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EDITORIAL COMMENT

Can Cardiac Magnetic Resonance Myocardial Scar Features Affect Treatment Decisions for Patients With Coronary Artery Disease and Heart Failure?*

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With the growing prevalence of type 2 diabetes, obesity, and the increasing average age of the population, coronary artery disease (CAD) has become an escalating health care burden in most western countries. CAD has been the most common cause of death in the U.S. for decades, and in recent years, this pattern has become a worldwide phenomenon (1). Despite the benefits of effective therapies developed in the past decades, the age-adjusted decline in CAD mortality in the U.S. has not been paralleled by a similar reduction in sudden cardiac death (SCD) (2). Some estimate that with the growing prevalence of CAD, the absolute number of SCDs is actually on the rise in the U.S. Although major multicenter studies have documented the importance of left ventricular ejection fraction (LVEF) and New York Heart Association functional class as the strongest predictors of risk for cardiac mortality in survivors of acute myocardial infarction (MI) (3), more novel risk-stratifying schemes are undoubtedly necessary in order to reduce SCD.

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In this issue of *iJACC,* Kwon et al. (4) reported results of an observational study assessing the implications of quantitative analysis of myocardial scar burden imaged by contrast-enhanced cardiac magnetic resonance (CMR) imaging to patient all-cause survival or a need for cardiac transplantation. The authors studied 349 patients with documented ischemic cardiomyopathy who were referred for assessment of myocardial viability by CMR. The authors performed cine steady-state free precession and late gadolinium enhancement (LGE) CMR imaging using standard techniques. Post-processing was carefully performed by semi-quantitative grading of segmental scar score, transmurality score, average segmental transmurality, and quantitative measurement of scar extent as a percentage of the total myocardium (scar percent), blinded to clinical outcome. After a mean follow-up of 2.6 years, 51 patients died and 5 underwent cardiac transplantation. Using Cox proportional regression analysis, it was concluded that quantitative scar percent and semi-quantitative average transmurality were the strongest predictors of death or cardiac transplantation. In particular, quantitative scar % was the strongest predictor of the combined events by multivariable selection. The strengths of the study include the relatively large number of patients and the long clinical follow-up in this high-risk group. The authors should be commended for their efforts in using quantitative or semi-quantitative LGE techniques in studying this group of very sick CAD patients with moderate to severe left ventricular dysfunction and a high burden of myocardial scar (average LVEF was approximately 24%, with scar involving 31% of the myocardium). This group represents not only the subset of CAD patients at the highest risk (15% mortality over mean follow-up of 2.6 years), but also those who potentially can gain the most from novel or even invasive therapeutic options. In this clinical scenario, novel noninvasive risk stratification can therefore be potentially invaluable in making treatment decisions.

In conjunction with other reports, this study provides adjunctive and growing evidence of patient

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prognostication using high-resolution myocardial tissue characterization by CMR (5–7). Kwon et al. (4) also provided compelling evidence that in high-risk CAD patients presenting with moderate to severe global dysfunction, scar burden provided an incremental patient prognosis to LVEF, which can be affected by the patient's hemodynamic states and myocardial loading conditions. Owing to a high contrast-to-noise ratio of LGE imaging, quantitative and reproducible analysis can be achieved rapidly after imaging, allowing more precise measurement of nonviable myocardial extent than with conventional nuclear techniques. However, readers need to consider several issues before these potentially encouraging results can be applied clinically.

Clinical presentation of infarction and timing from an index acute MI, among other factors, may modify the prognostic implication of the results by Kwon et al. (4). Population-based studies have indicated that patients found to have clinically silent myocardial infarction experienced a 10-year mortality of more than 45% (8,9). In the current study, details regarding the proportion of patients with a clinical history of MI or electrocardiographic evidence of a previous MI were not available. Therefore, it is unclear how many of these patients who were found to have LGE suffered clinically unrecognized MI. Patients found to have clinically unrecognized MI by LGE represent a particularly high-risk group of CAD patients and are likely to follow a survival distribution worse than that of patients who suffer a clinical MI. In addition, available clinical data suggest that there are bimodal risk periods after hospital discharge after an acute MI (10). SCD risk seems to be highest in the first several months after MI (11) during the unstable myocardial healing phase; this is followed by a lower long-term risk phase of subacute and a chronic phase of adverse cardiac remodeling. Quantitative assessment of myocardial scar, such as transmurality, scar mass, and percent of myocardium, are likely dynamic markers of post-MI remodeling that have different prognostic implications at different stages after an acute MI. In the current study, details regarding timing from the acute MI presentation were not provided. The ideal prognostic tool will need to incorporate the dynamism of remodeling risk, assessing these quantifiable changes at 2 or more time points after an acute MI. These must be addressed in future studies.

Apart from myocardial scar extent and LVEF, exquisite details of the left ventricular anatomy in 3 dimensions can aid treatment decisions. CMR can offer accurate assessment of the severity of the left ventricular geometric distortion and mitral regurgitation, which are factors that should be considered in selecting patients who may benefit from left ventricular or mitral valvular reconstructive surgery. At our institution, many cardiac surgeons routinely use CMR to gauge these variables, in addition to scar location and extent, in planning and assessing results before and after performing a Dor procedure. Owing to high spatial resolution and tissue contrast of LGE imaging by CMR, novel infarct characteristics such as microvascular obstruction (12,13), peri-infarct zone (6), and infarct surface area (14) by CMR have shown strong promise, beyond the predictive value of infarct size and LVEF, as novel predictors of patient mortality or surrogates of adverse cardiac events.

Increasing evidence supports the use of CMR LGE in addressing specific issues in the management of ischemic cardiomyopathy. Bleeker et al. (15) reported the use of LGE to identify nonresponders to cardiac resynchronization therapy beyond echocardiographic criteria of dysynchrony. Kim et al. (16) showed, in a landmark study, how the transmural extent of infarction accurately predicts segmental recovery of contractile function given successful coronary revascularization. Bello et al. (17) provided evidence of how benefits from beta-blocker therapy in ischemic heart failure patients can be predicted from LGE imaging. However, how we can use this information contributed by Kwon et al. (4) in guiding treatment decisions in these high-risk patients will need studies. Can quantifiable scar markers guide the implantation of internal cardioverter defibrillators to prevent SCD beyond the predictive value of LVEF? Possibly, but without information regarding the cause of death (cardiac or noncardiac, SCD or not), the relationship between scar extent and any likelihood of a life-threatening arrhythmic event will need further investigation. Is it more useful to assess the extent of viable myocardial segments, rather than the extent of myocardial scar, in selecting patients for high-risk revascularization surgery? Can the information provided by CMR lead to better treatment planning and at least improved symptoms or quality of life? Results using CMR from the anticipated STICH (Surgical Treatment of Ischemic Heart Failure) trial and other multicenter efforts may address some of these issues.

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REFERENCES

1. Murray CJ, Lopez AD. Mortality by cause for eight regions of the world: Global Burden of Disease Study. Lancet 1997;349:1269–76.
2. Huikuri HV, Castellanos A, Myerburg RJ. Sudden death due to cardiac arrhythmias. N Engl J Med 2001;345:1473–82.
3. Risk stratification and survival after myocardial infarction. N Engl J Med 1983;309:331–6.
4. Kwon DH, Halley CM, Carrigan TP, et al. Extent of left ventricular scar predicts outcomes in ischemic cardiomyopathy patients with significantly reduced systolic function: a delayed hyperenhancement cardiac magnetic resonance study. J Am Coll Cardiol Img 2009;2:34–44.
5. 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.
6. Yan AT, Shayne AJ, Brown KA, et al. Characterization of the peri-infarct zone by contrast-enhanced cardiac magnetic resonance imaging is a powerful predictor of post-myocardial infarction mortality. Circulation 2006;114:32–9.
7. Wu KC, Weiss RG, Thiemann DR, et al. Late gadolinium enhancement by cardiovascular magnetic resonance heralds an adverse prognosis in nonischemic cardiomyopathy. J Am Coll Cardiol 2008;51:2414–21.
8. Kannel WB, Abbott RD. Incidence and prognosis of unrecognized myocardial infarction. An update on the Framingham study. N Engl J Med 1984;311:1144–7.
9. Yano K, MacLean CJ. The incidence and prognosis of unrecognized myocardial infarction in the Honolulu, Hawaii, Heart Program. Arch Intern Med 1989;149:1528–32.
10. The Multicenter Research Group. Risk stratification and survival after myocardial infarction. N Engl J Med 1983;309:331–6.
11. Solomon SD, Zelenkofske S, McMurray JJV, et al., Valsartan in Acute Myocardial Infarction Trial Investigators. Sudden death in patients with myocardial infarction and left ventricular dysfunction, heart failure, or both. N Engl J Med 2005;352:2581–8.
12. Hombach V, Grebe O, Merkle N, et al. Sequelae of acute myocardial infarction regarding cardiac structure and function and their prognostic significance as assessed by magnetic resonance imaging. Eur Heart J 2005;26:549–57.
13. Wu KC, Kim RJ, Bluemke DA, et al. Quantification and time course of microvascular obstruction by contrast-enhanced echocardiography and magnetic resonance imaging following acute myocardial infarction and reperfusion. J Am Coll Cardiol 1998;32:1756–64.
14. Bello D, Fieno DS, Kim RJ, et al. Infarct morphology identifies patients with substrate for sustained ventricular tachycardia. J Am Coll Cardiol 2005;45:1104–8.
15. Bleeker GB, Kaandorp TA, Lamb HJ, et al. Effect of posterolateral scar tissue on clinical and echocardiographic improvement after cardiac resynchronization therapy. Circulation 2006;113:969–76.
16. Kim RJ, Wu E, Rafael A, et al. The use of contrast-enhanced magnetic resonance imaging to identify reversible myocardial dysfunction. N Engl J Med 2000;343:1445–53.
17. Bello D, Shah DJ, Farah GM, et al. Gadolinium cardiovascular magnetic resonance predicts reversible myocardial dysfunction and remodeling in patients with heart failure undergoing beta-blocker therapy. Circulation 2003;108:1945–53.

Key Words: myocardial infarction ■ cardiac magnetic resonance ■ mortality.