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

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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 \(\beta\)-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...
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 FFRC for guide interventional decision-making. Official CCTA interpretation by interventional cardiologists at early FFRC-adopting centers has demonstrated a seamless integration of noninvasive imaging and intervention.

Limitations of FFRC

Accurate interpretation of CCTA and FFRC 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 FFRC 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 FFRC, 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 FFRC, as well as predict and compare post-PCI FFRC. 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 FFRC 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

FFRC 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 FFRC 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.


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