Response to Michiels et al and Sen et al Regarding Article, "Diagnostic Accuracy of Combined Intracoronary Pressure and Flow Velocity Information During Baseline Conditions: Adenosine-Free Assessment of Functional Coronary Lesion Severity"

We would like to thank the correspondents for their interest in our work.[1] The debate on adenosine may well be an important factor hampering adoption of physiologically guided revascularization, and therefore the value of a vasodilator-free approach deserves consideration in the light of its possible clinical implications. However, we welcome the criticism employed by the correspondents, as we agree that a rise in adoption must not go hand-in-hand with a fall in accuracy. As such, although our results are favorable, baseline stenosis resistance index (BSR) is still in need of rigorous validation before the concept is of practical value in daily clinical practice.

Although we have primarily evaluated the diagnostic accuracy of BSR for ischemia on an independent noninvasive reference standard, the conclusion of Michiels and colleagues that FFR determined in our study was suboptimal is important for the interpretation of our results. However, several aspects contrasting their conclusion need consideration. First, the rate of inaccurate FFR in our study is in accordance with other investigations reporting on this subject within a similarly heterogeneous patient population and noninvasive stress testing as a reference standard.[2] Second, the use of low-dose (40 μg maximum) intracoronary adenosine has unequivocally been shown to equal intravenous (IV) (140 $\mu g \cdot kg^{-1} \cdot min^{-1}$) infusion in terms of FFR values.[3] Third, all validation studies, evaluating the relation between FFR and myocardial ischemia on noninvasive stress testing, were performed using either low-dose intracoronary or IV adenosine. Both approaches yield equal optimal cut-off values averaging 0.74; a clear indication of their equality. Finally, the search for true maximal hyperemia has indicated that IV adenosine does not induce maximal hyperemia.[4] Hence, one may safely conclude that a direct relationship between FFR and myocardial ischemia is unequivocally determined for both low-dose intracoronary and IV adenosine, whereas neither achieves true maximal hyperemia. Therefore, FFR determined in our study can be considered accurate from a diagnostic point of view and a comparison between FFR and BSR valid.

Indeed, the pressure gradient across a stenosis is flow-dependent. Importantly, the relation between this gradient and flow is unique for a given coronary stenosis geometry. This results in a unique and predictable course of this relationship from basal to hyperemic conditions.[5] Combining both pressure and flow information, BSR is a specific characteristic of the stenosis determined during basal conditions, with a high diagnostic accuracy for myocardial ischemia.[1] Sen and colleagues interestingly raise the extent of flow velocity as an explanation for the difference in discriminative value between BSR and hyperemic stenosis resistance index. We believe that this difference arises from 2 factors that are indeed related to the extent of flow velocity. First, the presence of a measurement error, which unequivocally accompanies any measurement method, induces an uncertainty toward the actual resistance of the stenosis. As basal stenosis resistance is substantially lower than hyperemic stenosis resistance, this uncertainty is more pertinent in basal conditions. Second, the difference in stenosis resistance between ischemic and nonischemic lesion is smaller in basal conditions compared with hyperemia. The combination of these factors makes that the extent of flow velocity may indeed be of influence on the discriminative value of stenosis resistance index.

We welcome the suggestion to evaluate stenosis resistance during the wave-free period. However, it must be borne in mind that the relationship between pressure and flow derived from diastole differs significantly from that derived from whole-cycle averages, which may be of influence on the assessment of stenosis resistance index. Nonetheless, in the light of the aforementioned effect of flow velocity, the intrinsically high coronary flow during the wave-free period may indeed provide a unique opportunity to further improve the discriminative value of stenosis resistance, and in our judgment deserves further evaluation.

The present study did not attempt to address the setting of acute myocardial infarction, in which an increase in minimal microvascular resistance results in a decrease in hyperemic flow, resulting in an increase in FFR. However, microvascular resistance normalizes over time, distal coronary pressure drops, and FFR decreases. As microvascular resistance is, per definition, a black box for FFR, and viable hibernating myocardium cannot practically be distinguished from necrotic tissue by measuring distal coronary pressure, there are other modalities more appropriate to evaluate myocardial viability.

Currently, guide wires are available equipped with both a pressure- and Doppler-velocity sensor, circumventing the need for separate wires.[5] The practical ease of thermodilution notwithstanding, HSR and BSR have only been validated with Doppler flow velocity as a surrogate of flow. Although theoretically equivalent, true equality of the 2 techniques has not yet been determined.

Disclosures

None.

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