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ORIGINAL ARTICLE

Comparison of Magnetic Resonance Analysis of Myocardial Scarring With Biomarker Release Following S-T Elevation Myocardial Infarction

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Background Late gadolinium enhancement (LGE) with cardiac magnetic resonance (CMR) is commonly assumed to represent myocardial fibrosis; however, comparative human histological data are limited, and there is no consensus on the most accurate method for LGE quantitation. We evaluated the relationship between CMR assessment of regional fibrosis and infarct size assessment using serial biomarkers after ST elevation acute myocardial infarction (STEMI).

Methods Ninety-three patients treated for STEMI (59 ± 10 years, 86% male) underwent CMR 6 months after infarction. Infarct size was quantified by CMR-LGE using manual and range of semi-automated thresholds (range: 2–10 standard deviations [SD]) above reference myocardium and the full width-half maximum

Abbreviations: AMI, acute myocardial infarction; STEMI, S-T segment elevation myocardial infarction; CMR, cardiac magnetic resonance imaging; LGE, late gadolinium enhancement; SD, standard deviation; cTNI, cardiac troponin I; CK, creatinine kinase; AUC, area under the curve; FWHM, full width half maximum; PCI, percutaneous coronary intervention; NYHA, New York Heart Association

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(FWHM) technique, and compared with the rise in serum biomarkers. The agreement between CMR and biomarker in the identification of large infarcts based on peak troponin (TnI) levels was also analysed.

Results Quantification methods had a strong influence on the infarct size assessment with CMR-LGE. Significant correlations were observed between LGE and biomarkers across all of the signal intensity thresholds. Whilst there was a wide variation with respect to the estimation of total LGE size (from 6.8 ± 7.7 to 32.1 ± 11.3 grams), the variation in the correlation with peak troponin level was much smaller (r-values ranging from 0.670 to 0.876). There was good agreement between CMR-LGE and biomarker assessment of infarct size; the best agreement between CMR-LGE and large infarction using a threshold of 8SD for peak TnI > 50 ng/mL (Cohen's kappa (κ) = 0.722), and a threshold of 4SD for peak TnI > 95 ng/mL (κ = 0.761).

Conclusions The correlation between CMR-LGE quantification of infarct size and biomarker release following STEMI at a range of semi-automated thresholds was consistently strong, with good agreement between measures across a range of thresholds.

Keywords Cardiac magnetic resonance • Late gadolinium enhancement • Infarct size • Fibrosis

Background

Following an acute myocardial infarction (AMI), there is necrosis of cardiac myocytes followed by replacement of myocyte necrosis with fibrosis, or scar tissue during the recovery process [1]. The size of the infarct determines the degree of fibrosis, which is fundamental in the pathogenesis of heart failure and the development of adverse outcomes. This has been demonstrated using both cardiac biomarker and cardiac imaging assessment of infarct size [2–4]. The ability to accurately detect and quantify fibrosis is critical to understanding the mechanisms of heart failure, determining viability and prognosis, and for assessing therapeutic response to pharmacotherapy or intervention [5–9].

Regional fibrosis can be detected by cardiac magnetic resonance imaging (CMR) using late gadolinium enhancement (LGE) imaging. The sensitivity of LGE imaging is outstanding and may detect a scar volume of less than 1 gram [10], however in isolation LGE imaging is unable to discriminate between acute and chronic infarction. Regional fibrosis is also observed in non-ischaemic diseases such as myocarditis, hypertrophic cardiomyopathy and sarcoidosis, and the pattern of fibrosis can aid in diagnosis [11].

Close correlation between fibrosis using CMR-LGE and cardiac biomarkers creatine kinase (CK) and troponin (TnI) has been described in several previous studies [12–14], however in these studies there has not been a consistent method for quantitation of LGE. Due to uncertainty regarding the optimal method for quantitative assessment, there is no consensus in the guidelines as to the optimal method for CMR-LGE quantification of scar [15].

In this study, we evaluated the relationship between CMR-LGE assessment of myocardial fibrosis 6 months after ST elevation acute myocardial infarction (STEMI) and biomarkers release obtained in the acute phase of STEMI. We used a range of CMR-LGE thresholds to quantify infarct size. We subsequently assessed agreement between LGE and biomarker in the discrimination of large from small myocardial infarction, and subsequently determined the size of infarction using CMR-LGE thresholds (as a percentage of myocardium) that best agreed with large cardiac biomarker release after STEMI.

Methods

Study Design

Cardiac magnetic resonance studies and analyses were conducted through the Alfred Hospital, Melbourne, Australia. This study involved a subset of patients recruited into the Air Verses Oxygen In myocarDial infarction (AVOID) study, a multicentre, prospective, randomised, controlled trial comparing oxygen (8 L/min) with no supplemental oxygen in patients with STEMI diagnosed on paramedic 12-lead electrocardiogram [16]. Biomarkers were collected during the inpatient admission. Contrast enhanced CMR at 6 months was offered to all patients with confirmed STEMI, who were agreeable to travel to the core site for scanning, and had no contraindications for CMR. Patients suspected of having pre-existing fibrosis (history of ischaemic heart disease) were excluded from analysis, as were patients with complications of AMI likely to result in additional troponin release such as cardiogenic shock. All patients in this study had full revascularisation, with reperfusion to TIMI III flow. Any patients with poor reperfusion were excluded to reduce the impact on kinetics of the cardiac enzymes. (Myocardial blush grade was not measured). The results have been presented previously in abstract form [17].

Biomarker Collection

To assess TnI and CK concentration, blood sampling was conducted at baseline and then 6-hourly for the first 24 hours and 12-hourly out to 72 hours after admission. This allowed estimation of both the peak CK and TnI level, and an estimation of the area-under-curve (AUC) for CK and TnI release over the first 72 hours using trapezoidal integration. The

AUC estimation for cTnI and CK was used to overcome the impact of renal function and variable kinetics of enzyme release and clearance after STEMI/PCI. All cardiac enzymes were assessed using the same cTNI and CK assays, however we did not use a core lab for all enzyme analysis.

CMR Image Acquisition

All CMR scans were performed using a clinical 1.5 T CMR scanner (Signa HD 1.5 T, GE Healthcare, Waukesha, WI, USA). A contiguous short-axis steady-state free precession cine stack (TR = 3.8 ms, TE = 1.6 ms, 30 phases) extending from the mitral valve annulus to the LV apex (8-mm slice thickness, no gap) was acquired to enable volumetric analysis of the left ventricle using the summation of disk method.

Late gadolinium enhancement (LGE) was evaluated 10 minutes after administration of a bolus of gadolinium diethylene triamine pentaacetic acid (0.2 mmol/kg body weight, Magnevist, Schering, Germany) to identify regional myocardial fibrosis using a T1-weighted inversion recovery gradient echo technique (repetition time = 7.1 ms, echo time = 3.1 ms; inversion time [TI] individually determined to null the myocardial signal; slice thickness, 8 mm; matrix, 256 192; number of acquisitions = 2). To enable accurate nullification of healthy myocardium, a TI optimisation sequence was performed 8 minutes after gadolinium administration with a fast gradient echo, inversion recovery, and gated multiphase acquisition, commencing at an inversion time of 150 ms and increasing in 25 ms increments to 250 ms in a single mid-ventricular short-axis slice. Late gadolinium enhancement imaging was performed using standard long-axis views of the left ventricle and a contiguous short-axis stack from the mitral valve annulus to the LV apex.

CMR Image Analysis

All CMR images were independently interpreted by two experienced readers (CMR fellowship trained, >1000 studies reported). The readers were blinded to the subjects' clinical information and the results of other diagnostic tests, including cardiac enzymes.

Regional fibrosis was identified by myocardial LGE, defined quantitatively by myocardial post-contrast signal intensity at a number of SD (range: 2–10) above that within a 0.5–1 cm^2 reference region of remote normal myocardium within the same slice, or the nearest reference slice (if all myocardium is replaced by scar) using commercially available software (CMR42; Circle Cardiovascular Imaging, Inc., Calgary, Canada). Fibrosis was also quantified using the FWHM measure [1], using a reference region around hyper intense myocardium to define maximal signal for the FWHM threshold. Areas corresponding to greater than half the maximum signal intensity are classified as scar.

Volumetric analysis of the left ventricle to calculate the left ventricle ejection fraction (EF) was performed using the summation of disk method. Endocardial and epicardial LV contours were drawn manually for each diastolic and systolic frame, excluding papillary muscles.

Infarct Size Assessment

We assessed the agreement between cardiac biomarkers and CMR threshold levels using a definition of large infarction (CMR-LGE infarct size >10% and peak troponin I > 55 ng/mL). These cut-offs were based on a study by Chia et al. [4], in which a 72-hour troponin I level > 55 ng/ml had good sensitivity and specificity for the detection of a large infarct (>10%) of myocardium as estimated by technetium (Tc)-99 m sestamibi single-photon emission computed tomography myocardial perfusion imaging (SPECT). This study also demonstrated adverse cardiovascular outcomes when the 72-hour troponin level was greater than 95 ng/mL.

We then assessed the troponin I cut-off best associated with a reduction in ejection fraction (LVEF < 50%) on the 6-month CMR using receiver-operator-characteristic (ROC) curve analysis. ROC curve analysis using this definition of large biomarker infarct was used to determine the optimal cut-off for determination of a large CMR-LGE infarct.

Statistic Analysis

All analyses were conducted using SPSS statistics software (version 23.0; SPSS Inc, Armonk, NY, USA). All data are expressed as mean ± SD unless otherwise indicated. We used a two-tailed Student's t-test to compare continuous data, with a p value <0.05 considered statistically significant. The distribution of the biochemical data was assessed using the Shapiro-Wilk test. As the data did not follow a normal distribution, the relationship between biomarkers and LGE was assessed by the Spearman's rank correlation coefficient. Two-way mixed intraclass correlation coefficients (ICC) with absolute agreement were used to compare CMR-LGE visual threshold with SD thresholds. Bland–Altman analysis was used to assess agreement and variability in these measurements. Qualitative variables were compared using Cohen's kappa (κ) to quantify the level of agreement between infarct size assessment by cardiac biomarkers and CMR. The strength of inter-modality agreement was considered excellent if κ = 0.81–1.00, good if κ = 0.61–0.80, moderate if κ = 0.41–0.60, fair if κ = 0.21–0.40, and poor if κ < 0.20. The sensitivity, specificity and diagnostic accuracy areas under the curve and cut-off values were derived using ROC curve analysis using the point that maximised the trade-off between specificity and sensitivity.

Results

Clinical and Demographic Data

Cardiac magnetic resonance was performed 6 months after STEMI on 139 patients of the 441 patients in the AVOID study. Of these patients, 24 had a prior history of ischaemic heart disease, (including previous STEMI or non-STEMI) so were excluded to reduce the likelihood of LGE from previous infarction. Six patients required resuscitation for cardiogenic shock or ventricular arrhythmias, and were also excluded. A further 16 studies were excluded from analysis due to reduced CMR image quality, leaving a total of 93 patients for analysis. Of the 93 studies, 86 had troponin levels

Table 1 Patient demographics and presenting characteristics.

Sex	
• Male	80 (86%)
• Female	13 (14%)
Age (years)	59 ± 10
BMI (kg/m2)	28 ± 5
Risk factors	
• Current or ex smoker	78 (80%)
• Diabetes mellitus	39 (41%)
• Hypertension	43 (45%)
• Dyslipidaemia	40 (42%)
• Renal impairment	0
CMR at 6 months	
• EF%	55 ± 10%
• LVEDV (mL)	176 ± 42
Biomarkers	
• Peak TnI (mcg/L)	71 (26–145)
• Peak CK (U/L)	1859 (954-3681)
Lesion	
• LAD	41 (43%)
• LCx	9 (9%)
• RCA	50 (51%)
PCI	100%

Data presented as n (%), mean ± SD or median (inerquartile range).
Abbreviations: BMI, body mass index; premature CAD, coronary artery disease in first degree relative before the age of 65 years; CMR, cardiac magnetic resonance imaging; EF, ejection fraction; LVEDV, left ventricular end diastolic volume; LAD, left anterior descending artery; LCx, circumflex artery; RCA, right coronary artery; PCI, percutaneous coronary intervention.
Renal imparment – creatinine > 120 mmol/L.

recorded, and all had CK levels recorded. All patients had an LGE pattern consistent with infarction, rather than an alternative diagnosis such as myocarditis or sarcoidosis. The mean time between onset of chest pain and reperfusion was 195 ± 117 minutes.

Peak TnI was recorded at 6 hours in 31 of 86 patients, and at 12 hours in 33 patients (mean 10 ± 6.3 hours). Peak CK was recorded at 6 hours following admission for STEMI in 46 of 93 patients (mean 10 ± 7.2 hours).

Patient characteristics for the 93 CMR studies are provided in Table 1.

Table 3 Correlation between infarct size assessment using biomarkers and CMR-LGE.

Threshold	LGE Mass (grams) (mean ± SD)	LGE % (mean ± SD)	Correlation of semi-automated mass with manual threshold ICC, (95% CI)
Manual	12.3 ± 9.3	14.6 ± 9.9	N/A
FWHM	13.5 ± 9.4	15.9 ± 9.6	0.927 (0.883-0.953)
2SD	24.5 ± 13.9	29.2 ± 12.5	0.537 (−0.092-0.823)
3SD	19.0 ± 12.4	22.1 ± 12.1	0.758 (0.013-0.917)
4SD	15.4 ± 11.2	18.2 ± 11.7	0.914 (0.537-0.969)
5SD	13.2 ± 10.7	15.6 ± 11.2	0.965 (0.942-0.978)
6SD	11.2 ± 9.6	13.5 ± 10.6	0.940 (0.902-0.962)
8SD	8.8 ± 8.4	10.3 ± 9.3	0.873 (0.252-0.957)
10SD	6.6 ± 6.9	7.7 ± 7.9	.696 (−0.033-.891)

Abbreviations: SD, standard deviation; ICC, intra-class coefficient; CI, confidence interval; FWHM, full width-half maximum; LGE, late gadolinium enhancement.

Correlation of LGE With Biomarkers

There was a wide range of infarct size quantification dependent on the threshold used. Well-delineated scar with good image quality had less variation across semi-automated thresholds. The results are displayed in Table 2.

The mass of fibrosis at a 5SD threshold was less than half that estimated at 2 SD.

Table 3 demonstrates LGE correlation between manual threshold, FWHM, and a range of SD thresholds (2–10 SD) with infarct size assessment using biomarkers. A strong, statistically significant correlation was found with all methods of quantification, (Spearman's R range: 0.670–0.874, see Table 4). The correlation was equally strong regardless of biomarker assessment. The relationship between a 5SD threshold and biomarkers is shown in Figure 1.

Comparison Between Manual and Semi-Automated Threshold for LGE

The mean infarct size as determined by manual assessment of LGE was 12.3 ± 9.3 g (14.6 ± 9.9% of myocardium). This was comparable to the automated thresholds at 4SD to 6SD and FWHM (Table 3, Figure 2) with excellent agreement at

Table 2 Spearman's rho: Biomarkers and LGE mass.

	n	Manual	FWHM	2SD	3SD	4SD	5SD	6SD	8SD	10SD
Peak CK	84	0.867	0.788	0.761	0.833	0.858	0.867	0.861	0.871	0.874
Peak TnI	84	0.847	0.783	0.734	0.800	0.841	0.851	0.858	0.856	0.842
AUC CK	84	0.801	0.719	0.684	0.761	0.778	0.778	0.771	0.776	0.779
AUC TnI	84	0.867	0.807	0.750	0.817	0.854	0.862	0.864	0.865	0.855

All correlation coefficients are significant at the level <0.001.
Abbreviations: CK, creatinine kinase; AUC, area-under-curve; Tnl, troponin; FWHM, full width-half maximum.

Table 4 Spearman's rho: Ejection Fraction and infarct size by LGE/biomarkers.

	Manual	FWHM	2SD	3SD	4SD	5SD	6SD	8SD	10SD	Peak CK	AUC CK	Peak TnI	AUC TnI
EF	-0.666	-0.654	-0.582	-0.614	-0.641	-0.646	-0.653	-0.634	-0.615	-0.634	-0.556	-0.664	-0.654

All correlation coefficients are significant at the level <0.001.

Abbreviations: EF, ejection fraction; FWHM, full width-half maximum; SD, standard deviation; CK, creatine kinase; AUC, area-under-curve; Tnl, troponin.

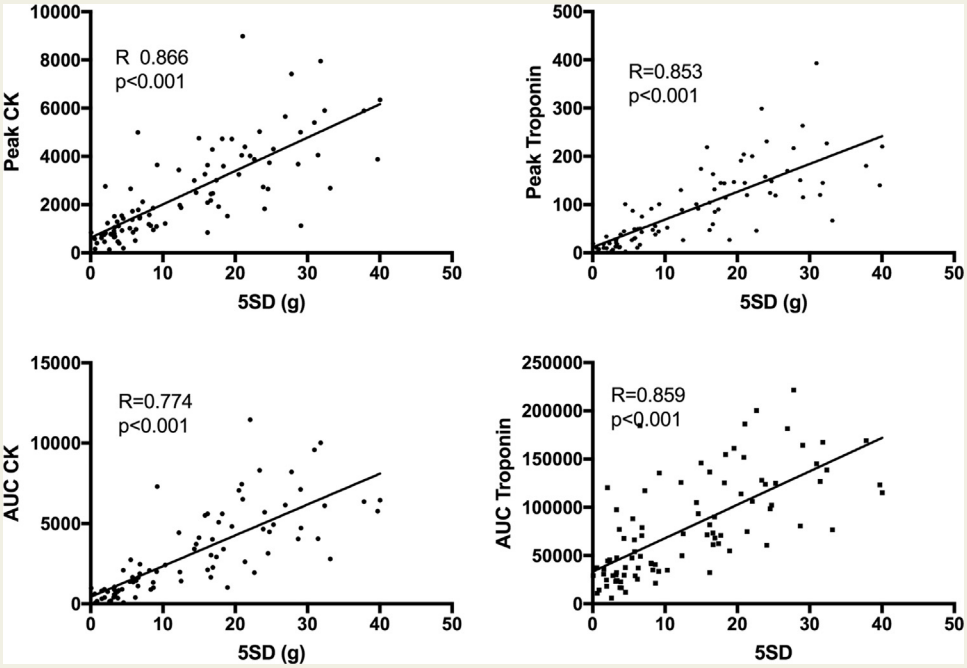

Figure 1 Graphical representation of the relationship between infarct size assessment by biomarkers and cardiac magnetic resonance-late gadolinium enhancement (CMR-LGE) at a 5SD threshold.

these thresholds (ICC 0.914–0.965). Inter-observer and intra-observer variation for the manually set threshold was assessed, and the ICC was 0.89 and 0.91, respectively, $p < 0.001$ for both measures.

Relationship of Infarct Size With Ventricular Function Acutely and at 6-Month Follow-Up

There was a modest negative correlation between ejection fraction and infarct size measured with LGE (at any threshold) and with biomarkers (Table 4, Figure 3). The highest correlation was between ejection fraction and a manually set threshold ($r = -0.666$, $p < 0.001$), however the confidence intervals overlapped for all methods.

Receiver-operator-characteristic curve analysis demonstrated a peak troponin >100 had an 85% sensitivity and 80% specificity for predicting a LVEF <50% at 6 months post revascularisation. The majority of patients (>94%) were NYHA class I at 6 months post revascularisation. There was no association between functional class and infarct size ($p = 0.84$).

Agreement Between CMR and Cardiac Biomarkers in the Diagnosis of a Large Myocardial Infarction

Using cut-offs thought to be sensitive for the determination of a large infarct (infarct size > 10% and peak troponin I >55 ng/mL), the strongest agreement (based on Cohen's kappa values) was found at 8SD, with good agreement for manual, FWHM and 4–8 SD threshold. Using higher thresholds for both CMR-LGE and peak troponin based on cut-offs associated with adverse cardiovascular outcomes [2,4] altered the strongest agreement to 4SD (Table 5, Figure 4), again with good agreement for the same signal intensity thresholds.

Using ROC curve analysis of our data a peak troponin >100 ng/mL had the best sensitivity and specificity for predicting a reduction in LVEF <50% at 6 months. Using a peak troponin of greater than 100 ng/mL as the biochemical reference standard for a large infarct (which is very close to the cut-off of 95 ng/mL advocated in previous studies), CMR-LGE had a very strong capacity to discriminate small from

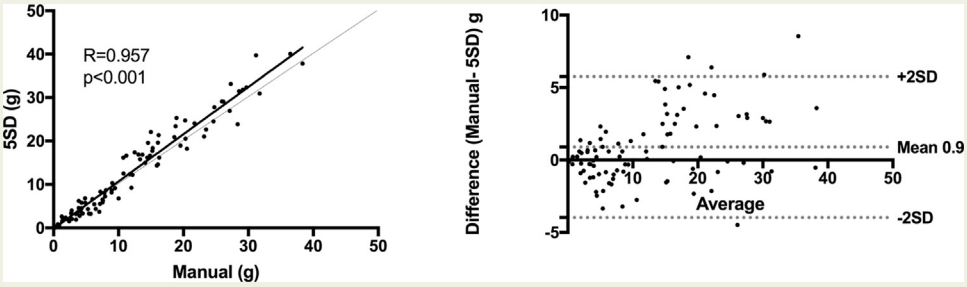

Figure 2 a: Caomparison of cardiac magnetic resonance-late gadolinium enhancement (CMR-LGE) measured using a manual threshold and 5SD threshold. The solid line is the trend-line, the dashed line is the line of identity. b: Bland-Altman plot of the mean values and differences between CMR-LGE at visual threshold and 5SD threshold.

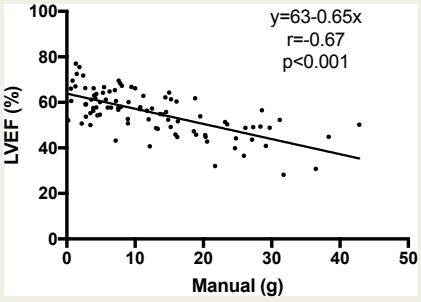

Figure 3 Comparison of cardiac magnetic resonance-late gadolinium enhancement (CMR-LGE) measured using a manual threshold with ejection fraction using a volumetric stack.

large myocardial infarction (Table 6, Figure 5). Table 6 provides a cut-off for large CMR-LGE myocardial infarction according the chosen signal intensity threshold.

Discussion

In this study we evaluated image intensity thresholds for quantitating fibrosis using CMR-LGE. Our results show a consistently strong correlation between cardiac biomarkers and CMR-LGE at all signal intensity thresholds.

There appears to be small, non-significant differences in the strength of the correlation between CMR-LGE quantification and biomarkers, whether using an automated SD, FWHM or a manually set threshold. By analysis of the agreement between CMR-LGE and cardiac biomarkers, 4SD had

Table 5 Agreement between biomarker and CMR_LGE in discriminating small from large infarction at set thresholds using Cohen's kappa.

n = 86	Manual	FWHM	2SD	3SD	4SD	5SD	6SD	8SD	10SD
>10% LGE/TnI > 55	0.716	0.543	0.159*	0.340	0.642	0.692	0.695	0.722	0.546
>19.5%LGE/TnI > 95	0.576	0.609	0.377	0.680	0.761	0.683	0.652	0.402	0.309

All kappa have $p < 0.001$ except those marked *, with a $p < 0.01$.

Abbreviations: LGE, late gadolinium enhancement; FWHM, full width-half maximum; SD, standard deviation.

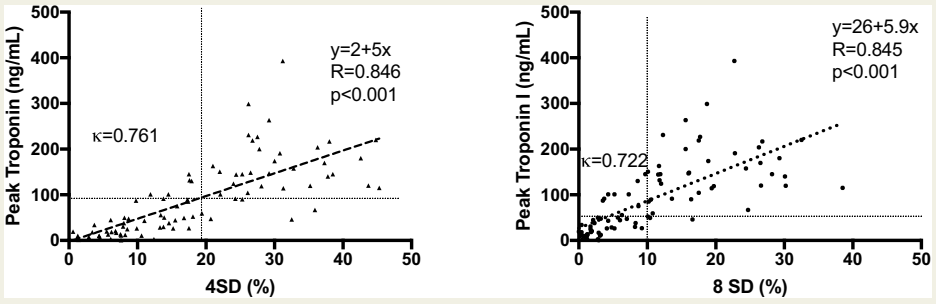

Figure 4 Comparison of cardiac magnetic resonance-late gadolinium enhancement (CMR-LGE) (at 4SD and 8SD) with peak troponin level. Cohen's kappa demonstrates the agreement between the two measures in defining a large infarct at pre-specified levels (dashed lines).

Table 6 CMR identification of large infarction defined biochemically as a peak troponin > 100 ng/mL.

n = 93	ROC AUC*	Infarct Size (%)	Sensitivity (%)	Specificity (%)
Manual	0.941	13	92	91
FWHM	0.907	17	86	86
2SD	0.892	26	83	84
3SD	0.919	21	86	84
4SD	0.931	17	89	86
5SD	0.935	15	89	84
6SD	0.931	13	86	87
8SD	0.934	9	89	88
10SD	0.907	5	86	84

Abbreviations: FWHM, full width-half maximum; SD, standard deviation; ROC, receiver operating characteristic; AUC, area-under-curve.
*There is no significant difference in AUC, with $p > 0.3$ for all comparisons using DeLong's method [24].

the strongest agreement when a larger infarct size was selected, while 8SD was the strongest when more specific criteria were chosen. While this does not suggest one is a better technique than another, it does suggest that selection of CMR-LGE thresholds should be selected with consideration of the study question. We have provided binary discriminator cut-offs for infarct size at the range of image intensity thresholds. Table 6 demonstrates the excellent predictive capacity to discriminate a large from a small infarct, and the percentage myocardium best associated with a clinically large infarct across thresholds. While no threshold was a better discriminator of infarct size, the variability in myocardial percentage across thresholds highlights the increasing specificity of LGE as the SD increases. For example, if using a signal intensity threshold of 5SD, we would consider a clinically significant, large infarct as an LGE percentage greater than 15% of the total myocardium.

Not surprisingly there was an association between the size of the infarct and heart function assessed by ejection fraction. The correlation was consistent across the range of semi-automated thresholds. The study was not powered to find a correlation with functional status (by New York Heart Association (NYHA) class), and we do not have data comparing the scar burden with other markers such as myocardial strain.

These findings are consistent with the histological findings of Iles et al. [18], where a 6SD threshold was recommended, and Moravsky et al. [19], where the closest correlation of histological fibrosis specimens was found at 5SD ($r = 0.78$, $p < 0.0001$). The correlation between biomarker release and CMR-LGE in our study (up to $r = 0.853$, $p < 0.001$ for AUC TnI at LGE 5 SD) was equally valuable, supporting the use of biomarkers as a readily available accurate predictor of infarct size at 6 months. Our findings are consistent with a study by Beek et al. [20], where thresholding contrast images at 6SD best predicted segmental functional outcome after revascularisation, but the difference with other methods was small and non-significant. Our results

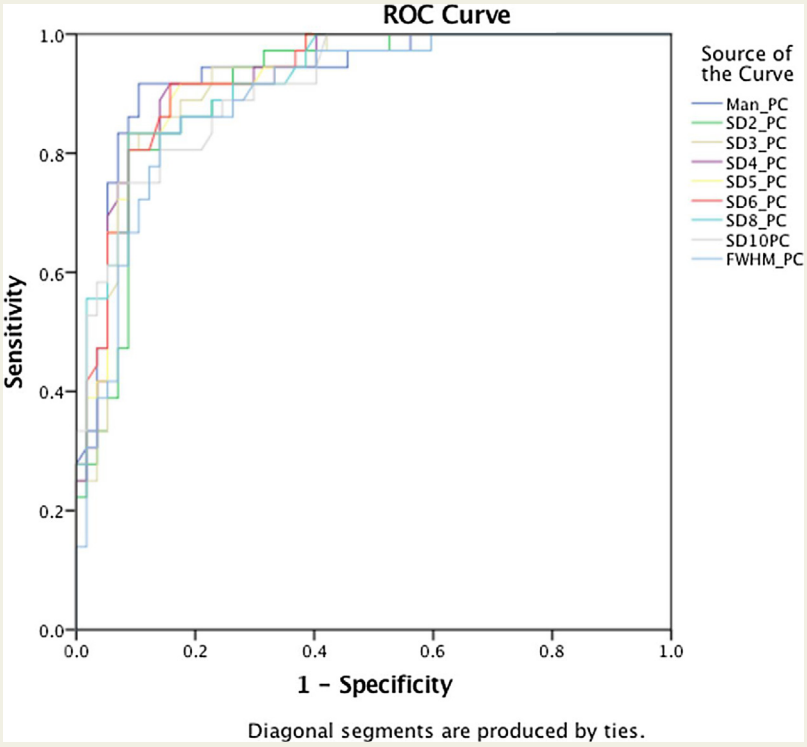

Figure 5 ROC curve of CMR-LGE thresholds and large infarction defined by peak troponin I greater than 100 ng/mL. Abbreviations: ROC, receiver operating curve; CMR, cardiac magnetic resonance; LGE, late gadolinium enhancement.

found that a manual threshold for CMR-LGE approximates that assessed using automated thresholds across a range of 4–6SD, and also has good agreement with the FWHM method.

Accurate detection of fibrosis is an important capability of CMR. Fibrosis has been shown to have an impact on prognosis in ischaemic and non-ischaemic cardiomyopathy [7,8]. The ability to accurately determine viability has been used clinically, impacting on decisions to proceed with revascularisation procedures, traditionally based on a visual estimate of scar thickness on CMR. Further investigation into the use of semi-automated thresholds to determine scar thickness has the potential to better define non-viable myocardium. Echocardiographic studies have demonstrated that reduced global longitudinal strain (GLS) in the acute phase of infarction is predictive of adverse left ventricular remodelling [21,22], and may be reflective of myocardial viability. The use of scar quantification may help further define the role of GLS in the early assessment of the myocardium post infarction. We believe that a consistent approach should be taken to the interpretation of myocardial fibrosis, however the choice of image intensity thresholds for the quantification of CMR-LGE still depends on individual preference and experience.

A limitation of the study is the effect of LV remodelling and differential scar shrinkage altering the size of scar relative to remote myocardium. We chose to perform CMR late (6 months, chronic phase) rather than in the acute phase of infarct recovery. This time period was selected to reduce the impact of swelling, oedema and capillary leakage in the assessment of infarct size using LGE, and was based on a hypothesis that late scar was proportional to myocyte necrosis and biomarker release. While patients with TIMI <3 were excluded, we were unable to correct for the variability in cardiac enzyme release in patients with microvascular obstruction despite TIMI 3 flow. However, in our study, the correlation between CMR-LGE in the chronic phase and cardiac biomarkers was significantly stronger than that reported using a range of signal intensity thresholds in the acute phase [23], supporting the use of the data in our analysis.

The lack of histological validation of infarct size assessment does limit the generalisability of this study, however, this is impractical in large-scale human studies. We also made the assumption that the baseline STEMI was solely responsible for the LGE seen at 6 months, however, it is possible that subjects had pre-existing scar or silent ischaemia during the follow-up period. However, we excluded cases where the size of biomarker release may have been contributed to by factors other than coronary occlusion (arrhythmia, cardiogenic shock, TIMI II flow post revascularisation), and cases where there was a high index of suspicion for prior infarction. The number of patients requiring exclusion is in itself a limitation of the study.

Conclusion

Infarct size assessment with biomarkers correlates strongly with CMR-LGE, irrespective of the method chosen to quantify scar, and has good agreement in the determination of large myocardial infarctions. Ultimately, the size of scar is heavily dependent on the chosen method, and this must be taken into consideration when interpreting CMR images.

Declarations

Ethical Approval and Consent to Participate

The study was approved by the Alfred Hospital Ethics Committee (Melbourne, Australia) and carried out under their guidelines. Prior to inclusion in the study written informed consent was obtained from all participants.

Consent for Publication

All authors declare their consent for publication.

Availability of Supporting Data

The anonymised datasets analysed during the current study are available from the corresponding author, on reasonable request.

Competing Interests

There are no competing interests.

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Authors' Contributions

BC – conception, design and analysis and interpretation of data, and drafting of the manuscript; DS – patient recruitment, analysis of data and revision of the manuscript; JH – conception and design and revision of the manuscript; AE – analysis and interpretation of data, revision of manuscript; XW – analysis and interpretation of data; SB, ZN, MS, JB, PC, BB, IM, DK – members of AVOID steering committee; LI – revision of manuscript; AJT – conception, design and analysis and interpretation of data, revision of the manuscript and final approval.

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