EDITORIAL COMMENT

CT Assessment of Coronary Artery Disease
Trends and Clinical Implications*

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In this issue of *JACC: Cardiovascular Imaging*, Bettencourt et al. (1) compare myocardial scar imaging with computed tomography (CT) and cardiac magnetic resonance (CMR). The data are based on a comprehensive clinical CT protocol, including coronary computed tomography angiography (CTA), myocardial stress–rest computed tomography perfusion (CTP), and computed tomography delayed enhancement scar imaging (CTDE). The report is part of a series of recent papers using apparently the same patient cohort (1-3). The prior publications demonstrate that stress CTP imaging has diagnostic accuracy comparable to stress–rest CMR and, when added to anatomic assessment of luminal stenosis alone, increases the diagnostic accuracy of CTA. In the current paper, the authors show that the addition of CTDE does not provide further diagnostic value for the identification of patients with functionally significant CAD (defined as luminal stenosis by conventional angiography $\geq 90\%$ [$\geq 50\%$ in the left main stem], or fractional flow reserve [FFR] $\leq 0.8$ in vessels $>2$ mm).

What future impact could the results have for cardiac CT? The diagnostic goals in symptomatic patients with suspected CAD are: 1) identification and localization of hemodynamically significant lesions, defined based on severity of luminal stenosis and/or effect on myocardial perfusion; 2) prediction of risk for future cardiovascular events; and 3) optimization of subsequent therapeutic management. Based on a significant amount of data from single- and multi-center studies intrindividually comparing noninvasive with invasive coronary angiography, CTA has been shown to be a useful noninvasive test (4). CTA is characterized by a high negative predictive value (> 95%) and low negative likelihood ratio (< 0.05), and can therefore reliably exclude significant stenosis in selected patient populations with intermediate pre-test probability (5). This is applied to patients presenting with stable chest pain or with acute chest pain in the emergency department (6,7). However, there are several technical limitations compared with invasive coronary angiography: 1) longer image acquisition windows (temporal resolution $>75$ ms vs. $>20$ ms), with increased susceptibility to motion artifacts; and 2) lower pixel dimensions (spatial resolution $0.5$ mm$^2$ vs. $0.1$ mm$^2$), with increased susceptibility to volume averaging. Volume averaging is most obvious for calcified plaques (“calcium blooming”) and indicates that a small calcified subvolume of dense calcium can increase the density of an entire voxel above the calcium threshold. These limitations degrade image quality...
extensive data have accumulated demonstrating the prognostic value of CTDE. On the other hand, intermediate-high pre-test probability of patients with low-dose CT delayed enhancement detects ischemic myocardial scar with moderate accuracy but does not necessarily lead to increased downstream testing (8,9). Therefore, coronary CTA is typically not recommended in patients with known significant CAD, most coronary stents, diffuse calcified atherosclerotic disease, and those with a high and irregular heart rate, excluding a significant percentage of patients.

These technical limitations have been alleviated, but not resolved, with the latest, most advanced scanner generations, and only gradual advances are expected in the near future. Another approach to increase the value of CT is to evaluate additional characteristics of coronary lesions, and specifically, their functional significance, that is, myocardial ischemia/scar. The role of perfusion imaging is well established with positron emission tomography/single-photon emission computed tomography, stress echocardiography, and stress CMR (10). Stress CTP is feasible, but data are still relatively limited (11,12). The series of papers by Bettencourt et al. (1) and recently published results from CARS-320 (Coronary Artery Stent Evaluation With 320-slice Computed Tomography–The CArS 320 Study) (13) provide evidence that combined coronary CTA and myocardial CTP may allow improved diagnostic accuracy compared with CTA alone, in patients with native CAD or stents.

In the current report, Bettencourt et al. (1) demonstrate that the addition of CTDE scar imaging did not add further diagnostic value. Segments with scar (CTDE+), but without ischemia (CTP−) were reclassified as significant disease. However, most segments with scar also demonstrated ischemia (9 of 11), explaining the lack of diagnostic impact. The negative results may simply demonstrate that scar imaging is not a good marker for the identification of functionally significant CAD. In fact, data from positron emission tomography/single-photon emission computed tomography and CMR demonstrate that the value of scar imaging is rather its prognostic value for future cardiovascular events and mortality (14).

The current study was too small to look at follow-up events, and there are very limited data describing the prognostic value of CTDE. On the other hand, extensive data have accumulated demonstrating the prognostic information of disease burden defined by CTA (stenosis and plaque burden) on future cardiovascular events (6,15). Specifically, a negative coronary CTA is associated with a pooled annualized event rate of 0.17% per year for major adverse cardiac events and 0.15% for death or myocardial infarction, comparable to healthy, low-risk populations adjusted for age.

On the basis of the preceding, we believe that the following trends can be identified for appropriate use of cardiac CT:

- Improvement in the selection of the most suitable patient populations remains important (16).
- Evaluation of the impact of CTA on therapeutic management is critical and is the objective of the large U.S. multicenter PROMISE (PROspective Multicenter Imaging Study for Evaluation of Chest Pain) (17) and RESCUE (Randomized Evaluation of Patients With Stable Angina Comparing Diagnostic Examinations) trials (18).
- In patients with intermediate stenoses on CTA, subsequent stress CTP may direct management, similar to invasive FFR (19). This is examined in the CORE320 (Combined Coronary Atherosclerosis and Myocardial Perfusion Evaluation Using 320 Detector Row Computed Tomography) trial (20).
- The recently described concept of CT-FFR is interesting, but incompletely understood, and further evaluation will be important to define its potential clinical role (21).
- Lastly, although feasible and intriguing, current data are not sufficient to support clinical use of CTDE scar imaging in the diagnostic work-up of patients with suspected CAD.

Coronary CTA has developed into a valuable diagnostic option for certain symptomatic patient populations. CTP and perhaps CTDE will likely expand CTA’s application, but further evaluation of their impact on therapeutic decision making is necessary, optimally in trials with clinical endpoints.

References

1. Bettencourt N, Ferreira ND, Leite D, et al. CAD detection in patients with intermediate-high pre-test probability: low-dose CT delayed enhancement detects ischemic myocardial scar with moderate accuracy but does not

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