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A non-contrast CMR risk score for long-term risk-stratification in reperfused ST-segment elevation myocardial infarction

Brief Title: Non-contrast CMR risk score for risk-stratification in STEMI

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Abstract

Background: A cardiovascular magnetic resonance (CMR) risk score including left ventricular ejection fraction (LVEF), myocardial infarct (MI) size and microvascular obstruction (MVO) was recently proposed to risk-stratify ST-segment elevation myocardial infarction (STEMI) patients.
Objective: We compared the prognostic value of a non-contrast CMR risk score for the composite of all-cause death, non-fatal myocardial infarction and new congestive heart failure.
Methods: The Eitel CMR risk score and Global Registry of Acute Coronary Events (GRACE) score were used as a reference (Score 1: acute MI size ≥19% LV, LVEF≤47%, MVO>1.4% LV and GRACE score). MVO was replaced by intramyocardial haemorrhage (IMH) in Score 2 (acute MI size ≥19% LV, LVEF≤47%, IMH and GRACE score). Score 3 included only LVEF≤45%, IMH and GRACE score.
Results: There were 370 patients in the derivation cohort and 234 patients in the validation cohort. In the derivation cohort, the 3 Scores performed similarly and better than GRACE score to predict the 1-year composite endpoint with C-statistics of 0.83, 0.83, 0.82 and 0.74, respectively. In the validation cohort, there was good discrimination and calibration of Score 3, with a C-statistic of 0.87 and P=0.71 in a Hosmer-Lemeshow test for goodness of fit, on the 1-year composite outcome. Kaplan-Meier curves for 5-years composite outcome showed that those with LVEF≤45% (high-risk) and LVEF>45% and IMH (intermediate-risk) had significantly higher cumulative events than those with LVEF>45% and no IMH (low-risk), log-rank tests: P=0.02, 0.03 respectively. The hazard ratio for the high-risk group was 2.3 (95%CI 1.1-4.7) and for the intermediate-risk group was 2.0 (95%CI 1.0-3.8), and these remained significant after adjusting for the GRACE score.
Conclusions: This non-contrast CMR risk score has comparable performance to an established risk score and STEMI patients could be stratified into low-risk (LVEF>45% and no IMH), intermediate-risk (LVEF>45% and IMH) and high-risk (LVEF≤45%).

Clinical Trial: Clinicaltrials.gov NCT02257294 NCT02072850

Key words: ST-segment elevation myocardial infarction, magnetic resonance imaging, risk-

Abbreviations:
PCI: percutaneous coronary intervention
STEMI: ST-segment elevation myocardial infarction
GRACE: Global Registry of Acute Coronary Events
TIMI: Thrombolysis in Myocardial Infarction
CMR: Cardiovascular magnetic resonance
MI: myocardial infarct
LVEF: left ventricular ejection fraction
MVO: microvascular obstruction
IMH: intramyocardial hemorrhage
RCT: randomized controlled trial
TIMI: Thrombolysis in Myocardial Infarction
LGE: late gadolinium enhancement
HR: hazard ratio

Introduction

In the current era of primary percutaneous coronary intervention (PCI), mortality in patients with acute ST-segment elevation myocardial infarction (STEMI) has fallen compared to previous years and has now plateaued, but morbidity remains significant(1). The prognosis of reperfused STEMI patients differ depending on their baseline risk profile, ischaemic time and infarct size(2–4). Therefore, early risk-stratification would be invaluable to stratify their management and onwards follow-up accordingly, in order to improve their long-term outcomes.

Several risk scores are available for risk-stratification of STEMI patients during the index hospitalization(5). The Global Registry of Acute Coronary Events (GRACE)(6,7), and the Thrombolysis in Myocardial Infarction (TIMI)(4) risk scores have been the most widely validated. The GRACE score can be used for all types of acute coronary syndromes and can predict in-hospital and 6-month mortality. On the other hand, the TIMI risk score specifically predicts the likelihood of mortality at 30-days post-STEMI (4). Of note, the cohorts from which these risk scores were derived consisted predominantly of patients treated by thrombolysis. Furthermore, these risk scores do not predict longer-term outcomes, including risk of developing heart failure. Cardiovascular magnetic resonance (CMR) is the reference test for quantifying myocardial infarct (MI) size, LV volumes, ejection fraction (LVEF) and infarct pathology (8–11). Stiermaier et al(12) recently proposed a CMR risk score (henceforth referred to as the Eitel CMR risk score) that included LVEF, MI size and microvascular obstruction (MVO) to predict a composite of all-cause death, non-fatal myocardial infarction and new congestive cardiac failure at 12 months. They found that the CMR parameters provided incremental prognostic value over clinical parameters(12). Of note, they did not include intramyocardial hemorrhage (IMH) in their model, yet this is known to have greater prognostic value than MVO(13,14).

Contrast-enhanced CMR for STEMI is not widely used in daily practice because of accessibility, patient selection (e.g. glomerular filtration rate > 30 ml/min/1.73m^2), lack of evidence of incremental clinical value, and cost.(10) Increasingly, new diagnostic possibilities are emerging with ultrashort CMR protocols without use of contrast media(15). Whether an abbreviated non-contrast CMR protocol, including data on LVEF and IMH only would have prognostic value comparable to a contrast-enhanced CMR study is unknown. A non-contrast CMR exam may be brief (15 – 20 minutes), better tolerated, and accessible to a broader, less selected population.

Therefore, in this study, we hypothesized that a non-contrast CMR risk score consisting of only LVEF and IMH on the acute CMR scan (henceforth referred to as Glasgow CMR Risk Score) would perform equally well compared to the Eitel CMR risk score(12) in predicting 1-year clinical outcomes, after adjusting for baseline clinical risk factors. Secondly. We aimed to assess the performance of the Glasgow CMR risk score to predict 5-years clinical outcomes.

Methods

We aimed to first assess the performance of the Glasgow CMR score against the Eitel CMR score to predict the 1-year composite outcome of all-cause death, non-fatal myocardial infarction and new congestive cardiac heart failure in the derivation cohort, after adjusting for baseline clinical risk factors (GRACE risk score). The Glasgow CMR score was then applied to the validation cohort to assess its discrimination and calibration for the 1-year composite outcome of the above endpoints. Lastly, the Glasgow CMR score was used to assess its prognostic performance on 5-years clinical outcomes.

The derivation cohort consisted of patients from the T-TIME trial (A Trial of Low-Dose Adjunctive Alteplase During Primary PCI; NCT02257294), which has been previously

published(16–19). This multi-centre trial recruited patients between March 2016 and December 2017, and investigated the effect of adjunctive low-dose intracoronary alteplase on MVO, in patients presenting within 6 hours of onset of STEMI(17). This trial was approved by the West of Scotland Research Ethics Service (reference: 13-WS-0119). Low-dose intracoronary alteplase failed to show a reduction in MVO (17) and in the subgroup presenting between 4 to 6 hours, low-dose intracoronary alteplase was associated with a greater extent of MVO(18). Follow-up data on the 1-year composite of all-cause death, non-fatal myocardial infarction and new congestive cardiac heart failure was available for this cohort.

The validation cohort (BHF MR-MI: NCT02072850) has been reported in previous studies(13,20–23). In brief, this was a prospective study with consecutive eligible patients recruited from a single centre between May 2011 and November 2012 following informed consent. This study was approved by the National Research Ethics Service (reference: 10-S0703-28). The eligibility criteria included an indication for primary PCI or thrombolysis for STEMI and exclusion criteria were standard contraindications to CMR. Follow-up data on 1-year and 5-years composite of all-cause death, non-fatal myocardial infarction and new congestive cardiac heart failure were available for this second cohort.

Only those patients with data on LVEF, MI size, MVO, IMH and GRACE score (GRACE 2.0, https://www.mdcalc.com/grace-acs-risk-mortality-calculator, which includes age, heart rate and systolic blood pressure on admission, creatine, cardiac arrest on admission, ST-segment deviation of electrocardiogram, abnormal cardiac enzymes and Killip Class) at baseline from both previous cohorts were included in this study. We used the GRACE score(6,7) in for risk prediction rather than the Thrombolysis in Myocardial Infarction (TIMI) risk score(4) as the former has previously been shown to perform better(24) in patients with acute coronary syndrome to predict long-term mortality.

CMR image analysis

The methods for CMR analyses have been published previously (13,17,18,20–23). In brief, MI size was quantified using computer-assisted planimetry of the late gadolinium enhancement (LGE) images acquired at 15 minutes post-contrast, and the territory of LGE was delineated using a signal intensity threshold of >5 standard deviations (SD) above a remote reference region and expressed as a percentage of total LV mass (%LV). MVO was defined as a dark zone on LGE imaging, quantified as %LV and in a binary fashion as present or absent. IMH was identified on the T2* CMR maps as a region of reduced signal intensity within the infarcted area with a T2* value of <20ms and was quantified as either present (if present on at least one short-axis T2* map) or absent (if absent on all of the basal, mid and apical short-axis T2* maps)(10).

LV volumes and LVEF were assessed using computer-assisted planimetry on the short-axis cine images with minimal manual adjustment when required and following standard recommendations(8).

The Eitel CMR risk score

The Eitel CMR risk score, as previously described(12) includes LVEF≤47%: 1 point; acute MI size ≥19% LV: 1 point; and MVO>1.4% LV: 2 points. Those with a score of 0 or 1 are considered to be in the low-risk group and those with a score of >1 are in the high-risk group.

Statistical analysis

Statistical analysis was performed using SPSS version 27 (IBM Corporation, Illinois, US). Continuous data were expressed as mean ± SD or median (lower and upper quartile) and categorical data were reported as frequencies and percentages.

For the risk predictions scores, Score 1 consisted of GRACE score and Eitel CMR risk score parameters (LVEF≤47%, acute MI size ≥19% LV and MVO>1.4% LV). MVO was

replaced by IMH (presence or absence) in Score 2 (GRACE score, LVEF≤47%, acute MI size ≥19% LV and IMH). Score 3 consisted of GRACE score, LVEF≤45% (rounded to the nearest 5% for simplicity) and presence of IMH only.

In the derivation cohort, the scores were assessed using multivariable binary logistic regression analysis and predicted probabilities for each score were generated to construct receiver operating characteristics (ROC) curves. C-statistics (area under the curve) were used to assess the discriminatory power of the risk prediction models and the ROC curves were compared using the method by De Long et al(25). In order to avoid over-fitting of the model, care was taken not to exceed the ratio of 10 events per variable included in the final model, which is the widely accepted minimum criterion(26). To test for non-inferiority between the Score 1 and Score 3, the non-inferiority threshold for the difference in area-under-the-curve between the 2 scores was set at ±0.10.

In the validation cohort, discrimination was assessed using the C-statistic for Score 3 to predict the 1-year composite outcome of all-cause death, non-fatal myocardial infarction and new congestive cardiac heart failure. Calibration was assessed by dividing the patient population into 6 groups based upon the magnitude of the derived risk score and plotting the predicted probability against the observed percentage of 1-year composite endpoints. The Hosmer–Lemeshow test was applied to determine goodness of fit. Kaplan-Meier curves were used to assess survival up to 5 years per group as stratified by the non-contrast CMR risk score and were compared using log-rank tests. The incidence of all-cause death, non-fatal myocardial infarction and new congestive cardiac heart failure during the follow-up period per CMR risk score group was analyzed using Cox proportional hazards regression (with censoring of data to the date of occurrence of the primary endpoint, lost to follow-up, withdrawal from the study) and the hazard ratios (HRs) were computed with 95% confidence interval. Adjusted HRs were also calculated after accounting for GRACE score (low/

intermediate risk: GRACE score <128; high risk: GRACE score ≥128). All statistical tests were two-tailed, and P<0.05 was considered statistically significant.

Results

There were 370 patients in the derivation cohort and 234 patients in the validation cohort with full CMR dataset and GRACE score.

Patient characteristics

The characteristics of the patients in both cohorts are detailed in Table 1. The mean age was similar but there were more women in the validation cohort. There were more patients with a pre-PCI TIMI (Thrombolysis in Myocardial Infarction) coronary flow grade of 0 and a post-PCI TIMI coronary flow grade of 3 in the validation cohort. Two thirds of the patients were in the high-risk group as per the GRACE score. All the participants in the derivation cohort completed 1-year follow-up. The median follow-up duration for the validation cohort was 2082 days (5.7 years), with an interquartile range of 1969 to 2198 days. Of note, CMR was performed on average 2 days later in the validation cohort than in the derivation cohort.

CMR characteristics

The CMR characteristics are summarized in Table 2. In the derivation cohort, the median acute MI size was 26(18-35)% LV mass, the mean acute LVEF was 49±8%, MVO occurred in 45% and IMH in 43% of the patients. On the other hand, in the validation cohort, the median acute MI size was lower at 18 (7-29)% LV mass, the mean acute LVEF was higher at 55±10%, but the incidences of MVO (53%) and IMH (41%) were similar.

In the combined cohort of 604 patients, all patients with IMH also had MVO and represented 87% of those with MVO. IMH occurred in 62% of patients with an MI size≥19% LV mass; in 93% of patients with MVO>1.4% LV mass; and in 67% of patients with LVEF<47%.

Clinical outcomes

The 1-year composite outcome of all-cause death, non-fatal myocardial infarction and new congestive cardiac heart failure occurred in 38/370 (10.3%) patients in the derivation cohort and in 25/234 (10.7%) patients in the validation cohort. The 5-years composite outcome in the validation cohort occurred in 49/234 (20.9%) patients.

Prognostic performance of the CMR risk scores to predict 1-year clinical outcomes in the derivation cohort

The C-statistic for GRACE score to predict the 1-year composite outcome was 0.74 (95%CI 0.65-0.82). The C-statistic of a score (Score 1) including GRACE score and Eitel CMR risk score (LVEF≤47%; acute MI size ≥19 % LV mass; and MVO>1.4% LV mass) was 0.83 (95%CI 0.77-0.90). When MVO was replaced by IMH (Score 2), GRACE score, LVEF≤47%, acute MI size ≥19 % LV mass and IMH performed similarly well with a C-statistic of 0.83 (95%CI 0.77-0.90). Lastly, when only GRACE score, LVEF≤45% and IMH were included (Score 3), the C-statistic was 0.82 (95%CI 0.75-0.88). Area-under-the-curve comparison showed no statistical difference between the 3 scores (Score 1 versus Score 2: P=0.86; Score 1 versus Score 3: P=0.33; Score 2 versus Score 3: P=0.32). However, all 3 scores performed better that GRACE score alone (p values for area-under-the-curve comparison for scores 1, 2 and 3 against GRACE score of 0.004, 0.005 and 0.03, respectively) (Figure 1).

Non-inferiority testing between Score 1 and 3 in the derivation cohort showed that the difference in area-under-the-curve was 0.02 with the 95%CI of -0.02 to 0.06 being within the non-inferiority margin of ±0.10.

Prediction of clinical outcomes in the validation cohort

Score 1 and 3 were highly correlated with a Pearson correlation coefficient of 0.96 between the 2 scores when their predicted probabilities of the scores were compared for 1-

year clinical outcomes. Score 3 showed good discrimination when it was applied to the validation cohort with a C-statistic was 0.87 (95%CI 0.78-0.96) (Figure 2a). There was also good calibration of Score 3, as shown on the calibration plot in Figure 2b with a P value of 0.71 by Hosmer-Lemeshow test for goodness of fit on 1-year clinical outcome.

Score 1 and 3 also performed well to predict 5-years clinical outcomes in the validation cohort with C-statistics of 0.68 (95%CI 0.59-0.76) and 0.65 (95%CI 0.56-0.74), respectively, with a P value of 0.22 and with a difference in area-under-the-curves of 0.03 (95%CI -0.02 to 0.07), which was within the non-inferiority margin. Furthermore, Scores 1 and 3 were highly correlated with a Pearson correlation coefficient of 0.86 between the 2 scores for the 5-years clinical outcomes.

The Eitel CMR risk score to predict 5-years clinical outcome

For the Eitel CMR risk score, those in the high-risk group (score >1) had a HR of 2.3 (95%CI 1.3-4.3), P=0.003, when using those in the low-risk group (score of 0–1) as reference and this remained significant [HR 1.3 (95%CI 1.3-4.2), P=0.005] after adjusting for GRACE score groups. Kaplan-Meier curve analysis confirmed that those with a score of >1 had significantly higher cumulative number of events of the composite endpoint than those with a score of 0–1 (log-rank test P=0.02) (Figure 3a).

The Glasgow CMR risk score to predict 5-years clinical outcome

The Cox proportional hazard analysis showed that the adjusted HR for the presence of IMH to predict the 1-year composite endpoint was 5.9 (95%CI 2.2-15.7), P<0.001, and that of LVEF≤45% was 7.2 (95%CI 3.2-16.6), P<0.001. Based on the HRs, a score of 1 was allocated for presence of IMH and for LVEF≤45%. Adjusted HRs for a score of 1 was 4.0 (95%CI 1.1-15.1), P=0.04 and that of a score of 2 was 7.6 (95%CI 5.7-70.1), P<0.001. However, 67% of patients with an LVEF≤45% also had IMH (P<0.001). Therefore, a

simplified risk score was constructed as follows: LVEF≤45% (irrespective of presence or absence of IMH): high-risk group; LVEF>45% and presence of IMH: intermediate-risk group; and the remainder of the patients would fall into a group with LVEF>45% and no IMH: low-risk group.

For the 5-years composite endpoint, the pooled event rates over the duration of follow-up were 15% (18/124), 27% (18/68) and 31% (13/42) for those for those in the low-risk, intermediate-risk and high-risk-group, respectively. Kaplan-Meier curves for the 5-years composite endpoint based on these 3 groups are shown in Figure 3b. With those in the low-risk group as reference, those in the intermediate-risk group had a HR of 2.0 (95%CI 1.0-3.8), P=0.04 and those in the high-risk group had a HR of 2.3 (95%CI 1.1-4.7), P=0.02. The HRs remained significant after adjusting for GRACE score groups with adjusted HRs of 2.0 (95%CI 1.1-3.9) and 2.1(95%CI 1.0-4.2), respectively.

Discussion

We have found that in a cohort of unselected STEMI patients, the Glasgow CMR Risk Score, including only LVEF and IMH data, performed as well as the Eitel CMR risk score, which included LVEF, MI size and MVO. Furthermore, this non-contrast CMR risk score performed well in the BHF MR-MI population despite this cohort having distinctly different characteristics in terms of inclusion criteria. Of note, unlike the Eitel CMR risk score that stratified patients into 2 groups, the Glasgow CMR Risk Score stratified patients into high-risk, intermediate risk and low-risk groups: those with LVEF≤45% at baseline (irrespective of presence or absence of IMH) had the worst prognosis in terms of the composite endpoint, followed by those with LVEF>45% and IMH; while those with LVEF>45% and no IMH had the best prognosis after a median follow-up of 5.7 years (Figure 3b). The simplicity and prognostic value of our score may be helpful in clinical practice.

Lastly, the Eitel CMR risk score also performed well to risk-stratify patients into low-risk and high risk up to 5 years follow-up.

The Glasgow CMR Risk Score performed similarly well with and without LGE or MVO as IMH occurred in the majority of patients with MI size≥19% LV mass (62%) and MVO>1.4% LV mass (93%). As a result, removing LGE and substituting MVO with IMH in the model did not change the C-statistic significantly.

The Glasgow CMR Risk Score represents a generalizable, clinically relevant advance when considered against prior studies (12). Although the number of patients in our study was less than that in Stiermaier et al(12) , we specifically evaluated IMH using T2* mapping and had follow-up data up to 5 years in the validation cohort.

Our findings are clinically relevant for the management of reperfused STEMI patients. First of all, since contrast media is not required, the abbreviated CMR protocol would facilitate its adoption into clinical practice; this approach would not preclude those with estimated glomerular filtration rate <30mL/min/1.73m^2; patients would potentially tolerate the scan better; and the associated cost would likely to be less. Secondly, this would open the way to investigate whether a management plan tailored to their risk profile, stratified by this risk score, would improve their outcomes. For example, those in the highest risk group could receive further novel adjunctive therapies (e.g. colchicine) on top of routine post-STEMI medications; more aggressive uptitration of their prognostic medications such as beta-blockers, angiotensin-converting enzyme inhibitors and mineralocorticoid receptor antagonists; in-depth monitoring for non-sustained ventricular tachycardia with implantable loop recorders and follow-up echocardiography to identify those developing adverse LV remodeling need for primary prevention ICD. Whether the prognosis of those in the intermediate risk group could be improved by initiating them on mineralocorticoid receptor antagonists (currently only indicated in those with LVEF≤40% and signs and symptoms of

heart failure or diabetes mellitus)(27) on top of routine post-STEMI medications and close monitoring for non-sustained ventricular tachycardia could be assessed in future studies. Lastly, whether those in the lowest risk group would benefit from early discharge from hospital and shorter treatment with beta-blockers and angiotensin-converting enzyme inhibitors and would fare equally well to those on longer term treatment warrants further investigation.

Limitations

Our study was retrospective in nature with post-hoc analysis of data from 2 previously published cohorts of moderate sample sizes. We included a cohort of relatively low-risk STEMI survivors with no contraindication to a comprehensive CMR scan. As a result, the number of events were relatively small at 1-year in both the derivation and validation cohorts. Although we tested our model in a validation cohort, it was a single-centre cohort and prospective studies are needed to confirm our findings in a multi-center setting, with larger patient numbers. Only 3 short-axis T2* maps were used for this study and therefore small areas of IMH may have been missed. However, the prognostic significance of these small areas of IMH is not known. Future studies could compare the performance of a minimum of basal, mid and short-axis T2* mapping or full LV-coverage T2* mapping and its impact on prognostic significance and scan time. Feature-tracking CMR data such as global longitudinal strain, which has previously been shown to be prognostic(28,29), were not available in our cohort and whether global longitudinal strain would improve the risk stratification over LVEF in the proposed model warrants future investigation.

Conclusion

Using the Glasgow CMR Risk Score, which can be acquired using an abbreviated non-contrast CMR protocol, reperfused STEMI patients could be stratified at a very early

stage following their index event into low-risk (LVEF>45% and no IMH), intermediate-risk (LVEF>45% and IMH) and high-risk (LVEF≤45%, irrespective of presence or absence of IMH) groups of developing long-term adverse clinical events. This score performed similarly well to the contrast enhanced CMR score previously proposed (the Eitel CMR risk score) and after adjusting for the baseline clinical risk profile (GRACE score). Future studies are required to confirm our findings and assess whether its implementation in clinical practice could be used to stratify therapies that would improve patients' outcomes.

Clinical Perspectives

Competency in medical knowledge

This study has shown that a non-contrast CMR scan with data on LVEF and IMH can risk-stratify reperfused STEMI patients equally well to an existing contrast-based CMR score using data on LVEF, MI size and MVO, on top of clinical risk score. The non-contrast CMR risk score (Glasgow CMR risk score) can stratify patients into high-risk (LVEF≤45%), intermediate-risk (LVEF>45%) and IMH present) and low-risk (LVEF>45% and IMH absent) groups.

Translational outlook

Further studies are needed to confirm the findings of this study and whether MI size by LGE could be dropped in future studies as this approach has the appeal of keeping scan time short, does not preclude patients with a contraindication to gadolinium chelate, would make a CMR scan cheaper for health providers and eventually more widely available to patients.

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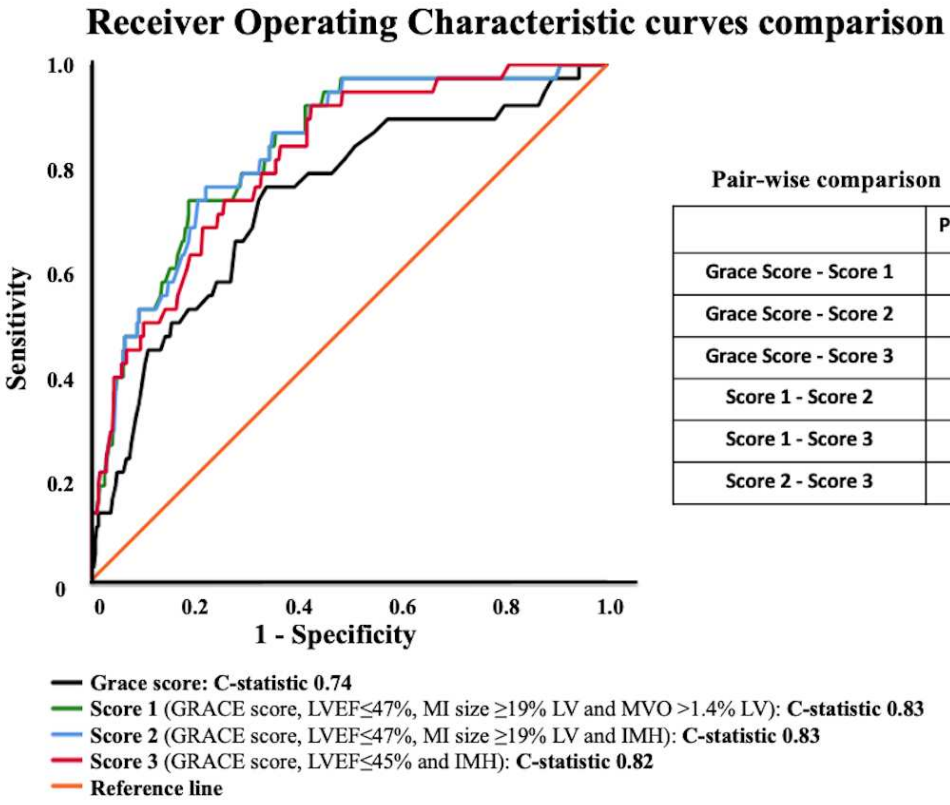
Figure Legends

Figure 1. Receiver operating characteristic curve comparisons of the 3 different scores against the GRACE score to predict 1-year clinical outcome
The 3 scores (Score 1: Grace score, LVEF≤47%, acute MI size ≥19%LV and MVO>1.4%LV; Score 2: GRACE score, LVEF≤47%, acute MI size ≥19%LV and IMH: Score 3: GRACE score, LVEF≤45% and IMH) performed equally well and better than the GRACE score to predict the composite outcome of all-cause death, non-fatal myocardial infarction and new congestive cardiac failure at 1 year.



Pair-wise comparison

	P values
Grace Score - Score 1	0.004
Grace Score - Score 2	0.005
Grace Score - Score 3	0.03
Score 1 - Score 2	0.86
Score 1 - Score 3	0.33
Score 2 - Score 3	0.32

Figure 2: (a) Discrimination and (b) calibration of the model including Glasgow CMR risk score and GRACE score in the validation cohort to predict 1-year outcome
(a): Receiver-operating characteristic curve showing good discrimination of the model with a C-statistic of 0.87.
(b): Calibration plot showing good calibration of the model, a P=0.71 by Hosmer-Lemeshow test for goodness of fit on 1-year clinical outcome.

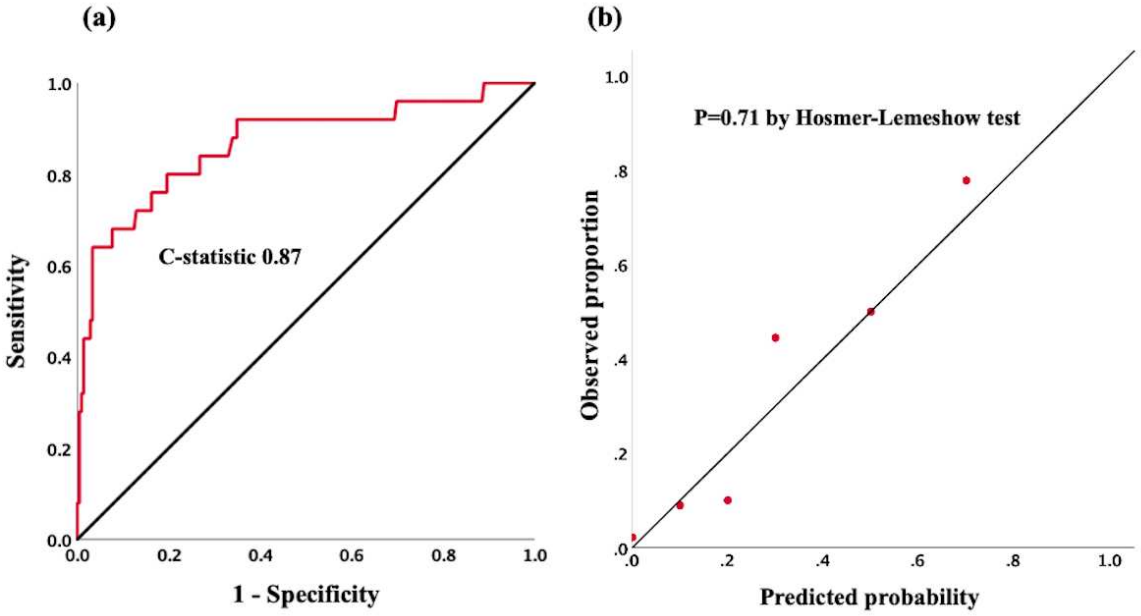
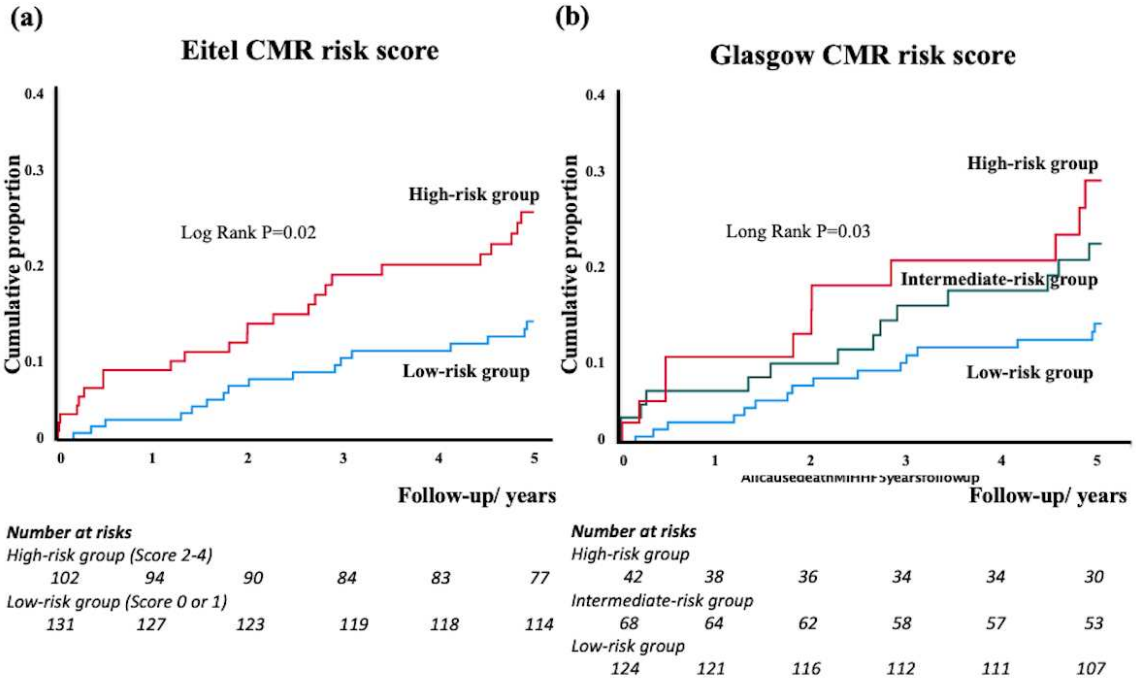


Figure 3. Kaplan-Meier curves of the cumulative event rates for the (a) Eitel CMR risk score and (b) Glasgow CMR risk score

(a): Kaplan-Meier curves of the cumulative event rates for those in the high-risk group (score >1) and those in the low-risk score (score 0 or 1) by Eitel CMR risk score

(b): Kaplan-Meier curves of the cumulative event rates for those in the high-risk group, intermediate-risk score and those in the low-risk score by Glasgow CMR Risk score



Number at risks						
High-risk group (Score 2-4)	102	94	90	84	83	77
Low-risk group (Score 0 or 1)	131	127	123	119	118	114

Number at risks						
High-risk group	42	38	36	34	34	30
Intermediate-risk group	68	64	62	58	57	53
Low-risk group	124	121	116	112	111	107

Central illustration. Non-contrast CMR for risk-stratification in STEMI
The top panel shows a representative patient with an anterior STEMI and undergoes PCI to the LAD. The patient then has an inpatient non-contrast CMR for risk-stratification. The bottom panel shows how the LVEF and IMH data could be used to risk-stratify patients into high-risk, intermediate-risk and low-risk group.

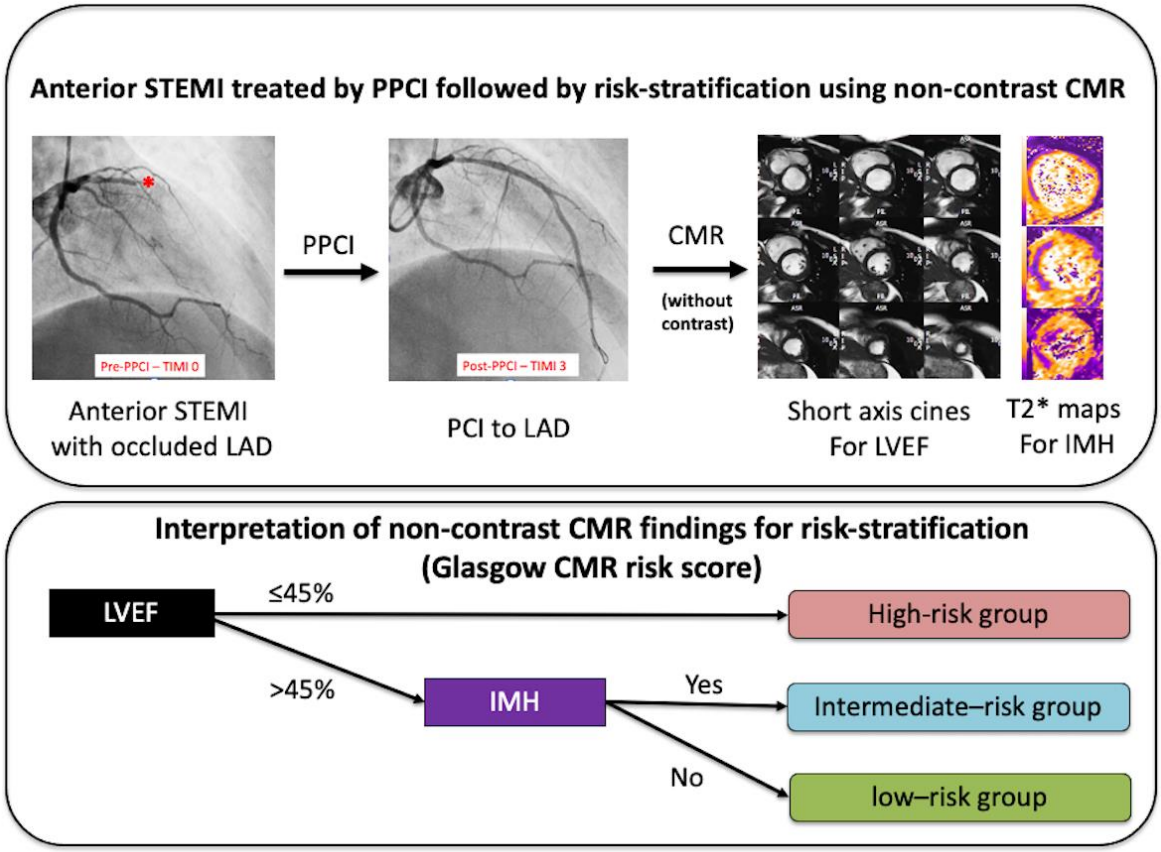


Table 1: Baseline demographics

	Derivation cohort (T-TIME) **N=370**	**Validation cohort (BHF MR-MI)** **N=234**
Age, mean ± SD	60±10	58±12
Male Gender	316 (85%)	178 (76%)
Diabetes Mellitus	43 (12%)	26 (11%)
Hypertension	109 (30%)	73 (31%)
Dyslipidaemia	76 (21%)	65 (28%)
Smoking history	239 (65%)	145 (62%)
Previous myocardial infarction	14 (4%)	16 (7%)
Systolic blood pressure/ mmHg	134±25	136±25
Diastolic blood pressure/ mmHg	80±16	80±14
Heart rate/ bpm	72±16	78±16
GRACE score		
<128	309 (84%)	158 (67%)

≥128	61 (17%)	76 (33%)
Symptom onset-to-balloon time/ mins	160 (118-221)	176 (122-329)
Infarct-related artery		
Left anterior descending artery	168 (45%)	93 (40%)
Circumflex artery	44 (12%)	44 (19%)
Right coronary artery	158 (43%)	97 (41%)
Pre-PCI TIMI flow		
0	299 (81%)	149 (64%)
1	27 (7%)	21 (9%)
2	39 (11%)	42 (18%)
3	5 (1%)	22 (9%)
Post-PCI TIMI flow		
0	0 (0%)	0 (0%)
1	10 (3%)	2 (1%)
2	61 (17%)	11 (5%)
3	297 (80%)	221 (94%)

GRACE: Global Registry of Acute Coronary Events; PCI: percutaneous coronary intervention; TIMI: Thrombolysis in Myocardial Infarction

Table 2: CMR characteristics.

	Derivation cohort (T-TIME) **N=370**	**Validation cohort (BHF MR-MI)** **N=234**
Acute MI size, median (IQR) % LV mass	26 (18-35)	18 (7-29)
MVO present	167 (45%)	125 (53%)
MVO, % LV mass	4.4 (2.3-9.7) N=167	5.2(1.9-12.7) n=125
IMH present	160 (43%)	96 (41%)
LVEF, %	49±8	55±10
LVEDV, ml	169 (144-198)	151 (127-175)
LVESV, ml	93 (78-113)	68 (51-86)
Timing of CMR/ days	4.4±2.1	2.1±1.8

MI: myocardial infarct; MVO: microvascular obstruction; LV: left ventricle; IMH: intramyocardial hemorrhage; LVEF: left ventricular ejection fraction; LVEDV: left ventricular end-diastolic volume; LVESV: left ventricular end-systolic volume; CMR: cardiovascular magnetic resonance.