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Clinical Decision Making With Myocardial Perfusion Imaging in Patients With Known or Suspected Coronary Artery Disease

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Myocardial perfusion imaging (MPI) to diagnose coronary artery disease (CAD) is best performed in patients with intermediate pretest likelihood of disease; unfortunately, pretest likelihood is often overestimated, resulting in the inappropriate use of perfusion imaging. A good functional capacity often predicts low risk, and MPI for diagnosing CAD should be reserved for individuals with poor exercise capacity, abnormal resting electrocardiography, or an intermediate or high probability of CAD. With respect to anatomy-based testing, coronary CT angiography has a good negative predictive value, but stenosis severity correlates poorly with ischemia. Therefore decision making with respect to revascularization may be limited when a purely noninvasive anatomical test is used. Regarding perfusion imaging, the diagnostic accuracies of SPECT, PET, and cardiac magnetic resonance are similar, though fewer studies are available with cardiac magnetic resonance. PET coronary flow reserve may offer a negative predictive value sufficiently high to exclude severe CAD such that patients with mild to moderate reversible perfusion defects can forego invasive angiography. In addition, combined anatomical and perfusion-based imaging may eventually offer a definitive evaluation for diagnosing CAD, even in higher risk patients. Any remarkable findings on single-photon emission computed tomography and PET MPI studies are valuable for prognostication. Furthermore, assessment of myocardial blood flow with PET is particularly powerful for prognostication as it reflects the end result of many processes that lead to atherosclerosis. Decision making with respect to revascularization is limited for cardiac MRI and PET MPI. In contrast, retrospective radionuclide studies have identified an ischemic threshold, but randomized trials are needed. In patients with at least moderately reduced left ventricular systolic function, viable myocardium as assessed by PET or MRI, appears to identify patients who benefit from revascularization, but well-executed randomized trials are lacking.
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Introduction

Several noninvasive imaging options are available for the assessment of suspected or known coronary artery disease (CAD) and for prognostication. These include coronary CT angiography (CCTA), SPECT, PET, and cardiac magnetic resonance (CMR). Stress echocardiography with myocardial perfusion imaging (MPI) is not commonly performed in the United States, as discussed elsewhere.[1] In this review, we address 3 fundamental questions that most clinicians might often get asked:

1. Who needs imaging and what are the advantages of the various testing options?
2. How do the imaging modalities perform in risk stratification?

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3. How do the results of individual tests guide decision making with respect to revascularization vs medical therapy?

With respect to the first question, the importance of accurate pretest risk assessment is addressed, and the advantages of each modality are framed within the context of anatomical or perfusion-based imaging. Newer techniques including coronary flow reserve (CFR) with PET and combined anatomical and perfusion-based imaging are emphasized. Regarding risk stratification and prognostication, the prognostic value of SPECT, CMR, and more recent studies with CCTA are discussed. Abnormal findings on PET CFR are usually a manifestation of macrovascular disease, microvascular disease, or a combination of both; the prognostic value of PET-based quantification of CFR is highlighted. Finally, studies that incorporate imaging results to identify patients who benefit from revascularization are discussed with the caveat that a well-executed randomized trial with imaging-guided revascularization vs medical therapy is lacking.

Diagnosis of Obstructive CAD

When is MPI Not Indicated?

In addition to further refinement of risk, a diagnostic test must more effectively classify a patient's risk such that downstream treatment is affected and subsequent morbidity and mortality attenuated. For patients at low risk of adverse cardiac events, initial imaging thus has low yield. Very few of these patients will have significantly discordant clinical and imaging results such that differential treatment has a major effect on outcome. Unfortunately, pretest risk assessment is frequently overestimated, and many of these patients undergo up-front MPI, leading to its overutilization.

In contemporary practice, patients are more likely to be treated for hypertension, hyperlipidemia, and diabetes mellitus. Moreover, over the years, patients will have varying success in treatment of these comorbidities. These temporal changes were illustrated in a study where pretest probability of CAD increased from 40.1%-49.2% from 1991-2009, yet the number of tests with abnormal findings on SPECT MPI decreased from 40.9%-8.7%.[2] During this time, use of aspirin, antihypertensive drugs, and lipid-lowering medications increased. Consequently, MPI may be frequently performed in patients labeled as having intermediate risk of disease but who may in fact be at low risk. As stress testing with MPI is best performed in patients with an intermediate probability of developing obstructive CAD, further study is needed to elucidate the current disconnect between pretest probability and subsequent demonstration of ischemia.

Exercise Results to Identify the Low-Risk Patient

In patients without known CAD who are able to exercise and have a normal baseline electrocardiography (ECG), exercise treadmill testing (ETT) is a reasonable initial test. The following 2 questions arise: Do any of these individuals benefit from perfusion imaging? In patients who can achieve an acceptable peak heart rate and exercise capacity, which test results should prompt follow-up imaging? With regard to the first question, a large single-center study showed that only 2.9% of exercising patients without typical angina had abnormal findings on SPECT MPI.[2] In the WOMEN trial, there was no difference in adverse cardiac events between women who underwent ETT vs ETT and MPI (1.7% vs 2.3%, $P = 0.59$).[3] It is noteworthy that the expected event rate was lower than predicted, again highlighting the frequent overestimation of pretest risk. Patients with excellent functional capacity are unlikely to benefit from further risk stratification with imaging. In a study of patients able to achieve more than 10 estimated metabolic equivalents, very few patients had evidence of ischemia, and the annualized cardiac event rate was 0.4%.[4]

Thus, most patients referred for testing to diagnose CAD who are able to adequately exercise are at low risk and should undergo ETT alone. The second question concerns the ETT results that should prompt imaging. Patients with very abnormal findings on tests frequently directly undergo invasive coronary angiography (ICA), but the appropriate management of inconclusive tests has been less well defined. A recent study addressed this issue by evaluating the yield of downstream MPI after ETT. Among patients with rapid recovery of ECG changes, none of the patients had positive results on imaging studies. Conversely, 21% had abnormal imaging findings following an ETT with typical angina but no ECG changes.[5] In conclusion, the yield of subsequent MPI is highest in patients whose ETT results change the probability of CAD from low to intermediate or high.

What Imaging Study Should You Order?

For truly intermediate-risk patients, noninvasive imaging has a well-established role to diagnose CAD in many different clinical scenarios.[6] As the options available to the clinician have increased, several questions concerning which test to order have become important: Is anatomical or perfusion-based testing preferable? Is one imaging modality better than another is? Finally, what is the role for combined anatomical and perfusion-based testing?

Anatomy-Based Approach

Regarding anatomy-based testing, in a summary of published studies examining the diagnostic accuracy of CCTA, the sensitivity and specificity per patient has been reported to be 94%-97% and 83%-90%, respectively.[7] In patients with no history of CAD, CCTA has an excellent negative predictive value. A meta-analysis that compared 64-slice multidetector computed tomography coronary angiography with ICA reported sensitivity, specificity, positive predictive values, and negative predictive values with 95% confidence intervals (CI) of 97.5% (CI: 0.96-0.99), 91% (CI: 0.88-0.94), 93%, and 96.5%, respectively.[8] CCTA can reliably exclude obstructive CAD, but the reported positive predictive value is lower. The ACCURACY trial reported a sensitivity of 93.8% and a