Invasive Testing for Coronary Artery Disease

FFR, IVUS, OCT, NIRS

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KEYWORDS

• Fractional flow reserve • Intravascular ultrasonography • Optical coherence tomography
• Near-infrared spectroscopy • Coronary artery disease

KEY POINTS

- Fractional flow reserve is a well-validated technique that can be used to characterize whether a coronary lesion is physiologically significant.
- Intravascular ultrasonography is a flexible technology that can be used to determine luminal area and the composition of a coronary lesion.
- Optical coherence tomography is an emerging technology that can help guide percutaneous coronary intervention and visualize deployed stent struts with high accuracy despite the presence of plaque or neointimal hyperplasia.
- At this time, the clinical applications of near-infrared spectroscopy remains unclear, but potential uses include determination of plaque composition to identify vulnerable plaques, and guidance of medical treatment strategies.

INTRODUCTION

Coronary angiography or cineangiography provides direct visualization of the coronary luminal anatomy and is the gold standard for the diagnosis of coronary artery disease.[1] However, since the development of angiography in the 1960s, the primary method for assessing the lesions that are of physiologic significance has been visual assessment by the operator,[2] which is prone to significant intraobserver and interobserver variability.[2–4] The significance of a given stenosis is not determined solely by the reduction in luminal diameter, because numerous additional factors such as lesion length, shape, and eccentricity affect the flow dynamics of the lesion and thus the physiologic significance.[5–9] Therefore, coronary angiography cannot solely be relied on to provide the physiologic or clinical significance of a stenosis, particularly when the vessel is narrowed to between 40% and 80% of its normal diameter.[10,11]

Because of the need for a more comprehensive method for determining the anatomic and functional characteristics of a coronary artery lesion, several techniques have been developed to augment standard cineangiography.[12,13] These novel techniques are centered on the physiologic assessment of lesions and advanced intravascular imaging to provide a more comprehensive anatomic assessment.

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This article discusses invasive testing for coronary artery disease. Fractional flow reserve (FFR), defined as the ratio of the distal pressure in the coronary artery to aortic pressure at a maximal hyperemic state, describes the physiologic significance of a coronary stenosis and can predict whether percutaneous coronary intervention (PCI) will be beneficial. Following FFR, the intravascular imaging modalities are reviewed: intravascular ultrasonography (IVUS), optical coherence tomography (OCT), and near-infrared spectroscopy (NIRS). These complementary imaging modalities can help overcome technical limitations in the ability to optimally visualize a particular lesion, and can provide information about the contour of the vascular lumen and the composition of the vascular wall.

FFR

FFR is an elegantly simple principle based on the fundamentals of fluid dynamics that was first derived and published by Pijls and colleagues[14,15] in the early 1990s. It has recently gained increased clinical traction because of several important long-term outcome studies that showed the usefulness of FFR in decision making with regard to lesion-specific treatment.[16–18] As previously discussed, it is critical that lesions with ischemic potential be evaluated in a manner that determines more than their appearance on arteriography.[19] A standard cineangiogram provides a two-dimensional representation of a three-dimensional structure, namely the lumen of the coronary artery. Because of the inherent limitations of these so-called lumenograms, standard clinical practice is to obtain numerous angiographic views of the epicardial coronary arteries, but two-dimensional imaging modalities inherently fail to accurately represent a three-dimensional structure.[6,13,20,21] Vasomotor tone, shape, length, eccentricity, collateral contribution, and several other factors of a lesion are critical in determining its clinical significance, but are lacking or absent in the assessment of lesions through the sole use of standard arteriography.[5–8]

FFR is defined as the ratio of distal coronary pressure in the coronary artery to aortic pressure at a maximal hyperemic state averaged over the cardiac cycle; this represents the maximum achievable blood flow in the presence of a stenosis divided by the maximum flow if there was no lesion.[14] FFR is particularly useful clinically in that it is independent of basal flow, changes in hemodynamics, and the microcirculation. For each coronary artery in a patient, a normal FFR is 1, because pressure in a normal epicardial coronary artery should equal aortic pressure throughout the artery.[14] Alternative methods of hemodynamic assessment such as coronary flow reserve (CFR) are subject to changes in hemodynamic conditions and fluctuations in microvascular resistance.[22] Instantaneous wave-free ratio (iFR) is another alternative in which the distal/reference pressure ratio is measured during a wave-free period during diastole. CFR and iFR lack large well-validated studies showing that their use results in a clear clinical benefit.

FFR uses standard interventional techniques and can be performed safely at the time of angiography.[23,24] A standard guide catheter is engaged in the artery of interest, followed by advancement of a pressure wire to the tip of the guide catheter.[23] Antithrombins and intracoronary nitroglycerin are administered.[24] The wire pressure is then equalized to the guide catheter pressure, and the wire passed distal to the lesion being interrogated. Hyperemia is induced, typically with intravenous adenosine (140 μg/kg/min), or through the use of intracoronary adenosine, intravenous regadenoson, or rarely dopamine, papaverine, and nitroprusside.[23,24] An FFR of less than 0.80 is considered to represent hemodynamic significance. **Fig. 1** shows an example of a positive FFR. A useful feature of the commercially available pressure wires is that they can be used interchangeably as interventional wires.[24] Thus if a positive FFR is obtained, coronary dilation catheters and coronary stent systems can be passed over the FFR wire. Following the procedure a postintervention FFR can be calculated, which has been shown to predict outcomes.

When assessing lesions of obviously high severity (>80%) or lesions that are clearly nonobstructive (<40%) visual assessment is adequate.[19] FFR shows its maximal utility for intermediate stenoses, which account for nearly half of the lesions seen during arteriography.[18,25] **Fig. 2** provides an example of lesions categorized by severity and FFR to illustrate that angiographic significance is not a reliable predictor of physiologic significance.[26] When an intermediate lesion is present and the translesional FFR is normal, then intervention can be deferred. The ability to intervene based on FFR data is based primarily on 3 pivotal studies: DEFER (Fractional Flow Reserve to Determine the Appropriateness of Angioplasty in Moderate Coronary Stenosis), FAME (Fractional Flow Reserve Versus Angiography for Guiding Percutaneous Coronary Intervention), and FAME II (Fractional Flow Reserve Versus Angiography for Multivessel Evaluation 2).

The DEFER study was a multicenter prospective randomized trial of 325 patients referred for single-vessel PCI based on a visual assessment of a greater than 50% de novo stenosis in a native