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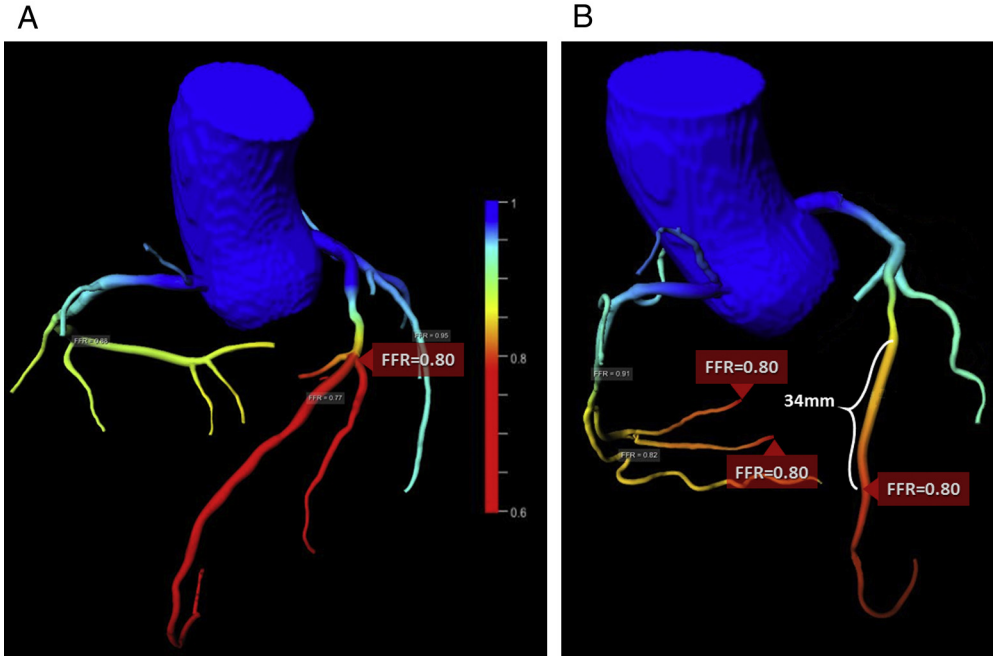
The Location of Distal Coronary Artery Pressure Measurement Matters for Computed Tomography-Derived Fractional Flow Reserve

We read with considerable interest a recent series of papers on clinical use of computed tomography-fractional flow reserve (CT-FFR) as a standalone method for evaluation of functional significance of coronary stenosis based on coronary CT angiography data (1,2). The presented studies comprise a continuous effort toward clinical deployment of this exciting diagnostic modality. The first step of clinical validation of CT-FFR involved correlating the simulated with the respective invasive FFR measurements taken at the same points distal to the coronary stenosis. Meticulous matching of these points was critical, because the FFR values unpredictably decrease toward the distal vessel, as seen in **Figure 1**. The next milestone, the PLATFORM (Prospective Longitudinal Trial of FFRct: Outcome and Resource Impacts), tested clinical utility of CT combined with CT-FFR applied already as an autonomous, noninvasive diagnostic method (3).

It went largely unnoticed though, that the leap from the validation studies with invasive FFR as the reference to the clinical use of CT-FFR as an independent noninvasive diagnostic tool lacked seminal interim data, namely: where CT-FFR should be measured when there is no invasive study to compare. This "original sin" may likely translate into diminished diagnostic value of the method, and given its expected turnover of multimillion exams a year, merits further discussion.

Because there were no preceding studies evaluating at which point distal to the stenosis the pressure should be measured for optimal result of CT-FFR, the assumption made by the investigators of PLATFORM and the cited studies was to sample the most distal part of the vessel (1-3). This approach not only is unsupported by any, but also is contrary to at least 2 currently available pieces of data: 1) according to recommendations, the invasive FFR should be measured 2 to 3 cm (or 5× to 10× the proximal vessel reference diameter) distal to the stenosis; 2) our

FIGURE 1 Coronary Pressure Gradients in 2 Patients With Similar Coronary Anatomy and Similar Stenosis Degree in LAD Artery



Coronary pressure gradients in 2 patients with similar coronary anatomy and similar stenosis degree in left anterior descending (LAD) artery, with high **(A)** and low **(B)** post-stenotic gradients. Additionally, in patient B, the distal right coronary artery shows computed tomography fraction flow reserve (FFR) values of 0.80. The most distal measurements as compared to those performed 2 to 3 cm below the stenosis increase sensitivity of computed tomography FFR while diminishing its specificity and accuracy, leading to overdiagnosis of significant coronary artery disease.

recent study showed that analogous rules apply to CT-FFR, and in addition, we showed that CT-FFR when measured at the end of the vessel led to increased sensitivity but significantly decreased both specificity and accuracy, which is exemplified in **Figure 1** (4). These are important considerations for the method, the role of which is to increase specificity of the diagnosis, as the add-on to an already sensitive method of coronary CT angiography. Another important consideration is that due to very low discriminatory power of CT-FFR within the gray zone of 0.75 to 0.85 (the diagnostic value of coin flipping), 0.80 threshold for clinical decision making should be discouraged rather than promoted (5).

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THE AUTHORS REPLY:

We thank Dr. Kruk and colleagues for their thoughtful comments to our reports on computed tomography-fractional flow reserve (CT-FFR) clinical utility (1). Current clinical recommendations for the measurement of invasive FFR are, somewhat paradoxically, based on anatomy ("2 to 3 cm distal to the stenosis"). In contrast to measured FFR, CT-FFR provides simultaneous calculation of pressure and flow across the entire coronary tree. So how is this plethora of data best utilized to optimize management of patients with stable chest pain? It has been demonstrated in patients with ≥1 intermediate range lesions that CT-FFR was positive (lowest value <0.80) in 56% of patients, whereas only 31% were positive for CT-FFR computed 2 to 3 cm distal to stenosis (2). Recently, Solecki et al. (3) demonstrated highest agreement between CT-FFR and stress cardiac magnetic resonance myocardial perfusion imaging when CT-FFR was computed 41 mm distal to stenosis. However, the "optimal" CT-FFR computation point may vary according to the applied CT-FFR methodology and reference standard, which would ideally be invasive physiology and downstream clinical outcomes.

In our reports on clinical utility, CT-FFR was read at the discretion of observers without formal standardization. Following clinical experiences and emerging published data, we agree with Kruk and colleagues that distal vessel CT-FFR positivity as a single interpretation criterion overestimates disease severity by myocardial perfusion imaging or invasive standards. In fact, employment of this interpretation approach during our clinical adoption of CT-FFR may have attenuated its full potential as a gatekeeper to the catheterization laboratory. Accordingly, it may be that some patients with a positive CT-FFR result are best managed by optimal medical treatment without needing further testing. Moreover, we agree with Kruk and colleagues that an absolute CT-FFR threshold of 0.80 should not drive clinical management, nor should it when adjudicated invasively. Accordingly, we propose a binary interpretation strategy only in patients with CT-FFR >0.80 or ≤0.75, whereas in the event of CT-FFR between 0.75 and 0.80, decisions should be based on additional information (1). Moreover, integrating information (beyond the CT-FFR value and pattern of pressure loss) of more patient-specific CT-derived data associated to flow obstruction such as plaque characteristics, myocardium at risk, and vessel-volume relative to myocardial mass may potentially increase the future diagnostic value of coronary CT angiography-CT-FFR testing. CT-FFR is in its infancy and has only recently been introduced for clinical assessment of stable patients. Extensive ongoing research and accumulating data on clinical utility and outcomes will expectedly provide us with information enabling definition of standardized CT-FFR interpretation criteria in the near future.