Fractional flow reserve in acute coronary syndromes

Bernard De Bruyne* and Julien Adjedj

Cardiovascular Center Aalst, OLV Ziekenhuis, Aalst, Belgium

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This editorial refers to ‘Fractional flow reserve vs. angiography in guiding management to optimize outcomes in non-ST-segment elevation myocardial infarction: the British Heart Foundation FAMOUS–NSTEMI randomized trial’†, by J. Layland et al. on page 100

Little doubt exists about the outcome benefit of an invasive strategy in patients with an acute coronary syndrome (ACS). Yet, once the revascularization is performed, the treatment strategy of patients admitted with an ACS is not always as straightforward in daily clinical practice as indicated in guidelines. The reasons for this are at least three-fold.

First, a sizable proportion of patients admitted for an ACS have multiple stenoses on the angiogram. Based on the clinical history, the electrocardiogram (ECG), and the angiogram, it is (usually) easy to identify the stenosis responsible for the acute clinical syndrome, but not to decide whether the non-culprit stenoses warrant treatment. Secondly, incomplete revascularization—whatever its definition—is associated with poor outcomes. While the timing of this additional revascularization procedure remains debated, leaving stenoses that induce ischaemia untreated is detrimental. Thirdly, assessing residual ischaemia after an ACS is less reliable than what is usually reported in patients with stable coronary artery disease. Many patients admitted with an ACS have several factors that make it difficult to perform or to interpret the results of non-invasive testing. These factors are not accounted for in most studies, reviews, and meta-analyses on accuracy of non-invasive tests. These factors are not accounted for in most studies, reviews, and meta-analyses on accuracy of non-invasive testing. In addition, the latter are based on the presence of a 50% diameter stenosis at angiography—a battered gold standard. Therefore, in patients with a recently revascularized myocardial infarction, non-invasive testing is much less applicable and less accurate than commonly reported, for detection, localization, and quantification of residual myocardial ischaemia.

Fractional flow reserve (FFR) is an invasive index that detects, localizes, and quantifies the potential of a stenosis to induce ischaemia. FFR is defined as the ratio of maximal myocardial flow in the presence of an epicardial stenosis, to maximal flow in its absence. In contrast to general belief, this definition does not assume the normalcy of microvascular function. Whether this function is normal or abnormal does not matter for the accuracy of the FFR measurements. It is even likely that most patients undergoing a coronary angiography have some degree of microvascular dysfunction. FFR tells the operator to what extent it will be possible to improve myocardial perfusion by re-establishing the conductance of a given epicardial segment in a given patient (who may or may not have microvascular dysfunction). What might constitute an issue for FFR measurements in ACS is not the microvascular dysfunction during the acute phase, but the transient changes in microvascular function that are thought to occur during the first hours, days, or weeks after the acute event. The magnitude of these changes depends on several factors, among which are the duration and the intensity of ischaemia, embolization of the microvasculature downstream of the occlusion, changes in filling pressures and in wall stress, the recovery of contractile function, and changes in systemic or local vasoconstrictors. These changes are expected to be more pronounced in ST-segment elevation myocardial infarctions (STEMIs) than in non-STEMIs (NSTEMIs). Whether or not, and to what extent they occur in the contralateral, non-infarcted, territory remains uncertain. The clinical impact of these changes on FFR measurements in non-culprit stenosis in ACS is, however, minimal.

Earlier data comparing FFR measurements in non-culprit lesions performed at the time of primary percutaneous coronary intervention (PCI) and repeated 6 weeks later showed no significant difference in FFR values, except in patients with very high left ventricular filling pressures during primary PCI. Stated another way, measuring FFR in the non-culprit lesion at the acute phase or 6 weeks later would have led to the same clinical decision about the need for revascularization. Why not obtain this information while the patient is on the table anyway?

Layland et al. now take us one step further in the routine use of FFR in patients with an ACS. In six UK centres, 350 NSTEMI patients referred for invasive management were randomly assigned to receive either an angiography-guided treatment strategy or an FFR-guided strategy (actually an angiography- and FFR-guided strategy). The primary outcome was the difference in the proportion of patients...
allocated to medical management alone. Clinical outcome data were only a secondary endpoint, as was the feasibility of routine FFR measurements. Since the trial was not powered to test a difference in clinical outcome, the latter should be interpreted with this in mind. In addition, the trial included patients on average 3 days after the index episode, suggesting a majority of stabilized unstable syndromes. Nevertheless, the main message is clear: ‘FFR guidance modifies the decision in \(~\approx\)20% of cases’. At first glance, this message conveys a feeling of déjà vu. In the FAME trial, 32% of patients presented with unstable angina or an NSTEMI.\(^\text{14}\) Much like the entire patient cohort, the patients with an ACS also benefit from FFR guidance.\(^\text{15}\)

References

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**References**


