Value-based imaging: Combining coronary artery calcium with myocardial perfusion imaging

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The unsustainable rising cost of healthcare has thrust us into an era in which the use of medical tests must be of proven clinical value. For diagnostic cardiac tests, this means determining if testing leads to some combination of improving outcomes or cost savings—the new era of ''value-based imaging.'' Notably, in this regard, it is not the *result* of a test which changes outcomes, but the *management* that occurs based on that result.

Radionuclide stress myocardial perfusion imaging (MPI) has been a routine part of the cardiology landscape for approximately 40 years. Its use during this time emerged from its proven ability to *predict* patient outcomes. How might this test fair best in the ''new marketplace'' in which the use of tests will now depend on their ability to *alter* patient outcomes?

The answer to this question is being affected by three important trends. First, since the late 1960s, the clinical presentation of coronary artery disease has markedly changed. While still the nation's leading cause of death, the annualized mortality rate of heart disease has decreased by 70%, myocardial infarction is both less frequent and less severe, and even the frequency of angina is diminishing. From 1991 to 2009, we noted a concomitant marked decline in the frequency of inducible myocardial ischemia on SPECT-MPI among diagnostic patients in the Cedars-Sinai experience, falling from a frequency of 30% in 1991 to only 5% in 2009.[1] Recent experiences in other large datasets, such as the patients recruited into the WOMEN[2] and PROMISE[3] trials have also demonstrated a concurrent low frequency of inducible myocardial ischemia as well as of obstructive CAD. Further, recent reports have also been documented that the likelihood of obstructive CAD is now far lower than that predicted by the standard approaches which are based on data from the 1970's.[3,4] Thus, a large majority of SPECT-MPI studies within diagnostic populations can now be expected to be normal. While the finding of a normal SPECT-MPI study without anatomic imaging may reduce referral to invasive coronary angiography (ICA), for the most part, it has little effect on patient management.[5]

Second, studies involving concomitant SPECT-MPI and coronary artery calcium (CAC) scanning have revealed that among patients referred for radionuclide stress testing, the frequency of abnormal CAC studies among patients with normal nuclear studies is quite high. In our earliest experience in this regard, among 1,119 patients with normal SPECT-MPI studies, 78% had evidence of CAC and in >30% of patients, the CAC score was >400, indicative of extensive atherosclerosis.[6] A limitation of radionuclide MPI-stress tests in general—is their inability to detect subclinical atherosclerosis, which is common among patients who are referred for cardiac stress testing. If the report were to include the presence and amount of CAC, i.e., adding anatomic imaging, greater change in management may follow.[7] Further, there is increasing awareness that SPECT-MPI frequently underestimates the extent of obstructive CAD and may misclassify patients with angiographic high-risk disease.[8] Knowledge of the presence of extensive coronary calcification could improve these assessments by better establishing the pre-scan likelihood of CAD as well as of high-risk CAD.

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Third, with respect to reporting risk, when the focus with radionuclide stress testing was previously simply aimed at short-term risk assessment, generally involving 2 to 3 years of follow-up, the test was famously known for producing a ''*warranty period*'' of low risk. We have subsequently learned, however, that there is heterogeneity in long-term outcomes among patients with normal SPECT-MPI studies, with risk increasing with both rising number of CAD risk factors [9-11] and with increasing CAC scores.[12,13] Accordingly, we have recently suggested that overall risk assessment, which can help provide for better disease management, can be complemented by identifying both short-term and long-term risk and conveying this information on nuclear stress test reports.[14]

Given these trends, use of CAC scanning before or combining it with SPECT- or PET-MPI can lead to a change in the clinical management to a greater degree than the use of SPECT-MPI in isolation in the following ways:

(1) *Improved selection of patients for stress testing* In the current era of low ischemic frequency and overestimation of the likelihood of obstructive CAD, methods to more reliably identify which patients truly need cardiac stress tests is desirable. Low CAC scores diminish the likelihood of obstructive CAD and inducible myocardial ischemia,[6,11,15] even among patients with an intermediate likelihood of CAD.[16] Thus, CAC scanning can reduce the number of patients who require SPECT-MPI due to low CAC scores. Conversely, the finding of a very extensive CAC score may lead to appropriate testing of patients who may not otherwise been identified as being at high risk. As a note of caution, the CAC score ''threshold'' for ischemia may be lower among patients with typical angina,[16] and more study is required regarding this important subgroup of patients. More study is also needed to assess how other clinical variables shape the relationship between CAC scores and inducible myocardial ischemia.[17]

(2) *Improved diagnosis* In 2016, the goal of diagnosis in patients with chest pain syndromes should not merely be the presence of obstructive CAD, but rather the identification of *any* CAD (i.e., any coronary atherosclerosis). CAC scanning provides identification of the presence and extent of subclinical atherosclerosis in a large percentage of patients who now have normal MPI studies during diagnostic work-up. Knowledge of the CAC in conjunction with a SPECT-MPI study could provide similar improvements in diagnosis, resulting in similar guidance of the intensity of medical therapy to that provided by coronary CTA. Moreover, CAC scanning can also be combined with other clinical methods to improve the Bayesian estimation of obstructive CAD.[18]

(3) *Improved risk assessment* CAC scanning can improve overall risk assessment in two ways. First, in patients with a normal MPI scan, short-term risk has been shown to be low regardless of the CAC score,[19] but after 5 to 6 years of follow-up, risk becomes heterogeneous, varying according to the magnitude of CAC abnormality.[12] Second, assessment of CAC score improves overall risk assessment across the spectrum of MPI abnormality.[12,13] Improved risk assessment could likely lead to wiser decisions as to the need for aggressive treatment vs minimization of wasteful spending. Of note in this regard, in the EISNER trial, randomization to risk factor counseling with CAC scanning (vs risk factor counseling without CAC scanning) led to improved patient risk factor profiles without increasing downstream testing or overall incurred medical costs during four years of follow-up.[4]

(4) *Improved test interpretation* Knowledge of the CAC score in individual patients frequently provides great assistance in the decision as to whether to report the otherwise equivocal MPI scan as normal or abnormal—and often increases interpreter certainty.[20] Improved interpretation should decrease the proportion of patients referred for ICA following SPECT who are found to have nonobstructive CAD and improve the identification of patients with high-risk CAD. These factors could improve the use of SPECT-MPI as a gatekeeper to ICA.

(5) *Improved physician/patient management* The CAC scan can affect the degree to which the patient implements heart-healthy behaviors following testing.[21,22]

PET-MPI is becoming increasingly common as the modality for radionuclide MPI, and the vast majority of PET-MPI studies are performed with PET/CT systems with which CAC scanning at the time of PET-MPI is readily available. SPECT-CT systems with similar capabilities for CAC assessments to those of the PET/CT systems are becoming increasingly used. Further, with these systems, the extent of CAC can be estimated with reasonable accuracy from the attenuation scans routinely performed for the PET or SPECT study.[23] And with the marked recent increase in the use of CAC scanning for the guiding aggressiveness of medical therapy, CAC scans that are separate from the MPI study are now commonly available.

So in which setting should routine use of CAC scanning with MPI be considered? Given the five advantages noted above, perhaps in all patients without

known CAD who are referred for these procedures. The combination of functional and anatomic assessments could increase the frequency of beneficial changes in patient management following testing, potentially allowing MPI to compete more effectively with coronary CTA in patients with an intermediate likelihood of CAD with respect to value-based imaging. The combined assessments should become the standard in future clinical trials involving nuclear MPI examinations.

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Disclosures

None.

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