Myocardial Deformation Imaging Based on Ultrasonic Pixel Tracking to Identify Reversible Myocardial Dysfunction

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Objectives
This study evaluated the predictive value of myocardial deformation imaging for improvement in cardiac function after revascularization therapy in comparison with contrast-enhanced cardiac magnetic resonance imaging (ceMRI).

Background
Myocardial deformation imaging allows analysis of myocardial viability in ischemic left ventricular dysfunction.

Methods
In 53 patients with ischemic left ventricular dysfunction, myocardial viability was assessed using pixel-tracking-derived myocardial deformation imaging and ceMRI to predict recovery of function at 9 ± 2 months follow-up. For each left ventricular segment in a 16-segment model, peak systolic radial strain was determined from parasternal 2-dimensional echocardiographic views using an automatic frame-by-frame tracking system of natural acoustic echocardiographic markers (EchoPAC, GE Ultrasound, Horton, Norway), and the relative extent of hyperenhancement using ceMRI.

Results
Of 463 segments with abnormal baseline function, 227 showed regional recovery. Compared with segments showing functional improvement, those that failed to recover had lower peak radial strain (15.2 ± 7.5% vs. 22.6 ± 6.3%; p < 0.001) and a greater extent of hyperenhancement (56 ± 29% vs. 14 ± 17%; p < 0.001). Using a cutoff of 17.2% for peak systolic radial strain, functional recovery could be predicted with high accuracy (sensitivity 70.2%, specificity 85.1%, area under the curve 0.859, 95% confidence interval 0.825 to 0.893). The predictive value was similar to that of hyperenhancement by ceMRI (sensitivity 71.6%, specificity 92.1%, area under the curve 0.874, 95% confidence interval 0.840 to 0.901, at a cutoff of 43% hyperenhancement).

Conclusions
Myocardial deformation imaging based on frame-to-frame tracking of acoustic markers in 2-dimensional echocardiographic images is a powerful novel modality to identify reversible myocardial dysfunction (The Use of Myocardial Deformation Imaging; NCT00476320). (J Am Coll Cardiol 2008;51:1473–81) © 2008 by the American College of Cardiology Foundation

Evidence of residual myocardial viability in patients with ischemic left ventricular (LV) dysfunction has important therapeutic and prognostic implications (1). The benefit of revascularization for functional recovery depends on the presence of viable myocardial tissue (2,3). Analysis of functional, cellular, or metabolic integrity has been used for assessment of myocardial viability and prediction of functional recovery after revascularization in patients with chronic myocardial infarction (4–7). Contrast-enhanced cardiac magnetic resonance imaging (ceMRI) has evolved into the noninvasive reference technique for the analysis of myocardial viability in chronic ischemic heart disease. It has been shown to have a high accuracy in the identification of reversible myocardial dysfunction before percutaneous or surgical revascularization (8,9).

Ultrasound myocardial deformation imaging using either tissue Doppler imaging or, more recently, frame-to-frame tracking of acoustic markers in 2-dimensional echocardiographic images has been shown in experimental as well as clinical studies to allow differentiation of different myocardial viability levels in chronic ischemic LV dysfunction (10–13). Previous studies evaluated myocardial deformation imaging either in experimental histologic studies or related the findings in clinical studies to ceMRI. The technique has not been validated in humans for prediction of functional recovery after myocardial revascularization procedures.
This study sought to define whether the assessment of myocardial viability based on myocardial deformation imaging allows the identification of reversible myocardial dysfunction and to compare its predictive value for segmental and global functional recovery after revascularization with ceMRI.

Methods

Patients. Between August 2004 and June 2006, 195 patients with LV dysfunction underwent ceMRI for the definition of myocardial viability. Patients had to be in sinus rhythm to be included. One hundred ten patients with nonischemic cardiomyopathy or acute coronary syndromes were excluded from the study to avoid possible acute ischemia or stunning. Among the remaining 85 patients with chronic ischemic heart disease, 6 patients refused participation in this study and 5 patients had echocardiographic windows insufficient for participation. Of the remaining 74 patients, 55 patients underwent revascularization and 19 had no revascularization. The mean interval between imaging studies and revascularization was 12 ± 11 days, and no patient had clinical evidence of infarction during this period. Twenty-one patients underwent coronary bypass surgery, and 34 underwent percutaneous transluminal coronary angioplasty. In the patients revascularized by coronary bypass surgery, bypass flow measurements were performed to confirm adequate myocardial perfusion; in the patients treated by percutaneous coronary intervention, the completeness of revascularization was confirmed by a final diameter stenosis less than 30% and a Thrombolysis In Myocardial Infarction flow grade 3 in all cases. One of the revascularized patients died, and 1 patient had biochemical evidence of myocardial infarction after coronary artery bypass surgery (creatine kinase-MB 3 times the upper limit). The remaining 53 patients (mean age 59 ± 8 years, 44 men) with revascularization comprised the study cohort. None of the patients had a clinical event indicative of myocardial infarction between revascularization and follow-up. This study was approved by the institutional review board of the University Aachen (EK 060/07). All patients gave written informed consent. Segmental and global functional recovery was assessed using echocardiographic images before and 9 ± 2 months after revascularization.

Echocardiography. Echocardiograms were performed before and 9 ± 2 months after revascularization with a Vivid Seven System (GE Ultrasound, Horton, Norway) equipped with a 2.5-MHz transducer. Parasternal long- and short-axis views at the basal, midventricular, and apical levels, as well as 3 standard apical views (4-chamber, 2-chamber, and long-axis) were acquired (frame rate 56 to 92 frames/s). Left ventricular ejection fraction was determined by manual tracing of end-systolic and -diastolic endocardial borders using apical 4- and 2-chamber views, employing biplane Simpson’s Method. The original 16-segment model of the American Society of Echocardiography was used to divide the LV.

Echocardiographic images obtained before revascularization and at follow-up were placed in a random order and analyzed by 2 independent observers who were unaware of the patient’s clinic and the findings of the other imaging modalities. Segmental wall motion was determined using the following score: 1 = normokinetic, 2 = hypokinetic, 3 = akinetic, or 4 = dyskinetic. A segment was considered to demonstrate functional improvement during follow-up if it improved by at least 1 grade. Global functional recovery was defined as an increase in ejection fraction >5% at follow-up.

Pixel tracking-based strain and strain rate analysis. The 3 acquired parasternal short-axis views at the basal, midventricular, and apical levels were analyzed considering the 16-segment model (6 segments for the basal and midventricular short-axis view and 4 segments for the apical short-axis view). Analysis was performed off-line with the aid of a dedicated software package (EchoPAC BT 05.2, GE Ultrasound). This system allows analysis of peak systolic radial and circumferential strain from short-axis views based on detection of natural acoustic markers. These markers are acoustic speckles that are equally distributed within the myocardium and can be identified as well as followed frame-to-frame during several consecutive images (14). The natural acoustic markers are expected to change their position from frame-to-frame in accordance with the surrounding tissue motion. The system calculates mean strain values for whole pre-defined LV segments, including all myocardial layers from the endocardium to epicardium.

Regarding the tracking quality, the system automatically generates a scale ranging from 1.0 for optimal to 3.0 for unacceptable for each analyzed segment, as described previously (14). We systematically dismissed segments with suboptimal tracking quality (grading >2.0 by the system) from the analysis. For the remaining segments, visual control of tracking quality was performed to ensure adequate automatic tracking. This was done by verifying adequate tracking quality of endocardial and epicardial borders by the system. End-systole was determined in the apical long-axis view as aortic valve closure. The time difference from the QRS complex was transferred to the other views. A medium degree of spatial and temporal smoothing was selected in the analysis algorithm of deformation parameters.

For each LV segment with adequate tracking, 9 peak systolic radial strain and peak systolic circumferential strain were automatically calculated. Radial strain relates to deformation (thickening or thinning) from the endocardium to the epicardium. Circumferential strain as a parameter of circumferential deformation relates to deformation along the curvature of the LV in the parasternal short axis.
Intraobserver and interobserver agreement in analysis of myocardial deformation parameters at this site have been determined before considering 10 subjects and have been reported previously (15). The coefficient according to Lin (16) was determined as an aggregate measure for agreement, which ranges between −1 and +1. It represents for continuous data an analog of the weighted kappa coefficient determined for ordinal data. For intraobserver agreement, the Lin coefficient was 0.99 (95% confidence interval [CI] 0.98 to 0.99) for radial strain and 0.95 (95% CI 0.90 to 1.00) for circumferential strain. For interobserver agreement, the Lin coefficient was 0.96 (95% CI 0.94 to 0.98) for radial strain and 0.93 (95% CI 0.89 to 0.97) for circumferential strain.

cMRI. All patients underwent cMRI within a few hours of the baseline echocardiographic study on a 1.5-T whole-body magnetic resonance scanner (Intera, Best, Philips, the Netherlands) using a 5-element phased-array cardiac coil with the patient placed supine. Each LV segment (according to the former 16-segment model of the American Society of Echocardiography) was scored as normokinetic, hypokinetic, akinetic, or dyskinetic by visual analysis. Fifteen minutes after intravenous injection of 0.2 mmol/kg body weight gadolinium (III)-diethyltriamine pentaacetic acid (Magnevist, Schering, Berlin, Germany), 8-mm short-axis slices were acquired with a prospectively electrocardiogram-gated gradient echo sequence with inversion pre-pulse. Imaging parameters were as follows: repetition time 2 heartbeats, echo time 5.0 ms, flip angle 25°, field of view 380 × 380 mm², 256 × 256 matrix, in-plane resolution 1.5 mm². The inversion time of the pre-pulse varied according to subjective visual judgment from 275 to 300 ms to achieve optimal signal suppression of normal myocardium and, consequently, optimal image contrast between infarcted and viable myocardium. Images were subsequently transferred to a workstation equipped with a dedicated cardiac software package (MassSoftware, Medis, Leiden, the Netherlands) for further analysis as described previously (17). Each myocardial segment was evaluated for the presence of hyperenhancement, defined as an area of signal enhancement ≥3 standard deviations of the signal intensity of nonenhanced myocardium. The total myocardial area and the contrast-enhanced area of each segment were traced manually. The segmental extent of hyperenhancement was calculated, defined as the percentage contrast-enhanced area of the total myocardial area ($\text{Area}_{\text{hyperenhancement}}/\text{Area}_{\text{myocardium}} \times 100$). Based on the percentage extent of hyperenhancement, a hyperenhancement category was determined for each segment related to the 5-point scale proposed by Kim et al. (8): 0% hyperenhancement (category 1), 1% to 25% hyperenhancement (category 2), 26% to 50% hyperenhancement (category 3), 51% to 75% hyperenhancement (category 4), and 76% to 100% hyperenhancement (category 5). Magnetic resonance imaging data were assessed by an experienced reader blinded to clinical data and results of the other imaging technique.

Statistical analysis. Data are expressed as mean ± standard deviation. Categorical data are presented by frequencies and percentages. Comparison between segments that showed functional recovery at follow-up and those that did not were performed with $t$ tests for continuous variables and chi-square tests for categorical variables. To address the issue of clustered data (data on multiple segments per patient used in the analysis), a generalized estimating equation approach with a Bernoulli variance function, a logistic link, and a working correlation matrix with exchangeable correlation assumption was used to explore the ability of strain parameters as well as hyperenhancement by magnetic resonance imaging to predict functional recovery (18). The output from this analysis allowed the derivation of receiver-operating characteristic (ROC) curves, which were used to designate cutoffs and calculate the area under the curve (AUC). To achieve a better comparability of the methods, we decided to keep the sensitivity fixed so that it did not fall below 70% and maximize the specificity over the set of eligible cutoff values. To show the equivalence of strain parameters and hyperenhancement by cMRI, a 95% CI for the difference of specificities was calculated. Two methods were regarded as equivalent if they did not differ by more than 10%; so if the CI for difference contained only values within the equivalence interval (−0.1, 0.1), we concluded that both methods were equivalent (19). In addition to continuous peak strain and percentage hyperenhancement analysis, categories of peak radial strain measures and extent of hyperenhancement were evaluated in this study. Similar to hyperenhancement, peak radial strain measures were assigned to quintiles of measures (categories were as follows: 1: >22.9%, 2: 22.9% to 17.2%, 3: 17.1% to 11.4%, 4: 11.3% to 5.6%, 5: <=5.5%). The categories considered the cutoff for prediction of segmental function recovery and aimed at coverage of all observed strain values with categories of similar width. All tests were 2-sided and assessed at the 5% significance level. All statistical analyses were performed using SAS version 9.13 (SAS Institute Inc., Cary, North Carolina) except for ROC statistics, for which we used SPSS version 14.0.1 (SPSS Inc., Chicago, Illinois).

Results

Study group. Clinical baseline characteristics of all patients are given in Table 1. Heart rate and systolic blood pressure did not change between baseline and follow-up examinations (74 ± 9 beats/min vs. 72 ± 6 beats/min, $p = 0.319$ and 144 ± 11 mm Hg vs. 145 ± 8 mm Hg, $p = 0.626$, respectively). There were 21 patients with recovery of global LV function at follow-up (ejection fraction at baseline vs. follow-up, 41 ± 8% vs. 53 ± 6%, respectively) and 32 patients without recovery of global LV function (ejection fraction baseline vs. follow-up, 39 ± 5% vs. 41 ± 5%). Patients did not differ in baseline characteristics.

In 771 LV segments (91%), echocardiographic image quality allowed visual assessment of segmental function and
myocardial deformation imaging at baseline and at follow-up studies; 308 segments had normal resting wall motion (41%), 259 segments had hypokinesia (33%), 135 segments akinesia (18%), and 69 segments dyskinesia (8%) at baseline studies. Myocardial deformation and ceMRI hyperenhancement parameters were evaluated on the 463 dysfunctional segments at baseline. Among these 463 dysfunctional segments at baseline, 227 segments (49%) showed functional recovery during follow-up after revascularization and 236 segments (51%) did not.

In the 19 patients in whom no revascularization was performed, there was no significant change in strain parameters from baseline to follow-up (radial strain from 13.5 ± 7.9% to 13.9 ± 7.3% and circumferential strain from −8.1 ± 6.5% to −8.5 ± 6.1%, respectively).

**Prediction of segmental functional recovery using echocardiographic deformation analysis.** Baseline peak systolic radial and circumferential strain data for the dysynergic segments are given in **Table 2**. Segments with functional recovery had significantly higher baseline peak systolic strain values compared with those without functional recovery. Figures 1 and 2 demonstrate strain curves of dysfunctional segments at baseline with and without functional recovery. A peak systolic radial strain >17.2% had a sensitivity of 70.2% and a specificity of 85.1% to predict segmental functional recovery (AUC = 0.859). Accuracies as well as the corresponding 95% CIs for peak radial and circumferential strain to predict segmental functional recovery are given in **Table 3**.

The peak systolic radial strain was significantly related to the likelihood of improvement in contractility after revascularization. When all segments that were dysfunctional before revascularization were analyzed and quintiles of peak systolic radial strain were considered, the proportion of improved contractility decreased progressively as the peak systolic radial strain measures decreased (p < 0.001) (Fig. 3). Thus, contractility increased in 82 of 93 segments (88%) with peak systolic radial strain >22.9% but in only 3 of 64 segments (5%) with peak systolic radial strain <5.5%.

**Prediction of segmental functional recovery using hyperenhancement imaging.** Baseline extent of hyperenhancement data for the dysynergic segments are given in **Table 2**. Segments with functional recovery had a lower extent of hyperenhancement and belonged to significantly lower hyperenhancement categories compared with segments without functional recovery (Table 2). Considering a cutoff point of 43%, transmural hyperenhancement allowed the prediction of functional improvement with a sensitivity of 71.6% and a specificity of 92.1% (AUC = 0.874) (Table 3).

The transmural extent of hyperenhancement was significantly related to the likelihood of improvement in contractility after revascularization (Fig. 3). Considering all segments that were dysfunctional before revascularization, the proportion of improved contractility decreased progressively as the transmural extent of hyperenhancement increased (p < 0.001). Thus, contractility increased in 117 of 140 segments (84%) with no hyperenhancement but in only 1 of 50 segments (2%) with hyperenhancement >75% of tissue.

**Relation between determined viability and improvement in global ventricular function.** For each patient, we estimated the percentage of the LV that was dysfunctional but viable

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**Table 1: Baseline Clinical Characteristics for Patients With and Without Global LV Functional Recovery**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Functional Recovery (n = 21)</th>
<th>No Functional Recovery (n = 32)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yrs</td>
<td>59 ± 10</td>
<td>57 ± 7</td>
<td>0.573</td>
</tr>
<tr>
<td>Men, n (%)</td>
<td>13 (62%)</td>
<td>20 (61%)</td>
<td>0.412</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>85 ± 11</td>
<td>87 ± 12</td>
<td>0.392</td>
</tr>
<tr>
<td>Height, m</td>
<td>1.70 ± 0.2</td>
<td>1.74 ± 0.1</td>
<td>0.671</td>
</tr>
<tr>
<td>Angina, CCS class</td>
<td>1.8 ± 0.4</td>
<td>1.7 ± 0.3</td>
<td>0.252</td>
</tr>
<tr>
<td>Heart failure, NYHA functional class, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>8 (38%)</td>
<td>11 (35%)</td>
<td>0.317</td>
</tr>
<tr>
<td>II</td>
<td>6 (29%)</td>
<td>10 (31%)</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>6 (29%)</td>
<td>9 (28%)</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>1 (5%)</td>
<td>2 (6%)</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>7 (33%)</td>
<td>12 (36%)</td>
<td>0.142</td>
</tr>
<tr>
<td>Hypertension (SBP/DBP &gt; 140/90 mm Hg), n</td>
<td>13 (62%)</td>
<td>19 (59%)</td>
<td>0.921</td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td>7 (33%)</td>
<td>11 (35%)</td>
<td>0.092</td>
</tr>
<tr>
<td>Hypercholesterolemia (cholesterol &gt;5 mmol/l), n</td>
<td>11 (52%)</td>
<td>16 (50%)</td>
<td>0.152</td>
</tr>
<tr>
<td>Family history, n</td>
<td>9 (44%)</td>
<td>14 (43%)</td>
<td>0.412</td>
</tr>
<tr>
<td>Ejection fraction baseline, %</td>
<td>41 ± 8</td>
<td>39 ± 5</td>
<td>0.198</td>
</tr>
<tr>
<td>Baseline LVEF &lt; 40%</td>
<td>6 (29%)</td>
<td>9 (28%)</td>
<td>0.692</td>
</tr>
<tr>
<td>Number of diseased vessels, n</td>
<td>1.2 ± 0.3</td>
<td>1.1 ± 0.3</td>
<td>0.259</td>
</tr>
<tr>
<td>Concomitant therapy, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACE/ARB</td>
<td>10 (48%)</td>
<td>17 (53%)</td>
<td>0.272</td>
</tr>
<tr>
<td>Beta-receptor blockers</td>
<td>17 (81%)</td>
<td>27 (84%)</td>
<td>0.671</td>
</tr>
<tr>
<td>Calcium-channel blockers</td>
<td>4 (20%)</td>
<td>7 (22%)</td>
<td>0.383</td>
</tr>
</tbody>
</table>

* Improvement of ejection fraction >5% at follow-up.

ACE = angiotensin-converting enzyme inhibitors; ARB = angiotensin II receptor blockers; CCS = Canadian Cardiology Society; DBP = diastolic blood pressure; LV = left ventricular; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; SBP = systolic blood pressure.

**Table 2: Myocardial Deformation and ceMRI Parameters Before Revascularization for Segments With and Without Functional Recovery at Follow-Up**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Functional Recovery (n = 227)</th>
<th>No Functional Recovery (n = 236)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radial strain (%</td>
<td>22.6 ± 6.3</td>
<td>15.2 ± 7.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Circumferential strain (%</td>
<td>−14.9 ± 6.5</td>
<td>−9.2 ± 5.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ceMRI Extent hyperenhancement (%)</td>
<td>14 ± 17</td>
<td>56 ± 29</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hyperenhancement category</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Category I</td>
<td>117</td>
<td>23</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Category II</td>
<td>72</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td>Category III</td>
<td>26</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td>Category IV</td>
<td>11</td>
<td>51</td>
<td></td>
</tr>
<tr>
<td>Category V</td>
<td>1</td>
<td>49</td>
<td></td>
</tr>
</tbody>
</table>

ceMRI = contrast-enhanced cardiac magnetic resonance imaging.
before revascularization using: 1) peak systolic radial strain measures; and 2) transmural extent of hyperenhancement. We calculated this percentage by adding the number of segments that were dysfunctional but predominantly viable and then dividing the total by the total number of segments in the L.V. For peak systolic radial strain, a cutoff point >17.2% and for the extent of hyperenhancement, 43% hyperenhancement was considered to define segmental viability. An increasing extent of dysfunctional but viable myocardium before revascularization correlated with greater improvement of ejection fraction after revascularization considering peak systolic radial strain \( r = 0.75, p < 0.001 \) as well as the extent of hyperenhancement by ceMRI \( r = 0.77, p < 0.001 \) (Fig. 4).

Comparison of myocardial deformation and hyperenhancement analysis for prediction of segmental and global functional recovery. By applying the optimal cutoff points for peak systolic radial strain measures as well as the extent of hyperenhancement from the ROC curves, we compared the sensitivity and specificity as well as AUC for the prediction of segmental functional recovery. There were no significant differences between the analyzed techniques in the prediction of segmental functional recovery (Table 3, Fig. 5, left).

The percentage of the L.V. that was dysfunctional but defined to be viable was calculated for both techniques and was used to predict global functional recovery (improvement in ejection fraction >5%). The AUC for the ROC curve considering peak systolic radial strain was 0.798 (95% CI 0.757 to 0.839, sensitivity 71%, specificity 78%), and the AUC for the ROC curve considering extent of hyperenhancement was 0.801 (95% CI 0.761 to 0.842, sensitivity 74%, specificity 75%). There was no significant difference in
the AUCs of the ROC curves of both techniques for prediction of global functional recovery (Fig. 5, right). There was a significant correlation between remaining myocardial wall thickness without hyperenhancement and circumferential strain \( r = 0.52, p < 0.001 \) and radial strain \( r = 0.50, p < 0.001 \). The thicker the remaining myocardial wall thickness, the higher the myocardial deformation.

### Discussion

The results of this study show that quantitative myocardial deformation imaging parameters determined at rest provide a feasible and accurate tool for identification of reversible segmental and global dysfunction. The predictive value of myocardial deformation parameters for functional recovery after revascularization of chronic ischemic LV dysfunction is comparable to ceMRI on a segmental and global LV level. **Magnetic resonance imaging.** Due to the ability to directly visualize the transmural extent of viable myocardium in each segment as well as to define the extent of viable myocardium within multiple segments, ceMRI has become the gold standard for assessment of myocardial viability \( 8,9,20–22 \). A strong correlation between the transmural extent of hyperenhancement and the recovery of regional function after revascularization has been described \( 8,20 \). Kim et al. \( 9 \) reported regional function improvement at 3 months of 78% in segments without hyperenhancement, improvement of 59% in segments with 1% to 25% hyperenhancement, but improvement of only 2% in segments with >75% hyperenhancement. In addition, the percentage of dysfunctional but viable myocardium by ceMRI correlates with recovery of global LV function after revascularization. The predictive power of hyperenhancement by ceMRI for functional recovery after revascularization found in this study was similar to previous reports: 117 of 140 dysfunctional regions (84%) identified as completely viable (without hyperenhancement) by ceMRI had an improvement in contractility after revascularization. In contrast, only 1 of 50 dysfunctional regions (2%) with >75% hyperenhancement demonstrated improvement after revascularization. There are some limitations to ceMRI, including costs, limited accessibility, and nonapplicability in patients with pacemakers or implantable defibrillators. Furthermore, fears of gadolinium-induced nephrotic systemic fibrosis have recently resulted in restrictions of the technique in patients with renal insufficiency \( 23 \). The frequent comorbidities of patients with ischemic cardiomyopathy may be a limiting factor for use of ceMRI in several of these patients. Other imaging modalities may be the preferred option in these patients.

**Myocardial deformation imaging to assess myocardial viability.** Experimental echocardiographic studies using Doppler-based myocardial deformation parameters have allowed accurate differentiation of nontransmural from transmural infarcts \( 10,11 \). Doppler-based strain analysis has also been found in a clinical study of 47 patients to allow definition of transmurality of myocardial infarction \( 12 \). However, Doppler-based strain imaging has found only limited access into clinical practice. The limiting factors have been a considerable angle dependency, a low signal-to-noise ratio, limited spatial resolution, and potential interactions by cardiac translational motion and tethering. Tracking of acoustic markers from frame-to-frame on the basis of 2-dimensional echocardiography has been proven to accurately determine regional and global LV function \( 14,15,24 \), including incremental function parameters like LV rotation and torsion \( 25 \). The novel technique overcomes most of the limitations of conventional tissue Doppler-based strain imaging. Recent experimental and clinical studies demonstrated high accuracy in the differentiation of subendocardial versus transmural myocardial infarcts defined by histology or by ceMRI \( 13,26,27 \). Radial strain analysis allowed detection of infarcted area greater than 50% with a sensitivity of 88% and a specificity of 95% in an ischemia-reperfusion model with histologic analysis of infarct extent \( 26 \). In a study of 80 patients with chronic ischemic cardiomyopathy, Chan et al. \( 27 \) determined significantly lower circumferential strain and strain rate measures in transmural infarct segments than in subendocardial infarcts. We have recently shown a sensitivity of 70.4% and a specificity of 71.2% for radial strain measures in transmural infarcts \( 10,11 \). Doppler-based strain analysis has also been found in a clinical study of 47 patients to allow definition of transmurality of myocardial infarction \( 12 \). However, Doppler-based strain imaging has found only limited access into clinical practice. The limiting factors have been a considerable angle dependency, a low signal-to-noise ratio, limited spatial resolution, and potential interactions by cardiac translational motion and tethering. Tracking of acoustic markers from frame-to-frame on the basis of 2-dimensional echocardiography has been proven to accurately determine regional and global LV function \( 14,15,24 \), including incremental function parameters like LV rotation and torsion \( 25 \). The novel technique overcomes most of the limitations of conventional tissue Doppler-based strain imaging. Recent experimental and clinical studies demonstrated high accuracy in the differentiation of subendocardial versus transmural myocardial infarcts defined by histology or by ceMRI \( 13,26,27 \). Radial strain analysis allowed detection of infarcted area greater than 50% with a sensitivity of 88% and a specificity of 95% in an ischemia-reperfusion model with histologic analysis of infarct extent \( 26 \). In a study of 80 patients with chronic ischemic cardiomyopathy, Chan et al. \( 27 \) determined significantly lower circumferential strain and strain rate measures in transmural infarct segments than in subendocardial infarcts. We have recently shown a sensitivity of 70.4% and a specificity of 71.2% for radial strain measures in the detection of nontransmural versus transmural infarction defined as >50% hyperenhancement by ceMRI \( 13 \). **Myocardial deformation imaging to predict functional recovery.** This study demonstrates that quantitative myocardial deformation parameters determined at rest can be used for identification of reversible myocardial dysfunction.
before revascularization procedures. We found that 82 of 93 dysfunctional segments (88%) with a radial strain value more than 22.9% had an improvement in contractility after revascularization. Similarly, prediction of improvement in global LV function was possible from analysis of myocardial viability in all dysfunctional LV segments. Importantly, the predictive power of myocardial deformation parameters for LV improvement was comparable to analysis of hyperenhancement by ceMRI. The AUC of peak systolic radial strain and extent of hyperenhancement by ceMRI for prediction of segmental functional recovery were similar: 0.859 and 0.874, respectively. Similarly, peak systolic radial strain and extent of hyperenhancement had similar AUCs to predict an improvement of LV ejection fraction by more than 5% after revascularization.

**Study limitations.** Matched analysis of LV function at baseline and at follow-up could be performed in only 91% of segments. Myocardial deformation parameters for analysis of myocardial viability and prediction of segmental functional recovery were not determined in 9% of segments. This was related to the inherent limitations of most echocardiographic techniques to display all LV segments with high image quality and the decision to reject all measurements of myocardial deformation parameters in case of a tracking quality generated by the system <2.0. Thus, 9% of segments that might have been analyzed by ceMRI were not accessible to echocardiographic prediction of functional recovery after revascularization. However, despite the inability of myocardial deformation imaging to determine viability in all segments, the predictive accuracy for recovery

![Figure 3](image1.png)

**Figure 3** Improvement in Segmental Function After Revascularization Related to Radial Systolic Strain and Hyperenhancement

Relation between peak systolic radial strain and likelihood of increased contractility after revascularization (left), and relation between transmural extent of hyperenhancement and likelihood of increased contractility after revascularization (right). Data are shown for all 463 dysfunctional segments before revascularization. The categories of hyperenhancement are given in the text. The categories of peak systolic radial strain were as follows: 1: >22.9%; 2: 22.9% to 17.2%; 3: 17.1% to 11.4%; 4: 11.3% to 5.6%; 5: <5.5% peak systolic radial strain.

![Figure 4](image2.png)

**Figure 4** Correlation Between the Percentage of the LV That Was Dysfunctional but Defined to Be Viable Before Revascularization and the Change in EF After Revascularization

The left panel shows the analysis considering the peak systolic radial strain; the right panel shows the analysis considering the extent of hyperenhancement by contrast-enhanced magnetic resonance imaging for assessment of global left ventricular (LV) viability. EF = ejection fraction.
of global LV function was similar to that obtained by analysis of hyperenhancement using ceMRI.

Quantitative analysis of the extent of myocardial hyperenhancement by ceMRI is used in clinical research (17,28). On the contrary, visual categorical analysis of hyperenhancement in ceMRI has been used in multiple previous studies and was shown to be very reliable due to the excellent image quality in most cases (8,9). It relates to the commonly used technique to define the extent of hyperenhancement in clinical practice. We used a quantitative analysis and transferred quantitative data to the categorical approach. Categories of radial strain were defined on the basis of the optimal cutoff to predict segmental recovery and aimed at coverage of all observed strain values with categories of similar width. This approach, although with arbitrary components, tried to define categories similar to those commonly used for ceMRI. Strain values were not zero, even in the group with the lowest myocardial deformation measures. This finding relates to previous observations with some deformation even in completely nonviable segments and has been explained by measurement artifacts related to tethering from adjacent segments (14,15).

Conclusions

This study demonstrates that myocardial deformation parameters obtained by tracking of acoustic markers within 2-dimensional echocardiographic images allows identification of reversible myocardial dysfunction. Regional and global functional recovery after revascularization can be predicted with an accuracy similar to the use of ceMRI.

REFERENCES


