Early Prediction of Infarct Size by Strain Doppler Echocardiography After Coronary Reperfusion

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Objectives
The objective of this study was to investigate whether strain Doppler echocardiography performed immediately after revascularization by percutaneous coronary intervention could predict the extent of myocardial scar, determined by contrast-enhanced magnetic resonance imaging (MRI).

Background
There is considerable variability in survival rate after percutaneous coronary intervention, and accurate early risk stratification is therefore of major clinical importance.

Methods
Thirty individuals with acute anterior myocardial infarction were examined with longitudinal strain by Doppler 1.5 h after revascularization. The extent of scarring 9 months later was analyzed by MRI in 16 corresponding myocardial segments. Strain in all left ventricular segments was averaged to obtain a global value. Infarct size was estimated by clinical parameters and cardiac markers.

Results
A good correlation was found between the global strain and total infarct size ($R^2 = 0.77, p < 0.00001$). A multivariate regression analysis showed that global peak strain and serum glutamic oxaloacetic transaminase correlated with the infarct size measured by MRI ($p = 0.0001$ and $p = 0.001$, respectively). Furthermore, a clear inverse relationship was found between the segmental strain and the transmural extent of infarction in each segment ($R = 0.67, p < 0.0001$).

Conclusions
This study demonstrates that assessment of regional and global strain at 1.5 h after reperfusion therapy correlates with size and transmural extent of myocardial infarction as determined by contrast-enhanced MRI. The novel global strain parameter is a valuable predictor of the total extent of myocardial infarction and may therefore be an important clinical tool for risk stratification in the acute phase of myocardial infarction. (J Am Coll Cardiol 2007;49:1715–21) © 2007 by the American College of Cardiology Foundation

Percutaneous coronary intervention (PCI) represents a major advance in the management of patients with acute myocardial infarction (AMI). The widespread use and recurrent improvements of the PCI method have resulted in a significant reduction in early and late mortality in patients compared with the use of pharmacological reperfusion therapy (1). Nonetheless, there is considerable variability in survival rate after PCI and, therefore, accurate early risk stratification is of major clinical importance. The currently available methods for risk assessment of mortality and morbidity after AMI are mainly derived from thrombolysis trials; therefore, their applicability in the PCI setting is uncertain.

Assessment of infarct size is important in risk stratification (2,3). This assessment can be achieved by biochemical (4), by electrocardiographic methods (5,6) or by imaging modalities, such as scintigraphy (7), grayscale echocardiography (8), wall motion score index (WMSI) (9), and contrast-enhanced magnetic resonance imaging (MRI) (10). When using MRI, one can quantify the extent of myocardial scarring after myocardial infarction with great accuracy (11–14). However, the use of MRI in the acute phase of AMI is limited. Echocardiography is more easily available and feasible technique in the acute setting.

The use of strain by Doppler quantifies regional myocardial deformation and can demonstrate abnormal myocardial function due to ischemia (15,16). There is currently no established echocardiographic method to quantify infarcted myocardium immediately after revascularization therapy. A recent animal experiment has demonstrated that combining
early systolic stretching and total shortening after reperfusion of myocardial infarction can distinguish between viable or necrotic myocardium (17). On the basis of these findings, we hypothesized that a substantial negative strain value measured shortly after reperfusion indicates viability and potential for functional recovery.

Furthermore, we hypothesized that the average of total myocardial shortening in all left ventricular (LV) segments reflects the total extent of necrotic myocardium and therefore may predict the final infarct size.

Methods

Patient population. Thirty consecutive patients (23 men, 7 women, 54 ± 9 years of age) with first AMI in the anterior LV wall were prospectively enrolled. All patients had typical chest pain and sustained ST-segment elevation demonstrated on electrocardiography (ECG). Patients were excluded if they had a previous history of myocardial infarction. Twelve (40%) of the patients underwent a rescue procedure. The coronary angiography showed total (n = 19) or subtotal (n = 11) occlusion of the left anterior descending coronary artery (LAD) and all underwent successful revascularization therapy. Seven (23%) of the patients had stenoses in 2 vessels. None had 3-vessel disease. After angioplasty, none of the patients had clinical evidence of recurrent coronary events in the period between the initial admission and the MRI scanning (8.7 ± 3.3 months after the AMI). Breath-hold cine images with a time resolution of 35 ms were acquired. Approximately 10 to 20 min after intravenous injection of 0.1 mmol/kg gadopentetate dimeglumine, late enhancement images were obtained from the long-axis views, followed by multiple short-axis slices covering the entire left ventricle. A breath-hold segmented magnetization-prepared turbo gradient echo sequence was used. The basal and midventricular short axis slices were divided into 6 segments, and the apical short axis slices were divided into 4 segments (18). In our study, findings in the apex were not used.

In each of the LV segments, the area of the entire myocardium was manually drawn. Infarct was defined as areas with pixel intensities >2 SD of the mean pixel intensity in normal myocardium in the same slice. In each segment, the infarct size was calculated as percentage of the total segment area. The total infarct size was reported as percent of LV mass and in units of grams of the infarcted myocardium.

Echocardiography. Examinations were performed with a digital ultrasonic device system (Vivid 7, GE Vingmed Ultrasound, Horten, Norway). The patients were examined within 2 h after revascularization. Tissue Doppler imaging recordings of LV were obtained from the apical long-axis, 4-chamber, and 2-chamber views (115 ± 21 frames/s). A new echocardiographic study was performed the same day as the MRI at 9 months after revascularization (121 ± 21 frames/s). The echocardiographic recordings were analyzed with dedicated software (EchoPac, GE Vingmed Ultrasound).

Left ventricular ejection fraction (LVEF) was assessed by Simpson’s method from the grayscale digital recordings (8). In our laboratory, this method has a rered uncertainty of 12%. The WMSI was calculated from the same cine loops as used for the strain analyses, in a standard 16-segments model (9,18). Strain was measured in the basal parts of each segment with a region of interest of 6 × 6 mm. The strain value used in this study was the maximum negative strain magnitude during systole or early diastole. The peak negative strain value measured in each segment was compared with the extent of delayed enhancement by MRI in the corresponding 16 segments (Fig. 1). Furthermore, the strain measurements from each segment were averaged to obtain a global strain value for the entire LV. Two different investigators unaware of each other’s results analyzed MRI and strain by Doppler measurements.

ECG. Standard 12-lead ECG was obtained from all patients before and after PCI as well as the following day. The simplified Selvester score was used for an estimation of infarction size by ECG (5).

Biochemistry. Serum was collected from each patient for measurement of troponin I, serum glutamic oxaloacetic transaminase, creatine kinase-myocardial band, and myoglobin before PCI and at 6, 12, and 24 h after the PCI procedure. The peak value for each marker was used in the statistical analysis.

Statistical methods. Values are expressed as mean ± SD. The acute global strain measurements were compared with WMSI, LVEF, ECG, biochemical markers, time to reperfusion, extent of coronary disease, residual diameter stenosis, and infarct size estimated by MRI using regression
analyses. We performed a multivariate regression analysis to find the best method for estimating final infarct size, using MRI as the reference method. Myocardial segments were divided in groups based on the transmural extent of infarction, and peak negative strain values between groups were compared by using 1-way analysis of variance with Bonferroni adjustment. Global strain values from the acute echocardiographic study and after 9 months were compared by using the paired Student t test.

For reproducibility, 10 patients were randomly selected, and strain in each segment was analyzed by 2 independent observers. Reproducibility was calculated by intraclass correlation (α value). SPSS 13.0 for Windows was used for all statistical analyses (SPSS Inc., Chicago, Illinois). We considered p < 0.05 statistically significant.

**Results**

Clinical characteristics are shown in Table 1. Of the 30 patients, 2 used angiotensin II receptor blocking agents; one used a beta-blocker, whereas none used angiotensin-converting enzyme inhibitors. Nine months after discharge from hospital, 6 patients used an angiotensin II receptor blocking agent, 27 were on a beta-blocker, and 9 used an angiotensin-converting enzyme inhibitor. During follow-up, none had recurrent angina, but 7 of the patients had a new PCI procedure of significant stenoses in nonculprit arteries, found during the acute PCI.

The time to reperfusion was close to 5 h (284 ± 138 min). Echocardiography was performed 87 ± 57 min after angioplasty. Global strain was $-13.5 ± 2.3%$. A total of 354 segments (81%) had sufficient image quality for strain analysis. Left ventricular ejection fraction by echocardiography was $42 ± 9\%$, and WMSI was $1.6 ± 0.3$. In 6 of the segments (1.3%), the wall motion abnormality was outside the expected LAD distribution area. Global strain nine months after revascularization was $-13.3 ± 2.8\%$ (p = NS from the acute measurement).

### Table 1 Clinical Characteristics and Biochemical Markers (n = 30)

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>54 ± 8</td>
</tr>
<tr>
<td>Time of ischemia (min)</td>
<td>284 ± 138</td>
</tr>
<tr>
<td>Infarct size by SSS (in % of left ventricle)</td>
<td>27 ± 11</td>
</tr>
<tr>
<td>Ejection fraction (by echocardiography)</td>
<td>42 ± 9</td>
</tr>
<tr>
<td>Wall motion score index (by echocardiography)</td>
<td>1.6 ± 0.3</td>
</tr>
<tr>
<td>Infarct size by MRI (in % of left ventricle)</td>
<td>16 ± 9</td>
</tr>
<tr>
<td>Infarct size by MRI (in g)</td>
<td>29 ± 19</td>
</tr>
<tr>
<td>Troponin I (µg/l)</td>
<td>102 ± 118</td>
</tr>
<tr>
<td>Myoglobin (µg/l)</td>
<td>1,051 ± 817</td>
</tr>
<tr>
<td>SGOT (U/l)</td>
<td>453 ± 292</td>
</tr>
<tr>
<td>CK-MB mass (µg/l)</td>
<td>273 ± 105</td>
</tr>
</tbody>
</table>

Values are mean ± SD.
CK-MB = creatine kinase isoenzyme myocardial band; MRI = magnetic resonance imaging; SGOT = serum glutamic oxaloacetic transaminase; SSS = Selvester QRS scoring system.
The infarct size by MRI was estimated to 29 ± 19 g, which represents 16 ± 9% of the left ventricle. Transmural extent was graded 51% to 100% in 39 segments, 1% to 50% in 162 segments, and no delayed enhancement in 153 segments.

**The relationship between myocardial strain and infarct size.** Figure 1 demonstrates typical strain traces from a patient with anterior wall infarction. Peak negative strain was $-4.5 \pm 4.3\%$ in areas of complete transmural delayed enhancement whereas normal systolic shortening ($-18.1 \pm 5.1\%$) was found in remote areas ($p < 0.00001$). Peak negative strain was measured during early diastole in 58% of all segments (104 ± 27 ms after end-systole). This postsystolic shortening was observed in ischemic segments only. The magnitude of postsystolic shortening was $53 \pm 37\%$ of total systolic shortening. Segmental strain $<-8.2\%$ had a specificity of 82% and a sensitivity of 78% to detect transmural scar extent ($\geq 50\%$ infarct size).

A significant correlation was found between the segmental strain value and the segmental infarct size by MRI ($R = 0.67$, $p < 0.00001$). An even better correlation was found between the global strain value in each patient and infarct size by MRI calculated as percentage of total volume ($R = 0.77$, $p < 0.00001$) (Fig. 3). Global strain $<-11.7\%$ in absolute values had a specificity of 96% and a sensitivity of 88% to reveal an infarct size larger than 18% of total LV volume ($19$). An averaged strain value from the infarct zone correlated well with the scar size when adjusted for the number of segments involved in each patient ($R = 0.81$, $p < 0.00001$). Both LVEF and WMSI by echocardiography exhibited significant correlations with infarct size by MRI ($R = 0.48$, $p = 0.007$ and $R = 0.45$, $p = 0.015$, respectively).

Correlations between global strain and cardiac and clinical markers are presented in Table 2. Table 3 shows a multivariate regression analysis with infarct size measured by MRI as the dependent variable. Only global peak negative strain and SGOT correlated significantly with the infarct size measured by MRI in this model. Global strain by Doppler assessed at the time of the MRI study showed a significant correlation to the myocardial scar ($R = 0.72$, $p < 0.0001$).

**Reproducibility.** The interobserver intraclass correlation for global peak negative strain was 0.91 ($p < 0.00001$). The corresponding intraobserver correlation was 0.95 ($p < 0.0001$).

**Discussion**

This study demonstrates that in patients with AMI measurements of global peak negative Doppler strain measured 1.5 h after revascularization therapy correlates well with...
Table 3. Multivariate Regression Analysis of All Parameters Versus Magnetic Resonance Imaging

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Correlation Coefficient (β)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strain by echocardiography</td>
<td>0.51</td>
<td>0.0001</td>
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<tr>
<td>SGOT</td>
<td>0.479</td>
<td>0.001</td>
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<tr>
<td>Time to reperfusion</td>
<td>-0.145</td>
<td>0.225</td>
</tr>
<tr>
<td>CK-MB</td>
<td>0.116</td>
<td>0.346</td>
</tr>
<tr>
<td>Myoglobin</td>
<td>-0.126</td>
<td>0.253</td>
</tr>
<tr>
<td>WMSI</td>
<td>0.127</td>
<td>0.273</td>
</tr>
<tr>
<td>ECG</td>
<td>-0.096</td>
<td>0.534</td>
</tr>
<tr>
<td>CAD</td>
<td>-0.068</td>
<td>0.548</td>
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<tr>
<td>Troponin I</td>
<td>0.055</td>
<td>0.681</td>
</tr>
<tr>
<td>TIMI post PCI</td>
<td>-0.042</td>
<td>0.831</td>
</tr>
<tr>
<td>LVEF</td>
<td>-0.007</td>
<td>0.973</td>
</tr>
</tbody>
</table>

CAD = extent of coronary artery disease; PCI = percutaneous coronary intervention; TIMI = Thrombolysis in Myocardial Infarction; other abbreviations as in Tables 1 and 2.

final infarct size assessed by contrast enhanced MRI. We introduce a novel strain index that combines strain from 16 LV segments. This global strain was found to be a better predictor of the total extent of myocardial infarction than LVEF. In addition to traditional echocardiography, global strain may thus add important information to early risk stratification after reperfusion of AMI.

Infarct size is a major prognostic factor for cardiovascular death, reinfarction, congestive heart failure, and stroke (3,19). Early information regarding the extent of the myocardial damage is therefore of major clinical importance. LVEF has traditionally been used to assess the degree of myocardial damage and as a marker of early and late complications after myocardial infarction (20,21). In our study, LVEF showed a poor correlation to the infarct size by MRI. One possible reason is that LVEF describes the global LV function whereas the infarcted area and reduced function is regional. A decrease in LVEF supposes that several LV segments are involved. Methods that measure LV regional function could therefore be more sensitive measures than EF to identify systolic dysfunction. The assessment of myocardial strain has been shown to be superior to wall motion analyses in acute ischemia and is fundamentally a regional technique (15,22). Different aspects of myocardial function are measured by the 2 techniques. Left ventricular ejection fraction primarily is a measurement of the radial contraction of the wall in addition to some longitudinal contraction reflected by the mitral plane movement. Global strain quantifies contraction only in the longitudinal direction. This longitudinal vector of the LV 3-dimensional contraction pattern is probably more sensitive to ischemia compared to radial contraction (23). Hence, we believe that our model with global strain could be a better indicator of myocardial damage due to ischemia.

Furthermore, the exact limitations of the endocardial borders are difficult to detect in patients with poor echocardiographic quality. Strain Doppler echocardiography therefore represents an important step forward in noninvasive assessment of the degree of myocardial damage after acute myocardial infarction and may become an improved marker of prognosis.

We have previously shown that strain by echocardiography is superior to tissue velocities by Doppler and wall motion analyses to detect the ischemic area in the acute ischemic myocardium (15). In this study we used the peak negative strain value, regardless of whether it appeared during systole or early diastole. This variable was used as a simplified measure for the sum of LV lengthening and shortening and might reflect the contractile reserve. The present study expands the use of strain by Doppler as a predictor of infarct size and demonstrates that strain is able to distinguish between different degrees of the transmural extent of infarction when obtained during the acute period of the infarction. This may add important information to the risk stratification in each patient. Moreover, it is independent of cardiac phase and easy to measure which facilitates its clinical use.

Our study showed a significant correlation between infarct transmurality and strain in corresponding segments, but the relationship was not as good as between total infarct size and global strain. An important reason for this finding is that the size and position of each myocardial segment by MRI and echocardiography is not identical. In addition, the effect of measurement variability of the two techniques is reduced by calculating total infarct size and global strain.

An important reason why the acute strain measurement could predict infarct size determined 9 months later was that global strain remained unchanged. After the acute episode when reperfusion has occurred, parts of the stunned myocardium becomes necrotic and other parts recovers with opposite effects on peak negative strain. One might speculate that these 2 effects balance each other.

Several risk scores using demographic and electrocardiographic variables have been developed from thrombolytic trials, but their applicability after primary PCI setting is more or less unknown. Contrast-enhanced MRI is today the best technique for assessing infarct size after AMI, and the prognostic value of this technique after infarction is well established (19). However, MRI is not commonly used as a routine examination and its use is limited because of economical factors and availability.

It is well known that the true anatomic infarct size might be overestimated by measurements of ejection fraction by echocardiography (24). Previous studies have shown modest correlation between wall motion by echocardiography and thallium-201 perfusion defects, creatine-kinase levels, hemodynamic changes, coronary angiography, and pathological findings (20,25). These discrepancies are probably explained by the fact that these techniques measure different aspects of the infarction process.

All functional indices based on myocardial deformation (including direct visual assessment, wall thickening, and strain measurements) are load-dependent. This load or local stress dependence is even more complex in the ischemic or infarcted part of LV, where the mechanical behavior of...
infarcted subendocardial myocardium is in large part dictated by that of the preserved subepicardial layers (26,27). Similarly, the function of preserved myocardium adjacent to the infarct border is heavily dependent on the mechanical behavior of remote noninfarcted regions (28,29). These factors may further have reduced the correlation between echocardiographic and MRI results in our study.

**ECG as a marker of myocardial infarction.** An ECG remains the most commonly used noninvasive tool for diagnosing and evaluating cardiac disease (6). The ECG classification system used in our study was designed to classify cardiac injury, infarct size, and LV function. Given the strong association between myocardial damage and death, this and similar classification systems have been used for predication of prognosis. In our study strain by Doppler correlated better with the total infarct size than the ECG estimated by the Simplified Selvester score.

**Biochemical markers of myocardial infarction.** Calculated peak activities of SGOT and creatine kinase-myocardial band have been shown to strongly correlate with the infarct size in patients with acute myocardial infarction. Peak troponin I has been found to correlate well with the infarct size by MRI in a recent study (30). Troponin and SGOT correlated equally well with the infarct size as strain by Doppler did. However, in contrast to echocardiography, biochemical markers do not have the same ability to describe the location of the infarct as echocardiography.

**Study limitations.** The MRI examination was performed several months after the acute phase of infarction whereas all other parameters were obtained during the acute phase. The objective of this study was, however, to clarify whether an early echocardiographic study was able to predict the final myocardial infarction size after remodeling as defined by MRI.

The superiority of the global strain value to LVEF in predicting infarct size and, therefore, LV regional function suggests that we may have obtained a better prognostic parameter than LVEF. Left ventricular ejection fraction is a global parameter, whereas the global strain actually is calculated from regional measurements. It is therefore not evident that this novel parameter is better than LVEF in assessing reduced myocardial function in diseases involving the whole LV.

The results presented in this study are from patients with anterior myocardial infarction after PCI treatment. Our results cannot be used in patients without reperfusion before the changes in global strain from the acute to the chronic phase have been explored. Follow-up angiography was not performed in our study. Even though none of the patients reported recurrent angina at follow-up, a late occlusion or progression of coronary disease, might be a confounder in our study.

Optimal strain measurements are not always easy to obtain in all parts of the myocardium, and infarction in other sites than the anterior wall may therefore be more difficult to assess. However, most infarctions would have been visualized by the three imaging planes used in this study.

**Conclusions**

Measurements of regional and global peak negative strain in acute anterior infarction 1.5 h after reperfusion therapy can predict final infarct size better than LVEF and correlate well with clinical indices of infarct size. It can be performed shortly after PCI and may have important diagnostic and therapeutic implications for the individual patient and lead to improved noninvasive risk stratification.

**REFERENCES**


