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EDITORIAL COMMENT

Comparing Outcomes and Costs Following Cardiovascular Imaging

A SPARC… But Further Illumination Is Needed*

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Stress single-photon emission computed tomography (SPECT) myocardial perfusion imaging is a historically robust, noninvasive technique, and represents the most common imaging method used in the United States for evaluation of patients with suspected or known coronary artery disease (CAD). On the basis of its diagnostic and prognostic evidence base—coupled with its familiarity of use—SPECT is endorsed for an array of clinical indications within clinical practice guidelines. In recent years, positron-emission tomography (PET) and coronary computed tomography angiography (CTA) have emerged as practical alternatives to SPECT, with contemporary published studies establishing a high diagnostic performance and prognostic utility that appears to match, if not exceed, that of conventional SPECT imaging. Yet, for the practitioner evaluating a patient being considered for noninvasive imaging for CAD, the choice of these and other noninvasive tests is ideally made, not only based upon consideration of test performance, but also for the ability of any test to inform therapeutic decision making in a timely, definitive, clinically effective, and cost-efficient manner. Given the recent introduction and adoption of PET and CTA, prospective effectiveness studies comparing these innovative noninvasive technologies to conventional SPECT are generally lacking, and thus, the role of PET or CTA in daily clinical practice has yet to be precisely elucidated.

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These issues were, in part, addressed by the SPARC (Study of Myocardial Perfusion and Coronary Anatomy Imaging Roles in Coronary Artery Disease) study, a prospective observational registry designed to compare post-test resource utilization and outcomes among patients who underwent SPECT, PET, or 64-slice coronary CTA between May 2006 and April 2008 (1). The SPARC investigators previously reported that among 1,703 patients without known CAD, patients referred for CTA experienced significantly higher 90-day rates of downstream invasive coronary angiography (ICA) testing and new prescriptions for aspirin and statins, as compared with those who underwent SPECT or PET (2). However, the clinical outcome and costs among these 3 testing cohorts have not been previously reported.

In this issue of the *Journal*, Hlatky et al. (3) extend their prior work by reporting the 2-year estimated costs and clinical outcomes among SPARC study participants without prior known CAD. Further, the authors estimate the long-term cost effectiveness of SPECT, PET, and CTA in models based upon the observed intermediate-term rates of all-cause mortality and myocardial infarction during the study period. Recognizing the significant differences in study populations being referred to SPECT, PET and CTA, the authors identified similar groups of individuals referred to each modality matched by propensity scoring. Similar to the initially reported 90-day results, the authors again observed that patients who underwent coronary CTA and PET experienced higher rates of subsequent ICA (16% and 15%, respectively) as compared with patients who underwent SPECT (7%). Patients who underwent PET and CTA were also more likely to undergo coronary revascularization, with the majority of ICA and revascularization occurring within 90 days of index testing. Given an expected non-normal distribution of costs associated with testing pathways, the median costs were no different among patients undergoing SPECT and CTA. Yet, despite the non-normality, mean costs were nevertheless reported and were higher for CTA (15%) and PET (22%) as compared with SPECT, stemming from higher rates of ICA and revascularization. Whether these findings underscore a superior diagnostic performance of CTA and PET compared with SPECT—with a higher rate of "true positive" patients referred for ICA—or higher rates of therapeutic revascularization for symptomatic angina from obstructive CAD remains unelucidated. Thus, although these data presented by the SPARC investigators represent an important step forward to address metrics beyond traditional measures of diagnostic and prognostic test performance, they nevertheless highlight the complexities associated with the conduct of such a study.

Given the observational design, patients enrolled into SPARC were clinically referred to specific tests based upon physician preference, a multifaceted decision that invariably resided in the context, not only of test type, but also of the results of prior testing, physician characteristics

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(e.g., familiarity with test modality, board certification), patient variables (e.g., symptom type, pre-test probability of CAD, patient preference), and test availability. Although many of these "confounding" variables could not be adequately accounted for within the SPARC registry, it is perhaps notable that many sites within the study did not even offer SPECT, PET, and CTA, thus rendering direct comparison of the 3 tests impracticable. Within sites offering more than 1 of these modalities, the locations of the imaging laboratories likely exhibited heterogeneity (office- versus hospital-based), and may have also contributed to referral patterns during the study period. Further, although standard clinical variables such as ejection fraction or renal function were not routinely collected for the study, important factors such as these likely influenced the choice of "which test for which patient." As an example, in addition to significant differences in age, comorbidities, and symptom status between testing groups, only 4% of patients who underwent SPECT had undergone any form of prior ischemic testing as compared with 29% of patients undergoing CTA. This 7-fold difference suggests the use of CTA as a "gatekeeper" or "arbiter," in part for individuals with stress tests that were abnormal or equivocal, respectively.

Notably, at its inception in 2006, the SPARC study hypotheses were and remain to this day novel and important. A comparative study of noninvasive imaging tests for costs and clinical outcomes that include 64-detector CTA—a modality introduced only in 2005—is as admirable as it had been contemporary. Yet, in the past 7 years, the rapid technological evolution of SPECT, PET, and CTA has emphasized the concept of technology assessment as a "moving target." As one example, iterative gains in CTA technology now enable test performance at radiation doses comparable to screening mammography and 10-fold lower than current generation single-isotope SPECT imaging (4). Similarly, advances in dual-energy CT now enable iodinated contrast doses up to 5-fold lower than traditional single-energy CTA. Perhaps most prominently, the practice of CTA over the past several years has gained, not only in utilization, but also in familiarity, and changing practice patterns based upon CTA test findings are now observed. Thus, although large-scale prospective studies of noninvasive CAD imaging are vital to our understanding of their integration into clinical practice, it remains a vexing proposition to conduct long-term or even intermediate-term investigations—such as is the case for SPARC—that represent a static moment in time for technologies whose development effectively outpaces the study.

Finally, the results of the present study emphasize the inextricable link between clinical effectiveness and economic efficiency. Germane to this, rates of post-test death or nonfatal myocardial infarction were highest for PET (6.5%), followed by SPECT (2.8%) and then CTA (1.6%), with patients undergoing PET older and with a greater prevalence of co-morbidities. A risk-adjusted trend ($p = 0.07$) was observed for lower all-cause mortality in individuals undergoing CTA versus SPECT, and although a significant benefit for CTA-based testing would be expected for a composite of mortality and myocardial infarction, this was not reported. Focused on SPECT as the conventional imaging test, the cost effectiveness of CTA was $10,700 per life-year added, with standard measures considering cost effectiveness at a threshold <$50,000 per quality-adjusted life-years saved. In the current study, CTA was cost effective in 89% of the bootstrap analyses, even when assuming a conservative estimate of 2 years of life lost due to myocardial infarction. Although these data are interesting and informative—and perhaps suggest a potential benefit of CTA use—the influence of residual confounding related to the aforementioned referral bias cannot be underestimated, particularly with respect to the increased rates of death in patients undergoing PET imaging. Further, post-test treatments and changes in patient behavior may have resulted in significant benefits, as well as harms associated with test-based strategies, and were regrettably not collected in the study.

Despite all of these limitations, the authors of the present study should be commended, not only for asking the right questions comparing the more contemporary imaging tests to more traditional ones, but also for guiding the field of noninvasive CAD imaging into investigations beyond diagnostic performance and prognostic utility. These observational studies will serve as the predecessors to ongoing randomized trials that will further inform the clinical practice community as to the advantages and disadvantages of the use of "which test when," all the while acknowledging that the imaging field is a perpetually evolutionary process that must consider technology development, test familiarity, and downstream testing and treatment. In this regard, the present study represents a "SPARC," but further illumination is invariably needed.

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