Angiogram-derived Physiology: Will it Change the Game or Miss the Boat?

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In this issue, Ghobrial *et al* describe the impact that one coronary angiogram-derived physiology system, Virtual FFR (vFFR), has on diagnosis and decision-making of cardiologists when assessing patients undergoing diagnostic angiography for either chronic coronary syndrome or non-ST elevation MI, when compared to angiography alone [1]. In 320 patients, the availability of vFFR data led to a significant reduction in the number of vessels considered to have important disease and changed the management in 22% of cases when compared to their classification using angiography alone. The authors logically suggest that the data, taken in the context of promising clinical results from this and other angiogram-derived physiology systems, indicate that vFFR should be used more routinely in clinical practice to improve the precision of patient diagnosis and management.

The paper indeed highlights the considerable clinical potential of angiogram-derived physiology systems. Reassuringly, the degree of reclassification of vessels with significant disease and overall change in management reported in VIRTU4 are remarkably similar to the results of RIPCORD [2], upon which this methodology was based, and several other studies that employed intracoronary pressure wire assessment of all coronary arteries of a size consistent with revascularisation and compared outcomes with angiographic assessment alone [3]. The vFFR results certainly therefore raise the possibility that such profound alterations in diagnosis and management could be harnessed in routine clinical practice to aid more accurate treatment for individual patients undergoing coronary angiography. The results of FAVOR3 and other studies using a variety of angiogram-derived physiology systems lend weight to this concept, with more on the way [reviewed in reference 4]. Why is this such an attractive construct for interventional cardiologists and their patients? In patients who are undergoing invasive coronary angiography (ICA) for clinical reasons, such systems could, in the future, offer a simultaneous and comprehensive assessment not just of angiographic appearance, but also of flow limitation in each vessel of interest. This could overcome the low uptake of pressure wire-based assessment in interventional cardiology despite the considerable evidence base favouring it over angiography alone. For example, in patients committed to PCI, the advantage of a pressure wire- versus angiogram-guided strategy to seen in FAME and FAME2 represent a Holy Grail in interventional practice, but could be routinely achieved using angiogram-derived physiology. Furthermore, given the promise of post-PCI optimisation using invasive pressure wire seen in DEFINE PCI , if such a concept can be further validated [5], this physiological optimisation could be achieved wire free if angiogram-derived physiology were routinely available. In achieving such lofty aims, angiogram-derived physiology systems could render the intracoronary pressure wire obsolete for many of its current indications.

Before we herald angiogram-derived physiology as a potential game changer in the routine care pathway, however, it is appropriate to step back and consider the wider context. Firstly, the number of patients who are committed to undergo ICA is, in general, clinically inappropriate. As is typical of much larger studies, in VIRTU4, 110 of the 197 (56%) "all comers" patents who were deemed unsuitable for the study at screening were excluded because they had normal coronary arteries. The widespread availability of CT Coronary Angiography (CTCA) coupled with well validated non-invasive models of flow limitation, in particular FFRCT (HeartFlow), should increasingly make such trips to the catheter lab obsolete. Specifically, the evidence base from observational and randomised trials unequivocally demonstrates that FFRCT significantly reduces both the number of ICA and the proportion of ICA that shows no significant coronary disease [6]. Furthermore, as confidence in this technology grows, heart team consensus will allow for patients to undergo CABG surgery based upon FFRCT results without the need for ICA. Thus, in the near future, the majority of patients who undergo ICA will be those with known coronary disease very likely to require PCI: those with unobstructed coronary arteries, mild disease and surgical disease will be detected and managed based upon non invasive testing. In addition, FFRCT data will already have provided the PCI operator with vessel-specific data regarding precise flow-limiting targets for stent deployment, as well as an estimate of the post stent result, this rendering lab-based assessments of physiology potentially redundant.

Second, the value of having routine and comprehensive information on coronary physiology at the time of ICA has consistently turned out to be lower than would be predicted from data derived from initial testing. Specifically, randomised trials including RIPCORD2 [7] and FUTURE have tested routine invasive and comprehensive pressure wire assessment at the time of ICA (as opposed to a population already committed to PCI) on populations with stable angina and NSTEMI and, perhaps surprisingly, found no clinical or financial benefit compared to angiographic assessment alone. Similarly, routine pressure wire assessment showed no benefit in FAME 3 or FLOWER MI [8]. Given the number of randomised trials showing that the strategy of comprehensive invasive FFR at the time of angiography yields no detectable outcome benefit, convincing positive data from randomised trials of vFFR and other angiogram-derived physiology systems will be required before use of such technology can be justified in routine practice.

In summary, the elegant paper by Ghobrial *et al* reinforces the considerable potential that vFFR and other angiogram-derived physiology systems could hold in improving the precision with which we diagnose and manage coronary artery disease on a personalised basis in the future. Based upon these and other data, randomised trials of the clinical outcome of the routine use of this and similar technologies are now needed. However, the promising observational data, yielding such similar results to those seen with comprehensive invasive FFR studies, must translate into clinical advantage in a manner that has never been achievable using the pressure wire itself... the true role of such exciting technologies as potential game changers in the process of diagnostic angiography now depends upon such trials. But these systems may have missed the boat if (a) a substantial proportion of these patients should never have reached the catheter lab in the first place, and (b) many of the rest will already have comprehensive anatomical and flow limitation data from FFRCT or similar systems?

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