

REPLY: Safety of the Deferral of Coronary Revascularization on the Basis of Instantaneous Wave-Free Ratio and Fractional Flow Reserve Measurements



We thank Dr. Biscaglia and colleagues and Dr. Alkhalil for their interest in our research (1). At a difference with the instantaneous wave-free ratio and fractional flow reserve groups in the 2 randomized trials used for our pooled analysis, the acute coronary syndrome (ACS) and stable groups used in our analysis are potentially fraught by case selection. Thus, inferring conclusions from the rates of revascularization in patients with ACS and those in stable condition is difficult. Compared with the context of stable angina, in ACS, interventionalists might be more selective at the time of performing pressure guidewire interrogation of nonculprit coronary arteries, because in some cases this would entail a second invasive procedure several days after treating the ACS culprit vessel. By doing so, in patients with ACS, pressure guidewire interrogation would more frequently occur in stenoses with higher angiographic likelihood of functional severity, resulting in a higher PCI rate than in patients in stable condition.

Unfortunately, evidence of a protective effect of the suggested drug treatments in patients who had revascularization of nonculprit coronary arteries deferred is still lacking. The prognostic implications of plaque composition and structure in nonculprit vessels deferred with FFR is currently under investigation in studies such as COMBINE (Combined Optical Coherence Tomography Morphologic and Fractional Flow Reserve Hemodynamic Assessment of Non-Culprit Lesions to Better Predict Adverse Event Outcomes in Diabetes Mellitus Patients) (2). By no means could we propose that stenting of nonculprit arteries is safer than deferral in patients with ACS; as demonstrated in our research, the 1-year event rate in patients with ACS with deferred vessels was much lower than in patients with ACS with treated vessels. The designs of both trials preclude drawing conclusions on quantitative angiographic data or on the location of a lesion causing an event during follow-up.

Overall, we believe that further research on how to improve further the safety of percutaneous coronary intervention deferral in patients with ACS is needed.

Javier Escaned, MD, PhD
Hernán Mejía-Rentería, MD
Hakim-Moulay Dehbi, PhD
Matthias Gotberg, MD, PhD
*Justin Davies, MD, PhD

*Imperial College NHS Trust
Hammermsith Hospital
London W12 0HS
United Kingdom
E-mail: justindavies@heart123.com

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REFERENCES

1. Escaned J, Ryan N, Mejía-Rentería H, et al. Safety of the deferral of coronary revascularization on the basis of instantaneous wave-free ratio and fractional flow reserve measurements in stable coronary artery disease and acute coronary syndromes. *J Am Coll Cardio Intv* 2018;11:1437-49.
2. Kennedy MW, Fabris E, Ijsselmuiden AJ, et al. Combined optical coherence tomography morphologic and fractional flow reserve hemodynamic assessment of non-culprit lesions to better predict adverse event outcomes in diabetes mellitus patients: COMBINE (OCT-FFR) prospective study. Rationale and design. *Cardiovasc Diabetol* 2016;15:144.

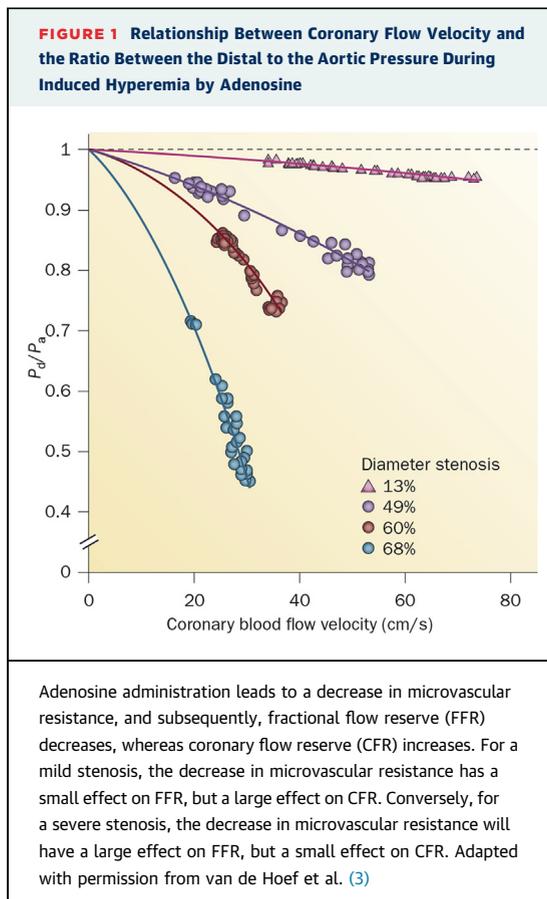
TO THE EDITOR

Go With the Flow When Instantaneous Wave-Free Ratio-Fractional Flow Reserve Discordance Occurs



Indeed, Beware When Relying on Fractional Flow Reserve Alone

With great interest we read the “Images in Intervention” case regarding discordance between instantaneous wave-free ratio (iFR), whole-cycle Pd/Pa, and fractional flow reserve (FFR) in the left main coronary artery and the left anterior descending coronary artery by Ihdahid et al. (1). Importantly, FFR should not be held as the “gold standard” to define ischemia, because there is abundant evidence that coronary flow is more important than coronary pressure in maintaining myocardial function (2,3). Even though disagreement between resting physiological indices and hyperemic FFR is more frequent in left main or proximal left anterior descending coronary artery lesions, this does not automatically mean that these lesions are indeed ischemia-causing. Prior research about FFR+/iFR- discordance has indicated that this indicates that lesions are non-flow-limiting (4). Fundamentally, this disagreement is based on differences in hyperemic coronary flow velocity, emphasizing once more the importance of assessing combined coronary pressure and flow measurements rather than relying solely on coronary pressure measurements such as FFR and iFR. In the presence of a stenosis, pressure loss occurs due



to: 1) viscous friction across the stenosis; and 2) convective acceleration and flow separation at the end of the stenosis, leading to a further loss of kinetic energy. Consequently, distal coronary pressure (P_d) decreases, leading to a low FFR value, whereas coronary flow remains high (see [Figure 1](#)). In conclusion, in FFR-positive, but iFR-negative, intermediate lesions as in the presented case, coronary flow reserve (CFR) can be as high as in angiographically nonobstructed vessels (4). The safety of deferring FFR-positive, but non-flow-limiting, lesions has been previously demonstrated (5).

Therefore, the take-home message in the presented case should be that FFR+/iFR- discordance usually means that the stenosis is non-flow-limiting, which in this case could have been confirmed by measuring CFR, after which PCI could most likely have been safely deferred.

Valérie E. Stegehuis, MD
Tim P. van de Hoef, MD, PhD
Jan J. Piek, MD, PhD
*Bimmer E. Claessen, MD, PhD

*The Icahn School of Medicine

1 Gustave L. Levy Place

Mount Sinai Medical Center

New York, New York 10029-6574

E-mail: Bimmer.Claessen@mountsinai.org

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REFERENCES

1. Ihdahid AR, Seneviratne SK, Cameron J, Ko B. Resting indexes in the functional assessment of left main and left anterior descending coronary stenoses: a case for caution. *J Am Coll Cardiol Intv* 2018;11:1531-3.
2. Smalling RW, Kelley K, Kirkeeide RL, Fisher DJ. Regional myocardial function is not affected by severe coronary depressurization provided coronary blood flow is maintained. *J Am Coll Cardiol* 1985;5:948-55.
3. van de Hoef TP, Meuwissen M, Escaned J, et al. Fractional flow reserve as a surrogate for inducible myocardial ischaemia. *Nat Rev Cardiol* 2013;10:439-52.
4. Cook CM, Jeremias A, Petraco R, et al. Fractional flow reserve/instaneous wave-free ratio discordance in angiographically intermediate coronary stenoses: an analysis using doppler-derived coronary flow measurements. *J Am Coll Cardiol Intv* 2017;10:2514-24.
5. van de Hoef TP, van Lavieren MA, Damman P, et al. Physiological basis and long-term clinical outcome of discordance between fractional flow reserve and coronary flow velocity reserve in coronary stenoses of intermediate severity. *Circ Cardiovasc Interv* 2014;7:301-11.

RESEARCH CORRESPONDENCE

Clinical Randomized Trial Evaluating Novel, Microcrystalline, and Biocompatible Polymer Paclitaxel-Coated Balloon for the Treatment of Femoropopliteal Occlusive Disease

The BIOPAC Trial

Paclitaxel-coated balloons (PCBs) have reduced restenosis and repeat revascularizations when compared with plain balloon angioplasty (PBA) alone after revascularization of superficial femoral arteries. On the other hand, concerns have been raised due to paclitaxel particle shedding during intervention and distal embolization. Second-generation PCBs consist of more homogenous and microparticle paclitaxel coatings that have shown

