血行再建術を回避しても安全な患者の見極め（Presentation #4028）

FAMOUS-NSTEMI：診断技術により、MI後の患者の5分の1が手術を回避できる

FAMOUS-NSTEMI: Diagnostic technique allows avoidance of surgery in one fifth of patients following an MI

非ST上昇心筋梗塞（NSTEMI）後患者における客観的冠動脈狭窄計測法である冠血流予備量比（FFR）計測は、これら患者の5分の1以上において血行再建術を回避するのに役立ち得る、とのスタディ結果が2014年European Society of Cardiology Congressホットラインセッションで発表され、同時に*The European Heart Journal*に掲載された。症状の安定した患者を対象とした過去のスタディでは、FFR値が0.80を超える患者は薬物療法で治療しても安全であるが、計測値が0.80以下である場合は血行再建術の適応であることが示されている。しかし、このFFRカットオフがNSTEMI患者においても妥当であるか否か、またはFFRがすべての冠動脈（責任病変および非責任病変）において使用できるかは不明である。スタディは350人の患者（平均年齢62歳、男性74%）を対象とした。FFRガイド下治療群にランダム化割り付けされた患者のうち、21.6%において治療方針が変更され最終的に22.7%が薬物療法を受けた（すなわち血行再建術を回避）のに対し、冠動脈造影を基に治療方針を決定された群では13.2%であった（p=0.022）。12か月後も血行再建術施行率はFFR群で低いままであり（79.0%対86.8%、p=0.054）、FFR群では経皮的冠動脈インターベンション（PCI）を72.2%に、冠動脈バイパスグラフト（CABG）を6.2%に施行されたのに対し、冠動脈造影に基づき方針を決定する群ではそれぞれ79.9%および6.9%であった。

Full Text

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

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, multicenter, randomized, 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," 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".

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 randomized to either receive this treatment (n=174), or to receive a subsequent diagnostic FFR (n=176) that 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 revascularization surgery, whereas measurements of 0.80 or less are an indication for revascularization. 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 randomized to FFR-guided treatment, while those who were randomized to angiographically guided treatment had their FFR results sealed until after study completion.

The study showed that among subjects randomized 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 revascularization) compared to 13.2% of those in angiographically-guided group (p=0.022; relative risk 1.72). At 12 months, revascularization 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.

Myocardial Infarction related to revascularization 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 revascularization 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 revascularization 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 multicenter, randomized, 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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Conference News