Case presentation: A 55-year-old man presents to the emergency department (ED) after an episode of substernal chest discomfort that lasted 2 hours. His pain occurred at rest and was not positional, pleuritic, or post-prandial. He has a history of hypertension and no known coronary artery disease (CAD). Vital signs and physical examination are unremarkable. His initial ECG, troponin, and serum creatinine are normal. How should this patient be evaluated?

The Challenge of Evaluating Acute Chest Pain
Chest pain is a common complaint in the ED, accounting for 10% to 15% of visits at an annual cost of $8 billion in the United States.1 However, missed myocardial infarctions occur in up to 2% of patients with acute chest pain2 and represent a leading cause of malpractice litigation. Because history alone is often inadequate to identify patients who may be safely discharged,3 it is common practice to use observation and serial cardiac biomarkers for patient evaluation. Additionally, exercise testing and vasodilator stress testing are commonly used, although such testing can be performed only after an observation period, which includes serial cardiac biomarkers. With increasing use of cardiac testing in an era of cost containment, a growing need exists to improve the efficiency and cost associated with the evaluation of acute chest pain.

Coronary Computed Tomographic Angiography: A Rapid Alternative to Usual Care
Coronary computed tomographic (CT) angiography (CTA) is a high-resolution, noninvasive technique to image the coronary arteries and to detect the presence, severity, and extent of CAD.4 The greatest utility of CTA lies in its high negative predictive value (≥95%) to exclude obstructive CAD and thus to identify patients who can be safely discharged without further diagnostic testing.5 In addition, this test can be performed rapidly because only 1 set of negative biomarkers is needed. Consequently, 4 randomized, controlled trials in the ED have compared CTA with usual care6–8 and single-photon emission CT,9 demonstrating a consistent ability of CTA to expedite discharge.10 Reassuringly, patients with a normal CTA or minimal CAD had very low downstream adverse cardiac events (<1%/y).

Strengths and Limitations
Although CTA avoids the inherent risks of stress testing in patients with suspected acute coronary syndrome (ACS), there are several strengths and limitations to consider (Table 1). Contrast and radiation remain potential concerns, but advances in CT hardware and software have improved overall patient safety. For instance, with prospective gated ECG triggering, the average effective dose is ≈3 to 4 mSv, equivalent to the annual level of background radiation from natural sources. Despite these advances, alternative tests (eg, treadmill testing, stress echocardiography) remain reasonable options in selected patients.

Patient Selection
The initial evaluation of acute chest pain requires an ECG and cardiac biomarkers (Figure 1A).11 Patients at very low risk for CAD and those with an alternative explanation for their symptoms require no further testing. Conversely, those with a high pretest probability for CAD may benefit from
a functional strategy (e.g., myocardial perfusion imaging or stress echocardiography) because CTA has reduced specificity to detect ischemia. Thus, ideal candidates for CTA are patients at low to intermediate risk of obstructive CAD (Figure 2). In addition, the use of CTA in the ED requires careful consideration of several key clinical, patient, and institutional factors (Table 2).

Beyond risk prediction for obstructive CAD, several scores are available to stratify patients for ACS risk and potential complications but have limited sensitivity to exclude ACS. Among available ED studies, 2 have used a Thrombolysis in Myocardial Infarction (TIMI) risk score of ≤2 or ≤4 among clinical features (e.g., history, ECG, biomarkers) to select potential candidates for CTA.

### Patient Preparation

In patients selected to undergo CTA, preparation with β-blockers and breathing instructions are paramount for achieving high image quality, although some scanners now permit rapid image acquisition, obviating the need for aggressive heart rate control. Large-bore (≈18 gauge) intravenous access is preferred for high-flow contrast administration. Unless contraindicated, all patients receive nitroglycerin before scanning.

### Management of CTA Findings

#### Normal CTA: No Plaque or Stenosis

Patients with normal CTA may be safely discharged and have an extremely low cardiac event rate (Figure 1B).

#### Nonobstructive CAD

In patients with nonobstructive CAD, a small potential for ACS remains despite the absence of significant stenosis. In the Rule Out Myocardial Infarction Using Computer Assisted Tomography (ROMICAT) I trial, in which providers were blinded to all CTA results, 6% of patients with nonobstructive CAD were ultimately categorized as having ACS, including 3 patients with myocardial infarction.

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**Table 1. Strengths and Limitations of CTA for Acute Chest Pain**

<table>
<thead>
<tr>
<th>Strengths</th>
<th>Limitations</th>
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<tbody>
<tr>
<td>Is noninvasive</td>
<td>Significance of anatomic lesions may be unknown</td>
</tr>
<tr>
<td>Detects the full spectrum of CAD</td>
<td>Incidental findings may require further workup</td>
</tr>
<tr>
<td>May affect preventive therapies</td>
<td>Intravenous contrast</td>
</tr>
<tr>
<td>Decreases time to diagnosis and length of stay</td>
<td>May increase downstream costs and revascularizations</td>
</tr>
<tr>
<td>Evaluates other causes of chest pain</td>
<td>Limited quality if elevated heart rate, arrhythmias, or morbid obesity is present</td>
</tr>
</tbody>
</table>

CAD indicates coronary artery disease; CTA, computed tomographic angiography; and ED, emergency department.

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**Figure 1.**

A. Proposed testing strategy in patients with possible acute coronary syndrome (ACS). *Contraindications to computed tomographic angiography (CTA) include renal disease, severe allergy to iodine contrast, inability to follow breath-hold instructions, and pregnancy. Also consider factors that may impair image quality: body mass index >40 kg/m², arrhythmias, high heart rate despite β-blockers, extensive coronary calcifications, and intolerance or contraindication to β-blockers or nitroglycerin. Adapted from Cheezum et al11 with permission from the publisher. Copyright © 2014 Informa Plc. Authorization for this adaptation has been obtained both from the owner of the copyright in the original work and from the owner of copyright in the translation or adaptation. **B.** Early imaging strategy implementing coronary CTA. CAD indicates coronary artery disease. Adapted from Cheezum et al11 with permission from the publisher. Copyright © 2014 Informa Plc. Authorization for this adaptation has been obtained both from the owner of the copyright in the original work and from the owner of copyright in the translation or adaptation.
who had a positive second set of cardiac biomarkers.13 Nevertheless, 2 subsequent randomized, controlled trials have demonstrated a very low event rate when patients with nonobstructive CTA findings were immediately discharged. On the basis of the available data, a conservative approach among patients who are found to have nonobstructive plaque is to check a second set of biomarkers. If negative, such patients can be discharged but require outpatient follow-up for preventive care (Figure 1B).

**Obstructive CAD**

In patients with obstructive CAD, admission and further workup are recommended to guide management. For the majority of these patients, particularly those with moderate stenosis (ie, 50%–70%), functional testing for ischemia (noninvasive or invasive) is recommended because it may reduce unnecessary coronary revascularizations (Figure 1B).

**CTA to Guide Preventive Therapy**

Patients with both nonobstructive and obstructive CAD have increased risk for long-term major adverse cardiac events relative to patients with no CAD. For example, among patients with nonobstructive plaque, the 2-year cardiac event rate in ROMICAT I was 4.6% (1.2% after excluding early [<30 day] major adverse cardiac events) versus 0% for patients with no CAD.14 Similarly, other studies have demonstrated that nonobstructive plaque on CTA, especially when multiple segments are involved, is associated with a higher rate of hard cardiovascular events compared with no plaque on CTA.9 Supporting the growing recognition that coronary plaque on CTA is associated with an increased event rate, multiple observational studies have shown that CTA is associated with intensification in preventive therapies and modification of CVD risk factors.15,16

**Unanswered Questions**

What is the Long-Term Cost-Effectiveness of CTA Relative to Usual Care?

Although CTA has been shown to reduce ED costs compared with usual care, available studies have shown no benefit in total hospital costs with CTA use. As a test designed to detect the anatomic presence of CAD, CTA has potential to increase downstream costs by unnecessarily triggering invasive angiography and coronary revascularization procedures. Although further research is needed to clarify the cost benefit of CTA, data suggest that when the prevalence or inability to exclude obstructive CAD is <30%, CTA offers cost savings relative to usual care for acute chest pain.17

Can Coronary Artery Calcification Testing Alone Safely Exclude ACS in Low-Risk Patients?

Coronary artery calcification (CAC) testing alone has been proposed as a rapid, inexpensive test that is easy to perform and can exclude ACS in a majority of low-risk symptomatic patients.18 National Institute for Health and Clinical Excellence guidelines have adopted this strategy on the basis of estimates of the cost-effectiveness of this approach.19
yet research and widespread use of CAC alone in symptomatic patients remain limited. Although data support favorable prognosis among patients with CAC of zero,20 further studies are needed to examine the safety of CAC for ruling out ACS and potentially to guide the need and type of further testing (eg, discharge when CAC=0, CTA when CAC=1–99, and perfusion imaging for patients with CAC >100).

Is There a Role for Triple Rule-Out Scanning?
Of relevance to the ED setting is the potential for CTA use as a “triple rule-out” (TRO) test to simultaneously exclude ACS, aortic dissection, and pulmonary embolism. Challenges to TRO use have limited its widespread application, with data suggesting that the rate of pulmonary embolism and aortic dissection detected by TRO testing is very low (≈1% of scans).21 Additionally, TRO scans require more contrast to opacify all 3 vascular beds with higher radiation doses compared with CTA. Although newer scanners and techniques should improve the risk-to-benefit ratio of TRO, appropriate use of TRO scanning remains uncertain.5

What Is the Role of High-Sensitivity Troponin Among Testing Strategies?
Initial studies have demonstrated a high accuracy for high-sensitivity troponin (c statistic=0.94) to exclude ACS in the first hour of presentation, with an ability to predict ischemia and CAD burden among patients with normal initial standard troponin levels.22 Although studies have shown that high-sensitivity troponin may offer prognostic value independently of CTA findings, its specificity for ACS appears to be more limited.23 Further research is needed to define the role of high-sensitivity troponin among available strategies.

Conclusions
Coronary CTA is now an established, noninvasive technique that can rapidly exclude obstructive CAD and identify patients who can be safely discharged from the ED. Although CTA appears to lower ED costs and may lead to intensification in preventive therapies, concern remains about the potential for this test to increase angiography and coronary revascularizations. Ultimately, appropriate patient selection will remain essential for ensuring optimal test use and patient management.

Case Resolution
Given the intermediate pretest probability of obstructive CAD and the absence of contraindications, the patient underwent CTA, demonstrating mild nonobstructive CAD (Figure 3). A second set of cardiac biomarkers was normal. He was discharged with follow-up for risk factor management and has remained free of adverse cardiac events.

Disclosures
None. The views expressed here are those of the authors only.

References


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