Papillary muscle ischemia and myocardial blood flow on N13-ammonia positron emission tomography myocardial perfusion imaging

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INTRODUCTION

The two-left ventricular (LV) papillary muscles (anterolateral and posteromedial) are small structures that are vital to mitral valve competence and LV function. Partial or complete papillary muscle rupture, complicating acute myocardial infarction, causes severe or even catastrophic mitral regurgitation, and is associated with increased morbidity and mortality.[1] However, despite the clinical significance of papillary muscle (PM) ischemia, the assessment of papillary muscle perfusion has been challenging with cardiac single photon emission computed tomography myocardial perfusion imaging (SPECT MPI) or Magnetic Resonance Imaging. Conventional nuclear imaging techniques like SPECT or gated radionuclide ventriculography lack the depth of spatial resolution in comparison to positron emission tomography (PET) for visualization of different patterns of papillary muscle ischemia.[2,3] PM visualization not only helps to diagnose PM ischemia but also differentiate between the various stages of ischemia, ranging from hibernation to infarction, which allows for better management of patients. Nakao et al. from Tokyo, Japan, in this issue of the Journal of Nuclear Cardiology ([4]) describe the role of N13-ammonia PET Myocardial Perfusion Imaging (MPI) in (1) detection of papillary muscle (PM) ischemia and (2) association of PM ischemia with global myocardial flow reserve (MFR) and its prognostic value in coronary artery disease (CAD).

The causes of coronary circulatory dysfunction in patients with risk factors for CAD are multifactorial, with a reduction in the bioavailability of endothelium-derived nitric oxide through various mechanisms, the probable common final pathway.[5] Endothelial activation plays a pivotal role in the pathogenesis of acute coronary syndromes. It is characterized by coronary plaque vulnerability, and paradoxical vasoconstriction, which likely contributes to plaque rupture.[6] Impairment of coronary circulatory function is expected to reflect in part the vulnerability of plaque, which in turn may explain the independent predictive value of coronary circulatory dysfunction for future cardiovascular events.[7] It may be concluded that functional alterations of the coronary circulatory function appear to reflect ongoing processes that modify the arterial wall's functional status. Thus, functional alterations of the coronary circulation appear to be more reliable in the assessment of CAD-related structural changes in predicting future cardiovascular clinical outcomes.[8–10]

The role of SPECT in myocardial perfusion assessment has been well-validated and established.[11] However, over the years, the use of PET for the evaluation of myocardial perfusion has emerged as a robust modality for the diagnosis, risk stratification, and management of patients with established or suspected CAD.[12] Cardiac PET MPI has critical advantages over SPECT, including (1) better diagnostic accuracy with

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fewer false positives, in turn, improving the specificity of diagnosing CAD (2) better spatial resolution allowing detection of smaller perfusion defects, in turn, improving sensitivity (3) reduced radiation exposure due to use of radiotracers with a shorter half-life (e.g., 13 N-Ammonia and 82 Rubidium) in comparison to SPECT tracers like thallium – 201 and technetium-99m agents (sestamibi or tetrofosmin) and (4) the ability to noninvasively quantify absolute myocardial blood flow (MBF) in ml per minute per gram of tissue and myocardial flow reserve (MFR).[13,14]

Although various other imaging modalities are being studied, PET remains the most robust noninvasive technology for MBF evaluation and to which other imaging modalities are compared.[15] It's validity and reproducibility has been well tested in both animals and humans.[16–18] MFR is the ratio of MBF during maximal coronary vasodilation to resting MBF. MFR signifies the relative reserve of the coronary circulation. The optimal value separating normal from abnormal MFR value is somewhat empirical considering different tracers and software used to derive the value and various studies with different cut-points.[15] However, in general, MFR >2.3 signifies a favorable outcome with <1.5 suggesting poor flow reserve and outcome. Since the landmark studies by Gould et al. in the late 70s. MFR has been advocated as the functional tool to assess the severity of CAD.[19,20] Studies have shown a good correlation between coronary artery stenosis on angiography and MFR obtained by PET using ^{15}O-water and ^{13}NH3 tracers.[21,22] Di Carli et al. showed similar correlations between the MFR and the severity of coronary stenosis.[23] Olivotto et al. suggested that diminished MBF commonly seen with microvascular dysfunction is a long term predictor of systolic dysfunction, whereas a preserved MBF has a protective effect.[24] The quantitative assessment of MBF and MFR can assist with the diagnosis of multivessel CAD and assess response to interventions, including lifestyle modifications or therapeutics. [15] PET tracers for measurement of MBF, which are well-validated, include 82Rb and 13N-ammonia. The evaluation of MBF and MFR using PET has revolutionized the assessment and management of patients with CAD and shifted the dependence from coronary angiogram for anatomical evaluation of blood flow in the epicardial coronaries to a functional one provided by PET, which provides a comprehensive assessment of the entire vascular bed.[15] The evaluation spectrum may range from endothelial dysfunction to early atherosclerosis to advanced diffuse atherosclerosis disease and noncoronary disease.

There have been extensive studies suggesting an incremental prognostic value of PET derived MBF and MFR in patients with CAD and other cardiac comorbidities.[24–26] ^{14}PET derived MFR can be done with the standard protocols currently utilized without requiring any extra time, radiation exposure, or additional cost, complementing the already improved assessment of relative myocardial perfusion. Over recent years, several observational studies have shown the potential value of MFR in clinical practice in patients with known or suspected CAD with ASNC PET guidelines too endorsing PET's potential clinical application.[27]

In the current issue of the Journal of Nuclear Cardiology, Nakao et al. study papillary muscle perfusion, its relationship to MFR and cardiac outcomes. The investigators identify PM ischemia in 31 out of 263 patients who underwent adenosine-stress N13-ammonia PET for known or suspected CAD. The left circumflex artery territory was the most frequently observed ischemic area, followed by the left anterior descending artery territory in cases with PM ischemia. A total of 22 patients (8.4%) were diagnosed with absent PM (defined as anterolateral or posteromedial nonvisualization in both stress and rest images), which could be related to the small size of PM's or infarction or severe ischemia. False-negative PM ischemia was thought to occur when PM perfusion is only mildly reduced. Interestingly global MFR was significantly lower in patients with either PM ischemia or absent PM than those with normal PM. Patients with PM ischemia had a statistically significant higher rate of major adverse cardiac events (MACE).

PET derived MFR is a powerful tool that provides a comprehensive picture of the health of the coronary vasculature ranging from the functional assessment of hemodynamically significant epicardial disease to microvascular dysfunction. High-spatial resolution N13- ammonia PET MPI also allows for detection of PM ischemia, which is associated with reduced global MFR and higher rates of MACE. Presence of PM ischemia complements MFR and many other known MPI variables in the risk stratification of CAD.

Disclosures

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