Myocardial Infarction

Relationship of Myocardial Strain and Markers of Myocardial Injury to Predict Segmental Recovery After Acute ST-Segment–Elevation Myocardial Infarction

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Background—Late gadolinium-enhanced cardiovascular magnetic resonance imaging overestimates infarct size and underestimates recovery of dysfunctional segments acutely post ST-segment–elevation myocardial infarction. We assessed whether cardiovascular magnetic resonance imaging–derived segmental myocardial strain and markers of myocardial injury could improve the accuracy of late gadolinium-enhancement in predicting functional recovery after ST-segment–elevation myocardial infarction.

Methods and Results—A total of 164 ST-segment–elevation myocardial infarction patients underwent acute (median 3 days) and follow-up (median 9.4 months) cardiovascular magnetic resonance imaging. Wall-motion scoring, feature tracking–derived circumferential strain (Ecc), segmental area of late gadolinium-enhancement (SEE), microvascular obstruction, intramyocardial hemorrhage, and salvage index (MSI) were assessed in 2624 segments. We used logistic regression analysis to identify markers that predict segmental recovery. At acute CMR 32% of segments were dysfunctional, and at follow-up CMR 19% were dysfunctional. Segmental function at acute imaging and odds ratio (OR) for functional recovery decreased with increasing SEE, although 33% of dysfunctional segments with SEE 76% to 100% improved. SEE was a strong predictor of functional improvement and normalization (area under the curve [AUC], 0.840 [95% confidence interval {CI}, 0.814–0.867]; OR, 0.97 [95% CI, 0.97–0.98] per +1% SEE for improvement and AUC, 0.887 [95% CI, 0.865–0.909]; OR, 0.95 [95% CI, 0.94–0.96] per +1% SEE for normalization). Its predictive accuracy for improvement, as assessed by areas under the receiver operator curves, was similar to that of MSI (AUC, 0.840 [95% CI, 0.809–0.872]; OR, 1.03 [95% CI, 1.02–1.03] per +1% MSI for improvement and AUC, 0.862 [0.832–0.891]; OR, 1.04 [95% CI, 1.03–1.04] per +1% SEE for normalization) and Ecc (AUC, 0.834 [95% CI, 0.807–0.862]; OR, 1.05 [95% CI, 1.03–1.07] per +1% MSI for improvement and AUC, 0.844 [95% CI, 0.818–0.871]; OR, 1.07 [95% CI, 1.05–1.10] per +1%SEE for normalization), and for normalization was greater than the other predictors. MSI and Ecc remained as significant after adjustment for SEE but provided no significant increase in predictive accuracy for improvement and normalization compared with SEE alone. MSI had similar predictive accuracy to SEE for functional recovery but was not assessable in 25% of patients. Microvascular obstruction provided no incremental predictive accuracy above SEE.

Conclusions—This multicenter study confirms that SEE is a strong predictor of functional improvement post ST-segment–elevation myocardial infarction, but occurs in a substantial proportion of dysfunctional segments with SEE >75%. Feature tracking–derived Ecc and MSI provide minimal incremental benefit to SEE in predicting segmental recovery.

Clinical Trial Registration—URL: http://www.isrctn.com. Unique identifier: ISRCTN70913605.

Key Words: late gadolinium enhancement ■ magnetic resonance imaging ■ myocardial infarction ■ myocardial viability ■ strain

Improvement in dysfunctional myocardium after acute ST-segment–elevation myocardial infarction (STMI) predicts long-term myocardial function and prognosis.1,2 Kim et al3 and Choi et al4 first demonstrated an inverse correlation between cardiovascular magnetic resonance imaging (MRI)–measured segmental late gadolinium enhancement (LGE) transmurality and functional recovery in hibernating myocardial viability.
and stunned myocardium, allowing the prediction of functional recovery without inotropic challenge.\(^1\)\(^2\) However, the evidence base in acute STEMI is limited by a small number of single-center studies and heterogeneity of LGE assessment.\(^3\)\(^–\)\(^5\) Moreover, several reports have shown that LGE, measured within days of STEMI, overestimates acute infarct size (IS) and underestimates the potential for functional recovery.\(^6\)\(^–\)\(^8\) The accuracy of segmental LGE expressed as segmental area of late gadolinium-enhancement (SEE) defined as enhanced percentage of segmental area,\(^9\)\(^–\)\(^12\) better than maximum transmurality in predicting segmental recovery in acute STEMI has shown promise.

Several other CMR markers of myocardial injury have been associated with functional recovery after STEMI. Circumferential strain (Ecc),\(^1\) myocardial salvage (MSI),\(^1\)\(^7\) LGE-derived microvascular obstruction (late MVO),\(^1\)\(^1\)\(^7\)\(^–\)\(^18\) and intramyocardial hemorrhage (IMH)\(^1\)\(^9\)\(^–\)\(^20\) have been assessed in a few small studies. There are no studies investigating whether they offer additive value to the predictive accuracy of LGE. Feature tracking (FT) is a novel postprocessing software for the quantification of myocardial strain from steady state free-precession cine images\(^16\)\(^–\)\(^20\) We have recently demonstrated greater robustness, reproducibility, and infarct correlation with FT-derived strain compared with tagging in acute STEMI.\(^2\)\(^1\)

We aimed to assess whether FT-derived Ecc, MSI, late MVO, and IMH predicted segmental functional recovery in acute STEMI and whether this was of additive value to SEE.

**Methods**

**Study Population**

Two hundred and three STEMI patients with multivessel coronary disease were recruited into the CMR substudy of a multicenter, prospective, randomized controlled study assessing infarct-related artery only versus complete revascularization.\(^2\)\(^2\) STEMI was diagnosed according to European Society of Cardiology definitions and patients underwent primary percutaneous coronary intervention (PPCI) within 12 hours of symptoms. The study was approved by the National Research Ethics Service and was conducted according to the Declaration of Helsinki, and patients provided written informed consent.

**Cardiovascular MRI**

CMR was performed in 5 of the 7 centers, at a median of 2.9 days post PPCI (acute CMR) and repeated at 9.4 months (follow-up CMR) on 1.5T platforms (4 Siemens Avanto, Erlangen, Germany and 1 Philips Intera; Best, Netherlands) with dedicated cardiac receiver coils. Follow-up CMR (median, 9 months) was completed in 164 patients who comprised the final study cohort. The acute CMR was performed as previously described with the addition of T2-weighted short-tau inversion recovery (T2w-STIR) covering the entire left ventricle (LV).\(^2\)\(^3\) The imaging protocol is detailed in Figure 1.

**MRI Analysis**

**Image Quality**

Image quality was graded on a 4-point Likert scale: 3=excellent, 2=good, 1=moderate, and 0=unanalyzable.

**Volumetric and Functional Analysis**

Analysis was performed using cvi42 v4.1 (Circle Cardiovascular Imaging, Calgary, Canada). LV volumes were calculated as previously described.\(^2\)\(^2\) Wall motion in the 16 American Heart Association myocardial segments was visually graded as: 1=normokinetic, 2=hy-pokinetic, 3=akinetically, 4=dyskinetic, and 5=aneurysmal.\(^2\) Segmental dysfunction was defined as wall motion score (WMS) of ≥2 at acute CMR and improvement as a decrease of ≥1, and normalization where WMS returned to 1 at follow-up CMR.\(^9\)\(^–\)\(^12\)\(^\)\(^0\)

**Infarct Characterization**

Edema (area-at-risk [AAR]) and infarct were quantified using cvi42 v4.1 on T2w-STIR and LGE imaging, using Otsu’s Automated Method and full-width half-maximum thresholding, respectively, as previously described by our group.\(^2\) Hypointense regions within enhancement on LGE and T2w-STIR imaging were included, corresponding to MVO and IMH, respectively, and expressed as present or absent for each of the 16 segments. SEE was calculated as percentage enhanced area for each myocardial segment (SEE=100\(\times\)segmental enhanced area/segmental area).\(^1\)SEE was additionally classified into 5 categories: SEE 0%, SEE 1% to 25%, SEE 26% to 50%, SEE 51% to 75%, and SEE 76% to 100% as previously described.\(^1\)\(^2\)\(^1\)\(^1\) Segmental MSI defined the proportion of the AAR that did not progress to infarction and was calculated as \((\text{segmental AAR–SEE})/\text{segmental AAR})\times 100.\(^\)\(^\

**Circumferential Strain Analysis**

Segmental peak endocardial Ecc was measured with FT using Diogenes Image Arena (Tomtec, Munich, Germany). Endocardial contours were manually drawn onto the end-diastolic image and propagated. The FT algorithm has been described previously.\(^2\)\(^1\) Suboptimally tracking segments were manually adjusted if the movement of contoured borders deviated from true myocardial motion by ≥50%.

**Statistical Analysis**

Normality was assessed using Kolmogorov–Smirnoff tests, histograms, and Q–Q plots. Normally distributed data were expressed as mean±SD, and comparisons between groups were conducted with ANOVA. Nonparametric data were expressed as median (25%–75% interquartile range), and compared with Kruskal–Wallis testing. Spearman rank correlation coefficient assessed the correlation between the predictors and the segmental function. We assessed whether (1) SEE, Ecc, MVO, MSI, presence/absence, and IMH (presence/absence) predicted improvement and normalization of dysfunctional myocardial segments at follow-up CMR using logistic regression analysis and (2) Ecc, MVO, MSI, and IMH provided incremental improvement in predictive accuracy above SEE alone. We developed logistic regression models with random effect to account for dependence of segments from the same patient. The likely clinical benefit for differences in predictive accuracy of SEE alone compared with SEE plus each of Ecc, MSI, MVO, and IMH was assessed using receiver operating characteristic curve analysis with the area under the curves (AUCs) compared using the method of Delong.\(^2\)\(^6\) On AUC, predictive accuracy of ≥0.9 was considered excellent, 0.8 to 0.9 very good, 0.7 to 0.8 good, 0.6 to 0.7 average, and <0.6 poor.\(^2\)\(^7\) The optimal cutoff values of SEE, segmental Ecc, and MSI for predicting functional recovery were identified by receiver operating characteristic curve analysis where sensitivity and specificity intersected. Intra- and interobserver agreement were assessed with intraclass correlation coefficient for absolute agreement\(^2\)\(^8\) and k statistic on a random selection of 10 patients. Intraobserver (J.N.K.) and interobserver agreement (J.N.K., S.A.N.) are reported in the Data Supplement. Statistical tests were performed using SPSS version 20 (IBM, New York, NY) and PROC GLIMMIX in SAS version 9.4 (Statistical Analysis Systems, NC). P<0.05 was considered significant.

**Results**

**Baseline Characteristics**

Demographic and CMR data are summarized in Table 1. Of the 203 enrolled patients, 164 underwent both acute and
follow-up CMR and hence comprised the study group. Reasons for patients not returning for follow-up CMR are shown in Figure 2. Image quality was diagnostic in all cine and LGE segments (n=2624), which were analyzable for WMS, SEE, Ecc, and MVO. Twenty-three percent of T2w-STIR segments (MSI, IMH) were nonanalyzable because of poor image quality or not being acquired because of significant breath holding and ECG gating difficulties. Thus 2020 segments were included in the assessment of CMR predictors of segmental recovery.

### Segmental Systolic Function Post STEMI

**Wall Motion Scoring at Acute and Follow-Up CMR**

On WMS, at acute CMR, 837 (31.9%) segments had contractile dysfunction (WMS 2: 499/2624 [19.0%]; WMS 3: 338/2624 [12.9%]). At 9-month follow-up CMR, 521 (62.2%) dysfunctional segments had improved, of which 372 (44.4%) had normalized and 495 (18.8%) remained dysfunctional (WMS 2: 350/2624 [13.3%]; WMS 3: 137/2624 [5.2%]; and WMS 4: 8/2624 [0.3%]).

**Segmental Function According to Segmental Extent of LGE and Strain**

Acutely, with worsening function on WMS, SEE, Ecc and presence of MVO and IMH increased, and segmental MSI decreased (Table 2). With increasing SEE, segmental function worsened (Figure 3). More than 98% of SEE 76% to 100% segments were dysfunctional at acute CMR. WMS correlated more strongly with SEE at acute (r=0.69; P<0.01) and follow-up CMR (r=0.62; P<0.01) than with MSI (acute, r=-0.523, P<0.01; follow-up: r=-0.514; P<0.01) and Ecc (acute: r=0.49; P<0.01; follow-up: r=0.49; P<0.01). At follow-up CMR, segmental function improved in each SEE grade (Figure 4). The proportion of dysfunctional segments improving or normalizing decreased with increasing SEE, with 90% of SEE 0% segments normalizing. Despite this, 33% of SEE 75% to 100% segments improved; however, only 5% normalized (Figure 4). The proportion of dysfunctional segments improving or normalizing increased with increasing MSI. Despite this, 43% of MSI 0% to 25% segments improved, but only 21% normalized (Figure 5).

### Predictors of Segmental Recovery in Dysfunctional Segments Post STEMI

**Predictors of Segmental Functional Improvement**

Individual Predictors: Results are shown in Table 3. SEE (P<0.001), MSI (P<0.001), Ecc (P<0.001), and the presence of MVO (P=0.021) and IMH (P=0.004) predicted functional improvement. SEE was a strong predictor of functional improvement (AUC, 0.840) with optimal cutoff being <34% (sensitivity=specificity=62%). Segmental MSI (AUC, 0.840; P=0.139), Ecc (AUC, 0.834; P=0.613), and MVO (AUC, 0.826; P=0.164) showed similar predictive value as SEE, but IMH (AUC, 0.818; P=0.041) did not. Revascularization strategy did not predict segmental improvement (P=0.206).

Predictors Combined With SEE: When SEE and Ecc were entered into the model together for functional improvement, both remained as significant predictors (P<0.001 SEE and P=0.027 Ecc), but the predictive value for functional improvement was similar for SEE+Ecc and SEE (AUC, 0.841 and 0.840; P=0.738). Similarly, MSI remained a significant predictor (P=0.031) after adjustment for SEE; however, the addition of MSI did not improve the predictive value compared with SEE alone (P=0.344). MVO (P=0.069) and IMH (P=0.756) did not predict segmental improvement when added to SEE.

**Predictors of Segmental Functional Normalization**

Individual Predictors: SEE (P<0.001), MSI (P<0.001), Ecc (P<0.001), and the presence of MVO (P<0.001) and IMH (P=0.001) predicted functional normalization (Table 3). SEE was a strong predictor of functional normalization (AUC 0.887) with optimal predictive cutoff being <29% (sensitivity=specificity=72%). The predictive value of SEE...
Table 1. Baseline Demographics and CMR Characteristics

<table>
<thead>
<tr>
<th>Baseline and Angiographic Characteristics</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients (n)</td>
<td>164</td>
</tr>
<tr>
<td>Age, y</td>
<td>63.0±9.5</td>
</tr>
<tr>
<td>Sex (male, %)</td>
<td>140 (85.4)</td>
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<tr>
<td>Diabetes mellitus, n (%)</td>
<td>24 (14.6)</td>
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<tr>
<td>Hypertension, n (%)</td>
<td>60 (36.6)</td>
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<tr>
<td>Symptom to PPCI time (min)</td>
<td>172 (128–280)</td>
</tr>
<tr>
<td>Left anterior descending artery culprit vessel, n (%)</td>
<td>50 (36.6)</td>
</tr>
<tr>
<td>Infarct-related artery only PCI, n (%)</td>
<td>80 (48.8)</td>
</tr>
<tr>
<td>Multivessel PCI, n (%)</td>
<td>84 (51.2)</td>
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</table>

CMR Characteristics

<table>
<thead>
<tr>
<th>Cine segments of diagnostic image quality (%) at acute CMR</th>
<th>100</th>
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<tbody>
<tr>
<td>LGE segments of diagnostic image quality (%) at acute CMR</td>
<td>100</td>
</tr>
<tr>
<td>T2w-STIR segments of diagnostic image quality (%) at acute CMR</td>
<td>76.8</td>
</tr>
<tr>
<td>Cine segments of diagnostic image quality (%) at follow-up CMR</td>
<td>100</td>
</tr>
<tr>
<td>Acute CMR time (d post STEMI)</td>
<td>2.9 (2.0–3.9)</td>
</tr>
<tr>
<td>Follow-up CMR time (mo post STEMI)</td>
<td>9.4 (8.9–10.0)</td>
</tr>
<tr>
<td>LV end-diastolic mass, g/m²</td>
<td>52.3 (45.9–61.0)</td>
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<tr>
<td>LV end-diastolic volume, mL/m²</td>
<td>89.5 (80.6–101.5)</td>
</tr>
<tr>
<td>LV end-systolic volume, mL/m²</td>
<td>47.5 (39.0–58.5)</td>
</tr>
<tr>
<td>LV ejection fraction, %</td>
<td>46.1±9.2</td>
</tr>
<tr>
<td>Infarct size (% LV mass)</td>
<td>12.7 (6.9–21.5)</td>
</tr>
<tr>
<td>Myocardial salvage index, %</td>
<td>58.7 (35.3–76.7)</td>
</tr>
</tbody>
</table>

Segmental Characteristics

<table>
<thead>
<tr>
<th>Dysfunctional segments at acute CMR, n (%)</th>
<th>837/2624 (31.9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dysfunctional segments at follow-up CMR, n (%)</td>
<td>495/2624 (18.9)</td>
</tr>
<tr>
<td>Segments with LGE at acute CMR, n (%)</td>
<td>1186/2624 (45.2)</td>
</tr>
<tr>
<td>Segments with LGE at follow-up CMR, n (%)</td>
<td>1009/2624 (38.5)</td>
</tr>
<tr>
<td>Segments with MVO at acute CMR, n (%)</td>
<td>165/2624 (6.3%)</td>
</tr>
<tr>
<td>Segments with IMH at acute CMR, n (%)</td>
<td>51/2624 (2.5%)</td>
</tr>
</tbody>
</table>

CMR indicates cardiovascular magnetic resonance imaging; IMH, intramyocardial hemorrhage; LGE, late gadolinium enhancement; MVO, microvascular obstruction; PPCI, primary percutaneous coronary intervention; STEMI, ST-segment–elevation myocardial infarction; T2w-STIR, T2-weighted short-tau inversion recovery.

Discussion

This is the largest study assessing CMR predictors of segmental functional recovery after acute STEMI treated with PPCI and the first to use multicenter data analyzed in a core laboratory. We have confirmed that early after STEMI, LGE overestimates IS despite using full-width half-maximum quantification, which gives lower values than 2 SD thresholding used by most previous studies. Functional improvement occurred in a significant proportion of near-transmurally enhanced segments although only 5% normalized. A key aim of conducting this study was to assess whether the accuracy of LGE to predict functional recovery after STEMI could be improved with the addition of other markers of myocardial injury. We have shown that baseline SEE is a strong predictor of recovery at 9 months. SEE was of similar predictive value to MSI, Ecc, and MVO for improvement, and a stronger predictor than MSI, Ecc, MVO, and IMH for normalization. In addition although Ecc and MSI remained as predictive after adjustment for SEE, they provided similar predictive values for recovery compared with SEE alone.

Prediction of Segmental Functional Recovery With LGE

Our observed inverse correlation between SEE and functional recovery is consistent with previous studies. The accuracy in predicting recovery was slightly lower than in the work of Kitagawa et al and Orii et al. LGE measured acutely overestimates necrosis by up to 30% in the first week post STEMI caused by myocardial edema. We undertook acute CMR at 3 days post PPCI to assess CMR in a real-world setting when patients are discharged and are less likely to undergo CMR at day 5 and 8 as in these 2 studies. Untreated multivessel disease with potential hibernating myocardium in noninfarct artery territories in our study, differences in LGE thresholding methods, and the smaller sample size of these studies may also have contributed to our slightly lower AUC. We used SEE because we felt that predictors did not significantly increase the predictive value for functional normalization (Ecc+SEE: AUC, 0.889; P=0.379 and MSI+SEE: AUC, 0.886; P=0.340). MVO (P=0.223) and IMH (P=0.221) did not predict segmental normalization when added to SEE.

SEE and Ecc as Predictors of Segmental Functional Recovery Where SEE≥50%

In dysfunctional segments with ≥50% SEE, SEE predicted improvement (P=0.002; AUC, 0.924) and normalization (P=0.002; AUC, 0.918; Data Supplement). MVO predicted functional normalization (P=0.002) and remained as significant after adjustment for SEE (P<0.009). Ecc, MSI, and IMH did not predict functional recovery and were not of additive value to SEE.

CMR Predictors of Segmental Functional Recovery Stratified by Revascularization Strategy

Full data are presented in the Data Supplement. The results for all analyses were similar in patients undergoing infarct related artery only (n=80) and complete revascularization (n=84) and were similar to those in the overall study cohort (n=164).

as measured by AUC was higher than that of segmental MSI (AUC, 0.862; P=0.007), Ecc (AUC, 0.844; P=0.001), MVO (AUC, 0.836; P<0.001), and IMH (AUC, 0.827; P<0.001). Revascularization strategy did not predict segmental normalization (P=0.463).

Predictors Combined With SEE: After adjustment for SEE, Ecc (P=0.001), and MSI (P=0.027) remained as significant predictors of functional normalization. However, compared with SEE alone (AUC, 0.887), the addition of these

Predictor combination that included both SEE and Ecc predicted functional normalization better than either alone (AUC, 0.924; P<0.009).

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it is a more accurate representation of segmental necrosis than transmurality of enhancement. Transmurality can overestimate segmental necrosis because a segment may be considered transmurally enhanced when only a small portion of segmental width demonstrates transmurality. Infarct extent based on transmurality has been compared with SEE in 1 study in hypertrophic cardiomyopathy and was 31% higher.\textsuperscript{29}

The recent study by Wong et al\textsuperscript{11} is the closest in design to our study. SEE and MVO were, however, stronger predictors of recovery in our study than their results (SEE: AUC, 0.840 versus 0.680; MVO: AUC, 0.836 versus 0.670). This may be because of their small study size (n=45), the fact that they only assessed LGE on 3 thin (6 mm) short-axis slices and hence provided incomplete LV coverage, and their later time point of acute CMR on day 8, by which time there may have been a degree of infarct and MVO resorption and functional recovery.

The optimal SEE cutoff for predicting recovery in our study of 34% is similar to that in the study by Becker et al,\textsuperscript{16} who also used SEE. It may be that if transmurality of enhancement overestimates necrosis relative to SEE, a smaller SEE cutoff predicts recovery. The commonly used arbitrary cutoff of 50% may need revising because it has been derived from historical work in chronic coronary artery disease\textsuperscript{3} where LGE is unlikely to overestimate necrosis.\textsuperscript{3} Importantly, SEE in our study was a strong predictor (AUC, 0.887) of functional normalization, which may be associated with long-term LV function and prognosis.\textsuperscript{1,2}

Late MVO and IMH were moderately strong predictors of segmental recovery. This is in keeping with the work of Kidambi et al\textsuperscript{18} who demonstrated that infarcts with MVO had no improvement in segmental function on midmyocardial and endocardial-strain in the infarct zone at 3 months, and that the

Figure 2. CONSORT diagram illustrating reasons for patients not returning for follow-up cardiovascular magnetic resonance imaging (CMR). RCT indicates randomized controlled trial; and STEMI, ST-segment-elevation myocardial infarction.

Figure 3. Wall-motion scoring (WMS) at acute and follow-up cardiovascular magnetic resonance imaging (CMR) by segmental extent of enhancement. SEE indicates segmental extent of enhancement.
presence of IMH further attenuated strain. Of note, MVO in our study was the only predictor of functional normalization in segments with SEE ≥50% in addition to SEE and provided incremental predictive benefit. This is likely to be a reflection of the more severe myocardial injury and adverse remodeling known to accompany MVO. Indeed, Kitagawa et al\textsuperscript{8} showed that segmental MVO extent <50% accurately identified recovering segments with SEE ≥50% enhancement. The lack of predictive accuracy of IMH in segments with SEE ≥50% in our study may be because of the relatively small number of segments with IMH and SEE ≥50% (n=41).

Our results have also shown that MSI performed equally and SEE to predict functional recovery. The moderate predictive accuracy of MSI is consistent with previous work highlighting

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Figure 4. Recovery in dysfunctional segments at follow-up cardiovascular magnetic resonance imaging (CMR) by segmental area of late gadolinium-enhancement (SEE).

Figure 5. Recovery in dysfunctional segments at follow-up cardiovascular magnetic resonance imaging (CMR) by segmental myocardial salvage index (MSI).
that MSI may underestimate functional recovery using segmental strain. The minimal incremental increase in predictive accuracy of MSI in addition to SEE is likely to result from the close relationship between SEE and MSI. Indeed, Spearman rank correlation coefficient for SEE and MSI was −0.89 \((P<0.001)\) in our study. Given that MSI significantly increases scanning time to acquire edema images, resulted in nonanalyzable images in 25% of patients and provided only minimal incremental value above SEE alone, there seems to be little merit in using MSI instead of or in addition to SEE. The close inter-relation between IS, MVO, and IMH is also likely to account for their lack of incremental predictive accuracy in our study.

**Prediction of Segmental Functional Recovery With Strain**

We recently compared FT and tagging strain assessment in acute STEMI and showed that FT-derived endocardial Ecc correlated strongest with infarct characteristics. This is likely to be a result of infarction firstly affecting the endocardium in the ischemic cascade. This is corroborated by the fact that Ecc was a strong predictor of segmental recovery in this study.

Our results are in keeping with those of Wong et al who showed an almost identical predictive accuracy (AUC, 0.823) to our study, of harmonic phase imaging-derived Ecc in identifying segmental recovery at 3 months. Unlike our study, they however demonstrated that Ecc was a significantly stronger predictor than SEE and MVO. This is likely to be because of methodological differences as discussed above. Our findings are similar to those of Orii et al who also showed a strong predictive accuracy of speckle-tracking echocardiographic Ecc for segmental functional recovery, and similar accuracy to SEE \((P=0.439)\). On a global level, our findings are supported by the recent work of Buss et al which showed that FT-derived global Ecc and LGE IS were moderately strong predictors of LV ejection fraction >50% at 6-month follow-up, and that Ecc was a non-inferior predictor compared with IS.

Our study is in contrast to the work of Neizel et al who used strain-encoded CMR–derived segmental Ecc and LGE SEE to predict severe, persistent dysfunction at 6 months defined as segmental Ecc <9%. Ecc was only a mildly strong predictor and was a significantly weaker predictor than SEE \((AUC, 0.74 versus 0.91)\). The weaker predictive accuracy of strain-encoded CMR Ecc compared with FT Ecc in their study may be because of the fact that Neizel divided the LV into 10 to 12, rather than 16 segments, thus potentially reducing the accuracy of strain assessment in basal and apical segments.

### Table 2. Segmental Extent of Myocardial Injury According to Degree of Dysfunction at Acute CMR

<table>
<thead>
<tr>
<th>WMS at Acute CMR</th>
<th>1. Normal (n=1787, 68%)</th>
<th>2. Hypokinetic (n=499, 19%)</th>
<th>3. Akinetic (n=338, 13%)</th>
<th>(P) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SEE, %</td>
<td>3.6±9.7</td>
<td>24.4±22.0</td>
<td>52.2±29.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Peak segmental Ecc, %</td>
<td>−23.5±10.2</td>
<td>−14.9±9.1</td>
<td>−9.6±7.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MSI, %</td>
<td>98.4 (71.2–100.0)</td>
<td>58.1 (25.7–83.2)</td>
<td>18.3 (0.0–52.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MVO, n (%)</td>
<td>7/1787 (0.4)</td>
<td>48/499 (9.6)</td>
<td>110/338 (32.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IMH, n (%)</td>
<td>1/713 (0.1)</td>
<td>12/241 (4.9)</td>
<td>41/198 (20.7)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

CMR indicates cardiovascular magnetic resonance imaging; Ecc, peak segmental circumferential strain; IMH, intramyocardial hemorrhage; MSI, myocardial salvage; and MVO, microvascular obstruction.

### Table 3. Segmental Extent of Myocardial Injury at Acute Cardiovascular Magnetic Resonance Imaging and Prediction of Functional Recovery at Follow-Up

<table>
<thead>
<tr>
<th>Predictor</th>
<th>AUC</th>
<th>95% CI</th>
<th>Optimal Cutoff</th>
<th>Odds Ratio ((P) Value)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Improvement</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SEE</td>
<td>0.840</td>
<td>0.814–0.867</td>
<td>&lt;34% (sens 62%, spec 62%)</td>
<td>0.97 per +1% SEE ((P&lt;0.001))</td>
<td>0.97–0.98</td>
</tr>
<tr>
<td>MSI</td>
<td>0.840</td>
<td>0.809–0.872</td>
<td>&gt;39% (sens 65%, spec 65%)</td>
<td>1.03 per +1% MSI ((P&lt;0.001))</td>
<td>1.02–1.03</td>
</tr>
<tr>
<td>Ecc</td>
<td>0.834</td>
<td>0.807–0.862</td>
<td>&lt;−11.4% (sens 59%, spec 59%)</td>
<td>1.05 per −1% Ecc ((P&lt;0.001))</td>
<td>1.03–1.07</td>
</tr>
<tr>
<td>MVO presence</td>
<td>0.826</td>
<td>0.798–0.853</td>
<td>NA</td>
<td>0.61 MVO present vs absent ((P=0.021))</td>
<td>0.40–0.93</td>
</tr>
<tr>
<td>IMH presence</td>
<td>0.818</td>
<td>0.779–0.857</td>
<td>NA</td>
<td>0.32 IMH present vs absent ((P=0.004))</td>
<td>0.15–0.67</td>
</tr>
<tr>
<td><strong>Normalization</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SEE</td>
<td>0.887</td>
<td>0.865–0.909</td>
<td>&lt;29% (sens 72%, spec 72%)</td>
<td>0.95 per +1% SEE ((P&lt;0.001))</td>
<td>0.94–0.96</td>
</tr>
<tr>
<td>MSI</td>
<td>0.862</td>
<td>0.832–0.891</td>
<td>&gt;48% (sens 71%, spec 71%)</td>
<td>1.04 per +1% MSI ((P&lt;0.001))</td>
<td>1.03–1.04</td>
</tr>
<tr>
<td>Ecc</td>
<td>0.844</td>
<td>0.818–0.871</td>
<td>&lt;−12.0% (sens 62%, spec 62%)</td>
<td>1.07 per −1% Ecc ((P&lt;0.001))</td>
<td>1.05–1.10</td>
</tr>
<tr>
<td>MVO presence</td>
<td>0.835</td>
<td>0.808–0.862</td>
<td>NA</td>
<td>0.19 MVO present vs absent ((P&lt;0.001))</td>
<td>0.12–0.31</td>
</tr>
<tr>
<td>IMH presence</td>
<td>0.827</td>
<td>0.789–0.865</td>
<td>NA</td>
<td>0.08 IMH present vs absent ((P&lt;0.001))</td>
<td>0.02–0.30</td>
</tr>
</tbody>
</table>

AUC indicates area under the curve; CI, confidence interval; Ecc, peak segmental circumferential strain; IMH, intramyocardial hemorrhage; MSI, myocardial salvage; and MVO, microvascular obstruction.
Indeed, no segments in their study had a strain value of zero, even those that were visually akinetic and contained MVO. In addition, strain-encoded CMR has a lower signal:noise ratio than steady state free-precession cine imaging. However, there are no data comparing strain-encoded CMR and FT strain assessment.

**Limitations**

Acute CMR was undertaken earlier than in some studies with potentially greater necrosis overestimation on LGE; however, this allows a closer representation of real-life practice where acute CMR would typically be undertaken predischARGE. All of our subjects had multivessel coronary disease, which may reduce comparability to previous studies. Only 164 of the 203 patients recruited had baseline and follow-up scans so there is a potential bias although there was no differences in clinical characteristics of those who did and did not have follow-up scans. Approximately 25% of patients did not have satisfactory T2w-STIR images to allow diagnostic segmental data for MSI and IMH, which may be improved with newer tissue characterization (mapping) techniques. Segmental MVO and IMH extent were not assessed because of this being currently unavailable in our analysis software. The same observer (J.N.K.) performed all CMR analysis; however, there was a 3-month gap between analysis of cine (WMS, Ecc), T2w-STIR (IMH, MSI), and LGE (SEE, MVO) imaging, ensuring blinded analysis of CMR predictors of segmental improvement.

**Conclusions**

The SEE of LGE is a strong predictor of functional recovery after PPCI, but recovery occurs in a substantial proportion of dysfunctional segments with SEE>75%. FT-derived Ecc and MSI provide only minimal incremental benefit to SEE in predicting segmental recovery after STEMI. Further work is required to optimally identify stunned, non-necrotic myocardium after PPCI.

**Acknowledgments**

Drs McCann and Khan conceived the study idea. Drs Khan, McCann, Greenwood, Peebles, Wong, and Nazir supervised study visits. Drs Khan and Lai performed statistical analysis. Dr Khan performed cardiovascular magnetic resonance imaging and statistical analyses, and wrote the article, which all authors critically reviewed and revised.

**Sources of Funding**

Medical Research Council and managed by the National Institute for Health Research (NIHR) Efficacy and Mechanism Evaluation programme (10-27-01). The main Culprit Versus Lesion-Only Primary PCI (CyLPRIT) trial was funded by the British Heart Foundation (SP/10/001) with support from the NIHR Comprehensive Local Research Networks. Dr McCann was funded by an NIHR career development (SP/10/001) with support from the NIHR Comprehensive Local Programme (10-27-01). The main Culprit Versus Lesion-Only Primary PCI (CyLPRIT) trial was funded by the British Heart Foundation (SP/10/001) with support from the NIHR Comprehensive Local Research Networks. Dr McCann was funded by an NIHR career development (SP/10/001) with support from the NIHR Comprehensive Local Programme (10-27-01).

**Disclosures**

None.

**References**


A benefit in being able to reliably identify patients whose left ventricular function will recover after ST-segment–elevation myocardial infarction is to identify a lower-risk group that will not require further monitoring and consideration of additional therapies, such as implantable cardiac defibrillators. Our results suggest that even patients with extensive late gadolinium enhancement still require further imaging to assess whether left ventricular function has recovered, with one third of patients with segmental area extent of late gadolinium enhancement >75% demonstrating functional recovery. This is likely to result from overestimation of necrosis on late gadolinium enhancement in the acute phase post-ST-segment–elevation myocardial infarction because of the presence of edema. Even when measured acutely, late gadolinium enhancement is still the best method available to predict functional recovery, but clinicians must be aware that some proportion of segments with near-transmural enhancement in the acute phase has the potential to recover function. If viability is the key determinant on deciding further management, then the options are either to wait until edema has settled (after 7–10 days) or to consider low-dose dobutamine assessment in patients with >50% segmental area extent of late gadolinium enhancement. Circumferential strain may have a role in predicting segmental recovery in patients with contraindications to gadolinium-based contrast agents.
Relationship of Myocardial Strain and Markers of Myocardial Injury to Predict Segmental Recovery After Acute ST-Segment–Elevation Myocardial Infarction

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SUPPLEMENTAL MATERIAL

Relationship of myocardial strain and markers of myocardial injury to predict segmental recovery following acute ST-segment elevation myocardial infarction

*Short Title: CMR predictors of segmental recovery in STEMI*

**Authors**

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Joyce Wong³, MRCP, MD

John P Greenwood⁴, FRCP, PhD

Gerry P McCann¹, MRCP, MD
Supplemental Results Data 1

**Intra and interobserver variability**

Observer agreement for segmental analyses were high. Intraobserver: WMS: ICC 0.900, kappa 0.81; SEE: ICC 0.955, SEE grade kappa 0.820; Ecc: ICC 0.872; MVO presence: kappa 0.971; IMH presence: kappa 0.971. Interobserver: WMS ICC 0.792, kappa 0.67; SEE: ICC 0.969, SEE grade kappa 0.774; Ecc ICC 0.796; MVO presence kappa 0.822; IMH presence kappa 0.750.
Supplemental Results Data 2

SEE and Ecc as predictors of segmental functional recovery where SEE ≥50%

Functional improvement

In dysfunctional segments with >50% SEE (SEE 4-5), SEE strongly predicted functional improvement (model p=0.002, ‘SEE 51-75%’: OR 2.3 vs. ‘SEE 76-100%’, p=0.008). AUC was 0.924 (p=0.002). The other variables did not predict improvement (Ecc: p=0.259; MSI: p=0.927; MVO: p=0.900; IMH: p=0.286). Combining SEE and the other variables did not improve predictive accuracy compared with SEE alone.

Functional normalisation

Similarly, SEE was a strong predictor of functional normalisation (model p=0.002, ‘SEE 51-75%’: OR 6.7 vs. ‘SEE 76-100%’, p=0.008). AUC was 0.918 (p=0.002). The only other variable that predicted normalisation was MVO (MVO: p=0.002; Ecc: p=0.427; MSI: p=0.837; IMH: p=0.117). Combining SEE and MVO did not improve the predictive accuracy compared with SEE alone (AUC= 0.863 vs. 0.918).
Supplemental Results Data 3

Segmental function according to segmental extent of LGE and strain stratified by revascularisation strategy

**IRA-only revascularisation**

<table>
<thead>
<tr>
<th>WMS at Acute CMR</th>
<th>1: Normal (n=826)</th>
<th>2: Hypokinetic (n=260)</th>
<th>3: Akinetic (n=150)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>SEE (%)</td>
<td>3.2±9.1</td>
<td>24.9±22.5</td>
<td>53.6±29.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Peak segmental Ecc (%)</td>
<td>-23.6±10.2</td>
<td>-15.1±8.7</td>
<td>-9.1±7.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MSI (%)</td>
<td>99.0 (74.5, 100.0)</td>
<td>57.2 (24.1, 83.5)</td>
<td>17.3 (0.0, 49.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MVO (n, %)</td>
<td>4/826 (0.5)</td>
<td>26/260 (10.0)</td>
<td>44/150 (29.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IMH (n, %)</td>
<td>1/365 (0.3)</td>
<td>8/118 (6.8)</td>
<td>14/73 (19.2)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

SEE= segmental extent of enhancement; Ecc= peak segmental circumferential strain; MSI= myocardial salvage; MVO presence of microvascular obstruction (MVO); IMH= intramyocardial haemorrhage. No segments had WMS of 4 or 5 at acute CMR.

Correlation between SEE at acute CMR and WMS at acute CMR was r=0.712 (p<0.001), and between SEE at acute CMR and WMS at follow-up CMR was r=0.631 (p<0.001). Correlation between Ecc at acute CMR and WMS at acute CMR was r=0.497 (p<0.001), and between Ecc at acute CMR and WMS at follow-up CMR was r=0.424 (p<0.01).

**Complete revascularisation**

<table>
<thead>
<tr>
<th>WMS at Acute CMR</th>
<th>1: Normal (n=961)</th>
<th>2: Hypokinetic (n=239)</th>
<th>3: Akinetic (n=188)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>SEE (%)</td>
<td>4.0±10.2</td>
<td>23.8±21.4</td>
<td>51.0±29.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Peak segmental Ecc (%)</td>
<td>-23.5±10.3</td>
<td>-14.8±9.6</td>
<td>-10.0±8.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MSI (%)</td>
<td>98.4 (71.2, 100.0)</td>
<td>58.1 (25.7, 83.2)</td>
<td>18.3 (0.0, 52.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MVO (n, %)</td>
<td>IMH (n, %)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-----------</td>
<td>------------</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3/958 (0.3)</td>
<td>0/348 (0.0)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>22/239 (9.2)</td>
<td>4/123 (3.3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>66/188 (35.1)</td>
<td>27/125 (21.6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SEE = segmental extent of enhancement; Ecc = peak segmental circumferential strain; MSI = myocardial salvage; MVO presence of microvascular obstruction (MVO) and IMH = intramyocardial haemorrhage. No segments had WMS of 4 or 5 at acute CMR.

Correlation between SEE at acute CMR and WMS at acute CMR was r=0.676 (p<0.001), and between SEE at acute CMR and WMS at follow-up CMR was r=0.603 (p<0.001). Correlation between Ecc at acute CMR and WMS at acute CMR was r=0.479 (p<0.001), and between Ecc at acute CMR and WMS at follow-up CMR was r=0.409 (p<0.01).

Predictors of segmental functional recovery in dysfunctional segments stratified by revascularisation strategy

IRA-only revascularisation

Functional improvement

SEE (p<0.001), MSI (p<0.001) and Ecc (p=0.007) predicted segmental functional improvement with similar accuracy: (SEE: AUC 0.852, MSI: AUC 0.841, Ecc: AUC 0.833). MVO (p=0.357) and IMH (p=0.275) did not predict functional improvement. MSI (p=0.113) and Ecc (p=0.574) became insignificant when combining with SEE in the prediction model.

Functional normalisation

SEE (p<0.001), MSI (p<0.001), Ecc (p<0.001) and MVO (p<0.001) predicted segmental functional normalisation. SEE (AUC 0.895) showed higher predictive values than the other
markers (MSI: AUC 0.87, Ecc: AUC 0.842, MVO: AUC 0.838). These variables became (marginally) insignificant (MSI p=0.110, Ecc = 0.048, MVO p=0.656) when combined with SEE in the prediction model. IMH (p=0.983) did not predict functional normalisation.

Complete revascularisation

Functional improvement

All of the individual variables predicted segmental functional improvement: SEE p<0.001, MSI p<0.001, Ecc p<0.001, MVO p=0.028, IMH: p=0.008. The predictive value of SEE (AUC 0.843) was similar to MSI (AUC 0.849), Ecc (AUC 0.849), MVO (AUC 0.837) and IMH (AUC 0.839). Combining with SEE, only Ecc remained as predictive (p=0.020).

Functional normalisation

All of the individual variables predicted segmental functional improvement: SEE (p<0.001), MSI (p<0.001), Ecc (p<0.001), MVO (p<0.001), IMH (p=0.016). The predictive value was similar for SEE (AUC 0.886), Ecc (AUC 0.855) and MSI (AUC 0.864). SEE showed higher predictive value than MVO (AUC 0.840) and IMH (AUC 0.824). Combining with SEE, only Ecc remained as predictive (p=0.004).