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EDITORIAL COMMENT

FFR-CT and CT Myocardial Perfusion Imaging

Friends or Foes?*

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The field of cardiac imaging has seen many developments in recent years, with the goal of optimizing coronary computed tomography angiography (CCTA) imaging for the anatomical analysis of coronary artery disease (CAD). As a result, CCTA is a reliable, clinically proven method, with high negative predictive value for ruling out CAD (1,2). Extensive evaluation of CCTA techniques also confirmed that CAD should be evaluated by combining anatomical and functional parameters to increase specificity instead of focusing on anatomical evaluation alone (3,4). With the perfection of the CCTA acquisition protocols, the focus is shifting again to the functional side of CAD evaluation. Many techniques have been invented, reinvented, and replaced for this purpose. These methods are focused mainly on 2 parallel approaches. The first approach includes the invasive real-life measurements of specific stenotic flow such as fractional flow reserve (FFR) measurements, whereas the second approach traditionally focuses on imaging-based measurements of myocardial perfusion through different imaging modalities.

Recent developments in both hardware and software technology shifted the interest from invasive FFR to CT-derived FFR (FFR-CT) and from PET and SPECT perfusion to CT myocardial perfusion imaging (CT-MPI). Both technologies are based on CT imaging merging both approaches into closely related technologies, allowing anatomical and functional evaluation within 1 modality. FFR-CT and CT-MPI are increasingly used to guide treatment decisions and evaluate the validity of stenosis-specific interventions. However, both technologies look at different levels of the ischemic cascade and are based on different physiological principles; therefore, it remains unclear whether these technologies will be competing or complementary techniques.

The paper by Pontone et al. (5) in this issue of *iJACC* is the latest in a series of investigations with the main purpose of evaluating the combined value of CCTA, FFR-CT, and CT-MPI. Previous studies investigated the value of static perfusion (6), the comparison of static and dynamic perfusion, and now the comparison of CCTA, FFR-CT, and dynamic CT-MPI.

The current reference standards for the assessment of myocardial perfusion are PET (absolute quantification) and SPECT perfusion (visual analysis). Especially in the United States, nuclear perfusion testing is well established and covered by insurance. Another popular option for myocardial perfusion imaging is magnetic resonance imaging (MRI), which has the capability to perform perfusion imaging in combination with late gadolinium enhancement for infarct evaluation. Dynamic CT-MPI has several disadvantages compared with these methods; most of them are a result of the limited research completed on a wide range of patient populations, scanner systems, and analyzation techniques. This resulted in diverging suggestions of myocardial blood flow (MBF) medians and cut-off values, hampering the clinical implementation of this promising technique. The current study provides much needed information on dynamic CT-MPI using absolute MBF values in combination with anatomical CCTA analysis in

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addition to combining and comparing results with FFR-CT. Pontone et al. (5) uses MBF values with a cut-off value of 101 ml/100 g/min, whereas other studies have described cut-offs ranging from 77 to 105 ml/100 g/min (7).

This contribution is different from other publications on the subject in that it is 1 of the few available studies that performed dynamic CT-MPI using a MDCT scanner with full heart coverage within 1 gantry rotation, whereas most other investigations use a DSCT system with a shuttle mode to provide full heart coverage. The respective scanner offers 160 mm of coverage, allowing the entire heart to be captured in one gantry rotation. However, the increased coverage also comes with a disadvantage: namely, the lower temporal resolution (TR) of 140 ms compared with 66 ms with a DSCT system (8). A lower TR may cause image blur and creates a less robust multisegment reconstruction. This will enhance the need for the use of beta blockers, as demonstrated in the current studies. Previous studies on the use of beta blockers during perfusion studies have shown that these can have an anti-ischemic effect and may influence the results of the perfusion study. Another consideration, when using a scan system with wide coverage, is the increase of cone-beam artifacts, amplifying the need or sophisticated 3D reconstruction algorithms.

There are various approaches to the use of FFR-CT: among them, an off-site computational flow approach such as the one used in this investigation and an on-site machine learning approach (9,10). Although both of them are increasingly used in research settings, the off-site analysis solution, executed by HeartFlow (HeartFlow, Redwood City, California), is the only FDA- approved approach that is clinically available in the United States, Europe, and Japan to date. On-site prototypes are available, however likely not for clinical application within the foreseeable future.

Although CT-MPI is limited by the need for additional scanning and pharmacological stressors, FFR-CT benefits from the fact that analysis can be done straight from the diagnostic CCTA acquisition, which is used for coronary artery evaluation and detection of stenosis. However, the current method for FFR-CT requires the exclusion of vessels or patients with stents and bypasses in addition to very strict image-quality requirements. These limitations are shown in the study by the fact that 87 (36%) of patients were excluded with previous stent/MI. A discussion emphasizing the difference between invasive FFR and FFR-CT is ongoing to determine the optimal location of FFR-CT measurement. Although invasive FFR is measured around a specific stenosis, FFR-CT allows for evaluation of the entire coronary tree. Very little research has been done on determining the optimal location, but few studies show that the location of measurement can highly influence the diagnostic accuracy of FFR-CT.

Pontone et al. (5) demonstrate that the combination of FFR-CT and CT-MPI improves the area under the curve (AUC: 0.876 and AUC: 0.878, respectively) for the detection of significant disease, compared with anatomical analysis alone (AUC: 0.826). Results from the MACHINE Registry (11) showed that CT-MPI, integrated with FFR-CT, improved the AUC from 0.70 to 0.85. This study used a DSCT system and an on-site algorithm; however, similar improvements are seen when anatomical analysis was combined with both functional technologies. In the current study, the increase in AUC from CCTA alone to an integrated approach was less pronounced than in MACHINE, mostly due to the high AUC of CCTA alone (0.70 vs. 0.83).

This study by Pontone et al. (5) confirms that CT-MPI and FFR-CT are complementary techniques and describes the necessity of developing an optimal decision-making algorithm for different patient populations. It is worth noting that the results are similar to studies with different FFR-CT and CT-MPI approaches and different CT systems, enhancing the generalizability of both of these technologies and pushing them toward clinical implementation.

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