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