

Final infarct size measured by cardiovascular magnetic resonance in patients with ST elevation myocardial infarction predicts long-term clinical outcome: an observational study

Jacob Lønborg^{1*}, Niels Vejlstrup¹, Henning Kelbæk¹, Lene Holmvang¹, Erik Jørgensen¹, Steffen Helqvist¹, Kari Saunamäki¹, Kiril Aleksov Ahtarovski¹, Hans Erik Bøtker², Won Yong Kim², Peter Clemmensen¹, and Thomas Engstrøm¹

¹Department of Cardiology, Rigshospitalet, Blegdamsvej 9, 2100 Copenhagen, Denmark; and ²Department of Cardiology, Skejby, Aarhus, Denmark

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Aims

Tailored heart failure treatment and risk assessment in patients following ST-segment elevation myocardial infarction (STEMI) is mainly based on the assessment of the left ventricular (LV) ejection fraction (EF). Assessment of the final infarct size in addition to the LVEF may improve the prognostic evaluation. To evaluate the prognostic importance of the final infarct size measured by cardiovascular magnetic resonance (CMR) in patients with STEMI.

Methods and results

In an observational study the final infarct size was measured by late gadolinium enhancement CMR 3 months after initial admission in 309 patients with STEMI. The clinical endpoint was a composite of all-cause mortality and admission for heart failure. During the follow-up period of median 807 days (IQR: 669–1117) 35 events (5 non-cardiac deaths, 3 cardiac deaths, and 27 admissions for heart failure) were recorded. Patients with a final infarct size \geq median had significantly higher event rates than patients with a final infarct size $<$ median (17 vs. 6%; Log rank $P = 0.002$). In a multivariable Cox regression analysis, including age, peak troponin T, LVEF, LV volume index, and heart rate, the final infarct size remained significantly associated with the occurrence of subsequent events (adjusted hazard ratio 1.13 per 1% increase (95% CI: 1.05–1.21; $P = 0.001$). The overall Wald χ^2 value of a model including known risk factors was 47.3, which increased to 57.9 when the final infarct size was added ($P = 0.001$ for the difference).

Conclusion

Assessment of the final infarct size by CMR 3 months after a STEMI provides strong independent prognostic information incremental to known risk factors including the LVEF, and may help to improve the risk stratification of STEMI patients.

Keywords

ST-Segment elevation myocardial infarction • Cardiovascular magnetic resonance • Prognosis • Final infarct size • Late gadolinium

Introduction

The recommended treatment for patients with ST-segment elevation myocardial infarction (STEMI) is timely reperfusion with primary percutaneous coronary intervention (PCI) in order to minimize the myocardial damage and thereby preserve left

ventricular (LV) function.¹ In patients with reduced LV ejection fraction (EF) following acute myocardial infarction, treatment with an implanted cardioverter-defibrillator and intensive medication is recommended.^{2,3} Thus, tailored heart failure therapy is based on clinical grounds and on assessment of the LVEF, which in terms of the indication for cardioverter-defibrillator

* Corresponding author. Tel: +45 35851885; fax: +45 35452705, Email: jacoblonborg@gmail.com

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implantation should be assessed >40 days after the infarction.⁴ It seems relevant to look for additional supplemental strategies to improve the risk stratification in STEMI patients, especially in the acute or subacute phase. Assessment of myocardial damage may help improve the prognostic evaluation of STEMI patients.

The myocardial damage following STEMI can be assessed accurately by late gadolinium enhancement (LGE) using cardiovascular magnetic resonance (CMR) imaging.⁵ Gadolinium is a contrast agent that is distributed in the extracellular space in the infarct region.⁶ In the acute phase of a STEMI, the extracellular space is increased in the infarct region due to a combination of necrosis, haemorrhage, and oedema. The extent of LGE in the acute phase has been related to the outcome in patients with STEMI.^{7–10} However, later on the necrotic tissue is replaced by fibrotic scar tissue also with increased extracellular space.¹¹ This process leads to ongoing 'infarct shrinkage' after the first week until the infarction reaches its final size after ~30 days.^{7,8,12–15} Measurement of LGE in the acute phase of an infarction might therefore overestimate the necrotic infarct size, whereas 'final LGE' extent is more precisely related to the amount of necrotic tissue.¹³ In STEMI patients the prognostic importance of the final infarct size assessed by LGE is not fully elucidated. This study aims to determine the prognostic importance of the final infarct size measured after 3 months by LGE CMR in consecutive patients with STEMI treated with primary PCI.

Methods

Study population and treatment

Patients in the present substudy were pooled from two randomized studies in STEMI patients.^{16,17} One study compared ischaemic post-conditioning (IPost) to conventional primary PCI¹⁶ and the other study compared i.v. administration of the GLP-1 analogue exenatide to placebo in primary PCI.¹⁷

This study includes patients with a first STEMI and symptom duration ≤ 12 h who were field-triaged directly to the PCI centre or transferred from a local hospital. STEMI was defined as ST-segment elevation in two contiguous electrocardiographic leads of >0.1 mV in V_4 – V_6 or limb leads II, III, and aVF, or >0.2 mV in leads V_1 – V_3 . Patients were not considered for enrolment if they presented with cardiogenic shock, unconsciousness, acute stent thrombosis, known renal insufficiency, previous myocardial infarction, or previous coronary artery bypass graft surgery. Furthermore, patients were excluded if cardiac biomarkers did not confirm the diagnosis (aborted STEMI). All patients eligible for primary PCI were pretreated with aspirin 300 mg orally or 500 mg i.v.; clopidogrel 600 mg orally; and unfractionated heparin 10 000 units i.v. On arrival at the catheterization laboratory, a coronary angiography was performed to identify the culprit lesion, and primary PCI was performed as previously described.^{16,17} A glycoprotein IIb/IIIa receptor antagonist was administered at the discretion of the operator if no contraindications were present. All patients were treated with clopidogrel 75 mg daily for 12 months and aspirin 75 mg daily indefinitely. Blood was drawn for assessment of plasma troponin T before, immediately after, 6 h after, and 12–18 h after intervention. All patients were informed verbally and in writing, and all gave their written consent. The study was performed according to the Helsinki declaration of good clinical practice, and The Danish National Committee on Biomedical Research Ethics approved the protocol.

Final infarct size and LV function by CMR

In the absence of contraindications a CMR scan was performed at a median of 90 (IQR: 80–96) days after the STEMI in order to assess the final infarct size using a 1.5 T scanner (Avanto scanner, Siemens, Erlangen, Germany) and a 6-channel body array coil. The final infarct size was assessed from delayed enhancement images obtained using a standard ECG-triggered inversion-recovery sequence (slice thickness 8 mm, slice gap 0 mm, TE 1.4 ms, field of view 300–360 mm, inversion time was adjusted in a single slice).^{18,19} The final infarct size was assessed using the freely available software Segment v1.8 (<http://segment.heiberg.se>) as shown in Figure 1.²⁰ This is a semi-automatic approach that calculates the mean signal intensity in five sectors in each slice. The 20% most endocardial and epicardial myocardium in each sector is excluded, leaving the middle 60% of the myocardial wall as the basis for calculation of the mean signal intensity. The region with the lowest mean signal intensity is considered 'remote' myocardium. A slice-specific threshold is then set as the mean of the remote sector plus 1.8 standard deviations. To take the partial volume effect into account, each pixel within the infarct region is then weighted according to the signal intensity, where the minimal detectable pixel is set as the 10%-weight. The endocardial and the epicardial borders were manually traced in all short-axis images and the LV myocardial mass calculated. Papillary muscles were considered parts of the LV cavity. A single observer (J.L. with 4 years of experience; SCMR level 2) trained in Cardiology performed all CMR analysis. Inter-observer variability in terms of the final infarct size was assessed in 50 randomly selected patients with a mean bias 0.8%LV and limits of agreement $\pm 2.6\%$ LV.

The LV volume and function were measured by CMR using a standard ECG-triggered balanced steady-state free-precession cine sequence (slice thickness 8 mm, slice gap 0 mm, echo time 1.5 ms, field of view 300 mm, frames 25 per heart beat) as shown in Figure 1. On short-axis cine CMR images the LV volumes were calculated by manually tracing the endocardial borders in all 25 phases. The diastolic and the systolic frames were automatically identified according to the size of the LV blood pool area, and the LV end-diastolic volume (EDV), LV end-systolic volume (ESV), and LVEF were calculated accordingly. All volumes were normalized according to the body surface area. Papillary muscles were considered parts of the LV lumen. The findings on CMR did not change the therapy or lead to admission.

Clinical endpoints

Clinical data were collected from hospital files and the clinical outcome was assessed as a composite of the all-cause mortality and any admission for heart failure (peripheral or pulmonary oedema as the main reason for admission). Admission for heart failure was only registered if the main reason for admission and the cause of treatment during admission was peripheral or pulmonary oedema. A reviewer blinded to all paraclinical data including CMR measurements carefully evaluated all readmissions during the follow-up period by evaluating the hospital files. Thus, the same person made the final decision whether an admission could be registered as an admission for heart failure. Patients who suffered an event or re-infarction before 3 months were excluded from the present analysis.

Statistical analysis

All statistical analyses were performed with SPSS software version 20 (SPSS, Inc., Chicago, IL, USA). A two-sided P -value <0.05 was considered statistically significant. The patients were stratified according to the final infarct size \geq median or $<$ median. Categorical variables were

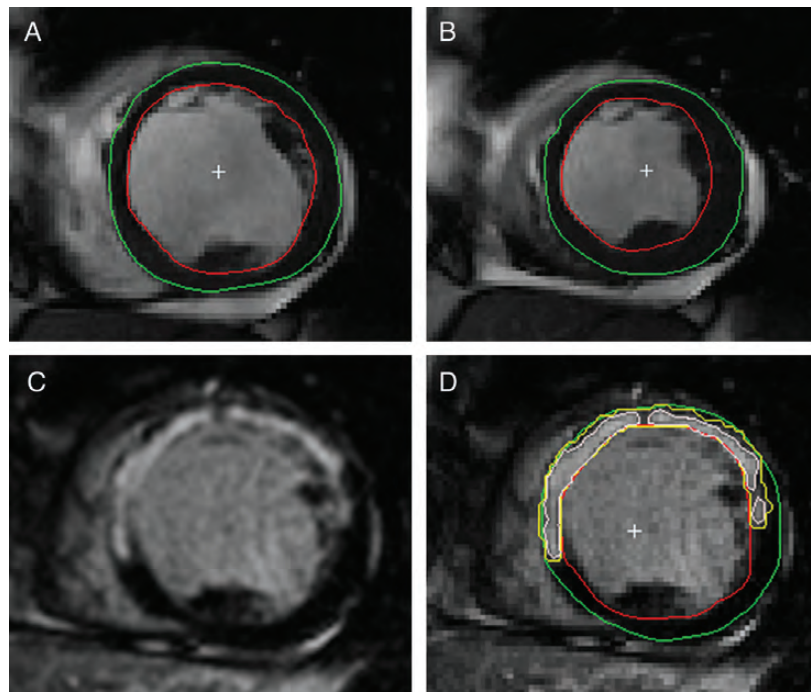


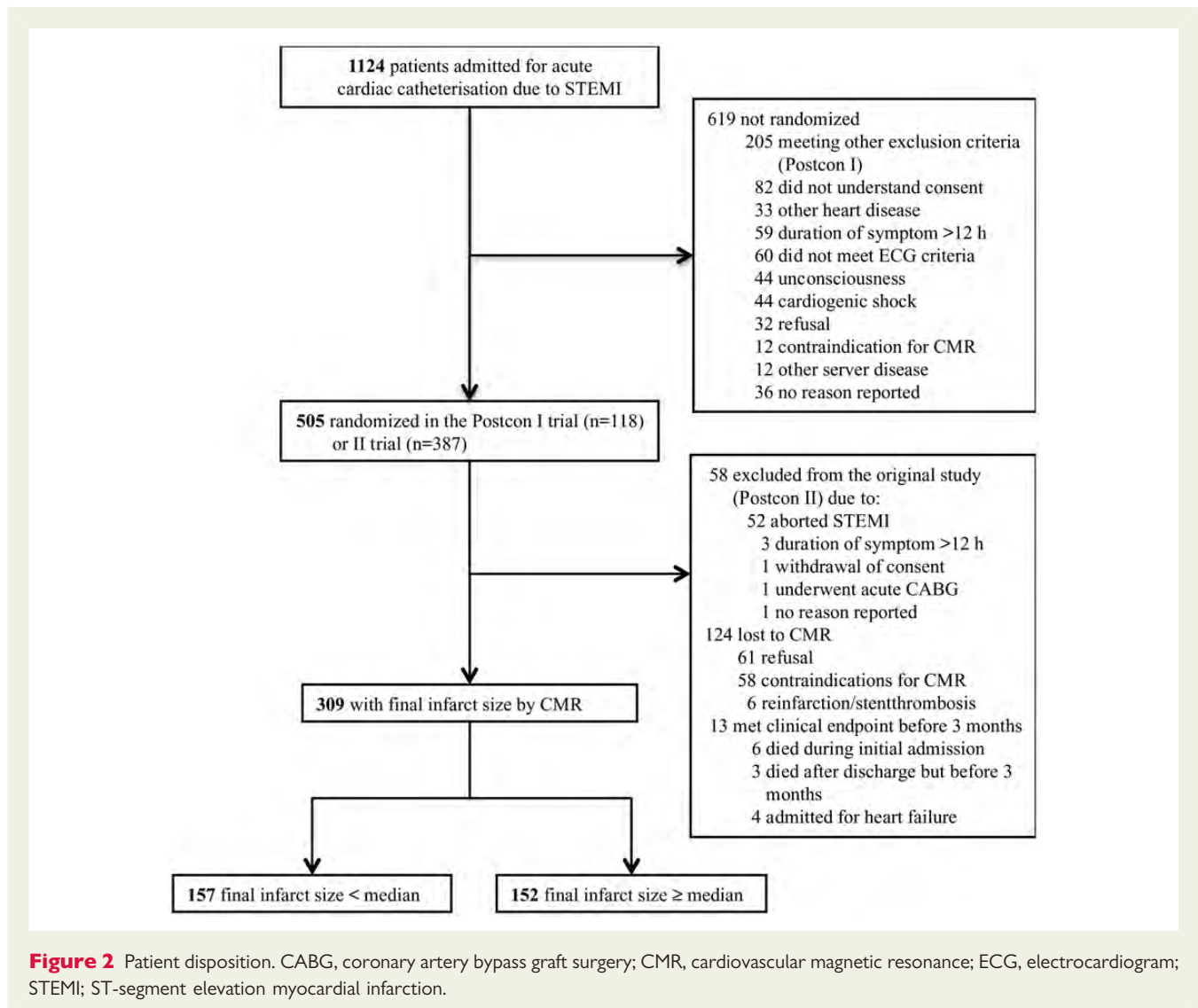
Figure 1 Cardiovascular magnetic resonance images. Cardiovascular magnetic resonance images from a patient with occlusion in the left anterior descending artery and subsequently anterior and septal infarct. Steady-state free-precession image in end diastole (A) and end systole (B) is used to calculate left ventricular volumes and ejection fraction (red, endocardial border and green, epicardial border). Infarction was assessed using a delayed enhancement inversion-recovery sequence (C) and the final infarct size (orange zone) was measured using the freely available software Segment v1.8 (<http://segment.heiberg.se20>) as shown here (D). To take the partial volume effect into account, each pixel within the infarct region (yellow zone) is then weighted according to the signal intensity, where the minimal detectable pixel is set as the 10%-weight.

compared using the χ^2 or Fisher's exact test, and continuous variables were compared using Student's *t* or the Mann–Whitney test. To assess the prognostic importance of the final infarct size 3 months after STEMI according to the median value, the Kaplan–Meier method was used with comparisons by the Log rank test. A univariable Cox proportional hazard analysis was performed evaluating the final infarct size as a continuous variable. To identify the independent prognostic value of the final infarct size, three different multivariable approaches were applied: (i) A multivariable Cox proportional hazard analysis was performed using all variables with $P < 0.10$ in the univariable analysis. (ii) A backward stepwise approach was used removing the variable with the highest P -value. The limit for exclusion was $P \geq 0.10$ and for inclusion $P < 0.10$. (iii) A Cox proportional hazard analysis was also performed adjusting for known prognostic predictors [age, LVEF, anterior infarct location, thrombolysis in myocardial infarction (TIMI) flow, and symptom onset-to-balloon dilatation duration]. The risk for events was expressed as hazard ratios with 95% confidence intervals (CIs). The overall Wald χ^2 value of a model containing all significant variables in the univariable analysis except the final infarct size was compared with the overall Wald χ^2 value of a model including all significant variables and the final infarct size. Owing to potential confounding effects of exenatide and IPost, a possible interaction with exenatide/IPost was evaluated. The Cox regression assumptions were checked for each variable by interaction, variable*variable (linearity—only continuous variable) and visually for proportionality.

Results

Study population

The patient inclusion is illustrated in *Figure 2*. A total of 505 patients were randomized in the two previous studies, of which 309 patients were eligible for inclusion in the present study and evaluated for the clinical outcome. The reasons for exclusion are listed in *Figure 2*; of the 58 patients who had contraindications for CMR, 25 patients had claustrophobia, 15 had nephropathy (estimated glomerular filtration rate < 60 mL/min), 6 had arrhythmia, making the ECG gating impossible, 7 had metallic implantation including pacemakers, 4 were unable to cooperate, and 1 could not enter the scanner due to severe obesity. The median final infarct size was 9.5% LV (IQR: 5.3–15.0). Baseline characteristics according to the final infarct size \geq median or $<$ median are shown in *Table 1*. Patients with the final infarct size \geq median were more likely to have anterior infarct location, lower TIMI flow grade, longer duration from symptom onset to balloon dilatation, and higher peak troponin T levels (*Table 1*). Furthermore, a final infarct size \geq median was related to a higher LV mass index, larger LVEDV and LVESV indices, and a lower LVEF (*Table 1*).



Clinical outcome

During the follow-up period of median 807 (IQR: 669–1117) days (calculated from time of CMR examination), a total of 35 (11.3%) events (5 non-cardiac deaths, 3 cardiac deaths, and 27 admissions for heart failure) were observed. Cancer was the cause of non-cardiac death in four patients and infection (sepsis) in one. A further number of 13 patients met a clinical endpoint before 3 months (Figure 2), of which 6 events occurred during the initial admission. Thus 7 events (17% of the total events) occurred between initial discharge and 3 months (Figure 2).

Predictors for clinical outcome

Patients with a final infarct size \geq median had significantly higher event rates than patients with a final infarct size $<$ median (17 vs 6%; $P = 0.002$) (Figure 3). The prognostic importance of a 5% LV increase in the final infarct size is shown in Figure 4.

As shown in Table 2, age, implantation of a stent (stentable lesion), peak in plasma troponin T, statin treatment after

3 months, LVEDV index, LVESV index, LVEF, heart rate at rest at 3 months, and final infarct size (%LV) all had a $P < 0.10$ in a univariable Cox proportional hazard analysis, and was therefore used in the multivariable analyses. In the multivariable models, using variables with $P < 0.10$ in the univariable analysis, the final infarct size remained significantly associated with the outcome even after a backward elimination process (Table 2). Furthermore, adjusting for known predictors (age, LVEF, anterior infarct location, TIMI flow, and symptom onset to balloon dilatation duration), the final infarct size remained significantly associated with the clinical outcome (adjusted hazard ratio 1.09 per 1% increase; 95% CI: 1.02–1.16; $P = 0.007$). Adjusting for exenatide/Post treatment in a Cox regression analysis, the final infarct size remained significantly associated with the outcome ($P < 0.001$), and no interaction was observed ($P = 0.48$). Stratifying patients according to the LVEF (LVEF $\geq 45\%$), the final infarct size was still significantly associated with the outcome in both groups: LVEF $\geq 45\%$: hazard ratio 1.57 (95% CI: 1.14–2.17) and LVEF $< 45\%$: hazard ratio 1.81 (95% CI: 1.16–2.83).

Table 1 Patient characteristics

	All patients (n = 309)	Final infarct size <median (n = 157)	Final infarct size ≥median (n = 152)	P-value
Age, years	61 ± 11	60 ± 11	61 ± 11	0.48
Male, n (%)	252 (82)	126 (80)	126 (83)	0.91
Body mass index, kg/m ²	27 ± 4	27 ± 4	27 ± 4	0.57
Diabetes mellitus, n (%)	21 (7)	11 (7)	10 (7)	0.83
Hypertension, n (%)	99 (32)	52 (33)	47 (31)	0.47
Hypercholesterolaemia, n (%)	146 (47)	75 (48)	72 (47)	0.94
Previous PCI, n (%)	23 (7)	9 (6)	14 (9)	0.28
Symptom onset-to-balloon dilatation, min	180 (125–269)	165 (120–249)	202 (130–308)	0.009
Anterior infarct location, n (%)	133 (43)	54 (35)	79 (52)	0.004
TIMI grade pre-PCI, n (%)				
0/1	236 (76)	101 (65)	135 (88)	
2	39 (13)	27 (17)	12 (8)	<0.001
3	34 (11)	28 (18)	6 (4)	
Multiple vessel disease, n (%)	53 (17)	28 (16)	25 (18)	0.65
Collateral flow (Rentrop grade 2/3), n (%)	49 (16)	21 (13)	28 (18)	0.28
TIMI grade 3 after procedure, n (%)	284 (92)	147 (94)	137 (91)	0.33
Stent implantation, n (%)	258 (84)	130 (84)	128 (87)	0.63
Randomized to exenatide/IPost, n (%)	170 (55)	92 (59)	78 (51)	0.25
Peak plasma troponin T, µg/L	4.4 (2.3–7.4)	2.7 (1.3–4.2)	7.3 (4.5–11–5)	<0.001
Medical treatment after 3 months, n (%)				
β-Blockers	282 (91)	138 (88)	144 (95)	0.07
Statin	307 (99)	156 (99)	151 (99)	1.00
Aspirin	307 (99)	156 (99)	151 (99)	1.00
Clopidogrel	305 (99)	152 (99)	143 (98)	0.36
ACE inhibitors	141 (46)	67 (44)	74 (51)	0.25
Heart rate at rest after 3 months, bpm	64 (56–71)	61 (55–71)	66 (58–72)	0.19
CMR parameters				
Final infarct size, %	10 (5–15)	6 (3–8)	15 (12–19)	<0.001
Final infarct size, g	12 (6–19)	6 (3–10)	19 (14–26)	<0.001
LV mass index, g/m ²	61 (53–67)	58 (51–64)	63 (55–71)	<0.001
LVEF, %	57 (49–62)	61 (55–65)	51 (45–58)	<0.001
LVEDV index, mL/m ²	80 (69–94)	76 (65–87)	87 (74–100)	<0.001
LVESV index, mL/m ²	35 (26–45)	30 (24–37)	42 (31–54)	<0.001

Data are presented as mean ± SD, median (IQR) or n (%) unless otherwise indicated.

ACE, angiotensin-converting enzyme; CMR, cardiovascular magnetic resonance; IPost, ischaemic postconditioning; LV, left ventricular; LVEF, LV ejection fraction; LVEDV, LV end-diastolic volume; LVESV, LV end-systolic volume; PCI, percutaneous coronary intervention; TIMI, thrombolysis in myocardial infarction.

The overall Wald χ^2 value of a model containing age, stent implantation, peak plasma troponin T, LVEF, LVEDV index, LVESV index, and heart rate at rest was 47.3 ($P < 0.001$). By adding the final infarct size to this model, the overall Wald χ^2 increased to 57.9 ($P < 0.001$), with a P -value of 0.001 for the difference (Figure 5).

Discussion

The main finding of this study was that the final infarct size determined by LGE CMR measured after 3 months is a strong predictor

for the prognosis in patients with STEMI treated with primary PCI, and provides independent prognostic information beyond that provided by the acute infarct size assessed as peak troponin T, LV function, and volume. Thus, the final infarct size by LGE CMR can be used to improve the prognostic evaluation in STEMI patients, and serve as a surrogate endpoint in clinical studies.

The extent of LGE assessed by CMR after scar remodelling has previously been associated with the clinical outcome.^{21–26} However, these populations were inhomogeneous and include patients with a variety of cardiac diseases. No differentiation was

made between patients with STEMI and non-STEMI patients or non-ischaemic cardiac disease, although these patient groups differ significantly in terms of myocardial damage, comorbidity, pre-existing diseases, and prognosis.^{27–29} Therefore, whether difference in disease and/or comorbidity affected the results cannot be ruled

out. Furthermore, in the previous studies patients were referred for a CMR based on a clinical indication, and in a substantial number of patients CMR was performed >2 years after the acute episode. The present study is therefore the first to evaluate the prognostic significance of routine assessment of the final infarct size by LGE CMR in a consecutive cohort consisting of only STEMI patients treated with primary PCI, and determines the final infarct size as an important predictor in these patients.

The amount of infarcted myocardium has been shown to decrease over time in porcine studies,³⁰ and the extent of LGE in reperfused myocardial infarction is significantly smaller in the sub-acute compared with the acute phase.¹¹ Similarly, the extent of LGE decreases 30–40% over time in humans after reperfusion.^{7,8,12–15} There is a rapid reduction in the extent of LGE within the first week following the infarction,¹² and thereafter the infarct size measured by LGE decreases slowly and remains almost constant after 30 days to 1 year.^{12,15} Therefore, measuring the final infarct size after 3 months seems to be reasonable. Despite a strong correlation between acute and subacute infarct size, the progressive change seems more pronounced in smaller infarcts, leading to the speculation that the small-sized infarctions may be underestimated in the subacute phase.³¹ On the other hand, acute measurement overestimates the size of necrotic tissue, because in the acute phase the infarct zone contains both necrotic myocytes and structurally normal but functionally compromised myocytes.³² Accordingly, the agreement between necrosis by histology and LGE is markedly improved in the chronic stage.³² Experimental studies have demonstrated that the

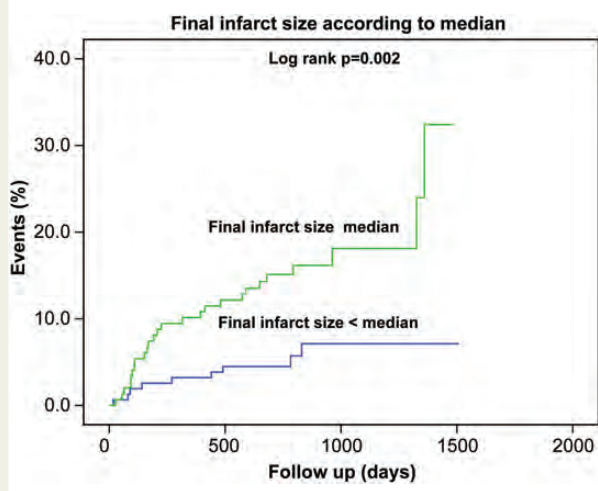


Figure 3 The association of median final infarct size with outcome. Kaplan–Meier curves of the incidence of events (all-cause mortality and admission for heart failure). Comparison by the Log rank test.

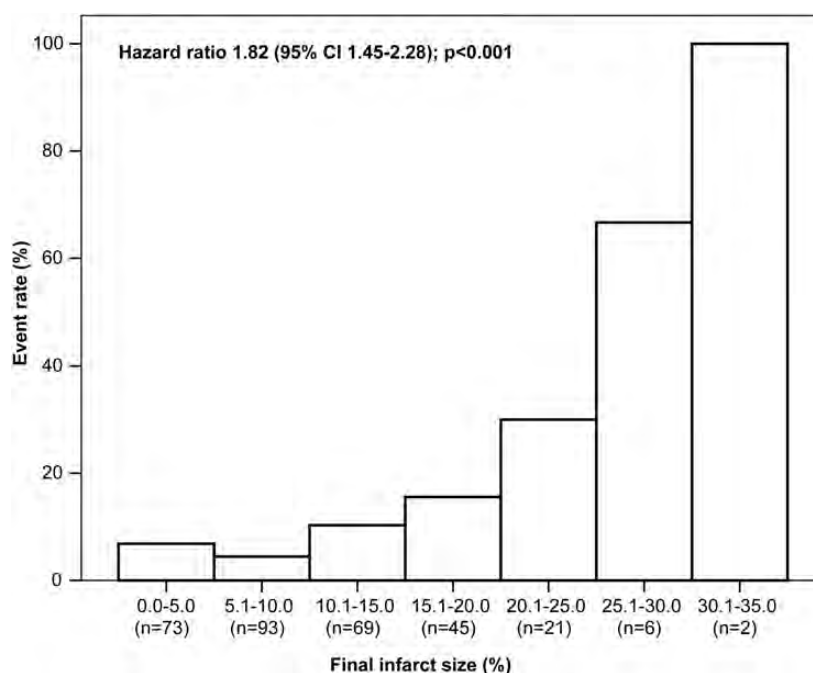


Figure 4 Event rates according to the final infarct size. Unadjusted event rates (all-cause mortality and admission for heart failure) for a 5% change in the final infarct size measured by cardiovascular magnetic resonance 3 months after ST-segment elevation myocardial infarction. CI, confidence interval.

Table 2 Uni- and multivariable Cox regression analysis of predictors for outcome

	Univariable		Multivariable model		Backward stepwise model	
	Hazard ratio (CI)	P-value	Adjusted hazard ratio (CI)	P-value	Adjusted hazard ratio (CI)	P-value
Age	1.03 (1.00–1.06)	0.08	1.02 (0.99–1.06)	0.18	1.03 (1.00–1.07)	0.045
Stentable lesions	0.44 (0.20–0.94)	0.035	0.31 (0.13–0.77)	0.011	0.34 (0.14–0.80)	0.014
Peak plasma troponin T	1.09 (1.03–1.15)	0.002	1.10 (1.00–1.20)	0.047	1.10 (1.01–1.20)	0.034
Final infarct size, per 5%	1.81 (1.48–2.34)	<0.001	1.80 (1.29–2.51)	0.001	1.92 (1.44–2.59)	<0.001
LVEF, per 5%	0.69 (0.60–0.79)	<0.001	0.90 (0.56–1.38)	0.58	—	—
LVEDV index, per 10 mL/m ²	1.02 (1.00–1.04)	0.016	1.45 (0.76–2.78)	0.27	—	—
LVESV index, per 10 mL/m ²	1.45 (1.26–1.67)	<0.001	2.14 (0.77–5.90)	0.17	1.32 (1.05–1.66)	0.017
Heart rate at rest after 3 months	1.25 (1.06–1.46)	0.041	1.02 (0.99–1.06)	0.28	1.03 (1.00–1.06)	0.09

The following parameters were tested in univariable analysis with $P \geq 0.10$: gender, body mass index, diabetes mellitus, hypertension, hypercholesterolaemia, randomized to exenatide/IPost, previous PCI, collateral flow, pre-procedural TIMI flow, symptom onset-to-balloon dilatation, TIMI flow 3 after procedure, anterior infarct location, multiple vessel disease, and LV mass index.

CI, confidence interval; IPost, ischaemic postconditioning; LV, left ventricular; LVEF, LV ejection fraction; LVEDV, LV end-diastolic volume; LVESV, LV end-systolic volume; PCI, percutaneous coronary intervention; TIMI, thrombolysis in myocardial infarction grade.

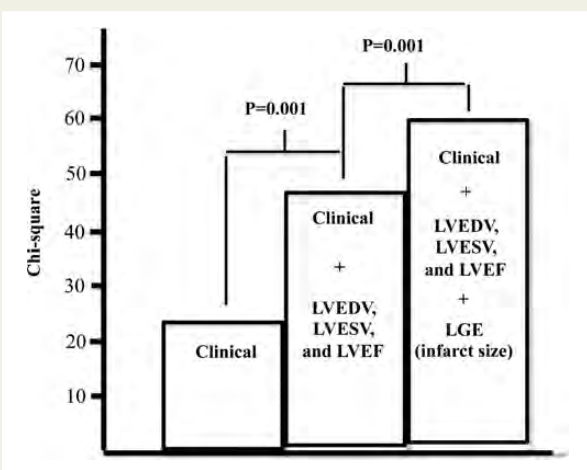


Figure 5 χ^2 value incremental value of the infarct size by late gadolinium enhancement as % of LV 3 months after ST-segment elevation myocardial infarction. Clinical data included age, stent implantation, and peak troponin T. LVEDV, LV end-diastolic volume. LVEF, left ventricular ejection fraction. LVESV, LV end-systolic volume.

infarction area measured by histology and LGE undergoes an initial expansion during the first 2–4 days after the coronary occlusion due to inflammation, formation of oedema, and haemorrhage.^{31,33} Thus, the most accurate timing for measuring the infarct size by LGE in patients with STEMI remains to be settled.

Measurement of the LVEF is important for the prognostic assessment of patients after a STEMI. However, the use of a global LVEF measured in the acute phase may be misleading both due to the compensatory hypercontractility of normal myocardium, and to stunned hypokinetic but viable myocardium that may recover in time. This may also help explain the discrepancy

between the LVEF measured before or after 40 days in terms of survival benefits of implanted cardioverter-defibrillator implantation.^{2,34} Nonetheless, it seems relevant to look for additional supplemental strategies to improve the risk stratification in STEMI patients, especially in the acute or subacute phase. LGE measured in the acute phase seems to be a stronger prognostic predictor than the LVEF, and seems to improve risk stratification.⁸ Still, LGE may overestimate the necrotic infarct size, and the extent of LGE can vary in size within a few days. As demonstrated in this study, LGE measurement in the subacute phase provides additional prognostic information to known risk factors including the LVEF. However, whether choosing the treatment strategy based upon assessment of the infarct size by LGE in addition to the clinical ground and the LVEF improves the prognosis remains to be settled in randomized settings.

Assessment of the final infarct size does not allow for evaluation of microvascular obstruction,^{35–38} LV thrombus, and haemorrhage,^{39,40} which is a limitation by using the final infarct size to risk-stratify STEMI patients. Conversely, assessment of the infarct size by CMR in the acute phase provides information regarding the acute infarct size and microvascular obstruction, information that also can be obtained by easier assessable and cheaper means such as angiographic myocardial blush grade,⁴¹ cardiac biomarkers, and ST-segment resolution. When it comes to evaluation of the final myocardial damage in the subacute or chronic phase after a STEMI, few methods exist, but as demonstrated in this study, CMR is a promising method. In contrast, measuring LGE in the subacute phase does not take the risk of suffering an event between discharge and the time of acquisition into account, which in this study accounted for 17% of the total events. Since the infarct size remains almost constant between 30 days and 1 year following an infarction, estimation of the final infarct size at 30 days might be preferable to later time points and has the potential for improved risk stratification. It should further be noted that risk assessment and stratification is most effective in the first few days post

myocardial infarction when patients are at a greatest risk. Acutely measured myocardial salvage index is related to the outcome following STEMI,⁴² but the prognostic information provided by the infarct size seems to be stronger than that provided by the myocardial salvage index.^{8,43} While the myocardial salvage index serves excellently as a surrogate marker in clinical studies, the additional prognostic value to the infarct size, microvascular obstruction, and haemorrhage may be limited. Moreover, it is feasible to calculate the myocardial salvage index from the final infarct size, which probably also is more representative of the actual myocardial salvage. This approach requires an additional scan to be performed within 1 week following the infarction to measure the area at risk, which limits the clinical relevance. Nevertheless, the optimal timing for performing CMR in terms of prognostic information remains to be settled, and the prognostic utility of CMR needs to be tested in randomized settings compared with usual care.

To date no consensus and standardization regarding the method for evaluation of the LGE infarct size exists. Several methods are used including thresholding by 2–6 SD above normal myocardium, manual quantification, ‘full width at half maximum’, and automatic detections.^{20,44} We chose to use an automatic approach as previously described, since it takes the partial volume into account and has proved superior to a 4.7 SD threshold approach in terms of variability and mean bias.²⁰ Since the same method was used for all patients, it is unlikely that using another method would affect the results and conclusions.

Limitations

The acute infarct size was only evaluated as peak troponin T. The area under the curve of troponin T might have provided additional information, but troponin T was measured at too few time points to perform area under the curve analysis. Patients in this study were randomized to placebo, exenatide or IPost, which could have affected the results. However, statistically, adjustment for treatment allocation did not alter the results and thus the conclusions. A total of 39% of the patients intentioned to analysis were lost to CMR, which induces a certain risk of selection bias. Furthermore, the excluded patients and the patients lost to CMR may present some of the most critically ill patients (e.g. patients with renal failure, unconsciousness, or cardiogenic shock). These patients are also most likely at higher risk and also more prone to have large infarcts introducing the risk of selection bias. On the other hand, patients with aborted myocardial infarction, representing those at low risk, were not included in this study. Finally, the limited number of patients included in our study with only 35 clinical events indicates that the results should be interpreted with caution due to the risk of overfitting the multivariable models.

Conclusion

Assessment of the final infarct size by CMR 3 months after a STEMI provides strong independent prognostic information incremental to known risk factors including the LVEF, and may help to improve the risk stratification of patients with STEMI.

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