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Prognostic Value of Quantitative Stress Perfusion Cardiac Magnetic Resonance

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ABSTRACT

OBJECTIVES This study sought to evaluate the prognostic usefulness of visual and quantitative perfusion cardiac magnetic resonance (CMR) ischemic burden in an unselected group of patients and to assess the validity of consensus-based ischemic burden thresholds extrapolated from nuclear studies.

BACKGROUND There are limited data on the prognostic value of assessing myocardial ischemic burden by CMR, and there are none using quantitative perfusion analysis.

METHODS Patients with suspected coronary artery disease referred for adenosine-stress perfusion CMR were included (n = 395; 70% male; age 58 ± 13 years). The primary endpoint was a composite of cardiovascular death, nonfatal myocardial infarction, aborted sudden death, and revascularization after 90 days. Perfusion scans were assessed visually and with quantitative analysis. Cross-validated Cox regression analysis and net reclassification improvement were used to assess the incremental prognostic value of visual or quantitative perfusion analysis over a baseline clinical model, initially as continuous covariates, then using accepted thresholds of ≥2 segments or ≥10% myocardium.

RESULTS After a median 460 days (interquartile range: 190 to 869 days) follow-up, 52 patients reached the primary endpoint. At 2 years, the addition of ischemic burden was found to increase prognostic value over a baseline model of age, sex, and late gadolinium enhancement (baseline model area under the curve [AUC]: 0.75; visual AUC: 0.84; quantitative AUC: 0.85). Dichotomized quantitative ischemic burden performed better than visual assessment (net reclassification improvement 0.043 vs. 0.003 against baseline model).

CONCLUSIONS This study was the first to address the prognostic benefit of quantitative analysis of perfusion CMR and to support the use of consensus-based ischemic burden thresholds by perfusion CMR for prognostic evaluation of patients with suspected coronary artery disease. Quantitative analysis provided incremental prognostic value to visual assessment and established risk factors, potentially representing an important step forward in the translation of quantitative CMR perfusion analysis to the clinical setting. (J Am Coll Cardiol Img 2017;■:■–■) © 2017 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

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ABBREVIATIONS AND ACRONYMS

AHA = American Heart Association

CABG = coronary artery bypass grafting

CMR = cardiac magnetic resonance

IQR = interquartile range

LGE = late gadolinium enhancement

MBF = myocardial blood flow

MPR = myocardial perfusion reserve

PCI = percutaneous coronary intervention

PET = positron emission computed tomography

ROI = region of interest

SCD = sudden cardiac death

SPECT = single-photon emission computed tomography

In recent years, stress perfusion cardiac magnetic resonance (CMR) has become one of the methods of choice for the diagnosis of coronary artery disease based on high diagnostic accuracy, lack of ionizing radiation, and the ability to simultaneously assess cardiac function, myocardial perfusion, and viability (1-3). In the clinical setting, perfusion CMR is assessed qualitatively with visual analysis (4). There are data that show that ischemia detection by visual assessment performs similarly or is at least noninferior to other noninvasive modalities such as positron emission tomography (PET) or single-photon emission computed tomography (SPECT) (5-7).

There is a growing body of evidence that shows that the mere presence of ischemia is of prognostic value (8-12); however, in recent years, the burden of ischemia has become an important focus (13,14). SPECT allows quantification of relative ischemic burden in terms of percentage of ischemic myocardium, and accepted thresholds have been shown to be of prognostic value in large nuclear data sets (13,15). The thresholds of ischemic burden used in SPECT have been extrapolated to CMR (16,17); however, evidence regarding the validity of these thresholds for CMR is lacking.

CMR perfusion quantification has been shown to be feasible and has been validated against invasive and noninvasive modalities, including fractional flow reserve (18) and PET (19). Although both visual and quantitative analysis can provide data on ischemic burden, there are data that suggest the diagnostic superiority of quantitative CMR perfusion analysis, specifically in the setting of multivessel coronary disease (20). A direct comparison between visual and quantitative perfusion CMR in terms of prognostic benefit has yet to be performed.

The main aim of this study was to assess the prognostic value of quantitative CMR perfusion analysis. Furthermore, we aimed to investigate the validity of accepted consensus-based thresholds for ischemic burden in the setting of adenosine stress perfusion CMR.

METHODS

STUDY DESIGN. Patients with suspected coronary artery disease referred on a clinical basis to King's College London CMR Service at St Thomas' Hospital (Guy's and St Thomas' NHS Trust) between January 2009 and January 2015 were considered for enrollment. Consecutive patients who underwent a clinical CMR scan that included assessment of cardiac function, ischemia testing with high-resolution dual-bolus adenosine stress, and resting perfusion imaging, followed by late gadolinium enhancement (LGE) imaging were included. Patients in whom regadenoson was used were excluded because the long half-life of the drug has the potential to result in the acquisition of resting perfusion images with a degree of residual hyperemia, which results in the underestimation of myocardial perfusion reserve (MPR) (21,22).

The study was conducted in accordance with the Declaration of Helsinki (2000) and was approved by the National Research Ethics Service. All patients provided written informed consent.

STUDY ENDPOINT AND PATIENT FOLLOW-UP. The start of follow-up was defined as the date of the CMR scan. The primary endpoint was a composite of cardiovascular death (death due to myocardial infarction, heart failure, or ventricular arrhythmia), nonfatal myocardial infarction (acute coronary syndrome with associated electrocardiographic changes and elevation of serum biomarkers of myocardial necrosis to >99th percentile of the assay upper limit of normal [23]), aborted sudden cardiac death (SCD) (documented ventricular fibrillation or sustained ventricular tachycardia with hemodynamic compromise requiring defibrillation or cardioversion not associated with acute myocardial infarction), and late revascularization (percutaneous coronary intervention [PCI] or coronary artery bypass grafting [CABG] >90 days after the start of follow-up). To avoid the potential effect of a positive CMR result leading to early revascularization, we excluded procedures within 90 days of the CMR scan from the definition of the endpoint revascularization (24). Patients who did not experience events were censored at the point of last follow-up. When patients experienced >1 event, only the first event was considered.

Follow-up was performed through interrogation of electronic patient records and patient notes. All events were adjudicated by consensus of 3 physicians blinded to CMR data. Mortality and cause of death were obtained from the Office for National Statistics and through review of medical records, death certificates, and post-mortem data where available.

IMAGE ACQUISITION. Patients were asked to refrain from nicotine and caffeine-containing foods and beverages for 24 h before the scan. Standard 2-, 3-, and 4-chamber cine images were acquired during breath hold. Contiguous short-axis slices were acquired from the base to the apex for calculation of left ventricular volumes, function, and mass. Following