JACC: CARDIOVASCULAR IMAGING VOL. 11, NO. 11, 2018

PUBLISHED BY ELSEVIER

EDITORIAL COMMENT

Noninvasive Assessment of Coronary Anatomy and its Hemodynamic Consequences During a Single Test

Are We There Yet?*

Amit R. Patel, MD,[a,b] Neha Goyal, MD[a]

The presence of ischemia in patients with coronary artery disease is an important determinant of prognosis and identifies those individuals who are likely to benefit from revascularization. It is well known that the severity of a coronary stenosis alone does not determine the downstream myocardial perfusion. In fact, several recent trials utilizing invasive fractional flow reserve (FFR) have shown that patient outcomes are improved when the decision to perform revascularization is based on whether a coronary stenosis is hemodynamically significant rather than just its anatomical severity (1). These studies also demonstrate that nonhemodynamically significant coronary stenoses can safely be treated with medical therapy alone; whereas, medical management alone of hemodynamically significant stenoses may be associated with worse outcomes. The use of FFR, which is an excellent tool for determining the hemodynamic significance of coronary stenosis, is still an invasive strategy and there continues to be a need for a robust noninvasive approach for determining the presence of a coronary stenosis and its hemodynamic significance. The ideal strategy would provide both anatomic and functional data about coronary artery disease in an accurate, cost-effective, and convenient way that would improve patient outcomes and guide treatment plans.

Coronary computed tomography (CCTA) is an accurate, noninvasive imaging test that provides a detailed anatomical assessment of the coronary arteries comparable to invasive coronary angiography. CCTA has a high negative predictive value and use of CCTA has also been shown to help identify patients with nonobstructive disease that may benefit from medical therapy. However, it does not, by itself provide information about functional significance of a visualized lesion. The assessment of severity of stenosis may also not be accurate in the presence of coronary calcification, coronary stents, and bypass grafts. When compared with functional testing in the PROMISE (Prospective Multicenter Imaging Study for Evaluation of Chest Pain) trial (2), CCTA alone as an initial test for evaluating chest pain had similar clinical outcomes over a 2-year period as a functional-only test such as treadmill stress testing, stress single-photon emission tomography, stress echocardiography, and so on. However, a recent meta-analysis reviewing all randomized trials comparing CCTA to functional testing for the evaluation of chest pain has suggested that the use of CCTA may be associated with a decrease in myocardial infarction rates (3). To date, there have not been any randomized, controlled trials comparing CCTA alone to cardiac magnetic resonance or positron emission tomography stress testing.

The use of CCTA offers the potential to evaluate both coronary anatomy and its hemodynamic status during a single examination using techniques such as computed tomography fractional flow reserve (CT-FFR) or computed tomography perfusion (CTP) (4). CT-FFR is a technique that uses computational fluid dynamics to derive FFR values for any

*Editorials published in *JACC: Cardiovascular Imaging* reflect the views of the authors and do not necessarily represent the views of *JACC: Cardiovascular Imaging* or the American College of Cardiology.

From the [a]Department of Medicine, University of Chicago Medicine, Chicago, Illinois; and the [b]Department of Radiology, University of Chicago Medicine, Chicago, Illinois. Dr. Patel has received research grants from Philips Healthcare, General Electric, Astellas Pharma, and Myocardial Solutions; and serves on the Speakers Bureau for Astellas Pharma; none of these organizations had any input with regard to this editorial. Dr. Goyal has reported that she has no relationships relevant to the contents of this paper to disclose.

ISSN 1936-878X/$36.00 https://doi.org/10.1016/j.jcmg.2017.12.021

particular coronary stenosis. It can be derived from standard CCTA images without need for pharmacologic stress agents, additional image acquisitions, or further contrast administration. Several recent trials have compared CT-FFR against a reference standard invasive FFR and found that the technique has a reasonable diagnostic performance with an average per-vessel sensitivity of 83% and specificity of 78% (5). It has additionally been suggested that the use of CT-FFR as a gateway to invasive coronary angiography could potentially reduce the cost of evaluating and treating patients with coronary artery disease while preserving patient outcomes and improving quality of life (6). The clinical utility and appropriate cutoff values of CT-FFR are yet to be fully elucidated; in fact, a recent study demonstrated that CT-FFR had a very high diagnostic accuracy for detecting very abnormal FFR values (i.e., <0.60) but performed much worse for detecting clinically more challenging coronary stenoses with FFR values between 0.60 and 0.80 (7).

An alternative strategy would be to perform vasodilator CTP in patients noted to have a potentially significant coronary artery stenosis during the CCTA exam to determine which stenoses are hemodynamically significant and potential targets for revascularization. Such a strategy would mandate the use of a pharmacologic stress agent, acquisition of additional CT images, and administration of additional contrast. CTP has been compared against invasive FFR in several studies and also has a reasonable diagnostic performance with an average per-vessel sensitivity of 78% and specificity of 86% (8). It has been suggested that a strategy that includes the addition of CTP to CCTA can significantly reduce the number of patients that must subsequently undergo invasive coronary angiography without compromising patient outcomes (9).

SEE PAGE 1611

In the randomized, multicenter study presented in this issue of *iJACC*, Sørgaard et al. (10) focused on the added value of CTP to CCTA in patients presenting with acute chest pain. Six hundred patients were randomized to either a CCTA-only arm or a CCTA + CTP arm within 2 weeks of chest pain presentation. Patients with >50% stenosis in the CCTA-only arm and those with >50% stenosis and a downstream perfusion defect in the CCTA/CTP arm were referred for invasive FFR-guided coronary revascularization. The investigators noted that there was a significant reduction in the number of patients referred for invasive coronary angiogram in the latter group (14% vs. 30%). Interestingly, however, the study suggested no significant difference in the frequency of coronary revascularization in each of the subgroup of patients referred for invasive coronary angiography (48% in the CCTA group vs. 50% in the CCTA + CTP group). One would have expected a higher rate of revascularization in the group of patients referred for invasive coronary angiography after undergoing a hybrid CCTA/CTP study because such an approach ought to only identify hemodynamically significant stenoses. The failure of the hybrid CCTA/CTP approach to result in a higher rate of revascularization in the patients referred for invasive coronary angiography may have been due to a 15% drop-out rate in the CTA + CTP arm. In fact, when patients that dropped out of the CTA + CTP arm were excluded from analysis, the CTA + CTP strategy was indeed associated with a higher rate of revascularization as initially expected. No significant differences were noted in the overall outcome of patients with both techniques suggesting that CTA + CTP may be a safe strategy to reduce the number of patients referred for invasive coronary angiography; unfortunately, the study was likely not powered to conclusively determine this outcome. This study highlights the advantages of obtaining both coronary anatomy and function in a single study. The proposed approach could shorten time to diagnosis and management as well as reduce costs. Another important aspect of this study to consider is that the CTP was performed on 320 slice scanners, which have several important advantages that likely improved the overall quality of CTP imaging. The results from this study may not be applicable to exams performed on other types of CT equipment.

CCTA has gained wide acceptance for its ease of use, availability, cost, and for its negative predictive value. This can be complemented further by adding CTP to achieve the advantage of having a single noninvasive test capable of providing a detailed anatomic and functional assessment. CTP has now been evaluated in several small studies against a variety of reference standards; however, it is still in an experimental stage and not widely performed. Its utility needs to be studied in larger population groups and standard protocols need to be devised with regard to image acquisition and interpretation. Although this study adds important and promising data related to a CTA + CTP strategy for evaluating patients with chest pain, given that such an approach requires the administration of a vasodilator drug along with additional iodinated contrast and radiation exposure, a definitive randomized-controlled trial demonstrating the superiority of CTA + CTP over CTA + CT-FFR will be necessary if the technique

JACC: CARDIOVASCULAR IMAGING, VOL. 11, NO. 11, 2018
NOVEMBER 2018:1622–4

is to be recommended as a primary CCTA-based strategy to be used in all patients. For the same reasons, it may also be incumbent on us to prove that CTA + CTP is at least as clinically effective as (if not better than) more established stress-testing techniques that do not utilize ionizing radiation. The most convincing level of evidence would come in the form of a large, well-designed randomized outcomes-based trial. However, such propositions would be very costly, and we may need to be satisfied with lower levels of evidence that might be obtained from high-quality, risk-adjusted meta-analyses of prospective trials with a focus on patient outcomes and cost-effectiveness.

ADDRESS FOR CORRESPONDENCE: Dr. Amit R. Patel, University of Chicago, 5758 South Maryland Avenue, MC9067, Chicago, Illinois 60637. E-mail: amitpatel@uchicago.edu. Twitter: @AmitRPatelMD.

REFERENCES

1. Jeremias A, Kirtane AJ, Stone GW. A test in context: fractional flow reserve: accuracy, prognostic implications, and limitations. J Am Coll Cardiol 2017;69:2748–58.

2. Douglas PS, Hoffman U, Patel MR, et al., for the PROMISE Investigators. Outcomes of anatomical versus functional testing for coronary artery disease. N Engl J Med 2015;372:1291–300.

3. Bittencourt MS, Hulten EA, Murthy VL, et al. Clinical outcomes after evaluation of stable chest pain by coronary computed tomographic angiography versus usual care: a meta-analysis. Circ Cardiovasc Imaging 2016;9:e004419.

4. Singh A, Mor-Avi V, Patel AR. Update on computed tomography myocardial perfusion imaging. Curr Cardiovasc Imaging Rep 2016;9. pii:19.

5. Danad I, Szymonifka J, Twisk JWR, et al. Diagnostic performance of cardiac imaging methods to diagnose ischaemia-causing coronary artery disease when directly compared with fractional flow reserve as a reference standard: a meta-analysis. Eur Heart J 2017;38:991–8.

6. Nørgaard BL, Gaur S, Leipsic J, et al. Influence of coronary calcification on the diagnostic performance of CT angiography derived FFR in coronary artery disease. a substudy of the NXT Trial. J Am Coll Cardiol Img 2015;8:1045–55.

7. Cook CM, Petraco R, Shun-Shin MJ, et al. Diagnostic accuracy of computed tomography-derived fractional flow reserve: a systematic review. JAMA Cardiol 2017;2:803–10.

8. Takx RA, Blomberg BA, El Aidi H, et al. Diagnostic accuracy of stress myocardial perfusion imaging compared to invasive coronary angiography with fractional flow reserve meta-analysis. Circ Cardiovasc Imaging 2015;8. pii:e0026666.

9. van Rosendael AR, Dimitriu-Leen AC, de Graaf MA, et al. Impact of computed tomography myocardial perfusion following computed tomography coronary angiography on downstream referral for invasive coronary angiography, revascularization and, outcome at 12 months. Eur Heart J Cardiovasc Imaging 2017;18:969–77.

10. Sørgaard MH, Linde JJ, Kühl JT, et al. Value of myocardial perfusion assessment with coronary computed tomography angiography in patients with recent acute-onset chest pain. J Am Coll Cardiol Img 2018;11:1611–21.

KEY WORDS chest pain, ischemia, noninvasive, outcome, revascularization