Multivessel Percutaneous Coronary Intervention Guided by Fractional Flow Reserve

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Introduction

Recent guidelines on myocardial revascularisation recommend revascularisation for ischaemia-related stenoses and medical therapy for non-ischaemic stenoses. However, non-invasive stress testing will not always provide adequate or complete information about the functional importance of coronary artery narrowings, particularly in patients with multivessel disease. Moreover, in such patients, one cannot rely on the angiogram to identify ischaemia-producing lesions when assessing stenoses between 50 and 90%.

By using fractional flow reserve (FFR) in patients with multivessel disease, the interventional cardiologist is able to accurately distinguish between coronary stenoses that induce myocardial ischaemia and stenoses that do not induce myocardial ischaemia. Consequently, it is possible to treat selectively the functionally significant stenoses (those responsible for reversible ischaemia, also called 'ischaemic stenoses') by stent placement and leave the non-ischaemic stenoses for medical treatment in such patients.

Fractional Flow Reserve

The index FFR is considered the gold standard for the detection of myocardial ischaemia, related to a particular stenosis. FFR indicates the physiological significance of a coronary stenosis and is defined as maximal blood flow in a stenotic artery as a ratio to normal maximal flow. It can be easily measured during coronary angiography by the ratio of distal coronary pressure (Pd) measured with a coronary pressure guidewire to aortic pressure (Pa) measured simultaneously with the guiding catheter (see Figure 1).

For measuring FFR, maximum hyperaemia is of paramount importance, which can easily be obtained by application of a hyperaemic agent. Particularly in multivessel disease assessment, the continuous infusion of adenosine through a central vein (femoral vein, intravenous [IV] adenosine* at a rate of 140 ug/kg/min) is recommended. Continuous hyperaemia enables the operator to benefit from the diagnostic features of FFR. A FFR value of 0.80 discriminates coronary stenoses responsible for ischaemia with an accuracy of more than 90%.

Fractional Flow Reserve in Multivessel Disease

The Fractional Flow Reserve versus Angiography in Multivessel Evaluation (FAME) study compared angiography-guided percutaneous coronary intervention (PCI) with FFR-guided PCI in patients with multivessel coronary artery disease. In both treatment
arms, coronary intervention was performed using drug-eluting stents. At 20 centres in Europe and the US, 1,005 patients were randomised. Patients with very complex multivessel coronary artery disease were excluded from the study. The primary outcome of the trial was a significant decrease in the composite endpoint of death, myocardial infarction or the need for repeat revascularisation at one-year with FFR guidance versus angiography-guidance (13.2 versus 18.3%, p=0.02) (see Figure 2).

The advantage of a FFR-guided strategy was maintained at two years in the FAME study. The combined rate of death and myocardial infarction, as well as the rate of myocardial infarction alone, increased in favour of the FFR-guided strategy. Moreover, while using less stents per patient, the FFR-guided approach resulted in equal relief of myocardial ischaemia and subsequent angina symptoms compared with the common angiography-guided approach. In addition, the use of FFR in the FAME study did not prolong procedure time, reduced the amount of contrast agent used and saved valuable healthcare resources.

**Specific Features of Fractional Flow Reserve**

Besides a very high specificity and sensitivity for the detection of inducible myocardial ischaemia related to a coronary artery stenosis, FFR has some additional advantageous and specific features that make it an easy and convenient practical index to be used in the catheterisation laboratory, particularly for the assessment of multivessel disease.

With respect to the interrogation of patients with multivessel disease by FFR, the fact that there is no need for a normal control artery to compare with is advantageous compared to non-invasive functional tests, like nuclear perfusion imaging (see Figure 3).

Furthermore, FFR has an unsurpassed high spatial resolution. The position of the pressure sensor on the sensor-tipped guidewire can be accurately located by fluoroscopy, and by changing its position along a coronary artery under continuous hyperaemia, the pressure changes can be followed in real-time. This feature allows an operator to distinguish between diffuse atherosclerosis and focal stenoses, even within a single coronary artery segment. Other functional tests, in contrast to FFR, only reach an accuracy per patient (exercise stress-testing with electrocardiogram [ECG]) or per coronary artery (nuclear perfusion imaging). The same feature can also be of help in the assessment of arteries with serial, ostial or bifurcation stenoses.

Serial stenoses are frequently encountered in multivessel disease cases. When several stenoses are present in the same artery, FFR remains a valid means of assessing the effect of the stenoses together. Yet, it is important to realise in such cases that each of several stenoses will influence hyperaemic blood flow and therefore FFR across the other one. The influence of the distal lesion on the proximal is more important than the reverse. Theoretically, FFR can be calculated for each stenosis individually. However, this is neither practical nor easy to perform and therefore of little use in the catheterisation laboratory. Practically, as for diffuse disease, a pullback manoeuvre under maximal hyperaemia is the best way to appreciate the exact location and physiological significance of sequential stenoses, and to guide the interventional procedure step-by-step.

**Conclusions**

FFR is considered the gold standard for the detection of myocardial ischaemia. The advantageous features of this index, like its high spatial resolution and applicability in all kinds of lesion subsets, make FFR the ideal tool for the guidance of multivessel PCI.

As proven by the FAME trial, PCI guided by FFR in patients with multivessel disease is one of those rare situations in medicine in which a new technology not only improves outcomes, but also saves resources.

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* Prior to using hyperemic agents, please review the instructions for use for a complete listing of indications, contraindications, warnings, precautions, potential adverse events and directions.