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# **Computerized Tomographic Coronary Angiography for the Evaluation** of ED Patients with Potential Acute Coronary Syndromes

Dear Colleagues,

The diagnosis of acute coronary syndrome (ACS) represents one of the most difficult tasks facing clinicians in the acute care environment. Accurately detacting ACS in patients presenting to the ED with chest discomfort or other high risk presentations for myocardial ischemia or infarction remains a complex diagnostic task. In addition, for emergency physicians, the evaluation of ACS is particularly stressful as the misdiagnosis of this disease process serves as a common source for medical malpractice litigation, resulting in approximately 20% of the dollars awarded annually. Currently, patients must be evaluated for myocardial necrosis, rest ischemia, and ultimately exercise-induced ischemia in the emergency setting to properly diagnose this condition in patients at risk for ACS. Myocardial biomarkers, serial 12-lead electrocardiograms, rest radionuclide imaging, graded exercise testing, and stress echocardiography and radionuclide imaging all represent usual approaches to a proper diagnosis in the ED. Ultimately, visualization of the coronary artery anatomy by cardiac catheterization remains the gold standard approach for diagnosis of atherosclerotic coronary artery disease, ruptured plague and intra-luminal clot in patients with ACS.

In this EMCREG-International Newsletter, Drs. Judd Hollander and Howard Litt describe an important new modality for visualizing the coronary artery anatomy in patients with possible ACS - using 64-slice multidetector computed tomography coronary angiography. With the enormous and rapid computational power available in today's CT scanners, the coronary artery anatomy can be examined in great detail by effectively "freezing" a single cardiac cycle. This allows a non-invasive look at the atherosclerotic burden of a coronary artery as revealed by wall thickness associated with the plaque and the presence of calcium in the plaque. Intra-luminal clot can also be visualized with this technique. For emergency physicians, this technology provides tremendous potential including the early diagnosis of a ruptured plaque in a patient with ACS and for patients without disease, the visualization of disease free coronary arteries. We hope that you will enjoy this discussion of a new and potentially powerful addition to the emergency physician's diagnostic armamentarium. It is the goal of EMCREG-International to bring cutting edge information to the clinician, hopefully improving patient care and ultimately outcome.

Sincerely.



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# Introduction

Of the nearly 6 million patients presenting annually to U.S. emergency departments for evaluation of chest pain,<sup>1</sup> up to 85% do not have a cardiac cause for their symptoms.<sup>2-4</sup> Given the prevalence and clinical significance of coronary artery disease, however, excluding a cardiac cause of chest pain remains a challenging clinical problem and often mandates extensive testing. There is little ambiguity in the management of high-risk patients: individuals with ST-segment elevation myocardial infarction (STEMI) are treated expeditiously with primary percutaneous intervention or fibrinolysis. Patients with unstable angina and non-STEMI are treated with antithrombin and antiplatelet agents with rapid transition to the catheterization laboratory. The management and disposition of patients with STEMI and non-STEMI are dictated by consensus expert guidelines.<sup>5,6</sup>

Conversely, the management and disposition of low-risk patients is considerably less clear. Most of these patients are not ultimately diagnosed with acute coronary syndromes (ACS), yet are admitted to the hospital for "rule out MI" protocols which increase health care costs. Moreover, these hospital admissions lead to inpatient bed shortages, emergency department (ED) crowding, and prolonged ED stays, all of which lead to poor resource utilization.<sup>7</sup>

Numerous studies have attempted to risk stratify these patients more effectively in order to identify those at risk for adverse outcomes and optimize care for all patients with ACS. These tools have employed a range and combination of variables such as historical information, clinical characteristics, markers of myocardial necrosis, ECG interpretations, computer algorithms as well as cardiac imaging. Most of these advances either do not achieve sufficient sensitivity to allow rapid and early release of patients from the ED or are difficult to accomplish logistically.<sup>8-18</sup>

# **Diagnostic Testing and Risk Stratification**

To have utility for the emergency practitioner, a risk stratification tool needs to be simple, use information available during the initial presentation, and be easily applied early in the clinical course. Current standard of care requires clinical risk stratification followed by cardiac markers and some form of imaging for most patients with potential ACS.



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## **Cardiac Biomarkers**

Cardiac biomarkers alone have not been able to accomplish the goal of immediately decreasing risk to such a low level that ED chest pain patients could conclusively be "ruled out" and discharged to home without further evaluation for underlying coronary artery disease. Serial CK-MB mass measurements have nearly 90% sensitivity three hours after ED presentation for myocardial necrosis but are only 36-48% sensitive when utilized at or shortly after presentation.<sup>19,20</sup> An analysis of four studies assessing the predictive properties of single cardiac troponin I values at the time of presentation for acute myocardial infarction (AMI) found a sensitivity of 39% and specificity of 93%.<sup>19</sup> Despite the fact that these markers are useful for both diagnosis and risk stratification of patients with chest pain, single measurements of either or both markers cannot be safely used to assist in the discharge decision - since making it would result in an unacceptable miss rate for both AMI and cardiovascular complications.

It is worth noting that combinations of two or more cardiac markers increase the early predictive value of these types of strategies, however no combination of commercially available markers has yet been demonstrated to approach 100% sensitivity on the initial



Most patients are either observed in an observation unit or admitted to the hospital for objective testing (usually stress testing or myocardial perfusion imaging) for possible ischemia or underlying coronary artery disease. sample.<sup>21-23</sup> Most patients are either observed in an observation unit or admitted to the hospital for objective testing (usually stress testing or myocardial perfusion imaging) for possible ischemia or underlying coronary artery disease.

# Stress testing and myocardial perfusion imaging

The most common diagnostic imaging modality used to evaluate patients with potential ACS is an exercise or pharmacologic stress test. The results of the stress test are typically the final step to "rule in" or "rule out" ACS during any given admission. They are used because they help risk stratify patients with respect to outcome over the subsequent months to years. Relative to patients with an abnormal stress test, patients with normal tests are at lower risk for subsequent AMI.<sup>24</sup> However, patients that present to the ED

with chest pain syndromes often return with similar symptoms. Shaver demonstrated there was no association between a negative evaluation for underlying coronary artery disease and subsequent cardiac related ED visits, admissions, or cardiac resource test utilization over the year following the index visit.<sup>25</sup> Thus, it appears that negative tests do not provide a sufficient level of comfort to patients or providers when patients have persistent or recurrent symptoms. Nerenberg et al. found that knowledge of a prior negative stress test did not affect the emergency physician disposition decision when patients returned to the ED.<sup>26</sup> They also found that patients with a prior normal stress



A recent cardiac catheterization with normal or minimally diseased vessels almost eliminates the possibility of an acute coronary syndrome.

test are at the same risk of adverse cardiovascular events as patients who have not previously undergone stress testing. Thus, knowledge of a previously normal stress did not and should not impact clinical decision making in the ED. From a pathophysiology perspective, this makes sense; stable angina is caused by a fixed obstruction to flow, however, unstable angina, NSTEMI and STEMI are caused by plaque rupture and thrombus formation in a lesion that may or may not have been significant enough to result in angina (or a positive stress test) prior to the acute process. Stress testing assesses whether or not a fixed obstruction to flow is present and cannot predict subsequent plaque rupture resulting in ischemia.

### **Cardiac catheterization**

Prior cardiac catheterization results are known to be very useful for risk stratification of patients. Patients who have previously been documented to have minimal (<25%) stenosis or normal coronary arteriograms have an excellent long term prognosis with greater than 98% free from myocardial infarction 10 years later.<sup>27</sup> Repeat cardiac catheterizations an average of 9 years later found that approximately 90% of patients did not develop even single vessel coronary artery disease.<sup>28</sup> Thus, a recent cardiac catheterization with normal or minimally diseased vessels almost eliminates the possibility of an acute coronary syndrome.

However, most patients that present to the ED do not receive cardiac catheterization and thus are likely to receive either no evaluation<sup>29</sup> or an evaluation via stress testing that does not appear to provide comfort when negative, for either the patient or the physician.<sup>25,26</sup>

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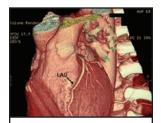
Alternative methods of risk stratification may prove to be more successful in terms of both risk stratification and impact on future symptoms. deFillipi et al showed that in low-risk patients, coronary angiography is more sensitive and more cost effective than exercise treadmill testing.<sup>30</sup> Patients with negative coronary angiography had fewer repeat ED visits, fewer hospitalizations, and had higher satisfaction rates and better understanding of their disease than patients who had negative stress tests.<sup>30</sup> Thus, using coronary angiography in place of stress testing for low risk patients may not only aid in patients' understanding of their disease, but may also decrease subsequent ED visits and hospitalizations as well as aid in physician disposition decision-making. Alternatively, computed tempography (CT) coronary againg arguing ar

computed tomography (CT) coronary angiography correlates very well with cardiac catheterization, potentially offering a noninvasive assessment of coronary anatomy with the same benefits for future clinical decision-making and patient understanding of their disease as cardiac catheterization.

### CT coronary angiography

Computed tomography angiographic evaluation of the coronary arteries shows great promise in the evaluation of patients with potential ACS (Figures 1 and 2). It is particularly appealing from the emergency medicine perspective.

Calcium scoring using electron beam CT (EBCT) is useful for detection of high grade stenosis and occlusion with a sensitivity of 92% and a specificity of 94%.<sup>31</sup> McLaughlin used EBCT to stratify ED chest pain patients without known coronary artery disease (CAD) and found that 1 of 48 patients with a negative test had



In low-risk patients, coronary angiography is more sensitive and more cost effective than exercise treadmill testing. a cardiac event.<sup>32</sup> Laudon et al. found a 100% negative predictive value in 53 patients compared to other assessments for coronary arterv disease.<sup>33</sup> Georgiou et al. performed a prospective observational study of ED chest pain patients.<sup>34</sup> They found the cardiovascular event rate to be 0.6% for the 76 subjects with a calcium score of 0 compared to 14% for the subjects with calcium scores greater than 400. These studies suggest that EBCT can provide valuable prognostic information for ED chest pain patients. Raggi et al studied 207 low to intermediate risk patients and found that EBCT has a sensitivity

of 74% and a specificity of 89% for the presence of obstructive coronary artery disease.<sup>35</sup> In their Bayesian analysis, EBCT provided a cost savings of 45-65% over a pathway including treadmill testing.

scoring, whether performed using EBCT or multidetector CT (MDCT) detects coronary calcium but does not detect plaque without calcification. While studies in ED patients have demonstrated the safety of using the absence of coronary calcifications as criteria for risk stratification;<sup>31-34</sup> the addition of MDCT coronary angiography to calcium scoring further enhances this diagnostic test allowing detection of coronary calcification, non-calcified



CT coronary angiography correlates very well with cardiac catheterization, potentially offering a noninvasive assessment of coronary anatomy.

atherosclerotic plaque, and coronary luminal stenosis. Leber et al reported a specificity of 97% for detection of atherosclerotic coronary stenosis.<sup>36</sup> Raff et al., compared cardiac catheterization results and CT coronary angiography in 1,065 coronary artery segments in 70 patients; finding a mean difference in percent stenosis of  $1.3 \pm 14.2\%$ .<sup>37</sup> Specificity, sensitivity, positive and negative predictive values of CT angiography for significant stenosis was: 86%, 95%, 66% and 98%, respectively. This study also demonstrated the reliability of a negative CT coronary angiogram in excluding CAD.

These data combined with findings that patients with normal or minimally diseased coronary arteries do well over the long term,<sup>27,28</sup> has led emergency physicians to generally eliminate an ACS from the differential diagnosis of patients with a recent normal cardiac catheterization. Such patients are routinely discharged from the ED without admission for further evaluation.

The combination of the outstanding sensitivity and negative predictive value of coronary calcium scoring in 3 studies of ED patients with potential ACS, together with documented correlation between CT coronary angiography and routine cardiac catheterization results, as well as the ability to obtain both calcium scores and visualization of the coronary arteries with CT coronary angiography has led several centers to both study and routinely utilize CT coronary angiography in "real time" clinical practice.





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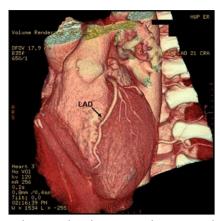
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### Clinical studies on CT coronary angiography in the ED

The clinical evaluation of CT coronary angiography and its optimal applications in the ED are currently underway. To date, the main focus has been on this technology's use for pre-discharge testing.

Gallagher et al.<sup>38</sup> compared the accuracy of CT coronary angiography with stress myocardial perfusion imaging for the detection of an acute coronary syndrome or 30-day major adverse cardiac events in low risk chest pain patients following a "rule out" in an observation unit. All patients had both rest and stress myocardial perfusion imaging and CT coronary angiography. Patients with abnormal myocardial perfusion imaging (reversible perfusion defects) or positive CT coronary angiography results (stenosis >50% or calcium score > 400) were considered for cardiac catheterization, and those with discordant results had a 30-

Figure 1. Images obtained by CT coronary angiography



Volume rendered LAO view shows normal LAD and diagonal branches in a 38 year old woman with atypical chest pain. Volume rendered images provide an overview of the coronary arteries but can not be used on their own to exclude stenosis.



Thin-slab maximum intensity projection reveals no stenosis in proximal LAD, circumflex, and ramus medianus (RM) arteries.

day re-evaluation. Of 85 study patients, 7 (8%) were found to have significant coronary stenosis and none had myocardial infarction or an adverse cardiovascular event during 30 day follow-up. The sensitivity of myocardial perfusion imaging was 71% (95% C, 36-92%) and CT coronary angiography was 86% (95% CI, 49-97%). The specificity was 90% (81-95%) for myocardial perfusion imaging and 92% (84-96%) for CT coronary angiography. The negative predictive value of myocardial perfusion imaging and CT coronary angiography was 97% (90-99%) and 99% (93-100%), and the positive predictive value was 38% (18-64%) and 50% (25-75%) respectively. Their data suggest that the performance of CT coronary angiography is at least as good as that of stress myocardial perfusion imaging for detection or exclusion of an acute coronary syndrome in low risk chest pain patients.



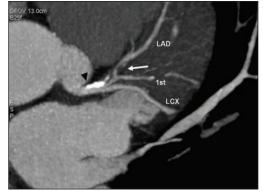
Curved multiplanar reformatted (MPR) projection demonstrates patent circumflex (arrow) coursing between the left atrium (LA) and left ventricle (LV)



Low density noncalcified plaque (arrow) causing >50% stenosis of the proximal right coronary artery. Ao=Aorta



Curved MPR projection demonstrates patent LAD and oblique long axis view of the left atrium (LA) and left ventricle (LV)



Calcified plaque resulting in 50% stenosis of the distal left main (arrowhead). Mixed calcified and noncalcified plaque resulting in 70% stenosis of the proximal LAD and mild stenosis of the proximal 1st diagonal (1st). Patent circumflex (LCX)

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Figure 2. Summary of CT Technologies for Coronary Artery Imaging

# Summary of CT Technologies for Coronary Artery Imaging

# Two CT technologies are in use for imaging of the coronary arteries:

Electron Beam CT (EBCT) - sometimes called "ultrafast" CT Multidetector CT (MDCT) - sometimes called multislice CT (MSCT)

### **Electron Beam CT (EBCT)**

EBCT operates without motion of a mechanical x-ray source around the patient. A magnetic field controls the direction of an electron beam, sweeping it across a fixed target ring, which produces an x-ray beam that in turn sweeps across a fixed detector ring on the opposite side of the gantry from the target ring. Because there are no mechanical parts, the x-ray beam rotates very rapidly, allowing a slice acquisition time of 50-100 msec, "freezing" the motion of the heart. Single slices, usually 3 mm thick, are acquired during each heart beat, so that exams of the entire heart may take 30-40 secs.

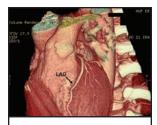
### Multidetector CT (MDCT)

In mechanical gantry MDCT systems, the entire x-ray tube and detector spin around the patient. Using MDCT, up to 64 slices of 0.5-0.75 mm thickness can be obtained during each heart beat, resulting in examination times of 6-12 seconds, which is within the breath hold capability of most patients. However, because a mechanical system is used, slice acquisition time (and therefore temporal resolution) has been limited to about 200 msec. This results in motion blurring at higher heart rates, and is the reason that most centers administer beta blockers to patients with heart rates > 65 bpm. The newest generation of MDCT scanners allows a temporal resolution of 83 msec, which may obviate the need for beta blockers in almost all patients.

In general, EBCT has superior temporal resolution but decreased spatial resolution and longer breath holds compared to MDCT. Additionally, EBCT scanners are not widely available, as only one manufacturer produces them. EBCT scanners have also not been implemented widely outside of cardiac imaging because of limitations in x-ray tube output. Both types of CT systems can be used for calcium scoring, but MDCT is the dominant technology currently in use for contrast enhanced coronary CT angiography. Regardless of whether one performs coronary CT angiography using EBCT or MDCT, imaging is performed during rapid intravenous injection (3-5 ml/sec) of 80-120 ml of high iodine concentration (300-400 mg) non-ionic contrast, so impaired renal function is a contraindication.



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Compared to the standard evaluation, the use of CT coronary angiogram resulted in reduced length of stay.

Goldstein et al.<sup>39</sup> studied 197 patients admitted to an observation unit. Patients were randomized to either standard evaluation or CT coronary angiography. CT coronary angiography patients with minimal disease were discharged home. Those with stenosis >70% underwent catheterization and patients with intermediate lesions or uninterpretable scans underwent nuclear stress testing. They found that CT coronary angiogram evaluation immediately excluded or identified a cardiac etiology of chest pain in 75% of cases. Sixty six patients with normal coronary arteries were discharged home and 9 with severe disease were referred for immediate invasive evaluation. The CT

coronary angiogram findings necessitated referral for stress testing in 24% of patients, including 13 with intermediate stenoses. Compared to the standard evaluation, the use of CT coronary angiogram resulted in reduced length of stay (12.5 versus 22.1 hours, p < 0.0001) and lower costs (\$1,586 versus \$1,872 p < 0.0001). Although this study was too small to conclusively comment on safety, no patient in either group died or had an acute myocardial infarction.

Moloo et al.<sup>40</sup> compared CT coronary angiography to myocardial perfusion imaging in patients being admitted to the hospital. They found a high degree of agreement between the tests but did not report the relationship between the tests and outcome. Nagurney et al.<sup>41</sup> found that CT coronary angiography results had a large impact on the post-test probability of disease in 40 patients admitted through the ED. Hoffman et al., in a study of 103 patients who received MDCT with results blinded to the clinician, found that in the 74 patients that either did not have plaque or had plaque without stenosis, none were diagnosed with an ACS within 5 months.<sup>42</sup>

Chase et al.<sup>43</sup> reported a different patient population – ED patients who had not yet been evaluated in an observation unit or had a complete "rule out protocol". Their clinical algorithm evaluated low risk (defined as TIMI score  $\leq$ 2) patients in the ED with CT coronary angiography after obtaining a serum creatinine level and a single set of cardiac markers (Figure 3). Patients with a negative CT coronary angiogram were immediately discharged home without further evaluation or other provocative testing. A negative CT coronary angiogram was defined as no stenosis or a stenosis less than 50% and a calcium score less than 100. Of the 41 EMERGENCY MEDICINE CARDIAC RESEARCH AND EDUCATION GROUP

patients enrolled, 33 were discharged from ED after having negative CT coronary angiograms. None of the patients in the study had an adverse event during index hospitalization or at 30 day follow up (0%; 95% CI, 0-7.3%). They used a 64 slice CT scanner for the majority of the patients. Some studies suggest that older model CT scanners (for example, 16 slice) do not appear to have the same diagnostic accuracy.<sup>44,45</sup> Khare et al<sup>46</sup> showed that CT coronary angiography may be very cost effective to exclude symptomatic coronary artery disease in ED patients. One might expect that if this new technology can rapidly exclude disease in ED patients, thus avoiding admission to observation units or the hospital, it would likely be very cost effective. Studies are now being designed to address both the safety and cost effectiveness of CT coronary angiography in the ED for patients with potential ACS.

# Conclusions

CT coronary angiography is a new technology that in early studies shows great promise in the management of ED patients with potential

ACS. Recent guidelines state, "A 'normal' CT coronary angiogram allows the clinician to rule out the presence of hemodynamically relevant coronary artery stenosis with a high degree of reliability" and give it a class IIa, Level of Evidence B recommendation for use in symptomatic patients.47 It combines a noninvasive approach to the evaluation of coronary artery disease with accuracy that rivals cardiac catheterization. Preliminary data suggest that it may be useful both for pre-discharge evaluation of possible coronary artery disease in patients who have ruled out for AMI and to exclude coronary artery disease obviating the need for a traditional "rule out" admission. If these promises are realized, the increased efficiency and decreased needs for telemetry beds might improve both hospital efficiency and revenues without increasing overall costs. Only time and appropriately designed studies can answer these questions definitively.



**CT** coronary angiography is a new technology that in early studies shows great promise in the management of ED patients with potential ACS. It combines a noninvasive approach to the evaluation of coronary artery disease with accuracy that rivals cardiac catheterization.

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**Figure 3.** Hospital of the University of Pennsylvania (HUP) Protocol for CT Coronary Angiogram in Low Risk Chest Pain Patients

# HUP Protocol for CT Coronary Angiogram in Low Risk Chest Pain Patients

# Eligible candidates

- 1. Patients with a chief complaint consistent with potential ACS
- 2. Electrocardiogram without acute ST or T wave changes
- 3. TIMI risk score of less than or equal to 2
- 4. No contraindications to CT coronary angiography:
  - lodinated contrast allergy
  - **Pregnant patients**

Heart rate > 80 beats per minute despite beta-blockade

Heart rate > 80 beats per minute with contraindication to beta-blockade:

- Hypotension
- Cocaine use in the past 72 hours
- Active asthma or COPD

Creatinine clearance < 60

## Interpretation of Results

# CT coronary angiography is considered negative if:

1. The calcium score is < 100

# AND

2. The patient has no stenosis or < 50% stenosis of the right coronary, left main, left anterior descending, or circumflex arteries or of their first-order branches

**NEGATIVE RESULTS:** Patients with negative CT coronary angiography are discharged home with outpatient follow up to further investigate the etiology of the symptoms.

**POSITIVE RESULTS:** Patients with positive CT coronary angiography are admitted to the appropriate inpatient service depending upon the next step in the evaluation process. This is commonly stress myocardial perfusion imaging for intermediate or equivocal results or cardiac catheterization for patients with high risk anatomy.



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- 1. Serial CK-MB mass measurements are nearly 90% sensitive when utilized at or shortly after presentation.
  - a. True
  - b. False
- 2. Patients minimal (<25%) stenosis or normal coronary arteriograms have an excellent long term prognosis.
  - a. True
  - b. False
- 3. According to the study by deFillipi, which of the following tests has been shown to be most cost effective for patients with low risk chest pain?
  - a. stress test
  - b. CT coronary angiogram
  - c. cardiac catheterization
  - d. resting MIBI scan

# 4. Which of the following are true regarding CT coronary angiography?

- a. CT coronary angiography is at least as good as that of stress myocardial perfusion imaging for detection or exclusion of an acute coronary syndrome in low risk chest pain patients
- When used in a chest pain observation unit, the use of CT coronary angiogram resulted in reduced length of stay and lower costs.
- c. When used in a chest pain observation unit, the use of CT coronary angiogram resulted lower costs.
- d. Data exist suggesting that CT coronary angiogram might have a role in the immediate evaluation of low risk chest pain patients.
- e. All of the above

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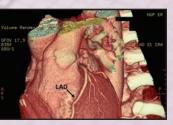
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