

EDITORIAL COMMENT

Variation on a Theme

CMR as the “One-Stop Shop” for Risk Stratification After Infarction?*

Katherine C. Wu, MD

Baltimore, Maryland

Predicting prognosis after acute myocardial infarction (AMI) remains clinically challenging, partly due to significant interpatient variability in risk profiles and what is often individualized therapeutic management. In addition, the risk of poor outcomes varies as a function of time from AMI, particularly in the period spanning initial hospital presentation to the time of discharge. Systematic approaches to risk assessment have been advocated, and a number of clinical risk scores have been developed that can potentially be applied at the bedside. These include and are not limited to the

center primary percutaneous coronary intervention (PCI) trials for AMI, the CADILLAC score predicts mortality at both 30 days and 1 year. The prognostic discriminatory capacity of all 3 scores, both for development and when tested against a validation cohort, as measured by the C-statistic, are reported at 0.78 to 0.83 and 0.75 to 0.79.

In addition to patient clinical characteristics, there are 2 other major determinants of both short- and long-term survival after myocardial infarction (MI). These 2 factors are left ventricular ejection fraction (LVEF) and the severity and extent of residual coronary artery stenoses that perfuse viable myocardium. The LVEF is influenced by both the amount of necrotic myocardium and the extent of residual myocardium at risk. Current clinical practice for post-MI risk stratification includes the assessment of LV function, generally by echocardiography. In addition, in patients in whom coronary catheterization is not performed, provokable myocardial ischemia is determined by post-MI stress testing with nuclear or echocardiographic techniques. Direct assessment of infarct size via imaging techniques is typically not routinely assessed, in part because it has not been definitively shown to provide additional prognostic and therapeutic information, except in small cardiac nuclear scintigraphic and cardiac magnetic resonance (CMR) studies. Furthermore, there is limited clinical emphasis placed on other potentially important factors such as adequacy of tissue level reperfusion (microvascular status) and regional wall motion abnormalities, both of which might provide independent but not definitively proven prognostic information.

The potential for CMR to provide a “one-stop shop” for the assessment of ischemic heart disease has long been proposed (5,6). CMR is uniquely able to integrate, in a single examination, the accurate

[See page 835](#)

Thrombolysis In Myocardial Infarction (TIMI) risk (1), Global Registry of Acute Coronary Events (GRACE) (2), and CADILLAC (The Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications) trial (3) scores. The TIMI and GRACE registries were both developed from cohorts involving 14,000 to 17,000 patients. The TIMI risk score was designed to predict 30-day mortality in fibrinolytic-eligible patients on the basis of initial presenting features. The GRACE model was developed from a multinational registry of acute coronary syndrome patients and predicts 6-month and 4-year mortality (4) from clinical features at hospital discharge. Derived from a database of >2,000 patients enrolled in multi-

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

From the Division of Cardiology, Department of Medicine, Johns Hopkins Medical Institutions, Baltimore, Maryland. Dr. Wu is supported by the Donald W. Reynolds Cardiovascular Research Center at Johns Hopkins University. She has received research grant support from GE Healthcare Technologies.

assessment of LV structure, global and regional systolic function, together with myocardial infarct sizing, adequacy of tissue level reperfusion (microvascular status), and myocardial ischemic burden/extent of viability with low-dose dobutamine. In the current issue of *JACC*, Bodi et al. (7) aimed to test the prognostic value of a comprehensive CMR assessment compared with known clinical risk profiles. They studied 214 survivors of first ST-segment elevation MI discharged from a single center with median follow-up of approximately 1.5 years. The majority of patients (58%) received thrombolytics, but a total of 92% were ultimately treated with coronary artery stenting during their hospital stay. CMR was performed at an average of 7 days after MI, and 4 CMR indexes were examined: number of myocardial segments with 1) resting wall motion abnormality; 2) wall motion abnormality with dobutamine; 3) microvascular obstruction; and 4) transmural necrosis >50% of the wall. Twenty-one major adverse cardiac events (MACE) were observed. The authors created a multivariate model, essentially using stepwise analysis, incorporating a multitude of clinical and CMR variables. They concluded that the only variables that independently predicted outcome seemed to be the number of segments with wall motion abnormality and transmural necrosis.

This study highlights the challenges and potential approach to demonstrating an improvement in prognostication strategies after MI, particularly when expensive, less accessible technologies such as CMR are proposed. Despite limitations with clinical risk scores, they are attractive because they can be easily applied at the bedside, cost nothing to perform, and on average can explain a large proportion of post-AMI mortality. It has also been shown that there is incremental value when LVEF is added to clinical prediction scores (3,8). Because LVEF is readily obtained clinically by echocardiography, a specific challenge for CMR is to demonstrate additive value of the other unique variables (infarct size, infarct transmural, microvascular obstruction, resting, and dobutamine-induced wall motion abnormalities) above and beyond a composite score of clinical characteristics and LVEF. Simply put, CMR performance should favorably compare with the discriminant ability of 0.78 of the CADILLAC score, for instance, which uses only 7 factors: age >65 years, Killip class, baseline LVEF, anemia, renal insufficiency, triple vessel disease, and post-procedural TIMI flow grade. In comparison, from the Bodi et al. study (7), the C-statistics for infarct

size, transmural necrosis, and number of segments with baseline wall motion abnormalities all exceeded 0.75 and might be potentially additive or even synergistic to a clinical risk score. Although this type of approach could be useful, to move beyond the hypothesis-generation stage of the Bodi et al. study (7), much larger patient cohorts are critical. In the current study, the low total MACE rates limit the extent to which multiple variables can be included in any model and thereby preclude any definitive conclusions regarding the strengths of the findings, particularly with respect to the relative values of the individual CMR indexes, as seen by the wide, overlapping confidence intervals of the C-statistics for each. Also, it will be increasingly important to investigate, with adequate statistical power, whether there is differential predictive value of the CMR indexes on individual, pathophysiologically related outcomes rather than composite end points (i.e., ischemia and reinfarction complications should be differentiated from heart failure admissions and heart failure deaths vs. arrhythmic complications such as sudden cardiac death).

In addition to needing larger cohorts of patients with CMR, perhaps collected in the form of a multicenter retrospective registry as an initial step, attention to the uniformity of the MI patient population studied is warranted, particularly with respect to other factors that determine outcome. One significant independent prognostic variable is the status of the infarct-related artery (IRA). In the current study, 198 of the 214 total patients were treated with stenting, either by primary PCI, rescue PCI, or delayed PCI post-thrombolytic therapy; the status of the IRA in the remaining 16 patients is unclear. Among the thrombolytic therapy group, 69% underwent late revascularization "during routine catheterization" at a "median of 2 days." Early reperfusion with an open epicardial IRA is clearly beneficial. In contrast, routine late reperfusion (>24 h) is no better than medical therapy (9). Although the groups with and without MACE were matched in terms of initial thrombolytic therapy, a more critical question in the thrombolytic group was the state of the IRA, ideally at 24 h or at the time of catheterization pre-intervention (as well as the time to actual epicardial revascularization).

In conclusion, Bodi et al. (7) provide a novel approach to validating a comprehensive CMR method of risk stratification after AMI. The authors certainly raise the bar against which CMR must favorably compare, to even be considered a viable clinical tool. However, the ongoing chal-

Challenges are many, and the current work does not definitively answer which of the CMR indexes are better than the others or which add incremental value to the knowledge of clinical information and LVEF. To do so, there needs to be fair comparisons with the multitude of the available risk scores not only the TIMI risk that determines short-term outcome, avoidance of composite end points, inclusion of much larger numbers of patients that allow both the development and validation of CMR

prediction models, and adequate control for epicardial reperfusion status. The promise of the CMR “one-stop-shop” survives but remains to be realized for clinical post-AMI risk stratification.

Reprint requests and correspondence: Dr. Katherine C. Wu, Division of Cardiology, Johns Hopkins Hospital, 600 North Wolfe Street/Carnegie 568, Baltimore, Maryland 21287. *E-mail:* kwu@jhmi.edu.

REFERENCES

1. Morrow DA, Antman EM, Charlesworth A, et al. TIMI risk score for ST-elevation myocardial infarction: a convenient, bedside, clinical score for risk assessment at presentation: an intravenous nPA for Treatment of Infarcting Myocardium Early II Trial substudy. *Circulation* 2000;102:2031-7.
2. Eagle KA, Lim MJ, Dabbous OH, et al. A validated prediction model for all forms of acute coronary syndrome: estimating the risk of 6-month postdischarge death in an international registry. *JAMA* 2004;291:2727-33.
3. Halkin A, Singh M, Nikolsky E, et al. Prediction of mortality after primary percutaneous coronary intervention for acute myocardial infarction: the CADILLAC risk score. *J Am Coll Cardiol* 2005;45:1397-405.
4. Tang EW, Wong C-K, Herbison P. Global registry of acute coronary events (GRACE) hospital discharge risk score accurately predicts long-term mortality post acute coronary syndrome. *Am Heart J* 2007;153:29-35.
5. Blackwell GG, Pohost GM. The evolving role of MRI in the assessment of coronary artery disease. *Am J Cardiol* 1995;75:D74-8.
6. Kramer CM. Integrated approach to ischemic heart disease. The one-stop shop. *Cardiol Clin* 1998;16:267-76.
7. Bodi V, Sanchis J, Nunez J, et al. Prognostic value of a comprehensive cardiac magnetic resonance assessment soon after a first ST-segment elevation myocardial infarction. *J Am Coll Cardiol Img* 2009;2:835-42.
8. Singh M, Reeder GS, Jacobsen SJ, et al. Scores for post-myocardial infarction risk stratification in the community. *Circulation* 2002;106:2309-14.
9. Menon V, Pearte CA, Buller CE, et al. Lack of benefit from percutaneous intervention of persistently occluded infarct arteries after the acute phase of myocardial infarction is time independent: insights from Occluded Artery Trial. *Eur Heart J* 2009;30:183-91.

Key Words: cardiac magnetic resonance.