Interview

New treatment approaches in coronary heart disease

Colin Berry speaks to Caroline Telfer, Assistant Commissioning Editor.

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■ **What attracted you to a career in interventional cardiology?**

For me, interventional cardiology integrates treating patients directly through a learned set of 'craft' skills, problem solving, science and technology. In my opinion, it is the most interesting and exciting medical specialty.

■ **What would you consider to be your greatest achievement to date?**

It is still early days. I have made various contributions in basic science and with new imaging methods. We are particularly excited about PROTECT, which is an MRC/BHF-funded first-in-man clinical trial of gene therapy to prevent saphenous vein graft failure after coronary artery bypass graft.

I have been a doctor for 20 years and involved in research for the past 15 years. I have observed substantial investments from scientists and their funders, sometimes with uncertain outcomes. I am increasingly attracted to the notion that simple ideas can successfully challenge established practices and directly result in improvements in patient health and wellbeing. In recent years, we have had some success and the benefits to patients are very obvious. One example would be our research into bleeding problems during angiography and percutaneous coronary intervention (PCI) with femoral artery access and the lowering of this risk with radial access. Other simple propositions are work-in-progress: pressure wire instead of angiography-guided treatment decisions in acute coronary syndrome (ACS) patients, deferred stenting instead of immediate stenting in primary PCI and so on.

■ **In light of your recent publications on the topic, what have you deduced about the usefulness of fractional flow reserve measurement in the field of interventional cardiology?**

Fractional flow reserve (FFR) is a new diagnostic option that can change management on an individual patient basis. The potential for FFR to optimize treatment decisions and patient outcomes in stable coronary disease has already been proven in FAME (St Jude Medical Inc., MN, USA). A more tantalizing clinical problem that has been 'off-limits' for pressure wire research is unstable coronary disease. Patients with a recent ACS who undergo invasive management do so as part of an urgent/emergency care pathway in which some of the usual diagnostic steps (e.g., stress testing) are missing. Potentially, invasive measurement of lesion-level ischemia with the pressure wire could help the clinician to make more informed treatment decisions with hopefully better clinical outcomes. However, the validity of FFR in ACS patients is not established, and for this reason, this area is ripe for research.

■ **And why do you think it is so important to improve the diagnostic efficiency in patients with non-ST-elevation myocardial infarction?**

There are treatment challenges in patients who have a non-ST-elevation myocardial infarction and they have an above average risk of future morbidity and mortality, so improvements are needed in terms of how these patients are managed in order

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to try and improve their long-term clinical outcomes.

■ **The results of the FAME II trial have recently been published, regarding the outcomes associated with FFR-guided procedures in the treatment of coronary artery disease. Can you elaborate on the purposes of this study?**

FAME II was a response to the COURAGE trial and FAME II was made possible by the technological developments and evidence base that supports FFR adoption in patients with stable angina. COURAGE suggested that patients with angina can be equally treated by tablets or by coronary interventions with angioplasty and stents. Although COURAGE was a large randomized controlled trial, conducted by internationally respected investigators, many cardiologists struggle to believe the results of this trial. I suspect these, and no doubt some other reasons too, were the main drivers for FAME II. As FAME II randomly compared PCI versus medical therapy in patients with invasive evidence of ischemia as revealed by FFR, so the ISCHEMIA trial involves random assignment of patients with ischemia revealed noninvasively. Both of these trials test the COURAGE trial results.

■ **So they compared the outcomes with FFR alone to those with FFR and best available treatment?**

FAME II has shown that, in patients with ischemia measured invasively by FFR, angioplasty with stenting is needed, albeit to prevent future unplanned hospitalizations for urgent coronary revascularization.

■ **In your opinion, how do these new findings build upon those from the original FAME trial?**

They reinforce the clinical utility of FFR in routine decision-making in the catheterization laboratory.

■ **What would you say are the most important results to come out of the FAME II trial?**

The most important results are the clinical and cost–effectiveness of revascularization in patients with ischemia as disclosed by FFR.

■ **When reviewing the results of the FAME II trial, were there any results that you did not expect?**

No, I thought the results were as predicted. Although some have questioned the importance of revascularization in the composite primary outcome, it would have required a much larger trial to assess for any impact when restricted to death and myocardial infarction since the annual event rate of these events in stable angina is low (typically <3%).

■ **You mentioned the cost–effectiveness. St Jude Medical have issued a press release 'Cost Effectiveness Study Determines FFR Can Improve Health While Reducing Economic Burden in the UK'. What are your opinions on this aspect of the treatment?**

I think treatment decisions based on FFR measurements have the potential to reduce morbidity, mortality and healthcare costs overall in patients with coronary heart disease. Treatment decisions in the catheterization laboratory that do not use FFR may be suboptimal and, therefore, associated with a future health and cost burden.

■ **Does it remove the unnecessary interventions?**

Yes, this was one of the main results in the FAME trial, and other studies have shown this too.

■ **How do you think the results of this study, and others alike, will change the field of interventional cardiology in the next 5 years?**

I think it is an evolving paradigm and more education and training around FFR are needed. As FFR is used more often, so health benefits for individual patients and for healthcare providers may be realized.

■ **Will therapy become more personalized?**

Yes.

■ **What do you think will be the long-term impact?**

Coronary heart disease is a chronic condition and as longevity improves so the community burden of coronary

heart disease may rise. Compared with angiography alone, treatment decisions informed by FFR are associated with improved health so it makes sense that FFR should be widely used, especially in patients with intermediate lesions and in those who have not had prior stress testing.

■ In terms of interventional cardiology in general, FFR seems to be beneficial, but is there anything else that is equivalent? In your opinion, what would be the next best thing?

Stress perfusion MRI, which provides a noninvasive assessment of ischemia. Unlike nuclear imaging and computed tomography angiography, MRI is safer since it does not involve ionizing radiation, which is associated with cancer.

■ Have they done trials into this?

Yes, but more trials are needed of stress MRI and I would point out three. The CE MARC II trial, the MR-INFORM trial and the ISCHEMIA trial. I think the approach to the diagnostic management of coronary heart disease will be quite different in 5–10 years time.

■ Is this with similar end points?

Generally, these are three important clinical trials in stable coronary heart disease. My own research interest is in unstable coronary heart disease and you mentioned about non-ST-elevation myocardial infarction earlier so we are looking to work out the potential health and economic benefits of FFR in patients with unstable coronary disease. Similarly with stress MRI as well.

■ Is there anything else that you wanted to add?

Yes, I am grateful for the support of my clinical colleagues, and our patients and funders, especially the British Heart Foundation and government agencies, such as the Scottish Funding Council, Chief Scientist Office and Medical Research Council. Without them, none of our work would be possible; and a final word, above all, for my wife.

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