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

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Patients with acute chest pain (ACP) represent a global health and economical challenge for the US healthcare system. The more than 8 million annual emergency department (ED) visits impart a significant economic burden in excess of $8 billion annually, particularly as 80% of these patients are admitted to the hospital and subsequently undergo extensive testing for what often turns out to be noncardiac chest pain. However, 2% to 8% of discharged patients inadvertently have acute coronary syndrome (ACS), which accounted for 26% of all money paid in closed malpractice claims in emergency medicine from 1985 to 2003.

Response by Hendel on p 263

Based on the current classification, diagnosis, and management of patients with ACP, this article reviews the role of currently available functional diagnostic tests and potential of cardiac CT to improve management of these patients by direct and noninvasive assessment of coronary artery disease (CAD). To provide a rationale for the use of cardiac CT, we provide a summary of available data on the accuracy of cardiac CT for the detection of coronary atherosclerotic plaque and stenosis, as well as the assessment of left ventricular function. Based on a discussion of the health and economic risk benefit aspects of this new technology, we suggest how cardiac CT could be implemented into the current guidelines to improve accuracy and efficacy of current treatment of patients with acute chest pain.

Classification of Acute Coronary Syndrome

Acute coronary syndrome is an operational term and describes a clinical syndrome that comprises both the diagnosis of acute myocardial infarction (AMI) and unstable angina pectoris. Although myocardial necrosis caused by ischemia is the histological substrate of AMI, unstable angina pectoris (UAP) is characterized by ischemia without sufficient myo-
cardial damage to release detectable quantities of markers of myocardial injury.\textsuperscript{10} The presence of characteristic ECG changes, for example, ST-segment elevation, and/or the detection of biomarkers of myocardial necrosis enable further differentiation of AMI into ST-segment elevation myocardial infarction (STEMI) or non–ST-segment elevation myocardial infarction (NSTEMI), respectively.\textsuperscript{11}

### Pathophysiology of Acute Coronary Syndromes

The most common mechanism for ACS is an imbalance between the myocardial oxygen supply and demand.\textsuperscript{12} As identified through histological studies of patients who died of ACS, sudden rupture of the thin fibrous cap of a lipid-rich atheroma (thin cap fibrous atheroma) is the most common cause (55% to 60%), followed by erosion of the cap (30%), and, less often, calcified nodules within a noncalcified plaque (less than 10%).\textsuperscript{13} Consistently, several studies have suggested that thrombosis of a previously nonstenotic plaque has the most dramatic consequences. Overall, significant luminal narrowing on the basis of CAD is the most common cause of ACS (greater than 90%), and such stenosis is found in nearly all STEMI and in approximately 90% of NSTEMI during subsequent coronary angiography.\textsuperscript{14,15} Additional factors are location of the stenosis, size of the dependent myocardial territory, preexisting CAD leading to formation of collateral circulation (a phenomenon known as preconditioning), and blood coagulatory state, with proximal stenosis location, lack of preconditioning, and hypercoagulability as predictors for sudden death or STEMI.\textsuperscript{16–19}

Less common causes of ACS include coronary vasospasm,\textsuperscript{20–23} coronary thrombosis from hypercoagulable states,\textsuperscript{24,25} coronary embolization,\textsuperscript{26,27} and potentially endothelial dysfunction.\textsuperscript{19,28} In addition, myocarditis may mimic ACS and has been suggested as a common finding in patients with normal coronary angiogram.\textsuperscript{29} Women are especially more likely to have normal angiography during investigation for acute chest pain.\textsuperscript{30,31}

### Current Management of Patients With Acute Chest Pain

Current guidelines recommend classification of patients with acute chest into (1) noncardiac diagnosis, (2) chronic stable angina, (3) possible ACS, and (4) definite ACS (Figure 1), based on the patient’s history, physical examination, 12-lead ECG, and initial biomarker tests.\textsuperscript{11} However, neither a single set of biochemical markers for myocardial necrosis (troponin I, troponin T, creatine kinase MB-type [CK-MB]),\textsuperscript{32,33} nor initial 12-lead ECG alone or in combination (acute cardiac ischemia time-insensitive predictive instrument) identifies a group of patients who can be safely discharged home without further diagnostic testing.\textsuperscript{34–36} Thus, accurate early triage of patients presenting with acute chest pain to the ED remains difficult.\textsuperscript{4,37}

As a result, special chest pain observation units (CPU), originally pioneered by Raymond Bahr in 1982, have gained popularity rapidly and have been adopted by ED departments worldwide to master the challenge of the sheer number of patients with acute chest pain and the intensive testing they require.\textsuperscript{38,39} The purpose of a CPU is to facilitate the standard “rule out” myocardial infarction (MI) protocol, which consists of serial ECG and cardiac biomarker measurements, and usually a diagnostic test to evaluate for obstructive CAD as the underlying etiology of the chest pain.\textsuperscript{40} Currently, the standard diagnostic test is a functional test, such as exercise treadmill testing. Although this strategy reduces the number of cases of missed ACS as compared with traditional in-hospital evaluation,\textsuperscript{41} this practice has also increased the overall number of hospitalized patients due to a lower threshold of admitting patients with acute chest pain to such units.\textsuperscript{2,42–45}
Current Standard Diagnostic Testing

Current American Heart Association/American College of Cardiology (AHA/ACC) guidelines recommend various testing strategies. Symptom-limited exercise treadmill testing is recommended in patients who are capable of exercise and who are free of confounding features on the baseline ECG (eg, left bundle-branch block, left ventricular hypertrophy, and paced rhythms; class I recommendation, level of evidence C). In the remaining patients, pharmacological stress testing with nuclear perfusion imaging, 2D echocardiography, or magnetic resonance should be considered (class I recommendation, level of evidence C).46

Data on the diagnostic performance of immediate stress ECG for the detection of ACS are limited.47–49 However, in a study of 100 patients with acute chest pain who underwent exercise ECGs <1 hour after admission, 23% had positive tests; 38% had negative tests, and 39% had nondiagnostic tests, whereas an uncomplicated non–Q-wave AMI was diagnosed in 2%, indicating limited feasibility of this test for early triage.48,49

Single-photon emission computed tomography (SPECT), the most commonly performed diagnostic test, is complex, costly, and time-consuming (ie, ≈150 minutes for stress SPECT). In addition, this test is generally not available 24/7 due to the need to have a specifically trained personnel on-site.48 A number of observational studies demonstrated that rest SPECT detects significant stenosis with excellent sensitivity >90% and good specificity (67% to 78%) when compared with coronary angiography.50–53 A large randomized multicenter clinical trial in 2475 patients by Udelson et al demonstrated that incorporating rest SPECT in the initial evaluation of patients with chest pain results in fewer hospitalizations among patients without acute cardiac ischemia (n=2146, 52% with usual care versus 42% with SPECT imaging; rate risk ratio, 0.84; 95% CI, 0.77 to 0.92) without missing more ACS.54 However, according to current guidelines, most CPU order stress SPECT if serial 12-lead ECG and cardiac biomarker measurements are normal, which has been shown to improve diagnostic accuracy.54,55 Conversion of nondiagnostic exercise studies (achieve <85% of maximal heart rate) to pharmacological stress (eg, adenosine) is recommended. A drawback to rest-stress SPECT studies is radiation exposure, which is estimated to average 11.3 mSv with sestamibi and 9.3 mSv with tetrofosmin and is greater than the exposure from most diagnostic invasive angiograms (average, 5 to 7 mSv).56 Studies performed with thallium and a combination of thallium and sestamibi can produce significantly greater exposure (eg, 21 to 29 mSv).

Although rest echocardiography is relatively inexpensive, easy to perform, and widely available, available data suggest a similar or slightly lower sensitivity of rest echocardiography when compared with rest SPECT for the detection of myocardial ischemia.57–59 Stress echocardiography adds significant value to functional assessment at rest and increases both negative predictive value (NPV) (98.8%) and positive predictive value (PPV) (78%), as demonstrated by Bedetti et al in 522 patients with acute chest pain, inconclusive ED evaluation, and normal resting left ventricular (LV) function. However, stress echocardiography requires highly experienced sonographers and interpreting physicians and is often not available 24/7.

Overall, available functional tests are limited in their utilization for early triage because of the complexities connected by their restricted use before the report of serial negative cardiac biomarkers, the specific training requirements on personnel, and the frequency of nondiagnostic tests. Although they provide valuable information for risk stratification, their diagnostic accuracy for the detection of significant CAD is limited, leading to unnecessary invasive coronary angiograms in 33% to 44% of patients with suspected ACS.48,60 Thus, treatment of patients with acute chest pain, especially early and safe triage of patients at low to intermediate risk for ACS, remains challenging.

Features of Cardiac CT That Make the Technology Suitable for ED Indications

There are a number of features that are unique to cardiac CT imaging, which predispose this technique to improve the diagnostic workup of patients with acute chest pain in a cost effective manner.

1. Cardiac CT is unique in its ability to noninvasively visualize CAD and to accurately detect significant stenosis. Moreover, this test extends the spectrum of disease by visualizing nonobstructive coronary atherosclerotic plaque. Recent AHA/ACC guidelines for the first time recommend coronary CT as an alternative to conventional stress testing (class IIa recommendation, level of evidence B).

2. Cardiac CT is a quick and relatively simple procedure that can be performed within 10 to 20 minutes. Administration of β-blockers before the scan, for example, with either intravenous metoprolol (often given in 5-mg increments every 5 minutes up to a total dose of 25 mg under cardiac monitoring) or oral atenolol or metoprolol, is recommended for heart rates >65 beats per minute, except when a scanner with a temporal resolution <100 ms are used.61

3. Advanced cardiac CT technology using at least 64-slice CT technology, spatial resolution of 0.5 mm in z axis, and temporal resolution of <250 ms to enable coverage of the entire coronary artery tree during a short breath hold with robust image quality62–64 is becoming widely available in EDs. Today, ~3000 cardiac CT systems based on at least 64-slice are installed around the country.

4. Information on noncoronary cardiac pathologies such resting global and regional LV function as well as extracardiac pathologies or “incidental noncardiac findings” can be obtained at no additional cost.

Proper Validation of Diagnostic Imaging for Clinical Indications

More rigorous validation of diagnostic imaging test for certain clinical indications is a relatively new requirement triggered by fast technical developments providing new
options for diagnosis and management as well as the fact that imaging costs account for a disproportionate share of the recent increases in national healthcare costs. There is not yet a clear understanding how to validate diagnostic tests. Thus, we suggest the following steps for validation of diagnostic tests in reference to the design pharmaceutical trials with a special emphasis on cardiac CT in patients with ACP.

**Phase I**
Feasibility studies determine the diagnostic accuracy of the technology compared with the gold standard for findings relevant to the clinical outcome (ie, cardiac CT for the assessment of coronary atherosclerotic plaque, stenosis, and LV function as compared with intravascular ultrasound, invasive coronary angiography, and MRI, respectively).

**Phase II**
Observational studies determine the population in which the test has the highest clinical utility by assessing the prevalence of findings in these populations, the diagnostic accuracy for clinical outcomes, and the prevalence of these outcomes. The diagnostic accuracy provides information on the safety of the test (ie, safe and early ED discharge) and the prevalence of these findings (ie, plaque and stenosis) and the outcomes (ACS) provides information on the efficacy. In addition, diagnostic test characteristics can be explored for several diagnostic thresholds. However, an unbiased assessment of these measures is valid only if a blinded design (subjects and caregivers remain blinded to the results of the diagnostic test) is used. Thus, such studies can usually be performed only at a stage when the new technology is not yet clinically adopted and equipoise exists for blinding the results. Overall, results from observational trials provide rationale for guidelines, management decisions, and cost-effectiveness analysis although they neglect variations in “physician-based decision-making.”

**Phase III**
Randomized diagnostic trials (RDT) determine the efficiency of a new diagnostic imaging test compared with the standard of care in the clinical world. They determine how information from the test will be used by physicians. These trials are performed unblinded, and information of the new test is used for decision-making and patient care. Effect measures for these trials are health outcomes (ie, myocardial infarction, cardiac death, revascularization) and management and cost end points (ie, discharge rates, length of hospital stay, time to diagnosis, diagnosis made, subsequent tests and treatment, costs). Most likely to change practice are trials that demonstrate superiority of health outcomes. Major characteristics of trial design are related to balance generalizability versus precision with respect to study of population, control of clinical decision-making, hospital setting, and knowledge and skills of participating physicians. Although less controlled designs permit more generalizable conclusions, it is sometimes more difficult to establish causality between results and conditions within the trial (ie, whether physician knowledge, hospital administration, technical challenges with tests).

**Phase IV**
Clinical algorithms and registries are performed to determine the clinical usefulness in a broader clinical setting and to confirm results of RDT. These studies are usually performed once major societies and regulatory bodies have established the test at least as a class 2A indication. Their problem is often an uncontrolled environment, which may make it even harder to explain the decision-making patterns encountered. The following paragraphs summarize the status of cardiac CT research and its role for the triage of patients with acute chest pain according to these phases.

**Phase I: Feasibility Studies on Cardiac CT**
**Feasibility for the Detection of Obstructive Coronary Artery Stenosis**
To date, >60 studies with >5000 patients have been published investigating the accuracy of cardiac CT to detect significant coronary artery stenosis. The majority of these studies are single-center studies typically including middle-aged white men at high risk for CAD (≈60% prevalence of significant CAD). The results indicate an excellent sensitivity and NPV and moderate to good specificity and PPV on a per-patient basis, consistent with the capability to efficiently rule out the presence of significant stenosis. In a recent systematic review, Stein et al summarized single-center results by pooling available data of 2045 patients on the diagnostic accuracy of 64-slice CT for the detection of significant coronary stenosis (>$50% luminal narrowing). In this analysis, the investigators derive a summary estimate of a sensitivity of 98% (96% to 98%), a specificity of 88% (85% to 89%), an NPV of 96% (94% to 97%), and a PPV of 93%. Recently published multicenter studies, with the exception of “Core 64,” have now confirmed the excellent sensitivity and NPV coupled with a moderate to good specificity and PPV across a wide range of disease prevalence (25% to 68%, Table 1).

For the population of patients with chest pain with a low to intermediate pretest probability of obstructive CAD, studies with a low prevalence of disease, such as the ACCURACY trial, are most relevant. They suggest that cardiac CT can safely rule out the presence of significant stenosis. However, they also indicate that the clinical impact of positive findings may be limited due to the low PPV (47%), which is most often due to severe calcification. In addition, a number of considerations that are relevant in the setting of acute chest pain have not been addressed yet.

1. Although it is known that severe coronary calcification impairs specificity for stenosis detection, there is no established calcification threshold based on a non–contrast-enhanced scan to suggest when not to perform the standard contrast-enhanced scan.
Table 1. Summary of Published Multicenter Trials on the Diagnostic Accuracy of Cardiac CT for the Detection of Significant Coronary Artery Stenosis (>50% Luminal Narrowing)

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Scanner</th>
<th>Patients</th>
<th>Exclusion Criteria</th>
<th>Population</th>
<th>Prevalence, %</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
<th>PPV, %</th>
<th>NPV, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Garcia et al</td>
<td>2006</td>
<td>16</td>
<td>187 pts</td>
<td>&lt;2-mm diameter</td>
<td>59.8 ± 9, 68% male</td>
<td>32</td>
<td>94 (89–100)</td>
<td>51 (43–59)</td>
<td>28 (19–36)</td>
<td>98 (94–100)</td>
</tr>
<tr>
<td>Marano et al</td>
<td>2006</td>
<td>16/64</td>
<td>327 pts</td>
<td>Sustained heart rate &gt;70 bpm</td>
<td>54 (19–83) y, 76% male</td>
<td>58</td>
<td>94 (89–97)</td>
<td>88 (81–93)</td>
<td>91 (86–95)</td>
<td>91 (85–95)</td>
</tr>
<tr>
<td>Budoff et al</td>
<td>2008</td>
<td>64</td>
<td>230 pts</td>
<td>&gt;40 y body mass index, &gt;40 calcium score &gt;600, vessels &lt;1.5-mm diameter</td>
<td>58 ± 10 y, 59% male</td>
<td>25</td>
<td>95 (85–99)</td>
<td>83 (76 to 88)</td>
<td>64 (53 to 75)</td>
<td>99 (96 to 100)</td>
</tr>
<tr>
<td>Miller et al</td>
<td>2008</td>
<td>64</td>
<td>291 pts</td>
<td>&gt;50 y and &gt;70 y</td>
<td>59 median; IQR, 52–66; 74% male</td>
<td>56</td>
<td>85 (79–90)</td>
<td>90 (83–94)</td>
<td>91 (86–95)</td>
<td>83 (75–89)</td>
</tr>
<tr>
<td>Mejboom et al</td>
<td>2008</td>
<td>64</td>
<td>360 pts</td>
<td>in Holland</td>
<td>60 ± 6 68% male</td>
<td>68</td>
<td>99 (88–100)</td>
<td>64 (55–73)</td>
<td>86 (82–90)</td>
<td>97 (94–100)</td>
</tr>
</tbody>
</table>

*Per-patient base analysis with nonevaluable segments graded as positive.†Per-patient on-site evaluation.

2. Studies have typically excluded smaller (<1.5 mm in diameter) side branches from their accuracy analysis, which may harbor culprit lesions of small infarcts.68,69
3. Most studies have used >50% stenosis as a criteria for significance; however, from an interventional point of view, >70% is typically considered significant. Moreover, although initial data suggest that quantitative measurement of the degree of stenosis is feasible and correlates well to invasive coronary angiography in selected high-image quality examinations,73 it remains unclear whether accurate separation between 50% and 70% can be achieved. Thus, the feasibility of CT to support indications for revascularization is unclear.

4. Finally, the feasibility of stenosis detection in a broader clinical setting that includes community hospitals and private practices has not been tested in a multicenter, multivendor feasibility trial.

Feasibility for the Detection and Characterization of Coronary Atherosclerotic Plaque

Several small studies using 16-slice74,75 and 64-slice CT technology76–78 demonstrated the feasibility of cardiac CT to detect and quantify nonobstructive coronary plaque in the proximal coronary segments of selected high-quality examinations (sensitivity, 83%; specificity, 94% for the detection of any atherosclerotic plaque79) as compared with intravascular ultrasound. Notably, the diagnostic accuracy for the detection of calcified plaque is significantly higher than for noncalcified plaque.76–78 Moreover, further characterization of noncalcified plaque into fibrous or lipid-rich plaque may not yet be possible.79 However, 2 studies have demonstrated that positive remodeling, higher prevalence of either spotty calcification or exclusively noncalcified plaque, and higher plaque volume but not the degree of stenosis differentiate culprit lesions in ACS patients from nonculprit lesions and lesions in patients with stable angina.80,81

Feasibility of Cardiac CT to Assess Global and Regional LV Function and Perfusion

The ability of cardiac CT to perform a combined assessment of coronary morphology and global and regional LV function without additional radiation exposure or contrast administration constitutes an attractive feature of the modality specifically in the setting of acute chest pain. Cardiac CT is highly reproducible (κ = 0.86) and accurate for the detection of global and regional LV dysfunction when compared with cine MRI (r = 0.91).82–87 Initial studies also suggest that CT may be feasible to detect myocardial perfusion abnormalities using first-pass and late enhancement techniques.88–90

Phase II: Observational Studies on Cardiac CT

In the 1990s, 3 major studies comprising >400 patients determined the clinical utility of non–contrast-enhanced electron-beam computed tomography imaging of coronary artery calcification (CAC) to rule out ACS in patients with acute chest pain but inconclusive initial ED evaluation and no known CAD. The results suggested that the occurrence of ACS among patients with no or minimal coronary calcification is extremely rare (NPV, 99% to 100%) but that the detection of CAC renders very limited PPV.91 Moreover, in a 5-year follow-up, none of the patients without CAC at baseline had a major adverse cardiovascular event (MACE), demonstrating the excellent midterm prognostic value of CAC.92

Only 1 observational cohort study using contrast-enhanced 64-slice CT (Rule Out Myocardial Infarction Using Computer Assisted Tomography, ROMICAT) has been published.93 Among 103 patients who presented with ACP but had an inconclusive initial ED evaluation (nondiagnostic ECG and negative cardiac enzymes) 14 had ACS (13% event rate). Both caregivers and patients were blinded to the results of CT. In this study, none of the patients without CAD (Figure 2) or stenosis <50% (Figure 3) had ACS (sensitivity, 100%; NPV, 100%). The data suggested that a significant fraction of patients (>40%) may be eligible for early and safe discharge by using CT, whereas the presence of stenosis (Figure 4) had limited PPV (47%). The study also suggested that CT is not feasible in patients with a history of CAD and
that the spectrum of CAD is extended compared to stress functional testing.

**Phase III: Randomized Diagnostic Trials**

To date, only 1 single-center, randomized controlled clinical trial in 197 subjects at very low risk for ACS has been published. Subjects with negative serial troponin and no history of CAD were randomly assigned to a cardiac CT-based triage system or a stress SPECT-based triage system. In the CT arm, those with no or minimal CAD were discharged from the ED, those with intermediate stenosis (25% to 75%) crossed over to the stress SPECT arm, and those with severe stenosis were referred to invasive coronary angiography. There were no events (MI, unstable angina) in the entire study population during index hospitalization or after 6 months’ follow-up (sensitivity and NPV: 100%). However, consistent with the superior sensitivity of cardiac CT for the detection of stenosis, the number of subsequent invasive coronary angiograms was increased (11.1% versus 3.1%, \( P < 0.03 \)). The results supported previous findings that subjects with no or minimal CAD on CT can be safely discharged. Furthermore, the CT-based strategy significantly shortened time to diagnosis (3.4 versus 15.0 hours, \( P < 0.001 \)) and reduced costs ($1586 versus $1872, \( P < 0.001 \)) as compared with the stress nuclear perfusion imaging strategy.

**Phase IV: Clinical Practice Algorithm Studies on Cardiac CT**

Given these encouraging results, there are a growing number of clinical centers that have incorporated cardiac CT in their clinical practice. An interesting design was applied in a small study of 58 patients, including those with a history of CAD, by Rubinstein et al. Patients received standard ED triage along with cardiology consultation, after which a presumptive diagnosis of ACS was made where warranted with recommendations for hospitalization and early invasive treatment. Cardiac CT was then performed in all patients and recommendations adjusted based on CT findings (discharge with <50% stenosis). Patients were followed for MACE over a mean of 12 months of follow-up. Cardiac CT results led to a revised ACS diagnosis in 18 of 41 patients, canceled hospitalizations in 21 of 47, and altered early invasive treatment in 25 of 58. Sensitivity of significant stenosis by cardiac CT for the detection of MACE during follow-up was 95% (NPV: 97%). The results confirmed that a negative CT has excellent NPV for ACS and MACE. There is also initial evidence

![Figure 2](http://circimaging.ahajournals.org/content/3/3/256/F2.large.jpg)

**Figure 2.** Cardiac CT of a 48 year-old woman who presented to the emergency room with atypical ACP. Initial cardiac biomarkers were negative and the ECG demonstrated nonspecific t-wave changes. On hospital admission, the patient underwent serial blood sampling and a stress nuclear perfusion imaging the next day. All tests were normal. Cardiac CT demonstrated the absence of significant coronary stenosis and plaque in all coronary vessels. A, Maximum-intensity projection of the right coronary artery (white arrows). B, Curved multiplanar reformation of the left anterior descending coronary artery (white arrows). C, 3D volume–rendered reconstruction of the left main coronary artery (black arrow), the left anterior descending coronary artery (white arrow), and the left circumflex coronary artery (arrowhead) in an anterior view of the heart. RV indicates right ventricle; LV, left ventricle; AA, ascending aorta.

![Figure 3](http://circimaging.ahajournals.org/content/3/3/256/F3.large.jpg)

**Figure 3.** A 56-year-old man with multiple risk factors who presented to the ED with 2 hours of substernal chest pain and in whom the initial ED evaluation was inconclusive. Cardiac CT performed before hospital admission demonstrated nonobstructive atherosclerotic plaque but no significant stenosis. A, Maximum-intensity projection of the right coronary artery demonstrating nonobstructive calcified plaque in the proximal and distal segment of the vessel (white arrows). B, Curved multiplanar reformation of the left anterior descending coronary artery demonstrating nonobstructive calcified (white arrow) and noncalcified plaque (dashed arrow). C, Curved multiplanar reformation of the left circumflex coronary artery (white arrow) demonstrating the absence of plaque and stenosis. RV indicates right ventricle; LV, left ventricle; AA, ascending aorta.
suggesting that cardiac CT is at least comparable to stress nuclear imaging for the detection and exclusion of an ACS in low-risk patients with chest pain. Gallagher et al96 in 92 patients reported a sensitivity of 71% and a NPV of 97% for stress nuclear imaging compared with 86% and 99% for cardiac CT for the detection of ACS, respectively. Notably, the end point of this study was the presence of significant stenosis (>50%). In a report of a clinical practice CT algorithm in large cohort, Hollander et al97 followed 568 patients who underwent cardiac CT either immediately in the ED (n=285) or after a brief observation period (n=283). Their results indicate that none of the discharged patients (n=476, 84%) who all had absence of significant stenosis (>50%) had a cardiovascular event (cardiovascular death, nonfatal myocardial infarction) during a 30-day follow-up period. Table 2 summarizes the major phase II and III studies.

Based on the existing evidence, Figure 5 lays out a proposal on how to use cardiac CT to manage patients with ACP and no history of CAD considering the latest ACC/AHA guidelines.

The “Triple Rule Out” Protocol
Recent technical developments now permit acquisition of high-quality images of the coronary arteries, thoracic aorta, and pulmonary arteries in a single comprehensive cardiothoracic CT scan. The so-called “triple rule out protocol,” referring to the ability to exclude obstructive CAD, pulmonary embolism, and aortic dissection at once may be an attractive option to evaluate patients with undifferentiated chest pain in whom any of the 3 dedicated CT scans may be performed as standard of care. Initial data suggest that the protocol is feasible and that extracardiac findings (such as pneumonia) will be detected in some patients, which will change management.99–101 However, research that clearly demonstrates a benefit of comprehensive CT in these populations is warranted before clinical implementation, especially given the overall extremely low event rate in such studies and the increased exposure to radiation due to the greater scan length needed to completely image the thoracic aorta.

Cost-Effectiveness Analysis
As very few questions and scenarios can be addressed within the confines of a clinical trial, decision-analytic Markov model–based approaches with the flexibility to model characteristics of populations, diagnostic tests, and patient care have been used to project possible economic and health consequences of diagnostic tests. These models enable us to assess the utility of diagnostic tests from a broader perspective that includes potential risks and benefits associated with the tests and a lifelong horizon. They are especially helpful considering that a broad adoption of cardiac CT as a noninvasive imaging option for CAD detection would have an enormous clinical and financial impact on systems of care. The results of various modeling approaches agree in their assessment that an appropriate use of cardiac CT in low- to intermediate-risk patients with ACP is associated with cost savings compared with stress testing, especially in younger men and women.102–104

Incidental Findings
Reporting of incidental findings is a hotly debated topic because subsequent testing and diagnoses of incidental find-
ings may impair cost savings by cardiac CT. In the ROMICAT study, clinically important findings were detected in up to 5% of patients, but only very few led to a direct change in patient treatment. Further imaging tests were recommended in 20% of patients, most often to follow up pulmonary nodules, resulting in invasive procedures and detection of cancer in few patients. Overall, it appears that reporting of incidental findings is mandatory in symptomatic patients for medical, ethical, and legal reasons.

**Radiation Exposure**

Cardiac CT, SPECT, and invasive angiography all expose patients to radiation. Radiation doses of retrospectively gated 64-slice CT typically range from 7 to 14 mSv when dose modulation strategies are used. This exposure is comparable to stress SPECT (9 to 12 mSv) and lower than a thallium myocardial perfusion scan (18 to 21 mSv) but higher than the effective radiation dose from an invasive coronary angiography (5 to 7 mSv). Model-based calculations suggest that lifetime cancer risk from standard cardiac CT scans varies from 1 in 143 (0.007%) for a 20-year-old woman to 1 in 3261 for an 80-year-old man (0.0001), with significantly lower risks using dose modulation (1 in 715 and 1 in 1911, respectively, for a 60-year-old woman and men. In comparison, US women have a 1 in 8 (12.5%) lifetime chance of developing invasive breast cancer, and the overall cancer risk for 75-year-old men/women is 6%. Thus, even if the model-based assumptions of the cardiac CT–based cancer risk estimates are valid, the incremental risk seems low but nonneglectable. Moreover, advances using prospective ECG gating indicate that a low radiation scan option (5 mSv) may be increasingly feasible to image-selected populations of ED patients.

**Table 2. Studies Examining the Diagnostic Value of Cardiac CT in Patients Presenting With Acute Chest Pain to the ED**

<table>
<thead>
<tr>
<th>Year</th>
<th>Study Type</th>
<th>n</th>
<th>Subjects</th>
<th>Outcome of Interest</th>
<th>Prevalence, %</th>
<th>CT Criterion</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
<th>NPV, %</th>
<th>PPV, %</th>
</tr>
</thead>
</table>
| Hoffmann et al103 ROMICAT 2006 Validation cohort 103 54±12 y, 60% male ACS or MACE at 6 mo 13.6 1. Sig stenosis 2. Plaque 100 82 100 47
| Gallagher et al104 2007 Clinical practice algorithm 85 49±11 y, 53% male Sig stenosis in ICA or MACE at 30 d 8 Sig stenosis 86 92 99 50
| Goldstein et al105 2007 Randomized diagnostic trial 99 in CT arm (197 total) 48±11 y, 43% male Sig stenosis or MACE 6 mo, costs, time to diagnose, no. of tests 8 Sig stenosis 100 97 100 73
| Rubinshtein et al106 2007 Clinical practice algorithm 58 56±10 y, 64% male 1. ACS during index hosp; 2. MACE 15-mo follow-up 34; 22 1. Sig stenosis; 2. Sig stenosis 100; 92 97 100; 97 87; 52

*Sig indicates significant.

*Testing costs were higher in the CT arm, but shorter average ED time resulted in lower total costs per patient (approximately $300) in the CT arm.

**Figure 5.** Proposed algorithm incorporating cardiac CT in the evaluation of patients with a low to intermediate pretest probability of CAD (and without history of CAD) who present with suspected ACS. CT results are used to classify subjects according to coronary findings (no plaque, plaque but no stenosis, nondiagnostic [unable to exclude significant stenosis], and significant stenosis) and the presence and absence of regional LV wall motion abnormalities (RWMA+ and RWMA−, respectively). SAP indicates stable angina pectoris. *If 2nd troponin is positive, admit to the hospital for further evaluation and management according to current guidelines.
Future Research and Open Questions

There are a number of major research efforts underway to complement available data, specifically randomized multicenter trials such as ROMICAT II and CT-STAT; and registries such as SPARC and the Michigan Blue Cross Blue Shield registry. We hope that these efforts will be able to answer some of the important remaining questions about cardiac CT in the ED, including:

1. How adequate and how safe is the criterion-significant CAD defined as 50% stenosis as a discharge criterion, given that between 10% and 15% of patients with non-STEMI ACS have no significant stenosis?

2. Cardiac CT improves the sensitivity for the detection of CAD in the population of low- to intermediate-risk patients. Will cardiac CT lead to an increase in percutaneous coronary interventions on lesions that would not have been detected as physiologically significant on functional imaging studies, or will cardiac CT lead to an increase in dual diagnostic testing?

3. Cardiac CT extends the detectable spectrum of CAD. Will the detection of nonobstructive plaque trigger medical therapy and result in decrease of future cardiovascular events in patients with CAD but no ACS?

4. Can patients be sent home on the basis of CT before a second troponin is available, which would constitute a major paradigm shift?

5. Would a negative CAC screening constitute sufficient evidence for discharge in very low-risk and low-risk patients?

6. Is there a minimal event rate that justifies the use of coronary CT and stress nuclear imaging?

7. What is the effect on care for other ED patients who could be treated more quickly?

Clinical Implementation of Cardiac CT in the ED

CT scanning for pulmonary embolism in the ED could potentially provide a paradigm for cardiac CT scanning in patients with ACP, which has been shown to improve patient outcomes and care. However, to achieve widespread use and acceptance by ED physicians, availability of such services 24/7 may be required. Readers will be required to have at least COCATS II criteria (2 months of training with at least 200 cases). Recent AHA/ACC consensus documents outline the standard requirements for reporting of cardiac CT scanning.

Conclusions

In summary, available data suggest that cardiac CT may be superior to competing tests in the management and especially the early triage of acute chest pain patients because (1) it is a fast, relatively simple, and robust test with the potential to be available 24/7 in both tertiary and community hospital settings, (2) it uniquely provides a direct and noninvasive visualization for CAD, (3) rapid early discharge of nearly half of all patients with cardiac pain may be possible by excluding CAD, (4) extending the spectrum of CAD through the detection of nonobstructive CAD may result in a more accurate short- and long-term prediction of cardiovascular event risk and in improved preventive strategies. However, the growing availability of cardiac CT in EDs across the United States not only expands the opportunities for its clinical application but also heightens the need to ensure that clinical practice is dictated by evidence-based medicine. Recent attention to radiation exposure, which is inherent with both SPECT and CT imaging, should also cause us to carefully consider the appropriate use of these modalities. Thus, a number of important questions need to be addressed to justify widespread routine clinical application.

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Disclosures

None.

References


Response to Hoffman and Bamberg

Robert C. Hendel, MD

Drs Hoffman and Bamberg provide an excellent review of the contemporary literature for computed tomography coronary angiography (CCTA), with a focus on acute chest pain syndromes. This scholarly work also provides an outstanding paradigm for the validation of CCTA. The data presented are factual but provide only limited support for the routine use of CCTA for acute chest pain and highlight using this technique in patients without known ischemic heart disease or only those at very low risk. The discussion regarding the threshold of a significant stenosis is intriguing, including that “the feasibility of CT to support indications for revascularization is unclear.” This certainly would be a limitation and provides support for physiological testing, such as with stress testing. Recent advances supporting the use of CT for “triple rule out” are exciting and may alter practice habits, but the additional radiation and contrast exposure must be considered. The authors correctly point out the frequent nondiagnostic nature of exercise ECGs, and I also share concern about providing single-photon emission computed tomography imaging on a 24/7 basis. However, CT coronary angiography also has significant logistic problems. Their proposed algorithm lacks advice regarding a postadmission strategy and excludes stress testing completely. In their conclusion, the authors state that “a number of important questions need to be addressed to justify widespread routine clinical application,” a point with which I completely concur. Although the technology provides great images and has outstanding clinical potential, it is still premature to state that CCTA is the most accurate and effective tool for acute chest pain evaluation.
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

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