

Cardiovascular Imaging and Diagnostic Thinking in the 21st Century: A Call to Action

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A few years ago, Patel and colleagues (1) showed that only 38% of patients who undergo invasive coronary angiography (ICA) for diagnostic purposes actually do have obstructive coronary artery disease (CAD), a true low proportion considering both the adverse events (2) and the radiation exposure (3) associated with ICA. The most common sequence of events for evaluating people with suspected CAD is performing a “gatekeeper” test, which is a typical functional test such as myocardial perfusion scintigraphy, followed by ICA if the results of the gatekeeper test are positive (COURAGE era) (4). Currently, approximately 9 million myocardial-perfusion-scintigraphic imaging studies are performed each year in the United States, and this test represents one of the single largest mankind contributions to radiation exposure in the U.S. population (3). Patel and colleagues rightly suggest that we need to optimize the application of gatekeeper tests such as myocardial perfusion scintigraphy in order to decrease the disturbingly large proportion of ICA procedures that yield negative results. There is evidence that, in many situations, a better gatekeeper test may yet be another radiographic imaging technique — namely, computed-tomographic (CT) angiography scan. A number of single-center and multicenter studies (5) have shown that CT scan has high sensitivity, reasonable specificity, and an extremely high negative predictive value. Moreover, two large-scale studies have shown that a strategy of CT scan used in emergency departments is associated with faster discharge, as compared electrocardiography, stress echocardiography, or nuclear stress testing, as standard care, without a significant difference in event rates (6,7). In the more recent trial (8), 10,003 symptomatic patients with suspected CAD were randomly assigned to either anatomical testing with the use of CT scan 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 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 CT scan group and 3.0% in the functional-testing group (adjusted hazard ratio, 1.04; 95% confidence interval, 0.83 to 1.29). So, in symptomatic patients with suspected CAD who required noninvasive testing, a strategy of initial CT scan as compared with functional testing, did not improve clinical outcomes over a median follow-up of 2 years. Of potential interest to insurers, there were fewer catheterizations after CT scan than after functional testing, probably owed to a lower false positive rate with CT scan. Comparative cost analysis may be relevant, because generally the cost of CT scan 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 CT scan than with functional testing was alleviated by the trial results. As CT scan 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, as well as the relatively short follow-up period. Moreover, 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) will help answer the latter question .

Today, the dream of cardiology community is to combine anatomical and functional information in one shop to refine the selection of patients who should undergo coronary revascularization. In the FAME era (9), for patients who arrived in catheterization laboratory without coronary functional test, the current standard for assessing the significance of coronary artery narrowing is conventional fractional flow reserve (FFR), which is invasive, involving insertion of a wire into the coronary artery. But by using computer simulations to calculate blood flow, non-invasive FFR-CT scan can give a

comprehensive evaluation of a patient's chest pain without the need of an invasive procedure. The PLATFORM (prospective longitudinal trial of FFR-CT: outcome and resource impacts) (10) trial examined the use of FFR-CT guidance in 584 patients (mean age 60.9 years; 39.6% women) with new-onset chest pain, no prior history of CAD, and an intermediate pretest likelihood of obstructive CAD who were treated at 11 European sites and Duke Clinical Research Institute between September 2013 and November 2014. The nonrandomized study included 2 cohorts of patients—a planned noninvasive testing group (n = 204) and a planned catheterization group (n = 380). Each cohort was further divided in other 2 groups and assigned to usual care or FFR-CT. Optimal medical therapy was encouraged in all groups, and local physicians made all subsequent clinical decisions following standard practice. At 90 days, there were high rates of finding no obstructive disease at invasive catheterization by core lab assessment in both the planned noninvasive and planned invasive groups, which were slightly lower on visual readings vs. core lab assessment. Similar results were found across subgroups. Radiation exposure was lower with usual care in the planned noninvasive group, but not in the planned invasive group. Rates of MACE and vascular complications were too low to assess. There were no differences in revascularization rates amongst patients allocated to CT angiography/FFR-CT vs. usual care in either the planned noninvasive or planned invasive groups. Invasive procedures were cancelled in 61% of patients after physicians received the CT angiography/FFR-CT results. The study shows that CT scan plus FFR-CT more effectively triages patients for invasive procedures than usual care strategies. The message is that for stable chest pain patients in whom elective ICA is recommended, consideration should be given to performing this new test first. The findings of PLATFORM trial, a small study, seems to reinforce the message of 2 recent large trials—PROMISE (8) and SCOT-HEART (11) and another small trial- EVINCI (12)-supporting the notion that CT scan can improve diagnostic assessment by appropriately altering planned investigations and treatment options, and, moreover, improve upon this by providing combined non invasive functional and anatomic data.

Thus, whether it is conceivable that the cardiovascular imaging might potentially change daily clinical practice, cutting a considerable number of unnecessary ICA and providing us an initial answer to Patel's question, on the other hand the proof concept of FFR-CT needs to be evaluated in larger trials, and its impact on daily clinical practice remains uncertain, before seeing how the cardiology community will adopt the suggestions of these new imaging facilities.

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