Contrast-Enhanced Computed Tomography Angiography for Coronary Artery Evaluation

Description

Contrast-enhanced computed tomography angiography (CTA) is a noninvasive imaging test that requires the use of intravenously administered contrast material and high-resolution, high-speed computed tomography (CT) machinery to obtain detailed volumetric images of blood vessels. It is a potential alternative to current diagnostic tests for cardiac ischemia, i.e., non-invasive stress testing and/or coronary angiography.

Background

Contrast-enhanced computed tomography angiography (CTA) can be applied to image blood vessels throughout the body; however, for the coronary arteries, several technical challenges must be overcome to obtain high-quality diagnostic images. First, very short image acquisition times are necessary to avoid blurring artifacts from the rapid motion of the beating heart. In some cases, premedication with beta-blocking agents is used to slow the heart rate below approximately 60–65 beats per minute to facilitate adequate scanning, and electrocardiographic triggering or gating (retrogressive or prospective) is used to obtain images during diastole when motion is reduced. Second, rapid scanning is also helpful so that the volume of cardiac images can be obtained during breath-holding. Third, very thin sections (1 mm or less) are important to provide adequate spatial resolution and high-quality 3D reconstruction images.

Volumetric imaging permits multiplanar reconstruction of cross-sectional images to display the coronary arteries. Curved multiplanar reconstruction and thin-slab maximum intensity projections provide an overview of the coronary arteries, and volume-rendering techniques provide a 3D anatomical display of the exterior of the heart. Two different CT technologies can achieve high-speed CT imaging. Electron beam CT (EBCT, also known as ultrafast CT) uses an electron gun rather than a standard x-ray tube to generate x-rays, thus permitting very rapid scanning, on the order of 50–100 milliseconds per image. Helical CT scanning (also referred to as spiral CT scanning) also creates images at greater speed than conventional CT by continuously rotating a standard x-ray tube around the patient so that data are gathered in a continuous spiral or helix rather than as individual slices. Helical CT is able to achieve scan times of 500 milliseconds or less per image and use of partial ring scanning or post-processing algorithms may reduce the effective scan time even further.
Multidetector row helical CT (MDCT) or multislice CT scanning is a technologic evolution of helical CT, which uses CT machines equipped with an array of multiple x-ray detectors that can simultaneously image multiple sections of the patient during a rapid volumetric image acquisition. MDCT machines currently in use have 64 or more detectors.

A variety of noninvasive tests are used in the diagnosis of coronary artery disease. They can be broadly classified as those that detect functional or hemodynamic consequences of obstruction and ischemia (exercise treadmill testing, myocardial perfusion imaging [MPI], stress echo with or without contrast), and others that identify the anatomic obstruction itself (coronary CTA and coronary magnetic resonance imaging [MRI]). (1) Functional testing involves inducing ischemia by exercise or pharmacologic stress and detecting its consequences. However, not all patients are candidates. For example, obesity or obstructive lung disease can make obtaining echocardiographic images of sufficient quality difficult. Conversely, the presence of coronary calcifications can impede detecting coronary anatomy with coronary CTA. Accordingly, some tests will be unsuitable for particular patients.

Evaluation of obstructive coronary artery disease (CAD) involves quantifying arterial stenoses to determine whether significant narrowing is present. Lesions with greater than 50% to 70% diameter stenosis accompanied by symptoms are generally considered significant and often result in revascularization procedures. It has been suggested that coronary CTA may be helpful to rule out the presence of CAD and to avoid invasive coronary angiography (ICA) in patients with a low clinical likelihood of significant CAD. Also of note is the interest in the potential important role of non-obstructive plaques (i.e., those associated with <50% stenosis) because their presence is associated with increased cardiac event rates. (2) Coronary CTA can also visualize the presence and composition of these plaques and quantify the plaque burden better than conventional angiography, which only visualizes the vascular lumen. Plaque presence has been shown to have prognostic importance.

The information sought from angiography after coronary artery bypass graft (CABG) surgery may depend on the length of time since surgery. Bypass graft occlusion may occur during the early postoperative period; whereas, over the long term, recurrence of obstructive CAD may occur in the bypass graft, which requires a similar evaluation as CAD in native vessels.

Congenital coronary arterial anomalies (i.e., abnormal origination or course of a coronary artery) that lead to clinically significant problems are relatively rare. Symptomatic manifestations may include ischemia or syncope. Clinical presentation of anomalous coronary arteries is difficult to distinguish from other more common causes of cardiac disease; however, an anomalous coronary artery is an important diagnosis to exclude, particularly in young patients who present with unexplained symptoms (e.g., syncope). There is no specific clinical presentation to suggest a coronary artery anomaly.

Coronary CTA has several important limitations. The presence of dense arterial calcification or an intracoronary stent can produce significant beam-hardening artifacts and may preclude a satisfactory study. The presence of an uncontrolled rapid heart rate or arrhythmia hinders the ability to obtain diagnostically satisfactory images. Evaluation of the distal coronary arteries is generally more difficult than visualization of the proximal and mid-segment coronary arteries due to greater cardiac motion and the smaller caliber of coronary vessels in distal locations.
Radiation delivered with current generation scanners utilizing reduction techniques (prospective gating and spiral acquisition) has declined substantially, typically to under 10 mSv. For example, an international registry developed to monitor coronary CTA radiation recently reported a median 2.4 mSv (interquartile range, [IQR]: 1.3 to 5.5) exposure. (3) In comparison, radiation exposure accompanying rest-stress perfusion imaging ranges varies according to isotope used, approximately 5 mSv for rubidium-82 (PET), 9 mSv for sestamibi (SPECT), 14 mSv for F-18 FDG (PET), and 41 mSv for thallium; during diagnostic invasive coronary angiography, approximately 7 mSv will be delivered. (4) EBCT using electrocardiogram (ECG) triggering delivers the lowest dose (approximately 0.7 to 1.1 mSv with 3-mm sections). Any cancer risk due to radiation exposure from a single cardiac imaging test depends on age (higher with younger age at exposure) and gender (greater for women). (5-7) Empirical data (8) suggest that every 10 mSv of exposure is associated with a 3% increase in cancer incidence over 5 years.

The use of electron beam CT or helical CT to detect coronary artery calcification is addressed in a separate policy (No. 6.01.03).

**Regulatory Status**

Coronary CTA is performed using multidetector-row CT (MDCT), and multiple manufacturers have received U.S. Food and Drug Administration (FDA) 510(k) clearance to market machines. Current machines are equipped with at least 64 detector rows. Intravenous iodinated contrast agents used for coronary CTA also have received FDA approval.

**Related Policy**

None

**Policy**

*This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.*

Contrast-enhanced computed tomography angiography for evaluation of patients without known coronary artery disease and acute chest pain in the emergency room/emergency department setting is considered **medically necessary**.

Contrast-enhanced computed tomography angiography for evaluation of patients with stable chest pain and meet guideline criteria for requiring a noninvasive test in the outpatient setting is considered **medically necessary**.

Contrast-enhanced computed tomography angiography for evaluation of anomalous (native) coronary arteries in patients in whom they are suspected may be considered **medically necessary** when conventional angiography is unsuccessful or equivocal and when the results will impact treatment.
Contrast-enhanced computed tomographic angiography for coronary artery evaluation is considered not medically necessary for all other indications.

Rationale

Literature Search

This policy is based in part on Technology Evaluation Center (TEC) Assessments performed in 2005, 2006, and 2011. (9-11) The objective of the 2005 TEC Assessment was to evaluate the clinical effectiveness of contrast-enhanced cardiac computed tomography angiography (CTA) using either electron beam computed tomography (EBCT) or multidetector-row computed tomography (MDCT) as a noninvasive alternative to invasive coronary angiography (ICA), particularly in patients with a low probability of significant coronary artery stenosis. Evaluation of the coronary artery anatomy and morphology was the most frequent use of cardiac CTA and primary focus of the TEC Assessment. The Assessment considered multiple indications, but computed tomography (CT) technology used in studies reviewed is now outdated (studies employed 16-slice scanners). The TEC Assessment concluded that the use of contrast-enhanced cardiac CT angiography for screening or diagnostic evaluation of the coronary arteries did not meet TEC criteria.

The 2006 TEC Assessment was undertaken to determine the usefulness of CTA as a substitute for ICA for 2 indications: in the diagnosis of coronary artery stenosis and in the evaluation of acute chest pain in the emergency department. Just 7 studies performed in the ambulatory setting utilizing 40 to 64 slice scanners were identified. Two studies performed in the emergency department used 4- or 16-slice scanners. Evidence was judged insufficient to form conclusions. Available studies at the time were inadequate to determine the effect of CTA on health outcomes for the diagnosis of coronary artery stenosis in patients referred for angiography or for evaluation of acute chest pain in the emergency department.

Three indications for cardiac or coronary CTA are considered in the policy: 1) evaluation of anomalous coronary arteries, 2) patients with acute chest pain without known coronary disease presenting in the emergency room (ER) setting, and 3) evaluation of stable patients with signs and symptoms of CAD in the non-ER setting.

Patients With Acute Chest Pain Presenting to the Emergency Setting

Diagnostic Validity

The diagnostic characteristics of coronary CTA have not been directly assessed in patients in the emergency setting. Because patients who test negative on CTA are discharged from care and the status of their disease is unknown, there is verification bias and diagnostic characteristics of CTA cannot be determined. The diagnostic characteristics of coronary CTA previously established in other studies was assumed to apply to patients in the ED setting and were tested in randomized trials to establish clinical utility.
Clinical Utility

A 2011 TEC Assessment examined evidence on the evaluation of patients with acute chest pain and without known coronary artery disease (CAD). (11) Randomized controlled trials (RCTs) and prospective observational studies were identified by searching the MEDLINE database and relevant bibliographies of key studies. Several RCTs of CTA conducted in emergency settings were identified. A 2007 RCT by Goldstein et al evaluated 197 randomized patients from a single center without evidence of acute coronary syndromes to coronary CTA with 64-slice scanners (n=99) or usual care (n=98). (12) Over a 6-month follow-up, no cardiac events occurred in either arm. ICA rates were somewhat higher in the coronary CTA arm (12.1% vs 7.1%). Diagnosis was achieved more quickly after coronary CTA.

A 2009 RCT evaluated a similar sample of 699 randomized patients from 16 centers: 361 undergoing coronary CTA with 64- to 320-slice scanners and 338 undergoing myocardial perfusion imaging (MPI). (13) Over a 6-month follow-up, there were no deaths in either arm, 2 cardiac events in the coronary CTA arm and 1 in the perfusion imaging arm. ICA rates were similar in both arms (7.2% after coronary CTA, 6.5% after perfusion imaging). A second noninvasive test was obtained more often after coronary CTA (10.2% vs 2.1%), but cumulative radiation exposure in the coronary CTA arm (using retrospective gating) was significantly lower (mean 11.5 vs 12.8 mSv). Time to diagnosis was shorter (mean, 3.3 hours) and estimated ED costs lower with coronary CTA.

A 2012 RCT by Litt et al also evaluated the safety of coronary CT in the evaluation of patients in the ED. (14) Although the study was a randomized comparison with traditional care, principal outcome was safety after negative CTA examinations. No patients who had negative CTA examinations (n=460) died or had a myocardial infarction (MI) within 30 days. Compared with traditional care, patients in the CTA group had higher rates of discharge from the ED (49.6% vs 22.7%), a shorter length of stay (median, 18.0 hours vs 24.8 hours), and a higher rate of detection of coronary disease (9.0% vs 3.5%). Three studies reported no cardiac events after a negative coronary CTA in the ED after 12- (N=481), (15) 24- (N=368), (16) or 47-month (N=506) (17) follow-up.

A 2012 RCT by Hoffmann et al compared length of stay and patient outcomes in patients evaluated with CTA versus usual care. (18) For patients in the CTA arm of the trial, mean length of hospital stay was reduced by 7.6 hours, and more patients were discharged directly from the ED (47% vs 12%). There were no undetected coronary syndromes and no differences in adverse events at 28 days. However, in the CTA arm, there was more subsequent diagnostic testing and higher cumulative radiation exposure. Cumulative costs of care were similar between the 2 groups.

A 2014 RCT by Hamilton-Craig et al compared length of stay and patient costs in 562 patients presenting to the ED with low-to-intermediate risk chest pain with CTA versus exercise stress testing. (19) Costs within 30 days of presentation were significantly lower in the CTA group than in the exercise testing group (mean, $2193 vs $2704 p<0.001). Length of stay was significantly reduced in the CTA patients compared with the exercise testing group (mean, 13.5 hours vs 20.7 hours, p<0.0001). Clinical outcomes at 30 days and at 12 months did not differ.
Section Summary: Acute Chest Pain Presenting to the Emergency Setting

The high NPV of coronary CTA in patients presenting to the ED with chest pain allows coronary disease to be ruled out with high accuracy. The efficiency of the workup is improved, as patients are safely and quickly discharged from the ED with no adverse outcomes among patients who have negative CTA examinations.

Other important outcomes that require consideration in comparing technologies include ICA rates, use of a second noninvasive test, radiation exposure, and follow-up of any incidental findings. Although there is uncertainty accompanying the limited trial evidence, it is reasonable to conclude that ICA rate after coronary CTA is not markedly different from that after noninvasive imaging. Two studies showed that subsequent diagnostic testing was more frequent in patients who received CTA. Studies have differed in which treatment strategy results in higher overall radiation exposure. Incidental findings after coronary CTA are common and lead to further testing, but the impact of these findings on subsequent health outcomes is uncertain.

Stable Patients With Angina and Suspected CAD

Before the introduction of coronary CTA, the initial noninvasive test in a diagnostic strategy was always a functional test. Current practice guidelines recommend a noninvasive test be performed in patients with intermediate risk of coronary artery disease. The choice of functional test is based on clinical factors such the predicted risk of disease, electrocardiogram interpretability, and ability to exercise. When disease is detected, treatment alternatives include medical therapy or revascularization (percutaneous coronary intervention or coronary artery bypass graft surgery). If revascularization is indicated, patients undergo ICA to confirm the presence of stenosis. Which approach to adopt is based on the extent of anatomic disease, symptom severity, evidence of ischemia from functional testing, and more recently, fractional flow reserve obtained during invasive angiography. Many studies have shown that only a subset of anatomically defined coronary lesions are clinically significant and benefit from revascularization. Other studies have shown only limited benefits of treating coronary stenoses in stable patients. Thus an assessment of the diagnostic characteristics of coronary CTA alone is insufficient to establish clinical utility. A difficulty in evaluating a noninvasive diagnostic test for CAD is that the patient outcomes depend on not only the test results, but the management and treatment strategy. The most convincing evidence of clinical utility compares outcomes after anatomic-first (coronary CTA) and functional-first (eg, perfusion imaging, stress echocardiography) strategies.

Relevant studies reviewed here include studies comparing diagnostic performance of coronary CTA with angiography, studies of outcomes of patients undergoing CTA versus alternative tests, and studies of incidental findings and radiation exposure.

Diagnostic Accuracy

At this time, there is a fairly large body of evidence evaluating the diagnostic characteristics of coronary CTA for identifying coronary lesions. The best estimate of the diagnostic characteristics of coronary CTA can be obtained from review of recent meta-analyses and systematic reviews. Table 1 shows
ranges of sensitivity and specificity for functional noninvasive tests from studies reviewed for the diagnosis and management of stable angina by Fihn et al. (20) Sensitivities tended to range between 70% and 90%, depending on the test and study, and specificities ranged between 70% and 90%.

For coronary CTA, estimates of sensitivity from various systematic reviews are considerably higher (see Table 2). The guideline statement from Fihn et al cited studies reporting sensitivities between 93% and 97%. (20) A meta-analysis by Ollendorf et al of 42 studies showed a summary sensitivity estimate of 98% and a specificity of 85%. A meta-analysis of 8 studies conducted by the Ontario Health Ministry showed a summary sensitivity estimate of 97.7% and a specificity of 79%. In the meta-analysis by Nielsen et al, sensitivity of coronary CTA varied between 98% and 99% (depending on the analysis group). (21)

<table>
<thead>
<tr>
<th>Noninvasive Test</th>
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<th>Specificity (Range or Single Estimates)</th>
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<tr>
<td>Exercise electrocardiography</td>
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<td>70%-77%</td>
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<tr>
<td>Pharmacologic stress echocardiography</td>
<td>85%-90%</td>
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<tr>
<td>Exercise stress echocardiography</td>
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<tr>
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<tr>
<td>Pharmacologic stress myocardial perfusion imaging</td>
<td>88%-91%</td>
<td>75%-90%</td>
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<table>
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<th>Study</th>
<th>Sensitivity (Range or Single Estimates)</th>
<th>Specificity (Range or Single Estimates)</th>
</tr>
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<td>Fihn et al (2012) guideline statement</td>
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<td>80%-90%</td>
</tr>
<tr>
<td>Ollendorf et al (2011) meta-analysis</td>
<td>98%</td>
<td>85%</td>
</tr>
<tr>
<td>Health Quality Ontario (2010) meta-analysis</td>
<td>97.7%</td>
<td>79%</td>
</tr>
<tr>
<td>Nielsen et al (2014) meta-analysis</td>
<td>98%-99%</td>
<td>82%-88%</td>
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</tbody>
</table>

Clinical Utility

Randomized Controlled Trials

For patients at intermediate risk of CAD, 5 RCTs were identified comparing net health outcomes following a coronary CTA strategy with outcomes from other noninvasive testing strategies.

The PROMISE trial randomized 10,003 patients to coronary CTA or exercise electrocardiography, nuclear stress testing, or stress echocardiography (as determined by physician preference) as the initial diagnostic evaluation. (24) For the composite end point of death, MI, hospitalization for unstable angina, or major procedural complication, the outcome rate between the 2 groups showed no statistically significant difference (hazard ratio [HR], 1.04; 95% confidence interval [CI], 0.83 to 1.29). Coronary CTA also did not meet prespecified noninferiority criteria compared with alternative testing.
Some clinical outcomes assessed at 12 months favored coronary CTA, but the differences were nonsignificant. Coronary catheterization rates and revascularization rates were higher in the coronary CTA group.

In the SCOT-HEART trial, 4146 patients were randomized to coronary CTA or standard care. The primary end point was the change in the proportion of patients with a more certain diagnosis (presence or absence) of angina pectoris. Secondary outcomes included death, MI, revascularization procedures, and hospitalizations for chest pain. Analysis of the primary outcome showed that patients who underwent coronary CTA had an increase in the certainty of their diagnosis relative to those in usual care (relative risk, 1.79; 95% CI, 1.62 to 1.96). Regarding health outcomes, the rate of heart disease death and MI was lower with coronary CTA (1.3% vs 2.0%; HR=0.62; p=0.053), but results were of marginal statistical significance.

A small trial by Min et al (2012) randomized 180 patients with stable chest pain to initial diagnostic evaluation using coronary CTA or MPI. The primary outcome was angina-specific health status. There were no significant differences at follow-up between groups on any measures of health status.

The FACTOR-64 trial randomized 900 subjects with diabetes to screening with coronary CTA or standard care. Patients in this trial were asymptomatic, but were considered to be at high risk for CAD due to long-standing diabetes. The primary outcome was a composite of mortality, nonfatal MI, or unstable angina requiring hospitalization. At a median follow-up of 4 years, there was no significant difference between the groups for the primary outcome (CTA, 6.2%; control, 7.6%; HR=0.80; p=0.38).

The CAPP trial randomized 500 patients with stable chest pain to coronary CTA or exercise stress testing. The primary outcome was the change difference in scores of Seattle Angina Questionnaire domains at 3 months. Patients were also followed up for further diagnostic tests and management. In the CTA arm, 15.2% of subjects underwent revascularization. In the exercise stress testing arm, 7.7% underwent revascularization. For the primary outcome, angina stability and quality of life showed significantly greater improvement in the coronary CTA arm than in the exercise stress testing arm.

Nonrandomized Studies

Four nonrandomized studies were identified comparing outcomes of patients following a coronary CTA strategy with outcomes following other noninvasive testing strategies. A nonrandomized study of coronary CTA with computed fractional flow reserve assessment is discussed in the Appendix. Some studies emphasized downstream utilization of diagnostic testing and procedures rather than patient outcomes.

Nielsen et al conducted an observational trial comparing patients who underwent coronary CTA and exercise stress testing. Patients had a low-to-intermediate pretest probability of CAD and presented with suspected angina. Patients were followed for 12 months after the initial test, and assessed for occurrence of major adverse events such as cardiac death and nonfatal MI. Subsequent utilization of cardiovascular tests and therapy was also compared between groups. Clinical outcomes were not compared formally because there were few clinical events. No deaths were reported during
the follow-up period. Three patients in the exercise testing group had MIs within 12 months. For downstream test utilization, the exercise test group had greater subsequent use perfusion imaging (9% vs 4%, p=0.03) and greater mean total 1-year costs (€1777 vs €1510, p=0.03). Rates of ICA and revascularization did not differ statistically significantly.

Shreibati et al used Medicare claims data to compare all-cause mortality, subsequent utilization of several cardiac tests, treatment, and total costs in patients who underwent initial noninvasive testing with either coronary CTA, stress echocardiography, MPI, or exercise electrocardiography. (31) In this study, patients undergoing coronary CTA had higher rates of several types of utilization subsequent to their test than patients undergoing MPI. The study also presented outcomes for both stress echocardiography and exercise electrocardiography, but they tended not to be any different than for MPI. There were increased rates of ICA (22.9% vs 12.1%) and revascularization (11.4% vs 4.6%). Total spending and CAD-related spending were also higher for coronary CTA than for MPI. There was no significant difference in all-cause mortality between coronary CTA and MPI. Although the mortality rate for coronary CTA was slightly lower than the mortality rate for MPI (1.05% vs 1.28%), the adjusted odds ratio (OR) showed a higher risk of mortality, which may be due to unusual confounding. However, there was a slightly lower likelihood of hospitalization for MI (adjusted OR=0.60; p=0.04).

In Min et al (2008), costs and clinical outcomes for patients undergoing initial coronary CTA were compared with patients undergoing initial MPI. (32) The data source for this study was a proprietary claims database from 2 regional health plans. Utilization of medical care was lower after coronary CTA. Overall costs were lower, the proportion receiving ICA was lower, and the proportion receiving revascularization was lower after coronary CTA. In terms of clinical outcomes, the proportion with a hospitalization for angina was lower in the coronary CTA group. The coronary CTA group also had a lower rate of a combined outcome of angina or MI hospitalization (HR=0.70; 95% CI, 0.55 to 0.90).

In 2825 patients evaluated for stable angina and suspected CAD in Japan, Yamauchi et al examined outcomes after initial coronary CTA (n=625), MPI (n=1205), or angiography (n=950). (33) Average follow-up was 1.4 years. In a Cox proportional hazards model adjusted for potential confounders, the relative hazard of major cardiac events after MPI or coronary CTA were lower than after angiography; annual rates were 2.6%, 2.1%, and 7.0%, respectively. Revascularization rates were higher after coronary CTA than MPI (OR=1.6; 95% CI, 1.2 to 2.2).

### Incidental Findings

Nine studies using 64+-slice scanners were identified. (34-42) Incidental findings were frequent (26.6%-68.7%) with pulmonary nodules typically the most common and cancers rare (~5/1000 or less). Aglan et al (2010) (34) compared the prevalence of incidental findings when the field of view was narrowly confined to the cardiac structures with that when the entire thorax was imaged. As expected, incidental findings were less frequent in the restricted field (clinically significant findings in 14% vs 24% when the entire field was imaged).
Radiation Exposure

Exposure to ionizing radiation increases lifetime cancer risk. (43) Three studies have estimated excess cancer risks due to radiation exposure from coronary CTA. (6, 7, 44) Assuming a 16-mSv dose, Berrington de Gonzalez et al (2009) (44) estimated that the 2.6 million coronary CTAs performed in 2007 would result in 2700 cancers or approximately 1 per 1000. Smith-Bindman et al (2009) estimated that cancer would develop in 1 of 270 women and 1 of 600 men age 40 undergoing coronary CTA with a 22-mSv dose. (7) Einstein et al (2007) employed a standardized phantom to estimate organ dose from 64-slice coronary CTA. (6) With modulation and exposures of 15 mSv in men and 19 mSv in women, calculated lifetime cancer risk at age 40 was 7 per 1000 men (1/143) and 23 per 1000 women (1/43). However, estimated radiation exposure used in these studies was considerably higher than received with current scanners.

Now typically under 1 contemporary machines and radiation reduction techniques. For example, in the 47-center PROTECTION I study enrolling 685 patients, the mean radiation dose was 3.6 mSv, using a sequential scanning technique. (45) In a 2012 study of patients undergoing an axial scanning protocol, mean radiation dose was 3.5 mSv, and produced equivalent ratings of image quality compared with helical scan protocols, which had much higher mean radiation doses of 11.2 mSv. (46)

Section Summary: Stable Angina and Suspected CAD

A number of studies have evaluated the diagnostic accuracy of CTA for diagnosing CAD in an outpatient population. In general, these studies report high sensitivity and specificity, although there is some variability in these parameters across studies. Meta-analysis of these studies showed that for detection of anatomic disease, coronary CTA has a sensitivity greater than 95%, which is superior to all other functional noninvasive tests. Specificity is at least as good as other noninvasive tests. However, the link between improved diagnosis and health outcomes is not as clear, and thus outcome studies are necessary to demonstrate the clinical utility of coronary CTA.

Direct clinical trial evidence comparing coronary CTA and other strategies in the diagnostic management of stable patients with suspected CAD has not demonstrated the superiority of coronary CTA in any of the single clinical trials. Clinical trials demonstrated greater utilization of ICA and subsequent revascularization procedures after coronary CTA. An important problem of interpreting the clinical trials is that the comparator strategies differ: in the PROMISE trial, the CAPP trial, and Min et al (2012), coronary CTA was compared with an alternative noninvasive test; in other studies, coronary CTA was supplement to usual care (which may or may not have included a noninvasive test). This design difference in the clinical trials is likely a reflection of how coronary CTA is used in clinical practice either as a substitute for another noninvasive test or as an addition to other noninvasive tests. The PROMISE trial explicitly compared coronary CTA with an alternative functional test as the initial diagnostic test. Although the trial did not show the superiority of coronary CTA and did not meet prespecified criteria for noninferiority, Examination of some secondary clinical outcomes supports a conclusion of “at least” noninferiority. The results of the other randomized trials are consistent with noninferiority of coronary CTA with other established noninvasive tests. Thus, the randomized studies indicate that outcomes of patients are likely to be similar with coronary CTA versus other noninvasive tests.
The nonrandomized studies of coronary CTA have several methodologic shortcomings including reliance on administrative data and inability to fully assess and adjust for potential confounding. The findings generally show little difference in patient outcomes between diagnostic strategies. Downstream utilization of medical care showed variable findings.

Although studies of incidental findings and radiation exposure raise issues regarding the potential for adverse effects of coronary CTA, there is not sufficient evidence that the magnitude of these effects is important for ascertaining the net benefit or risk of coronary CTA in this setting.

Anomalous Coronary Arteries

Anomalous coronary arteries are an uncommon finding during angiography, occurring in approximately 1% of coronary angiograms completed for evaluation of chest pain. However, these congenital anomalies can be clinically important depending on the course of the anomalous arteries. A number of case series have consistently reported that coronary CTA is able to delineate the course of these anomalous arteries, even when conventional angiography cannot. (47-50) However, none of the studies reported results when the initial reason for the study was to identify these anomalies, nor did any of the studies discuss impact on therapeutic decisions. Given the uncommon occurrence of these symptomatic anomalies, it is unlikely that a prospective trial of coronary CTA could be completed.

Other Diagnostic Uses of Coronary CTA

Given its ability to define coronary artery anatomy, there are many other potential diagnostic uses of coronary CTA including patency of coronary artery bypass grafts, in-stent restenosis, screening, and preoperative evaluation.

- Evaluating patency of vein grafts is generally less of a technical challenge due to vein size and lesser motion during imaging. In contrast, internal mammary grafts may be more difficult to image due to their small size and presence of surgical clips. Finally, assessing native vessels distal to grafts presents difficulties, especially when calcifications are present, due to their small size. For example, a 2008 meta-analysis including results from 64-slice scanners, reported high sensitivity 98% (95% CI, 95 to 99; 740 segments) and specificity 97% (95% CI, 94 to 97). (51) Other small studies have reported high sensitivity and specificity. (52, 53) Lacking are multicenter studies demonstrating likely clinical benefit, particularly given the reasonably high disease prevalence in patients evaluated.

- Use of coronary CTA for evaluation of in-stent restenosis presents other technical challenges: motion, beam hardening, and partial volume averaging. Whether these challenges can be sufficiently overcome to obtain sufficient accuracy and impact outcomes has not been demonstrated.

- Use for screening a low-risk population was recently evaluated in 1000 patients undergoing coronary CTA compared with a control group of 1000 similar patients. (54) Findings were abnormal in 215 screened patients. Over 18 months of follow-up, screening was associated with more invasive testing, statin use, but without difference in cardiac event rates.

Coronary CTA for preoperative evaluation before noncardiac surgery has been suggested, but evaluated only in small studies and lacking demonstrable clinical benefit.
Ongoing and Unpublished Clinical Trials

Some currently unpublished trials that might influence this review are listed in Table 3.

Table 3. Summary of Key Trials

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<th>NCT Number</th>
<th>Title</th>
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<td>NCT01384448</td>
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<td>NCT01283659</td>
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<td>The Correlation of Heart Hemodynamic Status Between 320 Multidetector Computed Tomography, Echocardiography and Cardiac Catheterization in Patients With Coronary Artery Disease</td>
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<td>NCT01559467</td>
<td>The Supplementary Role of Non-invasive Imaging to Routine Clinical Practice in Suspected Non-ST-elevation Myocardial Infarction (CARMENITA)</td>
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<td>NCT02400229</td>
<td>Diagnostic Imaging Strategies for Patients With Stable Chest Pain and Intermediate Risk of Coronary Artery Disease (DISCHARGE)</td>
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<td>NCT02291484</td>
<td>Comprehensive Cardiac CT Versus Exercise Testing in Suspected Coronary Artery Disease (2) (CRESSENT2)</td>
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<td>NCT00991835</td>
<td>Plaque Registration and Event Detection In Computed Tomography (PREDICT)</td>
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<td>Dec 2014</td>
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</tbody>
</table>

NCT: national clinical trial.

Practice Guidelines and Position Statements

ACCF/AHA/ACP/AATS/PCNA/SCAI/STS joint guidelines for management of patients with stable ischemic heart disease were published in 2012. (20) Guideline statements for use of coronary CTA were divided whether used in patients without diagnosed disease or those with known disease and a patient’s ability to exercise:

Diagnosis Unknown

Able To Exercise

Class IIb

“CCTA might be reasonable for patients with an intermediate pretest probability of IHD who have at least moderate physical functioning or no disabling comorbidity.” (Level of Evidence: B)
Unable to Exercise

Class IIa

“CCTA is reasonable for patients with a low to intermediate pretest probability of IHD who are incapable of at least moderate physical functioning or have disabling comorbidity.” (Level of Evidence: B)

“CCTA is reasonable for patients with an intermediate pretest probability of IHD who a) have continued symptoms with prior normal test findings, or b) have inconclusive results from prior exercise or pharmacological stress testing, or c) are unable to undergo stress with nuclear MPI or echocardiography.” (Level of Evidence: C)

For Patients With Known Coronary Disease:

Able To Exercise

Class IIb

“CCTA may be reasonable for risk assessment in patients with SIHD (stabile ischemic heart disease) who are able to exercise to an adequate workload but have an uninterpretable ECG.” (Level of Evidence: B)

Class III: No Benefit

“Pharmacological stress imaging (nuclear MPI, echocardiography, or CMR) or CCTA is not recommended for risk assessment in patients with SIHD who are able to exercise to an adequate workload and have an interpretable ECG.” (Level of Evidence: C)

Unable to Exercise

Class IIa

“Pharmacological stress CMR is reasonable for risk assessment in patients with SIHD who are unable to exercise to an adequate workload regardless of interpretability of ECG.” (Level of Evidence: B)

“CCTA can be useful as a first-line test for risk assessment in patients with SIHD who are unable to exercise to an adequate workload regardless of interpretability of ECG.” (Level of Evidence: C)

Regardless of Patients’ Ability to Exercise

Class IIb

“CCTA might be considered for risk assessment in patients with SIHD unable to undergo stress imaging or as an alternative to invasive coronary angiography when functional testing indicates a
moderate- to high-risk result and knowledge of angiographic coronary anatomy is unknown.” (Level of Evidence: C)

Class III: No Benefit

“A request to perform either a) more than 1 stress imaging study or b) a stress imaging study and a CCTA at the same time is not recommended for risk assessment in patients with SIHD.” (Level of Evidence: C)

Appropriate use criteria (55,56) and expert consensus documents (57) published jointly by ACCF/ACR/AHA/NASCI/SAIP/SCAI/SCCT address coronary CTA in the emergency setting.

“In the context of the emergency department evaluation of patients with acute chest discomfort, currently available data suggest that coronary CTA may be useful in the evaluation of patients presenting with an acute coronary syndrome (ACS) who do not have either acute electrocardiogram (ECG) changes or positive cardiac markers. However, existing data are limited, and large multicenter trials comparing CTA with conventional evaluation strategies are needed to help define the role of this technology in this category of patients.”

In 2013, ACCF/AHA/ASE/ASNC/HFSA/HRS/SCAI/SCCT/SCMR/STS published appropriate use criteria for detection and risk assessment of stable ischemic heart disease.(58) Coronary CTA was considered appropriate for:

- Symptomatic patients with intermediate (10%-90%) pre-test probability of coronary artery disease
- (CAD) and uninterpretable ECG or inability to exercise
- Patients with newly diagnosed systolic heart failure
- Patients who have had a prior exercise ECG or stress imaging study with abnormal or unknown results
- Patients with new or worsening symptoms and normal exercise ECG

**National Institute for Health and Care Excellence**

The National Institute for Health and Care Excellence considers coronary CTA indicated for patients with stable chest pain and Agatston coronary artery calcium score less than 400, when the pretest likelihood is between 10% and 29%.(59)

**U.S. Preventive Services Task Force Recommendations**

No U.S. Preventive Services Task Force recommendations for coronary CTA have been identified.

**Summary of Evidence**
The evidence for coronary CTA in patients who present with chest pain and suspected coronary artery disease in the emergency setting, at intermediate to low risk, includes several randomized controlled trials. Relevant outcomes are overall survival, morbid events, and resource utilization. The studies showed similar patient outcomes, with faster patient discharges from the emergency department, and lower short-term costs. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

The evidence for coronary CTA in stable patients who have chest pain, intermediate risk of coronary artery disease, and meet guideline criteria for requiring noninvasive testing (ie intermediate risk) includes studies of diagnostic accuracy of coronary CTA, randomized trials comparing coronary CTA with alternative diagnostic strategies, and observational studies comparing coronary CTA with alternative diagnostic strategies. Relevant outcomes are overall survival, test accuracy, morbid events, and resource utilization. Studies of diagnostic accuracy show that coronary CTA has higher sensitivity and similar specificity to alternative noninvasive tests. Although randomized trials do not show superiority of coronary CTA to other diagnostic strategies, they are consistent with noninferiority (ie, similar health outcomes) to other diagnostic strategies. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

The evidence for coronary CTA in patients who have a clinical scenario where anomalous coronary arteries are suspected includes case series. Relevant outcomes are overall survival, test accuracy, morbid events, and resource utilization. The studies show that coronary CTA can often detect anomalous coronary arteries that are missed by other diagnostic modalities. Anomalous coronary arteries are a rare condition, and formal studies to assess clinical utility are unlikely to be performed. In most situations, these studies would be insufficient to determine whether the test improves health outcomes. However, for this rare condition, evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

**Medicare National Coverage**

There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

**References**


Appropriate Use Criteria Task Force, the Society of Cardiovascular Computed Tomography, the American College of Radiology, the American Heart Association, the American Society of Echocardiography, the American Society of Nuclear Cardiology, the North American Society for Cardiovascular Imaging, the Society for Cardiovascular Angiography and Interventions, and the Society for Cardiovascular Magnetic Resonance. J Cardiovasc Comput Tomogr. Nov-Dec 2010;4(6):407 e401-433. PMID 21232696


Policy History

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Reason</th>
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</thead>
<tbody>
<tr>
<td>September 2012</td>
<td>New Policy</td>
<td>Policy updated with literature review, references 18, 19, 43, 45-48, 57-59 added, others removed. No change to policy statement.</td>
</tr>
<tr>
<td>March 2014</td>
<td>Update Policy</td>
<td>Policy updated with literature review through October 16, 2014; references 21, 23-24, 27, and 64 added; reference 65 updated. No change to policy statements.</td>
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</tbody>
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Keywords

Angiography, Computed Tomography
Computed Tomography Angiography
CTA
CT Angiography

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 18, 2016 and is effective April 15, 2016.

Signature on file
Deborah M. Smith, MD, MPH