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Review article – *Special issue: Imaging in Coronary Artery Disease*

Myocardial perfusion imaging in coronary artery disease

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ABSTRACT

Radionuclide myocardial perfusion imaging (MPI) can be used to demonstrate the presence of coronary heart disease and to risk stratify and guide management of patients with known disease. It has the ability to localize hemodynamically important coronary stenoses, and assess the extent and severity of coronary obstruction by the presence and extent of perfusion defects. A normal stress MPI indicates the absence of coronary obstruction and hence of clinically significant disease. Cardiac PET has the advantage from SPECT of higher spatial and temporal resolution, and a decreased radiation exposure to patients. Hybrid cardiac imaging combining SPECT or PET with CT data appears to offer superior diagnostic and prognostic information in patients with intermediate risk for CAD. A significant progress in better quantification of myocardial blood flow and coronary flow reserve has recently been seen. Also several studies have demonstrated that the combination of imaging apoptosis and matrix metalloproteinases production can help imaging vulnerable plaque and identifying the group of high-risk asymptomatic patients who will benefit most by an imaging procedure.

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Introduction

The accurate noninvasive diagnosis and functional evaluation of coronary artery disease (CAD) is an important step in selecting the appropriate management strategy. A complete assessment of CAD requires both anatomical and functional information. This can be obtained in a variety of ways and the common imaging techniques overlap in their capabilities, particularly for the assessment of myocardial viability, function, and coronary anatomy. Several noninvasive imaging options are available for the assessment of suspected or known coronary artery disease and for a long-term prognosis of the disease. Radionuclide tests occupy a central position within the cardiac imaging modalities, and among them myocardial perfusion imaging (MPI) has an obvious place because of its perfect validation for assessing myocardial perfusion. Patients with ECG abnormalities, poor exercise capacity, or intermediate pretest likelihood of disease according to the ECS guidelines, would be the best candidates for this noninvasive imaging [1].

The introduction of ^{201}Tl myocardial perfusion imaging as an adjunct to ECG treadmill studies in the mid-1970s has evolved into the discipline of nuclear cardiology today [2]. MPI provides direct assessment of myocardial perfusion and therefore has an important role in the diagnosis of CAD in patients presenting with chest pain and intermediate pretest likelihood. Techniques such as SPECT and PET currently allow evaluating occlusive coronary atherosclerosis by estimation of myocardial perfusion as well as effects of myocardial hypoperfusion on metabolic activity and contractile function. An inducible perfusion abnormality indicates impaired perfusion reserve, which in turn usually corresponds to epicardial coronary obstruction.

Diagnosis and prognosis of obstructive CAD

Exercise–ECG stress testing has an established role in assessment of patients for the detection of occlusive CAD and with known CAD; however, the progression from ECG-based stress testing to current SPECT and PET technologies has led to improvements in both diagnostic efficacy (sensitivity and specificity for detecting CAD) and resolution (identifying the culprit lesion for chest pain and myocardial ischemia) [3]. An additional advantage of myocardial perfusion-based stress testing over ECG-only testing is the applicability to patients with underlying ECG abnormalities that mask dynamic ischemic ECG changes. Nevertheless, many patients referred for stress testing have functional limitations from pulmonary, orthopedic, peripheral vascular or neurologic conditions that prevent sufficient physical exercise. Ischemic ECG signals may be uninterpretable among patients with abnormal baseline ST segment depression of >1 mm, electronic pacing, left bundle-branch block, or preexcitation pattern. These inadequacies as well as the limited sensitivity and specificity of ECG-based SPECT stress test have led to the development of alternate methods of stressors with pharmacologic agents that either simulate exercise, such as an adrenergic agent (dobutamine), or induce vasodilation (adenosine or dipyridamole) [4].

Myocardial uptake of a radiotracer used for MPI is a function of both delivery of the radiotracer to the cell surface (which is flow-dependent) and subsequent extraction and retention into the cell (which is dependent on cell membrane integrity and viability). Intravascular radiotracer is extracted by myocardial tissue in proportion to blood flow. Thus, the same mechanisms leading to insufficient oxygen delivery and subsequent ECG-detected myocardial ischemia on the treadmill can be assessed directly by interrogating regional myocardial perfusion. Regions of decreased myocardial uptake on SPECT and PET can then be correlated with specific coronary artery vascular territories and with a culprit atherosclerotic lesion responsible for the patient's symptoms. A repeated radiotracer injection and imaging after stress and at rest allows differentiating between reversible and fixed perfusion defects. Reversible defects correlate with myocardial ischemia as seen by dynamic ECG changes between resting and stress conditions. If the defect size decreases from rest to stress, this signifies hypoperfused but viable myocardium (hibernation), which predicts a high possibility for recovery of function after revascularization [4] (Fig. 1).

The distribution of radiotracers in various regions of the LV reflects the physiologic consequence of the coronary artery vascular territories, the extent of epicardial luminal narrowing and downstream adaptation by the resistance vessels and collaterals. Metabolic adaptation likely represents one of the earliest responses to myocardial ischemia, which is regulated to protect the structural and functional integrity of the heart. Ischemia may be transitory and reversible, or permanent and irreversible, leading to myocardial infarction. Myocardial ischemia may also lead to postischemic stunning, hibernation, and preconditioning. A decrease in oxygen delivery to the myocardium results in the downregulation of mitochondrial oxidative metabolism and reduced contractile function targeting intracellular metabolic processes. Radiotracers reflect changes in blood flow and myocardial extraction and this has become the basis for subsequent cardiac SPECT and later PET tracers for perfusion imaging. For SPECT, a family of technetium-99m (^{99m}Tc) based radiotracers was developed in the 1990s including now ^{99m}Tc-sestamibi and ^{99m}Tc-tetrofosmin. Despite widespread clinical use, those radiotracers are imperfect due partly to their nonlinear myocardial extraction at high flow rates and high initial hepatic uptake, which can make difficult interpretation of defects in the inferior wall due to adjacent photon scatter. Radiotracers that have minimal hepatic uptake or more rapid washout are continuously under investigation to ameliorate some of these limitations [5].

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