Imaging Update in ACS: Advances in Plaque and Ischemia Imaging

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Most acute coronary syndrome (ACS) events are triggered by plaque rupture and subsequent thrombosis formation. Therefore, identifying high-risk plaques is an important strategy for reducing ACS events. With recent advances in vascular biology, physicians have a better understanding of the morphological features, such as luminal narrowing, that distinguish high-risk vulnerable plaques from lower-risk lesions. With better options for assessing vascular stenosis, physicians have also refined various models for predicting long-term cardiovascular (CV) risk in patients with coronary artery disease (CAD). However, exploiting these discoveries requires accurate imaging of vascular structure and function.

In this special session on CV imaging, Frank E. Rademakers, MD, PhD, University Hospitals, Leuven, Belgium, described the role of new imaging technologies in the detection and management of atherosclerosis, CAD, and other vascular complications. Plaque imaging is important for identifying patients who may benefit from systemic or targeted treatment and comparing the efficacy of various treatment strategies. Ischemia imaging can support risk stratification, inform the selection of invasive versus noninvasive treatment, and guide coronary interventions. Several examples illustrate the importance of new imaging techniques in advancing the evaluation and treatment of patients with vascular disease.

The Case for Ischemia Imaging: Fractional Flow Reserve-Guided Revascularization

New technologies are emerging as important tools for guiding percutaneous coronary intervention (PCI). Pressure-derived fractional flow reserve (FFR) can be measured during coronary angiography and can identify coronary lesions that are responsible for ischemia. An FFR value of ≤0.80 identifies ischemia-causing coronary stenoses with an accuracy of >90%. The Fractional Flow Reserve Versus Angiography in Multivessel Evaluation (FAME) study compared angiography alone versus angiography that was guided by routine measurement of the FFR for guiding PCI with drug-eluting stents in patients with multivessel CAD. Lesions that required PCI were identified before randomization, based on their angiographic appearance. Patients who were randomly assigned to angiography-guided PCI underwent stenting of all indicated lesions, while those who were randomized to FFR-guided PCI underwent stenting only of those lesions that were indicated by FFR [Tonino PA et al. *N Engl J Med* 2009].

Compared with angiography-guided PCI, FFR-guided PCI significantly reduced the rate of the composite endpoint of death, nonfatal myocardial infarction (MI), and repeat revascularization at 1 year [Tonino PA et al. *N Engl J Med* 2009]. The benefits of FFR-guided PCI persisted throughout the FAME follow-up period. In the 2-year analysis, patients in the FFR-guided PCI group had significantly reduced mortality and MI rates compared with the standard angiography-guided PCI group [Pijls NH et al. *J Am Coll Cardiol* 2010].

To understand the mortality and morbidity benefits of FFR-guided PCI, FAME investigators evaluated the relationship between angiographic stenosis severity and functional stenosis severity, as measured by FFR [Tonino PA et al. *J Am Coll Cardiol* 2010]. In patients with multivessel disease, they found that angiographic stenosis severity corresponded poorly with the presence of myocardial ischemia and was inferior to FFR measurements in identifying which stenoses should be stented. The discrepancy between angiographic and functional stenosis was especially pronounced in cases of moderate (50% to 70%) and severe (71%

Highlights from the

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to 90%) stenosis range. Together, several reports from the FAME study indicate that FFR-guided PCI is superior to angiography-guided PCI and should be the new standard of care for patients with multivessel disease.

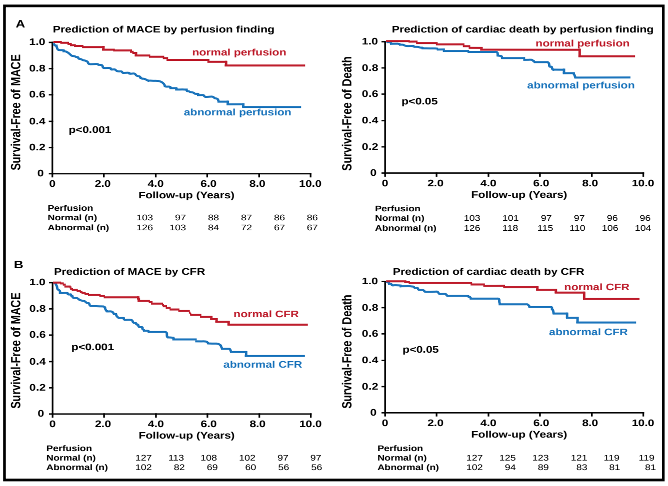
Hamilos and colleagues from the University of Crete, Greece, also showed the benefits of FFR-guided PCI in a prospective trial of 213 patients with left main coronary artery (LCMA) stenosis. In these patients, angiography alone underestimated the functional significance of the stenosis and provided inadequate information about the need for revascularization. By comparison, an FFR-guided strategy accurately identified which patients were most likely to benefit from revascularization and which patients could be successfully managed with nonsurgical interventions [Hamilos M et al. *Circulation* 2009]. Understanding when CABG is necessary and when surgery can safely be deferred may improve long-term survival in patients. Therefore, rather than basing revascularization decisions solely on angiography, FFR measurements should be obtained in patients with ambiguous LMCA stenosis.

PET Myocardial Perfusion Imaging

Positron emission tomography (PET) myocardial perfusion imaging provides an excellent measure of regional myocardial blood flow (MBF) that appears to be superior to standard single-photon emission computed tomography (SPECT) perfusion imaging. Using PET imaging to assess MBF at rest and during stress is a noninvasive strategy for revealing early and subclinical abnormalities in coronary arterial vascular structure and function.

Herzog and colleagues from the University Hospital Zurich, Switzerland, evaluated the value of PET myocardial perfusion imaging in predicting long-term prognosis in 256 patients with suspected myocardial ischemia. Abnormal myocardial perfusion predicted a higher incidence of major adverse CV events, including cardiac death, nonfatal MI, late revascularization, and hospitalization for cardiac reasons ($p<0.001$), as well as a higher incidence of cardiac death ($p<0.05$; Figure 1). In patients with normal myocardial perfusion, an abnormal coronary flow reserve (CFR) on PET imaging further distinguished patients with high annual CV event rates ($p<0.05$) and annual cardiac death rates ($p<0.05$) from those with low annual event rates. In patients with abnormal perfusion, CFR remained predictive of adverse outcomes throughout the 10-year follow-up ($p<0.001$). Therefore, CFR on PET imaging is an independent predictor of adverse outcomes that adds to the prognostic predictive value of perfusion findings alone [Herzog BA et al. *J Am Coll Cardiol* 2009].

Figure 1. Kaplan-Meier Survival Curves (Unadjusted) for the Entire Study Population.



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Future of Vascular Imaging

Future imaging technologies will provide options for evaluating vascular structure and function more precisely in patients with CAD. Some techniques will focus on quantifying MBF to assess coronary microvascular dysfunction and subclinical disease. In addition, tools for imaging vascular inflammation and plaque will provide measures of plaque attenuation, composition, and instability. Technical improvements, including the use of contrast agents and 3-dimensional technologies, will further enhance imaging capabilities.

Investigators at the VU University Medical Centre, Amsterdam, The Netherlands, have used (15)O-water images without attenuation correction to improve the accuracy of MBF and CFR measurements while reducing the total radiation burden and effective radiation dose in patients who undergo PET imaging [Lubberink M et al. *Nucl Med* 2010]. At the Washington University School of Medicine, St. Louis, Missouri, USA, researchers are exploring cardiac MRI methods as alternatives to radionuclide imaging in patients with myocardial ischemia. In particular, quantitative MRI oxygenation imaging is a promising noninvasive tool for directly evaluating myocardial energetics and efficiency [McCommis KS et al. *Circ Cardiovasc Imaging* 2010].

The management of ACS is moving toward the earlier identification of at-risk patients and the earlier treatment of subclinical atherosclerotic disease. Advanced imaging techniques may improve the diagnostic and prognostic evaluation of patients with atherosclerotic disease, enhance the selection of treatments that are tailored to each patient's individual level of risk, and facilitate the use of noninvasive therapy when possible.