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Picture perfect? Performance of quantitative coronary angiography-based vessel FFR versus pressure wire-based FFR

Colin Berry[1,2]*, BSc, MBChB, PhD, FRCP, FESC, FACC; Daniel T. Y. Ang[1,2], MBChB, MRCP

1. British Heart Foundation Glasgow Cardiovascular Research Centre, University of Glasgow, Glasgow, United Kingdom;
2. Department of Cardiology, Golden Jubilee National Hospital, Clydebank, United Kingdom

Measurement of fractional flow reserve (FFR) at the time of invasive coronary angiography is an established method for the assessment of epicardial coronary lesion severity. International guidelines recognise its role in guiding decisions on revascularisation[1,2], specifically, an FFR >0.80 facilitates a safe deferral of coronary intervention[3]. The use of FFR alters clinician management plans in the catheterisation laboratory[4], and more importantly, may lead to improved clinical outcomes in chronic and acute coronary syndromes[5,6].

Despite these developments, FFR adoption remains limited in clinical practice, primarily due to the requirement for coronary instrumentation, increased procedural time and cost, and patient intolerance to intravenous adenosine. With these challenges in mind, there is growing interest in non-invasive FFR measurements as an adjunct to anatomical imaging. These methods utilise computational flow dynamics, the foundations of which are based on the laws of Bernoulli and/or Poiseuille[7]. They are calculated by computational modelling using data acquired by computerised tomography (CT)[8] or invasive coronary angiography[9]. Their real strength lies in their capacity for multivessel assessment without the need for multi-coronary instrumentation. Results so far have shown good correlation between the non-invasive indices and invasive FFR[7].

In this issue of EuroIntervention, Masdjedi et al[10] provide new data from the FAST II (Fast Assessment of STenosis severity) study. This prospective, multicentre study enrolled patients from Europe, USA and Japan who had coronary disease of intermediate severity (30-70% on visual assessment). A total of 391 patients were recruited, with 54 (14%) excluded due to angiographic exclusion criteria and 3 excluded due to lack of FFR data. Of the final 334 patients, FFR was assessed in 1 vessel each and compared with the 3D-quantitative comparative analysis (QCA)-derived vessel FFR (vFFR). vFFR analysis was done offline by both a core laboratory, as well as trained site staff. Importantly, vFFR estimation was undertaken blind to the FFR result. Performance and accuracy of vFFR were assessed against the gold standard, invasive FFR.

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The study demonstrated moderate correlation between the core lab vFFR and pressure wire-based FFR (R=0.74; p<0.001), with good diagnostic performance of vFFR in identifying an FFR

**Corresponding author: BHF Glasgow Cardiovascular Research Centre, Institute of Cardiovascular and Medical Sciences, University of Glasgow, 126 University Place, Glasgow, G12 8TA, United Kingdom. E-mail: colin.berry@glasgow.ac.uk*

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≤0.80. Using a cut-off of vFFR ≤0.80, sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy were 81%, 95%, 90%, 90% and 90%, respectively. On-site vFFR was similar but with reduced sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy at 71%, 89%, 79%, 85% and 83%, respectively.

This study systematically builds upon previous retrospective analyses from FAST I and FAST Extend. These studies focus on patients with intermediate coronary artery disease, traditionally the cohort that derives most benefit from FFR assessment. The strengths of the FAST II study are its intercontinental population, blinded vFFR analysis and inclusion of a considerable (36%) proportion of patients with FFR ≤0.80. The software allowed for automated temporal alignment of analysed images, identification of end-diastolic frames and vessel contour detection. The automation of these analyses allows for greater efficiency and result consistency across sites. That said, almost 1 in 10 cases involved manual adjustment according to the standard operating procedure.

There are a few points worth further discussion. Angiography-derived estimates of FFR are limited by image quality. 3D-QCA requires 2 views ≥30° apart (ideally orthogonal), with minimal vessel tortuosity, overlap and foreshortening. These issues resulted in approximately 10% of the study population being excluded on angiographic criteria alone. Ostial lesions also precluded vFFR assessment.

The principles of haemodynamics assume steady laminar flow conditions, which do not necessarily apply in the setting of pulsatile blood flow and turbulence from coronary stenoses. These principles are even less applicable in tandem stenoses or diffuse disease, which often occur in clinical practice. More than 70% of the cases in this study had focal lesions, which limits extrapolation of vFFR accuracy to individuals with more diffuse disease. Another underserved subgroup are patients with microvascular angina, more specifically those with a raised index of microvascular resistance (IMR), in whom angiography-based FFR estimation may be less accurate[11]. Even if vFFR were to achieve 100% correlation and diagnostic accuracy with invasive FFR, we would still need to contend with the challenges of decision making in the "grey zone" FFR of 0.75-0.80.

Given the offline central analysis in this study, the authors have acknowledged some limitations for translation of their findings into clinical practice. QCA still requires manual correction for errors, which occurred in approximately 10% of cases. There was also a 10% inter-user variability for vFFR. These limitations are generic across other angiography-derived methods for FFR estimation, and not relevant to direct, automated measurement of FFR during stable hyperaemia.

The FAST III study is a randomised controlled, open-label, multicentre, international, non-inferiority, clinical trial of vFFR-guided versus FFR-guided coronary revascularisation in 2,228 subjects with intermediate coronary artery lesions (ClinicalTrials.gov: NCT04931771). The primary outcome is the composite of all-cause death, any myocardial infarction, or any revascularisation at 12 months. This study should answer many of the questions regarding clinical feasibility, applicability, cost, and prognostic benefit. Future studies should highlight the performance of vFFR in patients with "grey zone" FFR 0.70-0.80, the region where the greatest discrimination is required.

In conclusion, the FAST II study has highlighted the promising potential of non-invasive FFR. Ultimately, patient-specific factors (vessel tortuosity, overlap, ostial lesions) necessitate that invasive FFR will remain the gold standard test for the foreseeable future.

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Conflict of interest statement

C. Berry and D. Ang are employed by the University of Glasgow which holds consultancy and research agreements for work with Abbott Vascular, AstraZeneca, Auxilius Pharma, Boehringer Ingelheim, Causeway Therapeutics, Coroventis, Genentech, GSK, HeartFlow, Menarini, Neovasc, Siemens Healthcare, and Valo Health.

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