



A CELERIAN GROUP COMPANY

Open Meeting: Non-Invasive Flow Reserve (FFR) for Stable Ischemic Heart Disease

Meeting Date and Time:	October 13, 2020 2:00 p.m. EST
Facilitator:	Dr. Meredith Loveless
Location:	Teleconference
Attendees:	Not to disclose

Dr. Loveless began the meeting at 2:00 P.M. ET for the proposed policy of Non-Invasive Flow Reserve (FFR) for Stable Ischemic Heart Disease.

Introduction

This technology is used to estimate the change in coronary blood flow related to coronary artery stenosis and traditionally required catheterization. With the newer technologies that are being introduced, this can be calculated from a computer, from CT images and the degree of potential to stenosis is calculated with post-processing software. This allows the potential for patients to avoid an invasive procedure if it's not necessary.

The current policy, Non-Invasive Fractional Flow Reserve (FFR), has left main disease. We are focusing this policy on intermediate coronaries stenosis. The post-processing is done after the CT scan is complete. This is not amendable to acute evaluation and is limited to symptomatic and stable ischemic heart disease

- Left main from 30-50%
- Other vessels from 40-70%

There are multiple limitations to be discussed by the presenters.

Main Points

- Limited to patients with stable coronary symptoms
- It is performed after the base study is completed
- Higher grade stenoses are excluded because those patients are triaged to catheterization.
- Low grades to stenoses are excluded because those typically do not require additional confirmatory data
- More than two intermediate risk lesions are excluded because that typically would proceed directly to catheterization.

Comments

Please send comments to CMD.INQUIRY@cgsadmin.com by November 22, 2020.



Presentations

Dr. Roger Campbell disclosed that he is an employee of Heart Flow.

Pathway Overview

The basic pathway discussed is that patients who are stable, just as was described, present and then undergo Coronary CTA. That is the only test required in approximately three out of four patients. The FFRCT is then acquired, so there's this bifurcated pathway and then the FFRCT elements are provided to the physician to aid in his or her decision making about whether invasive evaluation may be warranted.

Exclusions

There are some concerns with the following about artifacts that might may introduce into the CTA images and would make it difficult or impossible to provide the FFRCT analysis.

- #1: Severe obesity(BMI >39 kg/m2)
- #2: Prior placement of prosthetic valves
- #9: Prior pacemaker or defibrillator lead placement

Recommendation is that rather than include these three as absolute exclusions, excluding some patients who may well be analyzable by heart flow. It should be reworded to say that if image quality is unacceptable that there will be feedback. There will be no FFRCT processing, no charge.

The next suggested revisions to draft exclusions were:

- #3: Known severe aortic stenosis
 - » Recommendation to remove entirely. There is not impact on physiology as LV mass is considered in the FFRCT analysis
- #5 Suspicion of acute coronary syndrome
 - » Revise to the following: Suspicion for acute coronary syndromes (where acute myocardial infarction or unstable angina have not been ruled out)
 - » This is the verbiage also used in Palmetto's final LCD version.
- #6 Intracoronary metallic stent
 - » There are specific instances where coronary stents can or cannot be analyzed, patients with those stents can be analyzed. Those are outlined in the instructions for use, it is not a pan.
 - » Recommendation that the revisions be revised to match what's is listed in HeartFlow's ISU and are cleared FDA clearance.

HeartFlow's Image Quality Assessment

A quantitative evaluation is done to determine if this scan meet the quality required for HeartFlow's FDA cleared process for FFR CT Evaluation. If the quality is impaired from a heart valve or a lead then the FFRCT does not need to be complete. There is not charge for the case since there is no FFRCT analysis. HeartFlow provides explanation for failed cases and training to help improve image quality of future studies.

The spectrum of image quality from coronary CT images were shown. Overall, there is a 90% acceptance rate for real-world use of this technology. The published literature and the references will be included in the written comments.

Invasive FFR

Of critical importance is the clause inclusion in the draft LCD which prohibits use of obtaining pressure by invasive pressure wire at catheterization.

- We believe this does not belong in the draft LCD. that there will absolutely be clinical utility to measuring invasive FFR or IFR using a pressure wire or other devices at the time of catheterization. In some patients after they have FFRCT

Inclusions

The percent stenosis range as measured in our largest study to date, which is 5000 patients, all of whom had CTA and FFRCT shows that by eliminating the range of 70 to 90% stenosis,

fully 25% of those lesions will be FFR negative. Physicians may use that information to avoid an invasive procedure depending on the clinical circumstances. By assuming all patients, over 70% will have a positive FFR, which was what would happen if this technology were not available to these patients. Is that that 25% of patients would be managed in a manner as to the physiology of their coronaries which may help them pursue a less invasive pathway.

The data we have on the outcomes for this are that if you look at patients with this range of stenosis, nearly two thirds will have a different management plan after FFRCT than they would have had with CTA alone. And this is all published in our peer reviewed publications.

Recommendation-The list of inclusions be revised to left main disease with intermediate coronary stenosis 30 to 50%.

In vessels other than the left main coronary disease with stenosis is uncertain functional significance lumen reduction of 40 to 90%.

Dr. Mark Rabbat disclosed that he is on the Advocacy Committee of the Society of Cardiovascular CT and a HeartFlow consultant.

FFR Fractional Flow Reserve is the gold standard invasive test to appropriately identify patients who benefit from revascularization. FFR can be derived noninvasively from a standard CT dataset and has been noted to have high diagnostic performance.

There have been multiple clinical trials in high impact journals demonstrating the improvement and long-term outcomes for patients with this diagnostic strategy with the demonstration of safe deferrals of unnecessary invasive coronary angiography ends in patients with coronary artery disease.

The patients included in these clinical trials had a diameters doses in the range of 30 to 90% diameter reduction. A significant percentage of individuals had stenosis in the 70 to 90%-severe range.

A significant proportion of those in the 70 to 90% stenosis category are able to safely defer unnecessary invasive coronary angiography. In addition, those just multi vessel severe coronary artery disease in the 70 to 90% range FFRCT to the CT anatomic dataset there's often a change management strategy.

For example, many patients get downgraded from more invasive coronary artery bypass graft surgery based off of the CT anatomy alone and that severe multi vessel disease category range to a single or two vessel percutaneous intervention after FFRCT in multi vessel disease.

Dr. Rabbat provided data of clinical experience of over 400 patients demonstrating that FFRCT is feasible in over 90% of patients. FFRCT was able to safely differ unnecessary ICA with no major adverse cardiac events. Of those who undergo ICA there's a high proportion of revascularization leading to more efficient utilization of the test lab. In this analysis, a significant proportion of patients in the 70 to 90% diameter reduction.

It is recommended for physicians who perform CT to follow SCCT guidelines for performance and acquisition.

As of April 2020, a positive FFRCT findings can be used in lieu of invasive FFR, IFR, CDR, TCI registries and the appropriate use criteria for stable ischemic heart disease. This was endorsed by both the American Heart Association as well as American College of Cardiology this year.

Exclusions

Recommendation criteria:

- Exclusion:
 - » Recommendation of updating to what Palmetto recently published.
 - Suspicion for coronary syndromes, where acute MI or unstable angina has not been ruled out
 - » Acceptable image quality as defined by HeartFlow criteria
 - » Only exclude anatomy that would affect hemodynamic accuracy
 - » NSTEMI/STEMI/UN (<=30 DAYS)
 - » New systolic heart failure with no prior invasive catheterization

Inclusion

- Left main disease with intermediate coronary stenosis (30-50%)

- Coronary artery disease with coronary stenosis of uncertain functional significance (40-90%)

Emphasizing the inclusion criteria to include coronary artery disease with coronary stenosis of uncertain, functional significance, in the 40 to 90% time under reduction. As a society not including those patients with 70 to 90% stenosis would be a disservice to the patients that we serve.

We also recommend including left main disease with intermediate coronary stenosis in this 30 -60% diameter reduction rang.

The American College of Cardiology underwent a CTA roundtable summit. There summary around more widespread CMS coverage and payment for both FFRCT and CTA being quite clear as a first line diagnostic test for patients with stable coronary artery disease.

Dr. Ragapopalan does not report any COI.

The criteria to include coronary artery disease between 40-90% is appropriate, given the fact that it's difficult to reach these vessels to establish functional significance. Having the ability to satisfy the functional significance of those lesions, 40% is greater than 40% all the way to 90%. I think one of the major goals of this technology is really a triage workflow, to help determine who indeed has cardiac diseases, essentially asking who truly deserve to go to the Cath lab. The second, the two other criteria around inclusion of patients, were allowing patients with (could not transcribe...) There's a good percentage of those pieces on the evaluation, especially the older patient population, health, concomitant disease, specifically diagnostic evaluation. It's an advantage to actually understand the physiology of coronary artery disease. In our experience, my experience, at least in many of those cases, it's still possible to evaluate the coronary arteries. It's best to send the images are sent to HeartFlow to make the validation. Whether or not these images are suitable diagnostic quantity in order to slow the process. So it's often dependent on position and if it interferes such as pacemaker. And one of the other comments made earlier during Dr. Rogers's presentation was the idea that, once you, once you have CT fractional flow invasive studies will not be reimbursed, I think, that is somewhat limited. Because, in many cases, there could be, although it's a small percentage of cases, sometimes you do fine some discordance as the ability to measure the flow in some cases where there is a concern.

Dr. Bruce Samuels

CTFFR advance to the understanding of coronary physiology utilizing computational fluid dynamics as opposed to direct measurements has been very useful.

There have been some limitations of documented literature to the utilization of CTFFR as a substitute for invasive coronary physiology. The Pacific trial, the re-assessed trial, and the multiple other studies that have been discussed today in comparison to invasive FFR correlation in general is quite good. This is driven primarily by the remarkable sensitivity with a poor overall specificity. The ability to rule out disease is extremely high with CT angiography CTFFR.

When you have a CTFFR that's been performed and it shows a negative physiologic results, It gives the interventionist or the clinician great diagnostics ability to be able to inform somebody who does not need to come to the cath lab.

When the test is abnormal and when it gets particularly close to the dichotomous threshold of 0.8 the diagnostic accuracy compared to invasive FFR starts to get very poor and the specificity approaches 50%. There are certain studies that have shown positive predictive value, but most of the studies have shown that the value can be trusted when under point .65.

A clinical decision is needed as the results are closer to the discriminatory value of 0.8 . The discriminatory value falls off and this was shown very well in multiple studies that are included in references sent to CGS.

When there is patient in the lab with a CTFFR that's been performed, which is getting near the discriminatory cutoff of 0.8. There will be time when clinically, what is being seen in the lab will jive with what was seen with the FFRCT.

To make a decision, which could be critical to the life of their patient by relying simply on a noninvasive test, which has limited positive predictive value and unlimited specificity in this extremely important clinical area.

James Men founder and CEO of Clearly

- The diagnostic performance characteristics of CT favor its use as a safe and effective referral management tool.

- » When reviewing the prior multi-center clinical trials that looked at CT versus invasive angiography for the detection and exclusion of high grade coronary stenosis, you can see from the sensitivity on the negative predictive value that it really is very high.
- » An image was shown that depicts a large-scale randomized controlled trial called conserve. 1600 randomized patients who are being referred to the cath lab, either to cath as they were normally being referred to do or to selective cath strategy where physicians were asked to perform a noninvasive CT angiogram first.
- » The end point was a 12-month end point at both economic and clinical outcomes. The 12-month mark, there was a 77% reduction in cath rates if you underwent that selective CT first strategy, that was associated with a 60% decrement and normal capped, at 21%, reduction in revascularization, and a 57% reduction in overall diagnostic cost.
- Real-world I interpretation of CT is associated with significant overestimation of stenosis
 - » The Promise Trail consisted of a 10,000 patient randomized trial where the CT core lab published this study where they looked at the concordance between the expert core lab and then the site interpretation of the CT scan
- Severe stenosis by CT should not be the primary focus
 - » In a study of 2500 patient who have either mild disease or no disease with less than 50% stenosis who were followed for 3.1 years for mortality. There is an increased risk of death.
- Atherosclerosis-guided evaluation and treatment improves prognostic risk stratification and patient-centered outcomes
 - » The evolution of the field of coronary CT angiography really came from 2005 with the introduction of 64 slice CT scanners. In 2015 there was this sort of frame shift where we realized that for the last 40-50 years we've been using stress testing to look for ischemia and invasive angiograms look for stenosis.
 - » Atherosclerotic plaque is very complex. When an artery is cut it is visibly noticeable that the plaques are different and have different features.

The ICONIC Study followed 25,000 patients 3.5 years and during that 3.5 years, 234 patients experienced an acute coronary syndrome. The patients were matched 1 to 1 with patients who did not experience the acute coronary syndrome sometime after their CT scan for all of these factors, including stenosis, severity.

- The majority of the patients who will have a heart attack in the future actually have mild stenosis that are less than 50%.
- The type of play is the strongest discriminant of future heart attack risk

SCOT-HEART randomized control trial demonstrated a 40% reduction in death myocardial infarction if somebody underwent a CT guided strategy. Better preventive medical therapy drove the benefit and outcome.

Atherosclerosis-guided evaluation and treatment is not feasible in current clinical practice

- Too time-intensive: up to 8 hours per patient analysis
- Too much data to process
- Too opaque

Cleerly aims to apply CT imaging into a digital care pathway to support doctors and patients improve diagnosis, prognostic risk stratification, and clinical decision making.

Cleerly Digital Care Pathway is a four step process.

- The disease phenotype-extract a CT scan into a cloud and the several hour image analytic time is reduce a matter of minute, and there's a cardiac CT technologists overseen by a doctor, who verifies that the machine learning that what the machine was supposed to do.
- Clinical solutions are delivered to all of the stakeholders in the care pathway.
- Patient solution
 - » Step 1-AI enabled comprehensive coronary artery disease evaluation
 - FDA objective and quantitative software
 - Rapid Turn Around Time
 - High Diagnostic Performance
 - Intuitive User Experience

- » Step 2-For the Imaging Physician
 - Deliver solutions to the stakeholders in the care pathway.
- » Step 3-For the Clinician
 - A second software platform called, Cleerly coronary that is intended for the doctor in the office who doesn't have an experience in imaging
 - Can be used for training
- » Step 4-For the Patient
 - The patient gets a 25-page report focused on the coronary artery disease
 - Helps the patient understand heart attack risk and how cleerly can help decipher their risk, and provide results

The AMA issued CPT codes for the Cleerly platform relating really to the quantification and characterization of coronary atherosclerotic plaque to assess the severity of coronary disease.

Conclusion

The research has shown that CT can be a highly effective referral management tool, if the interpretation is quantitative and accurate

CT identified atherosclerosis is what identifies the patient at risk and that preventive medical therapy can really improve the outcomes.

AI enabled analysis allows for comprehensive coronary disease evaluation

Empower every stakeholder in the care pathway so that they can improve their understanding, their diagnosis, risk stratification, and decision making.

Cleerly has a formal partnership with the American College of Cardiology to improve patient outcome.

Closing

Coronary artery disease is a major concern for the Medicare population and a large cause of morbidity and mortality.

Dr. Loveless gave thanks to all of the presenters, cardiologists, and providers who have joined us and their commitment to helping develop new technologies to improve the lives and outcomes for our beneficiaries and for the research and hard work that you do in order to help improve health long-term.

Presenters were asked to submit supporting literature with any comments.