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*

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Abstract

**Background:** Late gadolinium-enhanced cardiovascular MRI (CMR) overestimates infarct size and underestimates recovery of dysfunctional segments acutely post ST-segment elevation myocardial infarction (STEMI). We assessed whether CMR-derived segmental myocardial strain and markers of myocardial injury could improve the accuracy of late gadolinium-enhancement in predicting functional recovery following STEMI.

**Methods and Results:** 164 STEMI patients underwent acute (median 3d) and follow-up (median 9.4mth) CMR. Wall-motion scoring, Feature-Tracking derived circumferential strain ($Ecc$), segmental area of late gadolinium-enhancement (SEE), microvascular obstruction (MVO), intramyocardial haemorrhage and salvage index (MSI) were assessed in 2624 segments. We used logistic regression analysis to identify markers that predict segmental recovery. 32% of segments were dysfunctional acutely and 19% at follow-up. Segmental function at acute imaging and odds-ratio for functional recovery decreased with increasing SEE although 33% of dysfunctional segments with SEE 76-100% improved. SEE was a strong predictor of functional improvement and normalisation (AUC 0.840 [95% CI: 0.814-0.867], odds ratio [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 normalisation). 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], odds ratio [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 normalisation) and $Ecc$ (AUC 0.834 [95% CI: 0.807-0.862], odds ratio [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 normalisation), and for normalisation 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 normalisation compared to SEE alone. MSI had similar predictive accuracy to SEE for functional recovery but was not assessable in 25% of patients. MVO provided no incremental predictive accuracy above SEE.

**Conclusions:** This multicentre study confirms that SEE is a strong predictor of functional improvement post STEMI but recovery 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:** [ISRCTN70913605](http://www.isrctn.com/ISRCTN70913605)

**Keywords:** Myocardial infarction, late gadolinium enhancement, myocardial strain, cardiovascular magnetic resonance, viability.
Background

Improvement in dysfunctional myocardium following acute ST-elevation myocardial infarction (STEMI) predicts long-term myocardial function and prognosis\(^1,2\). Kim\(^3\) and Choi\(^4\) first demonstrated an inverse correlation between cardiovascular MRI (CMR)-measured segmental late gadolinium enhancement (LGE) transmurality and functional recovery in hibernating\(^3\) and stunned\(^4\) 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 centre studies and heterogeneity of LGE assessment\(^5-12\). Moreover, several reports have shown that LGE, measured within days of STEMI overestimates acute infarct size and underestimates the potential for functional recovery\(^13-15\). The accuracy of segmental LGE expressed as segmental extent of enhancement (SEE), defined as enhanced percentage of segmental area\(^10,12,16\) rather 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 following STEMI. Circumferential strain ($E_{cc}$)\(^11\), myocardial salvage (MSI)\(^17\), LGE-derived microvascular obstruction (late MVO)\(^11,17,18\) and intramyocardial haemorrhage (IMH)\(^18\) 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 post-processing software for the quantification of myocardial strain from steady-state free-precession (SSFP) cine images\(^19,20\). We have recently demonstrated greater robustness, reproducibility and infarct correlation with FT-derived strain compared with tagging in acute STEMI\(^21\).
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 multicentre, prospective, randomised controlled study assessing infarct-related artery only versus complete revascularisation. STEMI was diagnosed according to European Society of Cardiology definitions and patients underwent primary percutaneous coronary intervention (PPCI) within 12h of symptoms. The study was approved by the National Research Ethics Service, was conducted according to the Declaration of Helsinki and patients provided written informed consent.

Cardiovascular MRI

CMR was performed in 5 of the 7 centres, 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 LV. 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= unanalysable.

Volumetric and functional analysis
Analysis was performed using cvi42 v4.1 (Circle Cardiovascular Imaging, Calgary, Canada). LV volumes were calculated as previously described\(^2\). Wall motion in the 16 American Heart Association myocardial segments was visually graded as: 1= normokinetic, 2= hypokinetic, 3= akinetic, 4= dyskinetic and 5= aneurysmal.\(^2\) Segmental dysfunction was defined as wall motion score (WMS) $\geq 2$ at acute CMR and improvement as a WMS decrease of $\geq 1$, and normalisation where WMS returned to 1 at follow-up CMR.\(^{10-12, 16}\)

**Infarct characterisation**

Oedema (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* [segmental enhanced area/segmental area])\(^1\). SEE was additionally classified into 5 categories: SEE 0%, SEE 1-25%, SEE 26-50%, SEE 51-75%, SEE 76-100% as previously described\(^1, 12, 16\). Segmental MSI defined the proportion of the AAR that did not progress to infarction and was calculated as [(segmental AAR - SEE)/segmental AAR] x100.

**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.\(^2\)
Suboptimally tracking segments were manually adjusted if 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±standard deviation, and comparisons between groups were conducted with ANOVA. Non-parametric data were expressed as median (25%-75% interquartile range), and compared with Kruskal-Wallis testing. Spearman’s Rank Correlation Coefficient assessed the correlation between the predictors and segmental function. We assessed: (1) whether SEE, Ecc, MVO, MSI, (presence/absence) and IMH (presence/absence) predicted improvement and normalisation of dysfunctional myocardial segments at follow-up CMR using logistic regression analysis, and (2) whether 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-Operator Curve (ROC) analysis with the area under the curves (AUCs) compared using the method of Delong. On AUC, predictive accuracy of >0.9 was considered excellent, 0.8-0.9 very good, 0.7-0.8 good, 0.6-0.7 average and <0.6 poor. The optimal cut-off values of SEE, segmental Ecc and MSI for predicting functional recovery were identified by ROC analysis where sensitivity and specificity intersected. Intra and interobserver agreement were assessed with intraclass correlation coefficient for absolute agreement (ICC) and kappa statistic on a random selection of 10 patients. Intraobserver (JNK) and interobserver agreement (JNK, SAN) are reported in Supplemental Data 1. Statistical tests were
performed using SPSS v20 (IBM, New York, USA) and PROC GLIMMIX in SAS v9.4 (Statistical Analysis Systems, North Carolina, USA). P<0.05 was considered significant.

Results

Baseline characteristics

Demographic and CMR data are summarised 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 analysable for WMS, SEE, Ecc and MVO. Twenty-three percent of T2w-STIR segments (MSI, IMH) were non-analysable due to poor image quality or not being acquired due to 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%) of 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%) of dysfunctional segments had improved of which 372 (44.4%) had normalised and 495 (18.8%) remained dysfunctional (WMS 2: 350/2624 [13.3%], WMS 3: 137/2624 [5.2%], WMS 4: 8/2624 [0.3%]).

Segmental function according to segmental extent of LGE and strain

During, 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). Over 98% of ‘SEE 76-100%’ segments were dysfunctional at acute CMR. WMS correlated more strongly with SEE at acute ($r_s=0.69$, $p<0.01$) and follow-up CMR ($r_s=0.62$, $p<0.01$) than with MSI (acute: $r_s=-0.523$, $<0.01$; follow-up: $r_s=-0.514$, $<0.01$) and $Ecc$ (acute: $r_s=0.49$, $p<0.01$; follow-up: $r_s=0.49$, $p<0.01$). At follow-up CMR, segmental function improved in each SEE grade (Figure 4). The proportion of dysfunctional segments improving or normalising decreased with increasing SEE, with 90% of ‘SEE 0%’ segments normalising. Despite this, 33% of ‘SEE 75-100%’ segments improved, however only 5% normalised (Figure 4). The proportion of dysfunctional segments improving or normalising increased with increasing MSI. Despite this, 43% of ‘MSI 0-25%’ segments improved, but only 21% normalised (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 ($p<0.001$), $Ecc$ ($p<0.001$), as well as 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. Revascularisation 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 to 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 normalisation

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 as measured by AUC was higher than 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). Revascularisation strategy did not predict segmental normalisation (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 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 normalisation 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 normalisation (p=0.002) (AUC 0.918) (Supplemental Data 2). MVO predicted
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Functional normalisation (p=0.002) and remained as significant after adjustment for SEE (p<0.009). Ece, MSI and IMH did not predict functional recovery and were not of addictive value to SEE.

CMR predictors of segmental functional recovery stratified by revascularisation strategy

Full data are presented in Supplemental Data 3. The results for all analyses were similar in patients undergoing IRA-only (n=80) and complete revascularisation (n=84), and were similar to those in the overall study cohort (n=164).
Discussion

This is the largest study assessing CMR predictors of segmental functional recovery following acute STEMI treated with PPCI and the first to use multicentre data analysed in a core lab. We have confirmed that early after STEMI, LGE overestimates infarct size despite using FWHM quantification, which gives lower values compared with 2SD thresholding used by most previous studies. Functional improvement occurred in a significant proportion of near-transmurally enhanced segments although only 5% normalised. A key aim of conducting this study was to assess whether the accuracy of LGE to predict functional recovery following 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 normalisation. Additionally 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 and Orii. LGE measured acutely overestimates necrosis by up to 30% in the first week post STEMI due to myocardial oedema. 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 two studies. Untreated multivessel disease with potential hibernating myocardium in non-infarct 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 since we felt that it is a more accurate representation of segmental necrosis than
Superscript transmurality of enhancement. Transmurality can overestimate segmental necrosis since a segment may be deemed transmurally enhanced when only a small portion of segmental width demonstrates transmurality. Infarct extent based on transmurality has been compared with SEE in one study, in HCM and was 31% higher.

The recent study by Wong\textsuperscript{11} is the closest in design to our study. SEE and MVO were however stronger predictors of recovery in our study compared with their results (SEE: AUC 0.840 vs. 0.680, MVO: 0.836 vs. 0.670). This may be due to their small study size (n=45), the fact that they only assessed LGE on three thin (6mm) short-axis slices and hence provided incomplete LV coverage, and their later timepoint 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 cut-off for predicting recovery in our study of 34% is similar to that in the study by Becker\textsuperscript{16}, who also used SEE. It may be that if transmurality of enhancement overestimates necrosis relative to SEE, a smaller SEE cut-off predicts recovery. The commonly used arbitrary cut-off of 50% may need revising, since it has been derived from historical work in chronic coronary artery disease\textsuperscript{3} where LGE is unlikely to overestimate necrosis. Importantly, SEE in our study was a strong predictor (AUC 0.887) of functional normalisation, 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\textsuperscript{18} who demonstrated that infarcts with MVO had no improvement in segmental function on mid-myocardial and endocardial-strain in the infarct zone at 3 month, and that the presence of IMH further attenuated strain. Of note, MVO in our study was the only predictor of functional normalisation 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 remodelling known to accompany MVO. Indeed, Kitagawa\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 due to the relatively small number of segments with IMH and SEE ≥50% (n=41).

Our results have also shown that MSI performed equally as well as SEE to predict functional recovery. The moderate predictive accuracy of MSI is consistent with previous work highlighting that MSI may underestimate functional recovery using segmental strain.\textsuperscript{17} 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’s 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 oedema images, resulted in non-analysable images in 25% of patients and provided only minimal incremental value above SEE alone, there appears to be little merit in using MSI instead of or in addition to SEE. The close interrelation 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\textsuperscript{21}. This is likely to be a result of infarction firstly affecting the endocardium in the ischaemic cascade.\textsuperscript{30} This is corroborated by the fact that Ecc was a strong predictor of segmental recovery in this study.
Our results are in keeping with Wong who showed an almost identical predictive accuracy (AUC 0.823) to our study, of HARP-derived Ecc in identifying segmental recovery at 3 months\(^\text{11}\). Unlike our study, they however demonstrated that Ecc was a significantly stronger predictor than SEE and MVO. This is likely to be due to methodological differences as discussed above. Our findings are similar to those of Orii\(^\text{12}\) who also showed a strong predictive accuracy of speckle-tracking echocardiographic Ecc (AUC 0.899) 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\(^\text{31}\), which showed that FT-derived global Ecc and LGE infarct size were moderately strong predictors of LVEF >50% at 6-months follow-up, and that Ecc was a non-inferior predictor compared with infarct size.

Our study is in contrast to the work of Neizel\(^\text{12}\) who used strain-encoded CMR (SENC)-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 vs. 0.91). The weaker predictive accuracy of SENC Ecc compared to FT Ecc in their study may be due to the fact that Neizel divided the left ventricle into 10 to 12, rather than 16 segments, thus potentially reducing the accuracy of strain assessment in basal and apical segments. Indeed, no segments in their study had a strain value of zero, even those that were visually akinetic and contained MVO. In addition, SENC imaging has a lower signal-to-noise ratio than SSFP cine imaging\(^\text{32}\). However there are no data comparing SENC 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 pre-discharge. 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 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 characterisation (mapping) techniques. Segmental MVO and IMH extent were not assessed due to this being currently unavailable in our analysis software. The same observer (JNK) 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.

Clinical Summary

The main benefit in being able to reliably identify patients whose LV function will recover following STEMI is to identify a lower risk group who will not require further monitoring and consideration of additional therapies such as implantable cardiac defibrillators. Our results suggest that even patients with extensive LGE still require further imaging to assess whether LV function has recovered, with one third of patients with SEE >75% demonstrating functional recovery. This is likely to result from overestimation of necrosis on LGE in the acute phase post STEMI due to the presence of oedema. Our view on this is that measured acutely, LGE still appears to be the best method available to predict functional recovery, providing moderately strong accuracy but clinicians must be aware that a significant proportion of segments with seemingly near-transmural enhancement have the potential to recover function. If viability is the key determinant on deciding
Further management then the options are either to wait until oedema has settled (after 7-10 days)\(^{15}\) or consider low-dose dobutamine assessment in patients with >50% SEE\(^{33}\). Ecc may have a role in predicting segmental recovery in patients with contraindications to gadolinium-based contrast agents.

Conclusions
The SEE of LGE is a strong predictor of functional recovery following 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 following STEMI. Further work is required to optimally identify stunned, non-necrotic myocardium following PPCI.

Acknowledgments
GPM and JNK conceived the study idea. JNK and JPG recruited patients. JNK, GPM, JPG, CP, JW and SAN supervised study visits. JNK and FYL performed statistical analysis. JNK performed CMR and statistical analyses, and wrote the paper, which all authors critically reviewed and revised.

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Disclosures

There are no conflicts of interests for any of the authors.
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Figure Legends

Figure 1: MRI protocol
LV= left ventricle, RV= right ventricle, SAX= short axis, FOV= field of view, TR= repetition time, TE= echo time, TI= inversion time, IS= infarct size, MVO= microvascular obstruction

Figure 2: CONSORT diagram illustrating reasons for patients not returning for follow-up CMR

Figure 3: Wall-motion scoring at acute and follow-up CMR by segmental extent of enhancement
WMS= wall-motion score, SEE= segmental extent of enhancement

Figure 4: Recovery in dysfunctional segments at follow-up CMR by segmental extent of enhancement
SEE= segmental extent of enhancement

Figure 5: Recovery in dysfunctional segments at follow-up CMR by segmental myocardial salvage
MSI= myocardial salvage index
Table 1: Baseline demographics and CMR characteristics

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<th>CMR characteristics</th>
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<td>Cine segments of diagnostic image quality (%) at acute CMR</td>
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<td>LGE segments of diagnostic image quality (%) at acute CMR</td>
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<td>Acute CMR time (days post STEMI)</td>
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<tr>
<td>Left-ventricular end-systolic volume (ml/m²)</td>
<td>47.5 (39.0-58.5)</td>
<td></td>
</tr>
<tr>
<td>Left ventricular ejection fraction (%)</td>
<td>46.1±9.2</td>
<td></td>
</tr>
<tr>
<td>Infarct size (% LV mass)</td>
<td>12.7 (6.9-21.5)</td>
<td></td>
</tr>
<tr>
<td>Myocardial salvage index (%)</td>
<td>58.7 (35.3-76.7)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Segmental characteristics</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Dysfunctional segments at acute CMR (n, %)</td>
<td>837/2624 (31.9)</td>
<td></td>
</tr>
<tr>
<td>Dysfunctional segments at follow-up CMR (n, %)</td>
<td>495/2624 (18.9)</td>
<td></td>
</tr>
<tr>
<td>Segments with LGE at acute CMR (n, %)</td>
<td>1186/2624 (45.2)</td>
<td></td>
</tr>
<tr>
<td>Segments with LGE at follow-up CMR (n, %)</td>
<td>1009/2624 (38.5)</td>
<td></td>
</tr>
<tr>
<td>Segments with MVO at acute CMR (n, %)</td>
<td>165/2624 (6.3%)</td>
<td></td>
</tr>
</tbody>
</table>
Final manuscript accepted for publication in Circulation: Cardiovascular Imaging, 27th April 2016. DOI: 10.1161/CIRCIMAGING.115.003457.

| Segments with IMH at acute CMR (n, %) | 51/2016 (2.5%) |
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</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>

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.
Table 3: Segmental extent of myocardial injury at acute CMR 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>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>n/a</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>n/a</td>
<td>0.32 IMH present vs. absent (p=0.004)</td>
<td>0.15-0.67</td>
</tr>
</tbody>
</table>

<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>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>n/a</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>n/a</td>
<td>0.08 IMH present vs. absent (p=0.001)</td>
<td>0.02-0.30</td>
</tr>
</tbody>
</table>

AUC= area under the curve, 95% CI= 95% confidence interval, sens=sensitivity, spec=specificity, SEE= segmental extent of enhancement, Ecc= peak segmental circumferential strain, MSI= myocardial salvage, MVO= microvascular obstruction, IMH= intramyocardial haemorrhage