Journal of the American College of Cardiology
© 2014 by the American College of Cardiology Foundation
Published by Elsevier Inc.
Vol. 63, No. 11, 2014
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2013.11.048

STATE-OF-THE-ART PAPER

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,*† 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†

Utrecht and Maastricht, the Netherlands; and London, United Kingdom

The goal of this study was 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). Although the diagnostic value of CMR findings is established, the independent prognostic association with future cardiovascular events remains largely unclear. Studies published by February 2013, identified by systematic MEDLINE and EMBASE searches, were reviewed for associations between CMR findings (left ventricular ejection fraction [LVEF], wall motion abnormalities [WMA], abnormal myocardial perfusion, microvascular obstruction, late gadolinium enhancement, edema, and intramyocardial hemorrhage) and hard events (all-cause mortality, cardiac death, cardiac transplantation, and MI) or major adverse cardiovascular events (MACE) (hard events and other cardiovascular events defined by the authors of the evaluated papers). Fifty-six studies (n = 25,497) 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 [HRs]: 1.03 to 1.05 per % decrease) was independently associated with MACE. In patients with suspected or known CAD, WMA (adjusted HRs: 1.87 to 2.99), inducible perfusion defects (adjusted HRs: 3.02 to 7.77), LVEF (adjusted HRs: 0.72 to 0.82 per 10% increase), and infarction (adjusted HRs: 2.82 to 9.43) were independently associated with hard events, and the presence of inducible perfusion defects was associated with MACE (adjusted HRs: 1.76 to 3.21). The independent predictor of future cardiovascular events for patients with a recent MI was LVEF, and the predictors for patients with suspected or known CAD were WMA, inducible perfusion defects, LVEF, and presence of infarction. (J Am Coll Cardiol 2014;63:1031–45) © 2014 by the American College of Cardiology Foundation

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). Noninvasive imaging modalities such as 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 (MI) and suspected or known CAD (2–4).

See page 1046

CMR is a comprehensive and accurate imaging modality that combines anatomic 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 1 single examination, and absence of ionizing radiation. Furthermore, CMR is considered the current reference standard for the assessment of ventricular function

From the *Department of Cardiology, University Medical Center Utrecht, Utrecht, the Netherlands; †Department of Radiology, University Medical Center Utrecht, Utrecht, the Netherlands; ‡Julius Center of Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, the Netherlands; §Laboratory of Experimental Cardiology, University Medical Center Utrecht, Utrecht, the Netherlands; ‖Division of Imaging Sciences and Biomedical Engineering, St. Thomas' Hospital, London, United Kingdom; and the ¶Department of Cardiology, Maastricht University Medical Center, Maastricht, the Netherlands. Dr. Nagel has received significant grant support from Bayer Healthcare and Philips Healthcare. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Manuscript received September 10, 2013; revised manuscript received November 5, 2013, accepted November 26, 2013.

Abbreviations and Acronyms

CAD = coronary artery disease
CMR = cardiac magnetic resonance
HR = hazard ratio
IMH = intramyocardial hemorrhage
IPD = individual patient data
LGE = late gadolinium enhancement
LVEF = left ventricular ejection fraction
MACE = major adverse cardiovascular event(s)
MI = myocardial infarction
MVO = microvascular obstruction
WMA = wall motion abnormality/abnormalities

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 2 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 are limited, most often because of small sample sizes and/or the 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 February 25, 2013. The search syntax included synonyms for CMR imaging findings, combined with synonyms for the population of interest (i.e., patients with recent MI 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 papers were manually removed from the search results.

Selection of papers. Two authors (H.A. and A.A.) independently double screened all titles and abstracts, and they excluded papers on the basis of pre-defined criteria. Disagreements were resolved in a consensus review. An overview of the selection procedure is shown in Figure 1. Reasons for exclusion of papers on the basis of title or abstract were: 1) nonoriginal data (e.g., reviews, editorials, guidelines, and comments); 2) nonclinical data (e.g., technical, animal, or in vitro studies); 3) case reports (e.g., studies including <10 patients); 4) study populations investigated for clinical indications other than recent MI and suspected or known CAD; 5) studies that did not describe CMR findings of interest; and 6) studies with patients who were not followed up for cardiovascular events. The full text of the remaining papers 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 [WMA] 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; and 5) only patients with a low suspicion of CAD were included. (Low suspicion of CAD was defined as studies that only included patients with chest pain without electrocardiographic abnormalities and/or without negative cardiac enzymes, because those patients are generally considered to not be appropriate candidates for CMR [11].)

All references included in the remaining papers were reviewed to retrieve papers initially missed in the original search syntax.

Assessment of methodological quality. This systematic review complies with the preferred reporting items of PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) (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 types 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 (HRs) and odds ratios with accompanying 95% confidence intervals, 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 electrocardiographic findings, CMR findings, and treatment) included in the analysis were recorded. CMR imaging findings of interest were left ventricular ejection fraction (LVEF), 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 LGE, presence of edema, and presence of intramyocardial hemorrhage (IMH). For each of these imaging findings, the cutoff that was used in the paper for defining an imaging result as positive in the statistical analysis was noted. Outcomes of interest were hard events (defined as all-cause mortality, cardiac death, cardiac transplantation, and/or MI), and major adverse cardiovascular events (MACE). MACE was

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 ischemic heart disease OR ischemic 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.

ACS = acute coronary syndrome(s); CAD = coronary artery disease; CMR = cardiac magnetic resonance; CVD = cardiovascular disease; LGE = late gadolinium enhancement; MeSH = Medical Subject Headings; MI = myocardial infarction; MR = magnetic resonance; MRA = magnetic resonance angiography; MRI = magnetic resonance imaging; NMR = nuclear magnetic resonance; NSTEMI = non–ST-segment elevation myocardial infarction; STEMI = ST-segment elevation myocardial infarction.

defined as any combination of endpoints as defined by the authors of the original paper, including hard events and other events such as congestive heart failure, ischemia, unstable angina, arrhythmia, stroke, and/or revascularization.

If study data were used in multiple papers (e.g., when papers 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 paper with the largest number of patients. CMR imaging findings used for the analysis are listed in Tables 2 and 3. Based on clinical relevance, we divided the study populations into 2 groups: 1) patients with a recent MI; and 2) patients with suspected or known CAD (i.e., patients clinically referred for CMR).

Because 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 1 of the following 3 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 >1,000 patients. The summed number of patients included in studies with a significant result on multivariable analysis was >50% of the total number of evaluated patients.
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

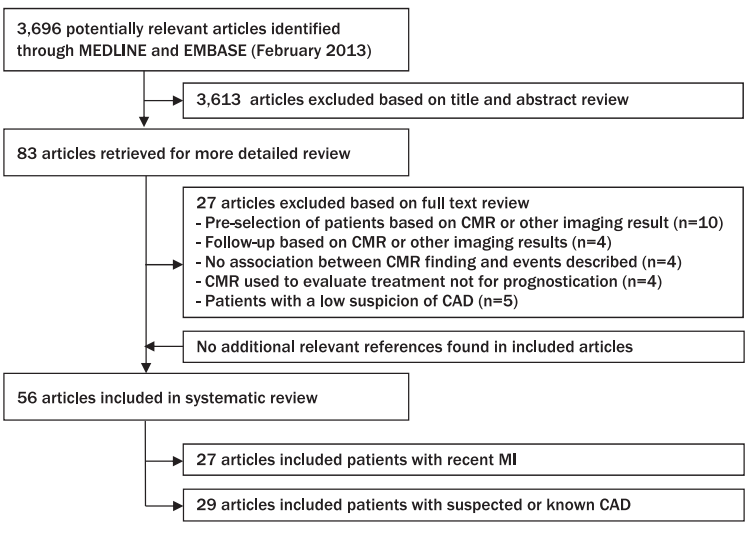

Figure 1 Literature Search and Selection Process of Studies Included in Systematic Review

Of 3,696 potentially relevant papers, 56 papers met our inclusion criteria and were included in the systematic review. CAD = coronary artery disease; CMR = cardiac magnetic resonance; MI = myocardial infarction.

Table 2 Study Characteristics: Patients With a Recent MI

Author, Year (Ref. #) Country (Inclusion Period)	Study Population: Number of Evaluable Results (Study Population)	Study Population: Definition of CAD (Time Between MI and MRI), Days	Important Exclusion Criteria
Ahn et al., 2013 (21) Korea (2007–2010)	135 (167)	STEMI (7 [4–15])	Prior MI or CABG multivessel intervention
Amabile et al., 2011 (22) France (2006–2008)	112 (173)	STEMI (4.7 ± 1.9)	Left bundle branch block
Bodi et al., 2010 (23) Spain (2004–2006)	119 (234)	First STEMI (7 ± 2)	Previous MI, cardiac surgery, decreased LVEF
Bodi et al., 2009 (24) Spain (2004–2006)	214 (250)	STEMI (7 ± 1)	Previous MI, cardiac surgery
Bruder et al., 2008 (25) Germany (2004–2005)	67 (143)	STEMI (4.5 ± 2.5)	—
Cochet et al., 2010 (26) France (2005–2007)	61 (78)	Non-STEMI (3–7)	Previous MI
Cochet et al., 2009 (27) France (2001–2005)	184 (190)	AMI (3–7)	—
Eitel et al., 2010 (28) Germany (nr)	128 (128)	STEMI (3 [2–4])	—
Eitel et al., 2011 (29) Germany (nr)	202 (267)	STEMI (3 [2–4])	Previous MI
Eitel et al., 2010 (30) Germany (2006–2008)	208 (267)	STEMI (3 [2–4])	Previous MI/fibrinolysis
Eitel et al., 2011 (31) Germany (2006–2009)	333 (407)	STEMI (3 [2–4])	Previous MI/fibrinolysis
Grothoff et al., 2012 (32) Germany (nr)	421 (524)	STEMI (1–4)	—
Husser et al., 2010 (33) Spain (2001–2009)	192 (231)	First STEMI (8 [6–11])	Cardiac surgery
Husser et al., 2013 (34) Spain (2001–2010)	304 (335)	First STEMI (6)‡	—
Jensen et al., 2010 (35) Germany (nr)	50 (70)	STEMI (2.9 ± 1.6)	Previous MI, previous PCI/CABG
Klug et al., 2012 (36) Austria (2005–2007)	107 (129)	STEMI (2 [2–4])	CHF
Larose et al., 2010 (37) Canada (nr)	103 (104)	STEMI nr	MI (<6 months), revas (<6 months)
Lønborg et al., 2013 (38) Denmark (nr)	199 (287)	First STEMI (2 [1–3])	Previous MI/CABG, acute stent thrombosis
Lønborg et al., 2013 (39) Denmark (nr)	309 (505)	First STEMI (90 [80–96])	Previous MI/CABG, acute stent thrombosis
Miszalski-Jamka et al., 2010 (40) U.S. (nr)	99 (105)	STEMI (3–5)	Severe pulmonary disease, CHD, VD, previous PCI/CABG
De Waha et al., 2012 (41) Germany (nr)	315 (322)	STEMI (3 [2–4])	Previous MI, prior fibrinolysis
De Waha et al., 2012 (42) Germany (2006–2008)	423 (512)	STEMI (3 [2–4])	Prior fibrinolysis
De Waha et al., 2010 (43) Germany (2006–2008)	422 (512)	STEMI (3 [2–4])	Prior fibrinolysis
Prunier et al., 2008 (44) France (1996–2001)	105 (124)	STEMI (7.8 ± 4.2)	Previous MI
Raman et al., 2010 (45) Italy (nr)	88 (100)	Non-STEMI (2.1 ± 1.5)	—
Wu et al., 2008 (46) U.S. (1999–2006)	113 (124)	STEMI (2 [2–4])	Previous MI, revas, AR
Wu et al., 1998 (47) U.S. (nr)	44 (44)	AMI (10 ± 6)	—

Values are n (N), median (interquartile range), n (%), mean ± SD, or range, except as otherwise indicated. ● = no overlap with other studies, and the CMR imaging finding is included in this systematic review; ⊛ = there is overlap with other studies, and the CMR imaging finding is not included in this systematic review; ○ = imaging finding is not described in the paper. *Low dose. † = fixed follow-up period. ‡Median.

ACM = all-cause mortality; AMI = acute myocardial infarction; AR = arrhythmia; As = adenosine; At = atropine; CABG = coronary artery bypass grafting; CHD = congenital heart disease; CHF = congestive heart failure; CM = cardiac mortality; CMP = cardiomyopathy; CP = chest pain; CT = cardiac transplant; CVA = cerebrovascular accident; Di = dipyridamole; Do = dobutamine; HF = heart failure; HT = hypertension; IMH = intramyocardial hemorrhage; LV = left ventricular; LVEF = left ventricular ejection fraction; MACE = major adverse cardiovascular event(s); MVO = microvascular obstruction; NA = not applicable; nr = not reported; NYHA = New York Health Association; OCAD = obstructive coronary artery disease; PCI = percutaneous coronary intervention; PE = pulmonary embolism; revas = revascularization; UA = unstable angina; VD = valvular disease; other abbreviations as in Table 1.

Continued on next page

Table 2 Continued

CMR									Events		
MRI Procedure		Imaging Characteristics									
Field Strength, T	Pharm. Use	LVEF	WMA	Perfusion	MVO	IS	ED	IMH	Follow-Up Duration, Months (SD/Range)	Hard Events, Definition n (%)	MACE, Definition n (%)
1.5	None	○	○	○	○	●	○	○	32 (22–41)	—	CM, MI, CHF: 12 (9)
1.5	None	●	○	○	●	○	●	●	11‡ (nr)	—	ACM, CHF, AR, ACS, revas: 32 (29)
1.5	None	◉	○	○	○	●	○	○	20 (10–41)	—	CM, MI, CHF: 18 (15)
1.5	Do*	◉	●	○	◉	●	○	○	18 (9–36)	—	CM, MI, CHF: 21 (10)
1.5	None	●	○	○	●	●	○	○	14 ± 2	—	CM, MI, CHF, UA, revas: 16 (24)
3.0	None	○	○	○	●	●	○	○	12† (NA)	—	CM, MI, UA, CHF: 15 (25)
1.5	None	●	○	○	●	●	○	○	12† (NA)	—	CM, MI, UA, CHF: 44 (24)
1.5	None	◉	○	○	◉	◉	○	○	19 (14–21)	ACM: 11 (9)	ACM, MI, CHF: 17 (13)
1.5	None	●	○	○	●	◉	●	○	19 (14–21)	ACM: 14 (7)	ACM, MI, CHF: 33 (16)
1.5	None	◉	○	○	◉	◉	●	○	6† (NA)	—	ACM, MI, CHF: 26 (13)
1.5	None	●	○	○	◉	●	○	●	6† (NA)	—	ACM, MI, CHF: 35 (11)
1.5	None	●	○	○	●	◉	○	○	21 (5–39)	ACM 11 (3)	ACM, MI, CHF: 73 (17)
1.5	None	◉	○	●	◉	●	○	○	22 (12–42)	—	CM, MI, CHF: 20 (10)
1.5	None	●	○	○	●	●	●	●	32 (11–50)	—	CM, MI, CHF: 47 (15)
1.5	None	◉	○	○	○	◉	○	○	32 ± 8	ACM MI 6 (12)	CM, MI, CHF, UA, revas: 27 (54)
1.5	None	●	○	○	●	●	○	○	53 (45–60)	—	ACM, MI, CVA, CHF, revas, ischemia, AF: 63 (59)
1.5	None	○	○	○	○	●	○	○	33 (24–42)	—	ACM, MI, AR, CHF, LVEF <35: 23 (22)
1.5	None	●	○	○	○	○	○	○	28 (24–38)	—	ACM, MI, HF, CVA: 40 (20)
1.5	None	●	○	○	○	●	○	○	27 (22–37)	—	ACM, HF: 35 (11)
1.5	None	●	○	○	●	●	○	○	38 ± 11	—	CM, MI, CHF: 41 (41)
1.5	None	○	○	○	◉	◉	○	○	20 (13–29)	—	ACM, CHF: 37 (12)
1.5	None	●	○	○	●	●	○	○	19 (11–27)	—	ACM, MI, CHF: 69 (16)
1.5	None	●	○	○	●	●	○	○	19 (11–27)	ACM 25 (6)	ACM, MI, CHF: 69 (17)
1.5	None	●	○	○	○	○	○	○	49 ± 20	—	ACM, MI, CHF: 24 (23)
1.5	None	○	○	○	○	○	●	○	6† (NA)	—	ACM, CHF, AR, ACS: 16 (18)
1.5	None	●	○	○	○	●	○	○	18 (7–23)	—	CM, MI, CHF: 16 (14)
1.5	None	○	○	○	●	●	○	○	16 ± 5	—	CM, MI, UA, CHF, CVA: 19 (43)

Table 3 Study Characteristics: Patients With Suspected or Known CAD

Author, Year (Ref. #) Country (Inclusion Period)	Study Population: Number of Evaluable Results (Study Population)	Study Population: Definition of CAD (Time Between MI and MRI)	Study Population: Important Exclusion Criteria
Bello et al., 2011 (48) U.S. (nr)	100 (100)	History of MI, prior PCI/CABG, significant stenosis	VD, CMP, myocarditis, CT, MI <1 month
Bertaso et al., 2012 (49) Australia (2008–2009)	362 (362)	Clinically referred	Prior CABG
Bingham et al., 2011 (50) U.S. (2002–2006)	908 (1,009)	Suspected CAD, clinically referred	Severe VD
Bodi et al., 2007 (51) Spain (2003–2006)	420 (420)	Clinically referred	MI/revas (3 months after CMR)
Bodi et al., 2012 (52) Spain (2007–2009)	1,722 (1,797)	Clinically referred	ACS
Buckert et al., 2013 (53) Germany (2003–2007)	1,152 (1,229)	Suspected/progression of known CAD	Prior MI (<3 months)
Catalano et al., 2012 (54) Italy (2002–2006)	376 (410)	Clinically referred	ACS (<6 weeks), HF, myocarditis, CMP
Charoenpanichkit et al., 2010 (55) U.S. (1997–2004)	353 (362)	Clinically referred, measurable LV mass	—
Cheong et al., 2009 (56) U.S. (2001–2010)	857 (905)	Clinically referred	CMP, myocarditis, sarcoidosis
Coelho-Filho et al., 2011 (57) U.S. (nr)	405 (424)	Clinically referred	AMI, UA, CHF, CMP, myocarditis
Di Bella et al., 2013 (58) Italy (2001–2007)	231 (231)	AMI (>3 months)	UA, recent ischemia, VD, HCM, malignancy
Gebker et al., 2011 (59) Germany (2005–2008)	1,532 (1,699)	Chest pain/dyspnea, suspected/known CAD	UA, myocarditis, endocarditis, AF
Hundley et al., 2002 (60) U.S. (1997–1999)	279 (338)	Clinically referred, inconclusive echo	—
Jahnke et al., 2011 (61) Germany (2001–2008)	679 (717)	Chest pain/dyspnea, suspected/known CAD	—
Jahnke et al., 2007 (62) Germany (2001–2005)	461 (513)	Chest pain/dyspnea, suspected/known CAD	—
Kelle et al., 2011 (63) Germany (2000–2004)	1,017 (1,463)	Suspected/known CAD, clinically referred	Early revas
Larose et al., 2007 (64) U.S. (nr)	147 (153)	>30 days after acute MI, clinically referred	Conditions affecting RV function
Lo et al., 2011 (65) Hong Kong (2003–2008)	203 (260)	Suspected or known CAD, clinically referred	Intermediate stenosis, CMP, myocarditis
Kaminski et al., 2011 (66) U.S. (nr)	210 (252)	HT, clinically referred	Previous MI, myocarditis, VD, NYHA IV
Korosoglou et al., 2010 (67) Germany (2004–2008)	1,493 (1,784)	Suspected or known CAD, clinically referred	No sinus rhythm, UA, severe HT, moderate/severe VD
Korosoglou et al., 2011 (68) Germany (2006–2009)	320 (382)	Suspected or known CAD, clinically referred	No sinus rhythm, UA, severe HT, moderate/severe VD
Krittayaphong et al., 2009 (69) Thailand (nr)	2,194 (2,272)	≥30 yrs of age, clinically referred	Urgent revas
Krittayaphong et al., 2011 (70) Thailand (2004–2008)	1,232 (1,232)	Suspected or known CAD	Previous MI
Krittayaphong et al., 2009 (71) Thailand (2002–2006)	1,366 (1,418)	Suspected or known CAD	Q-wave, non-CAD cardiac disease
Krittayaphong et al., 2010 (72) Thailand (2002–2007)	1,644 (1,644)	≥30 yrs of age, HT, clinically referred	Previous MI, urgent revas
Kwong et al., 2006 (73) U.S. (nr)	195 (221)	Suspected or known CAD, clinically referred	Previous MI, CMP, UA, myocarditis, NYHA IV, stenosis,
Kwong et al., 2008 (74) U.S. (nr)	107 (109)	Diabetes mellitus, clinically referred	Myocarditis, CMP myocarditis, NYHA IV, stenosis, UA
Steel et al., 2009 (75) Canada (nr)	254 (264)	Clinically referred	UA, CHF
Wallace et al., 2009 (76) U.S. (1997–2004)	221 (266)	Clinically referred, inconclusive echo	Men

Values are n (N), mean ± SD, n (%), or median (interquartile range), except as otherwise indicated. ● = no overlap with other studies, and the CMR imaging finding is included in a systematic review; ◉ = there is overlap with other studies, and the CMR imaging finding is not included in a systematic review; ○ = imaging finding is not described in the papers. *High dose. †Range. ‡Median. Abbreviations as in Tables 1 and 2.

Continued on next page

Table 3 Continued

CMR									Events		
MRI Procedure		Imaging Characteristics									
Field Strength, T	Pharm. Use	LVEF	WMA	Perfusion	MVO	IS	ED	IMH	Follow-Up Duration, Months	Hard Events, Definition	MACE, Definition
1.0 1.5	None	●	○	○	○	●	○	○	58 ± 19	ACM: 30 (30)	—
1.5	As	●	○	●	○	●	○	○	22 (18–25)	—	CM, MI, revas, ischemia: 38 (10)
1.5	As	●	●	●	○	●	○	○	31 ± 14	CM, MI: 35 (4)	ACM, MI, revas: 101 (11)
1.5	Di	●	●	●	○	●	○	○	16 ± 10	CM, MI: 23 (5)	CM, MI, UA: 41 (10)
1.5	Di	○	●	●	○	●	○	○	13 ± 10	CM, MI: 61 (4)	—
1.5	As	●	●	●	○	●	○	○	50 ± 25	—	CM, MI, CVA: 88 (8)
1.0	None	○	○	○	○	●	○	○	38 ± 21	—	ACM, HF: 56 (15)
1.5	Do*	●	●	○	○	○	○	○	72 ± 24	CM, MI: 71 (20)	—
1.5	None	●	○	○	○	●	○	○	53‡ (nr)	ACM, CT: 252 (29)	—
1.5	As/Di	●	●	●	○	●	○	○	30 (6–83)	CM, MI: 36 (9)	—
1.5	None	●	●	○	○	●	○	○	38‡ (nr)	—	CM, AR: 19 (8)
1.5	Do/At	○	●	○	○	○	○	○	25 ± 10	CM, MI: 30 (2)	—
1.5	Do,* At	◉	●	○	○	○	○	○	20 (nr)	CM, MI 18 (6) (ACM): 20 (7)	CHF, UA, revas: 97 (35)
1.5	Do*/As	◉	◉	●	○	○	○	○	57 ± 26	CM, MI: 77 (11)	CM, MI, revas: 306 (45)
1.5	Do*/As/At	●	◉	◉	○	○	○	○	27 ± 12	CM, MI: 19 (4)	—
1.5	Do,* At	●	●	○	○	○	○	○	44 ± 24	CM, MI: 46 (5)	ACM, MI, UA, CHF, AR, revas: 178 (18)
1.5	None	●	○	○	○	●	○	○	17 (6–53)	ACM: 26 (18)	—
NS	As	●	●	●	○	●	○	○	38 ± 19	CM, MI: 15 (7)	—
1.5	None	●	●	○	○	●	○	○	19 (6–47)	ACM: 21 (10)	ACM, MI, UA, CHF: 48 (23)
1.5	Do,* At	●	●	●	○	○	○	○	24 ± 12	CM, MI: 53 (4)	—
1.5	Do,* At	◉	●	○	○	○	○	○	28 ± 9	CM, MI: 35 (11)	—
1.5	None	●	○	○	○	●	○	○	30 ± 19	CM, MI: 92 (4)	CM, MI, UA, CHF, AR: 210 (10)
1.5	As	◉	◉	●	○	◉	○	○	35 ± 16	CM, MI: 40 (3)	CM, MI, UA, CHF: 135 (9)
1.5	None	◉	○	○	○	●	○	○	31 ± 16	CM, MI: 58 (4)	CM, MI, UA, CHF, AR: 157 (11)
1.5	None	◉	●	○	○	◉	○	○	28 ± 18	CM, MI: 62 (4)	CM, MI, UA, CHF, AR: 178 (11)
1.5	None	◉	●	○	○	●	○	○	16 (6–42)	CM: 17 (9)	CM, MI, UA, CHF, AR: 31 (16)
1.5	None	◉	◉	○	○	◉	○	○	17 (6–57)†	—	ACM, MI, AR, UA, HF, CVA: 38 (36)
1.5	As/Di	●	○	●	○	●	○	○	17 (8–56)	CM, MI: 28 (11)	CM, MI, UA, revas: 49 (19)
1.5	Do, At	◉	◉	○	○	○	○	○	74 ± 19	CM, MI: 36 (16)	ACM, MI, UA, CHF, revas: 89 (40)

Table 4 Characteristics of Patients With a Recent MI

First Author (Ref. #)	Evaluable Results (Study Population)	Age, Yrs	Men	History of CAD	Diabetes	HCL	Hypertension	Smoking	BMI, (kg/m^2)
Ahn et al. (21)	135 (167)	58 ± 12	87	NA	25	27	31	59	nr
Amabile et al. (22)	112 (173)	58 ± 12	83	NA	17	34	38	60	27 ± 1
Bodi et al. (23)	119 (234)	56 ± 11	90	NA	15	39	35	71	nr
Bodi et al. (24)	214 (250)	57 ± 12	84	NA	16	37	41	63	nr
Bruder et al. (25)	67 (143)	61 ± 12	81	NA	21	75	69	43	27 ± 4
Cochet et al. (26)	61 (78)	62 ± 12	77	NA	7	43	36	41	27 ± 4
Cochet et al. (27)	184 (190)	60 (50–72)	77	NA	10	39	36	47	26 (24–29)
Eitel et al. (28)	128 (128)	67 (55–76)	74	NA	23	34	69	37	nr
Eitel et al. (29)	202 (267)	66 (55–74)	70	NA	25	34	67	41	nr
Eitel et al. (30)	208 (267)	66 (55–74)	70	NA	25	34	67	41	nr
Eitel et al. (31)	333 (407)	64 (53–73)	74	NA	23	35	64	41	nr
Grothoff et al. (32)	421 (524)	66 ± 12	76	NA	26	34	69	42	nr
Husser et al. (33)	192 (231)	58 ± 12	82	NA	17	37	41	65	nr
Husser et al. (34)	304 (335)	58 ± 12	80	61	17	38	46	60	nr
Jensen et al. (35)	50 (70)	58 ± 11	82	NA	nr	nr	nr	nr	27 ± 5
Klug et al. (36)	107 (129)	57 ± 12	84	NA	8	81	60	56	26 ± 4
Larose et al. (37)	103 (104)	58 (55–60)	77	NA	8	49	34	52	nr
Lønborg et al. (38)	199 (287)	62 ± 11	79	NA	8	49	32	nr	nr
Lønborg et al. (39)	309 (505)	61 ± 11	82	NA	7	47	32	nr	27 ± 4
Miszalski-Jamka et al. (40)	99 (105)	57 ± 11	78	NA	20	92	72	32	28 ± 4
De Waha et al. (41)	315 (322)	65 (54–73)	74	NA	26	37	69	44	28 (25–30)
De Waha et al. (42)	423 (512)	65 (55–73)	75	NA	26	33	68	42	27 (25–30)
De Waha et al. (43)	422 (512)	65 (55–73)	75	NA	26	33	68	42	28 (25–30)
Prunier et al. (44)	105 (124)	59 ± 13	85	NA	12	43	33	62	nr
Raman et al. (45)	88 (100)	59 ± 12	65	NA	43	nr	78	51	29 (26–33)
Wu et al. (46)	113 (124)	57 ± 11	83	NA	17	53	43	52	nr
Wu et al. (47)	44 (44)	58 ± 9	75	NA	nr	nr	nr	nr	nr

Values are n/N, mean ± SD, %, or median (interquartile range).
BMI = body mass index; other abbreviations as in Tables 1 and 2.

>1,000 patients. The summed number of patients included in the studies with a significant result on multivariable analysis was <50% of the total number of patients.

3. Not enough evidence to establish the prognostic value of this finding: CMR findings were studied in a summed total of <1,000 patients and/or <3 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 <0.05 was considered statistically significant.

Results

Search results. Our search yielded 3,040 papers in MEDLINE and 656 papers in EMBASE. Of these, 3,613 papers were excluded on the basis of title and abstract, and 26 papers on the basis of full-text screening, including 5 papers investigating patients with a low suspicion of CAD (16–20) (Fig. 1). Reference cross-checking of the selected papers yielded no additional studies. Of the remaining 56 studies, 27 investigations reported on patients with a recent MI (21–47), and 29 studies reported on patients with suspected or known CAD (48–76). Study characteristics of the selected papers are listed in Tables 2 and 3 and patient characteristics in Tables 4 and 5. The total number of patients included in the studies ranged between 44 and 2,194, with a mean age ranging from 52 to 67 years and a follow-up duration between 6 and 74 months.

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 (Fig. 2). The results of the individual studies are listed in Online Table B. Several issues concerning the statistical analyses are given in Table 6. First, 31 of the 56 studies (55%) categorized 1 or more continuous prognostic variables used in the multivariable analysis. Second, 4 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 <10 (hard events 26 of 27 studies; MACE: 34 of 44 studies), leading to a possible overestimation of the reported HRs in those studies (77).

Table 5 Characteristics of Patients With Suspected or Known CAD

First Author (Ref. #)	Evaluable Results (Study Population)	Age, Yrs	Men	History of CAD	Diabetes	HCL	Hypertension	Smoking	BMI (kg/m^2)
Bello et al. (48)	100 (100)	66 ± 11	87	NA	23	67	49	nr	nr
Bertaso et al. (49)	362 (362)	62 ± 12	58	43	24	60	58	24	nr
Bingham et al. (50)	908 (1,009)	65 (55–74)	59	49	25	nr	64	6	nr
Bodi et al. (51)	420 (420)	64 ± 11	61	nr	26	44	50	15	nr
Bodi et al. (52)	1,722 (1,797)	64 ± 11	62	nr	28	55	62	22	nr
Buckert et al. (53)	1,152 (1,229)	62 ± 12	72	nr	21	57	63	24	27 ± 4
Catalano et al. (54)	376 (410)	64 ± 11	78	nr	21	57	58	59	26 ± 4
Charoenpanichkit et al. (55)	353 (362)	64 ± 12	54	nr	36	55	69	42	31 ± 7
Cheong et al. (56)	857 (905)	59 ± 14	66	75	37	12	nr	7	nr
Coelho-Filho et al. (57)	405 (424)	57 ± 14	59	nr	22	57	56	15	28 ± 6
Di Bella et al. (58)	231 (231)	64 ± 11	89	NA	33	52	55	49	26 (24–28)
Gebker et al. (59)	1,532 (1,699)	63 ± 10	67	48	23	74	65	31	28 ± 4
Hundley et al. (60)	279 (338)	63 ± 11	56	nr	37	66	76	59	nr
Jahnke et al. (61)	679 (717)	61 ± 10	69	54	23	74	78	35	27 ± 4
Jahnke et al. (62)	461 (513)	61 ± 9	67	52	19	70	76	43	27 ± 4
Kelle et al. (63)	1,017 (1,463)	61 ± 11	68	52	17	70	73	44	27 ± 4
Larose et al. (64)	147 (153)	63 ± 11	78	NA	37	89	63	33	nr
Lo et al. (65)	203 (260)	62 ± 12	59	16	30	46	70	29	25 ± 4
Kaminski et al. (66)	210 (252)	52 ± 16	59	20	34	65	nr	27	nr
Korosoglou et al. (67)	1,493 (1,784)	65 ± 13	74	55	19	53	71	18	26 ± 4
Korosoglou et al. (68)	320 (382)	64 ± 14	74	nr	22	56	76	22	26 ± 4
Krittayaphong et al. (69)	2,194 (2,272)	65 ± 11	53	nr	36	65	53	19	24 ± 3
Krittayaphong et al. (70)	1,232 (1,232)	65 ± 11	48	nr	35	62	63	15	nr
Krittayaphong et al. (71)	1,366 (1,418)	64 ± 11	55	nr	34	62	49	18	nr
Krittayaphong et al. (72)	1,644 (1,644)	65 ± 11	48	nr	37	65	NA	17	25 ± 4
Kwong et al. (73)	195 (221)	59 ± 13	68	29	25	56	53	32	29 ± 5
Kwong et al. (74)	107 (109)	59 ± 13	63	nr	NA	70	71	23	nr
Steel et al. (75)	254 (264)	58 ± 13	59	nr	25	61	57	11	29 ± 6
Wallace et al. (76)	221 (266)	63 ± 12	0	nr	38	57	73	38	33 ± 8

Values are n (N), mean ± SD, %, or median (interquartile range).
Abbreviations as in Tables 1, 2, and 4.

CMR imaging findings in patients with recent MI. Five studies analyzed hard events, including 1,223 patients after ST-segment elevation MI with a total of 67 hard events. The prognostic value of CMR findings and cardiovascular events are shown in Figure 3. 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 MI. Twenty-seven studies (N = 5,057 patients) analyzed 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 more than 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 HRs 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 7. The results of the individual studies are listed in Online Table 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 HRs of the included studies ranged between 1.87 and 2.99. As for the presence of perfusion defects, the reported HRs ranged

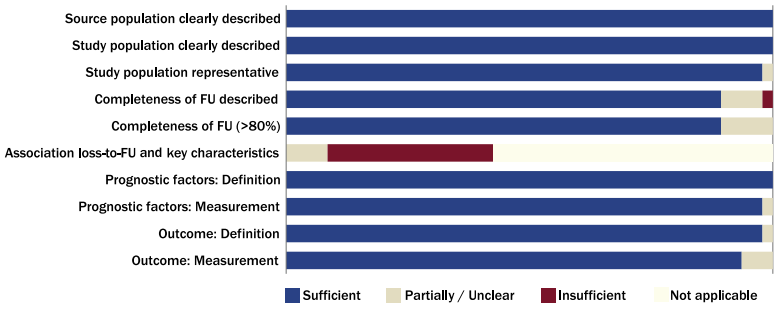

Figure 2 **Methodological Quality of Included Studies**

The methodological quality of the included studies was assessed on 4 domains of potential bias: study population, follow-up, prognostic factor, and outcome. FU = follow-up.

between 3.02 and 3.77. Furthermore, for both of these CMR findings, the risk of a hard event increased with the number of segments involved. For LVEF, HRs ranged between 0.72 and 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) analyzed 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 more than 1,000 patients and more than 3 studies. Of these CMR findings, the presence of inducible perfusion defects (range of reported HRs was between 1.76 and 3.21) and 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 7. The results of the individual studies are listed in Online Table A2.

Discussion

The results of this systematic review indicate that CMR features are independent predictors of cardiovascular events in patients with recent MI as well as in patients with suspected or known CAD. 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. A total of 56 papers with 25,497 patients with recent MI or suspected or known CAD were included. We found that most CMR findings were associated with cardiovascular events in the univariable analyses. However, because of the strong associations with established clinical, that is, non-imaging, cardiovascular prognostic variables, only a few CMR findings were independently related to prognostic events in multivariable analyses.

Patients with recent MI. No independent association was found between any of the investigated CMR findings and hard events (all-cause mortality, cardiac death, cardiac transplantation, and MI), 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 MI were not independent prognostic CMR findings in patients with a recent MI. 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 <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 1 of the few CMR findings that has been widely studied in patients after recent MI. 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 microthrombi 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 IMH (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 MI. Furthermore, the differences across studies between early and late MVO might be explained by differences in imaging time after ST-segment elevation MI 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 MI, 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

A

CMR imaging findings		Hard events				Major adverse cardiac events			
Finding	Criterion	Studies evaluated	Patients evaluated (multivariable analysis)	Weighted % of studies with significant result	Weighted % of studies with significant results on multivariable analysis	Studies evaluated	Patients evaluated (multivariable analysis)	Weighted % of studies with significant result	Weighted % of studies with significant results on multivariable analysis
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%	

B

CMR imaging findings		Hard events				Major adverse cardiac events			
Finding	Criterion	Studies evaluated	Patients evaluated (multivariable analysis)	Weighted % of studies with significant result	Weighted % of studies with significant results on multivariable analysis	Studies evaluated	Patients evaluated (multivariable analysis)	Weighted % of studies with significant result	Weighted % of studies with significant results on multivariable analysis
LVEF	%	12	7860	62%		9	6040	36%	
WMA (rest)	Presence	6	3784	8%		2	1839	0%	
	Segments	4	3369	0%		2	630	0%	
	Score	2	1212	84%		3	1578	15%	
WMA (induced)	Presence	3	2863	100%		1*	279	0%	
	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%	
Perfusion (induced)	Presence	5	4012	100%		5	3908	94%	
	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%	

Figure 3 **Prognostic Value of CMR Findings and Future Cardiovascular Events in Patients With a Recent MI and With Suspected or Known CAD**

(A) In patients with a recent MI, a finding was defined as an 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%. **(B)** In patients with suspected or known CAD, a finding was defined as an 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%. IMH = intramyocardial hemorrhage; LVEF = left ventricular ejection fraction; MVO = microvascular obstruction; NOS = not otherwise specified; WMA = wall motion abnormalities; other abbreviations as in Figure 1. * = studies only included the CMR imaging feature in the univariable analysis.

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 WMA and infarct size measurements are important in the prediction of future cardiovascular events.

In a recently published meta-analysis, Lipinski et al. (82) 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. Our systematic review extends this knowledge by comparing the independent prognostic

Table 6 Statistical Analysis of Included Studies

Analysis method (56 studies)		
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		
Pre-defined (e.g., 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)
<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)

Values are n (%).
MACE = major adverse cardiovascular event(s).

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 examinations 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 WMA, 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 because of 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 3 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, whereas others used binary divisions and other arbitrarily chosen (study-specific) cutoff values, resulting in larger HRs compared with 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 clearly overestimated HRs (84). As a rule of thumb, models should be developed with 10 to 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 and 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

Table 7 Summary CMR findings

	Independent Prognostic CMR Finding (Group 1)	No Independent Prognostic CMR Finding (Group 2)	Not Enough Evidence to Establish the Prognostic Value (Group 3)
Patients with recent MI			
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
Patients with suspected or known CAD			
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)

NOS = not otherwise specified; WMA = wall motion abnormality; other abbreviations as in Tables 1 and 2.

aggregated results is difficult and should be done with care. A separate analysis on individual component endpoints could overcome these difficulties given that 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 fulfill 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 recommendations for tumour MARKer prognostic studies) reporting guidelines in oncology, which can also be applied to noncancer diseases (91). Also, the recently published PROGRESS (Prognosis Research Strategy) recommendations can be translated to the cardiovascular imaging field (92–95).

Conclusions

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

We showed that in patients with a recent MI, LVEF is an independent prognostic variable. In patients with suspected or known CAD, the presence of inducible WMA, inducible perfusion defects, LVEF, and presence of infarction were independent prognostic variables of CMR imaging.

Acknowledgment
The authors thank Cees Haaring (Department of Radiology, University Medical Center Utrecht), for his support in data management.

Reprint requests and correspondence: Dr. Hamza El Aidi, Department of Cardiology, University Medical Center Utrecht, Heidelberglaan 100, P.O. Box 85500 HP E01.132, 3508 GA Utrecht, the Netherlands. E-mail: h.elaidi@umcutrecht.nl.

REFERENCES

1. Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012;380:2095–128.
2. Hulten EA, Carbonaro S, Petrillo SP, Mitchell JD, Villines TC. Prognostic value of cardiac computed tomography angiography: a systematic review and meta-analysis. J Am Coll Cardiol 2011;57:1237–47.
3. Bruder O, Schneider S, Nothnagel D, et al. EuroCMR (European Cardiovascular Magnetic Resonance) registry: results of the German pilot phase. J Am Coll Cardiol 2009;54:1457–66.
4. Jaarsma C, Leiner T, Bekkers SC, et al. Diagnostic performance of noninvasive myocardial perfusion imaging using single-photon emission computed tomography, cardiac magnetic resonance, and positron emission tomography imaging for the detection of obstructive coronary artery disease: a meta-analysis. J Am Coll Cardiol 2012;59:1719–28.
5. Simonetti OP, Kim RJ, Fieno DS, et al. An improved MR imaging technique for the visualization of myocardial infarction. Radiology 2001;218:215–23.
6. Semelka RC, Tomei E, Wagner S, et al. Interstudy reproducibility of dimensional and functional measurements between cine magnetic resonance studies in the morphologically abnormal left ventricle. Am Heart J 1990;119:1367–73.
7. Romero J, Xue X, Gonzalez W, Garcia MJ. CMR imaging assessing viability in patients with chronic ventricular dysfunction due to coronary artery disease: a meta-analysis of prospective trials. J Am Coll Cardiol Img 2012;5:494–508.
8. Nandalur KR, Dwamena BA, Choudhri AF, Nandalur MR, Carlos RC. Diagnostic performance of stress cardiac magnetic resonance imaging in the detection of coronary artery disease: a meta-analysis. J Am Coll Cardiol 2007;50:1343–53.
9. Kim RJ, Wu E, Rafael A, Chen EL, et al. The use of contrast-enhanced magnetic resonance imaging to identify reversible myocardial dysfunction. N Engl J Med 2000;343:1445–53.
10. Ingui BJ, Rogers MA. Searching for clinical prediction rules in MEDLINE. J Am Med Inform Assoc 2001;8:391–7.
11. Hendel RC, Patel MR, Kramer CM, et al. ACCF/ACR/SCCT/SCMR/ASNC/NASCI/SCAI/SIR 2006 appropriateness criteria for cardiac computed tomography and cardiac magnetic resonance imaging: a report of the American College of Cardiology Foundation Quality Strategic Directions Committee Appropriateness Criteria Working Group, American College of Radiology, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance, American Society of Nuclear Cardiology, North American Society for Cardiac Imaging, Society for Cardiovascular Angiography and Interventions, and Society of Interventional Radiology. J Am Coll Cardiol 2006;48:1475–97.
12. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Ann Intern Med 2009;151:264–9, W64.
13. Hayden JA, Cote P, Bombardier C. Evaluation of the quality of prognosis studies in systematic reviews. Ann Intern Med 2006;144:427–37.
14. Bouwmeester W, Zuithoff NP, Mallett S, et al. Reporting and methods in clinical prediction research: a systematic review. PLoS Med 2012;9:1–12.
15. Collins GS, Mallett S, Omar O, Yu LM. Developing risk prediction models for type 2 diabetes: a systematic review of methodology and reporting. BMC Med 2011;9:103.
16. Lerakis S, McLean DS, Anadiotis AV, et al. Prognostic value of adenosine stress cardiovascular magnetic resonance in patients with low-risk chest pain. J Cardiovasc Magn Reson 2009;11:37.
17. Hartlage G, Janik M, Anadiotis A, et al. Prognostic value of adenosine stress cardiovascular magnetic resonance and dobutamine stress echocardiography in patients with low-risk chest pain. Int J Cardiovasc Imaging 2012;28:803–12.
18. Lerakis S, Janik M, McLean DS, et al. Adenosine stress magnetic resonance imaging in women with low risk chest pain: the Emory University experience. Am J Med Sci 2010;339:216–20.
19. Vogel-Claussen J, Skrok J, Dombroski D, et al. Comprehensive adenosine stress perfusion MRI defines the etiology of chest pain in the emergency room: comparison with nuclear stress test. J Magn Reson Imaging 2009;30:753–62.
20. Ingkanisorn WP, Kwong RY, Bohme NS, et al. Prognosis of negative adenosine stress magnetic resonance in patients presenting to an emergency department with chest pain. J Am Coll Cardiol 2006;47:1427–32.
21. Ahn KT, Song YB, Choe YH, et al. Impact of transmural necrosis on left ventricular remodeling and clinical outcomes in patients undergoing

primary percutaneous coronary intervention for ST-segment elevation myocardial infarction. Int J Cardiovasc Imaging 2013;29:835–42.
22. Amabile N, Jacquier A, Shuhab A, et al. Incidence, predictors, and prognostic value of intramyocardial hemorrhage lesions in ST elevation myocardial infarction. Catheter Cardiovasc Interv 2012;79:1101–8.
23. Bodi V, Husser O, Sanchis J, et al. Contractile reserve and extent of transmural necrosis in the setting of myocardial stunning: comparison at cardiac MR imaging. Radiology 2010;255:755–63.
24. Bodi V, Sanchis J, Nunez J, et al. Prognostic value of a comprehensive cardiac magnetic resonance assessment soon after a first ST-segment elevation myocardial infarction. J Am Coll Cardiol Img 2009;2:835–42.
25. Bruder O, Breuckmann F, Jensen C, et al. Prognostic impact of contrast-enhanced CMR early after acute ST segment elevation myocardial infarction (STEMI) in a regional STEMI network: results of the "Herzinfarktverbund Essen". Herz 2008;33:136–42.
26. Cochet A, Lalande A, Lorgis L, et al. Prognostic value of microvascular damage determined by cardiac magnetic resonance in non ST-segment elevation myocardial infarction: comparison between first-pass and late gadolinium-enhanced images. Invest Radiol 2010;45:725–32.
27. Cochet AA, Lorgis L, Lalande A, et al. Major prognostic impact of persistent microvascular obstruction as assessed by contrast-enhanced cardiac magnetic resonance in reperfused acute myocardial infarction. Eur Radiol 2009;19:2117–26.
28. Eitel I, Nowak M, Stehl C, et al. Endothelin-1 release in acute myocardial infarction as a predictor of long-term prognosis and no-reflow assessed by contrast-enhanced magnetic resonance imaging. Am Heart J 2010;159:882–90.
29. Eitel I, Desch S, de Waha S, et al. Long-term prognostic value of myocardial salvage assessed by cardiovascular magnetic resonance in acute reperfused myocardial infarction. Heart 2011;97:2038–45.
30. Eitel I, Desch S, Fuernau G, et al. Prognostic significance and determinants of myocardial salvage assessed by cardiovascular magnetic resonance in acute reperfused myocardial infarction. J Am Coll Cardiol 2010;55:2470–9.
31. Eitel I, Kubusch K, Strohm O, et al. Prognostic value and determinants of a hypointense infarct core in T2-weighted cardiac magnetic resonance in acute reperfused ST-elevation-myocardial infarction. Circ Cardiovasc Imaging 2011;4:354–62.
32. Grothoff M, Elpert C, Hoffmann J, et al. Right ventricular injury in ST-elevation myocardial infarction: risk stratification by visualization of wall motion, edema, and delayed-enhancement cardiac magnetic resonance. Circ Cardiovasc Imaging 2012;5:60–8.
33. Husser O, Bodi V, Sanchis J, et al. Head to head comparison of quantitative versus visual analysis of contrast CMR in the setting of myocardial stunning after STEMI: implications on late systolic function and patient outcome. Int J Cardiovasc Imaging 2010;26:559–69.
34. Husser O, Monmeneu JV, Sanchis J, et al. Cardiovascular magnetic resonance-derived intramyocardial hemorrhage after STEMI: influence on long-term prognosis, adverse left ventricular remodeling and relationship with microvascular obstruction. Int J Cardiol 2013;167:2047–54.
35. Jensen CJ, Jochims M, Hunold P, Sabin GV, Schlosser T, Bruder O. Right ventricular involvement in acute left ventricular myocardial infarction: prognostic implications of MRI findings. AJR Am J Roentgenol 2010;194:592–8.
36. Klug G, Mayr A, Schenk S, et al. Prognostic value at 5 years of microvascular obstruction after acute myocardial infarction assessed by cardiovascular magnetic resonance. J Cardiovasc Magn Reson 2012;14:46.
37. Larose E, Rodes-Cabau J, Pibarot P, et al. Predicting late myocardial recovery and outcomes in the early hours of ST-segment elevation myocardial infarction: traditional measures compared with microvascular obstruction, salvaged myocardium, and necrosis characteristics by cardiovascular magnetic resonance. J Am Coll Cardiol 2010;55:2459–69.
38. Lonborg JT, Engstrom T, Moller JE, et al. Left atrial volume and function in patients following ST elevation myocardial infarction and the association with clinical outcome: a cardiovascular magnetic resonance study. Eur Heart J Cardiovasc Imaging 2013;14:118–27.
39. Lonborg J, Vejlstrup N, Kelbaek H, et al. Final infarct size measured by cardiovascular magnetic resonance in patients with ST elevation myocardial infarction predicts long-term clinical outcome: an observational study. Eur Heart J Cardiovasc Imaging 2013;14:387–95.
40. Miszalski-Jamka T, Klimeczek P, Tomala M, et al. Extent of RV dysfunction and myocardial infarction assessed by CMR are independent outcome predictors early after STEMI treated with primary angioplasty. J Am Coll Cardiol Img 2010;3:1237–46.
41. de Waha S, Eitel I, Desch S, et al. Time-dependency, predictors and clinical impact of infarct transmurality assessed by magnetic resonance imaging in patients with ST-elevation myocardial infarction reperfused by primary coronary percutaneous intervention. Clin Res Cardiol 2012;101:191–200.
42. de Waha S, Desch S, Eitel I, et al. Relationship and prognostic value of microvascular obstruction and infarct size in ST-elevation myocardial infarction as visualized by magnetic resonance imaging. Clin Res Cardiol 2012;101:487–95.
43. de Waha S, Desch S, Eitel I, et al. Impact of early vs. late microvascular obstruction assessed by magnetic resonance imaging on long-term outcome after ST-elevation myocardial infarction: a comparison with traditional prognostic markers. Eur Heart J 2010;31:2660–8.
44. Prunier F, Brette S, Delepine S, Geslin P, Le Jeune JJ, Furber AP. Three-dimensional MRI assessment of regional wall stress after acute myocardial infarction predicts postdischarge cardiac events. J Magn Reson Imaging 2008;27:516–21.
45. Raman SV, Simonetti OP, Winner MW 3rd, et al. Cardiac magnetic resonance with edema imaging identifies myocardium at risk and predicts worse outcome in patients with non-ST-segment elevation acute coronary syndrome. J Am Coll Cardiol 2010;55:2480–8.
46. Wu E, Ortiz JT, Tejedor P, et al. Infarct size by contrast enhanced cardiac magnetic resonance is a stronger predictor of outcomes than left ventricular ejection fraction or end-systolic volume index: prospective cohort study. Heart 2008;94:730–6.
47. Wu KC, Zerhouni EA, Judd RM, et al. Prognostic significance of microvascular obstruction by magnetic resonance imaging in patients with acute myocardial infarction. Circulation 1998;97:765–72.
48. Bello D, Einhorn A, Kaushal R, et al. Cardiac magnetic resonance imaging: infarct size is an independent predictor of mortality in patients with coronary artery disease. Magn Reson Imaging 2011;29:50–6.
49. Bertaso AG, Richardson JD, Wong DT, et al. Prognostic value of adenosine stress perfusion cardiac MRI with late gadolinium enhancement in an intermediate cardiovascular risk population. Int J Cardiol 2013;167:2055–60.
50. Bingham SE, Hachamovitch R. Incremental prognostic significance of combined cardiac magnetic resonance imaging, adenosine stress perfusion, delayed enhancement, and left ventricular function over preimaging information for the prediction of adverse events. Circulation 2011;123:1509–18.
51. Bodi V, Sanchis J, Lopez-Lereu MP, et al. Prognostic value of dipyridamole stress cardiovascular magnetic resonance imaging in patients with known or suspected coronary artery disease. J Am Coll Cardiol 2007;50:1174–9.
52. Bodi V, Husser O, Sanchis J, et al. Prognostic implications of dipyridamole cardiac MR imaging: a prospective multicenter registry. Radiology 2012;262:91–100.
53. Buckert D, Dewes P, Walcher T, Rottbauer W, Bernhardt P. Intermediate-term prognostic value of reversible perfusion deficit diagnosed by adenosine CMR: a prospective follow-up study in a consecutive patient population. J Am Coll Cardiol Img 2013;6:56–63.
54. Catalano O, Moro G, Perotti M, et al. Late gadolinium enhancement by cardiovascular magnetic resonance is complementary to left ventricle ejection fraction in predicting prognosis of patients with stable coronary artery disease. J Cardiovasc Magn Reson 2012;14:29.
55. Charoenpanichkit C, Morgan TM, Hamilton CA, et al. Left ventricular hypertrophy influences cardiac prognosis in patients undergoing dobutamine cardiac stress testing. Circ Cardiovasc Imaging 2010;3:392–7.
56. Cheong BY, Muthupillai R, Wilson JM, et al. Prognostic significance of delayed-enhancement magnetic resonance imaging: survival of 857 patients with and without left ventricular dysfunction. Circulation 2009;120:2069–76.
57. Coelho-Filho OR, Seabra LF, Mongeon FP, et al. Stress myocardial perfusion imaging by CMR provides strong prognostic value to cardiac events regardless of patient's sex. J Am Coll Cardiol Img 2011;4:850–61.
58. Di Bella G, Siciliano V, Aquaro GD, et al. Scar extent, left ventricular end-diastolic volume, and wall motion abnormalities identify high-risk patients with previous myocardial infarction: a multiparametric approach for prognostic stratification. Eur Heart J 2013;34:104–11.

59. Gebker R, Jahnke C, Manka R, et al. The role of dobutamine stress cardiovascular magnetic resonance in the clinical management of patients with suspected and known coronary artery disease. J Cardiovasc Magn Reson 2011;13:46.
60. Hundley WG, Morgan TM, Neagle CM, Hamilton CA, Rerkpattanapipat P, Link KM. Magnetic resonance imaging determination of cardiac prognosis. Circulation 2002;106:2328–33.
61. Jahnke C, Furundzija V, Gebker R, et al. Gender-based prognostic value of pharmacological cardiac magnetic resonance stress testing: head-to-head comparison of adenosine perfusion and dobutamine wall motion imaging. Int J Cardiovasc Imaging 2012;28:1087–98.
62. Jahnke C, Nagel E, Gebker R, et al. Prognostic value of cardiac magnetic resonance stress tests: adenosine stress perfusion and dobutamine stress wall motion imaging. Circulation 2007;115:1769–76.
63. Kelle S, Chiribiri A, Vierecke J, et al. Long-term prognostic value of dobutamine stress CMR. J Am Coll Cardiol Img 2011;4:161–72.
64. Larose E, Ganz P, Reynolds HG, et al. Right ventricular dysfunction assessed by cardiovascular magnetic resonance imaging predicts poor prognosis late after myocardial infarction. J Am Coll Cardiol 2007;49:855–62.
65. Lo KY, Leung KF, Chu CM, Loke KL, Chan CK, Yue CS. Prognostic value of adenosine stress myocardial perfusion by cardiac magnetic resonance imaging in patients with known or suspected coronary artery disease. QJM 2011;104:425–32.
66. Kaminski M, Steel K, Jerosch-Herold M, et al. Strong cardiovascular prognostic implication of quantitative left atrial contractile function assessed by cardiac magnetic resonance imaging in patients with chronic hypertension. J Cardiovasc Magn Reson 2011;13:42.
67. Korosoglou G, Elhmidi Y, Steen H, et al. Prognostic value of high-dose dobutamine stress magnetic resonance imaging in 1,493 consecutive patients: assessment of myocardial wall motion and perfusion. J Am Coll Cardiol 2010;56:1225–34.
68. Korosoglou G, Gitsioudis G, Voss A, et al. Strain-encoded cardiac magnetic resonance during high-dose dobutamine stress testing for the estimation of cardiac outcomes: comparison to clinical parameters and conventional wall motion readings. J Am Coll Cardiol 2011;58:1140–9.
69. Krittayaphong R, Boonyasirinant T, Saiviroonporn P, et al. Prognostic significance of left ventricular mass by magnetic resonance imaging study in patients with known or suspected coronary artery disease. J Hypertens 2009;27:2249–56.
70. Krittayaphong R, Chaithiraphan V, Maneesai A, Udompanturak S. Prognostic value of combined magnetic resonance myocardial perfusion imaging and late gadolinium enhancement. Int J Cardiovasc Imaging 2011;27:705–14.
71. Krittayaphong R, Maneesai A, Chaithiraphan V, Saiviroonporn P, Chaiphet O, Udompunturak S. Comparison of diagnostic and prognostic value of different electrocardiographic criteria to delayed-enhancement magnetic resonance imaging for healed myocardial infarction. Am J Cardiol 2009;103:464–70.
72. Krittayaphong R, Boonyasirinant T, Chaithiraphan V, et al. Prognostic value of late gadolinium enhancement in hypertensive patients with known or suspected coronary artery disease. Int J Cardiovasc Imaging 2010;26 Suppl 1:123–31.
73. Kwong RY, Chan AK, Brown KA, et al. Impact of unrecognized myocardial scar detected by cardiac magnetic resonance imaging on event-free survival in patients presenting with signs or symptoms of coronary artery disease. Circulation 2006;113:2733–43.
74. Kwong RY, Sattar H, Wu H, et al. Incidence and prognostic implication of unrecognized myocardial scar characterized by cardiac magnetic resonance in diabetic patients without clinical evidence of myocardial infarction. Circulation 2008;118:1011–20.
75. Steel K, Broderick R, Gandla V, et al. Complementary prognostic values of stress myocardial perfusion and late gadolinium enhancement imaging by cardiac magnetic resonance in patients with known or suspected coronary artery disease. Circulation 2009;120:1390–400.
76. Wallace EL, Morgan TM, Walsh TF, et al. Dobutamine cardiac magnetic resonance results predict cardiac prognosis in women with known or suspected ischemic heart disease. J Am Coll Cardiol Img 2009;2:299–307.
77. Peduzzi P, Concato J, Kemper E, Holford TR, Feinstein AR. A simulation study of the number of events per variable in logistic regression analysis. J Clin Epidemiol 1996;49:1373–9.
78. Kloner RA, Ganote CE, Jennings RB. The "no-reflow" phenomenon after temporary coronary occlusion in the dog. J Clin Invest 1974;54:1496–508.
79. Fishbein MC, J YR, Lando U, Kanmatsuse K, Mercier JC, Ganz W. The relationship of vascular injury and myocardial hemorrhage to necrosis after reperfusion. Circulation 1980;62:1274–9.
80. Moller JE, Hillis GS, Oh JK, Reeder GS, Gersh BJ, Pellikka PA. Wall motion score index and ejection fraction for risk stratification after acute myocardial infarction. Am Heart J 2006;151:419–25.
81. Mollema SA, Nucifora G, Bax JJ. Prognostic value of echocardiography after acute myocardial infarction. Heart 2009;95:1732–45.
82. Lipinski MJ, McVey CM, Berger JS, Kramer CM, Salerno M. Prognostic value of stress cardiac magnetic resonance imaging in patients with known or suspected coronary artery disease: a systematic review and meta-analysis. J Am Coll Cardiol 2013;62:826–38.
83. Royston P, Altman DG, Sauerbrei W. Dichotomizing continuous predictors in multiple regression: a bad idea. Stat Med 2006;25:127–41.
84. Babyak MA. What you see may not be what you get: a brief, nontechnical introduction to overfitting in regression-type models. Psychosom Med 2004;66:411–21.
85. Riley RD, Lambert PC, Abo-Zaid G. Meta-analysis of individual participant data: rationale, conduct, and reporting. BMJ 2010;340:c221.
86. Hemingway H, Philipson P, Chen R, et al. Evaluating the quality of research into a single prognostic biomarker: a systematic review and meta-analysis of 83 studies of C-reactive protein in stable coronary artery disease. PLoS Med 2010;7:e1000286.
87. Riley RD, Heney D, Jones DR, et al. A systematic review of molecular and biological tumor markers in neuroblastoma. Clin Cancer Res 2004;10Pt 1:4–12.
88. Collins GS. Opening up multivariable prediction models: consensus-based guidelines for transparent reporting. 2011. Available at: http://blogs.bmj.com.proxy.library.uu.nl/bmj/2011/08/03/gary-collins-opening-up-multivariable-prediction-models/. Accessed June 20, 2013.
89. Den Ruijter HM, Peters SA, Anderson TJ, et al. Common carotid intima-media thickness measurements in cardiovascular risk prediction: a meta-analysis. JAMA 2012;308:796–803.
90. Fox KA, Clayton TC, Damman P, et al. Long-term outcome of a routine versus selective invasive strategy in patients with non-ST-segment elevation acute coronary syndrome: a meta-analysis of individual patient data. J Am Coll Cardiol 2010;55:2435–45.
91. McShane LM, Altman DG, Sauerbrei W, Taube SE, Gion M, Clark GM. REporting recommendations for tumour MARKer prognostic studies (REMARK). Br J Cancer 2005;93:387–91.
92. Hemingway H, Croft P, Perel P, et al. Prognosis research strategy (PROGRESS) 1: a framework for researching clinical outcomes. BMJ 2013;346:e5595.
93. Riley RD, Hayden JA, Steyerberg EW, et al. Prognosis Research Strategy (PROGRESS) 2: prognostic factor research. PLoS Med 2013;10:e1001380.
94. Steyerberg EW, Moons KG, van der Windt DA, et al. Prognosis Research Strategy (PROGRESS) 3: prognostic model research. PLoS Med 2013;10:e1001381.
95. Hingorani AD, Windt DA, Riley RD, et al. Prognosis research strategy (PROGRESS) 4: stratified medicine research. BMJ 2013;346:e5793.

Key Words: cardiac magnetic resonance ■ prognosis ■ systematic review.

APPENDIX

For supplemental tables, please see the online version of this article.