Age and Ageing 2022; **51:** 1–11
https://doi.org/10.1093/ageing/afac248

RESEARCH PAPER

Prognostic value of cardiac magnetic resonance early after ST-segment elevation myocardial infarction in older patients

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All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

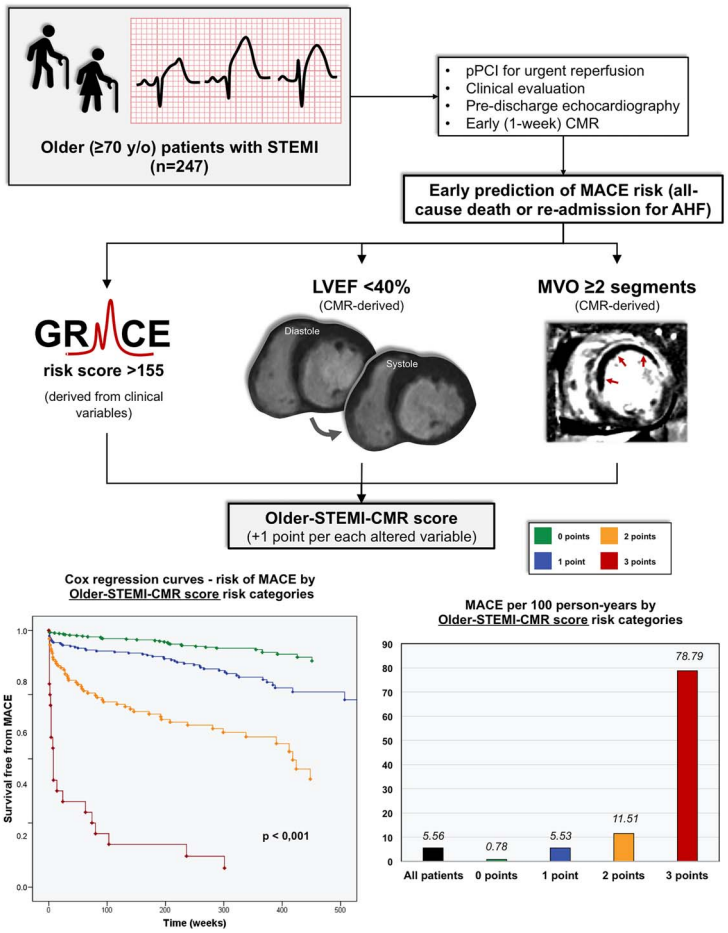
Abstract

Background: older patients with ST-segment elevation myocardial infarction (STEMI) represent a very high-risk population. Data on the prognostic value of cardiac magnetic resonance (CMR) in this scenario are scarce.
Methods: the registry comprised 247 STEMI patients over 70 years of age treated with percutaneous intervention and included in a multicenter registry. Baseline characteristics, echocardiographic parameters and CMR-derived left ventricular ejection fraction (LVEF, %), infarct size (% of left ventricular mass) and microvascular obstruction (MVO, number of segments) were prospectively collected. The additional prognostic power of CMR was assessed using adjusted C-statistic, net reclassification index (NRI) and integrated discrimination improvement index (IDI).
Results: during a 4.8-year mean follow-up, the number of first major adverse cardiac events (MACE) was 66 (26.7%): 27 all-cause deaths and 39 re-admissions for acute heart failure. Predictors of MACE were GRACE score (HR 1.03 [1.02–1.04], $P < 0.001$), CMR–LVEF (HR 0.97 [0.95–0.99] per percent increase, $P = 0.006$) and MVO (HR 1.24 [1.09–1.4] per segment, $P = 0.001$). Adding CMR data significantly improved MACE prediction compared to the model with baseline and echocardiographic characteristics (C-statistic 0.759 [0.694–0.824] vs. 0.685 [0.613–0.756], NRI = 0.6, IDI = 0.08, $P < 0.001$). The best cut-offs for independent variables were GRACE score > 155, LVEF < 40% and MVO ≥ 2 segments.

A simple score (0, 1, 2, 3) based on the number of altered factors accurately predicted the MACE per 100 person-years: 0.78, 5.53, 11.51 and 78.79, respectively ($P < 0.001$).
Conclusions: CMR data contribute valuable prognostic information in older patients submitted to undergo CMR soon after STEMI. The Older-STEMI–CMR score should be externally validated.

Keywords: myocardial infarction, older patients, cardiac magnetic resonance, risk, prognosis, older people

Graphical Abstract



In older (≥70 y/o) patients with STEMI submitted to undergo early (1-week) CMR, GRACE risk score > 155 points and CMR-derived LVEF<40% and MVO ≥ 2 segments conferred an increased risk of MACE during follow-up. Accurate patients risk stratification was performed based on an intuitive score derived from these variables. Abbreviations. AHF = Acute heart failure. CMR = Cardiovascular magnetic resonance. GRACE = Global Registry of Acute Coronary Events. LVEF = Left ventricular ejection fraction. MACE = Major adverse cardiac events. MVO = Microvascular obstruction. pPCI = Primary percutaneous coronary intervention. STEMI: ST-segment elevation myocardial infarction. y/o = years old.

Key Points

- The prognostic value of cardiovascular magnetic resonance (CMR) in older patients after ST-segment elevation myocardial infarction (STEMI) is unknown.
- Our cohort comprised 247 patients over 70 years of age who underwent CMR early (1 week) after STEMI.
- Global Registry of Acute Coronary Events score, CMR-derived left ventricular ejection fraction, and microvascular obstruction predicted long-term major adverse cardiac events (MACE).
- An intuitive score derived from these three predictors could accurately stratify MACE per 100 person-years in our cohort.
- CMR data contribute valuable prognostic information in older patients submitted to CMR soon after STEMI.

Introduction

Coronary artery disease is the main cause of mortality and morbidity in older patients [1–3]. ST-segment elevation myocardial infarction (STEMI), one of the paradigmatic manifestations of ischemic heart disease (IHD), has been traditionally associated with younger patients. However, steady population ageing in recent decades has led to a gradual increase in the incidence of STEMI in older patients, to the extent that currently over a third of STEMI patients are over 75 [4].

Older STEMI patients represent a very high-risk population. Not only an adverse prognostic factor in itself, age is also associated with other undesirable events such as longer delay between symptoms onset and therapeutic intervention, greater incidence of renal failure, worse Killip class and increased comorbidities [5–7]. Even if appropriate revascularization by percutaneous coronary intervention is performed, older STEMI patients have 4-fold increased risk of death or re-hospitalisation for heart failure (HF) after the acute event [1, 8].

Cardiovascular magnetic resonance (CMR) imaging is playing an increasingly important role in IHD patient evaluation, becoming the gold standard imaging test for structural assessment in this field [9–11]. Use of this non-invasive imaging technique for evaluation early after STEMI enables in-depth assessment of the structural consequences of myocardial infarction, and its predictive value has been widely demonstrated [12–14]. However, current scientific evidence about its prognostic usefulness in older patients is lacking.

In the present study, we aimed to: 1) assess whether CMR performed early after STEMI contributes prognostic value beyond routine clinical and echocardiographic evaluation in older patients, and 2) create a risk score that includes both clinical and CMR-derived variables to stratify the risk of major adverse cardiac events (MACE) in this setting.

Material and methods

Study group

The study group comprised older (≥70 years) patients discharged from hospital for a first STEMI treated with percutaneous coronary intervention and submitted to CMR from 2012 to 2017. Patients were prospectively included in a multicenter registry of three University Hospitals after informed consent was provided. Patients were managed by clinical cardiologists following current recommendations [5]. Previous analyses of this registry have been published [15].

Patient characteristics including Killip class at admission, peak creatine kinase MB mass, thrombolysis in myocardial infarction (TIMI) flow grade in the culprit artery (before and after reperfusion) and Global Registry of Acute Coronary Events (GRACE) and TIMI scores were recorded. Barthel index depicting patient's performance in activities of daily living was assessed by nurses during index admission.

The investigation conforms to the principles of the Declaration of Helsinki and was approved by the respective local Ethics Committees. The 'Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis' (TRIPOD) guidelines have been followed for design and reporting of the study.

Echocardiography

Transthoracic echocardiography was performed in all patients before discharge (5 ± 2 days post STEMI) by local cardiologists who quantified parameters and prospectively included the data in the respective databases. LVEF (%), LV end-diastolic volume (mL) and LV end-systolic volume (mL) were assessed using the biplane method of disks (modified Simpson's rule). Tricuspid annular plane systolic excursion (mm), as a proxy of right ventricle function, was measured in the apical 4-chamber view by means of M-mode. A wave velocity (m/s), E wave velocity (m/s) and left atrium diameter (mm) were also recorded.

CMR

CMR was performed in all patients at pre-discharge or shortly after discharge (7 ± 2 days post STEMI) as previously described [15], using the same CMR scanner characteristics (one in each institution), CMR study protocol and CMR software throughout. Local cardiologists specialised in CMR with more than five years' experience carried out the studies, quantified parameters using customised software (QMASS MR, 6.1.5, Medis, Leiden, The Netherlands) and prospectively included data in the registry.

Images were acquired by a phased-array body surface coil during breath holds and were triggered by electrocardiography. Cine images were acquired in two-, three- and four-chamber views, and in short-axis views using a steady-state free precession sequence (repetition time/echo time: 2.8/1.2 ms; flip angle: 58°; matrix: 256 × 300; field of view: 320 × 270 mm; slice thickness: 7 mm).

Breath-hold late gadolinium enhancement imaging was performed 10 min after administering gadolinium-based contrast (dimeglumine gadopentetate or dimeglumine gadobenate at 0.1 mmol/kg or gadoteric acid at 0.15 mmol/kg) in the same locations as in the cine images, using a segmented inversion recovery steady-state free precession sequence (repetition time/echo time: 750/1.26 ms; flip angle: 45°; matrix: 256 × 184; field of view: 340 × 235 mm; slice thickness: 7 mm). Inversion time was adjusted to nullify normal myocardium.

LVEF (%), LV end-diastolic and end-systolic volume indices (ml/m^2) and LV mass index (g/m^2) were calculated by manual planimetry of endocardial and epicardial borders in short-axis view cine images (Figure 1A–D). Areas showing late gadolinium enhancement were visually quantified by manual planimetry. IS (% of LV mass) was assessed as the percentage of LV mass showing late gadolinium enhancement (Figure 1E and F). MVO was defined as the number of segments without contrast uptake in the core tissue showing

late gadolinium enhancement (Figure 1G and H); the 17-segment model was applied.

Endpoint and follow-up

MACE was defined as a combined clinical endpoint including all-cause mortality or re-admission for acute decompensated HF, whichever occurred first. Current criteria for acute HF were used [16]. All events were prospectively adjudicated by consensus by clinical cardiologists by reviewing the electronic health record database at each hospital.

Statistical methods

All data were tested for normal distribution using the one-sample Kolmogorov–Smirnov test. Continuous normally distributed data were expressed as mean ± standard deviation and compared using Student's *t*-test. Non-parametric data were expressed as the median with the interquartile range and were compared using the Mann–Whitney U test. Proportions were compared by the Chi-square or Fisher's exact test as appropriate. The Chi-square for trend was applied for trends in more than two groups.

Variables achieving $P < 0.1$ significance in univariate analysis comparing MACE and non-MACE subgroups were added as cofactors in a multivariable Cox proportional hazard regression model to predict time to MACE. A hierarchical model was used to avoid overfitting of variables. The first model (clinical variables) included clinical variables associated with MACE on univariate analysis. The second model (clinical + echocardiographic variables) incorporated echocardiographic variables associated with MACE on univariate analysis. The third and final model (clinical + echocardiographic + CMR variables) incorporated CMR variables associated with MACE on univariate analysis. Hazard ratios with the corresponding 95% confidence intervals were computed.

To evaluate the additional prognostic contribution of CMR beyond baseline and echocardiographic characteristics, we computed changes in risk classification using the C statistic, the continuous net reclassification improvement (NRI) index and the integrated discrimination improvement (IDI) index. The two tested models were considered different if the 95% confidence intervals did not overlap the zero value.

Incidence rates of MACE (expressed as MACE per 100 person-years) were determined. Two-tailed *P*-values were obtained using mid-*P* adjustments.

Receiver operating characteristic (ROC) curves were computed to predict MACE, and variables that independently predicted MACE were dichotomized by means of the Youden index. To calculate the risk score, one point was scored for each altered parameter. The proposed cut-offs for GRACE score (>155 points), LVEF (<40%) and MVO (≥2 segments) are concordant with our previous experience in STEMI patients [14, 15].

Statistical significance was achieved at a two-tailed *P*-value < 0.05. The SPSS statistical package (version 15.0, SPSS Inc., Chicago, Illinois) and STATA (version 9.0, StataCorp, College Station, Texas) were used throughout.

Results

A total of 247 older (≥70 years) patients discharged for a first STEMI were included in the registry (Supplementary Figure S1). Mean age was 76.08 ± 4.68 years, most patients were male (67.2%), and the most prevalent cardiovascular risk factor was hypertension (63.6%). Half (50.2%) the population presented with anterior STEMI. TIMI flow grade 3 after PCI was accomplished in most patients (87.9%) (Table 1). Echocardiographic and CMR characteristics of the cohort are depicted in Table 2.

During a mean follow-up of 4.8 years, there were a total of 66 (26.7%) first MACE (27 all-cause deaths and 39 re-admissions for acute HF). On univariate comparison, patients who presented MACE during follow-up had higher heart rate and lower systolic blood pressure on admission, worse Killip class, an increased rate of anterior infarction (62.1% vs. 45.9%, $P = 0.03$), and higher GRACE and TIMI risk scores (Table 1). Regarding Echo and CMR indices (Table 2), this subgroup also had lower LVEF (either by Echo or by CMR), higher LV mass, more segments with MVO, and more extensive IS.

After inclusion in the hierarchical multivariable model, three variables were independent predictors of MACE occurrence: higher GRACE score (HR 1.03 [1.02–1.04], $P < 0.001$), more depressed CMR-LVEF (HR 0.97 [0.95–0.99] per percent increase, $P = 0.006$) and more extensive MVO (HR 1.24 [1.09–1.4] per segment, $P = 0.001$) (Table 3).

Adding CMR data significantly improved MACE prediction compared to the model with baseline and echocardiographic characteristics (C-statistic 0.759 [0.694–0.824] vs. 0.685 [0.613–0.756], NRI = 0.6, IDI = 0.08, $P < 0.001$).

The best cut-offs for independent variables were GRACE score > 155, CMR-LVEF < 40%, and MVO ≥ 2 segments. Each of these variables, if altered, was associated with reduced MACE-free survival (Supplementary Figure S2) as well as reduced survival free from each of the components of the combined MACE endpoint separately (Supplementary Figure S3).

We created a simple score (0–3 points) based on the number of altered factors, assigning one point for each of the following: GRACE score > 155, CMR–LVEF < 40% or MVO ≥ 2 segments. This Older-STEMI–CMR score accurately predicted MACE per 100 person-years, which was 5.56 per 100 person-years in the whole cohort (Figure 2). Patients with 0 points ($n = 76$, 30.7%) had an excellent prognosis and the lowest occurrence of MACE (0.78 per 100 person-years). Risk was increased if 1 ($n = 120$, 48.6%) or 2 points ($n = 39$, 11.5%) were scored, which conferred a risk of 5.53 and 11.51 MACE per 100 person-years, respectively. The highest risk was seen in patients with three points ($n = 12$,

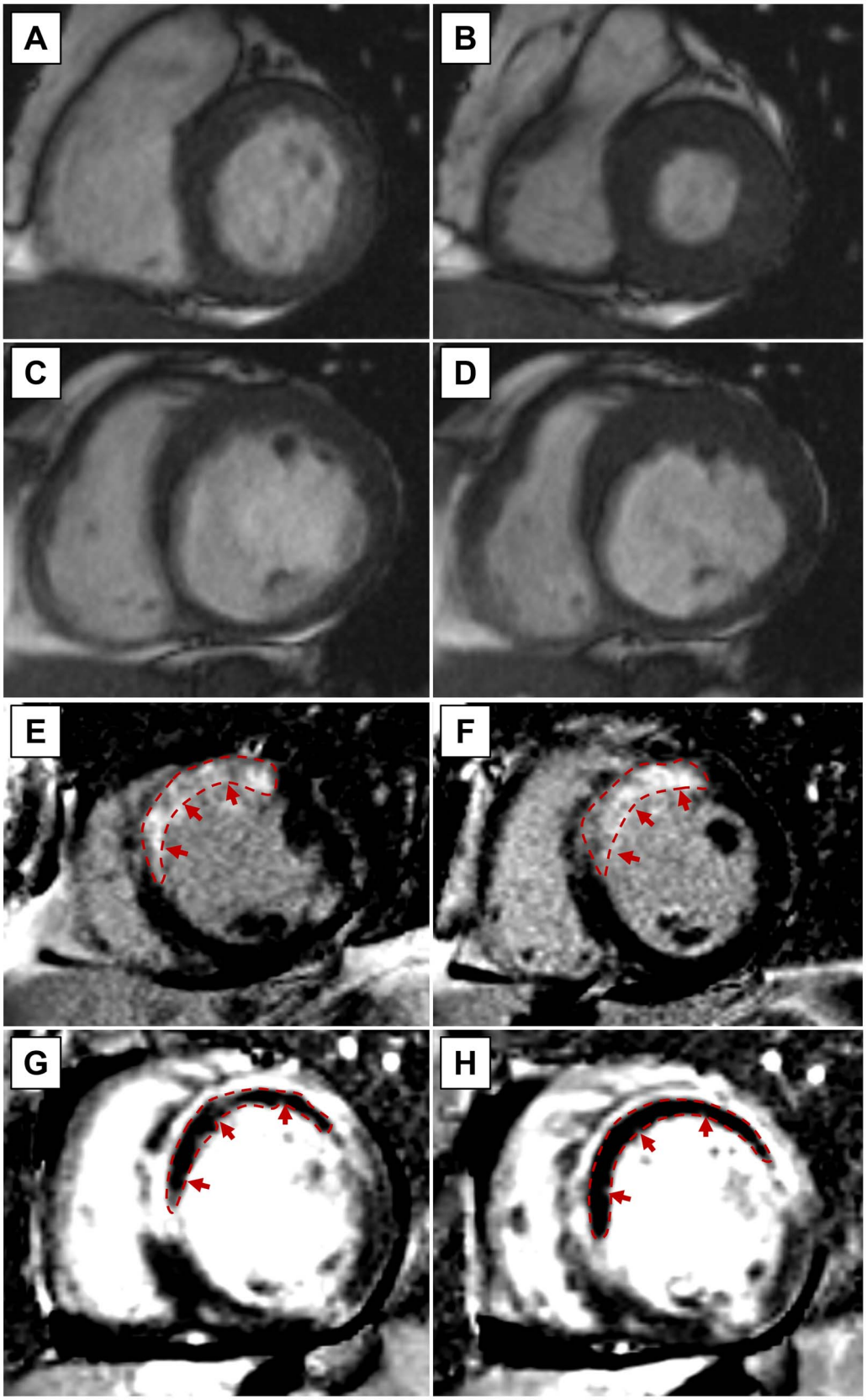


Figure 1. CMR parameters measured after STEMI. Cine images in diastole (left) and systole (right) showing preserved (A–B) and reduced (C–D) LVEF. The latter case corresponds to a patient with a recent inferior STEMI showing inferior–posterior akinesia. LGE imaging showing transmural necrosis (arrowheads) in anterior and anteroseptal segments after STEMI (E–F). Extensive

Table 1. Baseline characteristics of the entire cohort and of patients with and without MACE

	All patients ($n = 247$)	MACE ($n = 66$)	No MACE ($n = 181$)	P-value
Clinical variables				
Age (years)	76.08 ± 4.68	76.98 ± 5.31	75.75 ± 4.4	0.07
Male sex (%)	166 (67.2)	43 (65.2)	123 (68)	0.76
Ethnicity (%)				
Caucasian/white	241 (97.6)	64 (97)	177 (97.8)	0.79
Hispanic/latino	6 (2.4)	2 (3)	4 (2.2)	
Diabetes mellitus (%)	75 (30.4)	23 (34.8)	52 (28.7)	0.35
Hypertension (%)	157 (63.6)	40 (60.6)	117 (64.6)	0.56
Hypercholesterolemia (%)	96 (38.9)	23 (34.8)	73 (40.3)	0.46
Smoker (%)	75 (30.4)	21 (31.8)	54 (29.8)	0.76
Heart rate on admission (beats per min)	75 [63.25–85]	80 [68–90]	75 [63–84]	0.04
Systolic pressure (mmHg)	137.04 ± 32.22	129.94 ± 33.91	139.65 ± 31.27	0.04
Killip class (%)				<0.001
1	182 (73.7)	37 (56.1)	145 (80.1)	
2	49 (19.8)	19 (28.8)	30 (16.6)	
3	8 (3.2)	4 (6.1)	4 (2.2)	
4	8 (3.2)	6 (9.1)	2 (1.1)	
Time to reperfusion (min)	210 [150–330]	250 [159–411]	202.5 [148.5–300]	0.12
Peak creatine kinase MB mass (ng/ml)	187 [75–285]	221.05 [78.88–314.95]	167.4 [72.9–257]	0.09
Anterior infarction (%)	124 (50.2)	41 (62.1)	83 (45.9)	0.03
TIMI flow grade before PCI (%)				0.02
0	162 (65.6)	45 (68.2)	117 (64.6)	
1	13 (5.3)	0	13 (7.2)	
2	23 (9.3)	3 (4.5)	20 (11)	
3	49 (19.8)	18 (27.3)	31 (17.1)	
TIMI flow grade after PCI (%)				0.58
0	3 (1.2)	1 (1.5)	2 (1.1)	
1	2 (0.8)	0	2 (1.1)	
2	25 (10.1)	9 (13.6)	16 (8.8)	
3	217 (87.9)	56 (84.8)	161 (89)	
GRACE risk score	160.15 ± 25.68	175.04 ± 28.15	154.72 ± 22.46	<0.001
TIMI risk score	4 [3–6]	5 [4–7]	4 [3–5]	<0.001
Barthel index on admission	100 [80–100]	85 [55–100]	100 [80–100]	0.19

Abbreviations. GRACE = Global Registry of Acute Coronary Events. MACE = Major adverse cardiac events. PCI = Percutaneous coronary intervention. TIMI = Thrombolysis in Myocardial Infarction.

4.9%); that is, patients with GRACE score > 155, CMR–LVEF <40% and MVO ≥ 2 segments simultaneously. They depicted 78.79 MACE per 100 person-years ($P < 0.001$ for all comparisons). A similar risk stratification was noted for each of the components of the combined MACE endpoint separately (Supplementary Figure S4).

Discussion

The main findings of our study are that CMR performed early after STEMI can improve risk prediction in older (≥70 years) patients, and that a simple risk score comprised of three clinical and CMR-derived variables (GRACE score > 155, CMR–LVEF <40% and MVO ≥2 segments) accurately stratifies long-term risk of MACE in this population (Graphical Abstract).

Given that STEMI patients have an increased risk of short- and long-term complications and mortality, early risk assessment is systematically recommended in this population. Comprehensive clinical evaluation and analysis of echocardiographic prognostic predictors, especially LVEF, should be performed before hospital discharge in all these patients [5]. Lower echocardiography-LVEF values have been strongly associated with an increased risk of death and re-admission for HF [14, 15, 17, 18].

CMR imaging after STEMI has become well established in recent years. Not only does it provide the most accurate and reproducible measurement of LVEF [19], but it also enables comprehensive, non-invasive evaluation of the structural consequences of myocardial infarction [20–22]. The extent of infarcted myocardium and areas with MVO can be measured in late gadolinium enhancement sequences. The incremental prognostic value of these CMR parameters (LVEF, infarct size and MVO) early after the acute event has been robustly demonstrated in the STEMI population, emerging as the cornerstone of non-invasive risk

MVO (arrowheads) in a case of anterior STEMI (G–H). Abbreviations: CMR = Cardiovascular magnetic resonance. LVEF = Left ventricular ejection fraction. MVO = Microvascular obstruction. STEMI = ST-segment elevation myocardial infarction.

Table 2. Echocardiographic and CMR characteristics of the entire cohort and of patients with and without MACE

	All patients ($n = 247$)	MACE ($n = 66$)	No MACE ($n = 181$)	*P*-value
Echo indices at 1 week				
Echo-LVEF (%)	49.87 ± 10.56	47.18 ± 12.01	50.81 ± 9.9	0.03
Echo-LV end-diastolic volume (mL)	101.05 ± 38.38	107.21 ± 38.96	98.94 ± 38.23	0.37
Echo-LV end-systolic volume (mL)	50.71 ± 23.73	60.29 ± 25.36	47.43 ± 22.4	0.02
TAPSE (mm)	21 [19–23]	21 [19–24]	20 [18.25–22.75]	0.27
E wave velocity (m/s)	0.72 ± 0.59	0.72 ± 0.31	0.72 ± 0.66	0.98
A wave velocity (m/s)	0.87 ± 0.22	0.91 ± 0.33	0.85 ± 0.18	0.4
Left atrium diameter (mm)	36.5 [33–40.75]	37.5 [33–41]	36 [32–40]	0.35
CMR indices at 1 week				
CMR-LVEF (%)	50.77 ± 12.87	46.38 ± 14.58	52.37 ± 11.84	0.003
CMR-LV end-diastolic volume index (mL/m^2)	75.61 ± 20.19	77.41 ± 22.95	74.95 ± 19.1	0.44
CMR-LV end-systolic volume index (mL/m^2)	38.51 ± 17.68	43.52 ± 20.98	36.67 ± 15.97	0.02
LV mass (g/m^2)	68.9 ± 16.47	74.63 ± 19.7	66.82 ± 14.65	0.004
Microvascular obstruction (n of segments)	0 [0–2]	1 [0–3]	0 [0–2]	0.003
Infarct size (% of LV mass)	21.13 ± 13.58	26.74 ± 15.13	19.09 ± 12.4	<0.001

Abbreviations. CMR = Cardiovascular magnetic resonance. Echo = Echocardiography. LV = Left ventricular. LVEF = Left ventricular ejection fraction. MACE = Major adverse cardiac events. TAPSE = Tricuspid annular plane systolic excursion. In patients with atrial fibrillation at the time of echocardiography E and A wave velocities were not considered for analyses.

Table 3. Predictors of MACE: multivariable analyses

	Model 1		Model 2		Model 3	
	Hazard ratio [95% CI]	*P*-value	Hazard ratio [95% CI]	*P*-value	Hazard ratio [95% CI]	*P*-value
Baseline characteristics						
Age (years)	1.03 [0.95–1.12]	0.44	–	–	–	–
Heart rate on admission (beats per min)	1.01 [1–1.03]	0.06	–	–	–	–
Systolic pressure (mmHg)	1 [0.98–1.02]	1	–	–	–	–
Killip class II (%)	1.03 [0.34–3.13]	0.96	–	–	–	–
Killip class III (%)	1.73 [0.28–10.63]	0.56	–	–	–	–
Killip class IV (%)	1.43 [0.15–13.85]	0.76	–	–	–	–
Peak creatine kinase MB mass (ng/ml)	1 [0.99–1]	0.44	–	–	–	–
Anterior infarction (%)	1.89 [1.09–3.3]	0.02	2.3 [1.31–4.04]	0.004	1.31 [0.75–2.27]	0.34
TIMI flow grade 2 before PCI (%)	1.17 [0.6–2.29]	0.64	–	–	–	–
TIMI flow grade 1 before PCI (%)	0 [0–0]	0.97	–	–	–	–
TIMI flow grade 0 before PCI (%)	0.32 [0.08–1.27]	0.11	–	–	–	–
GRACE risk score	1.02 [1.01–1.03]	<0.001	1.02 [1.02–1.03]	<0.001	1.03 [1.02–1.04]	<0.001
TIMI risk score	1.07 [0.84–1.36]	0.6	–	–	–	–
Echo indices at 1 week						
Echo-LVEF (%)	–	–	0.99 [0.96–1.02]	0.56	–	–
Echo-LV end-systolic volume (mL)	–	–	–[a]	–[a]	–	–
CMR indices at 1 week						
CMR-LVEF (%)	–	–	–	–	0.97 [0.95–0.99]	0.006
CMR-LV end-systolic volume index (ml/m^2)	–	–	–	–	–[a]	–[a]
LV mass (g/m^2)	–	–	–	–	1.01 [0.99–1.03]	0.1
Microvascular obstruction (n of segments)	–	–	–	–	1.24 [1.09–1.4]	0.001
Infarct size (% of LV mass)	–	–	–	–	1.02 [0.99–1.04]	0.09

See text ('Statistical methods') for more details on the construction of the hierarchical multivariable approach used for analyses. Abbreviations. CMR = Cardiovascular magnetic resonance. Echo = Echocardiography. GRACE = Global Registry of Acute Coronary Events. LV = Left ventricular. LVEF = Left ventricular ejection fraction. MACE = Major adverse cardiac events. PCI = Percutaneous coronary intervention. TIMI = Thrombolysis in Myocardial Infarction. [a]Echo-LV end-systolic volume and CMR–LV end-systolic volume index were removed from multivariable analysis due to excessive collinearity [variance inflation factor > 5 for echo-LVEF and tolerance statistic < 0.2 for CMR–LVEF].

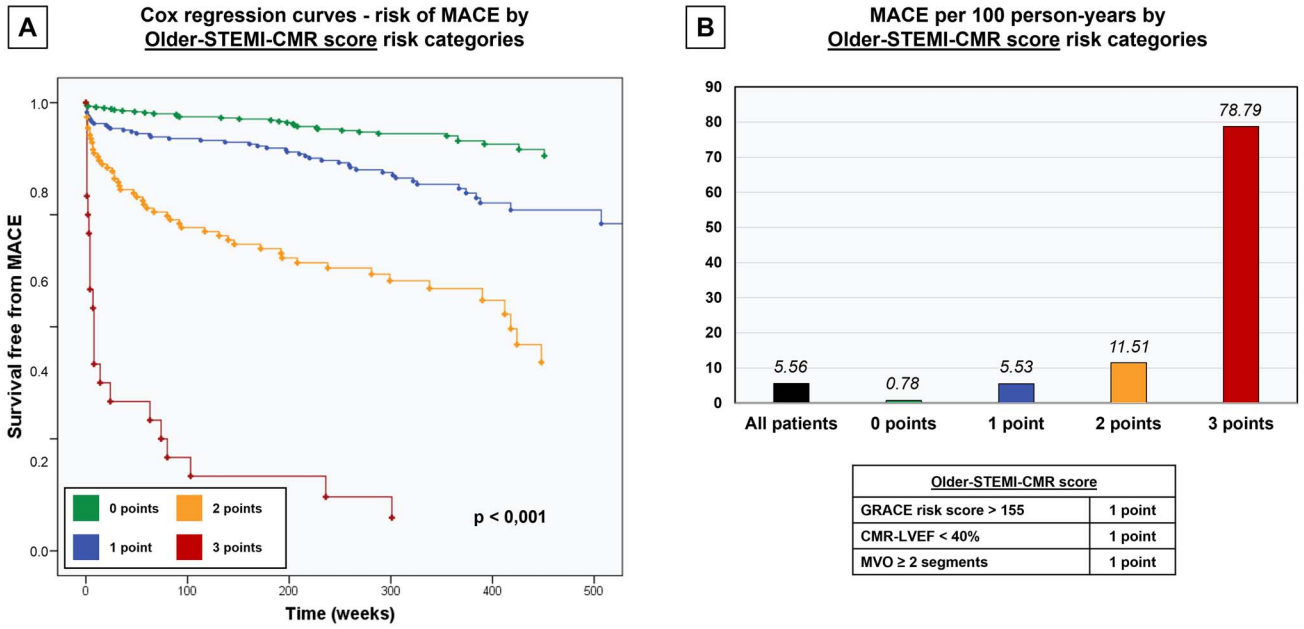


Figure 2. Survival analysis according to Older-STEMI–CMR score categories (0–3 points). (A) Cox regression curves depicting MACE-free survival by Older-STEMI–CMR score categories. (B) MACE per 100 person-years by Older-STEMI–CMR score categories; ($P < 0.001$ for all group comparisons). Abbreviations. CMR = Cardiovascular magnetic resonance. GRACE = Global Registry of Acute Coronary Events. LVEF = Left ventricular ejection fraction. MACE = Major adverse cardiac events. STEMI: ST-segment elevation myocardial infarction.

stratification based on data previously published by our group and current evidence [12, 22–24]. However, despite being a valuable prognostic tool, CMR availability is restricted in routine clinical practice for logistical and economic reasons. Several studies have attempted to discern which patients would benefit most from its use in terms of prognostic purposes, e.g. based on a pre-defined echocardiography–LVEF cut-off (<50%) [14].

Despite extensive testing of the prognostic value of CMR after STEMI, the mean age of patients included in most of these studies is around 60 years, and specific studies focusing on older patients are lacking. Older STEMI patients represent a subset with several particularities, such as increased risk of HF or mechanical complications [5, 25], more delay intervention, increased comorbidity [5–7], higher prevalence of previous history of IHD and multivessel involvement [5, 26, 27], and attenuated benefit of revascularization strategies [28]. While the prognostic value of stress CMR has been studied in older patients with chronic coronary syndrome [29], confirmation of whether CMR can be prognostically valuable in older STEMI patients is also desirable.

Our study shows that a higher GRACE score, more depressed CMR–LVEF and more extensive MVO were independent predictors of MACE in STEMI patients older than 70 years, in line with results in previously published literature. The GRACE score is an excellent predictor of in-hospital and 6-month mortality in patients with acute coronary syndrome and has also shown satisfactory accuracy for event prediction in older patients [30, 31].

Furthermore, in older patients LVEF is strongly associated with outcomes, and the presence of depressed LVEF has been shown to double the risk of MACE [32]. Along with other CMR parameters such as infarct size, MVO in early CMR after STEMI has been reported as a potent predictor of MACE; moreover, its presence does not differ with age [33, 34]. Unquestionably, patients with altered microcirculation have an increased risk of adverse left ventricular remodelling and adverse cardiac events. Regenfus et al. showed that MVO in reperfused STEMI was the strongest predictor of MACE across long-term follow-up and provided incremental prognostic value over clinical variables and LVEF [35]. Furthermore, leading on from our previous research, we can corroborate the prognostic value of CMR-derived LVEF and MVO in the general population soon after STEMI [12, 13, 15, 21]. However, there was no specific evidence in older patients, which further highlights the need for clinical integration with imaging in this population.

To enhance clinical applicability, we employed an integrated approach of MACE risk prediction, combining the usual clinical parameters with prognostic CMR-derived markers. By means of a simple risk score, the older-STEMI–CMR score, which included clinical (GRACE score) and CMR-derived (LVEF and MVO) variables, we demonstrated accurate early risk prediction and stratification after STEMI in older patients. Dichotomization of variables was performed for the sake of simplicity and applicability in routine clinical practice, using cut-offs recently validated by our group [13, 15, 36]. With this score we were able to

effectively discriminate patients into low, intermediate and high risk categories.

Almost a third of patients had a score of 0 points, i.e. a low risk clinical profile (GRACE score < 155), preserved LVEF and adequate microvascular reperfusion. This group has the lowest occurrence of MACE (0.78 per 100 person-years) and represents a very reassuring finding for the clinician since it identifies those patients with an excellent short- and long-term prognosis, comparable to that of younger STEMI patients. Most patients (48.6%) had a score of 1 point, which implies a relatively low risk of MACE (5.53 per 100 person-years). Therefore, these low-risk patients, accurately identified as those with 1 and especially 0 point scores, display excellent prognosis and could be managed similarly to other age groups.

Conversely, patients with the highest score (=3) possessed a prohibitive risk of MACE (78.79 per 100 person-years). The older-STEMI–CMR risk score could help identify those patients with truly high risk, who would benefit most from individualised management, closer follow-up and certain therapies, such as specific guideline-directed treatment in patients with LVEF $\leq$ 40%. Fortunately, the highest risk population represents only a minority of the cohort (4.9%). Nonetheless, more research is needed to explore the potential of this proposed risk score in terms of individualised patient management and decision making, especially in patients at very high risk (score 3).

Our results suggest that, after subsequent external validation, the risk score proposed could provide valuable prognostic information about older patients with STEMI submitted to CMR beyond a more traditional risk stratification based on baseline and echocardiographic parameters. This can help inform doctors about disease severity so that they take an individualised approach by giving more detailed information to patients and their relatives, respecting their preferences and involving them in the decision. Further studies should focus on selecting older patients who can benefit most from routine early CMR for accurate risk prediction after STEMI and exploring the implications of this approach on decision-making.

Study limitations

Several limitations of this study should be acknowledged. First, there is no well-established threshold to define the geriatric population, thus age 70 was selected as the cut-off in our cohort in accordance with most reviewed literature. Due to the observational nature of our study, we cannot exclude referral and survival bias, so patients referred for CMR may not be entirely representative of the whole older STEMI population. Also, reperfused patients are more likely representative of the robust subgroup amongst older STEMI individuals. Certain biochemical or clinical variables such as high-sensitivity cardiac troponin data, geriatric assessment, frailty evaluation and other imaging parameters, which could have played a role in patient prognosis were not included in the registry. Specifically, our study lacks a Comprehensive Geriatric Assessment beyond Barthel index which could have added important dimension in terms of prognostic assessment after STEMI. Finally, it would be desirable to validate our score in external datasets, ideally from different health systems and ethnicities.

Conclusions

CMR data can contribute valuable prognostic information in older patients submitted to undergo CMR soon after STEMI. A simple risk score including clinical (GRACE score > 155) and CMR (LVEF < 40% and MVO $\geq$ 2 segments) variables permits early MACE risk stratification soon after STEMI in older patients. The applicability of the older-STEMI–CMR score should be validated in external cohorts.

Supplementary Data: Supplementary data mentioned in the text are available to subscribers in *Age and Ageing* online.

Declaration of Conflicts of Interest: Siemens Healthcare provided financial support to conduct cardiac magnetic resonance studies in 94 subjects of this series.

Declaration of Sources of Funding: This work was supported by Instituto de Salud Carlos III and Fondos Europeos de Desarrollo Regional FEDER (grant numbers PI20/00637, PI15/00531, and CIBERCV16/11/00486, CIBERCV16/11/00420, CIBERCV16/11/00479), a postgraduate contract FI18/00320 to C.R.-N., CM21/00175 to V.M.-G. and JR21/00041 to C.B., Fundació La Marató TV3 (grant 20153030-31-32), La Caixa Banking Foundation (HR17-00527), by Conselleria de Educación—Generalitat Valenciana (PROMETEO/2021/008) and by Sociedad Española de Cardiología (grant SEC/FEC-INV-CLI 21/024). J.G. acknowledges financial support from the Agencia Estatal de Investigación (grant FJC2020-043981-I/AEI/10.13039/501100011033). D.M. acknowledges financial support from the Conselleria d'Educació, Investigació, Cultura i Esport, Generalitat Valenciana (grants AEST/2019/037, AEST/2020/029).

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Received 29 March 2022; editorial decision 30 August 2022