

EDITORIAL



Cardiovascular Imaging and Outcomes — PROMISEs to Keep

Christopher M. Kramer, M.D.

Noninvasive cardiovascular imaging is used on a daily basis to make crucial decisions regarding patient care. However, its rising use paralleled the doubling in Medicare spending on imaging services under the Part B physician fee schedule from 2000 to 2006, of which approximately one third was for cardiovascular imaging.¹ As a result, the American College of Cardiology Foundation and other societies developed appropriate-use criteria² for cardiovascular imaging that apply expert opinion to various imaging methods in common clinical scenarios to recognize those that are appropriate, may be appropriate, or are rarely appropriate in a given scenario. Cardiovascular imaging procedures and costs began to decrease as these criteria were implemented and as reimbursement declined coincidentally. In fact, total spending on imaging services has decreased by 28.4% since 2006.³

Experts in the field began to state that cardiovascular imaging was “at the crossroads”⁴ because proof of its value was required. The field needed to move beyond the assessment of the sensitivity, specificity, and accuracy of a given imaging test against a reference standard. Studies showing how imaging could affect hard cardiovascular outcomes were sorely needed. Yet outcomes are generally driven by therapy, not by the imaging study itself. It was against this backdrop that the National Heart, Lung, and Blood Institute (NHLBI) convened a panel of experts in 2008 to develop recommendations for randomized trials that use cardiovascular imaging in a number of clinical scenarios.⁵ One of the scenarios discussed at the workshop was the assessment of patients with chronic angina, and this discussion culminated in the design of the NHLBI-supported Prospective Multicenter Imaging

Study for Evaluation of Chest Pain (PROMISE), the results of which are now reported in the *Journal*.⁶

In this trial, 10,003 symptomatic patients with suspected coronary artery disease were randomly assigned to either anatomical testing with the use of coronary computed tomographic angiography (CTA) or to functional stress testing with the use of exercise electrocardiography, stress echocardiography, or nuclear stress testing. These tests drove subsequent care decisions, and the patients were then followed for a median of just over 2 years, with a composite primary end point of death, myocardial infarction, hospitalization for unstable angina, or major procedural complication. Event rates were low and similar in the two groups: 3.3% in the CTA group and 3.0% in the functional-testing group (adjusted hazard ratio, 1.04; 95% confidence interval, 0.83 to 1.29). So, no winner was declared. This result prompts the question: How will a tie for CTA change clinical practice?

A number of single-center and multicenter studies⁷ have shown that CTA has high sensitivity, reasonable specificity, and an extremely high negative predictive value. Two large-scale studies have shown that a strategy of CTA use in the emergency department is associated with faster discharge, as compared with standard care, without a significant difference in event rates.^{8,9} However, many insurers other than Medicare have balked at covering CTA, in part out of concern about clinicians using it to screen for coronary artery disease in asymptomatic patients, for which it is not indicated.¹⁰ The lack of evidence supporting CTA in randomized trials has also been cited. PROMISE answers the bell in that regard. Of potential interest to insurers,

there were fewer catheterizations after CTA than after functional testing, probably owing to a lower false positive rate with CTA. Comparative cost analysis may be telling, because generally the cost of CTA is lower than the cost of stress imaging but higher than that of stress electrocardiography. Certainly, any concern that radiation doses would be higher with CTA than with functional testing was alleviated by the trial results. As CTA technology advances, radiation doses continue to decrease, without a decrement in diagnostic accuracy.

Interpretation of the trial results is limited by the low event rates, which were driven in part by the high rate of appropriate medical therapy, including statins, in the two groups, as well as the relatively short follow-up period. Moreover, almost half the events were hospitalizations for unstable angina, which is the softest of the end points in the composite. Newer stress imaging methods, such as magnetic resonance imaging and positron-emission tomography, were not studied. Data from a third group of patients who received medical therapy but did not undergo testing might have been instructive, because we do not know whether event rates are lowered by any interventions that are guided by a positive test. The International Study of Comparative Health Effectiveness with Medical and Invasive Approaches (ISCHEMIA; ClinicalTrials.gov number, NCT01471522), in which randomized therapy (invasive vs. medical) is driven by the presence of extensive ischemia on functional stress testing, will help answer the latter question. Thus, the cardiovascular imaging field is delivering comparative effectiveness studies with results that are likely to change clinical practice. This is indeed a PROMISE kept.

Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

From the Departments of Medicine and Radiology, University of Virginia Health System, Charlottesville.

This article was published on March 14, 2015, at NEJM.org.

1. Medicare Part B imaging services: rapid spending growth and shift to physician offices indicate need for CMS to consider additional management practices. Washington, DC: Government Accountability Office, 2008 (<http://www.gao.gov/new.items/d08452.pdf>).
2. Carr JJ, Hendel RC, White RD, et al. 2013 Appropriate utilization of cardiovascular imaging: a methodology for the development of joint criteria for the appropriate utilization of cardiovascular imaging by the American College of Cardiology Foundation and American College of Radiology. *J Am Coll Cardiol* 2013;61:2199-206.
3. Imaging today: medical imaging trends in Medicare. Arlington, VA: Medical Imaging & Technology Alliance, September 20, 2012 (<http://www.medicalimaging.org/wp-content/uploads/2012/09/Medicare-2011-Data-MITA-Report-Final-9.20.2012.pdf>).
4. Shaw LJ, Min JK, Hachamovitch R, et al. Cardiovascular imaging research at the crossroads. *JACC Cardiovasc Imaging* 2010;3:316-24.
5. Douglas PS, Taylor A, Bild D, et al. Outcomes research in cardiovascular imaging: report of a workshop sponsored by the National Heart, Lung, and Blood Institute. *Circ Cardiovasc Imaging* 2009;2:339-48.
6. Douglas PS, Hoffmann U, Patel MR, et al. Outcomes of anatomical versus functional testing for coronary artery disease. *N Engl J Med* 2015;372:1291-300.
7. Budoff MJ, Dowe D, Jollis JG, et al. Diagnostic performance of 64-multidetector row coronary computed tomographic angiography for evaluation of coronary artery stenosis in individuals without known coronary artery disease: results from the prospective multicenter ACCURACY (Assessment by Coronary Computed Tomographic Angiography of Individuals Undergoing Invasive Coronary Angiography) trial. *J Am Coll Cardiol* 2008;52:1724-32.
8. Litt HI, Gatsonis C, Snyder B, et al. CT angiography for safe discharge of patients with possible acute coronary syndromes. *N Engl J Med* 2012;366:1393-403.
9. Hoffmann U, Truong QA, Schoenfeld DA, et al. Coronary CT angiography versus standard evaluation in acute chest pain. *N Engl J Med* 2012;367:299-308.
10. Kramer CM. All high-risk patients should not be screened with computed tomographic angiography. *Circulation* 2008;117:1333-9.

DOI: 10.1056/NEJMe1501924

Copyright © 2015 Massachusetts Medical Society.

EARLY JOB ALERT SERVICE AVAILABLE AT THE NEJM CAREERCENTER

Register to receive weekly e-mail messages with the latest job openings that match your specialty, as well as preferred geographic region, practice setting, call schedule, and more. Visit the NEJM CareerCenter at NEJMjobs.org for more information.