Circulation: Cardiovascular Imaging

EDITORIAL

Comparison of Computational Fluid Dynamics and Machine Learning–Based Fractional Flow Reserve in Coronary Artery Disease

See Article by Coenen et al

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Over 16.5 million Americans >20 years of age have coronary artery disease (CAD)—the leading cause of death in the developed and developing world. Currently, the gold standard for CAD detection remains invasive X-ray invasive coronary angiography (ICA), which has been recently augmented by calculation of the fractional flow reserve (FFR),[1] the ratio of flow across a stenotic artery with and without vasodilator. Although therapeutic interventions in the acute coronary space require access to the vasculature for ICA, patients with stable CAD[2–6] may not derive a similar benefit at the same level of risk (eg, vascular injury[7] or thromboembolic phenomena). These limitations have led to the consideration of noninvasive techniques, such as cardiac computed tomographic (CT) angiography (CCTA),[8–10] as a potential surrogate for ICA in patients who are not experiencing an acute coronary syndrome.

CCTA has emerged as a reliable method in the quantification, detection, and characterization of coronary plaque.[11] Advancements in the field of computational fluid dynamics (CFD)[12] have enabled modeling of coronary arterial flow from CCTA images. A CT-based FFR may be estimated with existing CCTA images, thereby obviating the need for invasive procedures or additional imaging. Clinical trials, such as DISCOVER-FLOW (Diagnosis of Ischemia-Causing Stenoses Obtained via Noninvasive Fractional Flow Reserve),[13] DeFACTO (Determination of Fractional Flow Reserve by Anatomic Computed Tomographic Angiography),[14] and the NXT trial (Analysis of Coronary Blood Flow Using CT Angiography: Next Steps),[15] have all demonstrated excellent correlation with ICA-based FFR. Nevertheless, CFD simulations of coronary arterial flow are complex because they are dependent on the contraction and relaxation of the heart. Coronary flow increases and decreases as the ventricles relax, and contract respectively, thus changing the intramyocardial pressure. Therefore, for an accurate model of coronary flow, both the heart and arterial model must be taken into consideration, leading to complex modeling, with a solution that is computationally inefficient. Preventing these delays in obtaining the diagnosis could be invaluable in patients who are at high risk for CAD, where the need for therapy may be more urgent.

Itu et al[16] directly address this call by estimating a CT-based FFR via machine learning (ML)–based approaches. Once the ML model is built, it can be used to estimate the FFR in near real time. Typically, large training data sets are required to develop (train) the ML model, after which time it can be applied to new (test) data not used in model development. This scheme provides a more realistic estimation of the parameters and is less prone to erroneous results because of model overfitting. Itu et al use a deep-learning model to estimate FFR from CCTA images from 87 patients and compare ICA-FFR, CFD-FFR, and ML-FFR. To develop the training

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data for the ML model, a large CCTA image database was constructed using 12 000 synthetically generated coronary anatomies in 3 stages. A fully connected deep neural network with 28 input features extracted from the synthetically generated database and 4 hidden layers was used to train the model and then applied to CCTA images from patients to test to model by estimating CT-FFR. The benefits of this approach include generalizability across a wide range of pathological CAD flow conditions and take advantage of nonlinear ML algorithms (eg, deep learning) that are highly accurate and suited to a large amount of input training data. Moreover, unlike traditional ML algorithms, the performance of any model does not tend to plateau because more data are added during the model-building process.

Using this approach, Coenen et al[17] present a multicenter study (comprising 351 patients with 525 vessels), comparing the detection of CAD by using CCTA alone, CFD-FFR, and the ML-FFR. The diagnostic performance of each technique was evaluated with ICA as reference. Of the 525 vessels investigated, 212 were considered to be hemodynamically significant (FFR≤0.8) using the ICA-FFR as reference. Whereas CCTA alone (with a 50% or 70% vessel stenosis cutoff) performed poorly, the CFD-based FFR and ML-based FFR detected CAD at much higher accuracy (78%; 75%–82%), with no discernable difference between the two. Of note, because nearly all the patients (≈96%) had a CCTA-defined stenosis >50%, for which they were referred to an ICA procedure, the number of false positives by CT angiography (CTA) alone is high (85 patients of 303). Impressively, using the ML-FFR, 62 patients were correctly reclassified out of the false-positive group, which indicate that not all stenoses identified by CTA contribute to hemodynamic severity. When the patients were subclassified based on their calcium scores, no appreciable difference was observed for all 3 modes of diagnosis. A substantial difference in accuracy by ML-FFR was observed, however, when the patients were grouped by their image quality; 75% (67%–83%) for the first tertile (lowest image quality) and 91% (86%–97%) for the third tertile (the highest image quality). This underscores the importance of having high-quality images both for training the ML algorithm and when it is applied to predict CAD on real-world clinical imaging data. The results indicate that the FFRs estimated from CFD and ML are indistinguishable, but the time required to perform the analysis decreased substantially. Both the ML model and the CFD used in this work are based on the same 3-dimensional segmentation model that requires 30 to 60 minutes to generate.

The ML results, which are based on anatomic features extracted from CTA, are nearly identical to the CFD results, which entails that advancements made in the CFD model of coronary arterial flow by the addition of plaque composition, minute changes in viscosity and density of blood, and other variables, such as the effect of current medications, would be faithfully reproduced in the ML model. Moreover, as shown in this multicenter study, the ML-FFR–based approach correctly reclassified 62 of 85 patients who were suspected of CAD using ICA-FFR as reference. This would, therefore, have important implications in risk stratification and subsequent referral to ICA procedures of patients suspected of having CAD. The limitations of this approach, as the authors point out, are in the CFD model that the ML model is based on; the ML model is only as accurate as the CFD model. Although the reduction in analysis time is impressive, there are several issues that have to be tackled in the clinical setting. The accuracy of detection of hemodynamically significant lesions is highly dependent on the image qualities as is shown in this work. Including a larger number and wider range of image qualities in the model-building/training phase may help ameliorate this issue. Extraction of the anatomic features from CTA still requires considerable amount of time (≈60 minutes), which currently is the rate-limiting step for instant analysis. But as more images are investigated and as ML-based image processing improves, the time required would indeed come down as well. Nevertheless, the authors need to be commended for their work demonstrating the clinical utility of using noninvasive CTA-based FFR estimation using ML methods in this multicenter trial.

ARTICLE INFORMATION

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Disclosures

None.

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