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Hamza El Aidi, MD Arthur Adams, MD Karel G.M. Moons, MD, PhD Hester M. Den Ruijter, PhD Willem P.Th.M. Mali, MD, PhD Pieter A. Doevendans, MD, PhD Eike Nagel, PhD Simon Schalla, MD, PhD Michiel L. Bots, MD, PhD Tim Leiner, MD, PhD

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Cardiac Magnetic Resonance Imaging findings and the risk of cardiovascular events in patients with recent myocardial infarction or suspected or known coronary artery disease – a systematic review of prognostic studies

Hamza El Aidi MD^{1,2}, Arthur Adams MD², Karel G.M. Moons MD, PhD³, Hester M. Den Ruijter PhD^{3,6}, Willem P.Th.M. Mali MD, PhD², Pieter A. Doevendans MD, PhD¹, Eike Nagel PhD⁴, Simon Schalla MD, PhD⁵, Michiel L. Bots MD, PhD³, Tim Leiner MD, PhD²

1. Department of Cardiology, University Medical Center Utrecht, Utrecht, The Netherlands
2. Department of Radiology, University Medical Center Utrecht, Utrecht, The Netherlands
3. Julius Center of Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, The Netherlands
4. Division of Imaging Sciences and Biomedical Engineering, St. Thomas' Hospital, London, United Kingdom
5. Department of Cardiology, Maastricht University Medical Center, Maastricht, The Netherlands
6. Laboratory of Experimental Cardiology, University Medical Center Utrecht, Utrecht, The Netherlands

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Short title: Prognostic value of CMR imaging findings and cardiovascular events

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Address for correspondence:

H. El Aidi, MD
Department of Cardiology
University Medical Center Utrecht
Heidelberglaan 100
P.O. Box 85500 HP E01.132
3508 GA Utrecht, the Netherlands
Telephone: +31 88 7559832
Fax: +31 30 2581098
E-mail: h.elaidi@umcutrecht.nl

Abstract

Objective To review the prognostic value of cardiac magnetic resonance (CMR) imaging findings for future cardiovascular events in patients with a recent myocardial infarction (MI) and patients with suspected or known coronary artery disease (CAD).

Background Although the diagnostic value of CMR findings is established, the independent prognostic association with future cardiovascular events remains largely unclear.

Methods Studies published until February 2013 identified by systematic MEDLINE and EMBASE searches were reviewed for associations between CMR findings (left ventricular ejection fraction [LVEF], (inducible) wall motion abnormalities [WMA], abnormal myocardial perfusion, microvascular obstruction [MVO], late gadolinium enhancement, edema, intramyocardial haemorrhage), and hard events (all-cause mortality, cardiac death, cardiac transplantation, and myocardial infarction) or major adverse cardiovascular events (MACE: hard events and other cardiovascular events defined by the authors of the evaluated articles) were included.

Results Fifty-six studies (25,497 patients) were evaluated. For patients with recent MI, too few patients were evaluated to establish associations between CMR findings and hard events. LVEF (range of adjusted Hazard Ratios (adjHRs): 1.03-1.05 per % decrease) was independently associated with MACE. In patients with suspected or known CAD, WMA (adjHR: 1.87-2.99), inducible perfusion defects (adj HR: 3.02-7.77), LVEF (adjHR: 0.72-0.82 per 10% increase), and infarction (adjHR: 2.82-9.43) were independently associated with hard events, and presence of inducible perfusion defects was associated with MACE (adjHRs 1.76-3.21).

Conclusion Independent predictors of future cardiovascular events were LVEF for patients with a recent MI and WMA, inducible perfusion defects, LVEF and presence of infarction for patients with suspected or known CAD.

Key words: Cardiac Magnetic Resonance, Prognosis, Systematic Review

List of abbreviations

CAD	coronary artery disease
CMR	cardiac magnetic resonance
IMH	intramyocardial haemorrhage
LGE	late gadolinium enhancement
LVEF	left ventricular ejection fraction
MACE	major adverse cardiac events
MVO	microvascular obstruction
WMA	wall motion abnormality

Introduction

Despite advances in prevention, detection and treatment in the last decades, coronary artery disease (CAD) remains a leading cause of morbidity and mortality in the Western world [1]. Non-invasive imaging modalities like ultrasound, computed tomography, and cardiac magnetic resonance (CMR) imaging have rapidly evolved and are increasingly used for diagnosis and treatment planning in patients with recent myocardial infarction and suspected or known CAD [2-4].

CMR is a comprehensive and accurate imaging modality that combines anatomical information with dynamic assessment of cardiac function. Advantages of CMR over other imaging modalities include high spatial and temporal resolution, the possibility to identify patients with ischemic heart disease in one single examination, and absence of ionizing radiation. Furthermore, CMR is considered the current reference standard for the assessment of ventricular function and myocardial fibrosis using late gadolinium enhancement (LGE) [5, 6]. In addition, CMR is able to assess myocardial viability and ischemia. CMR viability imaging can be performed using low dose dobutamine, LGE scar imaging, or a combination of both. Myocardial wall motion imaging during infusion of dobutamine and perfusion imaging during vasodilator administration are two CMR techniques to assess the presence of myocardial ischemia. The diagnostic performance of CMR for detection of myocardial ischemia and viability has been well investigated [7-9].

Besides being an important diagnostic tool, CMR may also provide prognostic information. However, data on prognosis from individual studies is limited, most often due to small sample sizes and / or a low number of events in these studies. Furthermore, the relative prognostic value of the available CMR imaging findings is unclear. Given this uncertainty, we performed a systematic review of studies reporting prognostic data from patients

undergoing CMR. We specifically aimed to identify those CMR findings that provide the best incremental prognostic information.

Methods

Literature search strategy

We performed a comprehensive systematic literature search in the MEDLINE and EMBASE electronic databases on the 25th of February 2013. The search syntax included synonyms for CMR imaging findings, combined with synonyms for the population of interest (i.e. patients with recent myocardial infarction within 2 weeks, and suspected or known CAD), and a validated list of synonyms to retrieve prognostic studies (Table 1) [10]. We applied no restrictions on publication date and language. Duplicate articles were manually removed from the search results.

Selection of articles

Two authors (HA and AA) independently double screened all titles and abstracts, and excluded articles based on predefined criteria. Disagreements were resolved in a consensus review. An overview of the selection procedure is shown in Figure 1. Reasons for exclusion of articles based on title or abstract were: (1) non-original data (e.g. reviews, editorials, guidelines, comments), (2) non-clinical data (e.g. technical, animal, or *in vitro* studies), (3) case-reports (e.g. studies including less than ten patients), (4) study populations investigated for clinical indications other than recent myocardial infarction and suspected or known CAD, (5) studies that did not describe CMR findings of interest, and (6) when patients were not followed up for cardiovascular events. The full text of the remaining articles was reviewed for information on the prognostic value of CMR imaging findings. Furthermore, studies were excluded if (1) only patients with a specific result on CMR or other imaging results were included (e.g. only patients with wall motion abnormalities on echocardiography were selected), (2) follow-up was only performed in a subgroup of patients defined by the result of

CMR imaging (i.e. only patients with a positive or negative CMR result), (3) no association between CMR finding of interest and cardiovascular events was described, (4) CMR was used to evaluate treatment and not for prognostication, (5) only patients with a low suspicion of CAD were included (Low suspicion of CAD was defined as studies only including patients with chest pain without ECG abnormalities and / or negative cardiac enzymes were not included, as those patients are generally considered not be appropriate candidates for CMR[11]).

All references of the remaining articles were reviewed to retrieve articles initially missed in the original search syntax.

Assessment of methodological quality

This systematic review complies with the preferred reporting items of PRISMA [12]. In contrast to randomized controlled trials and diagnostic studies, there are no criteria for quality appraisal of prognostic studies. We therefore adapted a quality scale from validated scales for other type of clinical studies and previously developed criteria for prognostic factor studies, and addressed study quality on all domains [13, 14]. To assess the quality of data analysis, reporting on treatment of continuous data, prognostic model building strategies, and number of predictors per event were recorded [15].

Data extraction and analysis

A standardized form was used to extract study data, including a description of the study population, CMR imaging findings, patient characteristics, cardiovascular risk factors, and nature and number of events. Hazard ratios (HR) and odds ratios (OR) with accompanying 95% confidence intervals (CI), and p-values of univariable and multivariable analysis were extracted. For multivariable results, the number and nature of variables (e.g. patient characteristics, laboratory and ECG findings, CMR findings, and treatment) included in the analysis were recorded. CMR imaging findings of interest were: left ventricular ejection

fraction (LVEF), wall motion abnormalities (WMA) at rest or after administration of pharmacological stress, myocardial perfusion at rest or after administration of pharmacological stress, early and late microvascular obstruction (MVO), presence and extent of late gadolinium enhancement (LGE), presence of edema, and presence of intramyocardial haemorrhage (IMH). For each of these imaging findings, the cut-off that was used in the article for defining an imaging result positive in the statistical analysis was noted. Outcomes of interest were hard events (defined as all-cause mortality, cardiac death, cardiac transplantation and/or myocardial infarction), and major adverse cardiac events (MACE). MACE was defined as any combination of endpoints as defined by the authors of the original article, including hard events and other events such as congestive heart failure, ischemia, unstable angina, arrhythmia, stroke and/or revascularization.

If study data was used in multiple articles (e.g. when articles referred to the same study, or assessed a comparable number of patients from the same hospital in the same inclusion period evaluating the same imaging findings), we only included the result of the imaging finding of the article with the largest number of patients. CMR imaging findings used for the analysis are listed in table 2. Based on clinical relevance, we divided the study populations in two groups: 1) patients with a recent myocardial infarction, and 2) patients with suspected or known CAD (i.e. patients clinically referred for CMR).

As there are no criteria established yet to identify independent prognostic variables in systematic reviews, we pre-specified the value of the CMR findings by categorizing each feature into one of the following three groups: 1) Independent prognostic CMR finding: the prognostic value of the CMR finding was assessed in at least 3 studies that included a summed total of more than 1,000 patients. The summed number of patients included in studies with a significant result on multivariable analysis divided by the total number of evaluated patients was more than 50%; 2) No independent prognostic CMR finding: the

prognostic value of the imaging finding was assessed in at least 3 studies that included a summed total of more than 1,000 patients. The summed number of patients included in the studies with a significant result on multivariable analysis divided by the total number of patients was less than 50%; 3) Not enough evidence to establish the prognostic value of this finding: CMR findings were studied in less than a summed total of 1,000 patients and / or less than three studies. For the findings that satisfied the criteria of an independent prognostic CMR finding, the ranges of adjusted HRs as reported in the investigated studies are reported. A p-value of less than 0.05 was considered statistically significant.

Results

Search results

Our search yielded 3,040 articles in MEDLINE and 656 articles in EMBASE. Of these, 3,613 articles were excluded based on title and abstract, and 26 articles based on full text screening, including five articles investigating patients with a low suspicion of CAD [16-20] (Figure 1). Reference cross-checking of the selected articles yielded no additional studies. Of the remaining 56 studies, 27 investigations reported on patients with a recent myocardial infarction [21-47] and 29 studies reported on patients with suspected or known CAD [48-76]. Study and patient characteristics of the selected articles are listed in Table 3 and 4, respectively. The total number of patients included in the studies ranged between 44 and 2194, with a mean age ranging from 52 to 67 years and a follow-up duration between 6 and 74 months. More details regarding study and patient characteristics, CMR imaging findings and patient characteristics, as well as observed numbers and types of events are listed in Tables 3 and 4.

Methodological aspects of the included studies

The study population, completeness and duration of follow-up, definition of prognostic variables and outcome were clearly described in most studies (Figure 3). Several issues

concerning the statistical analyses are given in Table 5. First, 31 of the 56 studies (55%) categorized one or more continuous prognostic variables used in the multivariable analysis. Second, four of the 53 included studies (8%) used previously published literature to determine the most relevant variables for subsequent multivariable analysis. Finally, in the majority of studies, the number of events per variable in multivariable analyses was less than 10 (hard events: 26 out of 27 studies; MACE: 34 out of 44 studies), leading to a possible overestimation of the reported hazard ratios in those studies [77].

CMR imaging findings in patients with recent myocardial infarction

Five studies analysed hard events, including 1,223 patients after STEMI with a total of 67 hard events. None of the CMR findings was assessed in more than 1,000 patients. Therefore, no inference can be made about the prognostic value of CMR findings and hard events in patients with a recent myocardial infarction. Twenty-seven studies (N= 5,057 patients) analysed the association between CMR findings and MACE (N=888 events). The independent prognostic value of LVEF, MVO not otherwise specified and presence or extent of infarct size was studied in over 1,000 patients and more than 3 studies. LVEF was an independent predictor in multivariable analysis of more than 50% of the studies (group 1). The multivariable hazard ratios of the included studies ranged between 1.03 and 1.05 per % decrease in LVEF. For the remainder of the CMR findings, not enough evidence was available to establish independent prognostic value (group 3). A summary of the results is given in Table 5A. The results of the individual studies are listed in Appendix A1.

CMR imaging findings in patients with suspected or known CAD

Twenty-four studies, comprising 18,212 patients with 958 hard events, studied the association between CMR findings and hard events in patients with suspected or known CAD. Of the CMR findings that were studied in more than 1,000 patients and in at least 3 studies, the presence of inducible WMA, the presence of inducible perfusion defects, LVEF, and

presence of infarct were important independent predictors of hard events (group 1). For the presence of inducible WMA, the multivariable hazard ratios of the included studies ranged between 1.87 and 2.99. As for the presence of perfusion defects, the reported HR ranged between 3.02 and 3.77. Furthermore, for both CMR findings the risk of a hard event increases with the number of segments involved. For LVEF, hazard ratios ranged between 0.72-0.82 per 10% increase in LVEF. As for the presence of infarct the HRs ranged between 2.82 and 9.43.

Eighteen studies (N=12,847 patients) analysed the prognostic value of CMR features for MACE (N=1,859 events). The independent prognostic value of LVEF, WMA score, presence of perfusion defects, and presence or extent of infarct size were studied in over 1,000 patients and more than 3 studies. Of these CMR findings the presence of inducible perfusion defects (range of reported HR between 1.76 and 3.21) presence or extent of infarct size were independent predictors of MACE in patients with suspected or known CAD (group 1). A summary of the results is given in Table 5B. The results of the individual studies are listed in Appendix A2.

Discussion

The results of this systematic review indicate that CMR features are independent predictors of cardiovascular events in patients with recent myocardial infarction as well as patients with suspected or known coronary artery disease. An important finding is that different CMR features are associated with events depending on the patient population under consideration.

This report is among the first comprehensive systematic reviews investigating the independent prognostic value of different CMR findings and the risk of future cardiovascular events. Fifty-six articles with 25,497 patients with recent myocardial infarction or suspected or known CAD were included. We found that most CMR findings were associated with cardiovascular events in the univariable analyses. However, due to the strong associations

with established clinical, i.e. non-imaging cardiovascular prognostic variables, only a few CMR findings were independently related to prognostic events in multivariable analyses.

Patients with recent myocardial infarction

No independent association was found between any of the investigated CMR findings and hard events (all-cause mortality, cardiac death, cardiac transplantation and myocardial infarction), because none of the CMR findings was studied in more than 1,000 patients.

LVEF was the only independent predictor independently associated with MACE.

Furthermore, MVO (not otherwise specified) and the presence or extent of myocardial infarction were no independent prognostic CMR findings in patients with a recent myocardial infarction. The other CMR findings did not meet our criteria for being considered independently associated (group 3). Although some of the CMR findings are promising in patients with recent MI, most of the findings were studied in less than 1,000 patients. More studies including a sufficient number of patients are required to establish the independent prognostic value of the results in recent MI patients.

Although LVEF has most often been used to describe left ventricular function, the prognostic value of LVEF after myocardial function has been questioned. A low LVEF may be the result of reduced contractile function due to extensive myocardial damage, continuing ischemia or presence of myocardial stunning. This systematic review showed that LVEF is one of the few CMR finding that has been widely studied in patients after recent myocardial infarction. Although other CMR findings may theoretically have more prognostic value than LVEF, this needs to be established in future studies with adequate sample sizes.

Histological studies have shown that areas of no-reflow contain capillaries with micro-thrombi that lead to obstruction [78]. Furthermore, hypoxia in this region of ischemia causes disruption of the endothelial layer and thereby extravasation of erythrocytes leading to intramyocardial haemorrhage [79]. This systematic review shows that there is not enough

evidence to support the use of MVO or IMH for prognostication in patients after a recent myocardial infarction. Furthermore, the differences across studies between early and late MVO might be explained by differences in imaging time after STEMI and time after contrast administration. More uniform definition and assessment of MVO are therefore required.

Even though CMR may be used as a diagnostic tool in patients after a recent myocardial infarction, current literature does not support the use of CMR for prognostication. Although CMR is the reference standard for LVEF, other more readily available and less expensive imaging modalities such as echocardiography are probably more suitable for this aim in clinical practice [80, 81].

Patients with suspected or known CAD

Among patients with suspected or known CAD, inducible WMA and inducible perfusion defects were the most important independent predictors of hard events. Other independent predictors were LVEF and infarct size. Furthermore, inducible perfusion defects and presence/extent of infarct were also associated with MACE. These results indicate that both inducible CMR as well as infarct size measurements are important in the prediction of future cardiovascular events.

In a recently published meta-analysis, Lipinski et al. found that a negative stress CMR is associated with a very low risk of cardiovascular death and MI in patients with known or suspected CAD[82]. Our systematic review extends this knowledge by comparing the independent prognostic value by evaluation of multivariable analysis of different CMR findings. We showed that stress CMR, LVEF and infarct size are the most important independent predictors of cardiovascular events in this patient-group.

In current clinical practice, CMR exams are mainly performed to guide clinical decision-making and not to assess future risk of patients. If a patient is found to have abnormal perfusion or wall motion abnormalities, physicians will generally refer them for

revascularization. Although most studies only included late revascularization, the close relation between CMR results and revascularization may have introduced bias in the relation between CMR result and subsequent patient risk because of the influence of revascularization in reducing post-CMR events. Along the same vein, it could have influenced the association between CMR result and MACE due to the inclusion of revascularization in MACE.

Aggregation of studies

Although the primary objective of this study was to give an overview of the available evidence, formal pooling of individual studies would have been problematic for three reasons. First, a large difference in classification and reporting of CMR findings was found. Some of the studies reported investigated variables on a continuous scale, while others used binary divisions and other arbitrarily (study specific) chosen cut-off values, resulting in larger hazard ratios compared to studies that used a scale with multiple points [83]. Second, the majority of the studies included too many variables in their multivariable analysis for the number of events in the study, leading to 'overfitting' and a clearly overestimated hazard ratios [84]. As a rule of thumb, models should be developed with 10-20 events per variable [77]. In case of a low event rate in a study, variables are best selected by using predictors established in literature. Third, the majority of studies reported MACE as a combination of cardiovascular outcomes. The use of MACE increases the event rates, statistical power and captures the overall prognostic value of the CMR imaging findings. However, because MACE included a variety of events with different importance for patients and clinicians, interpretation of aggregated results is difficult and should be done with care. A separate analysis on individual component endpoints could overcome these difficulties given sufficient studies and events are available.

Although the statistical analyses and reporting varied across studies the quality of the individual studies was good. This makes the studies suitable for a meta-analysis using

individual patient data (IPD). IPD is an analysis that uses original source data at the patient-level and has many advantages over a meta-analysis of summary results from the literature including standardizing statistical analyses, performing adjusted analyses in each study with consistent set of adjustment variables and explaining heterogeneity in prognostic variables across subgroups of patients [85-88]. Recent publications have shown that an IPD is achievable for prognostic variables [89, 90]. Several groups are now compiling a CMR registry, which could fulfil an important need [3].

To better facilitate future prognostic research, we recommend the development of reporting guidelines for prognostic studies in cardiovascular imaging. A good example is the REMARK reporting guidelines in oncology, which can also be applied to non-cancer diseases [91]. Also, the recently published PROGRESS recommendations can be translated to the cardiovascular imaging field [92-95].

In conclusion, CMR is capable of providing independent prognostic information that allows for risk stratification after myocardial infarction as well as in patients with suspected or known CAD.

In conclusion, we showed that in patients with a recent myocardial infarction LVEF is an independent prognostic variable. In patients with suspected or known CAD the presence of inducible wall motion abnormalities, inducible perfusion defects, LVEF, and presence of infarction were independent prognostic variables of CMR imaging.

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Figure legend

Figure 1 Literature search and selection process of studies included in systematic review
Of 3,696 potentially relevant articles, 56 articles met our inclusion criteria and were included in the systematic review. CAD=coronary artery disease; CMR= Cardiac Magnetic Resonance; MI= myocardial infarction

Figure 2A Prognostic value of CMR findings and future cardiovascular events, patients with a recent myocardial infarction

In patients with a recent MI a finding was defined as independent prognostic CMR finding if it was assessed in ≥ 3 studies, with a summed total of <1,000 patients and the weighted % of studies with a significant result on multivariable analysis (number of patients in studies with a significant result divided by total number of patients) of <50%. LVEF= left ventricular ejection fraction; WMA= wall motion abnormalities; MVO= microvascular obstruction, NOS= not otherwise specified; IMH= intramyocardial haemorrhage

Figure 2B Prognostic value of CMR findings and future cardiovascular events, in patients with suspected or known CAD

In patients with suspected or known CAD a finding was defined as independent prognostic CMR finding if it was assessed in ≥ 3 studies, with a summed total of <1,000 patients and the weighted % of studies with a significant result on multivariable analysis (number of patients in studies with a significant result divided by total number of patients) of <50%. LVEF= left ventricular ejection fraction, WMA= wall motion abnormalities; MVO= microvascular obstruction, NOS= not otherwise specified.

Figure 3 Methodological quality of included studies

The methodological quality of the included studies was assessed on four domains of potential bias: study population, follow-up, prognostic factor, and outcome. FU= follow-up.

Table 1 Description of the search strategy used to identify publications of interest

Population	((coronary artery disease OR coronary artery diseases OR CAD OR cardiovascular disease OR cardiovascular diseases OR CVD OR acute coronary syndrome OR acute coronary syndromes OR ACS OR coronary stenosis OR coronary stenoses OR heart infarction OR heart infarctions OR (MI NOT mitral insufficiency) OR myocardial infarction OR myocardial infarctions OR STEMI OR NSTEMI OR stable angina OR unstable angina OR angina pectoris OR coronary heart disease OR coronary heart diseases OR chest pain OR heart failure OR ischaemic heart disease OR ischaemic heart diseases OR ischemic heart disease OR ischemic heart diseases)))
Predictive variable	(Magnetic Resonance OR MRI OR CMR OR (MR NOT mitral regurgitation) OR NMR OR perfusion weighted imaging OR (late AND enhancement) OR LGE OR (delayed AND enhancement) OR late-enhancement OR (late AND enhanced) OR late-enhanced OR MRA)
Outcome	(((((Validat* OR Predict*[Title] OR Rule*)) OR (Predict* AND (Outcome* OR Risk* OR Model*))) OR (History OR Variable* OR Criteria OR Scor* OR Characteristic* OR Finding* OR Factor* AND (Predict* OR Model* OR Decision* OR Identif* OR Prognos*))) OR (Decision* AND (Model* OR Clinical* OR Logistic Models[MeSH]))) OR (Prognostic AND (History OR Variable* OR Criteria OR Scor* OR Characteristic* OR Finding* OR Factor* OR Model*))) OR ((risk OR multivariable OR multivariate) AND (association OR associated OR biomarker OR odds OR marker))
Search results (combined with AND)	MEDLINE: 3,040 EMBASE: 656

For MEDLINE, '[tiab]' was added to each search term, and for EMBASE, 'ti;ab' was added unless indicated otherwise.

Table 2 A Study Characteristics: patients with a recent myocardial infarction

First author, Year, Country, Inclusion period	Study population			CMR								Events					
	Number of evaluable result (study population)	Definition of CAD (time between MI and MRI)	Important exclusion criteria	MRI-procedure		Imaging characteristics						Follow-up duration (Months (SD / range))	Hard events		Major adverse cardiac events (MACE)		
				Field strength	pharm . use	LVEF	WMA	Perfusion	MVO	IS	ED		IMH	Definition	N (%)	Definition	N (%)
Ahn, K.T.[21] 2013 Korea (2007-2010)	135 (167)	STEMI (7 (4-15) ⁱ days)	Prior MI or CABG multi-vessel intervention	1.5 T	None	○	○	○	○	●	○	○	32 (22-41)	-	-	CM MI CHF	12 (9)
Amabile, N.[22] 2011 France(2006-2008)	112 (173)	STEMI (4.7±1.9 days)	Left bundle branch block	1.5 T	None	●	○	○	●	○	●	●	11 ^b (NS)	-	-	ACM CHF AR ACS revas	32 (29)
Bodi, V.[23] 2010 Spain (2004-2006)	119 (234)	first STEMI (7±2 days)	Previous MI, cardiac surgery, decreased LVEF	1.5 T	None	⊙	○	○	○	●	○	○	20 ^b (10-41)	-	-	CM MI CHF	18 (15)
Bodi, V.[24] 2009 Spain	214 (250)	STEMI (7±1 days)	Previous MI, cardiac surgery	1.5 T	Do ¹	⊙	●	○	⊙	●	○	○	18 ^b (9-36)	-	-	CM MI CHF	21 (10)

(2004-2006)																			
Bruder, O.[25] 2008 Germany (2004-2005)	67 (143)	STEMI (4.5±2.5 days)	-	1.5 T	None	●	○	○	●	●	○	○	14 ^a (2)	-	-	CM MI CHF UA revas	16	(24)	
Cochet, A.A.[26] 2010 France (2005-2007)	61 (78)	non-STEMI (3-7 days)	Previous MI	3.0 T	None	○	○	○	●	●	○	○	12 ^f (NA)	-	-	CM MI UA CHF	15	(25)	
Cochet, A.A.[27] 2009 France (2001-2005)	184 (190)	AMI (3-7 days)	-	1.5 T	None	●	○	○	●	●	○	○	12 ^f (NA)	-	-	CM MI UA CHF	44	(24)	
Eitel, I.[28] 2010 Germany (nr)	128 (128)	STEMI (3 (2-4) ⁱ days)	-	1.5 T	None	⊙	○	○	⊙	⊙	○	○	19 ^b (14-21) ⁱ	AC M	11 (9)	ACM MI CHF	17	(13)	
Eitel, I.[29] 2011 Germany (nr)	202 (267)	STEMI (3 (2-4) ⁱ days)	Previous MI	1.5 T	None	●	○	○	●	⊙	●	○	19 ^b (14-21)	AC M	14 (7)	ACM MI CHF	33	(16)	
Eitel, I.[30] 2010 Germany (2006-2008)	208 (267)	STEMI (3 (2-4) ⁱ days)	Previous MI/fibrinolys is	1.5 T	None	⊙	○	○	⊙	⊙	●	○	6 ^f (NA)	-	-	ACM MI CHF	26	(13)	
Eitel, I.[31] 2011 Germany (2006-2009)	333 (407)	STEMI (3 (2-4) ⁱ days)	Previous MI/fibrinolys is	1.5 T	None	●	○	○	⊙	●	○	●	6 ^f (NA)			ACM MI CHF	35	(11)	
Grothoff,	421 (524)	STEMI	-	1.5 T	None	●	○	○	●	⊙	○	○	21 ^b (5-	AC	11 (3)	ACM MI	73	(17)	

M.[32] 2012 Germany (nr)	(1-4 days)												39)	M		CHF)
Husser, O.[33] 2010 Spain (2001-2009)	192 (231)	first STEMI (8 (6-11) days)	cardiac surgery	1.5 T	None	⊙	○	●	⊙	●	○	○	22 ^b (12-42)	-	-	CM MI CHF	20 (10)
Husser, O.[34] 2012 Spain (2001-2010)	304 (335)	First STEMI (6 ^b days)	-	1.5 T	None	●	○	○	●	●	●	●	32 ^b (11-50)	-	-	CM MI CHF	47 (15)
Jensen, C.J.[35] 2010 Germany (nr)	50 (70)	STEMI (2.9±1.6 days)	Previous MI, previous PCI/CABG	1.5 T	None	⊙	○	○	○	⊙	○	○	32 ^a (8)	AC M MI	6 ⁾ (12)	CM MI CHF UA revas	27 (54)
Klug, G.[36] 2012 Austria (2005-2007)	107 (129)	STEMI (2 (2-4) ⁱ days)	CHF	1.5 T	None	●	○	○	●	●	○	○	53 ^b (45-60) ⁱ	-	-	ACM MI CVA CHF revas ischemia AF	63 (59)
Larose, E.[37] 2010 Canada (nr)	103 (104)	STEMI, Nr	MI (<6 months), revas (<6 months)	1.5 T	None	○	○	○	○	●	○	○	33 ^b (24-42) ⁱ	-	-	ACM MI AR CHF LVEF<35	23 (22)
Lønborg, J.T.[38] 2013 Denmark (nr)	199 (287)	First STEMI 2 (1-3) ⁱ days	Previous MI/CABG, acute stent thrombosis	1.5 T	None	●	○	○	○	○	○	○	28 ^b (24-38) ⁱ	-	-	ACM MI HF CVA	40 (20)
Lønborg, J.T.[39]	309 (505)	First STEMI	Previous MI/CABG,	1.5 T	None	●	○	○	○	●	○	○	27 ^b (22-37) ⁱ	-	-	ACM HF	35 (11)

2013 Denmark (nr)	(90 (80-96) ⁱ days)	acute stent thrombosis																
Miszalski-Jamka, T. [40] 2010 USA (nr)	99 (105)	STEMI (3-5 days)	Severe pulmonary disease, CHD, VD, previous PCI/CABG	1.5 T	None	●	○	○	●	●	○	○	38 ^a (11)	-	-		CM MI CHF	41 (41)
De Waha, S. [41] 2012 Germany (nr)	315 (322)	STEMI (3 (2-4) ⁱ days)	Previous MI, prior fibrinolysis	1.5 T	None	○	○	○	⊙	⊙	○	○	20 ^b (13-29) ⁱ	-	-		ACM CHF	37 (12)
De Waha, S. [42] 2012 Germany (2006-2008)	423 (512)	STEMI (3 (2-4) ⁱ days)	Prior fibrinolysis	1.5 T	None	●	○	○	●	●	○	○	19 ^b (11-27) ⁱ	-	-		ACM MI CHF	69 (16)
De Waha, S. [43] 2010 Germany (2006-2008)	422 (512)	STEMI (3 (2-4) ⁱ days)	Prior fibrinolysis	1.5 T	None	●	○	○	●	●	○	○	19 ^b (11-27) ⁱ	ACM	25 (6)		ACM MI CHF	69 (17)
Prunier, F. [44] 2008 France (1996-2001)	105 (124)	STEMI (7.8±4.2 days)	Previous MI	1.5 T	None	●	○	○	○	○	○	○	49 ^a (20)	-	-		ACM MI CHF	24 (23)
Raman, S.V. [45] 2010 Italy (nr)	88 (100)	Non-STEMI (2.1±1.5 days)	-	1.5 T	None	○	○	○	○	○	●	○	6 ^f (NA)	-	-		ACM CHF AR ACS	16 (18)
Wu, E. [46] 2008 USA (1999-2006)	113 (124)	STEMI (2 (2-4) ⁱ days)	Previous MI, revas, AR	1.5 T	None	●	○	○	○	●	○	○	18 ^b (7-23) ⁱ	-	-		CM MI CHF	16 (14)

Wu, K.C. [47] 1998 USA (nr)	44 (44)	AMI (10±6 days)	-	1.5 T	None	○	○	○	●	●	○	○	16 ^a (5)	-	-	CM MI UA CHF CVA	19 (43)
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Table 2B Study Characteristics: patients with suspected or known CAD

First author, Year Country, Inclusion period	Study population			CMR									Events					
	Number of evaluable result (study populati on)	Definition of CAD (time between MI and MRI)	Important exclusion criteria	MRI- procedure		Imaging characteristics							Follow -up durati on	Hard events		Major adverse cardiac events (MACE)		
				Field streng th	pharm. use	LVEF	WMA	Perfusion	MVO	IS	ED	IMH		Months (SD / range)	Definition	N	(%)	Definition
Bello, D. [48] 2011 USA (NS)	100 (100)	history of MI, prior PCI/ CABG, significant stenosis	VD, CMP, myocarditis, CT, MI <1 month	1.0 T 1.5 T	None	●	○	○	○	●	○	○	58 _a (19)	ACM	30 (30)	-	-	-
Bertaso, A.G.[49] 2012 Australia (2008- 2009)	362 (362)	Clinically referred	Prior CABG	1.5 T	As	●	○	●	○	●	○	○	22 (18- b 25)	-	-	CM MI revas ischem ia	38 (1 0)	
Bingham, S.E. [50] 2011 USA (2002-	908 (1009)	Suspected CAD, clinically referred	severe VD	1.5 T	As	●	●	●	○	●	○	○	31 _a (14)	CM MI	35 (4)	ACM MI revas	10 (1 1 1)	

Gebker, R.[59] 2011 Germany (2005-2008)	1532 (1699)	Chest pain/dyspnea, suspected/known CAD	UA, myocarditis, endocarditis, AF	1.5 T	Do/At	○ ● ○ ○ ○ ○ ○ ○	25 _a (10)	CM MI	30 (2)	-	-
Hundley, W.G.[60] 2002 USA (1997-1999)	279 (338)	Clinically referred, inconclusive echo	-	1.5 T	Do ^h , At	⊙ ● ○ ○ ○ ○ ○ ○	20 _a (NR)	CM MI (ACM)	18 (6) 20 (7)	CHF UA revas	97 (35)
Jahnke, C.[61] 2011 Germany (2001-2008)	679 (717)	Chest pain/dyspnea, suspected /known CAD	-	1.5 T	Do ^h /As	⊙ ⊙ ● ○ ○ ○ ○ ○ ○	57 _a (26)	CM MI	77 (11)	CM MI revas	30 (465)
Jahnke, C.[62] 2007 Germany (2001-2005)	461 (513)	Chest pain/dyspnea, suspected /known CAD	-	1.5 T	Do ^h /As/At	● ⊙ ⊙ ○ ○ ○ ○ ○ ○	27 _a (12)	CM MI	19 (4)	-	-
Kelle, S.[63] 2011 Germany (2000-2004)	1017 (1463)	Suspected/known CAD, clinically referred	Early revas	1.5 T	Do ^h , At	● ● ○ ○ ○ ○ ○ ○ ○ ○	44 _a (24)	CM MI	46 (5)	ACM MI UA CHF AR revas	17 (188)
Larose, E.[64] 2007 USA (nr)	147 (153)	>30 days after acute MI, clinically referred	Conditions affecting RV function	1.5 T	None	● ○ ○ ○ ● ○ ○ ○	17 (6- _b 53)	ACM	26 (18)	-	-
Lo, K.Y.[65] 2011 Hong Kong (2003-2008)	203 (260)	Suspected or known CAD, clinically referred	Intermediate stenosis, CMP, myocarditis	NS	As	● ● ● ○ ● ○ ○ ○	38 _a (19)	CM MI	15 (7)	-	-
Kaminski, M.[66] 2011 USA (nr)	210 (252)	HT, Clinically referred	Previous MI, myocarditis, VD, NYHA	1.5 T	None	● ● ○ ○ ● ○ ○ ○	19 (6- _b 47)	ACM	21 (10)	ACM MI UA	48 (23)

			IV											CHF				
Korosoglou, G.[67] 2010 Germany (2004-2008)	1493 (1784)	Suspected or known CAD, clinically referred	No sinus rhythm, UA, severe HT, moderate/severe VD	1.5 T	Do ^h , At	●	●	●	○	○	○	○	○	24 _a (12)	CM MI	53 (4)	-	-
Korosoglou, G.[68] 2011 Germany (2006-2009)	320 (382)	Suspected or known CAD, clinically referred	No sinus rhythm, UA, severe HT, moderate/severe VD	1.5 T	Do ^h , At	⊙	●	○	○	○	○	○	○	28 _a (9)	CM MI	35 (11)	-	-
Krittayaphong, R.[69] 2009 Thailand (nr)	2194 (2272)	≥ 30 years of age, clinically referred	Urgent revas	1.5 T	None	●	○	○	○	●	○	○	○	30 _a (19)	CM MI	92 (4)	CM MI UA CHF AR	21 (1 0 0)
Krittayaphong, R.[70] 2011 Thailand (2004-2008)	1232 (1232)	Suspected or known CAD	Previous MI	1.5 T	As	⊙	⊙	●	○	⊙	○	○	○	35 _a (16)	CM MI	40 (3)	CM MI UA CHF	13 (9 5)
Krittayaphong, R.[71] 2009 Thailand (2002-2006)	1366 (1418)	Suspected or known CAD	Q-wave, non-CAD cardiac disease	1.5 T	None	⊙	○	○	○	●	○	○	○	31 _a (16)	CM MI	58 (4)	CM MI UA CHF AR	15 (1 7 1)
Krittayaphong, R.[72] 2010 Thailand (2002-2007)	1644 (1644)	≥30 years of age, HT, clinically referred	Previous MI, urgent revas	1.5 T	None	⊙	●	○	○	⊙	○	○	○	28 _a (18)	CM MI	62 (4)	CM MI UA CHF AR	17 (1 8 1)
Kwong, R.Y.[73] 2006	195 (221)	Suspected or known CAD,	Previous MI, CMP, UA,	1.5 T	None	⊙	●	○	○	●	○	○	○	16 _b (6-42)	CM	17 (9)	CM MI	31 (1 6)

USA (nr)		clinically referred	myocarditis, NYHA IV, stenosis,													UA CHF AR	
Kwong, R.Y.[74] 2008			Myocarditis, CMP													ACM	38 (3)
USA (nr)	107 (109)	Diabetes mellitus, clinically referred	myocarditis, NYHA IV, stenosis, UA	1.5 T	None	◉	◉	○	○	◉	○	○	17 (6- b 57) ^f	-	-	MI AR	6
Steel, K.[75] 2009			UA, CHF	1.5 T	As / Di	●	○	●	○	●	○	○	17 (8- b 56)	CM MI	28 (11)	MI UA revas	49 (19)
Canada (nr)	254 (264)	Clinically referred														ACM	89 (40)
Wallace, E.L.[76] 2009			Men	1.5 T	Do, At	◉	◉	○	○	○	○	○	74 a (19)	CM MI	36 (16)	MI UA CHF revas	0
USA (1997- 2004)	221 (266)	Clinically referred, inconclusive echo															

a: mean, b: median, c: given as percentage, i: interquartile range; r: range; h: high dose; l: low dose; na: not applicable; nr: not reported; Do: dobutamine; At: atropine; As: adenosine; Di: dipyridamole; GE: General Electric; BMI: Body Mass Index (kg/m²); STEMI: ST-segment elevation myocardial infarction ; AMI: acute myocardial infarction; PCI: percutaneous coronary intervention ; CABG: coronary artery bypass grafting; T: Tesla; CMR: cardiac magnetic resonance imaging; CHD: congenital heart disease; CMP: cardiomyopathy; HT: hypertension; ACS: acute coronary syndrome; AS: aortic syndrome; VD: valvular disease; revas: revascularization; MI: Myocardial infarction; CM: cardiac mortality; ACM: all-cause mortality; LVEF: left ventricular ejection fraction; UA: unstable angina; CHF: congestive heart failure; NYHA: New York Health Association; CT: cardiac transplant; AR: arrhythmia; LV mass: left ventricular mass; PE: pulmonary embolism; CVA: cerebrovascular accident; OCAD: obstructive coronary artery disease; CP: chest pain; CAD: coronary artery disease; SD: standard deviation; ● no overlap with other studies, CMR imaging finding included in systematic review; ◉ overlap with other studies, CMR imaging finding not included in systematic review ○ Imaging finding not described in article

Table 3A Patient characteristics: patients with a recent myocardial infarction

Reference	N with evaluable result (N in study population)	Age (SD/range)	Men (%)	History of CAD (%)	Diabetes (%)	HCL (%)	Hypertension (%)	Smoking (%)	BMI (range/SD)
Ahn, K.T.[21]	135 (167)	58 12	87	na	25	27	31	59	nr
Amabile, N.[22]	112 (173)	58 ^a (12)	83	na	17	34	38	60	27 (1)
Bodi, V.[23]	119 (234)	56 ^a (11)	90	na	15	39	35	71	nr
Bodi, V.[24]	214 (250)	57 ^a (12)	84	na	16	37	41	63	nr
Bruder, O.[25]	67 (143)	61 ^a (12)	81	na	21	75	69	43	27 (4)
Cochet, A.A.[26]	61 (78)	62 ^a (12)	77	na	7	43	36	41	27 (4)
Cochet, A.A.[27]	184 (190)	60 ^b (50-72) ⁱ	77	na	10	39	36	47	26 ^b (24-29) ⁱ
Eitel, I.[28]	128 (128)	67 ^b (55-76) ⁱ	74	na	23	34	69	37	nr
Eitel, I.[29]	202 (267)	66 ^b (55-74) ⁱ	70	na	25	34	67	41	nr
Eitel, I.[30]	208 (267)	66 ^b (55-74) ⁱ	70	na	25	34	67	41	nr
Eitel, I.[31]	333 (407)	64 ^b (53-73) ⁱ	74	na	23	35	64	41	nr
Grothoff, M.[32]	421 (524)	66 ^a (12)	76	na	26	34	69	42	nr
Husser, O. [33]	192 (231)	58 ^a (12)	82	na	17	37	41	65	nr
Husser, O.[34]	304 (335)	58 ^a (12)	80	61	17	38	46	60	nr
Jensen, C.J. [35]	50 (70)	58 ^a (11)	82	na	nr	nr	nr	nr	27 (5)
Klug, G.[36]	107 (129)	57 ^a (12)	84	na	8	81	60	56	26 (4)
Larose, E. [37]	103 (104)	58 ^a (55-60) ⁱ	77	na	8	49	34	52	nr
Lønborg, J.T.[38]	199 (287)	62 ^a (11)	79	na	8	49	32	nr	nr
Lønborg, J.T.[39]	309 (505)	61 ^a (11)	82	na	7	47	32	nr	27 (4)
Miszalski-Jamka, T. [40]	99 (105)	57 ^a (11)	78	na	20	92	72	32	28 (4)
De Waha, S. [41]	315 (322)	65 ^b (54-73) ⁱ	74	na	26	37	69	44	28 ^b (25-30) ⁱ
De Waha, S.[42]	423 (512)	65 ^b (55-73) ⁱ	75	na	26	33	68	42	27 (25-30) ⁱ
De Waha, S. [43]	422 (512)	65 ^b (55-73) ⁱ	75	na	26	33	68	42	28 ^b (25-30) ⁱ
Prunier, F. [44]	105 (124)	59 ^a (13)	85	na	12	43	33	62	nr
Raman, S.V. [45]	88 (100)	59 ^a (12)	65	na	43	nr	78	51	29 (26-33) ⁱ
Wu, E. [46]	113 (124)	57 ^a (11)	83	na	17	53	43	52	nr
Wu, K.C. [47]	44 (44)	58 ^a (9)	75	na	nr	nr	nr	nr	nr

a: mean, b: median, c: given as percentage, i: interquartile range

Table 3B Patient characteristics: patients with suspected or known CAD

Reference	N with evaluable result (N in study population)	Age (SD/range)	Men (%)	History of CAD (%)	Diabetes (%)	HCL (%)	Hypertension (%)	smoking (%)	BMI (range/SD)
Bello, D. [48]	100 (100)	66 ^a (11)	87	na	23	67	49	nr	nr
Bertaso, A.G. [49]	362 (362)	62 ^a (12)	58	43	24	60	58	24	nr
Bingham, S.E. [50]	908 (1009)	65 ^b (55-74) ⁱ	59	49	25	nr	64	6	nr
Bodi, V. [51]	420 (420)	64 ^a (11)	61	nr	26	44	50	15	nr
Bodi, V. [52]	1722 (1797)	64 ^a (11)	62	nr	28	55	62	22	nr
Buckert, D. [53]	1152 (1229)	62 ^a (12)	72	nr	21	57	63	24	27 (4)
Catalano, O. [54]	376 (410)	64 ^a (11)	78	nr	21	57	58	59	26 (4)
Charoenpanichkit, C. [55]	353 (362)	64 ^a (12)	54	nr	36	55	69	42	31 (7)
Cheong, B.Y.C. [56]	857 (905)	59 ^a (14)	66	75	37	12	nr	7	nr
Coelho-Filho, O.R. [57]	405 (424)	57 ^a (14)	59	nr	22	57	56	15	28 (6)
Di Bella, G. [58]	231 (231)	64 (11)	89	na	33	52	55	49	26 (24-28) ⁱ
Gebker, R. [59]	1532 (1699)	63 ^a (10)	67	48	23	74	65	31	28 (4)
Hundley, W.G. [60]	279 (338)	63 (11)	56	nr	37	66	76	59	nr
Jahnke, C. [61]	679 (717)	61 ^a (10)	69	54	23	74	78	35	27 (4)
Jahnke, C. [62]	461 (513)	61 ^a (9)	67	52	19	70	76	43	27 (4)
Kelle, S. [63]	1017 (1463)	61 ^a (11)	68	52	17	70	73	44	27 (4)
Larose, E. [64]	147 (153)	63 ^a (11)	78	na	37	89	63	33	nr
Lo, K.Y. [65]	203 (260)	62 ^a (12)	59	16	30	46	70	29	25 (4)
Kaminski, M. [66]	210 (252)	52 ^a (16)	59	20	34	65	nr	27	nr
Korosoglou, G. [67]	1493 (1784)	65 ^a (13)	74	55	19	53	71	18	26 (4)
Korosoglou, G. [68]	320 (382)	64 ^a (14)	74	nr	22	56	76	22	26 (4)
Krittayaphong, R. [69]	2194 (2272)	65 ^a (11)	53	nr	36	65	53	19	24 (3)
Krittayaphong, R. [70]	1232 (1232)	65 ^a (11)	48	nr	35	62	63	15	nr
Krittayaphong, R. [71]	1366 (1418)	64 ^a (11)	55	nr	34	62	49	18	nr
Krittayaphong, R. [72]	1644 (1644)	65 ^a (11)	48	nr	37	65	na	17	25 (4)
Kwong, R.Y. [73]	195 (221)	59 ^a (13)	68	29	25	56	53	32	29 (5)
Kwong, R.Y. [74]	107 (109)	59 ^a (13)	63	nr	na	70	71	23	nr
Steel, K. [75]	254 (264)	58 ^a (13)	59	nr	25	61	57	11	29 (6)
Wallace, E.L. [76]	221 (266)	63 ^a (12)	0	nr	38	57	73	38	33 (8)

a: mean, b: median, c: given as percentage, i: interquartile range

Table 4 Statistical analysis of included studies

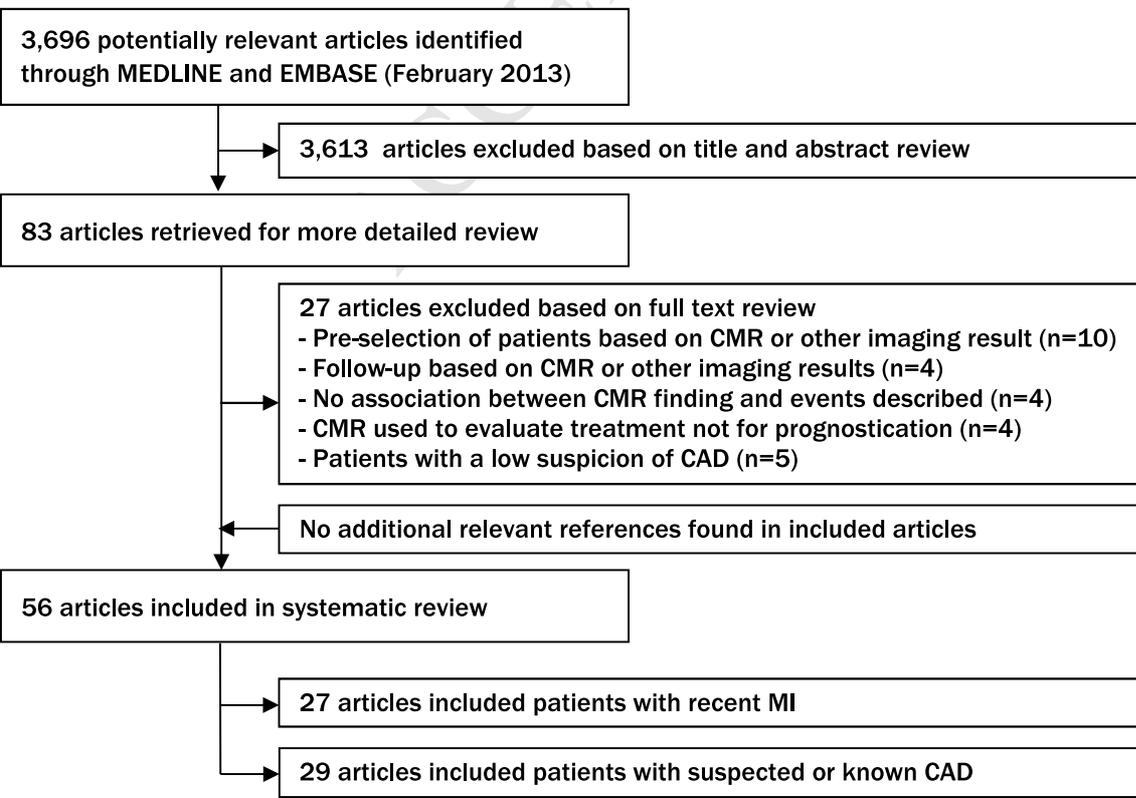
Analysis method (56 studies)	N	(%)
Treatment of continuous risk predictors		
All kept continuous	24	(43%)
All categorized/dichotomized	10	(18%)
Some categorized, some not	21	(38%)
Unclear	1	(2%)
Multivariable analysis (53 studies)		
Model building strategy		
Predefined (eg. based on previous studies or literature)	4	(8%)
Stepwise, forward selection, backward elimination	23	(43%)
All significant in univariable analysis	17	(32%)
Unclear	9	(17%)
Less than 10 events per predictor used		
In studies with hard events as outcome (27 studies)	26	(96%)
In studies with MACE as outcome (44 studies)	34	(77%)
Small sample size / chance findings discussed		
Sample size sufficient	9	(16%)
Small sample size, but chance finding discussed	19	(34%)
Small sample size, chance finding not discussed	28	(50%)

Table 5A Summary CMR findings: patients with recent myocardial infarction

	Independent prognostic CMR finding (group 1)	No independent prognostic CMR finding (group 2)	Not enough evidence to establish the prognostic value (group3)
Hard events	None	None	LVEF WMA (rest/induced) Perfusion (rest/induced) MVO (early/late/NOS) Infarct size (presence/extent/transmurality) Edema IMH
MACE	LVEF	MVO NOS Infarct size (presence/extent)	WMA (rest/induced) Perfusion (rest/induced) MVO (early/late) Infarct size (transmurality) Edema IMH

Table 5B Summary CMR findings: patients with suspected or known CAD

	Independent prognostic CMR finding (group 1)	No independent prognostic CMR finding (group 2)	Not enough evidence to establish the prognostic value (group 3)
Hard events	LVEF WMA induced (presence/segments) Perfusion induced (presence/segments) Infarct size (presence/extent/transmurality)	WMA rest (presence/segments)	WMA rest (score) WMA induced (score) Perfusion rest
MACE	Perfusion induced (presence) Infarct size (presence/extent)	LVEF WMA rest (score)	WMA rest (presence/segments) WMA induced Perfusion rest Perfusion induced (segments/score) Infarct size (transmurality)

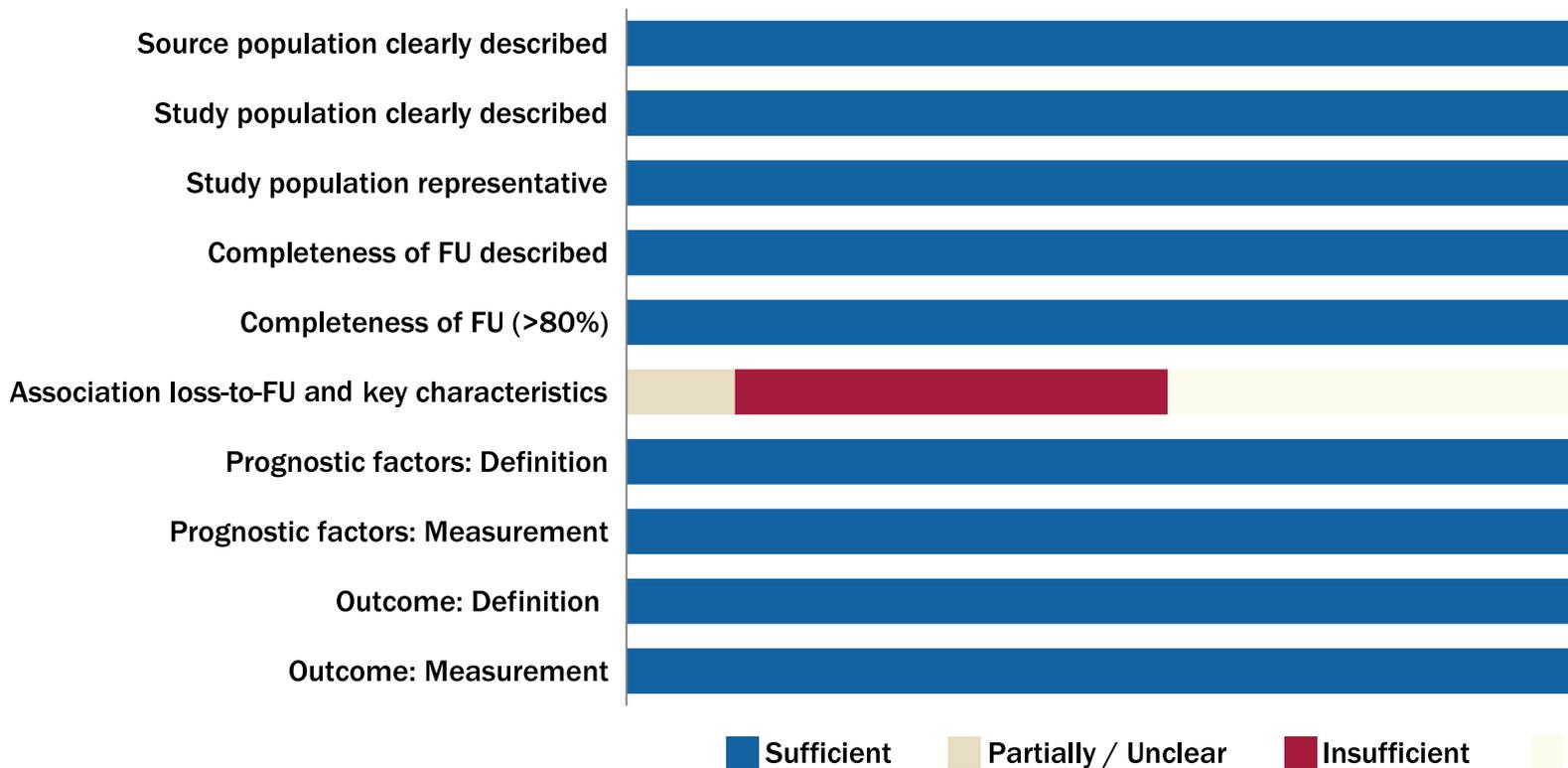


CMR imaging findings		Hard events				Major adverse cardiac events									
Finding	Criterion	Studies evaluated	Patients evaluated (multi-variable analysis)	Weighted % of studies with significant result	Weighted % of studies with significant results on multivariable analysis			Studies evaluated	Patients evaluated (multi-variable analysis)	Weighted % of studies with significant result	Weighted % of studies with significant results on multivariable analysis				
					0%	50%	100%						0%	50%	100%
LVEF	%	2	624	68%				11	2268	70%					
WMA (rest)	Segments	-						1	214	100%					
WMA (induced)	Segments	-						1	214	0%					
Perfusion (rest)	Segments	-						1	192	0%					
MVO	Early	1	422	0%				3	713	40%					
	Late	2	624	68%				3	668	100%					
	NOS	-						6	1047	11%					
Infarct size	Presence / extent	1	422	0%				13	2205	9%					
	Transmurality	-						1*	214	100%					
Edema	%	1	202	100%				3*	600	35%					
IMH	Presence	-						2*	416	100%					

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CMR imaging findings		Hard events				Major adverse cardiac events				
Finding	Criterion	Studies evaluated	Patients evaluated (multi-variable analysis)	Weighted % of studies with significant result	Weighted % of studies with significant results on multivariable analysis	Studies evaluated	Patients evaluated (multi-variable analysis)	Weighted % of studies with significant result	Weighted % of studies with significant results on multivariable analysis	
					0% 50% 100%					
LVEF	%	12	7860	62%		9	6040	36%		
	Presence	6	3784	8%		2	1839	0%		
WMA (rest)	Segments	4	3369	0%		2	630	0%		
	Score	2	1212	84%		3	1578	15%		
	Presence	3	2863	100%		1*	279	0%		
WMA (induced)	Segments	3	3159	68%		1	420	100%		
	Score	1	1017	0%		0*	0	-		
Perfusion (rest)	Presence	1	254	0%		1	254	0%		
	Score	1	254	0%		1	254	0%		
	Presence	5	4012	100%		5	3908	94%		
Perfusion (induced)	Segments	3	2592	82%		1	420	0%		
	Score	-	-	-		1*	254	0%		
Infarct size	Presence / extent	7	3774	63%		10*	6357	62%		
	Transmurality	3	3945	56%		1*	1366	100%		

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Appendix A1 Association between CMR imaging findings and cardiovascular events in individual studies

for patients with a recent myocardial infarction

Imaging feature	Reference	N	Test characteristic	Univariable	Multivariable	Number of variables adjusted for in multivariable analysis				
						Patient characteristics	Lab/ECG	CMR findings	Treatment	
Hard events										
LVEF	Eitel, I.	202	%	0.93 (0.90-0.97)	ns	2	-	3	2	
	De Waha, S.	422	% <35, 35-55, >55	2.31 (1.24-4.30)	2.51 (1.15-5.48)	1	1	2	2	
MVO	De Waha, S. Early	422	presence	3.20 (0.76-13.6)	2.43 (0.53-11.1)	1	1	2	1	
	De Waha, S. Late	422	presence	5.45 (1.28-23.1)	5.12 (1.09-24.1)	1	1	2	1	
Infarct Size	Eitel, I.	202	% LV	1.49 (1.19-1.88)	ns	2	-	3	2	
	De Waha, S.	422	presence	1.03 (1.00-1.05)	0.96 (0.92-1.01)	1	1	2	1	
Edema	De Waha, S.	422	% LV	1.03 (1.00-1.05)	0.96 (0.92-1.01)	1	1	2	1	
	Eitel, I.	202	MSI	0.95 (0.92-0.98)	0.93 (0.91-0.96)	1	-	3	2	
MACE										
LVEF	Amabile, N.	112	%	0.95 (0.92-0.98)	0.96 (0.92-0.99)	-	-	2	1	
	Lønborg, J.T.	199	%	0.95 (0.92-0.99)	nr	3	-	8	2	
	Husser, O.	304	%	0.95 (0.93-0.97)	0.95 (0.92-0.98)	7	1	8	1	
	Grothoff, M.	421	%	0.93 (0.94-0.97)	0.96 (0.93-0.99)	1	1	6	1	
	Prunier, F.	105	%	0.97 (0.97-0.99)	ns	4	2	2	2	
	Wu, E.	113	%	0.91 (0.87-0.95)	0.96 (0.88-1.05)	-	-	2	-	
	Miszalski-Jamka, T.	99	% 10↓	1.56 (1.15-2.11)	ns	-	-	2	-	
	Cochet, A.	184	% <40	2.40 (1.10-5.23) ^{OR}	1.20 (0.94-2.96) ^{OR}	1	-	2	-	
	Bruder, O.	67	% <48	2.02 (0.65-6.42) ^{OR}	ns ^{OR}	3	-	2	-	
	De Waha, S.	423	%	1.04 (1.02-1.06)	1.03 (1.02-1.05)	-	-	4	-	
	Eitel, I.	333	% <53	3.01 (1.36-6.63)	2.59 (1.12-6.01)	6	1	3	3	
	WMA (rest)	Klug, G.	107	% <40.6	ns	1.16 (0.67-1.99)	1	-	2	-
Bodi, V.		214	segments	sign	1.29 (1.11-1.49)	10	-	9	2	
WMA (induced)	Bodi, V.	214	segments	sign	ns	10	-	9	2	
Perfusion (rest)	Husser, O.	192	segments	p=0.004	ns	8	1	10	-	
	Early									
MVO	Cochet, A.	184	presence	3.05 (1.27-7.33) ^{OR}	2.25 (1.02-6.20) ^{OR}	1	-	2	-	
	De Waha, S.	422	presence	1.86 (0.92-3.75)	1.78 (0.77-4.08)	1	1	2	1	
	Klug, G.	107	presence	1.88 (1.04-3.40)	2.06 (1.04-4.09)	1	-	2	-	
	Late									
	Cochet, A.	184	presence	9.97 (4.14-23.99) ^{OR}	8.66 (3.55-21.1) ^{OR}	1	-	2	-	
	De Waha, S.	423	%LV	1.03 (1.01-1.04)	1.03 (1.02-1.05)	-	-	4	-	
	Cochet, A.	61	presence	18.33 (4.39-76.64)	10.4 (2.08-51.8)	1	-	1	-	
	NOS									
	Amabile, N.	112	% LV mass	1.9 (0.95-3.9)	ns	-	-	2	1	
	Bruder, O.	67	% >0.5 LVmass	3.9 (1.1-13.9) ^{OR}	sign	3	-	2	-	
	Grothoff, M.	421	% LV	1.04 (1.02-1.07)	ns	1	1	5	1	
	Husser, O.	304	segments	1.25 (1.14-1.38)	ns	7	1	8	1	
Miszalski-Jamka, T.	99	presence	3.1 (1.29-7.53)	ns	-	-	-	-		
Infarct size	Wu, K.C.	44	% LV	1.06 (1.01-1.11)	ns	-	-	2	-	
	Transmural									
	Bodi, V.	214	segments	Sign	1.30 (1.12-1.51)	10	-	9	2	

	Ahn, K.T.	135	≥ 5 segments	Sign	■	-	-	-	-
	<i>Other</i>								
	Bello, D.	100	% LV mass	1.03 (1.00-1.05)	ns	10	-	1	5
	Bodi, V.	119	mass (gr/m ²)	p=0.001	ns	10	-	9	2
	Bruder, O.	67	% LV mass (>7.3)	3.65 (1.04-12.9) ^{OR}	ns ^{OR}	3	-	2	-
	Cochet, A.	61	% myocardial volume	1.08 (1.01-1.15) ^{OR}	0.97 (0.89-1.06)	1	-	1	-
	Cochet, A.A.	184	% msa (>10)	2.72 (1.07-6.92) ^{OR}	0.64 (0.18-2.21) ^{OR}	1	-	2	-
	De Waha, S.	423	% LV	1.03 (1.01-1.05)	ns	-	-	4	-
	Eitel, I.	333	% LV (>17.5)	2.39 (1.13-5.06)	ns	6	1	3	3
	Klug, G.	107	Infarct mass (gr)	ns	0.69 (0.39-1.21)	1	-	2	-
	Husser, O.	304	% LV mass	1.04 (1.02-1.06)	ns	7	1	8	1
	Husser, O.	192	Infarct mass (gr)	sign	ns	8	1	8	-
	Larose, E.	103	% >23 total myocardium	10.1 (3.7-27.3)	1.27(1.43-2.01)	1	-	1	-
	Miszalski-Jamka, T.	99	% LV	1.03 (1.01-1.05)	1.03 (1.01-1.05)	-	-	2	-
	Wu, E.	113	%	1.08 (1.05-1.11)	1.06 (1.00-1.12)	-	-	2	-
	Wu, K.C.	44	% total myocardium	p<0.05	■	-	-	-	-
	Eitel, I.	208	MSI (>median)	0.95 (0.93-0.97)	0.93 (0.91-0.96)	1	1	3	1
Edema	Raman, S.V.	88	presence	sign	4.47 (1.00-20.0)	-	1	-	1
	Husser, O.	304	% LV mass	1.05 (1.03-1.07)	ns	-	-	-	-
	Husser, O.	304	Segments	1.29 (1.16-1.41)	1.17 (1.03-1.33)	7	1	8	1
IMH	Amabile, N.	112	Presence	3.4 (1.4-7.8)	2.8 (1.2-6.8)	-	-	2	1
	Eitel, I.	333	Presence	P<0.006	⊗	6	1	3	3

nr: not reported, sign: significant, ns: not significant, ■: No multivariable analysis performed; ⊗: not included in model based on clinical experience; ⊗: Not included in model, reason unclear; * Includes echocardiography; msa: myocardial surface area

Appendix A2 Association between CMR imaging findings and cardiovascular events in individual studies for patients suspected or known CAD

Imaging feature	Reference	N	Test characteristic	Univariable	Multivariable	Number of variables adjusted for in multivariable analysis					
						Patient characteristics	Lab/ECG	CMR findings	Treatment		
Hard events											
LVEF	Bello, D.	100	%↓	0.94 (0.91-0.97)	<i>sign</i>	10	-	1	5		
	Larose, E.	147	% 10 ↑	0.77 (0.60-0.98)	0.82 (0.61-1.01)	1	-	2	-		
	Coelho-Filho, O.R.	405	% 10 ↓	0.95 (0.93-0.97)	<i>ns</i>						
	Jahnke, C.	461	% 10 ↓	0.56 (0.40-0.79)	<i>ns</i>	7	-	4	-		
	Charoenpanichkit, C.	353	% <40	3.20 (1.78-5.76)	1.90 (0.98-3.69)	7	-	2	-		
	Cheong, B.Y.	857	% <30, 30-50, >50	p<0.0001	1.96 (1.32-2.91)	9	1	3	2		
	Lo, K.Y.	203	Nr	0.94 (0.92-0.97)	0.92 (0.88-0.96)	5	-	4	-		
	Kelle, S.	1017	%↓	0.96 (0.94-0.98)	<i>ns</i>	8	-	9	6		
	Kaminski, M.	210	% 10 ↑↓	1.03 (0.75-1.42)	<i>ns</i>	1	1	7	1		
	Krittayaphong, R.	2194	% 10 ↓	p<0.001	1.26 (1.06-1.51)	9	1	6	1		
	Korosoglou, G.	1493	%	scale p<0.01	p<0.05	3	-	3	-		
	Bodi, V.	420	%	p=0.1	p>0.05	5	-	5	-		
	Bodi, V.	1722	Segments	p<0.0001	<i>ns</i>	8	2	6	-		
	Bodi, V.	420	Segments	p=0.02	<i>ns</i>	5	-	5	-		
	WMA(rest)	Coelho-Filho, O.R.	405	Presence	7.06 (3.44-14.5)	<i>ns</i>	-	-	-	-	
Kelle, S.		1017	Presence	3.73 (1.99-6.99)	<i>ns</i>	8	-	9	6		
Lo, K.Y.		203	Presence	5.67 (2.04-15.79)	<i>ns</i>	5	-	4	-		
Korosoglou, G.		320	Presence	p<0.001	p<0.01	2	1	-	-		
Krittayaphong, R.		1644	Presence	5.26 (2.92-9.45)	<i>ns</i>	4	2	5	-		
Kwong, K.Y.		195	Presence	6.17 (2.23-17.1)	<i>ns</i>	3	1	7	2		
		195	Score	1.05 (1.02-1.09)	<i>ns</i>	3	1	7	2		
Kaminski, M.		210	Segments	1.49 (0.57-3.93)	<i>ns</i>	2	1	7	1		
Kelle, S.		1017	Segments	1.23 (1.16-1.30)	<i>ns</i>	8	-	9	6		
Kelle, S.		1017	Score	10.7 (5.48-21.0)	7.20 (3.30-15.7)	8	-	9	6		
Bodi, V.		1722	Segments	p<0.0001	1.17 (1.08-1.27)	8	2	6	-		
Bodi, V.		420	Segments	p=0.01	1.15 (1.05-1.26)	5	-	5	-		
WMA(induced)		Gebker, R.	1532	Segments	p<0.001	■	-	-	-	-	
		Charoenpanichkit, C.	353	Presence	2.44 (1.47-4.05)	1.87 (1.06-3.31)	7	-	2	-	
		Korosoglou, G.	1493	Presence	p<0.001	p<0.001	3	-	3	-	
	Kelle, S.	1017	Presence	3.28 (1.83-5.87)	2.99 (1.64-5.40)	8	-	9	6		
			Segments	1.24 (1.16-1.33)	<i>ns</i>	8	-	9	6		
Perfusion (rest)			Score	9.83 (4.90-19.73)	<i>ns</i>	8	-	9	6		
	Steel, K.	254	Presence	4.27 (2.00-9.09)	<i>ns</i>	4	-	12	-		
			Score	1.16 (1.08-1.25)	<i>ns</i>	4	-	12	-		
	Bodi, V.	420	Segments	p=0.02	p>0.05	5	-	5	-		
	Bodi, V.	1722	Segments	P<0.0001	1.10 (1.04-1.17)	8	2	6	-		
Perfusion (induced)	Coelho-Filho, O.R.	405	Presence	17.2 (6.65-44.3)	6.18 (2.07-18.5)	?	?	?	?		
			Segments	1.19 (1.14-1.24)	1.11 (1.03-1.19)	?	?	?	?		
	Jahnke, C.	471	presence (men)	3.12 (1.74-5.57)	3.02 (1.69-5.40)	4	-	3	-		
		208	presence (women)	4.57 (1.27-16.5)	4.08 (1.12-14.8)	1	-	3	-		
	Korosoglou, G.	1493	Presence	p<0.001	p<0.001	3	-	3	-		
Infarct size / mass	Krittayaphong, R.	1232	Presence	8.33 (3.84-18.09)	6.24 (2.7-14.4)	3	-	4	1		
	Lo, K.Y.	203	Presence	9.31 (3.18-27.3)	7.77 (2.50-24.2)	5	-	4	-		
	<i>Transmural</i>										
	Bodi, V.	1722	Segments	p<0.0001	<i>ns</i>	8	2	6	-		

	Cheong, B.Y.	857	Score	p<0.0001	1.26 (1.02-1.55)	9	1	5	2
	Krittayaphong, R.	1366	Score	7.81 (3.79-16.06)	3.44 (1.51-7.80)	5	4	1	3
	<i>Other</i>								
	Larose, E.	147	% 10 LV mass	1.03 (0.79-1.34)	0.91 (0.68-1.21)	1	-	2	-
	Bodi, V.	420	Segments	p=0.05	p>0.05	5	-	5	-
	Coelho-Filho, O.R.	405	Presence	3.08 (1.55-6.11)	ns	-	-	-	-
	Kaminski, M.	210	Presence	2.08 (0.78-5.59)	ns	1	1	7	1
	Krittayaphong, R.	2194	Presence	p<0.001	2.82 (1.53-5.18)	9	1	6	1
	Kwong, R.Y.	195	Segments	1.34 (1.17-1.54)	ns	3	1	7	2
			% LV Mass	1.10 (1.06-1.15)	ns	3	1	7	2
			Presence	10.9 (3.75-31.9)	9.43 (3.15-28.3)	3	1	7	2
	Lo, K.Y.	203	Presence	9.24 (3.27-26.08)	ns	5	-	4	-
MACE									
LVEF	Bodi, V.	420	%	p=0.009	p>0.05	5	-	5	-
	Bingham, S.E.	908	%	0.97 (0.96-0.99)	0.84 (0.71-1.00)	6	-	10	-
	Buckert, D.	1152	%	0.96 (0.95-0.98)	ns	7	-	4	-
	Di Bella, G.	231	%	0.97 (0.94-0.99)	0.97 (0.94-1.00)	1	-	9	-
	Lønborg, J.	309	% 5↑↓	0.69 (0.60-0.79)	ns	2	-	1	2
	Kaminski, M.	210	% 10 ↑↓	0.84 (0.68-1.04)	ns	2	1	7	1
	Krittayaphong, R.	2194	% 10 ↑↓	p<0.001	1.24 (1.10-1.40)	9	1	6	1
	Steel, K.	254	% 10 ↑↓	0.71 (0.56-0.90)	ns				
	Bertaso, A.G.	362	% <45	sign	ns	3	-	2	-
	Bodi, V.	420	Segments	p<0.001	p>0.05	7	-	5	-
WMA (rest)	Krittayaphong, R.	1644	Presence	3.77 (2.65-5.37)	ns	4	2	5	-
	Kwong, K.Y.	195	Presence	4.79 (2.32-9.92)	0.93 (0.30-2.91)	3	1	7	2
			Score	1.04 (1.01-1.07)	ns	3	1	7	2
	Kaminski, M.	210	Segments	1.49 (0.73-3.06)	ns	2	1	7	1
	Buckert, D.	1152	Score	1.09 (1.06-1.12)	1.07 (0.98-1.09)	7	-	4	-
WMA (induced)	Di Bella, G.	231	Score	3.07 (1.17-8.05)	2.80 (1.06-7.40)	1	-	9	-
	<i>Induced</i>								
	Bingham, S.E.	908	Presence	2.03 (1.33-3.01)	■	6	-	10	-
			Score	1.02 (1.01-1.04)	■	6	-	10	-
	Bodi, V.	420	Segments	p<0.001	1.15 (1.06-1.24)	7	-	5	-
Perfusion (rest)	Hundley, W.G.	279	Presence	2.0 (1.3-3.2)	1.6 (1.0-2.7)	10	-	1	-
	Steel, K.	254	Presence	3.17 (1.62-6.20)	ns	8	-	8	2
			Score	1.13 (1.05-1.22)	ns	8	-	8	2
Perfusion (induced)	Bodi, V.	420	Segments	p<0.001	p>0.05	7	-	5	-
	Krittayaphong, R.	1232	Presence	4.35 (2.93-6.47)	2.92 (1.86-4.60)	3	-	4	1
	Buckert, D.	1152	Presence	3.94 (2.58-6.00)	3.21 (2.06-5.00)	7	-	4	-
	Bertaso, A.G.	362	Presence	sign	sign	3	-	2	-
	Steel, K.	254	Presence	8.04 (3.76-17.17)	ns	8	-	8	2
			Score	1.07 (1.04-1.09)	ns	8	-	8	2
	Bingham, S.E.	908	Presence	2.00 (1.31-3.04)	1.76 (1.08-2.87)	6	-	10	-
	Score		1.04 (1.01-1.08)	■	6	-	10	-	
Infarct size	<i>Transmural</i>								
	Krittayaphong, R.	1366	Segments	5.71 (3.71-8.79)	2.55 (1.53-4.25)	5	4	1	3
	Catalano, O.	376	Score	4.82 (2.81-8.31)	☼	10	16	-	-
	<i>Other</i>								
	Bodi, V.	420	segments	p<0.001	p>0.05	7	-	5	-
	Bingham, S.E.	908	presence	2.17 (1.42-3.30)	2.10 (1.22-3.62)	6	-	10	-
	Kaminski, M.	210	presence	2.47 (1.22-5.00)	ns	2	1	7	1
	Krittayaphong R.	2194	presence	P<0.001	2.34 (1.58-3.45)	9	1	6	1
	Buckert, D.	1152	presence	3.17 (2.01-4.99)	ns	7	-	4	-
	Di Bella, G.	231	%LV Mass	1.03 (0.99-1.08)	1.04 (0.99-1.09)	1	-	9	-
Kwong R.Y.	195	presence	8.29 (3.92-17.5)	5.98 (2.68-13.3)	3	1	7	2	
		segments	1.29 (1.15-1.45)	ns	3	1	7	2	
		%LV Mass	1.09 (1.05-1.12)	ns	3	1	7	2	

Catalano, O.	376	%LV Mass \geq 45	13.61 (7.32-25.31)	5.25 (2.64-10.43)	10	16	-	-
Steel, K.	254	presence	8.09 (3.90-16.79)	2.7 (nr)	8	-	8	2
Lønborg, J.	309	% LV	1.81 (1.48-2.34)	1.09 (1.02-1.16)	2	-	1	2
Bertaso, A.G.	362	presence	sign	ns	3	-	2	-

nr: not reported, sign: significant, ns: not significant, ■: No multivariable analysis performed; ■: not included in model based on clinical experience; ■: Not included in model, reason unclear; * Includes echocardiography; msa: myocardial surface area; ↑ increase; ↓ decrease; ↑↓ unclear

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Appendix B Quality assessment (table)

Reference	N	Study population			Study attrition			Prognostic variable		Outcome	
		Source population clearly described	Study population clearly described	Study population representative	Completeness of FU described	Completeness of FU (>80%)	Association loss-to-FU –key characteristics	Definition	Measurement	Definition	Measurement
Recent Myocardial infarction											
Ahn, K.T. (2012)	135	●	●	●	●	●	na	●	●	●	●
Amabile, N. (2011)	112	●	●	●	●	●	○	●	●	●	●
Bodi, V. (2010)	119	●	●	●	●	●	na	●	●	●	●
Bodi, V. (2009)	214	●	●	●	●	●	na	●	●	●	●
Bruder, O. (2008)	67	●	●	●	○	○	○	●	●	●	●
Cochet, A.A. (2010)	61	●	●	●	●	●	na	●	●	●	●
Cochet, A.A. (2009)	184	●	●	●	●	●	na	●	●	●	●
Eitel, I. (2010)	128	●	●	●	●	●	na	●	●	●	●
Eitel, I. (2011)	202	●	●	●	●	●	○	●	●	●	●
Eitel, I. (2010)	208	●	●	●	●	●	○	●	●	●	●
Eitel, I. (2011)	333	●	●	●	●	●	○	●	●	●	●
Grothoff, M. (2012)	421	●	●	●	●	●	○	●	●	●	○
Husser, O. (2010)	192	●	●	●	●	●	na	●	●	●	●
Husser, O. (2012)	304	●	●	●	●	●	na	●	●	●	●
Jensen, C.J. (2010)	50	●	●	u	●	●	na	●	●	●	●
Klug, G. (2012)	107	●	●	●	●	●	○	●	●	●	○
Larose, E. (2010)	103	●	●	●	●	●	○	●	●	●	●
Lønborg, J. (2013)	309	●	●	●	●	●	na	●	●	●	○
Lønborg, J. (2013)	199	●	●	●	●	●	na	●	●	●	○
Miszalski-Jamka, T. (2010)	99	●	●	●	●	●	○	●	●	●	●
De Waha, S. (2012)	315	●	●	●	●	●	○	●	●	●	●
De Waha, S. (2012)	423	●	●	●	●	●	○	●	●	●	●
De Waha, S. (2010)	422	●	●	●	●	●	○	●	●	●	●
Prunier, F. (2008)	105	●	●	●	●	●	na	●	●	●	●
Raman, S.V. (2010)	88	●	●	●	●	●	○	●	●	●	●
Wu, E. (2008)	113	●	●	●	●	●	○	●	●	●	●
Wu, K.C. (1998)	44	●	●	●	○	○	○	●	●	●	●

●: sufficiently described; ○●: unclear or only partially described; ○: insufficiently described; na: not applicable; u: Unclear

Reference	N	Study population			Study attrition			Prognostic variable		Outcome	
		Source population clearly described	Study population clearly described	Study population representative	Completeness of FU described	Completeness of FU (>80%)	Association loss-to-FU –key characteristics	Definition	Measurement	Definition	Measurement
<i>Suspected or known CAD</i>											
Bello, D. (2011)	100	●	●	●	●	●	na	●	●	●	○●
Bertaso, A.G. (2012)	362	●	●	●	●	●	na	●	●	●	○●
Bingham, S.E. (2011)	908	●	●	●	●	●	○	●	●	●	●
Bodi, V. (2007)	420	●	●	●	●	●	na	●	●	●	●
Bodi V. (2012)	1722	●	●	●	●	●	na	●	●	●	●
Buckert, D. (2013)	1152	●	●	●	●	●	○	●	○●	●	●
Catalano, O. (2012)	376	●	●	●	●	●	○	●	○●	●	●
Charoenpanichkit, C. (2010)	353	●	●	●	●	●	na	●	●	●	●
Cheong, B.Y.C. (2009)	857	●	●	●	●	●	na	●	●	●	○●
Coelho-Filho, O.R. (2011)	405	●	●	●	●	●	na	●	●	●	●
Di Bella, G. (2013)	231	●	●	●	●	●	na	●	●	●	○●
Gebker, R. (2011)	1532	●	●	●	●	●	○	●	●	●	●
Hundley, W.G. (2002)	279	●	●	●	●	●	na	●	●	●	●
Jahnke, C. (2011)	679	●	●	●	●	●	○	●	●	●	●
Jahnke, C. (2007)	461	●	●	●	●	●	na	●	●	●	●
Kelle, S. (2011)	1017	●	●	●	●	●	na	●	●	●	●
Larose, E. (2007)	147	●	●	●	●	●	na	●	●	●	●
Lo, K.Y. (2011)	203	●	●	●	○●	○●	○●	●	○●	○●	●
Kaminski, M. (2011)	210	●	●	●	●	●	○	●	●	●	●
Korosoglou, G. (2010)	1493	●	●	●	●	●	na	●	●	●	●
Korosoglou, G. (2011)	320	●	●	●	●	●	○	●	●	●	●
Krittayaphong, R. (2009)	2194	●	●	●	●	●	na	●	●	●	●
Krittayaphong, R. (2011)	1232	●	●	●	○●	○●	○●	●	●	●	●
Krittayaphong, R. (2009)	1366	●	●	●	●	●	na	●	●	●	●
Krittayaphong, R. (2010)	1644	●	●	●	●	●	na	●	●	●	●
Kwong, R.Y. (2006)	195	●	●	●	●	●	na	●	●	●	●
Kwong, R.Y. (2008)	107	●	●	●	●	●	na	●	●	●	●
Steel, K. (2009)	254	●	●	●	●	●	na	●	●	●	●
Wallace, E.L. (2009)	221	●	●	●	●	●	na	●	●	●	●

●: sufficiently described; ○●: unclear or only partially described; ○: insufficiently described; na: not applicable; u: Unclear