Predicting Late Myocardial Recovery and Outcomes in the Early Hours of ST-Segment Elevation Myocardial Infarction

Traditional Measures Compared With Microvascular Obstruction, Salvaged Myocardium, and Necrosis Characteristics by Cardiovascular Magnetic Resonance

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Objectives
The aim of this study was to determine whether a very early imaging strategy improves the prediction of late systolic dysfunction and poor outcomes in ST-segment elevation myocardial infarction (STEMI) compared with traditional predictors.

Background
Earlier prediction of poor outcomes after STEMI is desirable, because it will allow tailored therapy at the earliest possible time, when benefits might be greatest.

Methods
One hundred and three patients with acute STEMI were studied by contrast-enhanced cardiovascular magnetic resonance within 12 h of primary angioplasty and at 6 months and followed 2 years. The primary end point was left ventricular (LV) dysfunction, whereas poor outcomes were a key secondary end point.

Results
Traditional risk factors were only modest predictors of late LV dysfunction. Late gadolinium enhancement (LGE) volume maintained a stronger association to LV ejection fraction change than infarct transmurality, microvascular obstruction, or myocardial salvage during STEMI (p < 0.02). Multivariable logistic regression identified LGE volume during STEMI as the best predictor of late LV dysfunction (odds ratio: 1.36, p < 0.03). An LGE ≥23% of LV during STEMI accurately predicted late LV dysfunction (sensitivity 89%, specificity 74%). The LGE volume provided important incremental benefit for predicting late dysfunction (area under the curve = 0.92, p < 0.03 vs. traditional risk factors). Twenty-three patients developed poor outcomes (1 death, 2 myocardial infarctions, 5 malignant arrhythmias, 4 severe LV dysfunction <35%, 11 hospital stays for heart failure) over 2.6 ± 0.9 years; LGE volume remained a strong independent predictor of poor outcomes, whereas LGE ≥23% carried a hazard ratio of 6.1 for adverse events (p < 0.0001).

Conclusions
During the hyperacute phase of STEMI, LGE volume provides the strongest association and incremental predictive value for late systolic dysfunction and discerns poor late outcomes. (J Am Coll Cardiol 2010;55:2459–69)

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Acute myocardial infarction (MI) has variable impact on long-term survival. After ST-segment elevation myocardial infarction (STEMI), patients who develop heart failure carry worse prognosis (1). Accordingly, decreased systolic function is sought after STEMI, because these sicker patients benefit most from pharmacological agents, coronary revas-
culation, and automated implanted cardioverter-defibrillator (AICD) implantation (2–4). Potential benefits might arise from earlier prediction and initiation of preventive treatment for heart failure during STEMI (5). However, left ventricular ejection fraction (LVEF) assessment performed very early after STEMI does not reliably predict late heart failure, because of heterogeneous LV remodeling and healing (6). In addition, the organization of acute STEMI care in many areas is based on centralized cathetizerization laboratories receiving STEMI patients directly from the field, to be transferred to a regional hospital 12 to 24 h after primary percutaneous coronary intervention (PCI), unless the patient is considered higher-risk and the transfer is delayed (7). Therefore, improved strategies are essential in the very early hours of STEMI to optimally risk-stratifity patients in order to initiate tailored treatment in a timely fashion and manage them securely.

Late gadolinium enhancement (LGE) measured by cardiovascular magnetic resonance (CE-CMR). Imaging was performed on a Philips Achieva 1.5-T system with a phased-array cardiac coil, ECG gating, and breath-holding in expiration (Philips Healthcare, Best, the Netherlands). To assess CE-CMR during the hyperacute phase of STEMI, protocol mandated imaging as early as logistically feasible, at the latest <12 h after angiography. Cine imaging for cardiac morphology and function was performed by 12-lead precordial leads; and 3) angiographically confirmed coronary artery acute occlusion or subocclusion (Thrombolysis In Myocardial Infarction flow grade 0 to 1). Exclusion criteria were a recent MI or revascularization procedure (<6 months), shock requiring balloon counterpulsation (but pressors were accepted), respiratory failure requiring mechanical ventilation (but oxygen by mask was accepted), and standard contraindications to cardiovascular MRI.

### Methods

#### Study population.
We enrolled consecutive patients with successfully reperfused acute STEMI in a prospective cohort study. The Institutional Review Board approved the study, and all patients signed informed consent. Acute STEMI was confirmed by: 1) presentation <12 h of typical chest pain onset; 2) ≥1 mm ST-segment elevation in 2 contiguous leads of electrocardiogram (ECG) (≥2 mm in precordial leads); and 3) angiographically confirmed coronary artery acute occlusion or subocclusion (Thrombolysis In Myocardial Infarction flow grade 0 to 1). Exclusion criteria were a recent MI or revascularization procedure (<6 months), shock requiring balloon counterpulsation (but pressors were accepted), respiratory failure requiring mechanical ventilation (but oxygen by mask was accepted), and standard contraindications to cardiovascular MRI.

#### Myocardial characterization by contrast-enhanced cardiovascular magnetic resonance (CE-CMR).
Imaging was performed on a Philips Achieva 1.5-T system with a phased-array cardiac coil, ECG gating, and breath-holding in expiration (Philips Healthcare, Best, the Netherlands). To assess CE-CMR during the hyperacute phase of STEMI, protocol mandated imaging as early as logistically feasible, at the latest <12 h after angiography. Cine imaging for cardiac morphology and function was performed by 12-lead precordial leads; and 3) angiographically confirmed coronary artery acute occlusion or subocclusion (Thrombolysis In Myocardial Infarction flow grade 0 to 1). Exclusion criteria were a recent MI or revascularization procedure (<6 months), shock requiring balloon counterpulsation (but pressors were accepted), respiratory failure requiring mechanical ventilation (but oxygen by mask was accepted), and standard contraindications to cardiovascular MRI.

#### Image analysis.
Image analysis was performed offline in an experienced core laboratory with a standardized approach after the 16-segment model (CMR Mass version 6.2.3, Medis, the Netherlands) (13,14). For ventricular volume analysis,
the endocardial border was determined for all 30 phases of the cardiac cycle, and the cardiac phases that demonstrated the largest and smallest ventricular cavity volumes were defined as end-diastole and -systole, respectively. Papillary muscles were included in the LV wall measurements (equivalent to weighting the LV) and excluded from LV cavity measurements (equivalent to blood pool techniques) (13). The LV end-diastolic volume, end-systolic volume, stroke volume, EF, and mass were computed with Simpson’s rule. The LV end-diastolic volume, end-systolic volume, and mass were adjusted to body surface area calculated by the Dubois formula (15). Segmental wall thickness was measured at end-diastole (20 to 30 chords/segment, by centerline method). Segmental thickening was measured by comparing average chord thickening at end-systole in each segment. LV function was reported as a continuous variable and also categorized as “normal” or “abnormal” (LVEF <50%) to reflect clinical practice (16).

Myocardial edema was defined as a mean signal intensity ±2 SDs of remote myocardium by semiautomatic software detection on T2 STIR and reported as a percentage of total myocardium on matched slices (10). Resting myocardial perfusion was assessed by the kinetics of myocardial enhancement during rapid intravenous injection of Gd contrast (17). The LGE was quantified by semi-automatic detection with the full-width at half-maximum approach as previously validated to maximize accuracy and reproducibility (18–22). The LGE size was reported in milliliters indexed to body surface area and calculated as a percentage of total myocardium. We also performed segmental analysis considering LGE to be “transmural” when LGE was at least 50% transmural in >50% of the segment’s total extension. Microvascular obstruction was quantified by visual detection on resting first-pass perfusion and reported as a percentage of total myocardium on matched slices (11). Salvaged myocardium was determined as the percent edematous myocardium from T2 STIR that was not necrotic on myocardium was determined as the percent edematous of total myocardium on matched slices (11). Salvaged on resting first-pass perfusion and reported as a percentage of total myocardium. We also performed segmental analysis considering LGE to be “transmural” when LGE was at least 50% transmural in >50% of the segment’s total extension. Microvascular obstruction was quantified by visual detection on resting first-pass perfusion and reported as a percentage of total myocardium on matched slices (11). Salvaged myocardium was determined as the percent edematous myocardium from T2 STIR that was not necrotic on myocardium was determined as the percent edematous of total myocardium on matched slices (11). Salvaged on resting first-pass perfusion and reported as a percentage of total myocardium. We also performed segmental analysis considering LGE to be “transmural” when LGE was at least 50% transmural in >50% of the segment’s total extension. Microvascular obstruction was quantified by visual detection on resting first-pass perfusion and reported as a percentage of total myocardium on matched slices (11).

**Follow-up.** Subjects were prospectively followed for a median of 33 months (range 24 to 42 months). Clinical follow-up based on a standard questionnaire was obtained from telephone interviews with the patients, relatives, or physicians or from hospital records. Survival status was obtained through a query of the government death index. Cardiovascular MRI was repeated at 6 months, because studies have demonstrated that infarct remodeling completes by this time (23). We collected major adverse cardiac events (MACE) defined as death, new MI, malignant arrhythmia (ventricular tachycardia/fibrillation), hospital stay for heart failure, or LVEF <35%.

**Statistical analysis.** Our primary end points were change in LVEF from STEMI to 6 months and LV dysfunction at 6 months. A key secondary end point was MACE as defined in the preceding paragraph.

Baseline characteristics are presented as mean (95% CI) for continuous variables and percentages for categorical data. Characteristics of patients with normal versus decreased 6-month LVEF were compared with a 2-tailed t test for continuous variables and chi-square test for categorical data. Changes in imaging variables from STEMI to 6 months were assessed with paired t tests.

We performed univariable and multivariable linear regression for association of variables measured during STEMI with percentage change in LVEF at 6 months. We also performed multiple linear regression analysis to determine the strongest association between change in LVEF and key CE-CMR parameters, including LGE percentage, nonviable segments, MVO, and SM.

Then we fit logistic regression models to estimate unadjusted odds ratios (ORs) with 95% confidence intervals (CIs) for: 1) LV dysfunction at 6 months; and 2) MACE. We performed 2 multivariable logistic regression analyses to assess any independent association of measurements made during STEMI with 6-month LV dysfunction and MACE. First, we aimed to build the best overall parsimonious model that provided association to LV dysfunction and MACE late after STEMI: stepwise forward selection was performed considering clinical or imaging variables listed in Tables 1 and 2 (variable entry or stay at p = 0.2). Second, we assessed the association of CE-CMR variables to 6-month dysfunction and MACE by adjusting for LVEF during STEMI and creatine kinase-myocardial band (CK-MB) rise.

Furthermore, we performed receiver-operator characteristic (ROC) analysis to identify an LGE percentage cutoff predicting LV dysfunction at 6 months and MACE while favoring superior sensitivity, to provide a better screening tool to identify patients who will develop heart failure after STEMI. The association between meeting this cutoff and MACE was verified by Cox proportional hazards analysis. Finally, ROC analysis was performed to determine any incremental value in LGE percentage for LV dysfunction beyond traditional risk factors; equality of the area under the curves (AUC) was tested with the algorithm suggested by DeLong et al. (24).

All final models were tested for goodness-of-fit and for influential observations to ensure that the assumptions of regression were satisfied. Analyses were performed with Stata version 9.2 (StataCorp LP, College Station, Texas) (25).

**Results**

One hundred and four consecutive subjects were prospectively studied. One was excluded between baseline and follow-up CE-CMR, because of dropout (claustrophobia). The remaining 103 subjects constituted the study cohort (99% successful enrolment and follow-up). Two patients had follow-up cardiovascular MRI before 6 months because urgent AICD implantation was scheduled for malignant arrhythmia, and 2 did not have follow-up cardiovascular MRI because of new MI during the follow-up period potentially altering the evolution of LVEF (adjudicated as adverse events). Median time separating coronary angiog-
raphy from initial CE-CMR was 4.5 h (interquartile range: 2.6 to 7.0 h). Significant LV dysfunction was present in 51% during STEMI and 30% at 6 months. Severe LV dysfunction (LVEF <35%) was present in 10% during STEMI and in 4% at 6 months. Demographic data and coronary artery disease risk factors did not differ between those who later developed LV dysfunction and those who did not, whereas STEMI characteristics significantly differed by greater pain-to-balloon time, presence of Q waves on ECG at STEMI presentation, and maximum CK-MB elevation in those who later developed LV failure (Table 1). Three percent of patients had treatment of STEMI with thrombus aspiration only, whereas all other patients underwent stenting (p = 0.8 between groups). All patients had Thrombolysis In Myocardial Infarction flow grade 3 in the infarct-related artery after angiography and no significant residual diameter stenosis (diameter stenosis 10.3%, 95% CI: 5.5 to 15.0%, p = 0.3 between groups). The use of medications shown to improve LV recovery and prognosis was very high with no difference between groups, whereas other potential causes of heart failure—including atrial fibrillation and significant heart valve disease—were very low and did not differ between groups (Table 1).

The study population presented a broad range of LV volumes and function during STEMI, which remodeled variably at 6 months (Table 2, Online Fig. 1). However, despite an average absolute increase in LVEF of 5.8 ± 14.1% (p < 0.00001), the changes in LVEF/individual
patient varied widely between a maximum relative decrease of 83% at one extreme and a maximum relative increase of 44% at the other extreme (Fig. 1). In total, 28% of the cohort incurred LVEF deterioration during infarct healing; 33% of the 52 patients without significant LV dysfunction at the time of STEMI (acutely compensated LVEF) developed systolic heart failure at 6 months (p < 0.001 for category change from normal to abnormal). In addition, of the 30 patients with systolic dysfunction at 6 months, 7 (23%) were acutely compensated (preserved LVEF) at the time of STEMI.

Three additional major infarct characteristics were assessed, namely percentage of transmural LGE segments, MVO percentage, and SM percentage. An increase in percentage of transmural LGE segments was significantly associated with a greater risk of late LVEF <50% in univariable analysis (OR: 1.93; 95% CI: 1.42 to 2.62, p < 0.00001). To a larger degree, an increase in MVO percentage was also associated with a significantly greater risk of late global LV dysfunction (OR: 11.0; 95% CI: 3.68 to 32.9, p < 0.00001). In addition, an increase in SM percentage was significantly associated with a decreased risk for late LVEF <50% (OR: 0.95; 95% CI: 0.87 to 0.99, p = 0.02).

Although each of these cardiovascular MRI-derived parameters has been investigated in different clinical contexts, we sought to determine which (among LGE percentage, percentage of transmural segments, MVO percentage, or SM percentage) measured early during STEMI best predicted global LVEF change over 6 months. Although univariable analysis indicated significant associations for all 4 parameters with change in LVEF, only LGE percentage maintained significant associations with LVEF change in multivariate analysis (coefficient: -0.94; 95% CI: -1.81 to -0.14, p = 0.02).

In the next step, we compared cardiovascular MRI variables with traditional predictors. Our first regression analysis tested for associations with percent change in LVEF from STEMI to 6 months. A first model built from stepwise forward selection and a second model—built with left anterior descending (LAD) artery infarct, presence of Q waves at presentation, LVEF during STEMI, maximum CK-MB rise, pain-to-balloon time, MVO, and SM—consistently identified LGE percentage (coefficient −1.27; 95% CI: −1.82 to −0.70, p < 0.0001, from the second model) and LVEF (coefficient −1.21; 95% CI: −1.61 to −0.89, p < 0.0001, second model) as the only variables present during STEMI that maintained significant independent associations to percentage change in LVEF from STEMI to 6 months.

Afterward, we performed logistic regression to determine associations with LVEF <50% at 6 months. After unadjusted analysis (Table 3), we developed 2 multivariable logistic regression models to determine which variables from hyperacute STEMI best predicted LVEF <50% at 6 months (Table 4). In the first stepwise multivariable approach built from the variables identified as significant in univariable analysis, LGE percentage was the only variable selected in forming the best overall model for LV dysfunction at 6 months. In the second multivariable approach,
LGE percentage in the hyperacute phase of STEMI maintained a significant association with 6-month LV dysfunction, independent of LVEF during STEMI and CK-MB rise.

The occurrence of LV dysfunction at 6 months invariably increased with greater LGE. The ROC analysis determined that a cutoff of ≥23% LGE measured at the time of STEMI predicted 6-month LV dysfunction with a sensitivity of 89%, specificity of 74%, positive likelihood ratio of 3.6, and negative likelihood ratio of 0.1. This cutoff was selected to screen for patients at risk for developing LV dysfunction late after STEMI, correctly classifying 80% of the population. The 23% LGE cutoff seemed useful in dichotomizing 2 groups with widely diverging recoveries in LVEF from baseline to 6 months, across the entire range of LVEF quartiles during STEMI (Fig. 2).

We verified whether LGE percentage during STEMI improved the prediction of late LV dysfunction beyond current risk factors. The ROC analysis indicated that LGE percentage measured during STEMI significantly improved the diagnostic accuracy for 6-month LV dysfunction (AUC: 0.92; 95% CI: 0.84 to 0.98) beyond pain-to-balloon time (AUC: 0.71; 95% CI: 0.60 to 0.82, p < 0.001 compared with LGE percentage), CK-MB rise (AUC: 0.79; 95% CI: 0.69 to 0.89, p = 0.01), and LVEF during STEMI (AUC: 0.84; 95% CI: 0.76 to 0.93, p = 0.03) (Fig. 3). The diagnostic accuracy of LGE percentage for predicting late LV dysfunction did not differ, whether the infarct territory

### Table 3

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yrs</td>
<td>1.00</td>
<td>0.96–1.04</td>
<td>1.00</td>
</tr>
<tr>
<td>Male</td>
<td>2.40</td>
<td>0.43–10.1</td>
<td>0.30</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.02</td>
<td>0.38–2.83</td>
<td>0.90</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>0.44</td>
<td>0.17–1.11</td>
<td>0.10</td>
</tr>
<tr>
<td>Active/recent smoking</td>
<td>0.71</td>
<td>0.29–1.74</td>
<td>0.80</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.13</td>
<td>0.21–6.23</td>
<td>0.90</td>
</tr>
<tr>
<td>LDL-cholesterol on STEMI presentation, mmol/l</td>
<td>1.80</td>
<td>0.93–3.48</td>
<td>0.08</td>
</tr>
<tr>
<td>Blood glucose on STEMI presentation, mmol/l</td>
<td>1.04</td>
<td>0.89–1.21</td>
<td>0.70</td>
</tr>
<tr>
<td>ECG Q waves on STEMI presentation</td>
<td>6.80</td>
<td>2.16–21.5</td>
<td>0.001</td>
</tr>
<tr>
<td>ECG total ST-segment elevation on STEMI, mm</td>
<td>1.06</td>
<td>0.97–1.16</td>
<td>0.20</td>
</tr>
<tr>
<td>LAD infarct territory</td>
<td>1.92</td>
<td>0.77–4.76</td>
<td>0.20</td>
</tr>
<tr>
<td>Pain-to-balloon time, min</td>
<td>1.10</td>
<td>1.03–1.17</td>
<td>0.005</td>
</tr>
<tr>
<td>Target vessel residual diameter stenosis*</td>
<td>1.01</td>
<td>0.99–1.03</td>
<td>0.40</td>
</tr>
<tr>
<td>Maximum CK-MB rise during STEMI, mmol/l</td>
<td>1.47</td>
<td>1.24–1.75</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td>LVEDV, during STEMI, ml/m²</td>
<td>1.10</td>
<td>1.05–1.15</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td>LVESV, during STEMI, ml/m²</td>
<td>1.16</td>
<td>1.08–1.23</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td>LVEF during STEMI*</td>
<td>0.87</td>
<td>0.82–0.93</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td>LV mass, g/m²</td>
<td>1.11</td>
<td>1.05–1.18</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td>LGE volume during STEMI, % LV</td>
<td>17.00</td>
<td>8.47–34.1</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td>Transmural LGE segments during STEMI*</td>
<td>1.93</td>
<td>1.42–2.62</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td>Microvascular obstruction during STEMI*</td>
<td>11.00</td>
<td>3.68–32.9</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td>Salvaged myocardium during STEMI*</td>
<td>0.95</td>
<td>0.87–0.99</td>
<td>0.02</td>
</tr>
</tbody>
</table>

n = 101. p value for univariable logistic regression. *Values given as percentages.

BSA = body surface area; CI = confidence interval; LDL = low-density lipoprotein; OR = odds ratio; other abbreviations as in Tables 1 and 2.

### Table 4

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Best overall multivariable model by stepwise forward selection including all significant variables from Table 3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presence of ECG Q waves at presentation</td>
<td>6.27</td>
<td>0.81–74.9</td>
<td>0.08</td>
</tr>
<tr>
<td>LGE during STEMI*</td>
<td>1.33</td>
<td>1.09–1.78</td>
<td>0.002</td>
</tr>
<tr>
<td>Pain-to-balloon time, min</td>
<td>1.15</td>
<td>1.01–1.32</td>
<td>0.09</td>
</tr>
</tbody>
</table>

Adjusted for LVEF during STEMI, LGE %, and CK-MB

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEF during STEMI*</td>
<td>0.95</td>
<td>0.88–1.03</td>
<td>0.20</td>
</tr>
<tr>
<td>LGE during STEMI*</td>
<td>1.36</td>
<td>1.11–1.66</td>
<td>0.004</td>
</tr>
<tr>
<td>Maximum CK-MB rise after STEMI, mmol/l</td>
<td>1.00</td>
<td>0.99–1.01</td>
<td>0.40</td>
</tr>
</tbody>
</table>

*Values given as percentages.

Abbreviations as in Tables 1 and 3.
The LGE ≥23% during STEMI identifies a subgroup of patients with significantly worse functional recovery compared with those with less LGE, across the entire range of LVEF quartiles during STEMI. Abbreviations as in Figure 1.

There is significant added value of LGE percentage during STEMI (per 1%, area under the receiver-operator characteristic curve [AUC]: 0.92) compared with traditional measures including LVEF during STEMI (per 1%, AUC 0.84, p = 0.03 vs. LGE), maximum creatine kinase-myocardial band (CKMB) (per 1 mmol/kg, AUC 0.79, p = 0.01 vs. LGE), and pain-to-balloon time (per 1 min, AUC 0.71, p = 0.001 vs. LGE) for the prediction of LV dysfunction at 6 months. Abbreviations as in Figure 1.
was LAD or not (AUC: 0.95 for LAD infarct vs. 0.89 for non-LAD infarct, \( p = 0.3 \)) and whether Q waves were present or not at STEMI presentation (AUC 0.93 for Q waves present vs. 0.88 for Q waves absent, \( p = 0.3 \)).

We additionally explored clinical outcomes: over 2.3 ± 0.4 year follow-up, MACE occurred in 23 (22%) subjects (1 death, 2 MIs, 5 malignant arrhythmias requiring AICD, 4 severe LV dysfunction <35%, 11 hospital stays for heart failure). The previously defined cutoff of LGE ≥23% measured during hyperacute STEMI incurred a significant risk of adverse events by univariable Cox proportional hazards regression (hazard ratio: 10.1; 95% CI: 3.7 to 27.3, \( p < 0.0001 \)) (Fig. 4). In addition, LGE percentage remained independently associated with MACE in multivariable Cox regression that included CK-MB rise and LVEF during STEMI (hazard ratio: 1.72; 95% CI: 1.43 to 2.01, \( p = 0.007 \)).

Discussion

The major finding of this study is that LGE quantification very early during STEMI predicts late heart failure and adverse events beyond traditional risk factors such as infarct territory, maximum CK-MB rise, pain-to-balloon time, presence of Q waves, and LVEF during STEMI. A second major finding is that, during the hyperacute phase of STEMI, LGE volume incurred the strongest association to LV function change, beyond infarct transmurality, MVO, and SM. Significant variability in preload and afterload conditions and difficulty in discriminating stunned from nonviable myocardium at the time of STEMI have rendered most early variables imperfect predictors of late systolic function and adverse events. However, strategies for the earliest possible risk assessment after STEMI have become essential not only to better target therapies but also to introduce these therapies in the timeliest manner while benefits might be greatest. We have demonstrated that, during STEMI, LGE percentage is the strongest predictor of late heart failure and adverse events, opening the door to improved strategies for very early risk stratification.

**LVEF measurement after STEMI.** Considerable effort has gone toward earlier risk stratification and faster implementation of prognosis-altering interventions in high-risk STEMI (5,26). Treatment strategies based on residual LVEF after STEMI have shown important survival benefits (2–4,27). However, LVEF measured very early after MI is an imperfect predictor of later LVEF recovery: normal global EF at the time of STEMI might beget low EF in later months—as observed in this study and others—likely as a result of the gradual disappearance of the compensatory increased contractility of healthy segments and remodeling (6,26). In addition, low EF at the time of STEMI might beget normal EF after infarct healing, as systolic dysfunction observed early after STEMI might be due to a combination of reversible myocardial stunning and irreversible necrosis (28,29). The failure of recent treatment strategies such as AICD implantation based on assessment of LVEF very early after STEMI, contrary to the success observed when LVEF was measured >40 days after MI, might be due to the observed variability in LV remodeling during early infarct healing (3,30).

**Predictors of residual systolic function after infarct healing and remodeling.** Systolic function after STEMI varies as a function of the infarct territory (31), the sum of ST-segment elevation on ECG (32,33), microvascular dysfunction (34,35), time to reperfusion (36), and time to peak CK (37). Although LVEF at the time of STEMI has been correlated to late systolic function in early studies (34), this has since been called into question by more accurate radionuclide (38) and volumetric techniques (9). In fact, LV remodeling is a particularly heterogeneous process, difficult

![Figure 4](image-url)
to predict and theoretically dependent on infarct size and territory, stunning, and the success of reperfusion including presence of collateral circulation and reversal of coronary thrombosis (39). In addition, global LVEF also relies on compensatory alterations of the remote territories that depend on circulation in the non–infarct–related coronary arteries and changes in local wall stress related to remodeling (40). A comprehensive assessment of LV remodeling predicting residual LVEF after infarct healing requires the consideration of all these variables. Our study demonstrates that, during this hyperacute period of STEMI, the predictive value of LVEF might be significantly improved by LGE measurement.

LGE during and after STEMI. The evolution of LV function over the first months after MI has been described with volumetric techniques (9,41–44). In a study of 20 subjects imaged within 1 week of acute MI and at 2 months, Ingkanisorn et al. (9) described an average 5% increase in LVEF and a 34% decrease in LGE. In another study examining 22 patients after primary PCI for STEMI, Baks et al. (45) described a 31% decrease in LGE between 5 days and 5 months after MI. These studies were not powered to examine multivariate predictors of LVEF after infarct healing. In addition, because of the measured decreases in LGE, concern was raised that early assessment of LGE might not be reliable. Although it has been suggested that LGE in the acute phase of STEMI might overestimate true infarct size either because of peri–infarct edema or partial volume effects (9,46), animal studies report that LGE during STEMI represents real myocardial tissue alterations (47), and therefore the observed decrease likely represents scar involution (48). Our study importantly adds that LGE during the hyperacute phase of STEMI holds a strong independent association with late heart failure and adverse events and therefore is likely biologically significant and not a simple overestimation.

Potential mechanisms underlying the predictive value of LGE during STEMI. Prior studies have reported associations between LGE measured within 1 week of MI and LVEF at 3 to 12 months; however, they could not take into account other risk factors or explore clinical outcomes. Wu et al. (49) have recently concluded that early LGE was a stronger predictor of clinical events than LVEF or LV end-systolic volume but did not take into account other infarct characteristics such as area at risk or salvaged myocardium. In addition, this study was performed outside the “hyperacute window” of STEMI, because patients were evaluated within 1 week, compared with within 12 h (median 4.5 h) in the present study. Although it seems likely that very early assessment might further improve patient care by allowing earlier risk stratification and more rapid initiation of tailored therapies, this remains to be demonstrated. Our study is the first step toward the evaluation of this strategy. We conclude in the STEMI population that infarct size measured by LGE carries a stronger association with heart failure and poor outcomes than traditional risk factors or other infarct characteristics.

Study limitations. We aimed to study the widest possible range of STEMI cases. Nevertheless, those requiring balloon counterpulsation or mechanical ventilation were excluded, because of logistical concerns and/or contraindications to cardiovascular MRI. In our current practice setting, however, mechanical ventilation or balloon counterpulsation are required in <3% of STEMI subjects. Although it might be argued that our population does not seem to carry severe disease, we present a faithful snapshot of contemporary STEMI with a representative rate of adverse events (Online Fig. 1). In addition, the definition of transmural necrosis we used was dichotomous (yes/no) on the basis of semiautomatic measurements of necrosis “thickness” along 20 to 30 chords/segment; although this provides objective measurements, it might differ from reports that define transmurality visually by 25% increments. Finally, given the relatively limited sample size, and despite a parsimonious statistical approach, it remains possible that our findings might be at least in part explained by some overfitting of regression models. Of the 2 logistic regression models developed to determine associations with LVEF <50%, the first model used stepwise forward selection including all significant variables from univariable analysis, therefore rendering it susceptible to overfitting and possibly yielding an overly optimistic model; however, the second model was adjusted only for LVEF during STEMI, LGE percentage, and CK-MB, therefore satisfying the prerequisites to avoid overfitting. Despite these potential limitations, our study is the largest to date investigating CE-CMR characteristics very early during STEMI, and seeking to clarify the added value of CE-CMR compared with traditional strategies by multivariate regression and ROC analysis. Our conclusions provide statistically sound and important data contributing to improved risk stratification early during STEMI.

Conclusions

This study demonstrates that, very early during STEMI, LGE volume is an accurate predictor of heart failure and adverse events, providing important incremental value beyond traditional risk factors, MVO, and myocardial salvage. Risk stratification based on CE-CMR infarct imaging very early during STEMI, and seeking to clarify the added value of CE-CMR compared with traditional strategies by multivariate regression and ROC analysis. Our conclusions provide statistically sound and important data contributing to improved risk stratification early during STEMI.

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**APPENDIX**

For a supplementary figure, please see the online version of this article.