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Letters

TO THE EDITOR

Functional Assessment and Acute Coronary Syndrome

"You Can't Blame Gravity for Falling in Love"

—Albert Einstein (1)

We read with great interest the paper by Escaned et al. (2), reporting a pooled analysis of the DEFINE-FLAIR (Functional Lesion Assessment of Intermediate Stenosis to Guide Revascularisation) and iFR-SWEDEHEART (The Instantaneous Wave-Free Ratio Versus Fractional Flow Reserve in Patients With Stable Angina Pectoris or Acute Coronary Syndrome) trials. The investigators should be complimented for providing a strong and relevant message, that deferring revascularization through functional assessment is related to a low event rate at 1 year (4%) in a contemporary population. These results reinforce the role of intracoronary physiology as a gatekeeper to revascularization in intermediate stenosis. At the same time, we were confused by the second message of the study, namely, that physiology may be less reliable in the setting of acute coronary syndrome (ACS). The investigators hypothesize a lower capability of pressure guidewires to identify stenosis that can be deferred in this setting (false negative). However, in this case, we would expect a higher rate of deferral in the ACS group, whereas the investigators show the exact opposite result, with a lower deferral rate in patients with ACS compared with those in stable condition (36% vs. 50%; $p < 0.001$). In addition, the investigators cite a possible risk related to vulnerable lesions amplified by ACS systemic inflammation state. If this were the case, the proper treatment would not be stenting, because no data support preventive stenting in these lesions but rather prolonged dual antiplatelet therapy, proprotein convertase subtilisin-kexin type 9, and interleukin-1β inhibitors. As correctly stated by the investigators, functionally guided revascularization has been validated mainly in a stable setting. However, we do not think that physiology should be blamed for the outcome difference between patients with ACS and those in stable condition. In the setting of ACS, the correct comparator of physiology should be visual estimation in nonculprit ACS lesions rather than deferred lesions in a stable setting.

Given that the investigators cleared the field from their previous hypothesis (3) showing the absence of an interaction between applied technology and outcomes in patients with ACS, the real challenge is now to increase the penetrance of physiological assessment in real-life practice. In the same issue of the journal, a prospective registry study showed that functional "believers" already use it in the setting of ACS (4), while functional "doubters" rely only on eyeballing, without distinguishing between patients with ACS and those in stable condition. To this end, generating randomized data comparing functionally and angiography-guided assessment in patients with ACS (especially non-ST-segment elevation ACS) could be more helpful than raising doubts regarding physiology in higher risk subgroups of patients just comparing them with lower risk ones or performing head-to-head comparison between different functional methodologies in a mainly stable setting.

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REFERENCES

1. Dukas H, Hoffmann B. Albert Einstein: the human side, Princeton, NJ, Princeton University Press, 2014:67.

2. 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 Cardiol Intv 2018;11:1437–49.

3. Götberg M, Cook CM, Sen S, Nijjer S, Escaned J, Davies JE. The evolving future of instantaneous wave-free ratio and fractional flow reserve. J Am Coll Cardiol 2017;70:1379–402.

4. Tebaldi M, Biscaglia S, Fineschi M, et al. Evolving routine standards in invasive hemodynamic assessment of coronary stenosis: the nationwide italian SICI-GISE cross-sectional ERIS study. J Am Coll Cardiol Intv 2018;11:1482–91.

TO THE EDITOR

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

Escaned et al. (1) reported a pooled analysis of the DEFINE-FLAIR (Functional Lesion Assessment of Intermediate Stenosis to Guide Revascularisation) and iFR-SWEDEHEART (The Instantaneous Wave-Free Ratio Versus Fractional Flow Reserve in Patients With Stable Angina Pectoris or Acute Coronary Syndrome) studies demonstrating equal safety of deferring revascularization using both instantaneous wave-free ratio (iFR) and fractional flow reserve (FFR) (4.12% vs. 4.05%; $p = 0.60$). Nonetheless, when the deferred patients were stratified according to their clinical presentation, there was a significantly higher rate of major adverse cardiovascular events in patients with acute coronary syndromes (ACS) compared with those with stable angina (5.91% vs. 3.64%; $p = 0.04$). Importantly, however, the definition of major adverse cardiovascular events was rather heterogeneous and did not allow delineation of events derived from the nonculprit artery above noise. In the PROSPECT (Prospective Natural-History Study of Coronary Atherosclerosis) (2), the cumulative rate of events related to the culprit artery was more than 60% of major adverse cardiovascular events. Therefore, the excess of events in patients with ACS, despite the physiological assessment of epicardial coronary stenosis, may not reflect the inadequacy of the used tools. Adjudicating events in relation to the culprit and the nonculprit artery would probably add insights into the role of FFR and/or iFR in patients with ACS.

Remarkably, the deferral rate of lesions was surprisingly lower in patients with ACS compared with those with stable angina (36% vs. 50%; $p < 0.001$). It is plausible that numbers of physiological evaluations per patient may be higher in patients with ACS compared with those with stable angina, as lesion severity has been demonstrated to be exaggerated in the nonculprit artery during the acute phase of ACS (3). Nonetheless, FFR of the nonculprit artery was shown to decrease, or at least not to significantly change, following the acute phase of ACS (4,5). This would suggest underestimation of lesion severity, if any, and possible less stenting of the nonculprit artery during the acute phase. Therefore, reporting the degree of luminal stenosis or the extent of coronary atherosclerosis stratified according to patient presentation to gauge potential mechanisms behind the lower deferral rate of revascularization in patients with ACS compared with those with stable angina patients in this study. This is important to enable early and detailed risk assessment of patients with ACS, which may be related to the inherent nature of possibly more extensive coronary atherosclerosis and not under- or overestimating ischemia burden by currently used tools in this high-risk group.

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REFERENCES

1. Escaned J, Ryan N, Mejia-Renteria 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 Cardiol Intv 2018;11:1437–49.

2. Stone GW, Maehara A, Lansky AJ, et al. A prospective natural-history study of coronary atherosclerosis. N Engl J Med 2011;364:226–35.

3. Hanratty CG, Koyama Y, Rasmussen HH, Nelson GI, Hansen PS, Ward MR. Exaggeration of nonculprit stenosis severity during acute myocardial infarction: implications for immediate multivessel revascularization. J Am Coll Cardiol 2002;40:911–6.

4. Ntalianis A, Sels JW, Davidavicius G, et al. Fractional flow reserve for the assessment of nonculprit coronary artery stenoses in patients with acute myocardial infarction. J Am Coll Cardiol Intv 2010;3:1274–81.

5. Wood DA, Poulter R, Boone R, et al. Stability of non culprit vessel fractional flow reserve in patients with ST-segment elevation myocardial infarction. Can J Cardiol 2013;29:S291–2.