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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 when measured early after 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 patients with STEMI and multivessel disease randomized in the CvLPRIT trial underwent acute (median 3 days) and follow-up (9 month) CMR. Wall motion score, Feature-Tracking derived circumferential strain (Ecc), segmental area extent of late gadolinium enhancement (SEE), microvascular obstruction, intramyocardial haemorrhage (IMH) and salvage index (MSI) on T2-weighted short tau inversion recovery imaging were assessed in 2624 segments. Accuracy of the markers in predicting segmental recovery was assessed using Receiver Operator Curves. 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 stronger predictor of functional improvement and normalisation than Ecc, microvascular obstruction and IMH, and none of these variables provided incremental predictive value above SEE alone. MSI had similar accuracy to SEE to predict functional recovery but was not assessable in 25% of patients.

Conclusions: This multicentre study confirms that functional recovery occurs in a substantial proportion of dysfunctional segments with SEE >75%. Feature Tracking derived Ecc, MSI, microvascular obstruction and IMH provide no incremental benefit to SEE in predicting segmental recovery following STEMI.

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}. Kim³ and Choi⁴ first demonstrated an inverse correlation between cardiovascular MRI (CMR)-measured segmental late gadolinium enhancement (LGE) transmuralities and functional recovery in hibernating³ and stunned⁴ 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.⁵⁻¹⁴ Moreover, several reports have shown that LGE, measured within days of STEMI overestimates acute infarct size and the potential for functional recovery¹⁵⁻¹⁷. The accuracy of segmental LGE expressed as segmental extent of enhancement (SEE), defined as enhanced percentage of segmental area^{12-14, 18} rather than maximum transmuralities 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 (Ecc)¹³, myocardial salvage (MSI)¹⁹, LGE-derived microvascular obstruction (late MVO)^{13, 19, 20} and intramyocardial haemorrhage (IMH)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 post-processing software that allows the quantification of myocardial strain from steady-state free-precession (SSFP) cine images^{21, 22}. We have recently demonstrated greater robustness, reproducibility and infarct correlation with FT-derived strain compared with tagging in acute STEMI²³.

We aimed to assess whether FT-derived Ecc, MSI, late MVO and IMH predict 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 in the CMR substudy of a multicentre, prospective, randomised controlled study assessing infarct-related artery only versus complete revascularisation (CvLPRIT-CMR: Complete versus Lesion-only Primary PCI Trial)²⁴. 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 all patients provided written informed consent.

Cardiovascular MRI

MRI 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 LV²⁵. 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.²⁶ 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.²⁷ Segmental dysfunction was defined as WMS ≥ 2 at acute CMR and improvement as a WMS decrease of ≥ 1 , and normalisation where WMS returned to 1 at follow-up CMR.^{12-14, 18}

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 group²⁸. 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 ($SEE = 100 * [\text{segmental enhanced area} / \text{segmental area}]$)^{13, 29}. SEE was additionally classified into 5 categories: SEE 0%, SEE 1-25%, SEE 26-50%, SEE 51-75%, SEE 76-100% as previously described^{13, 14, 18}. Segmental MSI defined the proportion of the AAR that did not progress to infarction and was calculated as $[(\text{segmental AAR} - \text{SEE}) / \text{segmental AAR}] \times 100$.

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 previously²³. Segments with sub-optimal tracking 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. Non-parametric data were expressed as median (25%-75% interquartile range). ANOVA and Kruskal-Wallis analyses were used to compare mean and median values between multiple groups respectively. Spearman's Rank Correlation Coefficient assessed the correlation between SEE, segmental Ecc and MSI and segmental function on WMS. The accuracy of SEE, segmental Ecc, MSI, MVO and IMH in predicting improvement and normalisation of dysfunctional myocardial segments at follow-up CMR was assessed initially using logistic regression, including revascularization strategy as a variable, and then using ROC curve analysis and calculation of AUC (area under the curve). AUCs were compared using the method of Hanley and McNeil.³⁰ The optimal SEE and segmental Ecc and MSI cut-off value for predicting functional recovery was that resulting in the greatest sum of sensitivity plus specificity. Appropriateness of logistic regression was confirmed using Hosmer-Lemeshow statistics. Intra and interobserver agreement were assessed with intra-class correlation coefficient for absolute agreement (ICC)³¹ and kappa statistic on a randomly selected sample of 10 patients. Intraobserver agreement (JNK) and interobserver agreement (JNK and SAN) are reported in Supplemental Data 1. Statistical tests were performed using SPSS V20. $p < 0.05$ was considered significant.

Results

Baseline characteristics

Demographic and CMR data are summarised in Table 1. 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 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%], WMS 4/5: 0/2624 [0%]). 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%], WMS 5: 0/2624 [0%]).

Segmental function according to segmental extent of LGE and strain

Acutely, with worsening function on WMS, SEE and presence of MVO and IMH increased, and segmental Ecc and MSI decreased (Table 2). With increasing SEE, segmental function worsened (Figure 2). 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 3). 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 3). 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 4).

Predictors of segmental recovery in dysfunctional segments post STEMI

Predictors of segmental functional improvement

SEE moderately predicted functional improvement (AUC 0.708, $p < 0.001$) (Table 3).

Optimal predictive SEE cut-off was $< 38\%$ (sensitivity 66%, specificity 66%). Segmental MSI predicted improvement with similar accuracy to SEE (AUC 0.700, $p < 0.001$; $p = 0.823$ vs. SEE). Segmental Ecc was a weak predictor of improvement (AUC 0.626, $p < 0.001$).

Segmental IMH presence was a weak predictor of improvement (AUC 0.565, $p = 0.027$), however MVO did not predict improvement (AUC 0.544, $p = 0.131$). Revascularisation strategy did not predict segmental improvement ($R^2 < 0.001$, $p = 0.73$). SEE was a stronger predictor of functional improvement than Ecc and the presence of segmental MVO and IMH ($p < 0.01$ for all). Combining SEE and Ecc, MSI, MVO or IMH did not improve the predictive accuracy³⁰ of identifying segmental improvement versus SEE alone (Figure 5).

Predictors of segmental functional normalisation

SEE was a moderately strong predictor of functional normalisation (AUC 0.807, $p < 0.001$) (Table 3). Optimal predictive SEE cut-off was $< 29\%$ (sensitivity 72%, specificity 74%).

Segmental MSI predicted normalisation with lower accuracy to SEE however the difference was not significant (AUC 0.765, $p < 0.001$; $p = 0.241$ vs. SEE). Segmental Ecc and MVO moderately predicted normalisation (AUC 0.691 and AUC 0.620 respectively, $p < 0.001$). Segmental IMH was a weak predictor of normalisation (AUC 0.590, $p < 0.001$).

Revascularisation strategy did not predict segmental normalisation ($R^2 = 0.001$, $p = 0.33$).

SEE was a stronger predictor of functional normalisation than Ecc and presence of segmental MVO and IMH ($p < 0.001$ for all). Combining SEE and Ecc, MSI, MVO or IMH

did not improve the predictive accuracy³⁰ of identifying segmental normalisation versus SEE alone (Figure 6).

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

In dysfunctional segments with $>50\%$ SEE, only SEE predicted improvement (AUC 0.606, $p=0.048$) and normalisation (AUC 0.763, $p=0.008$, Supplemental Data 1). Combining SEE and the other variables did not improve predictive accuracy versus SEE alone.

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 the FWHM technique for quantification, which gives lower values compared with 2SD thresholding used by most previous studies^{6, 8, 10, 11, 18}. Functional improvement occurred in a significant proportion of near-transmurally enhanced segments although only 5% normalised. The main 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 stronger predictor of recovery at 9 months than Ecc, MVO and IMH. Additionally Ecc, MSI, MVO and IMH add no incremental predictive value to SEE.

Prediction of segmental functional recovery with LGE

Our moderate inverse correlation between SEE and functional recovery is consistent with previous studies^{4, 5, 7, 8, 10-14}. Accuracy in predicting recovery was slightly lower than in some studies. LGE measured acutely overestimates extent of necrosis by up to 30% in the first week post STEMI due to myocardial oedema^{15, 17}. We undertook acute CMR at 3 days post PPCI to assess CMR in a 'real world' setting, when patients are discharged and are unlikely to undergo CMR at day 5-28 as per other studies^{4, 5, 7, 8, 10-14}. Untreated multivessel disease with potential hibernating myocardium in non-infarct artery territories in our study, differences in LGE thresholding methods^{4, 5, 7, 8, 10-12, 14} and the smaller sample size of other studies may also have contributed to our slightly lower AUC. We used SEE^{5, 8, 13, 12} since we felt that it is a more accurate representation of segmental necrosis than transmural extent of enhancement. It can overestimate segmental necrosis since a segment may be deemed transmurally enhanced when only a small portion of segmental width

demonstrates transmural^{4,9}. Infarct extent based on transmural extent of enhancement has been compared with SEE in one study, in HCM and was 31% higher³².

The optimal SEE cut-off for predicting recovery in our study of 38% is identical to that in the study by Becker et al¹⁸, who also used SEE. It may be that if transmural extent 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 disease³ where LGE is unlikely to overestimate necrosis³. Importantly, SEE in our study was a very strong predictor (AUC 0.807) of functional normalisation, accurately identifying segments likely to result in a significant improvement in long-term LV function and hence prognosis^{1,2}.

Late MVO and IMH were weak predictors of segmental recovery. This is in contrast to Kidambi et al²⁰ who demonstrated their accuracy in predicting absence of segmental recovery. This discrepancy may in part be explained by the fact that they performed follow-up at CMR at 3 months, where functional recovery may have been incomplete. Of note, MVO and IMH in our study did not predict functional recovery in segments with SEE >50%. This may be due to the high prevalence of MVO in such segments (42%) and thus their segmental extent is likely to be a more accurate predictor. Indeed, Kitagawa¹⁰ showed that segmental MVO extent <50% accurately identified recovering segments with >50% LGE enhancement.

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 when segmental strain at baseline and follow-up is assessed.¹⁹ MSI and SEE are closely related and given that MSI significantly increases scanning time to acquire oedema images, resulted in non-

analysable images in 25% of patients and did not perform any better than SEE alone, there is appears to be little merit in using MSI over SEE. The close interrelation between IS, MVO and IMH is also likely to account for the 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 characteristics²³. This is likely to be a result of infarction firstly affecting the endocardium in the ischaemic cascade.³³ However, endocardial Ecc was only a moderate predictor of segmental recovery in this study. This may be due to the lower observer agreement for segmental strain^{34, 35} compared with LGE assessment.^{6, 36} Additionally there may have been a significant proportion of patients with stunned myocardium in our study since we performed acute CMR early, in patients with multivessel disease.

Our results are in contrast to Wong¹³ who compared the predictive accuracy of segmental LGE (SEE) and HARP-derived mid-wall Ecc in identifying segmental recovery in acute STEMI. SEE predicted improvement with similar accuracy (AUC 0.680) to our study, however Ecc was a stronger predictor (AUC 0.820). This can explained by methodological differences. Firstly, Wong et al undertook acute CMR at day 8, and follow-up CMR at 3 months. Secondly, we excluded patients with previous STEMI from recruitment. Wong et al only excluded patients with previous STEMI within the infarct artery territory. Included chronic infarcts would invariably show no functional recovery, regardless of SEE. Thirdly, we assessed LGE on the full LV stack, unlike Wong et al who assessed only 3 thin (6mm) short-axis slices (basal, mid, apical) resulting in incomplete LV coverage. Finally, Wong et al provided no data on image quality and non-analysable

segments, which may be a significant limitation since up to 12% of tagged studies²⁰ are not analysable.

Although our study has only assessed Ecc using a single technique, FT, our results are consistent with previous work using CMR strain-encoded (SENC) analysis.³⁷ In that study SENC-derived segmental Ecc and LGE SEE were used to predict persistent dysfunction at 6 months post PPCI, defined as segmental Ecc <9%. SEE was a significantly stronger predictor for persistent segmental dysfunction than Ecc.³⁷

Clinical implications

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. The results suggest that even patients with extensive LGE still require further imaging to assess whether LV function has recovered. Despite the moderate accuracy of LGE, this technique still appears to be best method available although contractile reserve on low-dose dobutamine strain assessment³⁸ may offer incremental predictive accuracy to SEE. Ecc may have a role in predicting segmental recovery in patients with contraindications to gadolinium-based contrast agents. Undertaking acute CMR at a later timepoint (~7-10 days) may increase the predictive accuracy of SEE due to reduced overestimation of infarct extent of LGE and further work is required to test this hypothesis.

Limitations

Acute CMR was undertaken earlier than in some studies with potentially greater overestimation of necrosis on LGE, however this allows a closer representation of 'real life' practice where acute CMR would likely be undertaken pre-discharge. All of our subjects had multivessel coronary disease, which may reduce comparability to previous

studies. Approximately 25% of patients did not have satisfactory T2w images to allow diagnostic segmental data for MSI and IMH, which may be improved with newer tissue characterisation (mapping) techniques. The extent of MVO and IMH 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) and LGE (SEE, MSI) imaging, ensuring blinded analysis of CMR predictors of segmental improvement.

Conclusions

The SEE of LGE is a moderately strong predictor of functional recovery following PPCI but recovery occurs in a substantial proportion of dysfunctional segments with SEE >75%. Feature Tracking derived Ecc, MSI, microvascular obstruction and IMH provide no incremental benefit to SEE in predicting segmental recovery following STEMI and further work is required to optimally identify stunned, non-necrotic myocardium following PPCI. .

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GPM and JNK conceived the study idea. JNK and JPG recruited patients. JNK, GPM, JPG, CP, JW and SAN supervised study visits. 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.

Commentary

This multicentre study in patients with multivessel coronary artery disease has confirmed that late gadolinium enhancement performed early (day 3) after STEMI is a moderately strong predictor of functional recovery following PPCI but underestimates the potential for recovery in segments with near transmural enhancement. Other markers of injury such as microvascular obstruction, haemorrhage, myocardial salvage and Feature Tracking derived strain were not of additive value to late gadolinium enhancement. For clinicians who are faced with a patient who has severe left ventricular dysfunction following PPCI and wish to know whether that patient's function will recover have several options. If the CMR is performed early and shows that dysfunctional segments have less than 38% enhancement then left ventricular functional recovery is very likely. For patients where there is more enhancement, previous research has suggested that adding low dose dobutamine may help identify viable dysfunctional segments. An alternative is to perform the CMR subacutely (after 7-10 days) when myocardial oedema is resolving and the extent of late gadolinium enhancement is less likely to overestimate infarct size. Further work is required to optimally identify stunned, non-necrotic myocardium following PPCI.

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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: Wall-motion scoring at acute and follow-up CMR by segmental extent of enhancement

WMS= wall-motion score, SEE= segmental extent of enhancement

Figure 3: Recovery in dysfunctional segments at follow-up CMR by segmental extent of enhancement

SEE= segmental extent of enhancement

Figure 4: Recovery in dysfunctional segments at follow-up CMR by segmental myocardial salvage

MSI = myocardial salvage index

Figure 5: CMR predictors of segmental improvement assessed using Receiver Operator Curves

SEE=segmental extent of enhancement, MVO=microvascular obstruction, IMH=intramycardial haemorrhage, Ecc=circumferential strain, MSI= myocardial salvage index

Figure 6: CMR predictors of segmental normalisation assessed using Receiver Operator Curves

SEE=segmental extent of enhancement, MVO=microvascular obstruction, IMH=intramycardial haemorrhage, Ecc=circumferential strain, MSI= myocardial salvage index

Table 1: Baseline demographics and CMR characteristics

Baseline and angiographic characteristics	
Number of patients (n)	164
Age (years)	63.0±9.5
Gender (male, %)	140 (85.4)
Diabetes (n, %)	24 (14.6)
Hypertension (n, %)	60 (36.6)
Symptom to PPCI time (min)	172 (128-280)
Left anterior descending artery culprit vessel (n, %)	50 (36.6)
Infarct-related artery only PCI (n, %)	80 (48.8)
Multivessel PCI (n, %)	84 (51.2)
CMR characteristics	
Cine segments of diagnostic image quality (%) at acute CMR	100
LGE segments of diagnostic image quality (%) at acute CMR	100
T2w-STIR segments of diagnostic image quality (%) at acute CMR	76.8
Cine segments of diagnostic image quality (%) at follow-up CMR	100
Acute CMR time (days post STEMI)	2.9 (2.0-3.9)
Follow-up CMR time (month post STEMI)	9.4 (8.9-10.0)
Left ventricular end-diastolic mass (g/m ²)	52.3 (45.9-61.0)
Left ventricular end-diastolic volume (ml/m ²)	89.5 (80.6-101.5)
Left-ventricular end-systolic volume (ml/m ²)	47.5 (39.0-58.5)
Left ventricular ejection fraction (%)	46.1±9.2
Infarct size (% LV mass)	12.7 (6.9-21.5)
Myocardial salvage index (%)	58.7 (35.3-76.7)
Segmental characteristics	
Dysfunctional segments at acute CMR (n, %)	837/2624 (31.9)
Dysfunctional segments at follow-up CMR (n, %)	495/2624 (18.9)
Segments with LGE at acute CMR (n, %)	1186/2624 (45.2)
Segments with LGE at follow-up CMR (n, %)	1009/2624 (38.5)
Segments with MVO at acute CMR (n, %)	165/2624 (6.3%)
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

WMS at Acute CMR	1: Normal (n=1787, 68%)	2: Hypokinetic (n=499, 19%)	3: Akinetic (n=338, 13%)	p
SEE (%)	3.6±9.7	24.4±22.0	52.2±29.1	<0.001
Peak segmental Ecc (%)	-23.5±10.2	-14.9±9.1	-9.6±7.9	<0.001
MSI (%)	98.4 (71.2, 100.0)	58.1 (25.7, 83.2)	18.3 (0.0, 52.6)	<0.001
MVO (n, %)	7/1787 (0.4)	48/499 (9.6)	110/338 (32.5)	<0.001
IMH (n, %)	1/713 (0.1)	12/241 (4.9)	41/198 (20.7)	<0.001

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 according to degree of dysfunction at acute CMR

<u>Improvement</u>				
Predictor	AUC	95% CI, p	Optimal cutoff	Odds-Ratio
SEE	0.708	0.657-0.759, p<0.001	<38% (sens 66%, spec 66%)	SEE 0%: 23.1, SEE 1-25%: 4.9, SEE 26-50%: 2.9, SEE 51-75%: 2.3 (all OR vs. SEE 76-100%, p<0.001)
MSI extent	0.700	0.649-0.751, p<0.001	>43% (sens 59%, spec 73%)	1.02 per +1% MSI
Ecc extent	0.626	0.570-0.682, p<0.001	<-10.5% (sens 65%, spec 62%)	1.04 per -1% Ecc
MVO presence	0.544	0.487-0.602, p=0.131	n/a	0.55 where MVO present
IMH presence	0.565	0.507-0.623, p=0.027	n/a	0.84 where IMH present
<u>Normalisation</u>				
Predictor	AUC	95% CI, p	Optimal cutoff	Odds-Ratio
SEE	0.807	0.764-0.850, p<0.001	<29% (sens 72%, spec 74%)	SEE 0%: 170.3, SEE 1-25%: 33.1, SEE 26-50%: 10.2, SEE 51-75%: 6.7 (all OR vs. SEE 76-100%, p<0.001)
MSI extent	0.765	0.715-0.816, p<0.001	>61% (sens 59%, spec 84%)	1.03 per +1% MSI
Ecc extent	0.691	0.637-0.745, p<0.001	<-13.2% (sens 56%, spec 71%)	1.06 per -1% Ecc
MVO presence	0.620	0.564-0.676, p<0.001	n/a	0.62 where MVO present
IMH presence	0.590	0.534-0.646, p<0.001	n/a	0.40 where IMH present

AUC = area under the curve; 95% CI = 95% confidence interval; SEE= segmental extent of enhancement; Ecc= peak segmental circumferential strain;

MSI= myocardial salvage; MVO presence of microvascular obstruction (MVO) and IMH = intramyocardial haemorrhage