Assessment of Coronary Flow Reserve by Dynamic Single-Photon Emission Computed Tomography
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The latest SPECT cameras, such as cadmium zinc telluride ultra-fast cameras or the D-SPECT cameras, can capture sequential myocardial perfusion images with adequate quality to provide time activity curves of the left ventricular cavity and myocardial tissue. Although attenuation correction is not available in SPECT, from these curves and the single-compartment model, CFR is estimated as the ratio of the k1 parameter at stress to that at rest. Previous studies have confirmed the potential feasibility of SPECT-measured CFR on planar imaging compared with the gold standard [15O]H2O PET. Although the most commonly used method for the estimation of tissue CFR is PET studies using various flow tracers, the CFR estimated by SPECT or PET indicates the flow increase in myocardial tissue, but not the speed of coronary flow in the coronary conduit artery. Quantification of CFR is an emerging index used for improving both the diagnosis and risk stratification in patients with suspected coronary artery disease (CAD).

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tracers for PET are not yet available in many hospitals. Thus, the SPECT-measured technique is expected to increase the utility of CFR measurement in the clinical setting.

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CFR in CAD

The advantage of CFR measurement over perfusion imaging is that it can capture balanced ischemia, often underestimated by visual perfusion assessment, in patients with multiple coronary stenosis and diffuse atherosclerosis. Reduced CFR is a different concept from ischemia. Ischemia is caused by atherosclerosis in the conduit coronary artery, whereas a low CFR is caused by microvascular dysfunction associated with coronary risk factors in addition to coronary atherosclerosis. It is hard to predict the effects of the atherosclerotic burden on myocardial ischemia or CFR because atherosclerosis beyond the severity of luminal narrowing, such as plaque volume and morphology, and vascular remodeling cannot be clearly visualized by invasive coronary angiography. Because a low CFR indicates a continuous spectrum of disease severity of the conduit coronary artery and microvascular function, the measurement of CFR may be necessary to assess the functional disease activity of diffuse atherosclerosis at the individual patient level. Chronic ischemia with a low CFR might cause hibernation of the myocardium and consequently wall motion abnormality. Indeed, a recent study has demonstrated that revascularization by coronary artery bypass grafting in patients with high-risk CAD and a low CFR improves the prognosis compared with percutaneous coronary intervention or medical therapy alone. In addition, the COURAGE study suggests that improvement of ischemic burden is associated with a good prognosis. Improvement in the CFR is also potentially associated with a good prognosis. These studies suggest that it is important to identify for revascularization those patients who have functional flow-limiting coronary atherosclerosis as evaluated by inducible myocardial ischemia and a low CFR.

Clinical Use of CFR for the Identification of Obstructive CAD

The diagnostic value of SPECT is inferior to that of perfusion MRI, because of their different methodologies. SPECT delineates the relatively low perfused area against the epicaldial area. Quantitative CFR is considered to be a good functional index to overcome this limitation of SPECT. Indeed, previous studies using PET demonstrate that quantitative CFR has additive value to diagnose CAD over ischemic burden by perfusion imaging.

In particular, CFR has a high negative predictive value for ruling out obstructive coronary stenosis and diffuse atherosclerosis, because a normal CFR guarantees normal circulation throughout the entire coronary tree. However, a low CFR cannot distinguish coronary atherosclerosis from microvascular dysfunction, so it is not specific for ischemic burden. CFR is also reduced by microvascular dysfunction associated with coronary risk factors and aging. Accordingly, the cutoff value of CFR to detect the severity of coronary atherosclerotic burden might differ according to clinical status. The diagnostic value of PET improves from a receiver-operator characteristic curve area of 0.687, as determined using pre-CFR models such as pretest probability, summed stress score, and transit ischemic dilation index, to that of 0.731 using CFR models (cutoff value of CFR <1.93). Shiraiishi et al demonstrate the diagnostic value of SPECT-measured CFR; however, they did not test the statistical analysis of the incremental value of CFR over the summed stress score. On this matter, the sensitivity, specificity, positive predictive value, and negative predictive value of CFR alone were 0.86, 0.78, 0.57, and 0.94, respectively, although the values for the summed stress score are not provided.

Whether patients who have normal stress perfusion imaging and a low CFR should undergo invasive angiography is still unknown because of the low specificity of a low CFR for the detection of CAD in the clinical setting. Patients who have normal stress perfusion and normal CFR do not need to undergo angiography. We treated a patient with a normal CFR and coronary stenosis, and a patient with a very low CFR, extensive scar, and low ejection fraction (Figure). In our clinical experience, the CFR values of each patient with CAD should be determined in terms of both diagnosis and prognosis.

References


