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fluid dynamics and artificial intelligence deep-machine learning. Ko et al. (1) present the technical principles and general feasibility of yet another novel CT-based FFR prototype based on structural and fluid analysis to determine the physiological significance of coronary lesions. Compared with conventional coronary computed tomography angiography (CTA), the novel approach enabled a marked improvement in specificity (87% vs. 74%) and positive predictive value (74% vs. 60%), while the traditionally high sensitivity and negative predictive value of coronary CTA were preserved. The novel approach was reported to require short processing time (30 min) using a standard desktop computer.

We agree with the authors that the development of physician-driven, workstation-based analysis methods may be one of the necessary next steps to implement CT-derived FFR as a routine clinical test. In addition, we would like to direct the readers to additional studies using fast on-site algorithms. Our own laboratory investigated a different approach for workstation-based analysis using reduced-order computational fluid dynamics and recorded a mean duration of 37.5 ± 13.8 min for CT-FFR derivation including data pre-processing and coronary blood flow computation. In 67 lesions a significant improvement in specificity (85% vs. 34%) and positive predictive value (71% vs. 37%) was accomplished in comparison with coronary CTA alone (2). Using the same application, Kruk et al. (3) focused on the evaluation of patients with intermediate lesions (50% to 90%) and concluded that in approximately one-half of the patients CT-FFR allows for discrimination between ischemic and nonischemic stenoses.

Further, the performance of artificial intelligence deep-machine learning CT-FFR-derivation (4) is currently being evaluated by the MACHINE (Machine leArning Based CT angiograpHy derIved FFR: a MulticeNtEr registry) consortium (NCT02805621). With an estimated population of 352 patients from 5 centers we aim to investigate the comparative performance of computational fluid dynamic modeling and machine learning approaches for determining the functional significance of coronary artery stenosis validated against invasive FFR measurement.

What all these newer developments, including the one currently reported on by Ko et al. (1), have in common is their on-site, workstation-based, physician-driven availability. Besides arguably being better suited for routine clinical workflows, the integration of CT-FFR algorithms into a workstation environment also has potential to broaden the current focus on a single number (i.e., the FFR value) for guiding ad hoc patient management to a more comprehensive exploitation of the considerable richness of coronary CTA data. Our current workstations feature a broad spectrum of advanced, sophisticated tools for characterizing and quantifying the extent of atherosclerotic disease, features that have shown surprisingly powerful prognostic value in many investigations, most recently by harnessing our rapidly evolving machine learning capabilities (5). Integrating the ability of noninvasively determining lesion-specific ischemia with these powerful risk prediction and stratification methods may prove to be a readily available truth machine at our fingertips to determine which patient needs our help right now and in future.

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THE AUTHORS REPLY:

We would like to thank Dr. Baumann and colleagues for writing in support of the use of on-site, workstation-based analysis methods as one of the steps to

implement computed tomography (CT)–derived fractional flow reserve (FFR) as a routine clinical test. We also agree the evaluation of machine-based learning approaches may provide an alternative automated solution to noninvasively predict functionally significant stenoses.

While we and others have described early promise in its diagnostic performance (1,2), a number of important steps will be required before any functional technique including CT-FFR based on reduced-order modeling and workstation on-site analysis may enter into mainstream practice. These include: 1) prospective multicenter data demonstrating its diagnostic performance using separate core lab adjudication of coronary computed tomography angiography (CTA), CT-FFR, and invasive FFR; 2) refinements in processing and analysis algorithms that are focused on automating the process; better accounting for coronary calcium, myocardial thickness, and side branches; and developing an easy-to-use software interface; 3) provision of adequate staff training on workstation use; 4) real-world data demonstrating feasibility including in subsets with known coronary artery disease and prior revascularization; 5) cost effectiveness comparing with traditional functional approaches; and finally 6) outcome data demonstrating safety at short- and medium-term follow-up.

In this regard, the currently commercialized, Food and Drug Administration–approved CT-derived FFR based on remote analysis has and continues to undergo this vigorous process (3–5). However, each test does incur a significant per-use cost, which may make routine implementation across both private and public health sectors difficult. The important strength of an on-site workstation-based approach is that analysis does not involve additional costs above and beyond the coronary CTA alone, once centers are equipped with the workstations. For the same reason, multiple equipped centers may collaborate, which will facilitate the ease of mass data collection required for technique validation.

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