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DOI: 10.1056/NEJMc2211845

Fractional Flow Reserve or Intravascular Ultrasound for PCI

TO THE EDITOR: In the FLAVOUR trial, Koo and colleagues (Sept. 1 issue)[1] report that percutaneous coronary intervention (PCI) that was guided by fractional flow reserve (FFR) was noninferior to guidance by intravascular ultrasonography (IVUS) with respect to the composite outcome of death, myocardial infarction, or revascularization in patients with intermediate coronary stenosis. Although FFR-guided PCI has an established role among patients with intermediate coronary stenosis and stable ischemic heart disease,[2] whether IVUS has a similar role is unclear, except in those with left main coronary stenosis.[3] The decision to proceed with PCI in the IVUS group was based on a minimal lumen area measuring either 3 mm^2 or less or 3 to 4 mm^2 with a plaque burden of more than 70%. These measurements predicted future events among patients with acute coronary syndromes,[4] but it remains uncertain whether they would be predictive among patients with stable ischemic heart disease (the diagnosis in most patients in the FLAVOUR trial). Furthermore, there is no correlation between the morphologic features of plaque and FFR-positive flow-limiting lesions.[5] Thus, is the conclusion from this trial that either FFR or IVUS can guide the decision to proceed with PCI in patients with intermediate stenosis? Or was the trial exploring whether PCI outcomes with FFR guidance would be as good as those with IVUS guidance?

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No potential conflict of interest relevant to this letter was reported.

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DOI: 10.1056/NEJMc2212953

TO THE EDITOR: Whether a new treatment that is investigated in clinical trials should be used in patients depends on the balance between its efficacy and its safety.[1] The FLAVOUR investigators conclude that there was no difference in efficacy between PCI procedures that were guided by FFR or IVUS. However, the incidence of bleeding events (a safety metric) was not reported. The frequency of PCI was 44.4% among patients in the FFR group and 65.3% among those in the IVUS group, which led to the use of dual-antiplatelet therapy in a greater percentage of patients in the IVUS group. Therefore, prevailing wisdom suggests a greater number of bleeding events may also have occurred in the IVUS group.[2] It is a well-established fact that bleeding after PCI is associated with greater mortality.[2] In this trial, the number of deaths from any cause was greater in the IVUS group (and noncardiac mortality was twice as high), but the statistical power was insufficient to detect a between-group difference because the sample size was calculated on the basis of a composite end point. Thus, the findings of this trial that assessed only ischemic events could lead physicians to consider that the two guidance strategies are equivalent,

which could result in additional bleeding events and patient harm.

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No potential conflict of interest relevant to this letter was reported.

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DOI: 10.1056/NEJMc2212953

TO THE EDITOR: In the FLAVOUR trial, the use of FFR was found to be noninferior to IVUS with respect to clinical outcomes after 2 years of follow-up. In this trial, approximately 30% of the enrolled population (496 of 1682 patients) presented with an acute coronary syndrome. Although data support the use of FFR in patients with stable coronary artery disease, its value to guide revascularization in patients with acute coronary syndrome is controversial and still a matter of investigation. Some studies have shown higher rates of adverse events after FFR-based deferral of revascularization among patients with acute coronary syndrome than in those with stable angina.[1-3] Therefore, it would be more appropriate to evaluate patients with an acute coronary syndrome separately from those with stable coronary artery disease in order to better understand the real value of FFR and IVUS to guide PCI in different clinical scenarios.

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DOI: 10.1056/NEJMc2212953

TO THE EDITOR: The results of the FLAVOUR trial provide an opportunity to expose veiled attitudes in interventional cardiology. In the trial, cardiologists made a decision to proceed with target-vessel PCI of angiographic intermediate lesions at a higher frequency after IVUS guidance than after FFR guidance (58.4% vs. 33.2%). In practice, cardiologists select IVUS when they want to justify proceeding with PCI and use FFR when they do not, although asymptomatic patients with intermediate lesions have a low rate of cardiovascular events while receiving appropriate medical therapy alone.[1] The editorialist nicely clarified that the higher or lower frequency of PCI did not reduce cardiovascular events but implied that the results of the trial may be different in racial and ethnic groups outside Asia.[2] Is this implication valid, given that Craig Venter, one of the first scientists to sequence the human genome, said that "race is a social concept, not a scientific one"?[3] Should we be making treatment decisions regarding coronary revascularization on the basis of clinical indications, regardless of sex, race, or ethnic background?[4]

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No potential conflict of interest relevant to this letter was reported.

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DOI: 10.1056/NEJMc2212953

THE AUTHORS REPLY: In response to Elkaryoni: several trials have shown the prognostic implications of IVUS and other imaging-based measurements among patients with stable coronary artery disease. Furthermore, recent studies have shown that morphologic features of plaques are associated with FFR, which stem from the interactions between plaque and the hemodynamic environment.[1] Because PCI may have a plaque-sealing effect to prevent future events, the role of IVUS in guiding decision making for revascularization should be appreciated with its predictive value for clinical events. Therefore, the FLAVOUR trial is not simply comparing FFR with IVUS but is exploring the fundamental approach to diagnosis and treatment of both the patients and their lesions according to both physiologic features and imaging.

Shah proposes that the bleeding events in our trial, which could be higher in the IVUS group owing to a higher frequency of prescriptions for dual-antiplatelet therapy, should be considered in the interpretation of our trial results. It is true that the IVUS group may have had more bleeding events than those in the FFR group. However, the bleeding risk of dual-antiplatelet therapy after PCI should not be considered as a trade-off with the benefit of PCI. In addition, a previous trial showed that bleeding risk was increased by long-term dual-antiplatelet therapy only in patients who were at high risk for bleeding,[2] which suggests that bleeding events may not be a critical issue in our trial population.

Danzi and Piccolo raise an issue about the effect of clinical diagnosis. In the FLAVOUR trial, the cumulative incidence of clinical events among the patients with acute coronary syndrome was similar in the FFR group and the IVUS group (10.0% vs. 10.3%, for an absolute difference of −0.3 percentage points; 95% confidence interval, −5.6 to 5.0). Although this result should be interpreted with caution, it is in line with the findings in previous trials that support the use of FFR-guided PCI in patients with acute coronary syndrome.[3]

Bittl comments on the effect of demographic characteristics on the results. The cutoff value for FFR is not greatly influenced by demographic characteristics. However, anatomical variations according to sex, race, or ethnic group should be considered in determining the appropriate cutoff values for IVUS measures and their prognostic implications.[4] Therefore, the results of the FLAVOUR trial need to be interpreted in the context of demographic characteristics of enrolled patients as in other clinical trials.[5]

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Since publication of their article, the authors report no further potential conflict of interest.

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DOI: 10.1056/NEJMc2212953