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Diagnostic Performance of Fully Automated Pixel-Wise Quantitative Myocardial Perfusion Imaging by Cardiovascular Magnetic Resonance

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ABSTRACT

OBJECTIVES The authors developed a fully automated framework to quantify myocardial blood flow (MBF) from contrast-enhanced cardiac magnetic resonance (CMR) perfusion imaging and evaluated its diagnostic performance in patients.

BACKGROUND Fully quantitative CMR perfusion pixel maps were previously validated with microsphere MBF measurements and showed potential in clinical applications, but the methods required laborious manual processes and were excessively time-consuming.

METHODS CMR perfusion imaging was performed on 80 patients with known or suspected coronary artery disease (CAD) and 17 healthy volunteers. Significant CAD was defined by quantitative coronary angiography (QCA) as ≥70% stenosis. Nonsignificant CAD was defined by: 1) QCA as <70% stenosis; or 2) coronary computed tomography angiography as <30% stenosis and a calcium score of 0 in all vessels. Automatically generated MBF maps were compared with manual quantification on healthy volunteers. Diagnostic performance of the automated MBF pixel maps was analyzed on patients using absolute MBF, myocardial perfusion reserve (MPR), and relative measurements of MBF and MPR.

RESULTS The correlation between automated and manual quantification was excellent ($r = 0.96$). Stress MBF and MPR in the ischemic zone were lower than those in the remote myocardium in patients with significant CAD (both $p < 0.001$). Stress MBF and MPR in the remote zone of the patients were lower than those in the normal volunteers (both $p < 0.001$). All quantitative metrics had good area under the curve (0.864 to 0.926), sensitivity (82.9% to 91.4%), and specificity (75.6% to 91.1%) on per-patient analysis. On a per-vessel analysis of the quantitative metrics, area under the curve (0.837 to 0.864), sensitivity (75.0% to 82.7%), and specificity (71.8% to 80.9%) were good.

CONCLUSIONS Fully quantitative CMR MBF pixel maps can be generated automatically, and the results agree well with manual quantification. These methods can discriminate regional perfusion variations and have high diagnostic performance for detecting significant CAD. (Technical Development of Cardiovascular Magnetic Resonance Imaging; NCT00027170) (J Am Coll Cardiol Img 2018;■:■–■) 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

AIF = arterial input function

AUC = area under the curve

CAD = coronary artery disease

CMR = cardiac magnetic resonance

CTA = computed tomography angiography

CX = circumflex coronary artery

LAD = left anterior descending artery

LV = left ventricular

MBF = myocardial blood flow

MPR = myocardial perfusion reserve

PET = positron emission tomography

QCA = quantitative coronary angiography

rMBF = relative myocardial blood flow

rMPR = relative myocardial perfusion reserve

RCA = right coronary artery

ROC = receiver-operating characteristic

ROI = region of interest

Cardiac magnetic resonance (CMR) perfusion imaging has good diagnostic accuracy for detecting significant coronary artery disease (CAD) (1-3). Quantitative evaluation of dynamic contrast enhancement from the CMR perfusion time-signal intensity curves also accurately assess the severity of stenosis and myocardial ischemia in patients with known or suspected CAD (4-8).

There is an increased interest in fully quantitative assessment of myocardial blood flow (MBF) from CMR because it provides a wider range of perfusion estimates than semiquantitative perfusion indexes (9,10). It outperforms semiquantitative measures of perfusion and qualitative approaches in diagnosing patients with significant CAD (7,8). Absolute MBF estimates from CMR have been validated against microspheres (10,11) and positron emission tomography (PET) measurements of MBF (12-14). Preliminary studies that quantified MBF at a pixel level also validated these methods with microspheres (15), phantoms (16), and PET measurements (17). However, these validation studies required manual processing to delineate myocardial regions of interest (ROIs) and to quantify MBF. Those manual steps inevitably introduced inter- and intraobserver variability and created large barriers that prevented routine clinical usage.

In this study, we presented a fully automated image processing framework for quantitative pixel-wise assessment of MBF using first-pass CMR perfusion imaging. This work addressed the limitations of our previous techniques to generate perfusion pixel maps (15), which required manual image segmentation and were described as laborious and time-consuming (18,19). Most subcomponents of this automated framework were previously validated (15,20-22).

To evaluate the performance of automatically generated MBF pixel maps from the proposed framework, we aimed to: 1) compare fully automated and manual measurements of MBF; 2) characterize MBF and myocardial perfusion reserve (MPR) in healthy subjects and in patients; and 3) determine the diagnostic accuracy of absolute and relative measurements of MBF and MPR in patients with known or suspected CAD.

METHODS

STUDY POPULATION. Ninety-seven subjects were evaluated in this study, including 80 patients with known or suspected CAD and 17 healthy volunteers. This was a retrospective study of CMR stress and rest perfusion scans acquired as part of a clinical research protocol approved by the institutional review board of the National Heart, Lung, and Blood Institute. All subjects gave written informed consent (ClinicalTrials.gov Identifier: NCT00027170). Healthy volunteers were recruited specifically for validation purposes and needed to have a Framingham risk score of <1% and no history of cardiovascular disease. Patient studies were selected from the same time period as the healthy volunteers based on availability of invasive coronary angiography or coronary computed tomography angiography (CTA) within 90 days of the CMR scan. Patients were excluded if there was a change in symptoms in cases in which coronary angiography preceded CMR, if there revascularization occurred between the 2 studies, or if the digital angiography was not available for quantitative coronary angiography (QCA). Patients with CTA were excluded if they had an Agatston calcium score >0 or >30% noncalcified plaque in any major vessel.

DEFINITION OF SIGNIFICANT CAD. Significant CAD was defined as ≥70% stenosis in at least 1 major vessel or >50% stenosis in the left main coronary artery as confirmed by QCA. Nonsignificant CAD was defined by: 1) QCA of <70% stenosis; or by 2) CTA with <30% stenosis and a calcium score of 0 in all major vessels. QCA was performed by a physician blinded to the CMR perfusion results (Syngo QCA, Siemens Healthcare, Erlangen, Germany). CTA studies were performed on a 320-detector row scanner (Aquilion ONE, Toshiba, Otawara, Japan) and interpreted independently of CMR.

CMR PERFUSION IMAGING. CMR perfusion imaging was performed on a 1.5-T scanner (Siemens Healthcare, Erlangen, Germany). All subjects were instructed to abstain from caffeinated products for at least 24 h before the scan. Stress perfusion imaging was performed 70 s after a 400-μg intravenous bolus of regadenoson. Aminophylline 100 to 150 mg intravenous slow infusion was administered after stress imaging to minimize the residual effects of vasodilation. Perfusion at rest was performed 20 min later. A dose of 0.05 mmol/kg gadolinium intravenous at 2 to 5 ml/s (diethylenetriamine-pentaacetate, Magnevist, Berlex Laboratories, Wayne, New Jersey) was used and flushed with saline at 5 ml/s.

The perfusion imaging involved a steady-state free precession dual-sequence technique (23). The dual-sequence method acquired a low-resolution arterial input function (AIF) image, and 3 myocardial images every RR interval for 60 heart beats. Typical imaging