Journal of the American College of Cardiology
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Published by Elsevier Inc.

Vol. 44, No. 11, 2004
ISSN 0735-1097/04/$30.00
doi:10.1016/j.jacc.2004.09.004

EDITORIAL COMMENT

The Comprehensive Approach to Ischemic Heart Disease by Cardiovascular Magnetic Resonance Imaging

Are We There Yet?*

Christopher M. Kramer, MD, FACC
Charlottesville, Virginia

During the past decade, significant advances have been made in the imaging speed, resolution, quality, and versatility of cardiovascular magnetic resonance imaging (CMR). What was deemed unfeasible in cardiovascular patients in 1990 can now be achieved regularly as the result of the advent of more rapid imaging acquisition along with breath-hold techniques (1), diaphragmatic navigator gating (2), and real-time imaging (3) to counter the effects of respiratory motion. By the mid 1990s, imaging of myocardial function, resting myocardial perfusion, and infarct artery patency in patients with recent acute myocardial infarction could be performed in a single session of 45 to 50 min (4).

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At the start of the new millennium, CMR continued its rapid pace of development. Steady-state free precession cine imaging (5) and its enhanced contrast-to-noise ratio between myocardium and blood pool significantly improved image quality of functional imaging compared with older techniques. The accuracy of dobutamine stress testing is proven in comparison with X-ray angiography, as was shown in a sizable patient cohort (6), and also can be used to determine cardiac prognosis in the individual patient (7). New approaches to the rapid assessment of myocardial perfusion with semiquantitative measures of the first pass of the MR contrast agent gadolinium diethylenetriaminepenta-acetic acid (i.e., Gd-DTPA) through the myocardium were developed and validated against positron emission tomography (8). Delayed gadolinium enhancement was developed and validated as a method to sensitively detect myocardial infarction (9) and assess the likelihood of recovery of function in acute infarction (10) and chronic ischemic heart disease (11). Cardiovascular magnetic resonance imaging coronary angiography entered the era of multicenter trials, proving its utility in detecting left main and three-vessel coronary artery disease (CAD), albeit with suboptimal specificity in individual vessels (12).

It is against this backdrop that the concept of a comprehensive CMR approach to imaging patients with ischemic heart disease has been entertained (13). The first prospective step in this direction was that of Kwong et al. (14), who studied an intermediate-risk population of 161 consecutive patients who presented to the emergency room after experiencing 30 min of chest pain but whose electrocardiogram were nondiagnostic upon arrival. Within 12 h of presentation, comprehensive CMR, including cine imaging of function, first-pass gadolinium-enhanced myocardial perfusion, and delayed gadolinium-enhanced infarct detection, was performed with an examination time of 38 ± 12 min. Sensitivity and specificity of quantitative CMR, including wall thickening analysis and contrast indices for detecting acute coronary syndrome (ACS), in this population were 84% and 85%, respectively. Cardiovascular magnetic resonance imaging was more sensitive than troponin-I measures and Thrombolysis In Myocardial Infarction (TIMI) trial risk scores in detecting ACS. The detection of non–ST-segment elevation myocardial infarction was 100%. Wall motion, as was shown previously with echocardiography (15), was the most powerful single technique. Differentiation of acute versus chronic myocardial infarction was not feasible with the techniques used, but a recently described approach with a T_2-weighted sequence for imaging acute infarct-associated myocardial edema shows promise in this regard (16).

In this issue of the *Journal*, Plein et al. (17) take a similar approach but study a sicker cohort of patients with documented non–ST-segment elevation ACS (NSTE-ACS). The questions these authors propose are: can the patients that require invasive angiography be identified by comprehensive CMR and, if so, which of the imaging components performs best or is the comprehensive approach better? These authors previously had demonstrated the feasibility of this approach in a group of 10 stable outpatients awaiting coronary angiography (18). Included in the array of methods used were qualitative analysis of left ventricular function, adenosine stress and rest myocardial perfusion, infarct detection, and coronary angiographic techniques using established methods. Patients were imaged within 72 h of admission and within 24 h of X-ray angiography. Imaging itself required 62.5 ± 7.7 min, a time somewhat longer than was recorded in the study by Kwong et al. (14), undoubtedly because of the addition of coronary angiography.

The study by Plein et al. (17) certainly demonstrates that these techniques are both feasible and safe. The comprehensive CMR examination had a sensitivity of 97% and specificity of 83% for CAD requiring revascularization in this patient

*Editorials published in the *Journal of the American College of Cardiology* reflect the views of the authors and do not necessarily represent the views of *JACC* or the American College of Cardiology.

From the Departments of Medicine (Cardiovascular Division) and Radiology, University of Virginia Health System, Charlottesville, Virginia. Dr. Kramer is supported by NIH, NHLBI R01 HL-075792 and an American Heart Association Mid-Atlantic Affiliate Grant-in-Aid.

population, by all accounts an excellent result. The comprehensive approach worked better than any individual technique or other combination of techniques. The CMR approach performed better than TIMI risk scores. Perfusion imaging was the most sensitive for the end point chosen and, interestingly, wall motion was less accurate than in the study of Kwong et al. (14). This result may relate to differences in the patient population studied or to the fact that quantitative wall motion analysis was used by Kwong et al. (14) compared with the qualitative analysis performed in the present study.

The major question left incompletely answered by the present study is what is the true specificity of the combined CMR approach? The power of the study to accurately determine specificity was limited by the small number of patients (n = 12, 18%) who did not have CAD requiring revascularization. The confidence intervals for specificity are, therefore, quite wide. As with other noninvasive imaging modalities for risk stratification, Bayesian principles must be applied. If the prevalence of the end point in this population had been significantly lower, combining tests with relatively low specificity such as CMR coronary imaging (12,17) would have reduced the overall specificity of the combined approach. Any positive imaging component was counted as a patient with CAD requiring revascularization, which in a lower-risk population would have the net result of increasing the number of false-positive studies and reducing the specificity. The good specificity and excellent overall accuracy of the study by Plein et al. (17) is, therefore, in part, a direct reflection of the patient population studied. The inability to tell the difference in accuracy between combinations of two or three individual techniques also is related to the high prevalence of the end point chosen to study in this population. Further studies using the approach of Plein et al. (17) in a lower-risk population appear warranted.

The rationale for the present study was the assertion that one quarter to one half of patients who present with NSTE-ACS do not have obstructive CAD that requires re-vascularization. A review of the largest recent trials of similar populations comparing invasive with conservative therapies suggests that of those undergoing catheterization regardless of therapeutic strategy, between 60% and 80% eventually undergo revascularization (19–21). In the cohort studied by Plein et al. (17), 82% of patients had CAD requiring revascularization. How cost effective would a noninvasive imaging technique be that requires study of 100 patients to identify 20 or fewer who would not require the next step, invasive angiography? In addition, recent studies of similar populations suggest that delays in catheterization of high-risk populations with NSTE-ACS despite aggressive antithrombotic regimens may lead to an increase in adverse outcomes (21). Thus, this may not be the ideal setting for application of comprehensive CMR.

Certainly the feasibility of a comprehensive CMR approach, hinted at in recent years (13), has come to clinical reality. It can be performed safely, in a reasonable period of time, with excellent image quality in most patients. However, are we there yet? The real question remaining is: which test or tests for which patient population? The study by Plein et al. (17) tells us that in high-risk patient populations, a full-scale multimodality approach works well. In lower-risk patients, a combination approach using quantitative analysis and leaving out coronary imaging also performs well (14). Components of the comprehensive examination that are less specific, such as CMR coronary angiography in its present form (12,17), will likely not function as well in lower-risk populations. It may be that quantitative analysis of functional cine images and rest and stress perfusion imaging with delayed enhancement to exclude infarction as the cause of a perfusion defect will be the techniques of choice in the future. It will be up to the steadily growing number of CMR imagers (22) to answer these questions, a concept that just a decade ago seemed far from reality.

Acknowledgments

The author appreciates the helpful comments of Frederick Epstein, PhD; David Isbell, MD; Craig Meyer, PhD; and Walter Rogers, PhD.

Reprint requests and correspondence: Dr. Christopher M. Kramer, Departments of Medicine and Radiology, University of Virginia Health System, Lee Street, Box 800170, Charlottesville, Virginia 22908. E-mail: ckramer@virginia.edu.

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