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EDITORIAL COMMENT

Paving the Way for Clinical Implementation of Dynamic CT Perfusion*

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Coronary computed tomography angiography (CTA) has become an established diagnostic technique to diagnose and phenotype noninvasively coronary artery disease (CAD). Although coronary CTA performs well in ruling-out CAD, several studies have documented its low specificity in the detection of myocardial ischemia, limiting its value in the selection of patients who will benefit from coronary revascularization in addition to medical therapy (1,2). Distinct reasons may explain this, such as overestimation of lesion severity by visual assessment across all levels of stenosis (3). Moreover, the severity of coronary stenosis is only one of the factors involved in the pathophysiology of myocardial ischemia (4). This leads to the well-known mismatch between percent stenosis and impaired myocardial perfusion. Finally, the "intention to diagnosis" approach, frequently adopted in diagnostic performance studies involving coronary CTA, classifies as diseased coronary segments that are non-evaluable because of severe calcifications or motion artefacts, certainly leading to a higher rate of false positive findings (5).

The documentation of myocardial ischemia is a crucial step to guide clinical decision-making, especially in patients with intermediate coronary stenosis. Therefore, computed tomography perfusion (CTP) imaging was introduced as an attempt to overcome the limited ability of coronary CTA in detecting flow-limiting coronary stenoses (ie, causing myocardial ischemia) (6). Nowadays, CTP imaging has been performed by using either dual-source systems with shuttle mode technique (7) or wide-detector scanners, which allow the coverage of the entire myocardium in 1 gantry rotation (8). There are 2 different approaches to CTP imaging. Static CTP provides attenuation maps of the myocardium that can be inspected visually or semiquantitatively (9-11). On the other hand, dynamic CTP is a more appealing alternative since it allows quantification of myocardial blow flow (MBF) by applying mathematical models to time-attenuation curves constructed with data obtained from multiple acquisitions of the myocardium over time (7,8).

CTP is a physiological test that is not affected by the image quality and limitations of coronary CTA (eg, coronary stents and diffuse coronary calcifications). A recent meta-analysis demonstrated that adding the functional information of CTP to anatomical data increased coronary CTA specificity from 64% to 91% in detecting flow-limiting coronary stenoses (12). More importantly, in the CRESCENT II (Comprehensive Cardiac CT With Myocardial Perfusion Imaging Versus Functional Testing in Suspected Coronary Artery Disease) trial, implementation of dynamic computed tomography (CT) in the diagnostic work-up of patients with chronic coronary syndrome lowered the number of negative catheterizations compared with standard of care (13). Despite these undoubtful advantages, the use of dynamic CTP has been limited to a few centers and mainly to the research environment. This slow transition into clinical care may be the results of several factors, including the lack of standardization in acquisition protocols and image analysis, absence of an accepted cutoff value of MBF to identify myocardial ischemia, radiation dose, logistic challenges, and reimbursement issues.

In the this issue of *iJACC*, Nous et al (14) investigated the diagnostic performance of the combined use

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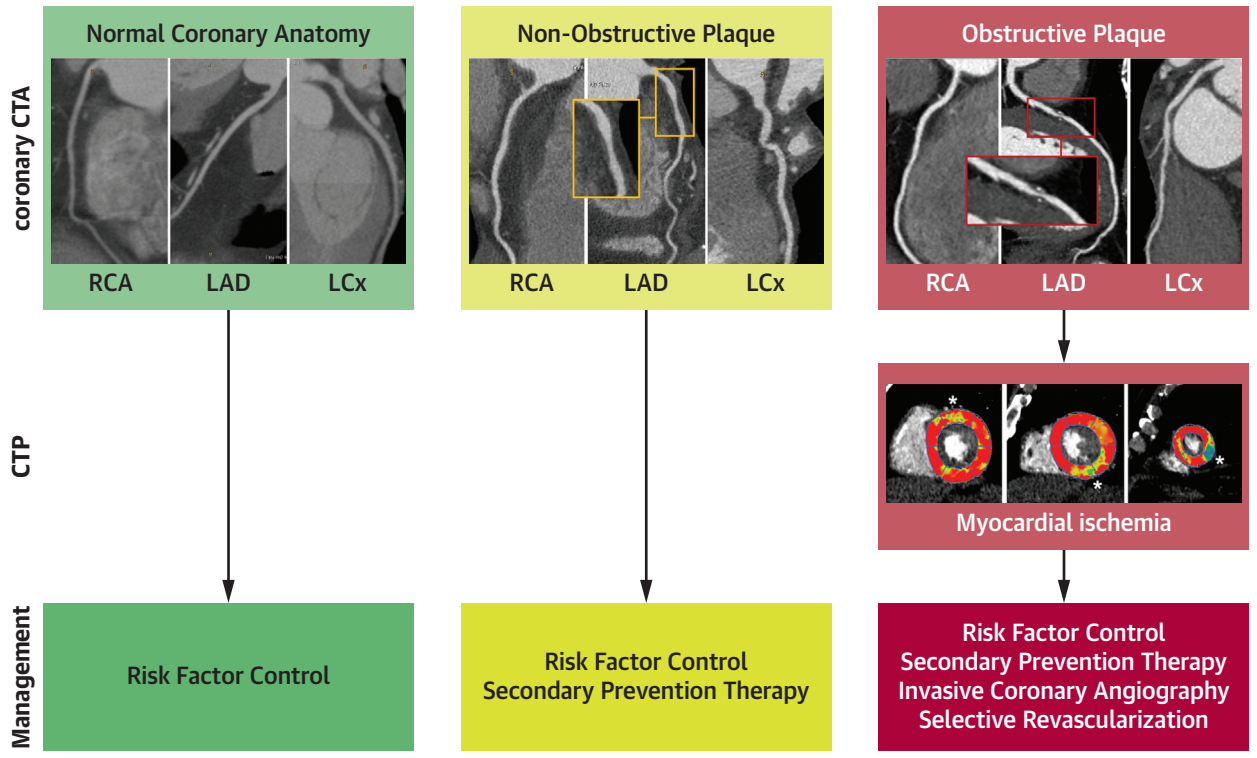
FIGURE 1 **Potential Role of CTP in the Management of Patients With Angina and Suspected Coronary Artery Disease**



*Presence of significantly reduced MBF in the anterior and infero-lateral walls of the left ventricle. Both territories are supplied by the LAD, which wraps around the left ventricular apex. CTA = computed tomography angiography; CTP = computed tomography perfusion; LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; RCA = right coronary artery.

of coronary CTA and dynamic CTP acquired during adenosine infusion for the detection of myocardial ischemia. The authors enrolled 132 patients with suspected CAD. All patients were referred for invasive coronary angiography and intermediate lesions (25%-90% diameter stenosis) were investigated with fractional flow reserve (FFR). In case of discordant coronary CTA and CTP findings, CTP overruled coronary CTA results. In line with previous published data, the current study confirmed the incremental diagnostic value of dynamic CTP when compared with coronary CTA alone, and this was predominant in moderately stenosed vessel (50%-69%).

The SPECIFIC (dynamic Stress PErfusion Ct for detectIon oF Inducible myoCardial ischemia) trial is the first prospective, observational, multicenter study investigating the diagnostic performance of dynamic CTP by using a third-generation dual-source CT scanner. We congratulate the authors for the rigorous analysis performed and for the use of independent core laboratories for each of the technologies involved. Moreover, the results of this study help solve some of the open issues related to CTP, thus contributing to strengthen the position of this novel imaging technology in the field of current cardiovascular medicine (**Figure 1**). First, the authors demonstrated that technical failure of CTP acquisition was comparable between centers with previous experience (>50 CTPs performed) and those with no experience. Second, the cutoff value of 0.80 for relative MBF is in the range reported in previous studies (7,15,16), demonstrating its robustness and consistency. Last, radiation dose decreased by nearly 50% compared with previous dual-source technologies, and therefore, it has become comparable to that reported for single-photon emission tomography studies.

However, several questions remain. One of the main advantages of quantitative perfusion techniques over visual analysis is the ability to detect myocardial ischemia in patients with 3-vessel

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disease. This aspect could not be evaluated in the study by Nous et al (14) because most patients included had either 1- or 2-vessel disease. Although the technical feasibility was not influenced by the experience of the center, the learning curve of the operator and the reproducibility of image analysis are still unknown, and they warrant further investigation. Although FFR is considered the clinical reference standard to document myocardial ischemia, MBF and FFR are not interchangeable because they measure 2 different aspects of coronary physiology. Indeed, FFR represents the hyperemic pressure gradient across a specific epicardial coronary artery, whereas MBF is a direct index of myocardial perfusion and considers both epicardial circulation and microvascular resistance (17). At the present time, robust studies comparing CTP with quantitative perfusion techniques, such as positron emission tomography and cardiac magnetic resonance, are still lacking.

The evaluation of diagnostic performance is only a small, although essential piece of the puzzle in the critical evaluation of a new imaging modality. In this regard, the multicenter prospective CTP-PRO (impact of stress Cardiac computed Tomography myocardial Perfusion on downstream resources and PROgnosis in patients with suspected or known coronary artery disease) study (18) is ongoing with the aim of comparing CTP against consolidated stress imaging tests, in a more unselected patient population, to evaluate the prognostic impact and cost-effectiveness of this emerging technique. Only fulfilling these mandatory steps, dynamic CT perfusion imaging will "climb up the ladder" in the real world.

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