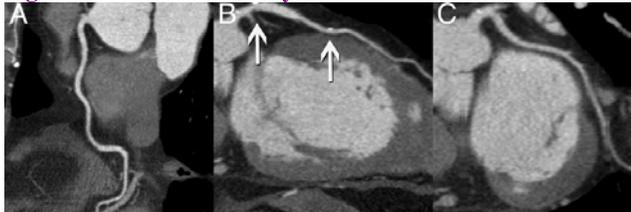


Cardiac CT Angiography: Window to our Hearts “Not as Clear as Advertised”

Cardiac computed tomographic angiography (CCTA) is revolutionizing our approach to the identification and management of coronary artery disease (CAD)—Figure 1. CCTA has the unique ability to assess extracoronary cardiac findings within the standard field of view, including the anatomy of cardiac structures—the atria, ventricles, valves, pericardium, great vessels, and venous anatomy—and any related abnormalities.

Figure 1. CCTA of coronary arteries.



A. right coronary artery, B. left anterior descending coronary artery (LAD), and C. left circumflex coronary artery.

Appropriate clinical applications include evaluation of intermediate-risk patients with acute chest pain and those with suspected coronary anomalies, uninterpretable or equivocal stress test results, or suspected cardiac morphologic abnormalities. Optimization of this diagnostic examination requires close attention to details such as minimizing motion and attaining sufficient contrast opacification. Iso-osmolar contrast can help achieve maximum patient comfort with the smallest elevation of heart rate and variability, as well as minimize the risk of acute kidney injury. Newer scanning

equipment and protocols have improved image quality in difficult cases, including obese patients, and those with heavy coronary calcification or metal artifacts. Current imaging protocols have reduced exposure to ionizing radiation and continue to improve safety. This *Heartbeat* will review recent studies to determine if CCTA is living up to the hype.

A Bridge Too Far and Too Soon

Systematic analysis of published studies using CCTA to determine the presence of coronary obstruction show marked variation in results and were inconclusive.¹ Two more recent studies suggest a lot more study is needed. The first, published in July 2008 is one of the first studies to examine the utility of CCTA as a screening tool for the detection of CAD in asymptomatic individuals.² The authors conclude that CCTA has the potential to provide good insight, but after weighing the pros and cons, they say it is far too soon to recommend this as a strategy. "On the basis of our results and considering present radiation-exposure data, we cannot recommend that CCTA be used as screening tool for this population at this point." They advocate that further studies be done.

The second was from John Hopkins, published in November 2008. It was an international, multi-center study in which the study population had a higher prevalence of disease than is seen in the general outpatient population, demonstrating that

CCTA is accurate in identifying coronary stenoses and in characterizing disease severity in symptomatic patients who have coronary calcium scores of 600 or less.³ However, multi-detector CCTA cannot be used as a simple replacement for conventional coronary angiography, given its negative predictive value of 83% and positive predictive value of 91% in this population of patients. In an accompanying perspective piece,⁴ Redberg and Walsh note that the study “does not advance our knowledge of the appropriate use and possible benefits of the technology.” *Until we have solid evidence of benefits and clarity about how best to incorporate the evidence into decision making, routine use of CCTA should be avoided to assess patients for CAD.*

The latest study to compare the diagnostic accuracy of CCTA to the gold standard—conventional coronary angiography (CCA)—indicates that the technology does a good job of ruling out significant CAD but overestimates disease severity, likely leading to more tests and their inherent risks.⁵ Study researchers emphasize that a rule-out test is a key asset for a screening tool, but an accompanying editorial by Dr Steven Nissen (Cleveland Clinic, OH) takes a dimmer view, suggesting that the implications of a false-positive study far outweigh the benefits of a rule-out test.⁶

The study included 360 symptomatic patients with acute and stable angina referred for CCA at one of three European centers. In addition to CCA, all patients also underwent a calcium scan and CCTA using one of several different brands of 64-slice scanners. Using CCA as the gold standard, researchers reported that CCTA had a sensitivity of 99% for detecting patients with at least one significant coronary stenosis, but a specificity of 64%, a negative predictive value of 97%, but a positive predictive value of 86%. On a per-segment basis, the sensitivity was lower but the specificity was higher. More strikingly, while the negative predictive value was nearly

100%, the positive predictive value, on a per-segment basis, was less than 50%.

The authors note that the high sensitivity of CCTA is in keeping with other, smaller, mostly single-center evaluations of CCTA, but that the disappointing specificity of 64% is lower—other investigators have typically published specificity results ranging from 79% to 100%. This study included all available coronary segments, regardless of image quality leading to lower specificity to more closely mimic a situation in which patients with a positive CCTA result or a nonevaluable CT scan would end up undergoing CCA. The lower specificity also points to the fact that patients in this study had a high pretest likelihood of significant CAD. Most feel that using CCTA in the moderately high-risk group (10-20% pretest likelihood of CAD) as a screening test will make it a little more sensitive and specific.

Giving us pause

But Nissen, in his editorial, says the results “should give us pause.” “When applied routinely in symptomatic patients at risk of coronary disease, in more than 50% of subjects, CCTA ‘detected’ coronary obstructions that simply were not there.” Indeed, he points out, of 98 patients in whom CCTA detected three-vessel disease, only 19 patients were found, on CCA, to actually have three-vessel disease, a false positive rate of 81%. *“This high false-positive rate has potentially serious implications, leading to unnecessary and potentially risky procedures that threaten to accelerate already-excessive healthcare costs.”*

According to Nissen, arguments by advocates of CCTA—that CT could be used in tandem with physiological testing or that its true value is as a rule-out test—ignore the costs and safety concerns of stacking additional tests. “CCTA is being deployed rapidly, and there exist no incentives for industry or physician advocates to seek the clinical-trial data we need to effectively use this imaging modality.” (A CT scanner costs about a million dollars. And a patient scan runs between \$500 and \$1,500. Last year an estimated

150,000 people in the U.S. got a CT scan at a total cost of more than \$100 million.)

"Accordingly, we need a restricted use of CT angiography until adequate clinical evidence becomes available showing the cost-effectiveness and safety of this approach," along with "real-world" trials and studies demonstrating that CT leads to improved patient outcomes.

In response, **Dr Pim de Feyter** (Erasmus University Medical Center), senior author on the study, tried to balance Nissen's concerns. "I agree with his conclusion that indiscriminate use of CTA should be prevented," de Feyter told **heartwire**. "Many aspects of the role of CCTA with regards to other noninvasive tests are not known and require more studies. However, many studies have shown that CT is reliable in ruling out the presence of CAD, and this may be, at present, where CT may be useful. We still consider CT a research tool, and in a few instances CT may be helpful to rule out CAD."

CT is not (yet) "running amok"

Dr Michael Budoff (UCLA), likewise, pointed out editorials like Nissen's overlook the fact that these types of studies are necessary and meaningful. "I thought this study was excellent," he said, particularly since it reinforces the negative predictive value of CCTA seen in other studies, including the **ACCURACY** trial, which looked at a lower-risk population. "This is a multicenter, multivendor trial that validates the potential for this test to be used to rule out CAD. It also reinforces the fact that this is *not* an ideal test when the prevalence of disease is high. . . . We need to use this when we're not sure that patients need to go to the cath lab, not when we're sure."

The problem, says Budoff, is that critics of CCTA angiography seem to forget that the test needs to be validated against the gold standard before other comparative studies (against nuclear imaging or stress echocardiography) or outcome studies can be done. "This is just a validation study. People are trying to take these early

validation studies to mean that these are not the definitive proof that we should do this test, and I would agree with that. This is one piece of the puzzle, but it's an important first piece." Budoff believes that the impression emerging from editorials like Nissen's and others imply that CT tests are being used widely and inappropriately. In fact, cardiac CT angiograms make up just a few hundred thousand of the 62 million CT scans being done per year, and use of CT angiography is 1/100th of that of nuclear imaging, he says. Moreover, the types of studies that critics are calling for *are* being done and in many cases have been presented at the major meetings. So the information "is out there," he says. Indeed, the appropriateness criteria published by the **ACC**, in partnership with seven other organizations, concisely describe the clinical situations (intermediate risk) in which CCTA angiography is a reasonable option

Perspective:

CCTA seems to be a step backward. Compared with conventional angiography, the angiograms produced by multi-detector CT scanners are much lower in quality and are suboptimal for diagnostic purposes—superimposed on the usual limitations of routine CCA, including the absence of physiological information and poor correlation with histology, but it is further constrained by poor image quality. To overcome quantum statistical noise and other quality limitations, larger radiation dosages are used, typically averaging 15 mSv, with specific organ systems receiving substantially higher exposure levels, about 5 to 7 times the dosage used for an optimal invasive CCA.⁷

In chronic ischemic CAD, symptoms result principally from the ability of stenoses to blunt increases in blood flow in response to increases in metabolic demands. This phenomenon is called coronary flow reserve (CFR). It is thought that CFR remains normal (typically a 5- to 7-fold increase in flow) until the stenosis approaches 75%. Between 75% and 95%, CFR decreases progressively. Accordingly, the angiographic

differences between moderate and severe lesions may be only a few tenths of a millimeter. Such differences are difficult to discern given the limitations in resolution of the best CCA and impossible to resolve with CCTA.

Furthermore, CCTA drives us back to making decisions based on luminal obstruction and the *oculostenotic reflex*. Last month's *Heartbeat* was spent on emphasizing functional anatomy (non-invasive risk stratification) along with CCA results with a strong push to calculate fractional flow reserve as part of the complex evaluation in difficult cases to determine need for revascularization.⁸ Based on the present data CCTA would add increased cost and radiation exposure without any proven benefit.

Risk

CT scanning in U.S. cardiology practices has increased threefold in the last two years and is expected to continue to rise. The cancer risk from a single CCTA is small but not negligible. The **FDA** has announced a small chance of developing a fatal cancer due to a 10-mSv CT study. The risk for women was found to be higher than for men and the risk to younger patients was higher than for older ones. But concerns about increases in cancer risk from increased radiation exposure remain. It must be remembered that many patients receive radiation exposure (CT scanning) for multiple other conditions and the doses are additive.

A study including 21 university and 29 community medical centers this month concluded, median doses of CCTA differ substantially (6 times the lowest dose) between study sites compared and CT systems.⁹ Effective strategies to reduce radiation dose are available, but some strategies are infrequently used. On February 2nd in *Circulation*, the American Heart Association issued an advisory to doctors urging the judicious use of CT scans for CVD. *Further study is needed to show that the potential benefits of screening outweigh the harmful effects of CCTA.*

Anything wrong with this picture?

CCTA imaging systems advertise the promise of safe and painless detection of CAD. Weekend courses are being offered everywhere to allow cardiologists to “learn” this new technology and apply it routinely for patient-care. Equipment manufacturers are glad to show practitioners how they can rapidly recoup their million-dollar investments. Interestingly, officials of Medicare had decided last summer not to reimburse for CCTA outside of study trials. After extensive lobbying by six societies (American College of Cardiology, American Society of Nuclear Cardiology, American College of Radiology, Society for Cardiovascular Angiography and Interventions, North American Society for Cardiac Imaging, and the Society of Cardiovascular Computed Tomography (SCCT) —who all signed onto a statement expressing their disagreement with the proposed national determination and argued for keeping existing payment—the decision was reversed.

Increasing use of CCTA is part of a much larger trend in American medicine. A faith in innovation, often driven by financial incentives, encourages doctors and hospitals to adopt new technologies before there is proof that they work better than older techniques. Patient advocacy groups and some doctors are clamoring for such evidence. But the story of the CCTA is a sobering reminder of the forces that overwhelm such efforts, making it very difficult to rein in a new technology long enough to determine whether its benefits are worth its costs.

Some medical experts say our devotion to the newest, most expensive technology is an important reason that the US spends more on health care than other industrialized nations — more than \$2.2 trillion in 2007, an estimated \$7,500 a person, about twice the average in other countries — without providing better care. This is an extremely important issue relevant to the dire straits of our present economy, the costs of

health care and the number of uninsured and under-insured.

CCTA as the new *window to our hearts* may not be as translucent as anticipated—thus far—based on our review. These studies suggest it may be risky, overused, inaccurate and too costly. **Restricted use of CCTA is called for until more studies are done regarding its accuracy, safety and improved outcomes.**

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