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EDITORIAL COMMENT

The New Era of Computational Fluid Dynamics in CT Angiography

Far Beyond the FFR Number*

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For nearly 4 decades, functional stress testing has served as standard practice in suspected coronary artery disease (CAD). However, a contemporary analysis from the National Cardiovascular Data Registry noted the low diagnostic yield from invasive coronary angiography (ICA) after traditional stress testing with less than one-half of patients found to have obstructive CAD (1). However, the identification of obstructive CAD is only part of the story of the relationship between coronary stenosis and ischemia. The concept of invasive fractional flow reserve (FFR) as a valid tool to detect the functional relevance of CAD was introduced in the early 1990s (2), showing nearly 2 decades later in both the FAME (Fractional Flow Reserve versus Angiography for Multivessel Evaluation) and the FAME-II trials that in patients with multivessel disease, FFR-guided revascularization strategy was more cost effective and improved outcomes than angiography-guided revascularization (3,4). Accordingly, over the past few years, there has been a strong interest in computing FFR noninvasively by using coronary computed tomography angiography (CTA). HeartFlow FFR derived from coronary CTA datasets (FFR_{CT}) applies computational fluid dynamics (CFD) to calculate FFR values in all epicardial coronary arteries without the need to change the imaging protocol. To date, several multicenter clinical trials of FFR_{CT} with nearly 1,400 patients have been completed (5–8). The most recent NXT (Analysis of Coronary Blood Flow Using CT Angiography: Next Steps) trial reported per-vessel sensitivities and specificities of 84% and 86%, respectively (7). Beyond its strong diagnostic performance, the recent PLATFORM (Prospect Longitudinal Trial of FFRct: Outcome and Resource Impact) trial reported that a diagnostic strategy guided by FFR_{CT} safely canceled 61% of ICA, reduced ICAs with no obstructive CAD by a dramatic 83%, improved quality of life for patients, and reduced health care costs (8,9). For FFR_{CT}, 3-dimensional geometric modeling and computationally intense blood flow analysis require off-site supercomputing power, and boundary conditions are determined by allometric scaling laws and assumptions regarding microvascular resistance (10). In this issue of *iJACC*, Ko et al. (11) present an alternative technique for FFR_{CT} with

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boundary conditions derived from structural deformation of coronary lumen and aorta and reduced order or 1-dimensional fluid modeling. The authors should be congratulated on this novel alternative technique for quantifying FFR. They reported higher specificity and positive predictive values for CT-FFR than for CTA alone, as well as good reproducibility. These findings are consistent with prior work with FFR_{CT} and other reduced order computations of FFR (7,12). As reduced order fluid modeling is less computationally intense than 3-dimensional FFR_{CT} analysis, current average processing times are generally shorter. It is important to mention several points. First, overall accuracy of CT-FFR was no different than CTA alone. This is in contrast to the recent NXT trial, which noted a statistically significant delta increase in area under the characteristic curve from 0.79 for CTA alone to 0.93 for FFR_{CT} ($p < 0.0001$) (7). Second, HeartFlow FFR_{CT} is actually the only U.S. Food and Drug Administration-approved CFD technique. Third, FFR_{CT} has been validated in other plaque subtypes such as intermediate and calcified lesions (13). On the contrary, it has yet to be determined whether reduced order modeling will maintain its diagnostic performance in these important patient populations. Fourth,

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all scans in the current study were performed using 320-detector CT, and the feasibility of CT-FFR in CT hardware with a lower number of detectors is unknown. The proposed CFD with FFRCT technique could be problematic in faster heart rates, as the entire diastolic phase of the cardiac cycle was used to assess changes in coronary lumen and aorta. On the other hand, FFR_{CT} necessitates a single phase in either systole or diastole. Finally, one of the patients who was excluded from the validation cohort had intramyocardial bridging. Bridging is a very common finding on CTA, and the potential inability to perform CT-FFR on these patients would be problematic. These and other issues need to be investigated further in large multicenter prospective studies.

HeartFlow FFR_{CT} is reported with an analysis time of 1 to 4 h. However, with advancement of automated image analysis, based on deep machine learning requiring less need for human editing, FFR_{CT} will soon be enabled for <1 h turnaround time, enabling its use outside stable ischemic heart disease and into the emergency room setting. Trials such as CREDENCE (Computed Tomography Evaluation of Atherosclerotic Determinants of Myocardial Ischemia; NCT02173275), comparing FFR_{CT} to myocardial perfusion with single-photon emission CT, positron emission tomography, or cardiac magnetic resonance, and PERFECTION (Comparison between Stress Cardiac Computed tomography Perfusion versus Fractional Flow Reserve measured by Computed Tomography Angiography in the Evaluation of Suspected Coronary Artery Disease) (14), comparing FFR_{CT} to stress CT, are underway. If FFR_{CT} is declared to be superior, the field of cardiology will likely see a major transition away from traditional noninvasive functional testing to testing driven primarily by coronary CTA plus FFR_{CT} as the first-line diagnostic strategy for those suspected of having CAD. Simultaneously, diagnostic ICA will continue to decline, and the catheterization laboratory will likely be transformed into a purely interventional suite.

The scope of FFR_{CT} reaches far beyond identification of specific ischemic lesions. New measurements, such as percentage of myocardium at risk, are on the horizon, which will further help clinicians in their therapeutic decision making. Similar to our practice in the invasive arena, the SYNTAX III (A Randomized Study Investigating the Use of CT Scan and Angiography of the Heart to Help the Doctors Decide Which Method is the Best to Improve Blood Supply to the Heart in Patients With Complex Coronary Artery Disease; NCT02813473) trial will evaluate to utilize the anatomic and functional information derived from FFR_{CT} to calculate SYNTAX (Synergy Between PCI with Taxus and Cardiac Surgery) scores, aiding clinicians in deciding between percutaneous coronary intervention or coronary artery bypass graft surgery. Finally, exciting data from the EMERALD (Exploring the mechanism of the plaque rupture in acute myocardial infarction; NCT02374775) study were recently presented at the last EuroPCR, using CFD-based noninvasive hemodynamics for the prediction of acute coronary syndromes. Culprit lesions had significantly lower FFR_{CT} and higher delta FFR_{CT} (across lesions), axial plaque, and wall shear stress than nonculprit lesions. In fact, these noninvasive hemodynamic parameters were better at identifying culprit lesions causing acute coronary syndrome than stenosis severity or high risk plaque features. Besides determining the burden of atherosclerotic disease, severity of stenosis, and adverse plaque features, the bridge of CFD to coronary CTA is taking us 1 step closer to identifying the vulnerable patient. We have entered a new era of computational fluid dynamics in coronary CTA. Its clinical adoption is very disruptive to standard practice diagnosis and management of CAD. As a medical community, we need to embrace this novel technology, recognize its value, and appreciate the extraordinary potential far beyond the FFR number. If the promise of CFD modeling and coronary CTA hold true and we are able to not only accurately identify specific ischemic lesions but individual plaques that are at risk to rupture, causing acute coronary syndromes, this may be one of the great advancements of our time.

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