Diagnostic technique allows avoidance of surgery in one fifth of heart attacks

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A method for measuring coronary artery blockage in heart attack patients can help more than one fifth of them avoid stents or surgery, according to a British study presented at the ESC Congress 2014 today.

The findings "are highly relevant to contemporary clinical care and, as a 'proof-of-concept', the trial sets the scene - which needs to be examined further in a much larger trial - for a more objective approach to treating heart attack patients," said senior author Colin Berry, PhD, from the Institute of Cardiovascular and Medical Sciences at the University of Glasgow, in Glasgow, United Kingdom.

Results of the prospective, multicentre, randomised, controlled FAMOUS-NSTEMI trial were presented as a Hot Line at the congress and published simultaneously in The *European Heart Journal*.

The findings support more research with this technique, known as Fractional Flow Reserve (FFR) measurement, in patients who have recently suffered the most common type of heart attack, known as Non-ST-Segment Elevation Myocardial Infarction (NSTEMI), said Professor Berry.

"Most NSTEMI patients undergo coronary angiography to allow cardiologists to evaluate the severity of coronary stenosis (blockage)," he explained. "Decisions about treatment are then based on visual interpretation of the angiogram. But this is a subjective interpretation that could potentially lead to misdiagnosis and incorrect treatment

decisions," he said.

"FFR measurement is an objective alternative, and this trial that has shown clearly that compared with standard angiography-guided management, FFR-guided management differentiates patients for drug treatment that would otherwise have been treated surgically or with stents" (tubes inserted to unblock the artery).

The study involved 350 patients (mean age 62 years, 74% male) from 6 acute care hospitals in the United Kingdom.

To be included, all patients needed a diagnosis of acute NSTEMI, at least one risk factor for coronary artery disease (e.g. diabetes mellitus), and have either urgent invasive management planned within 72 hours of their heart attack, or a history of recurrent symptoms within 5 days.

Additionally, angiography needed to show at least one coronary artery for which FFR measurement might have diagnostic value, meaning blockage of at least a 30% and normal blood flow.

A decision to treat with either drug therapy, stents, or surgery was made by the attending physicians based on assessment of each subject's baseline angiogram.

Subjects were then randomised to either receive this treatment (n=174), or to receive a subsequent diagnostic FFR (n=176) which would refine the treatment decision.

FFR assesses the physiological severity of a coronary blockage using a pressure-sensitive guidewire. Until now, absence of evidence has meant the role of FFR in NSTEMI patients is uncertain.

Previous studies in patients with stable symptoms have shown that

patients with FFR values above 0.80 can be safely treated medically, without the need for coronary revascularisation surgery, whereas measurements of 0•80 or less are an indication for revascularisation. However, it remains uncertain whether this FFR cut-off is valid in NSTEMI patients, and whether or not FFR might be used in all arteries (culprit and non-culprit). FAMOUS-NSTEMI was a developmental trial designed to gather information on these uncertainties

While all subjects in this study received the diagnostic FFR, results were only consulted for those who were randomised to FFR-guided treatment, while those who were randomised to angiographically-guided treatment had their FFR results sealed until after study completion.

The study showed that among subjects randomised to FFR-guided treatment, more than one fifth (21.6%) had a revised treatment plan based on the FFR measurement and ultimately 22,7% of them received drug therapy (i.e. avoided revascularisation) compared to 13.2% of those in angiographically-guided group (p=0.022; relative risk 1,72). At 12 months, revascularisation remained lower in the FFR group compared to the angiographically-guided group (79.0% vs. 86,8%, p=0,054), with 72.2% percutaneous coronary intervention (PCI) and 6.2% coronary artery bypass grafting (CABG) in the FFR group compared to 79.9% PCI and 6.9% CABG in the angiographically-guided group.

Heart attack (myocardial infarction) related to revascularisation also tended to be lower (p=0.12) and all major adverse cardiac events (MACE) were similar (p=0.89). Spontaneous MACE excluding procedure-related heart attack tended to be higher (p=0.25) in the FFR-guided group, but the number of events in this trial is too small to draw any conclusions about health outcomes. In fact, one of the main conclusions is that a larger trial is needed.

The trial results raise the question of competing risks, noted Professor

Berry.

"On the one hand revascularisation and heart attacks related to these procedures are reduced. On the other hand, spontaneous MACE events tended to be higher in the FFR-group that was managed with medical therapy. However, the number of events is small and the affected patients had heterogeneous characteristics. Of the additional events in the FFR group only a minority (four of ten patients), were associated with a decision to change treatment from revascularisation to medical therapy based on the FFR disclosure. This suggests other factors may be relevant."

In terms of cost, mean material costs were higher in the FFR-guided group compared to the angiography-guided group (£1,095 vs £822) because of the cost of the pressure wire, however because length of stay and other hospital costs were less in the FFR group, the overall in-hospital healthcare costs were similar (£7,289 and £7,484, respectively).

"The FAMOUS-NSTEMI trial is unique since it is the first multicentre, randomised, controlled trial to assess FFR-guided management specifically in patients with recent heart attack, and in whom all treatment options (drugs therapy, stents or surgery) were possible. FAMOUS-NSTEMI extends the evidence of the DEFER, FAME, FAME-2 and RIPCORD studies which were focused on patients with stable symptoms rather than on patients with recent heart attack," noted Professor Berry.

Use of FFR to inform treatment decisions in invasively-managed NSTEMI patients is not the standard of care mainly because of a lack of evidence, he added.

"The results support the case for a larger definitive trial informed by the results of the FAMOUS-NSTEMI study to fully assess the effects of

FFR-guided management on health outcomes and cost-effectiveness in the longer term."

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