Is FFR of the Left Main Coronary Artery Stenosis Reliable?

Understanding the technique and limitations of its applications.

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Fractional flow reserve (FFR), the ratio of translesional pressures across a stenosis, measured when microvascular resistance is fixed and minimal, has a strong association with ischemia. When used for guiding percutaneous coronary intervention compared to angiography alone, FFR produces better clinical and economic outcomes.[1,2] However, like any diagnostic test, the technique and limitations of its applications should be understood for best results. FFR may be associated with predictable false-positive and false-negative results (Table 1). Because the decisions regarding revascularization of the left main (LM) coronary stenosis are critical, accuracy of FFR is especially important (Figure 1). This brief review will assist in understanding when LM FFR requires more information for optimal use.

Numerous studies support the use of FFR to assess LM coronary stenoses.[3-9] In the largest of these studies, Hamilos et al demonstrated the long-term outcomes of FFR-guided decisions in 213 patients with an angiographically equivocal narrowing of the LM coronary artery.[9] The 5-year survival and event-free survival rates were similar, 89.8% and 74.2%, respectively, in the nonsurgical medically treated group (FFR ≥ 0.80) and 85.4% and 82.8%, respectively, in the surgical group (FFR < 0.80) (P = .48 and P = .50, respectively). Of note, these patients had both simple (isolated LM stenoses) and complex (LM with other multivessel) coronary artery disease. There were no significant differences in outcomes when separated by degree of disease. The reliability of FFR for simple lesions is rarely an issue, but an understanding of FFR for complex LM stenoses with additional lesions in the left anterior descending (LAD) and/or circumflex artery (Cx) branches requires the operator to have a more in-depth appreciation of the physiology as applied in this important anatomic subset.

A simple, isolated LM stenosis is easily assessed by FFR in the routine fashion. One caveat to increase reliability is that ostial FFR assessment requires that the guide catheter be removed from the ostium while infusing intravenous adenosine to avoid the artifact of guide catheter pressure damping. A distal LM stenosis involving the bifurcation of the LAD and Cx can be assessed with two FFR measurements, one in the LAD and another with the pressure wire in the Cx. However, interpreting the LM FFR in the presence of significant downstream branch lesions, such as an LAD stenosis, is more complicated because the LM and LAD lesions act like serial lesions, and the true flow across the LM is potentially reduced by a severe downstream stenosis, artifactually elevating the LM FFR when measured in the unobstructed vessel.

For an accurate FFR, maximal hyperemia must be achieved across the LM stenosis. Flow through the LM artery is the sum of both the LAD and left Cx (LCx) branch flow, the magnitude of flow being proportional to the size of each artery's viable myocardial bed. When LM FFR is measured in the unobstructed Cx artery, the reliability of this measurement will depend on whether the LAD stenosis is severe enough to impair flow. The lower LM flow would produce an erroneously elevated FFR because true maximal hyperemia would not be achieved.

In practice, the LM FFR in the setting of LM and LAD disease is assessed by placing the pressure wire sen-

TABLE 1. CAUSES OF FALSE-NEGATIVE AND FALSE-POSITIVE FFR

False-Negative FFR	False-Positive FFR
• Guide catheter pressure damping (ostial narrowing, side hole catheters) • No hyperemia: wrong drug, concentration, infusion failure • STEMI, culprit vessel • LM FFR, complex CAD with $FFR_{epicardial}$ < 0.6 • Serial lesion FFR of individual lesion (use gradient only) • Pressure signal drift, technical errors	• Technical errors: incorrect zero, failure to normalize • Pressure signal drift • Loose pressure connections, air bubbles, transducer connector errors

Abbreviations: CAD, coronary artery disease; FFR, fractional flow reserve; LM, left main; STEMI, ST-segment elevation myocardial infarction.

sor distal to the LAD lesion, administering adenosine hyperemia (either intravenously or intracoronary), and calculating the FFR across both lesions, which is called $FFR_{epicardial}$. If $FFR_{epicardial}$ is > 0.80, neither lesion is physiologically significant and no further intervention is needed. However, if the $FFR_{epicardial}$ is ≤ 0.80, the operator can measure FFR in the Cx. An apparent LM FFR (FFR_{app}) in the Cx, of > 0.80 would seem to indicate that the LAD, but not the LM, is hemodynamically significant. However, this is not always correct. A disadvantage of this assumption is that after the LAD lesion is stented, LM flow increases and the FFR_{app} may now become significant, mandating further revascularization. If unprotected LM stenting is not planned, performing percutaneous coronary intervention of a downstream LAD lesion, which would lead to a significant LM FFR, may not be the best option.

Fearon et al have brought clarity to this conundrum by identifying the degree of severity of downstream lesions, which makes the FFR_{app} unreliable.[10] To validate this concept, a model of a complex LM and LAD stenosis was created in patients in the catheterization lab after LAD stenting. An intermediate LM stenosis was created by positioning a partially deflated balloon catheter in the normal LM and another balloon catheter in the newly stented LAD. Using two pressure wires, the effect of increasing the severity of the LAD lesion and its impact on LM FFR measured in the unobstructed Cx was demonstrated. The true LM FFR (FFR_{true}), measured in the non-diseased (ie, Cx) vessel, was compared with the FFR_{app}, measured in the presence of an increasingly severe LAD created during LAD balloon inflation. The FFR_{true} was statistically but clinically insignificantly lower than FFR_{app} (0.81 ± 0.08 vs 0.83 ± 0.08; P < .001), a difference that correlated with the severity of the downstream disease (r = 0.35; P < .001). In all cases in which FFR_{app} was > 0.85, the FFR_{true} was > 0.80. The important observation of this study was that the FFR_{true} was significantly lower than FFR_{app} only when downstream stenoses in the LAD (or LCx) were very severe with $FFR_{epicardial}$ < 0.60. In these situations, an intravascular ultrasound assessment of the

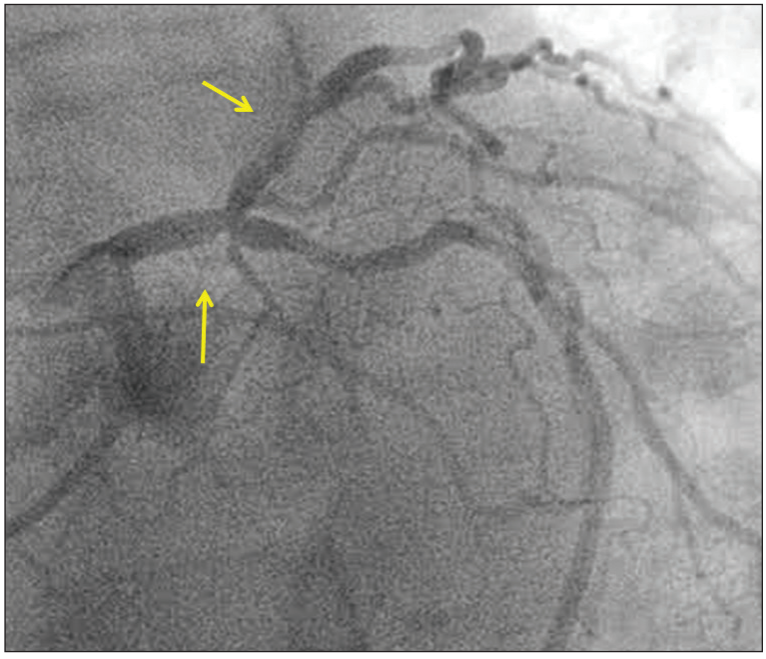

Figure 1. A cineangiograph frame displaying complex LM and LAD coronary artery disease.

LM with a threshold minimal luminal area of < 6.0 mm^2 is recommended.

The reliability of the LM FFR will always depend on operator technique, accurate hemodynamic signal acquisition, and adequate maximal hyperemia. The complex LM FFR can be used in nearly all cases, as $FFR_{epicardial}$ > 0.60 is a very common result. It should be reassuring to the practitioner that the data from in vitro, animal, and human studies of LM stenosis demonstrate that in most cases, downstream disease does not have a clinically significant impact on the assessment of FFR across an intermediate LM stenosis.[9-11] ■

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