Coronary and Cardiac Computed Tomography in the Emergency Room

Current Status and Future Directions

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Abstract: In the United States, chest pain is the second leading reason for patients to present to an emergency department (ED). Previously, those patients suspected to have acute coronary syndrome were monitored for 24 hours to determine the presence of serum biomarkers consistent with myocardial injury. However, more recently, imaging has been used to more efficiently triage these individuals and even discharge them directly from the ED. There are multiple cardiac imaging modalities; however, cardiac computed tomography now plays a significant role in the evaluation of patients with suspected acute coronary syndrome who present to the ED. In this review, we discuss the available state-of-the-art techniques for evaluating this cohort of patients, including clinical evaluation, serum biomarkers, and imaging options. Further, we analyze in detail evidence for the use of coronary computed tomography angiography to determine whether these patients can safely be discharged from the ED. Finally, we review some of the related future techniques that may become part of the accepted clinical management of these patients in the future.

Key Words: coronary computed tomography angiography, acute coronary syndrome, chest pain, emergency department

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In 2007, there were about 117 million visits to the emergency department (ED) in the United States. Approximately 8 million of these patients—the second largest cohort—presented with chest pain.[1] Generally, 15% to 30% of patients who present to the ED with nontraumatic chest pain have acute coronary syndrome (ACS).[2–7] The 28-day mortality rate for ACS among patients in developed nations is approximately 10% but varies with the severity of disease and the treatment provided.[8,9] Patients with ACS or acute myocardial infarction (AMI) can present with a wide variety of symptoms, making diagnosis difficult.[3] As a result, there has traditionally been a low threshold for hospital admission of such patients to exclude ACS, with a historically low percentage of patients found to be actually experiencing cardiac ischemia (15% to 30%) and resulting in hospital stay costs of about $8 to $10 billion a year.[2–7] Interestingly, 2% to 5% of patients with ACS were still being inappropriately discharged from the ED, leading to increased morbidity and mortality.[3,6,7] Consequently, the initial investigational strategy is now focused on rapidly and accurately excluding those diagnoses with the greatest short-term mortality risk. The differential diagnosis of chest pain includes other life-threatening conditions such as aortic dissection, pulmonary embolism (PE), tension pneumothorax, pericardial tamponade, and mediastinitis.

In this article, we review the current state-of-the-art techniques for management of chest pain in the ED, discussing in particular the application of coronary computed tomography angiography (CCTA) in the workup of these patients. We also examine some novel technologies that may find routine clinical application in the future.

INITIAL EVALUATION

Evaluation of chest pain patients in the ED, allowing risk stratification into high-risk, intermediate-risk, and low-risk groups, begins with history taking and a physical examination. The characteristics of the pain and associated symptoms are most reliable in "ruling in" high-risk patients but are less reliable when being used to "rule out" myocardial ischemia.[10] In the presence of symptoms, traditional cardiac risk factors (such as hypercholesterolemia, hypertension, family history, and tobacco use) are often assessed but remain poor predictors of risk for myocardial infarction (MI) or ACS.[11,12] Similarly, use of a physical examination to distinguish patients with ACS from patients with noncardiac chest pain is limited.

The standard 12-lead electrocardiogram (ECG) is the single best test to identify patients with ST-segment elevation MI (STEMI) immediately upon presentation to the ED. However, it cannot conclusively exclude ACS and should be used in conjunction with clinical history and cardiac markers.[2,13] The presence of clear ischemic changes on the initial ECG identifies a patient with ACS in whom admission and rapid management is mandatory. However, diagnostic ECG findings are present in only a minority of patients, leaving the majority within the differential diagnosis of possible myocardial ischemia and "suspected" ACS.

BIOMARKERS

The optimal biomarker for ACS remains elusive. Ideally, a marker with high sensitivity and high negative predictive value would allow safe discharge from the ED, whereas markers with high specificity and positive predictive values would lead to aggressive care for patients at high risk for cardiovascular complications. Table 1 summarizes the predictive properties of cardiac biomarkers used for diagnosis of ACS in the ED.[14] Despite improved early diagnosis and risk stratification of AMI with multimarker panels[15,16] and new, high-sensitivity cardiac

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TABLE 1. Summary of Predictive Properties of Cardiac Markers of Diagnosis of AMI

Marker at Time of Presentation	No. Studies	No. Subjects	Sensitivity (95% CI)	Specificity (95% CI)	Diagnostic Odds Ratio (95% CI)
Creatine kinase	12	3195	37 (31-44)	87 (80-91)	3.9 (2.7-5.7)
CK-MB	19	6425	42 (36-48)	97 (95-98)	25 (18-36)
Myoglobin	18	4172	49 (53-55)	91 (67-94)	11 (8-15)
Troponin I	4	1149	39 (10-76)	93 (66-97)	11 (3.4-34)
Troponin T	6	1346	39 (26-53)	93 (90-96)	9.5 (5.7-16)
CK-MB and myoglobin	3	2263	83 (51-96)	62 (66-90)	17 (7.6-40)

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CI indicates confidence interval.

troponin assays,[17,18] it has been shown that even with enhanced sensitivity, cardiac troponin was not universally elevated in those patients with unstable angina or transient myocardial ischemia.[19] Patients with negative markers still require evaluation and testing as dictated by their clinical presentations. Moreover, other medical conditions such as myocarditis, PE, and heart failure can be associated with elevations in cardiac troponin levels and would necessitate continued clinical evaluation.

Some markers of inflammation and platelet activation have shown promise as a biomarker of inflammatory activation in ACS. For example, myeloperoxidase has been recently considered a possible marker of vulnerable plaque that can be used to identify patients at increased risk for major adverse cardiac events (MACE) who might not otherwise be identified without invasive diagnostic testing, independently of evidence of myocardial necrosis.[20]

RISK STRATIFICATION

Several risk stratification algorithms have been studied and validated. Although clinical and computer algorithms can successfully stratify patients according to risk, they are unable to reliably identify a group of patients at such low risk for ACS that they can be safely discharged from the ED. The Goldman risk score, based on ECG findings and chest pain, stratifies patients into groups with risks for AMI varying from 1% to 77%. However, it does not identify the group with $<1\%$ risk, who could safely be discharged. Even in the group of patients deemed to be at low risk, the addition of initially negative cardiac troponins was still associated with a 5% rate for adverse outcomes.[21,22] Computer-aided detection/diagnosis (CAD) methods such as acute cardiac ischemia time-insensitive predictive instrument,[23] and artificial neural networks–based paradigms, reportedly provide somewhat improved performance, particularly when applied by nonemergency medicine house staff; however, they have not been shown to make a clinically relevant difference in diagnostic accuracy compared with contemporary emergency physician judgment.[24]

The Thrombolysis in Myocardial Infarction (TIMI) risk score, comprising 7 equally weighted parameters, was initially developed for use in patients with unstable angina or non-STEMI and has been shown to assist in risk stratification.[25] Only when cardiac biomarker testing was combined with a TIMI risk score of zero, occurring in approximately 10% of all ED patients, did it identify patients considered at such low risk that further evaluation was not needed and they could be discharged directly from the ED.[26] For patients with confirmed ACS, several scoring methods can be applied to identify patients in the coronary care unit who may benefit most from therapies. These methods include the PURSUIT (2000), GRACE (2003), and FRISC (2004) risk scores. However, none of these risk scores has been used for the identification of ACS in the emergency setting.[27] The more recently developed HEART score (2008) is specifically designed to stratify all chest pain patients in the ED.[28] The HEART score was validated in a retrospective multicenter study in 880 patients and proved to be a strong predictor of event-free survival and potentially also of future life-threatening cardiac events.[29] An "event" was defined as a combined endpoint of MI, percutaneous coronary intervention, coronary artery bypass grafting, or death within 6 weeks of presentation. The HEART score facilitates risk stratification of chest pain patients in the ED into low-risk (0 to 3), intermediate-risk (4 to 6), and high-risk groups (7 to 10), with mean risks for an event of 0.9%, 12%, and 65%, respectively. Consequently, an evidence-based decision may be made to discharge the patient from the ED or to admit for clinical observation or immediate aggressive therapies.

Three studies have shown that strong clinical suspicion of an alternative, noncardiac diagnosis might reduce the likelihood of death or major cardiovascular events, although not to a low enough level to allow safe and immediate release from the ED. In a large multicenter study of 17,737 patients, Miller et al[30] found that, of patients believed to have noncardiac disease at the conclusion of the ED evaluation, 6.8% had possible and 2.8% had definite 30-day adverse cardiovascular events. Disla et al[31] examined patients given a diagnosis of costochondritis, confirmed by a rheumatologist, of whom 6% had sustained an AMI. Hollander et al,[4] in a study on 1995 ED patients with potential ACS, found that patients with a definite alternative noncardiac diagnosis still had a 4% event rate at 30 days (95% confidence interval, 2.4%–5.6%). Thus, use of this criterion alone for safe and immediate release of ED patients who present with potential ACS is not possible.

MANAGEMENT PATHWAYS: EARLY IMAGING VERSUS OBSERVATION WITH SERIAL BIOMARKERS

If history, initial ECG results, and biomarkers with or without the use of risk scores are diagnostic for ACS, a triage decision to admit and treat should be made, and an evidence-based treatment strategy should be initiated. If the initial data are sufficient to result in a diagnosis that is not ACS (such as pericarditis), or reveal a very low probability for ACS, consideration can be given to early discharge from

the ED with appropriate follow-up. However, after this initial information, uncertainty often continues to exist regarding an ACS diagnosis. It is in this population of patients with suspected ACS that further workup and risk stratification is warranted using 1 of 2 pathways: early imaging or observation.

Early Imaging Pathway

In the early imaging strategy, imaging is carried out early in the evaluation process, with the goal of ruling in or ruling out ACS or MI without the added delay of waiting for serial biomarkers. Modalities include CCTA, echocardiography, cardiac magnetic resonance imaging (CMR), and single-photon emission CT myocardial perfusion imaging (SPECT MPI). Tests in this pathway do not require induction of stress physiology but rather image anatomy (CCTA), function (echocardiography, CMR), or perfusion (resting SPECT MPI, CMR) at rest. The potential advantage of this strategy is that a normal imaging study (given a high negative predictive value) in a patient with low to intermediate clinical suspicion for ACS may be sufficient to enable early discharge without the need for prolonged observation.

Resting SPECT MPI with technetium-99m sestamibi is useful in the setting of suspected ACS.[32–35] Technetium-99m sestamibi is taken up by the myocardium in proportion to myocardial blood flow and retained within the myocardial mitochondria with minimal redistribution after injection. This allows injection during symptomatic episodes, with subsequent imaging after patient stabilization. Several reports have concluded that the use of resting SPECT MPI in the ED is associated with shorter length of stay, lower cost, and fewer unnecessary hospital admissions.[36–38] A large body of literature based upon observational studies established a high negative predictive value for a normal resting SPECT MPI to rule out MI or short-term cardiac events. There are, however, significant practical issues that have prevented widespread implementation. Tracers and interpreting personnel may not be available at all hours for testing. Decreased accuracy occurs if the patient is not injected with the tracer during or shortly after the occurrence of acute symptoms, making timely injection essential. Radionuclide tracers used for resting MPI involve radiation exposure and thus should not be used during pregnancy. Recently introduced cadmium zinc telluride SPECT camera technology has the potential to significantly reduce ionizing radiation exposure and imaging times compared with traditional protocols while maintaining image quality and diagnostic accuracy.[39,40]

Resting 2-dimensional (2D) echocardiography is rapid and noninvasive but may not be readily available in the ED, particularly after hours. 2D echo provides information on myocardial ischemia by evaluating segmental wall motion and ejection fraction,[41,42] but the positive predictive value is poor (0% to 44%),[41,43,44] and 2D echo is limited in distinguishing acute versus chronic ischemia. In addition, resting echo cannot determine the presence of underlying high-grade coronary stenosis in the absence of impaired myocardial perfusion at rest that results in wall motion abnormalities. It can detect other possible causes of chest pain, including valvular disease, pericarditis, and cardiomyopathy. When contrast agents are used, echocardiography is reported to achieve higher sensitivity (79% to 97%) compared with wall motion analysis alone with both rest and stress.[45–49]

CMR can image coronary anatomy, regional and global ventricular function, myocardial perfusion, and myocardial fibrosis/scar. When used in ED patients, generally in observational studies with modest numbers of patients, contrast-enhanced perfusion, delayed enhancement, and cine evaluation of wall motion have been shown to have a sensitivity of 70% to 85% to detect ischemic conditions.[50–52] A normal CMR study has been associated with very low risk and good prognosis. Although the reported diagnostic accuracy of coronary magnetic resonance angiography for the detection of lesions is 72%,[53] the inferior spatial resolution compared with CTA limits clinical applications. Although both rest and rest-stress CMR protocols can be used, the technology and expertise is not widely available. CMR with pharmacological stress (eg, adenosine, dobutamine/atropine) can be used but has even less availability in the emergency room setting. In patients with acute chest pain, T2-weighted CMR is able to identify acute or recent myocardial ischemic injury and has been used to distinguish ACS from non-ACS as well as acute from chronic MI.[54] Miller and colleagues evaluated 110 ED patients having intermediate or high probability for ACS without ECG or biomarker evidence of AMI who were randomized to stress CMR in an observation unit versus standard inpatient care. Compared with inpatient care, an observation unit strategy involving stress CMR reduced incident cost without any cases of missed ACS in patients with emergent chest pain.[55]

Although catheter angiography remains the gold standard for diagnosis of coronary artery disease, it is not considered appropriate for the initial evaluation of patients at less than high risk for ACS. It should be reserved for confirmation of ACS in patients with positive screening results and interventions in the case of hemodynamically significant stenosis or occlusion. In addition, there is very little evidence for the implementation of non-CT modalities in the ED setting. Most of the studies to date have reported anecdotal evidence in patients with MI rather than in patients with suspected ACS.

Observational Pathway

The observational strategy, which was historically followed at most tertiary care centers even as recently as 5 years ago, requires serial analysis of cardiac biomarkers to rule in or rule out myocardial necrosis and MI. In the absence of an acute event, this is typically followed by an imaging test that may involve imaging coronary anatomy and/or imaging function and perfusion to look for evidence of ischemia. If serial biomarkers are negative, stress imaging or stress ECG is often incorporated.

Appropriate Use Criteria

A multisociety collaboration updated the criteria for appropriate use of CCTA in 2010.[56] For patients without known coronary artery disease presenting with suspected ACS, CCTA was determined to be appropriate in the setting of either (1) normal ECG and biomarkers, (2) uninterpretable ECG, or (3) nondiagnostic ECG or equivocal biomarkers for patients with either a low or intermediate pretest probability for CAD. In patients with a high pretest probability, persistently abnormal ECG after exclusion of MI, or with acute chest pain with multiple potential cardiac and noncardiac etiologies, the benefit of CCTA was uncertain. Finally, in patients with proven AMI, there is no

role for CCTA; these patients benefit more from immediate therapeutic intervention—that is, catheter angiography.

CORONARY CALCIUM SCORING

Coronary artery calcification (CAC) is considered to be a marker of atherosclerotic plaque. Studies have suggested that detection of coronary calcium by cardiac CT is useful for the evaluation of chest pain in the ED.[57] In a follow-up study by the same group comprising 263 patients who were evaluated in the ED with low to intermediate risk for ACS, 51% with absent or minimal CAC experienced no adverse cardiac events at 30 days, 1 year, and 5 years, with a negative predictive value of 99% for the test in this setting.[58] A 1031-patient prospective observational study conducted at an urban tertiary care hospital showed that a CAC of zero was associated with a low rate of cardiac events acutely and during the ensuing 6 months on normal SPECT.[59]

However, the role of calcium scoring alone in ACS risk stratification in the ED continues to be debated. Prior studies have shown that noncalcified plaques are more likely to be present in younger cohorts,[59–61] in diabetic patients,[62] and in patients with ACS compared with those with stable CAD.[63] A calcium score of zero may not predict the absence of CAD.[64–66] Further, CAD in younger, more atypical patients would be missed. Chang et al[61] found that positive calcium scores did not identify all patients with CAD and that the addition of coronary calcium scoring to CCTA findings did not help to predict 30-day cardiovascular events. Radiation exposure also remains a matter of concern: calcium scoring alone accounts for an estimated effective dose of 1.5 mSv.[67] Chang et al[61] also addressed the concern about the quality of images when the coronary calcium score exceeds 400, reporting that only 23 of 1049 patients had a coronary calcium score in this range, and 13 of those patients had interpretable coronary imaging.

CONTRAST-ENHANCED CCTA

At a growing number of medical centers, CCTA has become a hallmark of the early imaging pathway, available nearly 24/7 in the ED and quickly interpreted to further management and disposition of the patient.[68,69] Patients with hemodynamically significant stenoses can be admitted for further treatment and intervention (eg, cardiac catheterization or stress testing), whereas those with normal CCTA results or nonhemodynamically significant lesions can be medically managed and discharged.

Multiple studies have demonstrated the safety of CCTA for triage of patients at low to intermediate risk who present to the ED with chest pain and suspected ACS. In a cohort study of 568 patients with chest pain, those with a low TIMI risk score, negative ECG, and negative CCTA had no MACE 30 days after discharge from the ED.[70] One-year follow-up in this same cohort affirmed the initial findings: none of the patients experienced an acute MI, and only 1 patient died from an unclear cause.[71] The ROMICAT I trial, a single-center cohort study of 368 ED patients with acute chest pain, demonstrated a high negative predictive value for ACS in patients with a normal CCTA examination, as well as a decreased risk for MACE during the 2 subsequent years.[72,73] A strong correlation between plaque characterization, percentage of stenosis, and ACS was also noted. A subsequent prospective, multicenter, randomized control trial (ROMICAT-II) of 1000 patients with suspected ACS additionally showed that CCTA in low-risk patients with chest pain resulted in quicker hospital discharge, often directly from the ED, as well as no undetected ACS after 28 days.[74] Another prospective, multicenter trial (CT-STAT) randomized patients to receive either CCTA or SPECT MPI and found no statistically significant difference in MACE between the 2 noninvasive modalities.[75] A more recent multicenter study of 1370 subjects randomized to either CCTA or traditional observational therapy demonstrated that CCTA was a safe option for evaluation of low-risk and intermediate-risk patients with chest pain in the ED.[69]

Protocols

Protocols for CCTA have evolved according to available technology. Initially, most studies were carried out with retrospectively ECG-gated helical CT, allowing for reconstruction of multiple phases of the cardiac cycle as well as functional evaluation in addition to assessment for the presence and extent of atherosclerotic plaque. However, the disadvantage of retrospective ECG gating is the increased amount of ionizing radiation required to obtain data throughout the cardiac cycle. In light of this concern, prospective ECG triggering and axial CT became more widely used.[76] The advantage of prospective ECG-triggered axial imaging is the comparative reduction in radiation dose, with the limitation that functional assessment cannot be obtained because data are no longer acquired during the cardiac cycle. Newer technology has enabled dual-source, high-pitch helical CT with prospective ECG triggering.[77] This technique provides diagnostic quality imaging with even less ionizing radiation, but the fast scan time (approximately 250 ms) requires that patients have a low heart rate (ideally around 60 beats/min) so that the heart is in the same phase of the cardiac cycle throughout the imaging examination

To ensure the production of diagnostic quality images, optimal heart rate control is critical to minimize motion artifacts. This can be achieved with the administration of oral or intravenous β-blockers in patients without contraindications (eg, sinus bradycardia, hypotension, active/unstable small airway disease).[78] Heart rate optimization is important regardless of imaging protocol (retrospective ECG gating vs. prospective ECG triggering). In addition, vasodilation of the coronary circulation using sublingual nitroglycerin is also valuable for improving the contrast-to-noise ratio of the CCTA examination.[78] Specific contraindications to nitroglycerin administration exist, including recent phosphodiesterase inhibitor therapy (used for erectile dysfunction or pulmonary hypertension), hypotension, and critical aortic stenosis.

Advantages

The contrast-enhanced phase of CCTA is used to characterize the anatomy of the coronary arterial circulation, determine dominance, and identify any luminal abnormalities or anomalous connections.[79,80] The incidence of anomalous coronary arteries in the United States is thought to be slightly $<6\%$, whereas the incidence of myocardial bridging is approximately 10%.[81] Aside from anomalies with a clearly malignant (ie, interarterial) course of the left anterior descending coronary artery, the significance of these anomalies is unclear.

In patients with suspected ACS, CCTA is used to detect atherosclerotic plaque, classify it as calcified, noncalcified, or mixed, and characterize the resulting degree of stenosis. Figure 1 demonstrates $>90\%$ stenosis in the proximal left anterior descending artery of a patient, shown

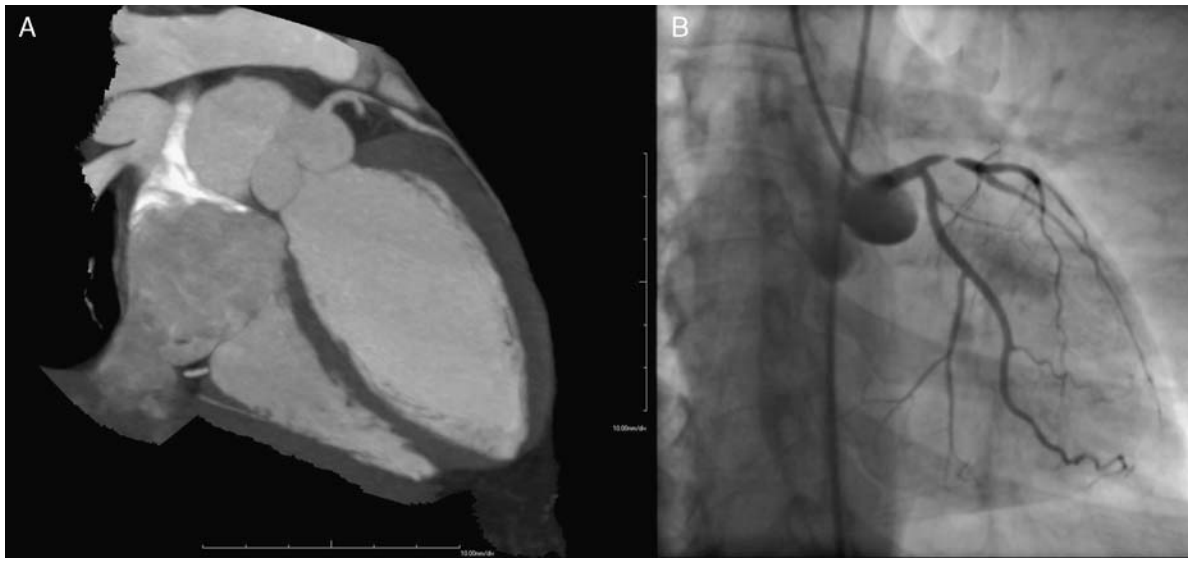

FIGURE 1. Correlation between CCTA (A) and catheter angiography (B) demonstrating >90% stenosis in the proximal left anterior descending artery of a patient before stent placement.

both on multiplanar reformats from a CCTA and on the corresponding angiographic projection before stent placement. In a prospective cohort study of 304 patients, high-risk plaque (plaque with CT attenuation < 30 Hounsfield units with or without accompanying positive remodeling) was shown to have greater prognostic value than the combination of percentage of stenosis on CCTA and stress difference scores (SDS) from SPECT MPI.[79] Plaque composition has been shown to vary on CCTA between patients with stable CAD and those with unstable angina.[63]

Yet another advantage of CCTA is the fact that it can be used to identify potential causes of chest pain other than ACS. This is a feature unique to CCTA over other non-invasive cardiac imaging modalities such as echocardiography, exercise stress testing, and MPI.[4,82] Further, CCTA can often reveal occult conditions for which a patient would benefit from treatment, such as previously undiagnosed malignancies of the lung and female breast.[83–89] It is important to examine extracardiac structures captured on full field-of-view (FOV) imaging, such as the calcium scoring series, which may not always be captured on the smaller FOV angiographic series.[90] Figure 2 demonstrates some extracardiac findings that have been captured on CCTA.

Historically, CCTA has been criticized for exposing patients to significant radiation for a diagnostic imaging examination.[91] However, customizing x-ray tube voltage (kVp) to patient size to achieve diagnostic image quality with less radiation has resulted in lower-dose protocols.[92] Further, the PROTECTION III trial showed that prospectively ECG-triggered axial imaging reduced the amount of radiation required by up to 69% compared with retrospectively ECG-gated imaging and to a level considerably lower than that of conventional SPECT MPI.[93] Other studies have also shown that CCTA can be performed using less radiation compared with SPECT MPI.[74] With the current state-of-the-art CT scanners, CCTA can be performed with estimated effective doses on the order of 1 mSv.[94] Concomitant implementation of dose-reduction technologies such as iterative reconstruction can result in diagnostic quality images with even lower estimated effective doses.[95–97]

Limitations

An often-noted limitation of CCTA is its inability to provide information on the functional significance of an anatomic stenosis. By its nature, CCTA provides an anatomic assessment of the degree of stenosis but cannot elaborate on whether the observed stenosis causes significant myocardial ischemia. Meijboom et al[98] showed only a moderate correlation between percentage of stenosis on CCTA and fractional flow reserve (FFR) measured with quantitative coronary angiography. However, Motoyama et al[79] showed that assessment of plaque architecture/composition on CCTA outperformed the combination of percentage of stenosis from CCTA and stress difference score from SPECT MPI (structural *and* functional information) in a small single-center trial.

One of the sharpest criticisms of CCTA is that, although it may decrease the length of stay and cost of care during an initial ED visit for chest pain, it ultimately leads to increased costs and added morbidity from unnecessary intervention in patients without completely normal examinations.[74] ROMICAT-II showed that CCTA led to a higher rate of subsequent invasive coronary angiography in intermediate-risk patients compared with the observational pathway.[74] In addition, among Medicare recipients, it was found that CCTA in non-ED patients led to more invasive coronary angiography compared with SPECT MPI.[99]

Many studies on extracardiac findings identified on CCTA would suggest that obtaining and evaluating a full FOV series, as part of CCTA, is beneficial to patients. However, some would argue that this additional information is actually to a patient's disadvantage. Budoff et al[100] argued that the benefits of full FOV CCTA outweigh the risks associated with follow-up imaging, including exposure to ionizing radiation, increased cost, and potential associated morbidity. For example, incidental pulmonary nodules detected on CCTA often require repeat follow-up CTs to assess for interval change and may even lead to positron emission tomography/CT scans or biopsy of indeterminate nodules.

High-attenuation material adjacent to the lumen of a coronary artery can significantly impact the assessment of the

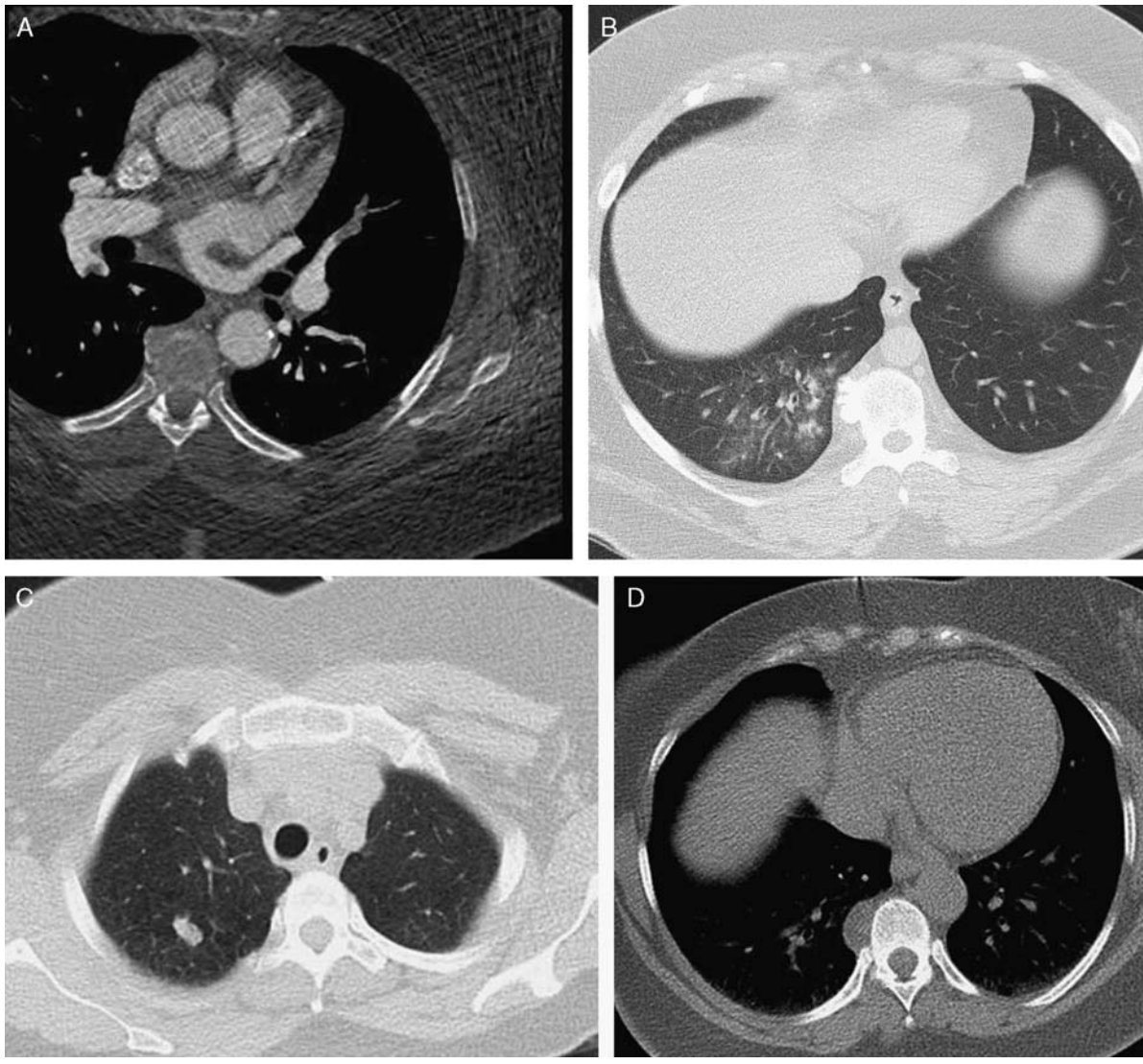

FIGURE 2. Examples of extracardiac findings detected on CCTA, including (A) bilateral pulmonary emboli, (B) right lower-lobe pneumonia, (C) a right upper-lobe nodule and (D) a right paravertebral mass, found in the same patient as shown in (C).

vessel lumen. In patients with a very high coronary calcium score, blooming artifacts from dense calcified plaques can limit evaluation of the adjacent lumen. Calcium scores >400 have been shown to detect stenosis on CCTA.[101] Similarly, evaluation of coronary patency in patients with known coronary artery disease and history of prior percutaneous coronary intervention and stenting is difficult in the native vessel immediately proximal and distal to a metallic stent as well as within the stent itself because of blooming artifacts.[102,103]

TRIPLE RULE-OUT (TRO) CTA

Patients in whom the initial workup is inconclusive can undergo an imaging study potentially excluding the most critical diagnoses, including troponin-negative non-ST elevation ACS, aortic dissection or other acute aortic syndrome, and acute PE. This type of approach is usually referred to as TRO. TRO is a modified contrast-enhanced CTA designed to image more of the chest (eg, aortic arch to the base of the heart or thoracic inlet to diaphragm) using additional contrast to maintain pulmonary artery opacification. Several studies have confirmed the feasibility of this approach, providing good coronary, pulmonary, and aortic image quality with negative predictive values in the range of 99.4% to 100%.[104–108] Relative disadvantages of a TRO include increased scan length, additional radiation exposure, 20% to 50% more contrast volume (to maintain pulmonary artery opacification), and added protocol complexity. The average effective dose estimate for a TRO study is 30% higher compared with CCTA if scanned from the aortic arch to the base of the heart and 50% to 125% higher when the entire thorax is imaged.[104,107,108]

The necessity of TRO in patients presenting with acute chest pain remains under discussion. The incidence of PE and aortic dissection in the population with low to intermediate ACS risk seems to be quite low and may not justify the increased radiation dose.[70,82,106] One study suggests that the TRO approach may have a role in patients at intermediate to

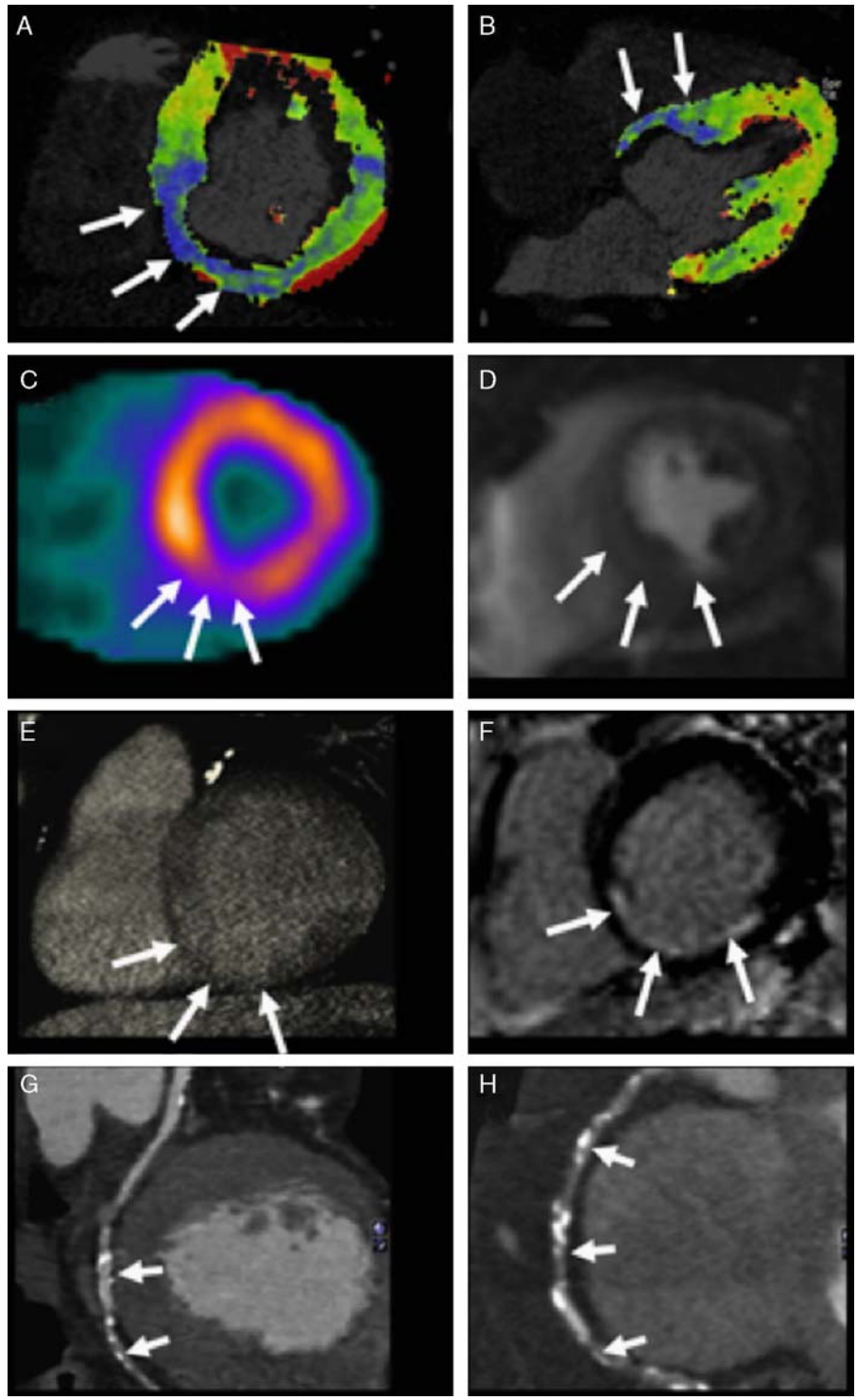

FIGURE 3. Images of a 55-year-old male patient with a family history of coronary artery disease who presented to the ED after several episodes of acute chest pain. Color-coded dynamic first-pass myocardial stress perfusion CT images in short-axis (A) and long-axis (B) views reveals a perfusion defect in the inferoseptal and lateral wall of the left ventricle, equivalent to the vascular territories of the right coronary artery and left circumflex artery (arrows). Corresponding short-axis stress SPECT thallium myocardial perfusion (C) and stress perfusion MRI (D) illustrate perfusion defects (arrows) in the same myocardial territory. Delayed-phase CT in short view (E) displays inferoseptal delayed subendocardial myocardial hyperenhancement, correlating well with delayed-phase MRI in short-axis orientation (F) (arrows). CCTA of left circumflex artery (G) and right coronary artery (H) depicts diffuse calcified and noncalcified atherosclerotic disease throughout the course of both vessels, causing several high-grade and subtotal stenoses (arrows). MRI indicates magnetic resonance imaging. (Image and caption reproduced with permission from Weininger et al.[112])

high risk for PE.[108] Pulmonary artery opacification on CCTA may not be adequate to exclude PE.[109] Nevertheless, this diagnosis is very uncommon in ED patients with chest pain and suspicion of ACS.[70,82] Most patients will have negative TRO results. Aortic dissection is not missed in any kind of protocol, whereas intramural hematoma may be missed on all protocols. Newer techniques such as prospective ECG triggering, large-volume detectors, and high-pitch helical dual-source CT may reduce radiation dose, leading to more widespread adoption of the TRO method.

COST-EFFECTIVENESS

At present, there appears to be conflicting evidence as to the cost-effectiveness of CCTA as a triage measure in the ED. Multiple studies have shown that CCTA is cost-effective in patients with < 50% pretest probability for ACS and also more cost-effective when used alone than when combined with SPECT MPI.[110] ROMICAT-II showed no significant difference in the cumulative mean cost of care for patients who underwent CCTA as opposed to an alternative noninvasive imaging modality.[74] Although patients with negative CCTA examinations had shorter hospital stays on their initial visit, they underwent more downstream testing and ultimately received more radiation exposure. In contrast, other studies have shown that in low-risk patients CCTA results in a higher discharge rate, shorter length of stay, and more cost-effective management of patients without a statistically significant difference in MACE when compared with non-CCTA groups.[69,75] One critic suggests that, just as patients with a negative CCTA can be discharged safely from the ED, so can patients with

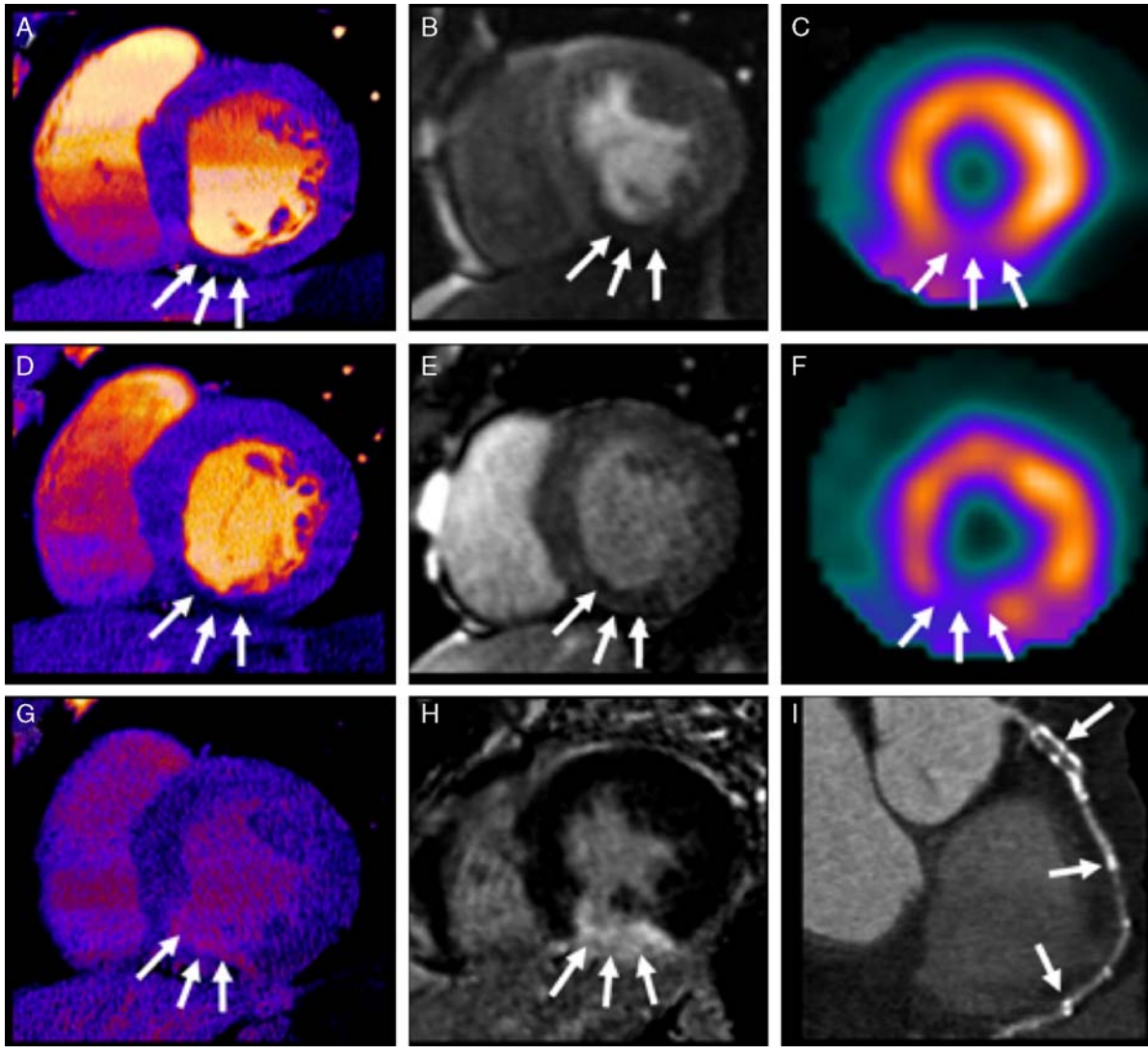

FIGURE 4. A 58-year-old man with a history of coronary artery disease and atypical chest pain. Dual-energy images in short-axis view (A) reveal an iodine defect of the inferior wall of the left ventricle (arrows), which could be confirmed by rest examinations of MRI (B) and SPECT (C) (arrows). In combination with adenosine-induced stress DECT (D), stress MRI (E), and stress SPECT (F) examinations, this inferior wall defect (arrows) was classified as a fixed defect. Delayed myocardial hyperenhancement (arrows) can be depicted in both late-phase DECT (G) and late-phase MRI (H). Corresponding CCTA (I) illustrates multiple hemodynamic relevant calcified and non-calcified plaques in the right coronary artery. DECT indicates dual-energy CT; MRI, magnetic resonance imaging. (Image and caption reproduced with permission from Weininger et al.[112])

negative ECG results and cardiac biomarkers, thereby saving the added expense of an additional CT examination.[111]

FUTURE DIRECTIONS

One recent innovation in the evaluation of chest pain in the ED is myocardial stress perfusion imaging using CT (Fig. 3) after administration of adenosine.[112–116] Historically, this type of analysis has been performed using first-pass perfusion and delayed enhancement CMR, which requires a low volume of intravenous contrast and does not use ionizing radiation. However, feasibility studies have demonstrated that both real-time and first-pass perfusion myocardial stress perfusion CT in patients with acute chest pain have higher sensitivity and specificity compared with stress/rest SPECT and CMR in detecting areas of decreased myocardial perfusion.[112,116] Although acknowledging the limitations of radiation exposure and increased contrast volume, we consider this technique to be a viable alternative in patients who cannot undergo contrast-enhanced CMR.

The use of dual-energy cardiac CT with simultaneous or alternating imaging at 2 different x-ray tube potentials is also being explored from multiple avenues (Fig. 4). One application has been the analysis of plaque composition. A decrease in blooming and beam hardening artifact associated with densely calcified plaque was noted with dual-energy CCTA in an anthropomorphic moving heart phantom.[117] Difference between calcified and noncalcified plaque in ex vivo human specimens has also been demonstrated.[118] In addition, dual-energy CT has been widely utilized for myocardial stress perfusion analysis.[112–116,119] Iodine maps obtained by analyzing dual-energy CT images have been shown to be comparable to SPECT MPI with >90% sensitivity and specificity.[120] When compared with 3 T CMR, dual-energy CT performs with 77% sensitivity and 98% specificity for evaluation of areas of chronic MI, with the added benefit of decreased metal artifact.[121] The combination of dual-source CCTA and dual-energy myocardial stress CT perfusion has been shown to have incremental benefit over CCTA alone.[115]

FFR is a conventional angiographic technique used to determine the volume of coronary blood flow that can be achieved in the presence of a stenotic lesion. It effectively provides an estimate of lesion-specific ischemia. Revascularization of a lesion with positive FFR (typically defined as ≤ 0.75 or ≤ 0.8) has been shown to be associated with decreased ischemia and more positive outcomes.[122] More recently, a noninvasive estimate of lesion-specific ischemia from CCTA, termed CT FFR (FFR_{CT}), has been developed (Fig. 5). For intermediate lesions (defined as 40% to 69% stenosis) causing ischemia, FFR_{CT} was found to have

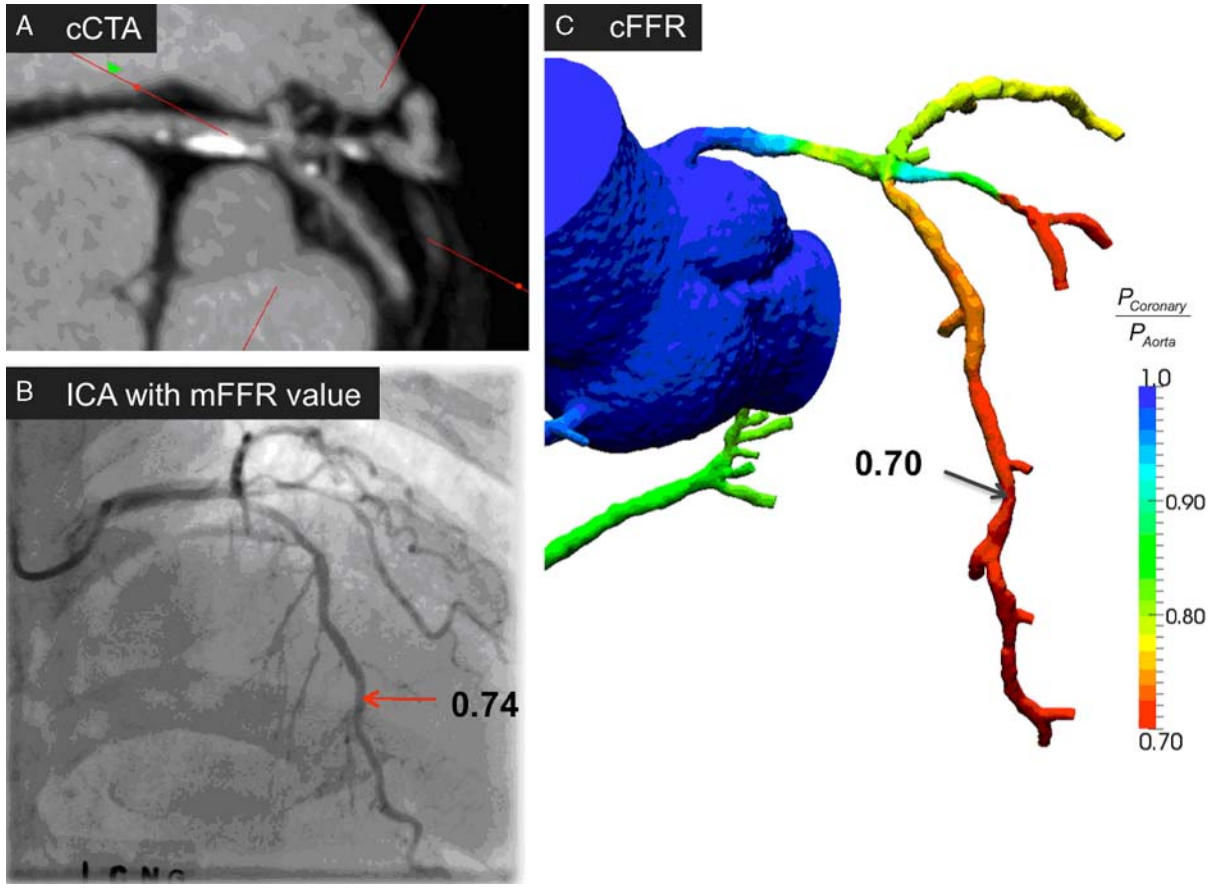

FIGURE 5. Comparison of (A) multiplanar reformat of CTA, (B) invasive coronary angiography (ICA) with FFR value, and (C) FFR_{CT} showing a hemodynamically significant stenosis of the left anterior descending artery (arrows, FFR < 0.8). Figure courtesy of Dr Bon-Kwon Koo, Seoul National University Hospital. (Image and caption reproduced with permission from Min et al.[123])

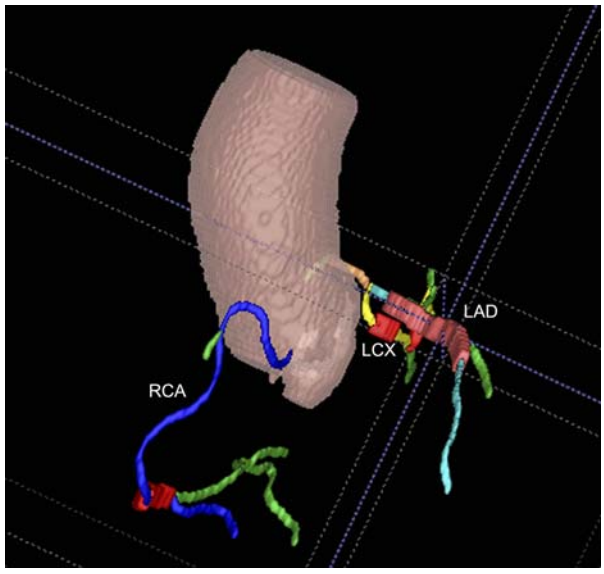

FIGURE 6. Automated extraction of plaque and characterization of stenoses using CAD identifies calcified plaque in the mid-left anterior descending artery (LAD), noncalcified plaque in the mid-circumflex, calcified plaque in the proximal circumflex, and mixed plaque in the distal right coronary artery (RCA); these segments are highlighted in red. LCX indicates left circumflex artery.

90% sensitivity and nearly 83% specificity, as well as statistically significant correlation with angiographic FFR. In addition, FFR_{CT} was also shown to outperform angiographic FFR and assessment of percentage of stenosis from CCTA for partially calcified or noncalcified plaque.[124] The DeFACTO trial, a multicenter prospective comparison of FFR_{CT} with angiographic FFR, showed 73% specificity and 90% specificity for the diagnosis of obstructive CAD.[125] However, FFR_{CT} still performed better than anatomic CT alone.

CAD of coronary artery disease is another interesting application that may gain traction in the imaging evaluation of patients in the ED (Fig. 6). Computer-aided simple triage analysis of CCTA has been used to automatically segment and label the coronary artery tree and also detect stenoses.[126,127] Such a system is designed to alert clinicians to the presence or absence of critical stenoses present on a CCTA in order to focus study interpretation toward rapid patient triage.

CONCLUSIONS

CCTA has now been validated using several large multicenter trials that demonstrate its safety and efficiency. However, concerns remain about increased resource utilization and radiation exposure, and the role of new biomarkers may change how we practice. Specifically, patients with negative ultrahigh-sensitivity troponins may not require imaging; however, these new biomarkers are rarely unequivocally negative. In addition, we must consider the long-term downstream consequences of additional imaging and interventions—are we actually preventing future events or just making unnecessary use of limited resources?

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