Cardiovascular CT in the Emergency Department

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Abstract

Acute-onset chest pain is one of the most common presentations in the emergency department (ED) and despite a thorough, time intensive, and costly ED evaluation utilizing the standard strategy, there is a non-negligible clinical risk of missed acute coronary syndrome (ACS) with 2–5 % of these patients being discharged inappropriately. The resultant consequences are, increased risk of short and long term mortality. This chapter discusses the current role of cardiac computed tomography in the evaluation of patients with acute chest pain in the ED and evaluates the current evidence supporting accuracy and safety of cardiac computed tomography, as well as it's ability to reduce ED cost.

Keywords

Acute coronary syndrome • Cardiac • Chest pain • Emergency department • Coronary computed tomography angiography

Current State of the Literature

Acute chest pain is one of the most frequent reasons for patient visits to the emergency department (ED) in the United States and a large amount of expense and time is spent in the workup of these patients. It is estimated that as many as 6 million people per year visit the ED with chest pain [1]; however, only a small minority of these patients ultimately receive a diagnosis of acute coronary syndrome (ACS) as the etiology of their chest pain [2]. Although most of these patients do not have a life-threatening underlying condition, a large proportion of these patients undergo routine evaluation of acute chest pain that includes hospital admission or observation unit stay to rule out ACS with the use of serial electrocardiography (ECG) and cardiac biomarker assessment. Such an approach is costly, time-consuming and puts additional strain on already limited resources.

Diagnosis of ACS

The term ACS describes clinical manifestations of acute myocardial ischemia induced by coronary artery disease (CAD). The American Heart Association (AHA) differentiates among ACS that involve myocardial infarction (MI) with acute ST segment elevation (STEMI), MI without ST segment elevation (non-STEMI), and unstable angina (UA) [3–5]. The diagnosis of STEMI is clear by ECG alone, but diagnosis of non-STEMI and UA is more challenging and requires additional data to risk stratify patients appropriately [6]. The third universal definition of MI, published in 2012, states that the diagnostic criteria for MI require a rise and/or fall of cardiac biomarkers (preferably troponins) with at least one value above the 99th percentile of the upper reference limit. In addition, patient should have symptoms of ischemia with new ECG changes and imaging evidence of a new loss of viable myocardium or new regional wall motion

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abnormality, or the identification of an intracoronary thrombus by angiography or autopsy [7]. However, the initial standard ED evaluation of patients with acute chest pain [8] does not often provide a firm diagnosis for appropriate triage decision and to safely rule out ACS based on negative cardiac troponin and ECG.

Risk Assessment in the Emergency Department

Patients with acute chest pain are generally stratified into high, intermediate, or low risk categories during their early clinical assessment in the ED. This risk assessment work-up traditionally includes patient's history of prior cardiovascular events, repeated physical examinations, and serial electrocardiographic and biochemical marker measurements [9–11]. Patients who are at high-risk of ACS or have STEMI based on ECG findings should be admitted and treated promptly as per guidelines [8]. Patients who are at low to intermediate risk carry a 5–20 % risk of an ACS and the current standard of care for these patients includes serial ECG and cardiac troponin measurements followed by stress testing with or without imaging to exclude myocardial ischemia [8]. This approach leads to prolonged hospital stay and significant cost burden and eventually only 2–8 % of this patient group is diagnosed with ACS [12].

Multiple risk stratification models based upon multivariable regression techniques have been created in order to help clinicians in therapeutic decision making and includes the Thrombolysis in Myocardial Infarction (TIMI) risk score, Global Registry of Acute Coronary Events (GRACE) risk score, and the Platelet Glycoprotein IIb/IIIa in Unstable Angina: Receptor Suppression Using Integrillin Therapy (PURSUIT) risk model [13–15]. The TIMI risk score is a simple and easily applied scoring system that has been validated for patients who present to the ED, and aids in assessing the likelihood of developing an adverse cardiac outcome (death, reinfarction, or recurrent severe ischemia requiring revascularization) within 14 days of presentation in patients presenting with UA and NSTEMI [14].

Despite these clinical risk scores, uncertainty often exists as to the etiology of a patient's symptoms and the potential adverse prognosis associated with them. This uncertainty emphasizes the need for diagnostic strategies that facilitate rapid and reliable early triage of patients who are at low-to-intermediate risk for ACS [16].

Supporting Evidence for Cardiac CT Use in the Emergency Department

With improvements in imaging capabilities, coronary computed tomography angiography (CCTA) has emerged as a new and promising imaging modality for the detection and assessment of coronary stenosis and atherosclerotic plaque, and has become integral in the assessment of patients with suspected ACS. Several single-center and multicenter studies have demonstrated the feasibility, safety, and accuracy of cardiac CT in the ED to exclude the presence of CAD [9, 17–30]. Most patients with ACS have significant coronary stenosis, and ACS is rare in the absence of coronary atherosclerosis [31, 32]. Therefore, the detection of obstructive CAD may be effective in identifying patients with ACS and the exclusion of coronary atherosclerosis may be helpful in ruling out ACS.

Given the excellent predictive value, CCTA allows for improved risk stratification of patients and appropriate triage, and can be considered an alternative to standard ED evaluation of acute chest pain patients. Furthermore, CCTA has been shown to reduce length of stay in the hospital. A meta-analysis comparing CCTA to standard care triage of acute chest pain in a total of 3266 low-to intermediate risk patients presenting to the ED noted that only 1.3 % overall MIs occurred mostly during the index hospitalization. In addition, length of stay in the hospital was significantly reduced with CCTA compared to standard care strategy. It was also found that CCTA significantly increased invasive coronary angiography (8.4 % versus 6.3 %) and revascularization (4.6 % versus 2.6 %). This meta-analysis included three major multicenter trials, CT-STAT [28], ACRIN-PA [30], and ROMICAT II [29], which have been pivotal in demonstrating the safe use of CCTA for early triage of patients in the ED [33]. In each of these trials, patients with no ECG changes and a negative initial troponin were randomized to either CCTA or standard treatment with serial cardiac markers and ECGs.

The CT-STAT (Coronary Computed Tomographic Angiography for Systematic Triage of Acute Chest Pain Patients to Treatment) is a multicenter trial of low risk ED patients that prospectively included 699 patients who were either randomly allocated to CCTA (n =361) versus myocardial perfusion imaging (MPI) (n=338). The investigators sought to compare the efficiency, cost, and safety of using CCTA in the evaluation of patients with acute chest pain and low risk of ACS [28]. The primary outcome of the study was time to diagnosis. The investigators also showed a cost reduction in patients randomized to CCTA. Those in the CCTA arm had a 54 % reduction in time to diagnosis and 38 % reduction in costs. There was no difference in major adverse cardiac events (MACE) between the two study groups [28].

The ACRIN-PA (American College of Radiology Imaging Network- Pennsylvania) multicenter trial was designed to evaluate the safety of CCTA strategy, defined as the absence of MI or cardiac death during 30-day follow-up, in low-to-intermediate risk patients in the ED [30]. This trial

included 1370 patients randomized in a 2:1 ratio to CCTA versus standard of care. The trial concluded that utilization of CCTA early in the ED was safe and of the 640 patients with negative CCTA examinations, none of them died or had a myocardial infarction within 30 days of presentation. They also found that early CCTA led to a shorter mean hospital stay (18 versus 24.8 h) and subsequently more frequent ED discharge when compared to standard of care (50 % versus 23 %) [30].

The ROMICAT II (Rule Out Myocardial Infarction Using Computer Assisted Tomography) trial is a multicenter comparative effectiveness trial that randomized patients to early implementation of CCTA versus standard ED evaluation in 1000 low-to-intermediate risk patients recruited from nine centers in the United States with suspected ACS [29]. The primary endpoint was length of stay. Approximately 8 % of the study patients developed ACS. The study showed that early CCTA utilization decreased the mean length of stay in the hospital by 7.6 h compared to standard ED evaluation and patients were more often discharged directly from the ED (47 vs. 12 %). Additionally, there were no missed cardiac events within 72 h, making CCTA a viable alternative for low-intermediate risk patients in the ED. However, increased diagnostic testing and higher radiation exposure was observed in the CCTA group. While there was a reduction in ED costs with an early CCTA strategy, there was no overall reduction in the cost of care during index hospitalization or 28-day follow-up [29].

In aggregate, these studies support the use of CCTA as an efficient and safe alternative to the more traditional triaging methods for low and low-to-intermediate risk patients as an option to exclude obstructive CAD as the etiology of chest pain, while allowing for a faster ED discharge and ED cost savings. However, such use of CCTA has been associated with increases in downstream invasive coronary angiography (ICA) and coronary revascularization, and the benefit of this approach requires further study.

Appropriate Use and Guidelines

The use of CCTA in patients presenting to the ED with acute chest pain and low-to-intermediate risk of ACS is supported by the current literature, as previously discussed. The Society of Cardiovascular Computed Tomography (SCCT) has recently published guidelines for the use of CCTA in the diagnosis of acute chest pain in patients with suspected ACS in the ED [34]. A summary of these guidelines is presented in Tables 27.1 and 27.2.

The ACCF/SCCT/ACR/AHA/ASE/ASNC/NASCI/SCAI/SCMR 2010 Appropriate Use Criteria for Cardiac Computed Tomography lists the use of CCTA as appropriate for "detection of CAD in symptomatic patients without known heart disease—acute symptoms with suspicion of ACS (urgent presentation) (Appropriate, score 7)" in patients with the following [35]:

- Normal ECG and cardiac biomarkers and low pretest probability of CAD
- Normal ECG and cardiac biomarkers and intermediate pretest probability of CAD
- ECG uninterpretable and low pretest probability of CAD
- ECG uninterpretable and intermediate pretest probability of CAD
- Non-diagnostic ECG or equivocal cardiac biomarkers and low pretest probability of CAD
- Non-diagnostic ECG or equivocal cardiac biomarkers and intermediate pretest probability of CAD

Evolution of Coronary CT Angiography Technology

Since the introduction of CT as a tool for medical imaging, there has been a desire to apply this technology for imaging of the heart. Electron-beam CT (EBCT) had been proposed earlier to the introduction of multi-detector row CT (MDCT) scanners, for the evaluation of patients arriving in the ED with acute chest pain. EBCT had better temporal but inferior spatial resolution as compared to MDCT, and this approach relied on the total coronary calcium score, called the Agatston score [36] as a measure of overall plaque burden, and showed high sensitivity but low specificity for the detection of obstructive CAD. Technologic development continued to 16-detector row and subsequently the 64-detector row MDCT scanners in 2002 and 2005, respectively, which were used to obtain ECG-synchronized images of the heart at high spatial and temporal resolution [37], to quantify coronary artery calcium [38], and to detect coronary artery stenosis [37, 39]. These scanners were capable of image acquisition with high spatial resolution (0.5–0.8 mm isotropic resolution), high temporal resolution (350–400 ms), and sufficient Z-axis coverage (20–40 mm). Scan times with these scanners were less than 10 s when only the heart is evaluated and less than 20 s when the entire thorax is imaged with ECG synchronization. The field of CCTA has continued to improve since 2005 with the introduction of MDCT scanners capable of even greater spatial resolution (up to 0.23 mm in-plane resolution), higher temporal resolution (via dual-source and high-pitch helical technology), and increased volume coverage (through 256- or 320-detector arrays). Broader 256- or 320- detector arrays allow complete volume coverage of the heart in a single heartbeat, thus reducing limitations concerning arrhythmia, and high and variable heart rates [37, 38, 40].

Table 27.1 Society of cardiovascular computed tomography (SCCT) guidelines on the use of CCTA for patients presenting with acute chest pain in the ED [34]

I. **Site Requirements**
Equipment
Required equipment:
≥64 detector rows scanner that is equipped with coronary artery-specific capabilities Advanced cardiac life support (ACLS) equipment to be present in the patient preparation and scanner areas Image interpretation platforms with three-dimensional post-processing software Prior year CCTA, with a minimum volume of 300 scans per year CT laboratory accreditation
Recommended equipment:
Scanner that is equipped to perform prospectively triggered axial scanning protocols in appropriate patients should be available for radiation dose reduction
Quality assurance program goals:
Achieving a diagnostic-quality scan rate of ≥95 % Quarterly median radiation dose rate within target reference level, established by the SCCT guidelines on radiation dose and dose-optimization strategies in cardiovascular CT Quarterly review of CCTA interpretation compared with invasive angiography, achieving at least 75 % per-patient accuracy
Staffing requirements:
At least one technologist is required with prior volume experience of at least 100 CCTA scans Current ACLS certification is required for technologists performing scans without the immediate proximity of an ACLS-certified nurse For beta-blocker premedication of patients, properly trained ACLS-certified nursing staff is required For prompt response to urgent or emergent complications, rapid response team and/or ACLS-certified physician must be available Scanner operation and availability, and staffing-service hours must satisfy ED minimum requirements
II. Interpreting Physician Requirements
Requirements:
At least one physician with a minimum of 2 years of clinical experience and/or at least 300 prior CCTA scan interpretations All other interpreting physicians must attain and maintain level-2 or the equivalent CCTA certification Interpreting physicians must be promptly available in person or by phone for consultation about patient preparation and scan protocol Interpreting physicians must be trained in the best-practice protocol selection of the scanners in use A qualified physician must interpret all non-cardiac anatomy on all scans
Recommendations:
Certification Board of Cardiovascular Computed Tomography certification or American College of Radiology Board certification or dedicated fellowship training in advanced cardiac imaging
III. Patient Selection
Appropriate indications:
Patients with acute chest pain with clinically suspected coronary ischemia ECG negative or indeterminate for myocardial ischemia Low to intermediate pretest likelihood by risk stratification tools (e.g., Thrombolysis in Myocardial Infarction [TIMI] grade of low [0–2] or intermediate [3–4]) Equivocal or inadequate previous functional testing during index ED hospitalization or within the previous 6 months
Uncertain indications:
High clinical likelihood of ACS by clinical assessment and standard risk criteria (e.g., TIMI grade >4) Previously known CAD (prior myocardial infarction, prior ischemia, prior revascularization, coronary artery calcium score >400)
Relative contraindications:
In case of history of allergic reaction to iodinated contrast without history of anaphylaxis or allergic reaction after adequate steroid/antihistamine preparation, alternative testing should be preferred Glomerular filtration rate (GFR) <60 Previous substantial volume of contrast within 24 h Factors leading to potentially non-diagnostic scans (vary with scanner technology and site capabilities) Heart rate is greater than the site maximum for reliable diagnostic scans after beta-blockers Contraindications to beta-blockers and inadequate heart rate control Atrial fibrillation or other markedly irregular rhythm Body mass index >39 kg/m^2
Absolute contraindications:
ACS: definite GFR <30 unless on chronic dialysis or evidence of acute tubular necrosis Previous anaphylaxis after iodinated contrast administration Previous episode of contrast allergy after adequate steroid/antihistamine preparation Inability to cooperate, including inability to raise arms Pregnancy or uncertain pregnancy status in premenopausal women
Patient preparation, scan protocol, and reporting should follow the SCCT guidelines. In addition, interpretation of the CCTA should be tailored according to the needs of the ED

Table 27.2 An example of management recommendations [34]

Sample management recommendations to emergency department physicians
Stenosis 0–25 % (ACS unlikely): Reasonable to discharge the patient Follow-up at physician's discretion
Stenosis 26–49 % (ACS unlikely): Reasonable to discharge the patient Outpatient follow-up is recommended for preventive measures
Stenosis 50–69 % (ACS possible): Further evaluation of the patient is indicated before discharge
Stenosis >70 % (ACS likely): Admit the patient for further evaluation

Coronary Artery Calcium Quantification

Prior to discussion of CCTA in the evaluation of acute chest pain patients presenting to the ED, the role of non-contrast coronary artery calcium (CAC) scanning is worthy to mention. CAC scan is relatively cheaper and faster to conduct and interpret. Due to the strong correlation of CAC to overall coronary artery atherosclerotic disease burden, there has been interest to use CAC scan in low-to-intermediate risk patients and to exclude CAD in patients with CAC score of zero. An American College of Cardiology Foundation/American Heart Association consensus statement endorsed the use of CAC testing for low-risk symptomatic patients as a "filter" for further cardiovascular testing. It is recommended that CAC scoring may be used in a binary fashion such that CAC of zero excludes CAD and no further testing is performed as compared to CAC >0, for which additional functional stress testing for obstructive CAD can be considered [41].

In contrast, a recent analysis from the CONFIRM registry demonstrated that CCTA findings were superior to CAC scoring for adverse cardiovascular outcomes in 10,037 low-to-intermediate risk patients, albeit stable rather than acute in presentation, undergoing both CAC and CCTA. CCTA occasionally demonstrated significant luminal stenosis of ≥50 % in patients with zero CAC score (3.5 % incidence). The investigators concluded that in symptomatic patients with a CAC score of 0, obstructive CAD is possible and is associated with increased cardiovascular events [42].

The major disadvantage of CAC scan is the inability to visualize non-calcified plaque, which may be present in a large proportion of patients. Moreover, non-calcified plaque carries with it important prognostic value that can be readily assessed by CCTA but not by CAC scan. Therefore, CAC scan is not widely considered a first-line test because of its inability to rule out stenosis by non-calcified plaque and low specificity for obstructive CAD, and CCTA may be a preferable option for most patients with acute chest pain.

Detection of Coronary Plaque by CCTA

CCTA is a contrast-enhanced CT scan used for non-invasive evaluation of the coronary arteries. The prognostic value and cost-effectiveness of CCTA have been described by many studies [43–55]. As opposed to non-contrast coronary calcium scoring, contrast-enhanced CCTA can identify calcified, non-calcified, and partially calcified (calcified and non-calcified) lesions of the coronary arteries. There is supporting evidence that the manual quantification of the coronary plaque volumes by CCTA for non-calcified and partially calcified plaques correlate closely with invasive intravascular ultrasound [56–59]. The detection of non-calcified plaque is more challenging compared to calcified plaque detection, and optimal image quality is required that can be achievable by using 64-slice scanners.

Beyond high-grade coronary stenoses, specific coronary plaque features are linked with ACS and other adverse cardiovascular events. Studies have shown that potentially vulnerable plaques have distinct features that include large plaque volume, large necrotic core size, attenuated fibrous caps, and positive arterial remodeling (growth of atherosclerotic plaque into the vessel wall rather than the vessel lumen) [60, 61]. Furthermore, the presence of "spotty" plaque calcifications has been associated with acute MI. CCTA can assess some of these "adverse" features of potentially vulnerable plaques [62]. Therefore, CCTA assessment of plaque may prove prognostically useful when including identification of adverse plaque features. The "adverse" plaque features associated with ACS and other adverse cardiovascular events to date include low attenuation plaque, positive remodeling, spotty calcifications, and the "napkin-ring sign". Studies have demonstrated the characteristics of coronary plaque in patients presenting with ACS [63–66]. Patients with ACS had greater portions of non-calcified plaque, had larger plaque volumes, presented more often with "spotty" calcifications, and included plaques with greater positive remodeling and lower CT attenuation than patients with stable angina [63, 64, 66]. Furthermore, the presence of a napkin-ring sign has also been shown to be a sign of high-risk coronary plaque [64, 67, 68].

Beyond these plaque features that require generally arduous measurements, prior investigations have also shown that major adverse cardiac events (MACE) were associated with more easily identifiable characteristics, including a higher amount of non-calcified plaque in non-obstructive CAD. Conversely, the amount of calcified plaque was not significantly associated with an increased risk for MACE [51].

Non-coronary CCTA Findings

A multitude of additional information proffered by CCTA may be of benefit in the acute and long-term assessment of

the ED patients. This includes evaluation of non-coronary cardiac findings, including left ventricle volume and ejection fraction; left ventricular mass; right heart dimensions and function; and great vessel pathology; as well as non-cardiac thoracic pathology of a patient's chest pain [69–75]. Furthermore, identification of pulmonary nodules as a non-cardiac incidental finding can improve follow-up related to potentially adverse findings [76–79].

The assessment of non-cardiac thoracic pathology by utilizing CCTA may include aortic dissection, pulmonary embolism, pneumonia, pericardial disease, abscesses, effusions, and cancer [45, 80, 81]. In this regard, some investigators have considered whether acute chest pain needs to be evaluated with a "triple rule-out" protocol which effectively increases the Z-axis coverage of the CT scan, and allows for exclusion of ACS, aortic dissection, and pulmonary embolus in a single scan; but there is no clear clinical benefit to this extended approach which has the disadvantage of significantly increased radiation dose, higher imaging costs, and longer interpretation and reporting time. Thus, routine use of a "triple rule-out" protocol is not currently recommended [34].

Diagnostic Accuracy of CCTA

Prospective multicenter diagnostic performance have demonstrated the ability of CCTA to accurately detect coronary stenosis when compared to invasive coronary angiography (ICA) as a reference standard. In the ACCURACY (Assessment by Coronary Computed Tomographic Angiography of Individuals Undergoing Invasive Coronary Angiography) trial [18], 230 patients underwent both CCTA and ICA for non-emergent typical or atypical chest pain. The study investigators demonstrated CCTA to have a sensitivity of 95 %, specificity of 83 %, positive predictive value of 64 %, and negative predictive value of 99 % for prediction of obstructive CAD with >50 % stenosis by ICA. The high negative predictive value of 99 % at both the patient and the vessel level demonstrated that cardiac CT is an effective non-invasive alternative to ICA to rule out obstructive CAD [18]. Furthermore, a meta-analysis of 40 ACCURACY studies concluded that in comparison with ICA, the sensitivity and specificity of CCTA to detect ≥50 % stenosis were 99 % and 89 %, respectively at per patient level, and 90 % and 97 %, respectively at per segment level [82]. Particularly germane to the topic at hand, CCTA in low-to-intermediate risk patients suspected to have ACS retains its very high sensitivity (92 %) and negative predictive value (99 %), with MACE at 30 days, 6 months, or at 1 year equal to zero or minimal in patients who were discharged with a normal CCTA or when CCTA demonstrated mild non-obstructive disease [25, 26, 83].

The ability of CCTA to rapidly exclude obstructive CAD among ED patients helps in identifying patients who can be safely and rapidly discharged from the ED relative to standard of care [33, 84]. The American College of Cardiology (ACC)/American Heart Association (AHA) guidelines have incorporated CCTA among current noninvasive tests for use in low-to-intermediate risk patients with suspected ACS. However, current literature still lacks a standardized approach to guide ED patient management based on cardiac CT findings.

Radiation Risk

Although CCTA has evolved as a useful diagnostic imaging modality in the assessment of CAD, the potential risks due to ionizing radiation exposure associated with CCTA have raised concerns, particularly with regard to potential long-term risks of radiation-induced malignancy, and has led to the "As Low As Reasonably Achievable (ALARA)" principle of radiation protection [85]. In spite of the fact that the increased risk of malignancy from CCTA remains controversial, the ALARA principle prevails in clinical practice. The clinical usefulness of CCTA for the rapid evaluation of chest pain in the ED must be weighed against the radiation exposure. Improvements in CCTA technology, including prospective ECG triggering, tube voltage reduction to 100 kV or less in non-obese patients, use of iterative image reconstruction, and high-pitch helical acquisition, have allowed for substantial reduction of radiation doses by CCTA to <1 mSv. These 1 mSv scans, though theoretically attractive, are still not routine due to certain challenges such as higher heart rates and arrhythmias, and large body habitus.

Indications

The use of cardiac CT to rule out ACS, especially in low-to-intermediate risk patients, is supported by the recent SCCT guidelines [34], which recommends CCTA in the setting of acute chest pain in patients with low-to-intermediate likelihood of ACS with negative initial electrocardiographic and biochemical markers, and TIMI grade ≤4. The indications according to these guidelines are as follows [34]:

Appropriate Indications

- Patients with acute chest pain with clinically suspected coronary ischemia
- ECG negative or indeterminate for myocardial ischemia
- Low-to-intermediate pretest likelihood by risk stratification tools (e.g., TIMI grade of low [0–2] or intermediate [3–4])
- Equivocal or inadequate previous functional testing during index ED hospitalization or within the previous 6 months

Uncertain Indications

- High clinical likelihood of ACS by clinical assessment and standard risk criteria (e.g., TIMI grade >4)
- Previously known CAD (prior MI, prior ischemia, prior revascularization, coronary artery calcium score >400)

Moreover, the ACCF/SCCT/ACR/AHA/ASE/ASNC/NASCI/SCAI/SCMR 2010 Appropriate Use Criteria for Cardiac Computed Tomography lists the use of CCTA as appropriate for "detection of CAD in symptomatic patients without known heart disease—acute symptoms with suspicion of ACS (urgent presentation) (Appropriate, score 7)" [35], as previously discussed.

Contraindications

CCTA is contraindicated in patients with severe renal impairment because of the high risk of contrast-induced nephropathy (CIN). In addition, pregnancy is a contraindication due to radiation exposure. Prior contrast reactions are a relative contraindication; such patients can frequently be pre-treated with the use of a steroid and anti-histamine medications one day prior to the CT examination. The absolute and relative contraindications to CCTA according to SCCT recently published guidelines include the following [34]:

Absolute Contraindications

- ACS: definite
- GFR <30 unless on chronic dialysis or evidence of acute tubular necrosis
- Previous anaphylaxis after iodinated contrast administration
- Previous episode of contrast allergy after adequate steroid/antihistamine preparation
- Inability to cooperate, including inability to raise arms
- Pregnancy or uncertain pregnancy status in premenopausal women

Relative Contraindications

- Alternative testing should be preferred in these cases: history of allergic reaction to iodinated contrast without history of anaphylaxis or allergic reaction after adequate steroid/antihistamine preparation
- Glomerular filtration rate (GFR) <60
- Previous substantial volume of contrast within 24 h (this will vary with the GFR)
- Factors leading to potentially nondiagnostic scans (vary with scanner technology and site capabilities)
  - Heart rate is greater than the site maximum for reliable diagnostic scans after beta-blockers
  - Contraindications to beta-blockers and inadequate heart rate control
  - Atrial fibrillation or other markedly irregular rhythm
  - Body mass index >39 kg/m^2

Summary of Strengths

CCTA is unique from prior forms of imaging in that it does not require stress provocation to determine burden of CAD. Multiple single-center and multicenter trials have established CCTA as a noninvasive diagnostic test with excellent sensitivity (97.2 %) and good specificity (87.4 %) for the detection of obstructive CAD with >50 % stenosis [17, 18]. The major strength of CCTA is its high negative predictive value for stenosis (99 %). In addition, CCTA is highly sensitive (90 %) and specific (92 %) for the detection of calcified and non-calcified coronary atherosclerotic plaque [57, 59, 86].

Summary of Limitations

A significant limitation of the CCTA is its lower specificity that may be attributable to a spatial resolution of about 0.5 mm. This non-ideal specificity of CCTA is concerning and could lead to increased downstream testing and, possibly, ICA with revascularization, thus warranting further improvements in CCTA technology. Another important limitation is that patients with extensive coronary calcification may have non-diagnostic scans because of calcium "blooming" and "beam hardening" artifacts. Cardiac dysrhythmias and inadequate heart rate control during imaging are other factors leading to sub-optimal scans for diagnostic purposes.

Moreover, assessment of CAD by cardiac CT requires ionizing radiation exposure and administration of contrast dye, compared to other modalities (e.g., exercise treadmill, rest echocardiography, exercise or pharmacologic stress echocardiography, rest or stress cardiac magnetic resonance imaging). Patients with significant contrast dye allergies or renal insufficiency are not candidates for CCTA. Morbid obesity can compromise image quality and thus reduce diagnostic accuracy or require higher doses of radiation. Higher heart rates and arrhythmias can cause misregistration artifacts, leading to poor visualization of the coronary arteries.

Future Directions

Chest pain is so commonly encountered in the practice of medicine and future advancements in CCTA technology are expected to improve the overall accuracy of CT-determined stenosis in comparison with reference standard fractional

flow reserve (FFR) measurements during ICA. Currently, investigators are interested in changing the face of how ACS is diagnosed and managed by improving the specificity of qualitative determination of coronary stenosis by fractional flow reserve derived from CT, or FFR_{CT}, a novel non-invasive method that applies computational fluid dynamics for the calculation of FFR from typically acquired CCTA studies. This technique has been demonstrated to have higher diagnostic performance for ischemia-causing lesions than any other functional imaging method [87]. Importantly, given its ability to obviate the requirement for use of adenosine or for additional scanning, this technique offers the added safety to not require increased radiation doses. In the future, it is expected that the maturation of dual-energy CT may further improves stenosis assessment and diagnostic accuracy in patients with heavy coronary calcifications, and may allow for further radiation reduction. In aggregate, noninvasive coronary imaging by CT is likely here to stay.

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