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Coronary Computed Tomography Angiography for Evaluation of Chest Pain in the Emergency Department

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Coronary computed tomography angiography has emerged as an important diagnostic modality for evaluation of acute chest pain in the emergency department for patients at low to intermediate risk for acute coronary syndromes. Several clinical trials have shown excellent negative predictive value of coronary computed tomography angiography to detect obstructive coronary artery disease. Cardiac biomarkers such as troponins and creatine kinase MB, along with history, electrocardiogram, age, risk factors, troponin score, and Thrombolysis in Myocardial Infarction score should be used in conjunction with coronary computed tomography angiography for safe and rapid discharge of patients from the emergency department. Coronary computed tomography angiography along with high-sensitivity troponin assays could be effective for rapid evaluation of acute chest pain in the emergency department, but high-sensitivity troponins are not always available. Emergency department physicians are not quite comfortable making clinical decisions, especially if the coronary stenosis is in the range of 50% to 70%. In these cases, further evaluation with functional testing, such as nuclear stress testing or stress echocardiogram, is a common approach in many centers; however, newer methods such as fractional flow reserve computed tomography could be safely incorporated in coronary computed tomography angiography to help with clinical decision-making in these scenarios. (Tex Heart Inst J. 2022;49(6):e217550)

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Chest pain accounts for approximately 6.5 million annual visits to emergency departments (EDs) in the United States, 260,000 of which are because of acute myocardial infarction.¹ In the United States, the estimated annual cost of evaluating patients with chest pain in the ED exceeds \$5 billion.²⁻⁶ Missing occult acute coronary syndrome (ACS) in such patients leads to morbidity and mortality and significant malpractice litigation.⁷ At the same time, ED physicians are obligated to perform more-rapid and accurate triage of chest pain patients to shorten the ED length of stay and to prevent ED return within 72 hours of discharge. Apart from ACS, other causes of acute chest pain that are concerning to ED physicians are aortic dissection and pulmonary embolism. Not surprisingly, every ED physician wishes there were a single imaging test that could rule out all the acute causes of chest pain for safe and timely discharge of patients.

Although history, physical examination, electrocardiogram (ECG), and serial troponins can rule out ACS and aid prompt discharge of patients, there is always a moment of indeterminacy when it is difficult to decide whether additional tests are warranted. The History, ECG, Age, Risk factors, and troponin (HEART) and Thrombolysis in Myocardial Infarction (TIMI) scores were developed in an effort to help clinical contextualization of the biomarkers assay.⁸ Patients with an intermediate risk for ACS (HEART score of 4-6 and TIMI score of 0-2) often are admitted to the observation unit overnight to undergo a stress echocardiogram and/or nuclear stress testing, which generally happens on the following day. Nuclear stress testing is often performed on these patients. However, nuclear stress testing is associated with large amounts of radiation exposure and has poor diagnostic accuracy to predict significant stenosis in the catheterization lab.⁹ The results of the Initial Invasive or Conservative Strategy for Stable Coronary Disease (ISCHEMIA) trial also suggest that stress testing is a poor predictor of adverse events.¹⁰

Landmark Clinical Studies Using CT Angiography for Evaluation of Chest Pain

Coronary computed tomography angiography (CCTA) has evolved as a rapid noninvasive test with a very high negative predictive value (NPV) to rule out significant stenosis and can be used as a roadmap by the catheterization lab to determine the severity of coronary artery stenosis (Fig. 1). Numerous clinical studies have validated the diagnostic accuracy of CCTA to evaluate obstructive coronary artery disease (CAD). The Assessment by Coronary Computed Tomography Angiography of Individuals Undergoing Invasive Coronary Angiography (ACCURACY) trial¹¹ was a prospective multicenter trial of patients with chest pain but without known CAD that showed that 64-multidetector row CCTA had a sensitivity of 95% and NPV of 99% to detect more than 50% stenosis. Similar results were found in the Coronary Artery Evaluation Using 64-Row Multidetector Computed Tomography Angiography (CORE-64) study,¹² which enrolled patients with suspected symptomatic CAD. The study by Meijboom et al¹³ enrolled symptomatic patients with stable or unstable angina symptoms and showed that CCTA accurately detects significant CAD and is reliable for ruling out significant CAD.

To the authors' knowledge, the first single-center randomized clinical trial comparing coronary computed tomography with standard diagnostic evaluation was published by Goldstein et al¹⁴ in 2007; in that study, 197 low-risk patients were randomized to CCTA vs rest-stress myocardial perfusion imaging (MPI). The major advantage of CCTA was that it could rapidly and accurately delineate the absence of CAD or the presence of severe stenosis, thereby facilitating more-rapid discharge and lowering costs. Patients who underwent CCTA required fewer repeat evaluations for recurrent chest pain. This trial was followed in 2011 by the mul-

ticenter Coronary Computed Tomographic Angiography for Systematic Triage of Acute Chest Pain Patients to (CT-STAT) trial,¹⁵ which randomized 699 low-risk patients at 16 study sites to either CCTA or rest-stress MPI. The CCTA resulted in a 54% reduction in time to diagnosis compared with MPI (2.9 h vs 6.3 h, respectively; $P < .001$) and was associated with 38% lower cost than MPI (\$2,137 vs \$3,458, respectively; $P < .001$).

Rule out Myocardial Infarction Using Computer Assisted Tomography I (ROMICAT I) was an observational study published in 2009, in which 368 patients with chest pain and low to intermediate risk for ACS with normal initial troponin (conventional troponin I) underwent CCTA before admission.¹⁶ Coronary computed tomography angiography had 98% NPV but only 77% sensitivity for the detection of ACS during index hospitalization. It also showed that 50% of these patients with chest pain had no CAD by CCTA.

Rule out Myocardial Infarction Using Computer Assisted Tomography II (ROMICAT-II) was a multicentric randomized controlled trial in which 1,000 patients with symptoms suggestive of ACS without ECG changes or an initial positive troponin test (conventional troponin I) were randomized to early CCTA or to standard of care (SOC) in the ED.¹⁷ The SOC included any available management strategy deemed appropriate by the treating physicians. These choices included ECG treadmill testing, stress echocardiogram, and stress single-photon emission computed tomography, as well as no further diagnostic testing as an option. In the CCTA group, the mean length of stay in the hospital was reduced by 7.6 hours compared with the SOC group ($P < .001$) without any significant difference in the ACS, major adverse cardiac events, mean cost of care ($P = .65$). However, there was more downstream testing in the CCTA group.

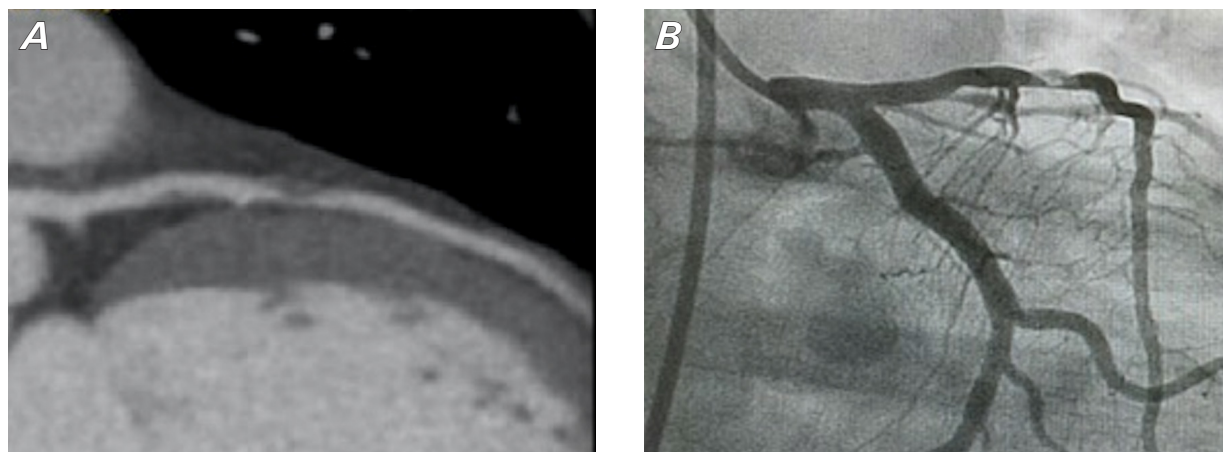


Fig. 1 Coronary computed tomography angiogram curved multiplanar view showing **A)** severe stenosis of the middle portion of the left anterior descending artery, and **B)** the corresponding lesion seen in the angiogram.

Coronary Computed Tomography Angiography Compared to Exercise ECG (CT-COMPARE) was another randomized single-center trial of 562 low- to intermediate-risk patients with chest pain undergoing CCTA or exercise stress ECG after the first negative troponin test.¹⁸ At 30 days, use of CCTA had provided a 35% relative reduction in length of stay ($P < .0005$) and a 20% reduction in hospital costs ($P < .001$), as well as superior diagnostic performance compared with exercise stress ECG for ACS. The overall results suggest that CCTA is useful as a first-line assessment for chest pain in the ED.

The well-powered, multicentric Computed Tomography for Safe Discharge of Patients with Possible Acute Coronary Syndromes (ACRIN-PA) trial⁴ randomized 1,370 patients with low to intermediate risk presenting with possible ACS in a 2:1 ratio to CCTA or to traditional care, looking at safety in patients with negative CCTA as the primary end point. Safety was defined as the absence of myocardial infarction and cardiac death during the first 30 days after presentation. Of 640 patients with a negative CCTA examination, there was no instance of death from myocardial infarction within 30 days. Patients in the CCTA group had a higher rate of discharge from the ED (50% vs 23%), a shorter length of stay (18 h vs 25 h), and a higher rate of detected coronary disease than did the traditional care group.

High-sensitivity troponin assays (hs-troponins) have become standard practice in many institutions because they allow for ACS to be ruled out more accurately and quickly. Whether hs-troponins will erode the potential clinical, logistic, and economic benefits of CCTA is an important clinical question. The Better Evaluation of Acute Chest Pain with Coronary Computed Tomography Angiography (BEACON) trial is a European randomized trial that compared a diagnostic strategy supplemented by early CCTA with SOC for patients suspected of having ACS in the era of hs-troponins.¹⁹ The BEACON trial showed that in a European setting, early CCTA was safe, less expensive, and had less subsequent outpatient testing than did SOC alone. However, the study also showed that early CCTA did not identify more patients with significant CAD who required coronary revascularization, did not reduce the length of stay, and did not allow more expedited discharge from the ED. As a result of this study, some might argue against the role of CCTA in the ED; however, it is important to consider here that by performing CCTA, physicians will not just rule out ACS but will also obtain more information about the etiology of presenting chest pain; this will lead to less subsequent outpatient testing. Emergency physicians may also use CCTA for triple rule out—that is, to rule out ACS, pulmonary embolism, and aortic dissection all at the same time. Although more outcome studies need to be conducted to suggest the effectiveness of this approach, it seems that triple rule out will

facilitate early discharge and reduce testing if patients come to the ED with similar symptoms in subsequent visits. Furthermore, it is important to consider that not all hospitals have hs-troponins available, and as a result, it is difficult to quickly discharge patients with timely follow-up. A study at our urban public hospital was performed to look at the positive predictive value of stress testing (exercise stress test and nuclear stress test) in the detection of obstructive CAD requiring percutaneous coronary intervention (PCI) or coronary artery bypass graft surgery and compared the results of stress testing with those of CCTA. We found that the proportion of positive CCTAs that had indications for PCI was significantly higher than that from the nuclear perfusion tests ($P = .0063$).²⁰ As we do not yet have hs-troponins in our clinical setting, CCTA seems to be an optimal choice for safe discharge of patients at our institution.

Patient Selection

Patients suitable for CCTA in the ED should have reasonable clinical suspicion of ACS but should not have objective evidence of ACS on ECG or myocardial necrosis by biomarkers. A TIMI or HEART score should be completed for risk stratification. Patient with known prior myocardial infarction or stents may not be well suited for testing. However, with newer and faster scanners, even patients with extensive atherosclerosis or stents could be reasonably ruled out for ACS or obstructive CAD. Generally, however, the best patient to get a CCTA in the ED is someone with low to intermediate risk of having ACS based on history, physical exam, TIMI score less than 4, and with low HEART ACS likelihood. High-risk patients should go for the invasive angiogram.²¹

Patient Preparation and Contrast Protocol

Coronary computed tomography angiography is generally a 20-minute procedure and requires anywhere from 15 minutes to an hour for interpretation, depending on the severity of disease. Heart rate control is a crucial step in reducing motion artifact and producing better image quality.²² Nitroglycerine either sublingually or applied in spray form is administered to dilate the coronary vessels. It also helps to use the images later for evaluation of fractional flow reserve computed tomography (FFRCT) if indicated.²³ Contrast is chosen based on the renal function of the patient. If the glomerular filtration rate (GFR) is higher than 60 mL/min, iodinated contrast is given at 5 mL/s, followed by the same amount of saline. If the GFR is 45 to 60 mL/min, iso-osmolar contrast at 5 mL/s is given after premedicating with acetylcysteine. If the GFR is 30 to 45 mL/min, we consider adding gadolinium or declining to perform CT. Patients with end-stage renal disease can have iodinated contrast at 5 mL/s if they are getting their regular dialysis. For CCTA, it is desired to have a high concentration of

contrast on the left side of the heart and low levels on the right.

Image Quality and Dose-Reduction Techniques

Image quality is a key component of any CCTA, as undiagnostic image quality leads to confusion, wastes resources, and exposes patients to unnecessary radiation. To minimize motion artifact, the heart is typically scanned at 75% of the cardiac cycle (mid-diastole) if the heart rate is lowered to a target of less than 65/min. If the heart rate is higher than 65/min, the heart is scanned at 40% of the cardiac cycle (end systole).

Calcium scanning is done without the use of intravenous contrast, and at the study center where this study was conducted, calcium scanning is performed for all patients undergoing CCTA in the ED. A calcium score of 0 often helps downgrade the risk of having substantial disease.²⁴ This is particularly useful in situations where CCTA cannot be obtained for various reasons, such as intravenous line dysfunction, poor renal function, or patient concern about intravenous contrast allergy. A calcium score of 0 suggests a low risk of acute myocardial infarction but does not predict the severity of stenosis, especially in a patient presenting to the ED with chest pain. Also, patients under the age of 40 years often have 0 calcium but could possibly have high-grade stenosis.

Although low-dose ionizing radiation and cancer risk has been debated for a long time,²⁵ CCTA should be performed based on the “as low as reasonably achievable” principle to minimize radiation exposure. A prospective protocol (scanning only in certain phases of cardiac cycle) should be used in every case, unless the heart rate is high, at which point a retrospective protocol (scanning throughout the cardiac cycle) should be used. Radiation is a measure of dose-length product, so the scan length should be appropriately chosen. Calcium scans can be helpful in finding the superior and inferior extent of the coronaries, which is information that can be used for CCTA. The radiation dose generally ranges from 0.5 to 1 millisieverts (mSv) for a calcium scan and 1 to 4 mSv for CCTA (prospective triggering), with an average of 1.3 mSv.

Interpreting Coronary CT Angiography Findings

At the study center, the final CCTA report details calcium score, severity of stenosis, plaque type, high-risk features, and burden. All segments of the coronary tree are analyzed using the 18-segment model from axial images and multiplanar reconstructions of the minimum available slice thickness. Maximal-intensity projections and curved multioblique views are often used. Diagnostic uncertainty resulting from motion artifact can be resolved by viewing multiple phases and by using

the SnapShot Freeze technique. Coronary computed tomography angiograms are typically read by a cardiologist, whereas noncardiac findings are reported by radiologists. All emergency scans are reported verbally to the ED staff.

Patient Management

Patients with no disease or mild disease are discharged home, whereas those with severe stenosis often proceed to the catheterization lab. However, ED physicians managing acute chest pain may not be familiar with the CCTA grading, especially when making clinical decisions if the stenosis is in the range of 50% to 70%. Further evaluation with functional testing using nuclear stress testing or stress echocardiogram is a common approach in many centers. In this context, FFRCT is a relatively new and promising modality that uses data from CCTA, creates models based on computational fluid dynamics, and can detect lesion-specific ischemia. In many clinical trials, the diagnostic accuracy of FFRCT has been shown to be similar to invasive FFR.²⁶⁻²⁸ Hlatky et al²⁹ showed that the use of FFRCT to select patients for invasive coronary angiography and PCI would result in 30% lower costs and 12% fewer events at 1 year than those with the most commonly used invasive coronary angiography/visual strategy. The Assessing Diagnostic Value of Non-Invasive FFRCT in Coronary Care (ADVANCED) registry enrolled 5,083 patients with clinically suspected CAD who underwent CCTA and FFRCT. The 1-year outcome showed less revascularization and lower cardiovascular death or myocardial infarction rates in patients with FFRCT of more than 0.8 (significant disease) vs patients with FFRCT of 0.8 or less (less-significant disease).³⁰ In the future, we will see FFRCT technology advance enough that it can be used to inform a road map to the catheterization lab. Based on the authors' experience with CCTA and the available evidence, it is appropriate to develop an approach for evaluation of patients presenting with chest pain in the ED (Fig. 2).

Conclusion

Emergency department physicians face the most challenging task when it comes to managing patients with acute chest pain, especially because of increasing pressure to reduce hospitalization, reduce length of stay, and prevent revisits to the ED. At the same time, it is also unacceptable to miss a chance to diagnose ACS. Improving upon the traditional risk factor assessment tools, which include history, physical examination, biomarkers, and risk-scoring algorithms such as the HEART score/TIMI score, CCTA has emerged as a new imaging modality with exceptional NPV that can be used to rule out significant coronary artery stenosis. Adding

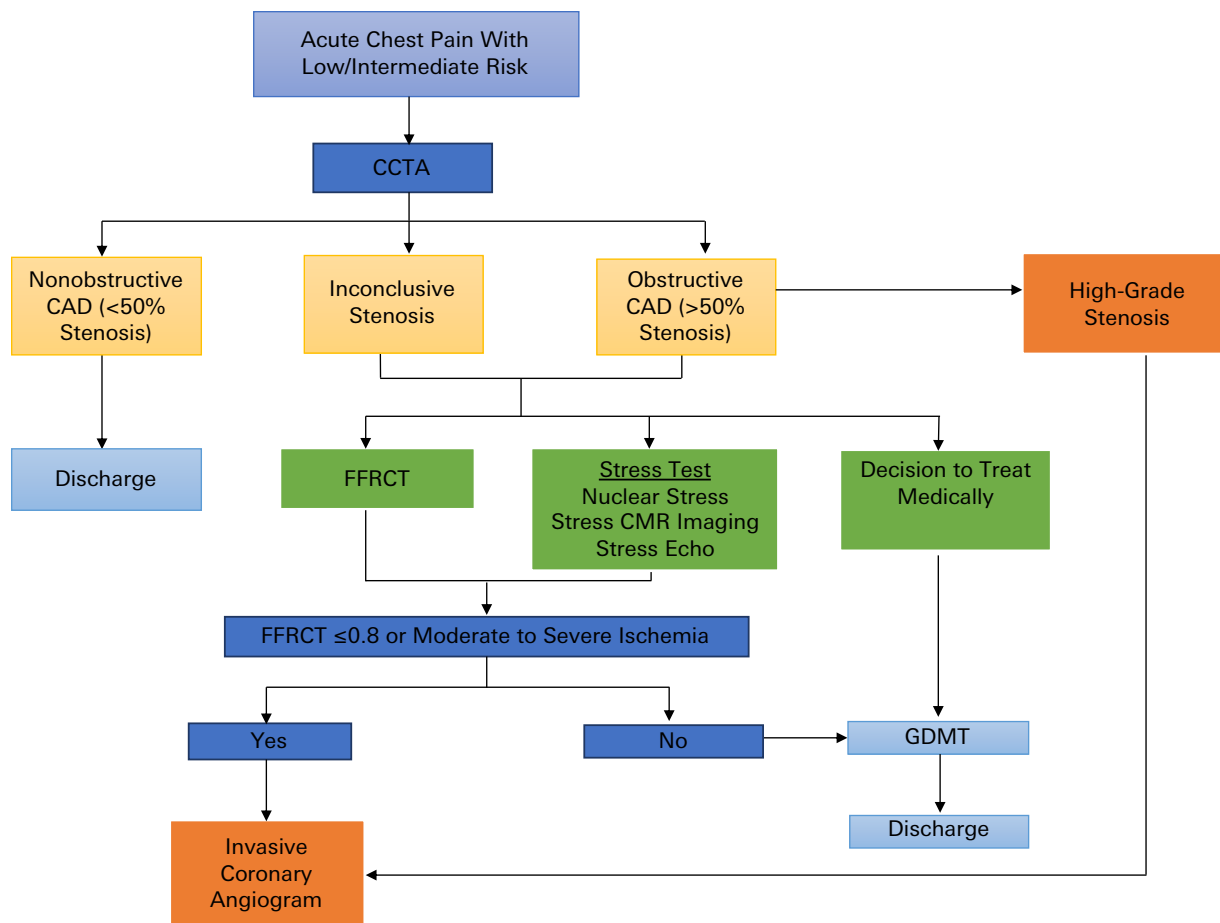


Fig. 2 Evaluation algorithm for low- to intermediate-risk patients presenting with acute chest pain in the emergency department.

CAD, coronary artery disease; CCTA, coronary computed tomography angiography; CMR, cardiac magnetic resonance; Echo, echocardiogram; FFRCT, fractional flow reserve computed tomography; GDMT, guideline-directed medical therapy.

functional value to the anatomy, FFRCT has supplemented the CCTA to make accurate clinical decisions if there is stenosis of uncertain clinical significance. Coronary computed tomography angiography was recently given a class 1A recommendation for patients with stable and acute chest pain in the 2021 American Heart Association/American College of Cardiology/American Society of Echocardiography/CHEST/Society for Academic Emergency Medicine/Society of Cardiovascular Computed Tomography/Society for Cardiovascular Magnetic Resonance guideline for the evaluation and diagnosis of chest pain.³¹ In the future, large clinical trials are needed to study CCTA and FFRCT and their role in care in the ED in terms of clinical outcomes and downstream cost-effectiveness.

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