Is Computed Tomography Coronary Angiography the Most Accurate and Effective Noninvasive Imaging Tool to Evaluate Patients With Acute Chest Pain in the Emergency Department?

CT Coronary Angiography Is the Most Accurate and Effective Noninvasive Imaging Tool for Evaluating Patients Presenting With Chest Pain to the Emergency Department: Antagonist Viewpoint

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The presentation of a patient with acute chest pain remains one of the most vexing problems in contemporary medicine. It is estimated that more than 6 million visits to the emergency department (ED) occur annually in the United States, with a primary complaint of chest pain.1,2 Although an acute coronary syndrome (ACS) accounts for only a small portion of these presentations, the concern of regarding a “missed” diagnosis is high, as failure to detect an ACS may place a patient in significant medical jeopardy and occurs as frequently as 4% of all cases.2 Due to the high medical penalties of a missed diagnosis, including an elevated risk-adjusted mortality rate,2 it is not surprising that medical malpractice claims for a failure to diagnose myocardial infarction/ACS constitute the most common reason for medical litigation, accounting for up to 20% of all medical lawsuits.3 The financial exposure from these claims, as well as the defensive posture frequently undertaken to avoid such litigation, results in more than $7 to $10 billion of “unnecessary” health care expenditures annually.1,4

Response by Hoffmann and Bamberg on p 275

Chest pain with clear ECG changes or elevations in serum biomarkers, such as CK-MB or troponin, do not pose a clinical dilemma, and management algorithms are quite clear. However, more than 80% of patients with chest pain in the ED do not have a final diagnosis of ACS, and few if any have findings suggestive of ischemic heart disease. A wide variety of approaches for these patients exist. Chest pain evaluation strategies include detailed clinical assessment, serum biomarkers, resting ECG, and determination of overall risk for ACS such as with the Thrombolysis in Myocardial Infarction (TIMI) score.5 However, even the most validated of these approaches lacks diagnostic accuracy and often did not predict an ACS.5 Additionally, short-term outcomes, including the need for revascularization, were not predicted, and noninvasive testing was thought to be indicated.6 Although this diagnosis may be made on clinical grounds in the majority of individuals, this level of “sensitivity” is not acceptable given the potential risk for missing unstable angina or myocardial infarction. Therefore, it is clear that additional methods for triage of patients with acute chest pain of an unknown etiology are needed and may include early stress testing, rest single-photon emission computed tomography (SPECT), myocardial perfusion imaging (MPI), echocardiography, stress imaging, and cardiac CT. In summary,
there is no debate regarding the clinical problem and the desire for an accurate decision-making solution.

Cardiac CT

A plethora of medical literature has been developed over a very short time, primarily focused on the diagnostic accuracy of CT coronary angiography (CCTA). The field has rapidly expanded, especially since the development of 64-slice technology, which has demonstrated outstanding diagnostic accuracy and a marked reduction in technically inadequate examinations, compared with the older 8- or 16-slice devices. A recent review of 64-slice CT demonstrated sensitivities of ≥90%, with specificity of 88%. Thus, a negative CCTA appears to reliably exclude significant coronary artery disease (CAD). Therefore, this article will focus exclusively on 64-slice CCTA because this should now be considered the standard for the field; no extrapolations should be made for older, less sophisticated technology because by definition, these scanners should be considered obsolete and inadequate for coronary angiography.

Recently, 2 important multicenter trials of 64-slice CCTA have been published, showing high diagnostic accuracy. Both trials wisely incorporated an intention-to-treat design, whereby all segments were included in the analysis, and in 1 study, an unevaluable segment was designated “abnormal.” The ACCURACY Trial compared CCTA with invasive coronary angiography (ICA) in 230 patients without known CAD. The patient cohort was unique and consisted of low-intermediate risk patients, similar to a potential ED population. Outstanding sensitivity and a negative predictive value of 99% were achieved, effectively excluding the presence of CAD. Although it is tempting to extrapolate these results to suspected acute chest pain syndromes, the authors appropriately point out that as all patients were already referred for ICA, the conclusions should not be extended to an ED population. Specificity, however, was probably compromised (83%) due to the all-inclusive nature of the design; the low specificity may lead to frequent downstream testing, which may be inappropriate in ED patients. A second multicenter evaluation of 64-slice CCTA was also commendable in that no patients, vessels, or coronary segments were excluded by design by Budoff et al and confirmed that a negative CCTA effectively ruled out significant CAD. However, 11% of patients who had insignificant stenoses on ICA were thought to have obstructive disease on CCTA, and the overall specificity was only 64%.

As noted, although these 2 multicenter studies of 64-slice CT were well designed and were able to exclude obstructive CAD as defined by ICA, both had low specificity (64% to 83%) and low positive predictive value (64% to 86%). If this approach was transferred to ED patients, a large number of patients probably would require additional diagnostic testing. Prospective ECG gating was not used in either study, and no dose modulation was used in 1 trial to provide maximum information and to minimize unevaluable vessels; the radiation dose was therefore high (5 to 18 mSv). This strategy raises questions about the use of dose modulation in ED settings, where there is a clear need to maximize diagnostic information and to exclude CAD whenever possible.

CCTA in the ED

Despite the interest and proliferation of cardiac CT, there remains limited data regarding the specific application of this technology to patients who present to the ED with acute chest pain, especially when restricted to a 64-slice scanner. Sixteen-slice devices are suboptimal for use with coronary angiography and may deliver inferior diagnostic accuracy, including only an 83% sensitivity. Despite the passing of several years since the dissemination of 64-slice CT machines, there are still few published reports of CCTA in ED patients; many of these studies have small numbers of patients, often fewer than 100. Additionally, none of the trials have been multicenter investigations, although several such studies are underway. Furthermore, few trials have been adequately randomized or controlled to eliminate either selection or treatment bias.

Trials examining CCTA for patients with suspected ACS are inconsistent with regard to patient selection criteria. This is extremely important when attempting to define which cohort of patients is best suited for this new technology. Although some trials focused on low-risk patients, others selected intermediate-risk patients and occasionally a wide range of risk (very low to intermediate risk) was included. Additionally, many studies excluded patients with known CAD, thereby limiting applicability for many ED patients.

End point selection for these clinical trials also varied widely. The most definitive and probably useful measure for the value of CCTA in ED patients would be a final diagnosis of an ACS, based on biomarkers and ECG findings. However, this end point was used in few trials and the actual frequency of ACS in several studies was zero, probably because of the low-risk cohort. In 1 of the larger trials of CCTA in the ED, Holland et al examined more than 500 low-risk patients (low TIMI score and nonischemic ECG) and demonstrated that 84% of patients could be discharged after CCTA, with no cardiac events in the 30-day follow-up period. It is likely, however, that these low-risk patients may have done just as well without the performance of a CT scan.

Several trials have used a composite end point, which may include findings from ICA and/or SPECT MPI. However, combined end points may be misleading because they may not truly reflect the ability of CCTA to risk-stratify potential patients with ACS. One of the key concerns with much of the CCTA/ACS literature is the use or incorporation of an anatomic end point, based on ICA. It is logical that CCTA, being a determinate of coronary anatomy, would favorably agree with ICA, another anatomic end point. Although diagnostic correlation between CCTA and ICA has been well documented and supported in this report, it does not validate the selection of ICA as a clinically meaningful end point for stratification of patients with suspected ACS. The importance of end point...
The failure of CCTA to detect an obstructive coronary lesion noted on ICA is infrequent with 64-slice CCTA, although not absent. However, the lack of high-grade stenosis may not eliminate a possible ACS. Etiologies such as myocardial bridging, variant (Prinzmetal) angina, and microvascular disease (Syndrome X) may account for a patient with acute chest pain to be diagnosed with ACS in the absence of significant angiographic disease. In fact, angiographically normal coronary arteries have been demonstrated in up to 8.5% of documented ACS.\(^{23}\) Thus, the ability to risk-stratify patients with suspected ACS with CCTA should not be based solely on the detection of an obstructive stenosis. Atherosclerotic plaque characterization is an intriguing application of CCTA and may be useful for assessment of patients with suspected ACS\(^{24,25}\) because calcium and an obstructive stenosis are not necessarily present in lesions that cause ACS. The evaluation of plaque morphology holds promise for use in patients with acute chest pain in the ED but has yet to rigorously define the key factors, including plaque density and extent; the clinical utility of plaque characterization is, at this point, unproven.

Conversely, does a CCTA study demonstrating obstructive CAD confirm an ACS, which is the critical question in the ED? Once again, the physiological importance of the stenosis is paramount. Although the detection of subclinical (and non-ACS) atherosclerosis may have long-term importance, the most vital data for the ED physician is the patient’s risk of a major cardiac event and the possibility of a missed ischemic event. When CCTA demonstrates a high-grade obstructive lesion, it appears logical to consider the patient’s chest pain as possibly related to ischemic heart disease. For intermediate lesions with approximately 50% to 70% diameter narrowing, the clear lack of correlation with physiology prohibits firm conclusions about risk of an ACS, as will be discussed.

Although pundits applaud the high negative predictive value and superb sensitivity of CCTA, with which there is consensus, false-positive rates raise another concern. The ROMICAT study examined 103 patients with chest pain in whom the results of CCTA were compared with a final diagnosis of ACS,\(^{20}\) which was a composite end point. Although superb sensitivity and negative predictive value were described, the specificity and positive predictive value of 82% and 47%, respectively, may lead to additional and possibly unwarranted testing and therapy. Similarly, in a recent editorial discussing the work of Meijboom et al,\(^{10}\) the presence of false-positive CCTA results was thought to lead to unnecessary and potentially hazardous procedures, as well as continuing to escalate health care expenditures.\(^{26}\) Nissen notes that >50% of patients studied with 64-slice CT were found to have obstructive lesions, which were not confirmed on ICA. Thus, although CCTA may exclude CAD in many ED patients, it has the potential to lead to additional diagnostic testing and possibly unneeded therapeutic interventions.

One key issue at the center of attention regarding CCTA use in the ED is the capacity for rapid and effective triage of patients with chest pains. There is no debate that CCTA provides a rapid and sometimes effective means of diagnosis and risk assessment. However, current trials do not necessarily support conclusions of streamlined care and cost-effectiveness. This is illustrated in the trial by Goldstein et al,\(^{22}\) who examined the value of CCTA in 187 ED patients with chest pain. Although length of stay and expenses were reduced in a cohort of patients undergoing CCTA when compared with routine care, which included stress/rest SPECT MPI, this measure is confounded by study design that stipulated that the non-CCTA arm required a “rule out myocardial infarction” protocol before performing stress SPECT imaging, thereby markedly increasing the length of stay. Additionally, rest MPI was not used for patients with persistent chest pain, which may have reduced time and expense associated with MPI strategies for acute chest pain.\(^{27}\) Another problem identified by this study was the need for further testing after CCTA in 25% of the patients to delineate risk due to either un evaluable images or intermediate severity stenoses on CCTA. It is imperative that these downstream testing procedures induced by CT be included in cost-effectiveness determinations and efficacy evaluations. Therefore, the conclusion that CCTA use in the ED leads to accurate and efficient decision-making for patients with acute chest pain remains debatable.

In an effort to define how best to use cardiac imaging and to define when it is reasonable to perform a specific procedure, various appropriate-use criteria have been developed during the past 5 years, including 1 document that examines CCTA utilization.\(^{28}\) These appropriate-use criteria consider the evaluation of acute chest pain in patients at intermediate likelihood for CAD as an appropriate indication for the use of CCTA. However, in low or high likelihood groups, CCTA was determined to be of uncertain appropriateness. Although more data are now available and these criteria are in need of a revision, there is no support for the use of CCTA as the preferred method for evaluation of all patients with acute chest pain presenting to an ED.

The “Triple Rule Out”

Although a coronary etiology for chest pain is often the focus of ED triage decisions, 2 other critically important pathological conditions may cause a patient to present to the ED with acute chest pain. Both aortic dissection and pulmonary embolism mimic symptoms of ACS and possess great potential for morbidity and mortality. However, all 3 entities may be readily diagnosed but often require multiple testing procedures. The idea behind a CT-based “triple rule out” protocol is to permit a comprehensive evaluation of chest pain with a single procedure. However, imaging all 3 structures simultaneously is technically demanding, if even possible, at the current time. To do so requires very precise timing of the bolus of contrast material, an increased volume of contrast, and a prolonged acquisition, thereby necessitating
greater radiation exposure. Standard CCTA sequences do not permit the effective evaluation of the pulmonary vasculature. When acquisitions are modified, assessment of the aorta, coronary arteries, and pulmonary arteries is feasible with a single breath-hold, although questions of image quality and broad applicability remain. To date, very limited data on the “triple rule out” protocol are available, and the ability to perform this method in all EDs remains to be demonstrated. This approach is not currently well accepted, and the appropriateness of use for the “triple rule out” protocol is uncertain. Furthermore, the increased radiation and contrast exposure, along with increased health care costs, especially when this method is applied indiscriminately, provide concern. In conclusion, the “triple rule out” protocol has engendered much enthusiasm, based more on concept than data. Overall, many CCTA experts as well as professional organizations do not currently advocate for this approach.

**Limitations for CCTA Use in the ED**

As noted previously, it is clear that 64-slice devices are needed for optimal diagnostic accuracy. This expensive equipment is not on-site at all emergency facilities, and, even when present, access to scanner time may be limited. Even in clinical studies examining the value of CCTA for ED patients with chest pain, limited times of CCTA performance were noted. The capital expenditures required for 64-slice CT and cardiac software are substantial, especially for smaller and rural hospitals. Also, costs are not only related to the initial purchase but to ongoing expenses related to maintaining highly skilled staff and physicians. A key limitation of CCTA use at the current time remains the ability to recoup expenditures, as reimbursement for this procedure remains limited.

Personnel must be available to supervise not only image acquisition but also for β-blocker and contrast administration. A physician trained in the expert interpretation of CCTA must also be readily available and should be able to perform a complete review of the image set on a workstation, although remote viewing may be an increasing available alternative.

The use of ionizing radiation is always at least a theoretical risk associated with CCTA and is often reported as 6 to 11 mSv. If plaque characterization is performed, the dose may be as high as 16mSv. Therefore, CCTA is associated with a “not negligible” lifetime risk of cancer, one that is especially important in younger women, who constitute many of the patients with chest pain seen in the ED. Although efforts continue to reduce radiation burden with dose modulation and prospective gating, these methods may not be applicable or advisable for ED patients, in whom preservation of optimal diagnostic accuracy is essential. Thus, even if readily available and easy to perform, CCTA should not be used indiscriminately and ordered only with forethought, as would be other methods using ionizing radiation, such as SPECT or PET.

Screening ED patients with chest pain for contraindications to contrast administration is critical, including assessment for possible dye allergy or renal insufficiency. Additionally, the current use of metformin also prevents the use of contrast, as does frank hyperthyroidism. Patients undergoing CCTA require heart rate adjustment, at least until the development of more advanced technology. However, those with bronchoplastic lung disease, as well as those with constrictions disturbances, are not candidates for β-blockade, making CT unfeasible. Additionally, coronary vasospasm has been reported as a result of β-blocker administration.

Cardiac arrhythmias may lead to problems with ECG gating, thereby producing imaging artifacts and rendering a study with unevaluable areas. Atrial fibrillation, with an irregular ventricular response, as well as frequent supraventricular or ventricular ectopy, are both relative contraindications for CCTA, at least with 64-slice scanners. Even persistent tachycardia may produce a suboptimal study (Figure 1).

Beyond the performance of CCTA, other factors may limit use in ED patients. Uninterpretable areas on 64-slice CCTA may lead to the inability to evaluate 6% to 11% of patients with chest pain. Prominent calcification, even when limited in scope, may cause a “blooming” artifact, preventing accurate interpretation of that segment (Figure 2). Excessive cardiac motion, potentially related to excessive heart rate, may cause a motion artifact, with degradation of imaging quality and “banding” (Figure 1). Intracoronary stents may cause “blooming” and prevent accurate assessment of patency (Figure 3). Additionally, coronary artery bypass grafts, although easily assessed for patency, may be very challenging to evaluate for lesions at the insertion point. In fact, many studies of CCTA for ACS applications have excluded patients with chest pain with prior revascularization, who constitute an increasingly common presentation due to the inability to
exclude a significant stenosis. When taken as a whole, indeterminate results for CCTA have been reported as occurring in up to 17% of ED subjects.\textsuperscript{20}

The aforementioned contraindications and limitations may limit performing CCTA to 25% to 60% of ED patients\textsuperscript{20,21} (Table). The most frequent reasons for not performing CCTA include renal insufficiency, arrhythmias, suspected allergy, taking metformin, hypothyroidism, and an inability to complete the study due to dye extravasation or claustrophobia. Few studies provide complete details regarding the ability to provide a definitive diagnosis; Goldstein et al\textsuperscript{22} demonstrated that 36% of consecutive ED patients with chest pain were excluded from the study because of (1) an inability to receive \( \beta \)-blockers, (2) potential for a contrast reaction, (3) atrial fibrillation, and (4) renal insufficiency. Furthermore, 11% of those who underwent CCTA had “nondiagnostic” studies, and an additional 24% required additional testing (SPECT) to establish a diagnosis. Therefore, up to 70% of ED patients with chest pain did not have a firm diagnosis established by CCTA.

### Coronary Anatomy and Physiology

From the anatomic standpoint, ICA is the benchmark for diagnosis of CAD, although it has long been recognized as an imperfect gold standard.\textsuperscript{35} Variability among observers exists in assigning the degree of stenosis,\textsuperscript{36} and no consensus is present regarding the threshold for what constitutes a “significant” lesion. Furthermore, poor correlation exists with postmortem findings, and, most importantly, discordance with physiological assessment.\textsuperscript{37} Although CCTA does provide some potential advantages over ICA, such as plaque

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**Table. Limitations of CCTA for ED Patients With Chest Pain**

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<th>Availability of 64-slice CT</th>
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<td>Not already in use</td>
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<td>Availability of personnel</td>
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<td>To modify heart rate</td>
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<td>Bronchoconstrictive lung disease (asthma, chronic obstructive pulmonary disease)</td>
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<td>Allergy</td>
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<td>Frequent supraventricular or ventricular ectopy</td>
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<td>Contrast related</td>
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<td>Bypass grafts</td>
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<td>Ionizing radiation</td>
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**Figure 2.** Severe calcification in the left anterior descending artery, with “blooming,” preventing assessment of luminal stenosis. Calcium score was 1100. Cross-sectional images demonstrate the extent of the “bloom.” (Courtesy of L. Samuel Wann, MD.)

**Figure 3.** Extensive “blooming” from stent preventing reliable assessment of possible in-stent restenosis. (Courtesy of L. Samuel Wann, MD.)
characterization, CCTA has inferior spatial and temporal resolution, thus lower image quality. Therefore, CT retains all of the limitations of ICA, with the addition of reduced image quality and inferior radiation dosimetry.

Symptoms such as angina pectoris result largely from the ability of stenosis to prevent requisite increases in coronary blood flow in response to metabolic needs, that is, coronary flow reserve (CFR). CFR stands as the hallmark of the physiological importance of a coronary stenosis, with a drop in CFR usually occurring with a stenosis between 75% and 95% of cross-sectional area, or approximately 50% diameter stenosis. Therefore, a very small change in lumen size (<1 mm) may cause substantial flow reductions. However, because of the limited ability to accurately determine the true coronary cross-sectional area, great variance occurs when comparing the degree of stenosis with CFR (Figure 4). This relationship may be even more disparate with CTA, based on its inferior resolution. Factors beyond the degree of stenosis must also be considered when evaluating coronary blood flow and ischemic potential, including the metabolic state of the myocardium, ventricular hypertrophy, and microvascular disease.

Most diagnostic studies evaluating ICA or CCTA define a significant stenosis as being >50% diameter narrowing. However, many analyses have examined both ≥50% and ≥70% cutoffs for the gold standard ICA, reinforcing uncertainty. Changing angiographic criteria may have substantial impact, as a CCTA study demonstrated when comparing a 50% or 75% threshold, with marked changes in diagnostic performance. Although most trials examining the value of CCTA for ED patient use ≥50%, a recent comparison between CCTA and SPECT MPI recommend that 70% should be used to delineate a stenosis of functional significance. Within the intermediate range of stenosis (40% to 70%), there is a gradual reduction in hyperemic flow with progressive levels of stenosis within this range. The determination of minor differences in percent stenosis with CCT is challenging and therefore assessment of physiological significance is more difficult.

In addition to the definition of a “significant” coronary stenosis remaining elusive, the clinical importance of coronary artery stenosis of moderate severity is often difficult to determine. Several trials examining stenoses of intermediate severity have noted poor correlation with physiological parameters (Figure 5), such as predicted translesional gradients, intracoronary assessment of coronary flow reserve, fractional flow reserve or exercise-induced ischemia. The answer for improved correlation with physiology does not lie with quantification, leading to the conclusion by Fisher et al that “Neither visual assessment of an angiography by experienced interventional cardiologists nor QCA can accurately predict the physiological significance of most moderate (40% to 70%) narrowings.”

In contrast to the known limitations in measuring coronary narrowing and its poor agreement of angiographic data with physiology, SPECT MPI has been shown to correlate highly with coronary blood flow measures such as CFR or fractional flow reserve. This is illustrated in Figure 4, which shows a poor correlation of percent diameter coronary stenosis with coronary flow reserve as measured by intracoronary Doppler flow wire. (From reference 45.)

Figure 5. A, Stress and redistribution (RD) thallium-201 images from a man with a 60% diameter stenosis of left anterior descending (LAD) coronary artery and with normal CFR (3.0). SPECT images are normal. B, Similar stenosis but with a markedly reduced CFR and a prominent reversible defect in the septal, anterior, and apical walls, consistent with a flow-limiting LAD lesion. (Courtesy of Jeffrey A. Leppo, MD.)
reserve, with agreement noted in 88% to 94% of lesions.\textsuperscript{43–45,47,48} In fact, reversible defect on SPECT MPI was the best predictor of an abnormal fractional flow reserve\textsuperscript{47} (Figure 5).

Multiple studies have demonstrated that CCTA has high sensitivity and that a “negative” study excludes the presence of hemodynamically significant coronary disease in most but not all patients compared with SPECT MPI.\textsuperscript{39,49–51} The lack of ischemia with MPI did not exclude the presence of a \( \geq 50\% \) luminal stenosis,\textsuperscript{50} as only 50% of the SPECT studies had abnormal perfusion despite a “significant” angiographic stenosis. This suggests that ischemia may be produced by mechanisms other than epicardial coronary disease. Other studies have shown that a “significant” coronary stenosis is often not accompanied by a reversible perfusion defect.\textsuperscript{39,49–52} In a study of 79 patients undergoing CCTA and SPECT MPI, the diagnostic accuracy for a physiologically significant stenosis by visual or quantitative CCTA assessment was only 49% and 71%, respectively.\textsuperscript{53} Similar to the aforementioned studies using ICA, only a weak correlation was demonstrated between CCTA (or ICA) and fractional flow reserve,\textsuperscript{53} further illustrating the discordance between anatomy and physiology.

Physiological markers also have important prognostic value. When examining patients with intermediate-grade stenoses, (50% to 75% diameter narrowing), CFR as measured by ECG-derived Doppler was correlated with outcome, as a physiologically significant lesion increased risk of subsequent myocardial infarction by 24-fold\textsuperscript{53}; no angiographic finding was associated with subsequent events. Likewise, in patients with an intermediate stenosis but normal fractional flow reserve, excellent outcomes were noted for more than 1 year afterward, even without revascularization.\textsuperscript{48,54} These data suggest the need for functional assessment when planning revascularization. Similarly, it has long been recognized that the presence of spontaneous or stress-induced myocardial ischemia is an important predictor of patient outcome.\textsuperscript{55,56} Although the presence of a coronary stenosis is the hallmark of atherosclerosis, limited prognostic value has been associated with anatomic findings, especially within an acute setting. When a coronary stenosis without hemodynamic significance is left unrevascularized, there is not an adverse impact on outcome.\textsuperscript{33,57,58} Furthermore, intervention on a lesion without clearly physiological and prognostic importance leads to exposure of a patient to risk and expense. In contrast, when ischemia is present, the risk for ischemic events is increased,\textsuperscript{55,56} thereby providing justification for coronary revascularization. Unfortunately, the documentation of myocardial ischemia remains infrequently performed\textsuperscript{59} despite guidelines and documents delineating this requirement for appropriateness in revascularization.\textsuperscript{60}

Therefore, it is evident that degree of stenosis does not predict the physiological significance impact of the lesion as determined by either direct flow measurements or the production of ischemia on imaging studies. In the assessment of chest pain in the ED, where an ACS is suspected, the finding of a coronary stenosis may or may not be the tipping point for additional evaluation and treatment. It is interesting to note that in 1 of the key trials for CCTA use in ED patients with chest pain, Goldstein et al\textsuperscript{22} state: “Failure to diagnose myocardial ischemia as the cause of acute chest pain has serious public health consequences and causes substantial malpractice litigation.” This and the preceding discussion then suggest that determination of coronary physiology, with the demonstration of ischemic potential, may be a more logical decision point in patient care algorithms than the assessment of the degree of coronary stenosis. The widespread use of CCTA “threatens to take us back to the overly simplistic approach of our predecessors. . . .”\textsuperscript{26} that being the treatment of any lesion with intervention, the so-called “occulostenotic reflex.”\textsuperscript{61} To follow this path would be to ignore the large body of evidence in support of functional assessment of ischemic heart disease as well as medical societies’ recommendations.\textsuperscript{60}

### Alternatives to CCTA in the ED

The clinical history is unquestionably the most important aspect for the evaluation of patients with chest pain in the ED. In addition to the description of symptoms, risk factor assessment should be undertaken as a key determinant in decision-making regarding additional evaluation. For example, in the setting of a low-risk patient with highly atypical symptoms, no additional diagnostic evaluation may be required. For those at a higher risk for an ACS, observation units and serial biomarkers (troponin)/ECG may be effective for initial triage, as has been the standard of care. If the initial set of biomarkers is negative, functional testing with exercise or pharmacological stress testing, with or without imaging, may follow. In fact, low-risk patients with a normal ECG may proceed directly to early ECG stress testing, providing a rapid, low-cost, and definitive evaluation in most cases.\textsuperscript{62–64} Early stress/rest SPECT MPI\textsuperscript{56,65–68} and stress echocardiography\textsuperscript{69–71} are also effective techniques. In fact, the sensitivity and negative predictive value of early SPECT (99% to 100%) may exceed that achieved with CCTA.\textsuperscript{66,68} Importantly, these techniques permit the physiological assessment of a patient with suspected ischemic heart disease and enables well-proven risk stratification.\textsuperscript{56,57} As a principal investigator and advocate of CCTA has stated, “...the benefits of clinical and noninvasive testing with the use of stress testing and myocardial scintigraphy are well established”\textsuperscript{14} (Figure 6).

Another method for the safe, rapid, and highly effective triage of patients presenting to the ED with acute chest pain is with the use of rest MPI. Multiple studies,\textsuperscript{56} including 2 prospective, randomized, controlled clinical trials,\textsuperscript{27,67} have shown clinical utility and effectiveness,\textsuperscript{27,66,67,72,73} with very high negative predictive values and clear impact on triage decision-making. The ERASE chest pain study randomly assigned 2456 patients to a strategy of either usual ED care or with a supplemental resting Tc-99m sestamibi scan.\textsuperscript{27} While maintaining safety, there was a 19% reduction of hospital admission rates in the MPI cohort, resulting in significant cost-savings. These studies, along with many others, serve as the basis for rest MPI use in ED.
Figure 6. A case study from January 2009 involving a 61-year-old man with atrial fibrillation. A, CCTA study depicts a low-density area in the left anterior descending coronary artery (arrow) suggestive soft plaque, along with a calcified region, which was interpreted as a 50% stenosis. B, >50% stenosis in the mid right coronary artery (arrow). C, Due to the uncertain significance of the CCTA findings, a SPECT study was performed that revealed normal perfusion. D and E, Invasive coronary angiography failed to demonstrate any high-grade stenosis. (Courtesy of Patrick Fenner, MD.)
patients with chest pain, with a Class I, Level A evidence recommendation, the highest level of support from clinical guidelines. Additionally, the use of rest SPECT MPI is thought to be appropriate for chest pain presentations to the ED.

The wealth of medical literature strongly supports methods other than CCTA for use in evaluating patients with suspected ACS, including a thoughtful clinical assessment. CCTA should not replace the history and physical examination. With regard to diagnostic testing, randomized controlled trial data and strong guidelines support the use of acute SPECT MPI. It is therefore hard to conceive of why CCTA should be considered the “most accurate and efficient” imaging procedure for acute chest pain evaluation. This is especially true given the known limitations related to an anatomic assessment when an ACS may be present.

**Cost-Effectiveness**

Limited information regarding the cost-effectiveness of CCTA is available, including for use in ED patients with chest pain. Goldstein et al demonstrated that using CCTA as part of the triage process is more efficient and more cost-effective than routine care, as the length of stay is shorter and overall expenses related to the diagnostic evaluation are less. However, this study fails to consider the large number of patients ineligible for this approach, the multiple design flaws previously described, the frequent requirement for additional downstream testing, and the lack of a true cost analysis. Two recent publications have reported the cost-effectiveness of CCTA for acute chest pain using modeling techniques. Khane et al stated that CCTA was cost-effective when compared with strategies incorporating an observation period and then either ECG or echocardiographic stress testing. However, no consideration was given to rest imaging or the early performance of functional testing. Additionally, this study suggested cost-effectiveness even in low-risk patients, a group that many authors have expressed concern regarding overall expenditures. The other study, also a simulation, demonstrated only modest overall cost-effectiveness but actually increased costs in men.

In contrast, SPECT MPI has been shown to be a cost-effective tool in the early detection of ischemic heart disease in patients with chest pain, contributing substantially to their risk stratification. When used for acute chest pain syndromes, cost-effectiveness of rest SPECT MPI has been shown in several studies including a controlled, multicenter trial with true cost data. Similarly, dobutamine-atroprine echocardiography as well as contrast echocardiography have both been shown to be cost effective in ED patients by reducing admissions, length of stay, and downstream resource utilization.

In summary, the efficiency and cost-effectiveness of CCTA remains unclear, especially when compared with other strategies. Well-controlled studies are clearly necessary, especially when performed in usual clinical settings, in view of the potential of this method to generate downstream testing.

**Conclusion**

CCTA is undoubtedly an intriguing and promising technology for the detection and evaluation of coronary atherosclerosis. With the advent of 64-slice technology and resultant improvements in image quality, the diagnostic value of CCTA is high. However, many questions remain, especially with regard to the use of CCTA in the evaluation of acute chest pain. Presently, there are few well-controlled, unbiased, multicenter data regarding CCTA for ED patients, thereby limiting conclusions regarding widespread applicability.

It is not well defined for which ED patients CCTA should be used, as very low-risk patients probably will not gain decision-making benefits. Additionally, it is unclear how often CCTA will be clinically applicable in this population, as upward of 60% of patients with acute chest pain presenting to an ED may be either ineligible for CCTA or obtain a nondiagnostic result. The real-world clinical value has yet to be defined for CCTA application in the ED.

An important concern about CCTA is the absence of functional information as it pertains to ischemia. Coronary physiology is the key determinant for prognosis and is the critical decision point for consideration of revascularization. The known discordance between anatomic and physiological variables, along with the well-documented prognostic benefits of ischemia determination, raise questions regarding CT use in the ED.

Alternative strategies for triage of ED patients have been published for many years, with a high level of evidence and support of expert panels for some modalities, such as SPECT MPI. It is therefore hard to conclude that CCTA is currently the most accurate and effective method. Yet, when high-quality images are obtained, CCTA undoubtedly is a rapid and accurate test for assessing CAD. Additionally, CCTA is a valuable tool when equivocal diagnostic information is present.

Overall, CCTA remains a promising technology for chest pain evaluation at the current time, one that may be cost-effective. Despite the excellent negative predictive value of CCAT in ED patients, substantial numbers of false-positive studies exist. This concern is further deepened by the inability of anatomic findings to delineate the substrate for ACS and document the presence of ischemia. This raises concern about stimulating downstream testing as well as unnecessary revascularization, which has caused local and national health plans to question reimbursement for this technique, prompting the suggestion of “a restricted use of CT angiography until adequate clinical evidence becomes available showing the cost-effectiveness and safety of this approach.” Although a moratorium on the use of CCTA seems unnecessary, additional validation, including outcomes data, are needed before concluding that CCTA is appropriate, or the most accurate and effective evaluation method, for all patients with chest pain in the ED.

**Disclosures**

Dr Hendel is a consultant for Astellas Pharma, PGx Health, and GE Healthcare and is a member of the speakers bureau for Astellas Pharma.

**References**


Response to Hendel

Udo Hoffmann, MD, MPH; Fabian Bamberg, MD, MPH

Dr Hendel rightfully emphasizes the limitations to use the degree of coronary artery stenosis as a sole criterion to diagnose acute coronary syndrome (ACS) or to indicate coronary intervention. However, the most effective and urgent therapeutic options in patients with suspected ACS are still limited to treating clot formation and/or relieving coronary luminal narrowing. Although conditions such as coronary vasospasm or microvascular disease may be the cause for ACS in a small subset of patients, treatment options are generally limited. Moreover, the exclusion of significant coronary disease may deliver important diagnostic clues in these conditions as well. The ability to rule out significant coronary artery disease, the cause of ACS in 90% of patients, quickly, noninvasively, and accurately will effectively prevent unnecessary further testing in populations with a low prevalence of disease such as patients with acute chest pain. Although data from randomized clinical trials support the use of rest myocardial perfusion imaging in suspected ACS, this technique is rarely applied in clinical practice. Such data are not available for stress myocardial perfusion imaging. Functional testing is undoubtedly beneficial for risk stratification but resulting changes in management, apart from referral to invasive coronary angiography, is often similar to those based on conventional risk factor assessment. Moreover, the efficacy of functional testing for the diagnosis of significant coronary artery disease is poor, as 40% to 50% of patients referred to invasive coronary angiography do not have significant coronary artery disease. Improved spatial and temporal resolution and the ability to combine anatomic with functional assessment will further improve the clinical utility of cardiac computed tomography but needs to be demonstrated in ongoing and future randomized trials.
Is Computed Tomography Coronary Angiography the Most Accurate and Effective Noninvasive Imaging Tool to Evaluate Patients With Acute Chest Pain in the Emergency Department?: CT Coronary Angiography Is the Most Accurate and Effective Noninvasive Imaging Tool for Evaluating Patients Presenting With Chest Pain to the Emergency Department: Antagonist Viewpoint

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doi: 10.1161/CIRCIMAGING.109.858167

Circulation: Cardiovascular Imaging is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2009 American Heart Association, Inc. All rights reserved.
Print ISSN: 1941-9651. Online ISSN: 1942-0080

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