FFRCT: Why Should Interventional Cardiologists Care?

Is FFRCT the holy grail of combined noninvasive coronary anatomic and physiologic evaluation?

BY OMAR KHALIQUE, MD, FACC, FASE, FSCCT, FSCMR

The history of coronary artery evaluation originated with anatomic evaluation via invasive coronary angiography (ICA). Since that "ancient time," testing for coronary artery disease (CAD) has evolved. Currently, a number of noninvasive tests are available and can be divided into two categories: functional and anatomic. The former category has been dominant in the recent past. Functional noninvasive tests include stress echocardiography, single-photon emission CT (SPECT), positron emission tomography, and stress cardiac MRI. Noninvasive anatomic testing is limited to cardiac CTA (CCTA). However, despite the plethora of available noninvasive imaging modalities, none of the existing data have proven the superiority of any one modality.[1,2]

UTILIZATION OF CCTA

With the rapid development and increased application of CCTA in the 2000s, a lot of excitement percolated around anatomic characterization of the coronary arteries, which could theoretically obviate diagnostic ICA for CAD characterization. However, it turned out that CCTA has a very powerful negative predictive value but poor positive predictive value and is hampered by blooming artifacts in the presence of calcification. Due to the high sensitivity and negative predictive value, CCTA performs an excellent function as a gatekeeper modality when CAD is ruled out. Based in part on the results of the SCOT-HEART trial,[3] the United Kingdom has adopted CCTA as a first-line imaging modality for all patients presenting with new-onset chest pain due to suspected CAD. However, clinical usage of CCTA has remained low in the United States, and practice patterns have heavily favored SPECT. The large amount of data behind functional testing such as nuclear myocardial perfusion imaging and stress echocardiography as well as difficulties in CCTA reimbursement have remained challenges for this technology.

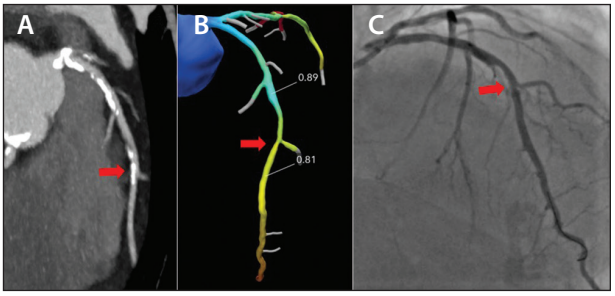
DIAGNOSIS AND PREDICTION OF OBSTRUCTIVE CAD

Observational studies of thousands[4] or hundreds of thousands[5] of patients with suspected CAD have shown that only about half of patients had invasively proven obstructive CAD despite the use of noninvasive stress testing. Although multicenter, multimodality imaging studies are often difficult to interpret due to heterogeneity in imaging methods and expertise, studies such as these clearly suggest that there is significant room for improvement in detecting ischemic epicardial CAD. Although functional stress testing is often positive due to epicardial CAD, there are other reasons for a positive test. For example, global wall hypokinesis may be induced by severe hypertension or valvular disease during stress imaging and perfusion abnormalities may occur from microvascular disease or artifacts.

FFRCT IMAGING

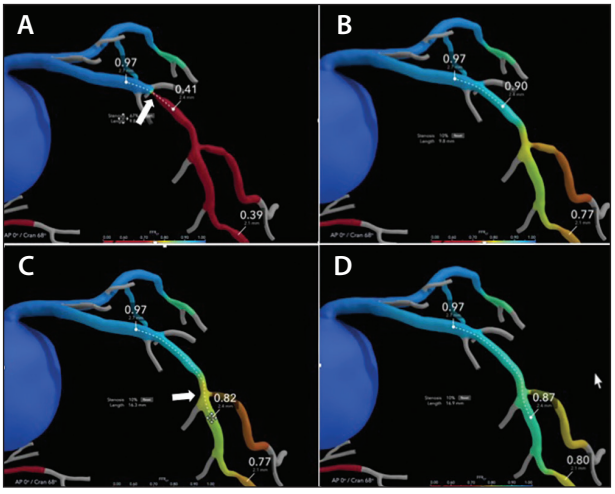
Technology

Fractional flow reserve derived from CT (FFRCT) has rapidly progressed and is being used clinically in Europe, Canada, Japan, and the United States. FFRCT is based on standard CCTA imaging and utilizes heart rate control with β-blockers and sublingual nitroglycerin to achieve hyperemia. FFRCT is more accurate than CCTA for identifying narrowing in heavily calcified coronary arteries.[6] FFRCT may be particularly useful to adjudicate intermediate stenosis found on CCTA. The method



Courtesy of Elvis Cami, MD.

Figure 1. FFRCT of an intermediate lesion in a symptomatic patient with multivessel disease. Panel A shows a maximum intensity projection of the left anterior descending (LAD) coronary artery on CCTA, where a mid LAD lesion (red arrow in all panels) was read as intermediate severity, with 50% to 70% stenosis. Panel B shows FFRCT analysis with a value of 0.81 beyond the lesion. On invasive angiography for PCI of a severe left circumflex lesion, the FFRinv value was 0.85, supporting the decision-making from the FFRCT study (C).



Courtesy of Elvis Cami, MD.

Figure 2. Interactive FFRCT planning tool. Simulates post-PCI FFRCT. Panel A shows an FFRCT value of 0.41 across a mid LAD lesion (white arrow). Panel B shows a normalized FFRCT value after virtual stenting of the lesion. A more distal LAD lesion in the same patient shows a borderline FFRCT value of 0.82 (C), with an improvement to 0.87 after PCI (D). Note: This tool is produced by HeartFlow and is currently for investigational use only.

developed by HeartFlow, Inc. is currently the only FDA- and CE Mark–cleared FFRCT technology. In short, a three-dimensional (3D) anatomic model of the epicardial coronary arteries, aorta, and myocardium is created. Machine learning techniques aid in creating a mesh of the coronary lumen with subvoxel accuracy.[7] These same machine learning techniques allow for interpretation of the lumen for 3D anatomic modeling in calcified vessels that is superior to that of the human eye. For each vessel supplying the myocardium, resting and hyperemic microvascular resistance are quantified by the 3D anatomic and microvascular resistance models. Using computational fluid dynamics, a color-coded, 3D anatomic model with FFRCT values available in every location of the coronary tree is generated. A simple point-and-click tool can then be used to display FFRCT values in the desired location. When the FFRCT value is combined with the patient-specific anatomic coronary map, functionally significant lesions can be identified (Figure 1).

FFRCT Versus FFRinv

It has long been known that an invasive FFR (FFRinv) value of < 0.80 across a coronary lesion is a worthy target for percutaneous coronary intervention (PCI), based on the currently available data.[8-10] FFRCT has shown a per-vessel accuracy of 86%, sensitivity of 84%, specificity of 86%, positive predictive value of 61%, negative predictive value of 95%, and area under the curve value of 0.93 when compared with FFRinv.[11,12]

FFRCT and the Interventional Cardiologist

Given the potential inaccuracies with FFRCT assessment, what promise does it hold for the interventional cardiologist? The very title of interventional cardiologist may provide an answer. The 1-year results of the PLATFORM trial showed a reduction in the total number of ICAs performed and an increase in the percentage of interventions performed during ICA in patients with suspected CAD using an FFRCT-guided invasive approach as compared with a standard invasive approach.[13] What interventional cardiologist would not desire a more efficient interventional practice whereby a higher percentage of ICAs result in interventions? Increasing use of and expertise with FFRCT may lead to fewer unnecessary diagnostic catheterizations and more efficient throughput of patients with lesions requiring intervention.

Cost-effectiveness is an important consideration for the interventionalist as well. In the era of burgeoning health care costs, a more cost-effective system that has positive effects on patient care benefits everyone. The PLATFORM study showed an approximate 26% cost reduction when using an FFRCT-guided invasive strategy versus a usual care invasive strategy. Positive cost data have driven the recent approval for reimbursement by the Centers for Medicare & Medicaid Services and by many private insurers.

Due to rapid advancements in technology, cardiac imaging is at the forefront of cardiology decision-making. In structural heart and valve programs around the world, interventional cardiologists are reading and interpreting structural heart CTAs for transcatheter aortic valve

replacement and increasingly for other valvular procedures. This allows vertical integration and preprocedural understanding of the anatomy to be encountered during the procedure. It behooves the coronary interventionalist to apply the same integration to CCTA with FFRCT to guide interventional decision-making. Official CCTA interpretation by interventional cardiologists at early FFRCT-adopting centers has demonstrated a seamless integration of noninvasive imaging and intervention.

Limitations of FFRCT

Accurate interpretation of CCTA and FFRCT depends on image quality. Typical issues, such as arrhythmias, high heart rate, and other artifacts, will hinder interpretation. Long calcified areas may also present a challenge for the 3D anatomic modeling required for FFRCT calculation. Regional reimbursement and embedded practice patterns across the United States may hinder adoption despite the advantages of the technology. Changes in United States guidelines favoring CCTA based on recent data will also be needed to increase utilization moving forward.

Future Directions

Although procedural planning is robust with CCTA and FFRCT, the technology is advancing to new levels. Although not yet available for clinical use, PCI planning tools are being evaluated in the research setting. One such interactive tool under investigation enables the user to simulate treatment scenarios and noninvasively predict the resulting FFRCT, as well as predict and compare post-PCI FFRCT. This could be of particular use in intermediate and sequential lesions (Figure 2). Early evaluations have shown the feasibility of this approach.[14,15] Randomized trials such as the PRECISE trial will further evaluate and refine the role of FFRCT in clinical practice. Early investigation is being performed on noncoronary intracardiac flows using computational fluid dynamics, which would be a related exciting advancement in cardiac CT imaging.[16]

SUMMARY

FFRCT is an exciting new technology that blends anatomy and physiology for CAD assessment. The increasing involvement of the coronary interventional cardiologist in pre-PCI CCTA and FFRCT assessment, similar to the vertical integration approach of the structural heart and valve interventionalist, as well as relevant changes in guidelines to increase appropriate usage of CCTA will be key factors in driving the field forward. ■

1. Douglas PS, Hoffmann U, Patel MR, et al. Outcomes of anatomical versus functional testing for coronary artery disease. N Engl J Med. 2015;372:1291-1300.
2. Greenwood JP, Ripley DP, Berry C, et al. Effect of care guided by cardiovascular magnetic resonance, myocardial perfusion scintigraphy, or NICE guidelines on subsequent unnecessary angiography rates: the CE-MARC 2 randomized clinical trial. JAMA. 2016;316:1051-1060.
3. SCOT-HEART Investigators, Newby DE, Adamson PD, et al. Coronary CT angiography and 5-year risk of myocardial infarction. N Engl J Med. 2018;379:924-933.
4. Chinnaiyan KM, Raff GL, Goraya T, et al. Coronary computed tomography angiography after stress testing: results from a multicenter, statewide registry, ACIC (Advanced Cardiovascular Imaging Consortium). J Am Coll Cardiol. 2012;59:688-695.
5. Patel MR, Dai D, Hernandez AF, et al. Prevalence and predictors of nonobstructive coronary artery disease identified with coronary angiography in contemporary clinical practice. Am Heart J. 2014;167:846-852.
6. Norgaard 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. JACC Cardiovasc Imaging. 2015;8:1045-1055.
7. Min JK, Taylor CA, Achenbach S, et al. Noninvasive fractional flow reserve derived from coronary CT angiography: clinical data and scientific principles. JACC Cardiovasc Imaging. 2015;8:1209-1222.
8. De Bruyne B, Pijls NH, Kalesan B, et al. Fractional flow reserve-guided PCI versus medical therapy in stable coronary disease. N Engl J Med. 2012;367:991-1001.
9. Smits PC, Abdel-Wahab M, Neumann FJ, et al. Fractional flow reserve-guided multivessel angioplasty in myocardial infarction. N Engl J Med. 2017;376:1234-1244.
10. Tonino PA, De Bruyne B, Pijls NH, et al. Fractional flow reserve versus angiography for guiding percutaneous coronary intervention. N Engl J Med. 2009;360:213-224.
11. Norgaard 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;63:1145-1155.
12. Koo BK, Erglis A, Doh JH, et al. Diagnosis of ischemia-causing coronary stenoses by noninvasive fractional flow reserve computed from coronary computed tomographic angiograms. Results from the prospective multicenter DISCOVER-FLOW (Diagnosis of Ischemia-Causing Stenoses Obtained Via Noninvasive Fractional Flow Reserve) study. J Am Coll Cardiol. 2011;58:1989-1997.
13. Douglas PS, De Bruyne B, Pontone G, et al. 1-year outcomes of FFRCT-guided care in patients with suspected coronary disease: the PLATFORM study. J Am Coll Cardiol. 2016;68:435-445.
14. Kim KH, Doh JH, Koo BK, et al. A novel noninvasive technology for treatment planning using virtual coronary stenting and computed tomography-derived computed fractional flow reserve. JACC Cardiovasc Interv. 2014;7:72-78.
15. Modi BN, Sankaran S, Kim HJ, et al. Predicting the physiological effect of revascularization in serially diseased coronary arteries. Circ Cardiovasc Interv. 2019;12:e007577.
16. Lantz J, Gupta V, Henriksson L, et al. Intracardiac flow at 4D CT: comparison with 4D flow MRI. Radiology. 2018;289:51-58.

Omar Khalique, MD, FACC, FASE, FSCCT, FSCMR
Director, Multimodality Cardiac Imaging
Structural Heart and Valve Center
Assistant Professor of Medicine
Columbia University Medical Center
New York, New York
ok2203@cumc.columbia.edu
Disclosures: None.