More evidence for prognostic value of quantification of myocardial perfusion

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Measurement of myocardial blood flow (MBF) in absolute units ($mL \cdot min^{-1} \cdot g^{-1}$ of myocardial tissue) using positron emission tomography (PET) can improve risk assessment over relative perfusion imaging.[1] The independent prognostic value of impaired MBF and myocardial flow reserve (MFR) in response to vasodilator stress has been demonstrated in several cohorts.[2-6] More recently, coronary flow capacity (CFC) integrating stress MBF and MFR has been introduced to aid in the interpretation of physiologic severity of coronary artery disease (CAD).[7]

In the study by de Dietz et al. published in this issue of the journal of Nuclear Cardiology,[8] investigators evaluated the prognostic value of global stress MBF, global MFR, and regional CFC in 234 patients undergoing ^{82}Rb PET myocardial perfusion imaging for evaluation of myocardial ischemia. During an average follow-up of 652 days, 47 patients experienced an adverse event, including 5 cardiac deaths, 13 non-fatal myocardial infarctions, 10 late revascularizations, and 19 hospitalizations for congestive heart failure or de novo angina pectoris. The main finding of the study is that after adjustment for clinical risk factors, reduced global stress MBF (< 1.94 $mL \cdot min^{-1} \cdot g^{-1}$), reduced global MFR ($< 1.98$), and severely reduced regional CFC in $> 3.2\%$ of the left ventricular myocardium emerged as independent predictors of adverse events (hazard ratios 4.5, 3.1, and 3.67, respectively). Furthermore, when stress MBF, MFR, and CFC were included in the same model, reduced global stress MBF remained as an independent prognostic factor. An additional aspect of the current study is that the use of silicon photomultiplier PET technology allowed for reduction of the injected dose of the tracer, with subsequent reduction in radiation exposure to the patient.

The findings of Dietz et al. are in line with previous studies showing that quantitative myocardial perfusion metrics by PET, both globally and regionally are powerful predictors of cardiovascular events in patients with CAD.[2-6] In a large cohort of 4029 patients undergoing clinically indicated PET myocardial perfusion imaging, Gupta et al. found that both global stress MBF and global MFR were independent predictors of cardiovascular mortality after adjustment for other prognostic factors, including clinical cardiovascular risk factors, left ventricular ejection fraction, myocardial scar and ischemia, and revascularization.[9] Furthermore, in that study MFR was a stronger predictor of cardiovascular mortality than stress MBF (hazard ratios 1.83 and 1.35 per unit decrease, respectively) and provided incremental prognostic value over global stress MBF.[9] However, some studies have found global stress MBF to be a particularly strong predictor of the risk of death or non-fatal myocardial infarction.[2,4,5] The findings of Dietz et al. support the prognostic value of both global stress MBF and MFR. It should be noted however, that the number of patients was relatively small and events differed from previous studies in that late revascularization and hospitalization due to either angina or heart failure were included in addition to mortality and myocardial infarction.

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The concept of CFC integrates regional stress MBF and CFR into a single parameter in order to achieve more comprehensive assessment of physiologic severity of CAD.[7] Indeed, studies have found that reduction of both stress MBF and MFR is associated with the highest rate of death or non-fatal myocardial infarction, whereas patients with reduction in either stress MBF or MFR are at an intermediate risk.[4,9] Observational studies have found that the reduced MFR may identify patients with survival benefit from early revascularization as compared to medical therapy.[10,11] In the study of Gupta et al., patients with concordant reduction in stress MBF and MFR had a high burden of myocardial scar and ischemia, whereas patients with discordant reduction in MFR, but preserved stress MBF had low scar and ischemia burden.[9] Thus, stress MBF and MFR may identify different prognostic phenotypes, which may influence selection of therapy.

Originally, CFC was developed based on per-pixel combinations of hyperemic MBF and CFR by ^{82}Rb PET that were associated with clinical features of ischemia.[7,12] Subsequently, Gould et al. showed that severely reduced CFC was associated with an increased risk of major adverse cardiac events, which was significantly reduced by coronary revascularization.[12,13] Gould et al. also demonstrated that identification of patients with severely reduced CFC could improve risk stratification compared to the use of stress MBF or MFR alone, indicating the potential complementary nature of these parameters.[13] More recently, CFC has been adopted in studies using PET with ^{15}O-water and ^{13}N-ammonia.[14,15] In addition to PET imaging, CFC can be derived from any imaging modality allowing for quantification of absolute coronary flow, and studies using intracoronary flow measurements have also reported a significant improvement in the prediction of major adverse cardiac events compared to coronary flow reserve and fractional flow reserve.[16,17] Dietz et al., derived a threshold of $>$ 3.2% of the left ventricular myocardium with severely reduced severely reduced CFC (pixels having both MFR $\leq$ 1.5 and stress MBF $\leq$ 1.1 mL·min^{-1}·g^{-1}) that predicted adverse events. This approach could easily be tested in other cohorts as well. However, the absolute values and thresholds likely vary between the different tracers and imaging methodologies and the presented thresholds may not be ideal for other imaging methods.

The study by Dietz et al. adds to the evidence that quantification of myocardial perfusion both globally and regionally is a strong predictor of outcomes. Although their study included a relatively small cohort, it adds important information on performance of different quantitative perfusion metrics to predict outcomes in patients undergoing PET myocardial perfusion imaging for evaluation of suspected ischemia.

Disclosures

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