A man in his late 70s who had undergone prior coronary artery bypass graft surgery presented with unstable angina. Angiography demonstrated widely patent grafts to the left anterior descending and right coronary arteries and a totally occluded graft to the obtuse marginal branch, which was known from a prior cardiac catheterization. Disease in the obtuse marginal branch appeared stable, but there was worsening of disease in the ramus branch, where 2 serial lesions were identified. Intravenous adenosine was administered at 140 μg/kg/min to induce maximal hyperemia, and fractional flow reserve (FFR) was measured in the ramus, revealing a nadir value of 0.43 across both lesions (Figure 1). A slow, pull-back maneuver across the distal lesion demonstrated that the proximal lesion had an FFR value of 0.82.

**WHAT WOULD YOU DO NEXT?**

A. The proximal lesion is ischemic while the distal lesion is nonischemic. Only the proximal lesion should have a stent placed.

B. The distal lesion is ischemic while the proximal lesion is nonischemic. Only the distal lesion should have a stent placed.

C. Both lesions are ischemic and should have a stent placed.

D. FFR with adenosine should be remeasured after placing a stent in the distal lesion to better assess the proximal lesion.
Diagnosis
Uncertain whether the proximal lesion is ischemic

What to Do Next
D. FFR with adenosine should be remeasured after placing a stent in the distal lesion to better assess the proximal lesion.

Discussion
Coronary angiography provides limited information regarding the functional significance of a coronary stenosis, and alone, can be unreliable for guiding revascularization, with significant interobserver variability. The FFR is an accurate and lesion-specific physiological test that indicates whether a particular coronary stenosis or segment can be held responsible for ischemia. An intracoronary pressure wire is advanced beyond the lesion or lesions of interest and maximal vasodilatation and hyperemia is achieved with either intravenous or intracoronary administration of vasodilators such as adenosine. The FFR is defined as the ratio of coronary pressure distal to a coronary artery stenosis and aortic pressure under conditions of maximal hyperemia (range, 0.7-1; normal value, 0.94-1).2

An FFR value less than 0.75 is considered flow limiting and is invariably associated with ischemia; therefore, a lesion with such an FFR value is appropriate for revascularization (sensitivity, 88%; specificity, 100%).2 In contrast, FFR values greater than 0.80 exclude ischemia in more than 90% of patients, with a low cardiac event rate (<1% per year) with medical therapy alone.2 Although FFR values between 0.75 and 0.80 are sometimes considered “gray zones,” more recent outcomes trials have used 0.80 as the ischemic threshold for revascularization and 0.80 is the routinely used cutoff value in clinical practice as well.2,4-5 False-negative FFRs can occur in the setting of inadequate hyperemia, certain technical issues (eg, deep-seated guide catheter, small coronary ostium, or electrical drift), and patient-related characteristics (eg, acute STEMI, severe left ventricular hypertrophy, or elevated left-sided filling pressures).

FFR has clinical utility also in patients with multiple lesions in the same coronary artery, as illustrated in this patient. Once hyperemia is induced, a pull-back maneuver is performed across all lesions to determine which lesion has the largest pressure gradient drop. To accurately assess the functional significance of the other lesion, it is imperative to repeat the FFR measurement under maximal hyperemia again once a stent has been placed in the primary lesion, because treating the primary lesion increases flow through the vessel overall, including through the other lesion. The lesion-specific distal pressure may therefore be lower and may affect its functional significance.6 Relying solely on a pull-back maneuver in this patient (as is sometimes done in clinical practice) would have erroneously implied that only the distal lesion, not the proximal lesion, needed to be treated. However, in this patient, a change in the FFR of more than 0.1 across the proximal lesion suggested that the lesion would likely be significant, despite the hyperemic distal pressure to aortic pressure ratio between the 2 lesions being 0.82. Also, for tandem lesions, the proximal (or distal) lesion may need to be treated if the inflow (or outflow) appears compromised, independent of hemodynamics, to minimize the risk of stent thrombosis.

In this patient, a 2.5 x 23-mm everolimus-eluting stent was initially placed in the distal lesion since it was the more hemodynamically significant lesion. FFR with adenosine was repeated after this procedure for the proximal lesion, which revealed a nadir value of 0.78. Accordingly, the proximal lesion was treated with an overlapping 2.75 x 18-mm everolimus-eluting stent (Figure 2). After placing a stent in both lesions, the repeated FFR value with adenosine was 0.93. An ideal FFR after placement of a stent should be greater than 0.95,7 but in this patient this FFR likely represents residual proximal disease that can be medically treated.

Figure 2. Ramus intermedius after final angiography.

ARTICLE INFORMATION
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REFERENCES