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EDITORIAL COMMENT

The Complexity Involved in Assessment of Left Main Coronary Artery Disease*

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About the size of the average cigarette butt, the left main coronary artery is a relatively small vessel, yet it is arguably 1 of the most valuable sections of real estate within the body. Since Herrick's description 100 years ago, we are well aware of the lethality of left main disease (1). Stenosis of the left main coronary is 1 of the few, specific coronary lesions in which revascularization reduces the likelihood of death compared with medical therapy (2–4). Thus, seeking out and revascularizing left main disease has become established as 1 of the tenets of modern cardiology.

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Identification of significant left main disease is not always easy. Angiography routinely underestimates and overestimates the degree of left main narrowing. This is particularly true for ostial, distal bifurcation, and diffusely diseased segments or in the presence of dense calcium or eccentric disease (Fig. 1). Wary of missing a potentially lethal condition, clinicians tend to "overcall" lesions and refer patients for bypass surgery who might not actually have significant stenosis. When this happens, grafts may occlude or become atretic (5). Thus, there are consequences to both missing the diagnosis as well as overestimating disease severity. It is really important to get this right.

Adjunctive methods, including fractional flow reserve (FFR) and intravascular ultrasound (IVUS), have been employed in the assessment of ambiguous left main lesions (6–12). For IVUS, minimal luminal area (MLA) is measured; the cutoff value defining significance is not entirely clear. The lower range for a normal left main stem is 7.5 mm^2 (6). An MLA <5.9 mm^2 has been shown to correlate with an ischemic FFR in 1 study (7), but in another study, an MLA <4.8 mm^2 best predicted FFR <0.80 (8). It appears safe to defer revascularization if the MLA by IVUS exceeds 6.0 mm^2 or if FFR is greater than 0.80 (7–12).

There are important considerations when performing FFR of an ambiguous left main lesion. Ostial disease may dampen the catheter pressure and falsely raise FFR. Therefore, it is recommended that the operator disengage the guide catheter after the pressure wire is positioned distal to the stenosis and use intravenous rather than intracoronary adenosine (13). In addition, the presence of disease in other vessels may affect the measurement of FFR. This is especially important because isolated left main disease is actually quite rare. In an unselected series of patients undergoing coronary angiography, isolated left main disease was present in only 9%; 17% had left main plus 1-vessel disease, 35% had left main plus 2-vessel disease, and 38% had left main plus 3-vessel disease (14). In the SYNTAX (Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery) trial, isolated left main disease was observed in only 6.1% of patients (15). Thus, we expect to find significant coronary disease in other vessels in more than 90% of patients with left main disease. This creates a challenge because if there is disease in both the left main and the left anterior descending artery (LAD), the operator cannot simply position the pressure sensor across just the left main lesion into the LAD and measure FFR. The LAD stenosis may hamper maximal hyperemia and falsely raise the FFR (13). Complex methodology to measure the FFR of each lesion in series has been described but is not practical for clinical use (16,17). Therefore, if there is disease in the left circumflex artery (LCX) or LAD, FFR of the left main is performed by positioning the transducer across the left main lesion into the uninvolved artery. But is this methodology sound? It is plausible that a stenosis in either vessel might still impair total flow across the left main. How does a proximal stenosis in the LCX or LAD influence the accuracy of FFR measurement when the pressure transducer is placed in the uninvolved artery?

This question was elegantly addressed by Daniels et al. (18) in this issue of *JACC: Cardiovascular Interventions*. Using an in vitro, experimental model of the coronary circulation, they first determined the "true FFR" of the left main segment in the absence of a downstream stenosis and then remeasured FFR ("FFR apparent") in the presence of variable degrees of stenosis in the LAD or the LCX with the sensor in the uninvolved artery. They found that, in the presence of mild to moderate disease in the LAD or LCX, the FFR across the left main did not differ from the true FFR. However, in the presence of significant disease in the LAD or LCX (which they arbitrarily defined as a composite FFR <0.65), FFR across the left main was higher than the true FFR. This was particularly evident for lesions in the LAD compared with disease in the LCX.

How should this study affect practice? Although this work was not performed or subsequently validated in hu-

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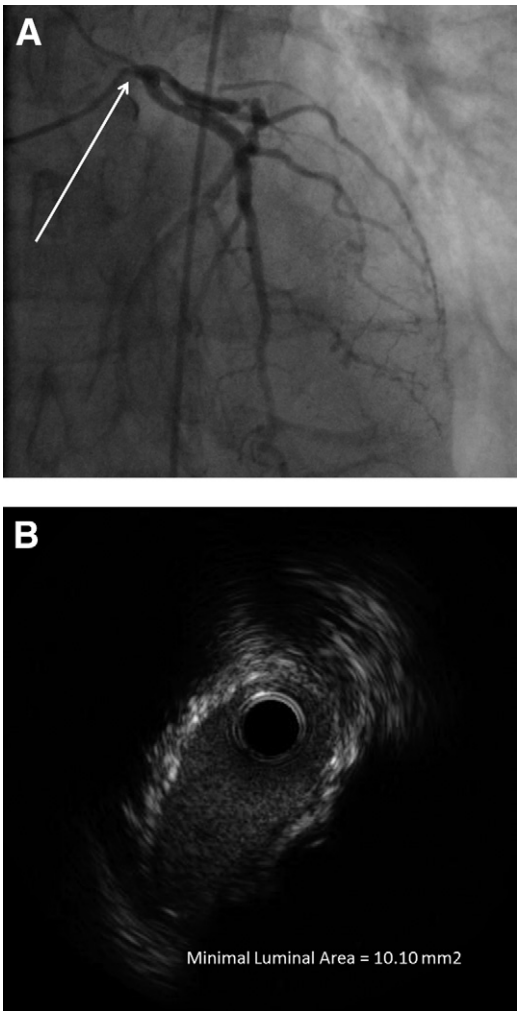

Figure 1. Example of an Ambiguous Left Main Lesion Involving the Ostium

In this case, the ostium of the left main appeared normal in some views but narrowed significantly in the right anterior oblique cranial view **(A).** Intravascular ultrasound noted an eccentric and elliptical lumen with a minimal luminal area of 10.10 mm^2 **(B).**

mans, the clinical implications are clear. If there is mild or moderate disease in the LAD or LCX, then FFR of an ambiguous left main can be performed with the wire positioned in the uninvolved artery. If there is concern about the severity of disease in the LAD or LCX, a composite FFR can be performed with the wire placed across both lesions; if this composite FFR is >0.65, then FFR of the left main with the wire repositioned into the uninvolved artery will be reliable. However, if the composite FFR is <0.65, then the left main should be assessed by IVUS using the cutoff value for MLA of 6.0 mm^2.

Obviously, verification of these results in humans with left main disease will be interesting and important but will prove difficult to accomplish. Unlike the experimental model used by Daniels et al. (18), the variable location, extent, and severity of coexisting disease cannot be controlled. It is possible that a small cohort in whom FFR of the left main is performed before and after treatment of a stenosis in the LAD or LCX can be studied to provide some validation of these findings, but these patients will be difficult to find and enroll.

This study raises additional questions. How might FFR of the left main be influenced by occlusive disease in a large right coronary? One might theorize that collaterals emanating from the left will, in effect, increase the size of the vascular bed of the left main and result in greater flow than normal, potentially falsely lowering the FFR and perhaps misleading the operator to conclude that the left main is significant when it may not be in the absence of an occluded right coronary. Similarly, this study did not take into account collateral dependence to the LCX or LAD in the event of occlusive disease in these vessels nor did it address the impact of disease in large branches of these vessels.

It is clearly important for clinicians to understand the message provided by this study and to recognize the complexity involved in assessment of a left main lesion. As we increase our understanding of these nuances, we will be more likely to "get it right" and make the correct decisions for patients with disease in this small but crucial segment of the coronary circulation.

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Key Words: fractional flow reserve ■ intravascular ultrasound ■ left main disease.