Introduction
Significant stenosis of the left main coronary artery (LMCA), generally defined as >50% reduction in vessel diameter, is found in approximately 4% of patients undergoing diagnostic coronary angiography. A significant narrowing of the LMCA puts a patient at high risk, as the stenosis jeopardises a large amount of the myocardial mass. According to current guidelines, any stenosis of the LMCA >50% should be treated surgically, regardless of the presence of symptoms or objective signs of ischaemia. However, this recommendation is based on studies conducted several decades ago and does not take into account recent changes in medical practice and angiographic quality. The question of how percutaneous coronary intervention (PCI) of the LMCA compares with surgical revascularisation for LMCA disease is currently being evaluated in large randomised trials. But the question of how to define a ‘truly’ significant LMCA lesion is a major concern that has not received the same attention.

Limitations in the Methods Used to Diagnose Left Main Coronary Artery Disease
Myocardial Perfusion Imaging
Non-invasive coronary testing has not been performed in the vast majority of patients undergoing PCI. Non-invasive coronary testing, particularly myocardial perfusion imaging (MPI), has proved to be highly sensitive and specific in detecting and localising ischaemia in patients with single-vessel disease and normal left ventricular function. However, it should be noted that the use of MPI in diagnosing LMCA stenosis is less well established due to the balanced reduction in perfusion during stress that is responsible for false-negative findings. In addition, since LMCA stenoses are rarely isolated, MPI is of little help in guiding revascularisation due to its limited spatial accuracy.

Angiography
Revascularisation decisions in everyday clinical practice are often made on the basis of angiographic estimation using the gold standard of a >50% reduction in vessel diameter. While it is commonplace to state that angiography is a poor predictor of the actual severity of a stenosis, this is particularly true in the case of LMCA stenosis. In the Collaborative Study in Coronary Artery Surgery (CASS), still considered a landmark study outlining the preferred treatment strategy for patients with LMCA disease, there was large intra- and inter-observer variability in the evaluation of LMCA stenoses severity. In a recently published study, two independent observers assessed LMCA disease in 213 patients with angiographically equivocal stenoses using both visual and quantitative coronary angiography (QCA). Fractional flow reserve (FFR) was measured in all patients to assess the actual severity of the LMCA lesion(s). Angiographic assessment of the lesions, either by QCA or by visual estimation, failed to correctly identify the significance of the stenosis in 29% of patients. Lesion severity was underestimated in most of these patients (23%). It is concerning that even in recent studies (SYNTAX, PRCOMBAT), patient management decisions were based only on angiography. As a result, it is likely that many patients who would have benefited from revascularisation were denied treatment on the basis of a stenosis that was considered angiographically non-significant or, conversely, other patients received surgical treatment on the basis of a stenosis that was falsely considered significant.

There are several reasons for the discrepancy between angiographic and haemodynamic assessment of LMCA lesions. These include:

• Catheter overlap with the LMCA, resulting in contrast medium spillover and incomplete mixing of blood and contrast medium in the proximal part of the LMCA.
• Short LMCA with diffuse distribution of atherosclerosis so that a normal comparator segment is lacking.
• The myocardial mass dependent on the LMCA is large and, thus, the amount of blood that flows through it is great.

Intravascular Ultrasound
Intravascular ultrasound (IVUS), an invasive diagnostic modality that provides more anatomically detailed images than angiography, is often advocated as a tool to evaluate LMCA stenoses. Since...
the physiological severity of a stenosis depends not only on the percent stenosis but also on the mass of myocardium perfused by that given segment and on the collateral circulation, an IVUS theoretically shares the same limitations as angiography in the evaluation of a LMCA stenosis. For this reason, a given cross-sectional area (CSA) will have a completely different physiological meaning in the LMCA than in a small diagonal branch. Consequently, the IVUS cut-off values for indicating significant LMCA stenosis vary from 4.8 to 8 mm² (CSA), and can often be confusing.2–20 Nevertheless, IVUS provides a more accurate and detailed anatomical estimation of lesion severity than angiography, and can be a helpful tool in evaluating LMCA stenosis in cases when PCI is under consideration.

Advantages of Fractional Flow Reserve in Left Main Coronary Artery Lesion Assessment

FFR is a validated, lesion-specific index that accurately reflects the functional significance of a coronary stenosis. FFR provides a precise estimation of the coronary blood supply for a specific myocardial territory, independent of haemodynamic parameters, such as heart rate, blood pressure or changes in myocardial contractility.21 Recent, large, randomised studies have consistently shown that FFR-guided revascularisation strategy using a cut-off value of 0.80 is associated with reduced cost and excellent clinical outcomes.21–23 These advantages are all applicable to the functional assessment of LMCA disease.24 A recent study has demonstrated that an FFR-guided revascularisation strategy can be safely applied to patients with LMCA stenosis. The patients had an equivocal LMCA stenosis on angiography, and coronary artery bypass grafting (CABG) was performed only on patients with an FFR <0.80 across the LMCA stenosis.25 Mortality was surprisingly low for patients who were deferred CABG, based on FFR measurements.

Fractional Flow Reserve Tips, Tricks and Limitations

Although measuring FFR of the LMCA is not technically demanding, the physician should keep some tips and tricks in mind to help ensure accurate measurements:

- A pullback curve should always be obtained in the case of lesions in left anterior descending (LAD) or left circumflex artery (LCx) in order to allow complete functional mapping of the epicardial coronary vasculature.
- The guiding catheter should be disengaged from the ostium when performing measurements.

The main caveat when measuring FFR in the LMCA is that lesions are rarely isolated, making evaluation more complicated. Coexisting stenoses in the LAD or in the LCx will tend to increase the FFR measured across an LMCA stenosis. The influence of downstream lesions on the FFR measurement in the LMCA depends on the severity of those lesions and on the size of the vascular territory supplied by the vessels. A recent experimental study showed that less-severe downstream lesions have only a minor impact on the FFR of the LMCA.26 In general, this problem can be partially solved by using the pullback curve as previously mentioned.

Conclusion

FFR helps ensure ‘correct’ decisions are made in equivocal LMCA lesions where anatomical information provides insufficient guidance, and there are limitations in the value of invasive tests. Ambiguous LMCA lesions can effectively be evaluated using FFR, providing valuable insight into optimal therapeutic decisions. Proper identification of patients who are most likely to benefit from revascularisation is indispensable since unnecessary interventions, or conversely revascularisations that are denied when actually needed, often lead to unfavourable clinical outcomes.

Main Points

- Angiography is a poor predictor of the actual severity of stenosis and usually underestimates the severity of LMCA lesions.
- LMCA lesions are rarely isolated, making evaluation more challenging.
- Coexisting stenoses in the LAD or in the LCx tend to increase the FFR measured across an LMCA stenosis.
- FFR can play a significant role in evaluating ambiguous LMCA lesions and impact physician decision-making in this challenging patient population.