JACC: CARDIOVASCULAR IMAGING
VOL. 9, NO. 10, 2016

ISSN 1936-878X/$36.00
PUBLISHED BY ELSEVIER
http://dx.doi.org/10.1016/j.jcmg.2016.01.037

EDITORIAL COMMENT

Pulling the RIPCORD

FFR_{CT} to Improve Interpretation of Coronary CT Angiography*

William F. Fearon, MD,[a] Jang Hoon Lee, MD[b]

The ideal method for identifying which patients warrant invasive coronary angiography to define the extent of coronary artery disease and the need for revascularization remains elusive. The traditional technique has been the clinical history combined with evidence of myocardial ischemia with reproduction of angina symptoms during electrocardiographic stress testing. Because of the relatively low sensitivity and specificity of the electrocardiogram in isolation, imaging modalities, such as echocardiography and myocardial perfusion scintigraphy, are often added to improve diagnostic accuracy. However, a major limitation of these approaches is the lack of anatomic data. The continued technical improvements with coronary computed tomography angiography (CTA) allow it to provide excellent anatomic information regarding coronary stenosis severity such that CTA compares favorably to traditional stress imaging modalities, which provide only functional data (1). Yet, CTA has been fraught with low specificity, resulting in unnecessary performance of invasive coronary angiography in a significant portion of patients. An ideal diagnostic tool would combine the anatomic resolution of CTA with reliable data regarding the functional significance of the visualized stenoses.

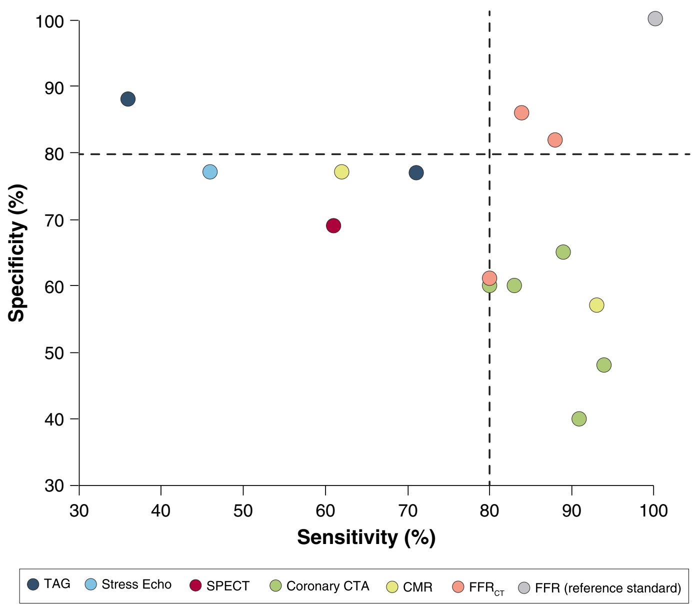
Myocardial fractional flow reserve (FFR), defined as the ratio of maximal myocardial flow in the presence of a coronary stenosis to maximal flow in the theoretical absence of the stenosis, has become the reference standard for determining the functional significance of a coronary stenosis (2). Conventionally, FFR is measured invasively using a coronary pressure wire at the time of coronary angiography to assess the ratio of mean distal coronary pressure (a reflection of flow when resistance is minimized during hyperemia) to mean proximal coronary pressure (measured with the guiding catheter and a reflection of normal flow in the absence of any stenosis) during hyperemia, typically induced by administration of adenosine. FFR has been validated against a noninvasive reference standard for diagnosing ischemia (3), and its use to guide revascularization decisions has been shown to improve outcomes in a variety of clinical settings (4).

By using the anatomic data derived from CTA combined with computer modeling of the flow characteristics across a given stenosis and solving the governing equations of fluid dynamics, Taylor et al. (5) introduced a method for noninvasively calculating FFR, which they termed computed tomography-derived fractional flow reserve (FFR_{CT}), and which allows CTA to provide not only useful anatomic data but also important functional data for each individual stenosis. The addition of FFR_{CT} significantly improves the diagnostic accuracy of CTA compared with invasively measured FFR, with correlations between FFR_{CT} and invasive FFR that appear more favorable than reported in previous studies comparing other noninvasive stress imaging modalities with invasive FFR (**Figure 1**) (6). For example, in the recently published multicenter NXT (Analysis of Coronary Blood Flow Using CT Angiography: Next Steps) trial comparing CTA and FFR_{CT} with invasively measured FFR in 484 patients, FFR_{CT} had a significantly improved specificity on a per vessel basis of 86% compared with 60% ($p < 0.0001$) and a significantly improved overall diagnostic accuracy of 86% compared with 65% using CTA alone ($p < 0.0001$) (7). Based on these results and others, FFR_{CT} has now been approved for clinical use in the United States by

*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]Division of Cardiovascular Medicine, Stanford University, Stanford, California; and the [b]Department of Internal Medicine, Kyungpook National University Hospital, Daegu, South Korea. Dr. Fearon has received research support from St. Jude Medical and Medtronic; and serves as a consultant to Medtronic and HeartFlow. Dr. Lee has reported that he has no relationships relevant to the contents of this paper to disclose.

FIGURE 1 Chart Comparing Sensitivity and Specificity of Numerous Commonly Used Methods for Noninvasively Detecting Ischemia-Producing Coronary Artery Disease Compared With a Reference Standard of Invasively Measured Fractional Flow Reserve



CMR = cardiac magnetic resonance myocardial perfusion imaging; CTA = computed tomography angiography; FFR$_{CT}$ = computer tomography-derived fractional flow reserve; SPECT = single-photon emission computed tomography; TAG = transluminal attenuation gradient. Modified with permission from Nørgaard et al. (6).

the Food and Drug Administration. The logistics regarding reimbursement for this technique and more rapid derivation of FFR$_{CT}$ and transfer of results are expected to be solved in the near future.

SEE PAGE 1188

In this issue of *iJACC,* the FFR$_{CT}$ RIPCORD study by Curzen et al. (8) provides further data supporting the utility of broadly applying FFR$_{CT}$ to our patients undergoing CTA. Leveraging data from the NXT trial, they reanalyzed 200 consecutive patients in whom CTA was performed for clinical reasons and FFR$_{CT}$ was then performed as part of the original trial. In the present study, 3 interventional cardiologists (presumably proficient at interpreting CTA) reviewed the CTA for each patient and by consensus decided on a management plan of medical therapy, percutaneous coronary intervention, coronary artery bypass graft surgery, or the need for more information. The FFR$_{CT}$ data for each patient were then revealed, and the group revised their plan accordingly.

The investigators found that the FFR$_{CT}$ data changed their plan in 36% of cases. Of the 38 patients in whom more information was required based on CTA alone, all were reallocated to medical therapy or to revascularization; 8 patients allocated to medical therapy moved to revascularization; and 26 of the patients assigned to percutaneous coronary intervention based on CTA alone were reassigned to medical therapy. Amazingly, 30% of vessels with >90% stenosis on CTA had FFR$_{CT}$ >0.80, suggesting the stenosis was not functionally significant, whereas almost 10% of vessels with narrowing <50% had FFR$_{CT}$ ≤0.80. These findings highlight the effect FFR$_{CT}$ can have on decision processes even when used routinely in a consecutive group of patients. Because of the high negative predictive value of a normal CTA, one would not anticipate much added benefit from FFR$_{CT}$ in cases with normal CTA, which appeared to be a significant minority in this study. Therefore, if one only applied FFR$_{CT}$ to cases in which the CTA was abnormal, one could anticipate even more dramatic differences in the treatment plan before and after incorporation of the FFR$_{CT}$ data.

Missing from this study are the data from the invasively measured FFR, which was performed in all patients in the original NXT trial. It would have been interesting to see how well the management plan based on the FFR$_{CT}$ data correlated with the ultimate treatment decision on the basis of the invasive coronary angiogram and FFR assessment. It is also unclear why the investigators did not include all 484 patients in the NXT trial, except for their desire to mimic the original RIPCORD study (9). Finally, demonstration that FFR$_{CT}$ improves clinical outcomes will be necessary before its routine application. A step in this direction came from the recently published PLATFORM (Prospective Longitudinal Trial of FFR$_{CT}$: Outcomes and Resource Impacts) study, which compared a strategy of CTA with adjunctive FFR$_{CT}$ to either a routine noninvasive stress testing strategy or a routine invasive coronary angiography strategy and showed that CTA and FFR$_{CT}$ can reduce the number of unnecessary coronary angiograms without missing cases of obstructive coronary artery disease (10). The study also found that, compared with routine noninvasive stress testing, FFR$_{CT}$ improves quality of life at a similar cost (11). Curzen et al. (8) should be congratulated for providing further evidence that it is time to "pull the ripcord" on relying on CTA alone for treatment decisions in our patients with stable chest pain by adding FFR$_{CT}$ to our algorithm.

REPRINT REQUESTS AND CORRESPONDENCE: Dr. William F. Fearon, Stanford University Medical Center, 300 Pasteur Drive, H2103, Stanford, California 94305. E-mail: wfearon@stanford.edu.

REFERENCES

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

2. Pijls NHJ, van Son JAM, Kirkeeide RL, De Bruyne B, Gould KL. Experimental basis of determining maximum coronary, myocardial and collateral blood flow by pressure measurements for assessing functional stenosis severity before and after percutaneous transluminal coronary angioplasty. Circulation 1993;86:1354–67.

3. Pijls NHJ, De Bruyne B, Peels K, et al. Measurement of fractional flow reserve to assess the functional severity of coronary-artery stenoses. N Engl J Med 1996;334:1703–8.

4. Fearon WF. Percutaneous coronary intervention should be guided by fractional flow reserve measurement. Circulation 2014;129:1860–70.

5. Taylor CA, Fonte TA, Min JK. Computational fluid dynamics applied to cardiac computed tomography for noninvasive quantification of fractional flow reserve: scientific basis. J Am Coll Cardiol 2013;61:2233–41.

6. Nørgaard BL, Jensen JM, Leipsic J. Fractional flow reserve derived from coronary CT angiography in stable coronary disease: a new standard in non-invasive testing? Eur Radiol 2015;25:2282–90.

7. Nørgaard BL, Leipsic J, Gaur S, et al. Diagnostic performance of noninvasive fractional flow reserve derived from coronary computed tomography angiography in suspected coronary artery disease: the NXT trial (Analysis of Coronary Blood Flow Using CT Angiography: Next Steps). J Am Coll Cardiol 2014;63:1145–55.

8. Curzen NP, Nolan J, Zaman AG, Nørgaard BL, Rajani R. Does the routine availability of CT-derived FFR influence management of patients with stable chest pain compared to CT angiography alone? The FFR_{CT} RIPCORD study. J Am Coll Cardiol Img 2016;9:1188–94.

9. Curzen N, Rana O, Nicholas Z, et al. Does routine pressure wire assessment influence management strategy at coronary angiography for diagnosis of chest pain? The RIPCORD study. Circ Cardiovasc Interv 2014;7:248–55.

10. Douglas PS, Pontone G, Hlatky MA, et al. Clinical outcomes of fractional flow reserve by computed tomographic angiography-guided diagnostic strategies vs. usual care in patients with suspected coronary artery disease: the prospective longitudinal trial of FFRCT: outcome and resource impacts study. Eur Heart J 2015;36:3359–67.

11. Hlatky MA, De Bruyne B, Pontone G, et al. Quality-of-life and economic outcomes of assessing fractional flow reserve with computed tomography angiography: PLATFORM. J Am Coll Cardiol 2015;66:2315–23.

KEY WORDS chest pain, computed tomography angiography, computed tomography angiography-derived fractional flow reserve