HTN (n, %)</td>
<td>284 (41.4)</td>
<td>133 (39.2)</td>
<td>151 (43.5)</td>
<td>0.255</td>
</tr>
<tr>
<td>Diabetes (n, %)</td>
<td>145 (21.1)</td>
<td>68 (20.1)</td>
<td>77 (22.2)</td>
<td>0.494</td>
</tr>
<tr>
<td>Smoking (n, %)</td>
<td>355 (51.7)</td>
<td>177 (52.2)</td>
<td>178 (51.3)</td>
<td>0.810</td>
</tr>
<tr>
<td>Previous PCI (n, %)</td>
<td>29 (4.2)</td>
<td>12 (3.5)</td>
<td>17 (4.9)</td>
<td>0.376</td>
</tr>
<tr>
<td>Previous ischemic stroke (n, %)</td>
<td>25 (3.6)</td>
<td>15 (4.4)</td>
<td>10 (2.9)</td>
<td>0.281</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>130.0 ± 31.0</td>
<td>135.5 ± 29.7</td>
<td>124.6 ± 31.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>78.1 ± 19.7</td>
<td>83.9 ± 17.4</td>
<td>72.5 ± 20.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Killip class 2–4 (n, %)</td>
<td>142 (20.7)</td>
<td>76 (22.4)</td>
<td>66 (19.0)</td>
<td>0.272</td>
</tr>
<tr>
<td>eGFR (mL/min)</td>
<td>85.7 ± 32.9</td>
<td>88.1 ± 35.5</td>
<td>83.3 ± 30.0</td>
<td>0.052</td>
</tr>
<tr>
<td>Log NT-proBNP (ng/L)</td>
<td>5.20 ± 1.85</td>
<td>5.37 ± 1.97</td>
<td>5.03 ± 1.70</td>
<td>0.017</td>
</tr>
<tr>
<td>Log troponin I (ng/mL)</td>
<td>3.97 ± 1.29</td>
<td>3.94 ± 1.48</td>
<td>3.99 ± 1.09</td>
<td>0.554</td>
</tr>
<tr>
<td>Symptom-to-balloon time (hour)</td>
<td>5.59 ± 4.57</td>
<td>5.61 ± 4.39</td>
<td>5.56 ± 4.75</td>
<td>0.875</td>
</tr>
<tr>
<td>Post PCI TIMI 3 flow (n, %)</td>
<td>645 (94.0)</td>
<td>319 (94.1)</td>
<td>326 (93.9)</td>
<td>0.933</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>49.1 ± 10.5</td>
<td>46.0 ± 10.5</td>
<td>52.1 ± 9.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GLS (%)</td>
<td>−14.0 ± 4.1</td>
<td>−12.4 ± 3.8</td>
<td>−15.7 ± 3.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>All-cause mortality (n, %)</td>
<td>64 (9.3)</td>
<td>35 (10.3)</td>
<td>29 (8.4)</td>
<td>0.376</td>
</tr>
<tr>
<td>Hospitalization for HF (n, %)</td>
<td>17 (2.5)</td>
<td>11 (3.2)</td>
<td>6 (1.7)</td>
<td>0.202</td>
</tr>
<tr>
<td>Composite adverse events (n, %)*</td>
<td>77 (11.2)</td>
<td>45 (13.3)</td>
<td>32 (9.2)</td>
<td>0.093</td>
</tr>
</tbody>
</table>

BMI = body mass index; eGFR = estimated glomerular filtration rate; GLS = global longitudinal strain; HF = heart failure; HTN = hypertension; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NT-proBNP = N-terminal pro-natriuretic peptide; PCI = percutaneous coronary intervention; SBP = systolic blood pressure; TIMI = thrombolysis in myocardial infarction.

*Composite incidence of all-cause mortality and hospitalization for heart failure; only first events were counted.
group, compared to the dotted line of nonanterior MI group). Additionally, the mean GLS in the anterior MI group was worse than that in the nonanterior MI group, even after controlling for LVEF (13.2 ± 0.2 vs. 14.9 ± 0.2% [mean ± standard error]; P < 0.001). We divided the study cohort into quartiles according to the LVEF (Fig. 2). LVEFs were not significantly different between anterior and nonanterior MI group except the third quartile, whereas GLSs were consistently worse in anterior MI group regardless of any quartile groups. Those tendencies were indicating that GLS decreased more severely in anterior MI than in nonanterior MI even in the condition of similar LVEF level.

**Difference in the Prognostic Implications of GLS between Anterior MI and Nonanterior MI:**

Table II displays risk factors for 2-year outcome using the univariate and multivariate analysis models for 2-year outcome. GLS (or LVEF) entered in multivariate Cox proportional hazard model together with significant risk factors in univariate analysis. GLS (or LVEF) was an independent predictor for 2-year outcome in the multivariate analysis model. We analyzed the prognostic values of GLS in anterior and nonanterior MI group using Cox proportional hazard model (Fig. 3). Crude hazard ratios (HR) of GLS were 1.292 (95% confidence interval [CI] 1.185–1.410) in anterior MI group and 1.154 (95% CI 1.067–1.248) in nonanterior MI group, respectively. There was an interaction between GLS and infarction territory (P for interaction = 0.048, Fig. 3). The difference in prognostic impact of GLS depending on the infarction territory persisted even after adjusting the prediction model with clinical confounders of baseline characteristics, biomarker, and interventional success from univariate analysis. Figure 3 demonstrated that there were significant interactions between GLS and infarction territory in both the crude and adjusted models, whereas LVEF showed consistent prognostic impact on outcomes regardless of infarction territory in all models, which showed that GLS was a more sensitive predictor in anterior MI group than that in nonanterior MI group.

**Discussion:**

This study addressed the difference in the prognostic impact of GLS depending on infarction territory in patients with STEMI. The main findings
from the present study were that (1) GLS decreased in a more sensitive manner in patients with anterior MI than in those with nonanterior MI, even when LVEF was similar and (2) GLS more sensitively predicted prognosis in patients with anterior MI than in those with nonanterior MI.

Unlike Doppler tissue image–derived parameters, speckle tracking–derived GLS has the advantage of angle independency and measures myocardial contractility excluding translational movement. Speckle tracking GLS measurements have also shown excellent reproducibility. Based on these important advantages, GLS has been validated as a novel parameter for the assessment of left ventricular systolic function and as a prognostic marker in various cardiac conditions, including ischemic heart disease, heart failure, atrial fibrillation, post cardiac surgery, and valvular heart disease.

GLS has been known to be closely associated with left ventricular remodeling and to have significant prognostic implications for patients with acute MI. Some previous studies have proposed superior prognostic implications of GLS compared to LVEF in patients with acute MI. Although the results of ROC curve analyses in the present study could not present the superiority of GLS in prognostic implication compared to LVEF in patients with STEMI, GLS obviously seemed to be as potent as LVEF in predicting prognosis. However, the present study suggested some differences in characteristics between GLS and LVEF in acute myocardial infarction. The results showed that GLS decreased more sensitively in anterior MI than nonanterior MI compared to LVEF, which might imply that GLS values can be modulated by the infarction territory in patients with STEMI in contrast to LVEF. A possible explanation for these findings may be predicated on the hypothesis that GLS depends more heavily on apical than on basal segments. A left ventricular contraction consists not only of a longitudinal component, but also of many other complex mechanisms such as radial, circumferential movement, twist, and torsion. GLS exhibits only longitudinal deformations, and it may be more dominantly affected by apical motion of left ventricle, whereas LVEF, as a volumetric measurement, may not be. A previous study conducted by Carnabuci et al. demonstrated regional differences in longitudinal strain and a relatively higher endocardial longitudinal strain in the left ventricular apical region in a dog model. A study...
including human subjects by Leitman et al.\textsuperscript{5} also demonstrated higher degrees of longitudinal strain in the apical endocardial myocardium than in the basal segments. The greater sensitivity to decreases associated with GLS than those associated with LVEF in anterior MI may underlie the mechanism of GLS as a more potent predictive parameter in anterior MI than in nonanterior MI.

**Study Limitations:**
This study had some limitations. First, this was a single-center retrospective study. Relatively small numbers of patients reached the outcome to affect the robustness of analysis. Second, there was absence of data about serial changes in left ventricular function and volumes. The outcomes were evaluated only depending on the clinical events without any surrogate markers. Third, the mortality outcome of this study was limited to all-cause mortality and causes of death were not investigated fully. Lastly, a single type of echocardiographic machine and speckle tracking analysis software was used. Thus, findings from this study have limited generalizability and may be affected by vendor-specific characteristics.

**Conclusion:**
Speckle tracking GLS measurement in patients with STEMI showed that GLS decreases in a more sensitive manner in patients with anterior MI than in those with nonanterior MI, even when LVEF was similar. Furthermore, GLS was a more sensitive prognostic indicator in patients with anterior MI than in those with nonanterior MI.

**References**
3. Munk K, Andersen NH, Terkelsen CJ, et al: Global left ventricular longitudinal systolic strain for early risk assess-

Supporting Information
Additional supporting information may be found online in the supporting information tab for this article.

Figure S1. Flow chart of patient selection.