

Dear Colleagues,

Noninvasive evaluation of symptoms thought to be related to coronary artery disease (CAD) occupies a considerable portion of provider time and contributes significantly to cost of care of both commercial and Medicare populations. Noninvasive diagnostic options, which have become available over the past 50 years, can broadly be divided into two categories: anatomical and physiological. Anatomical testing provides direct imaging of the coronary arteries and includes modalities such as coronary CTA and coronary MRI. Physiological testing does not provide direct images of the arteries but instead, relies on some parameter indicative of reduced coronary blood flow (impaired wall motion, reduced myocardial radio tracer uptake). Although there has been ongoing debate as to whether physiological or anatomical testing is superior, the fact remains that neither is perfect, as evidenced by the fact that upwards of 60% of patients referred for diagnostic coronary angiography do not have obstructive CAD.

It has long been thought that the “Holy Grail” of noninvasive CAD imaging would be an approach that would provide **both** anatomical **and** physiological information. That combination is now being tested, with the advent of software which allows calculation of fractional flow reserve (FFR) from standard coronary CTA imaging – so called FFR_{CT}. FFR measured in the catheterization lab involves the use of Doppler flow wires to measure pressure and flow in a diseased vessel. It has been shown to be useful in determination of the necessity of revascularization. Based on a limited number of studies, FFR_{CT} measurements appear to correlate with the FFR values derived from invasive cardiac catheterization (correlations range from 63% to 82% across studies)¹, demonstrating that a patient who undergoes CCTA with FFR_{CT} may be evaluated both anatomically and physiologically.

The clinical and economic implications of CCTA with FFR_{CT} could be immense. If that approach proves to be more accurate in diagnosis or exclusion of myocardial ischemia than other noninvasive testing currently available, then the use of other testing (myocardial perfusion imaging, stress echocardiography, perfusion PET and MRI protocols) would become second-line approaches. Utilization of diagnostic coronary angiography in the non-acute setting would be rare and percutaneous coronary intervention (PCI) would be reserved for those patients in whom FFR_{CT} demonstrated significant flow limitation and symptoms were not relieved by medical therapy.

However, one caveat is that FFR_{CT} has only been evaluated in relatively small patient samples, and further studies are required to confirm the accuracy and clinical outcome/impact, especially longer-term outcomes. Furthermore, FFR_{CT} is not considered a standard of care currently and is performed at certain centers only.

How much evidence-support does CCTA with FFR_{CT} currently have?

- The NXT trial² demonstrated a per-patient sensitivity and specificity for diagnosis of myocardial ischemia by FFR_{CT} of 86% and 79% respectively (using FFR derived in the catheterization lab as a gold standard). Although no head-to-head comparisons with other available technologies are available FFR_{CT} compares better with FFR than myocardial perfusion imaging (the modality most often used in this scenario).
- The PLATFORM trials^{3,4} demonstrated the feasibility and safety of CCTA with FFR_{CT} as an alternative to conventional evaluation pathways. Importantly, in patients for whom cardiac catheterization was planned as part of their clinical evaluation, CCTA/FFR_{CT} significantly reduced the likelihood of diagnostic cardiac catheterization showing no significant obstructive CAD. Furthermore, there was no change in major adverse cardiovascular events with incorporation of FFR_{CT} into clinical workflows. However, it is worth noting that the tested population has been limited to stable patients, and with only short-term observational data. There are no longer-term data currently.
- Resource utilization and cost of care impact of protocols incorporating FFR_{CT} have recently been addressed in the literature.^{5,6} Although economic benefit has been demonstrated in subgroups of

patients, the information continues to evolve. It is likely, however, that by reducing downstream utilization of diagnostic cardiac catheterization and PCI, CCTA/FFR_{CT} will realize cost savings (at best) or will be cost neutral at worst. It is noteworthy that the National Institute for Health and Clinical Excellence, which develops best practices for the British National Health Service (and incorporates cost in developing its recommendations), has concluded that there are cost savings associated with the use of CCTA/FFR_{CT}.

In summary, our clinical and research team behind-the-scenes at our Cardiology Solution vigilantly keeps on top of new technologies such as CCTA with FFR_{CT} as part of our efforts to provide appropriate, safe, and affordable health care services and keep you, our medical directors and chief medical officers informed. With new technologies always emerging, we will keep a sharp eye on CCTA with FFR_{CT}. Is it the "Holy Grail"? Only time will tell. One thing is certain - you will hear more about it, and hopefully, we can provide the most up-to-date information to keep you informed on its progress.

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