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 (retrospective 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 tomographic angiography for evaluation of anomalous (native) coronary arteries in symptomatic patients 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 the 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 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.

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. (12-15) 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. Thus, a policy statement includes this application (i.e., evaluating anomalies in native coronary arteries) as medically necessary in symptomatic patients only when conventional angiography is non-diagnostic and when the result will have an impact on treatment.
Patients with Acute Chest Pain Presenting to the Emergency Setting

A 2011 TEC Assessment examined evidence surrounding the evaluation of patients with acute chest pain and without known coronary artery disease (CAD). (11) Randomized controlled trials and prospective observational studies reporting prognosis were identified by searching the MEDLINE database and relevant bibliographies of key studies.

Several (RCTs) of CTA conducted in emergency settings were identified. An RCT of Goldstein et al. evaluated 197 randomized patients from a single center without evidence of acute coronary syndromes to coronary CTA (n=99) or usual care (n=98). (16) Over a 6-month follow-up, no cardiac events occurred in either arm. Invasive coronary angiography rates were somewhat higher in the coronary CTA arm (12.1% vs. 7.1%). Diagnosis was achieved more quickly following coronary CTA. A second trial (CT-STAT) evaluated a similar sample of 699 randomized patients from 16 centers—361 undergoing coronary CTA and 338 myocardial perfusion imaging (MPI). (17) 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. Invasive coronary angiography rates were similar in both arms (7.2% after coronary CTA; 6.5% after perfusion imaging). A second non-invasive test was obtained more often following coronary CTA (10.2% versus 2.1%), but cumulative radiation exposure in the coronary CTA arm (using retrospective gating) was significantly lower—mean 11.5 versus 12.8 mSv. Time to diagnosis was shorter (mean 3.3 hours) and estimated emergency room 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 emergency department. (18) Although the study was a randomized comparison to traditional care, the principal outcome was the safety outcomes of subjects with negative CTA examinations. No patients who had negative CTA examinations (n=460) died or had a myocardial infarction within 30 days. Compared with traditional care, patients in the CTA group had higher rates of discharge from the emergency department (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),(19) 24- (N=368), (20) or 47-month (N=506)(21) follow-up.

A 2012 RCT by Hoffmann et al compared length of stay and patient outcomes in patients evaluated with CTA versus usual care.22 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 2013 RCT by Linde et al (CATCH) compared ICA referral rate, positive predictive value (PPV) for detection of significant coronary artery stenosis, and subsequent revascularization in consecutive patients hospitalized at a single hospital in Denmark with suspicion of ACS but normal or nondiagnostic electrocardiogram (ECG) and normal cardiac troponin. (23) After discharge, patients were randomized in a block design to coronary CTA-guided care (n=299) or usual care (n=301). To maintain blinding, all patients underwent both coronary CTA and a functional test (bicycle exercise-ECG and/or MPI). Mean
(SD) pretest probability (using Diamond Forrester criteria based on age, sex of the patient, and type of chest pain) was approximately 37 (27) in both groups. In the CTA group (n=299), patients with significant stenosis (≥70% or >50% in the left main artery) were referred for ICA, and stenosis less than 50% was considered nonsignificant; management of patients with intermediate stenosis was individualized based on lesion location, stress test results, and clinical information. ICA referral rate did not differ statistically between groups (17% with CTA vs 12% with standard care; \( \chi^2 \) test for all comparisons, p=0.1). There were statistically significant between-group differences in ICA-identified significant stenosis (defined as ≥70% stenosis or reduced fractional flow reserve [FFR] ≤0.75 in intermediate stenoses [50%-70%]; 12% CTA vs 4% standard care; p=0.001); subsequent revascularization (10% CTA vs 4% standard care; p=0.005); and, in 85 patients who underwent ICA (49 [17%] in the CTA group and 36 [12%] in the standard care group), PPV for detection of significant stenosis (71% CTA vs 36% control; p=0.001). Negative predictive value (NPV) could not be calculated because not all patients underwent ICA. At 3-month follow-up, clinical events (cardiac death, MI, unstable angina, revascularization, readmission for chest pain) occurred in 3% of patients in the CTA group versus 5% in the standard care group (p=0.1). Median (interquartile range) radiation exposure for protocol-specified CT calcium score plus coronary CTA was 4.7 (3.8-6.0) mSv.

**Section Summary.** An overall assessment of the studies provides the following conclusions. Owing to the high negative prognostic value of coronary CTA in this population of patients presenting to the ED with chest pain, the test offers an alternative for patients and providers to exclude the presence of CAD. Evidence obtained in the emergency setting, similar to more extensive results among ambulatory patients, indicates a normal coronary CTA provides a prognosis at least as good as other negative non-invasive tests. The efficiency of the workup is improved, as patients are more quickly discharged from the emergency department with no adverse outcomes among patients who have negative CTA examinations.

Other important outcomes that require consideration in comparing technologies include invasive coronary angiography rates, use of a second non-invasive test, radiation exposure, and follow-up of any incidental findings. While there is uncertainty accompanying the limited trial evidence, it is reasonable to conclude that the invasive angiography rate following coronary CTA is not markedly different to that following perfusion imaging. Two studies showed that subsequent diagnostic testing was more frequent in subjects receiving CTA. Studies have differed in which treatment strategy results in higher overall radiation exposure. Incidental finding on subsequent health outcomes is uncertain.

**Stable Patients with Angina and Suspected Coronary Artery Disease**

Before the introduction of coronary CTA, the initial noninvasive test in a diagnostic treatment strategy was always a functional test. The choice of functional test is based on clinical factors such as gender, ECG abnormalities, and chest pain characteristics. Patients with suspicious findings are often referred to invasive angiography. When disease is detected, treatment alternatives include medical therapy or revascularization (PCI or coronary artery bypass graft [CABG] surgery). Which approach to adopt is based on the extent of anatomic disease, symptom severity, and evidence of ischemia from functional testing, noninvasive testing, or more recently, fractional flow reserve obtained during invasive angiography. A difficulty in evaluating a non-invasive diagnostic test for CAD is that it is part of testing...
and treatment strategy. The most informative and convincing evidence would accordingly compare outcomes following an anatomic-first (coronary CTA) and functional-first (e.g., perfusion imaging, stress echocardiography) strategies. Lacking direct comparative evidence, the steps or links in the testing-treatment pathway must be examined including diagnostic accuracy, need for invasive angiography following a non-invasive test, prognosis after a negative test, and likely outcomes of treatment based on information provided by the test.

Relevant studies identified included multicenter studies comparing diagnostic performance of coronary CTA to angiography for evaluation of native arteries, studies of incidental findings, radiation exposure, prognosis, outcomes, and studies of downstream or subsequent testing—all important considerations when comparing coronary CTA in the diagnostic-treatment pathway to alternatives.

Diagnostic Accuracy

In 2014, Nielson et al published a systematic review and meta-analysis to compare diagnostic accuracy and outcomes after coronary CTA (≥16 slice) or functional testing (exercise-ECG and single-photon emission computed tomography [SPECT]) in patients suspected of stable CAD. (24) Literature was searched through January 2013; 11 studies comparing diagnostic accuracy (for ≥50% stenosis on ICA; total N=1575) and 7 studies comparing outcomes (total N=216,603) were included. Diagnostic performance of coronary CTA for detecting significant CAD was statistically better compared with both exercise ECG and SPECT: For CTA versus exercise ECG, respectively, per-patient sensitivity was 98% (95% CI, 93 to 99) versus 67% (95% CI, 54 to 78; p<0.001), and specificity was 82% (95% CI, 63 to 93) versus 46% (95% CI, 30 to 64; p<0.001). For CTA versus SPECT, respectively, sensitivity was 99% (95% CI, 96 to 100) versus 73% (95% CI, 59 to 83; p=0.001), and specificity was 71% (95% CI, 60 to 80) versus 48% (95% CI, 31 to 64; p=0.14). In random effects (for high [>20%] statistical heterogeneity) or fixed (for homogeneity) meta-analyses, coronary CTA was associated with increased downstream test utilization (pooled odds ratio [OR] for 8 studies, 1.38 [95% CI, 1.33 to 1.43]; p<0.001; I²=99%), increased ICA (pooled OR for 8 studies, 2.25 [95% CI, 2.17 to 2.34]; p<0.001; I²=98%), increased coronary revascularization (pooled OR for 7 studies, 2.63 [95% CI, 2.50 to 2.77]; p<0.001; I²=89%), and decreased non-fatal MI (pooled OR for 6 studies,: 0.53 [95% CI, 0.39 to 0.72]; p<0.001; I²=0%) compared with exercise-ECG/SPECT.

Four multicenter studies evaluated the diagnostic accuracy of coronary CTA employing ICA as referent standard. All patients enrolled in the 4 studies were scheduled for ICA; the population of interest here is patients at intermediate risk only, a minority of whom would proceed to ICA.

ACCURACY (Assessment by Coronary Computed Tomographic Angiography of Individuals Undergoing Invasive Coronary Angiography) compared coronary CTA with ICA in 230 of 245 individuals experiencing typical or atypical chest pain referred for nonemergent ICA. (25) Three readers blinded to ICA results interpreted coronary CTA scans. Of the 143 normal coronary CTA scans, ICA was normal in 142 (NPV 99%); the false-positive rate was 17%. Radiation dose, prevalence of incidental noncardiac findings, and follow-up were not reported. Using a 50% stenosis cutoff, disease prevalence was 25%, with 13% having 70% or greater stenosis. Estimated pretest disease probability was not reported.
CORE 64 (Coronary Artery Evaluation Using 64-Row Multidetector Computed Tomography Angiography) evaluated 405 individuals referred for ICA to evaluate suspected CAD at 9 centers. There were 89 patients (22%) excluded from analyses due to Agatston calcium score greater than 600; results from 291 of 316 remaining individuals were analyzed. Coronary CTA was the initial diagnostic test, and investigators and physicians were subsequently blinded to coronary CTA results. Sensitivity was 85%; NPV, 83%; and false-positive rate, 10%. Coronary CTA radiation dose was 13.8±1.2 mSv for men and 15.2±2.4 mSv for women. Noncardiac findings were reported to the treating physician but were not described in the report. Disease prevalence was 56%, using a 50% stenosis cutoff. Pretest disease probability was not reported. In a subsequent analysis of this study that included all eligible patients regardless of Agatston calcium score, diagnostic performance of coronary CTA was similar between groups defined by suspected acute coronary syndrome (ACS) (typical angina at rest for at least 20 minutes, or relieved with nitrates at <20 minutes with associated ischemic ECG changes; angina-equivalent symptoms with associated transient ST segment changes on ECG; or angina-equivalent symptoms associated with abnormal cardiac enzymes; n=94) or non-ACS (no ACS features present; n=277). Sensitivity, specificity, PPV, and NPV were 90% (95% CI, 80 to 96), 88% (95% CI, 70 to 98), 95% (95% CI, 87 to 99), and 77% (95% CI, 58 to 90), respectively, in the ACS group, and 87% (95% CI, 81 to 92), 86% (95% CI, 79 to 92), 91% (95% CI, 85 to 95), and 82% (95% CI, 74 to 89), respectively, in the non-ACS group.

Meijboom et al (2008) evaluated 433 individuals, aged 50 to 70 years, seen at 3 university hospitals referred for ICA to evaluate suspected stable or unstable angina; 371 consented to participate and 360 completed the study. Tests were interpreted in blinded fashion. Sensitivity was 99%; NPV, 97%; and false-positive rate, 36%. Estimated radiation exposure based on instrument parameters was 15 to 18 mSv. Frequency of noncardiac findings was not reported. Disease prevalence was 68%, using a 50% stenosis cutoff; pretest probability was not reported.

Chow et al (2011) obtained consent from 181 patients and examined 169 of 250 eligible patients referred to ICA for evaluation of CAD (n=117) or structural heart disease (n=52). Four centers evaluated differing numbers of patients: 102 (60.3%), 40 (23.7%), 16 (9.5%), and 11 (6.5%), respectively. Overall sensitivity for obstructive CAD was 81%; NPV, 85%; and false-positive rate, 7%. Performance characteristics differed substantially and significantly by site. The center enrolling most of the patients reported sensitivity, specificity, NPV and PPV of 93%, 93%, 91%, and 95%, respectively; the other 3 centers reported values of 67%, 93%, 92%, and 71%, respectively. Estimated mean (SD) radiation exposure was 11.0 (6.8) mSv. Disease prevalence was 53%, using a 50% stenosis cutoff and mean estimated pretest probability of CAD 47%.

There was variability in coronary CTA diagnostic accuracy reported from these multicenter studies spanning different disease prevalence populations. The lower sensitivity reported by Chow et al (29) is notable, as well as the considerable between-center variability. In contrast to the others, the study used visual ICA assessment as a referent standard. Although arguably, visual assessment is most often used in practice, it is prone to imprecision. (30,31) Although Chow et al (29) reported high interobserver agreement for ICA (κ=0.88), Zir et al found 4 experienced observers agreed 65% of the time whether a stenosis exceeded 50% in 20 angiograms. Finally, the small number of patients enrolled
from 3 centers relative to overall annual coronary CTA volume (center 1: 102/1325; 2: 40/1539; 3: 11/1773; 4: 16/268) might reflect sampling variability (screening procedures or whether consecutive patients were approached was not reported).

Patient populations included in each study varied, as did disease prevalence. Estimates of pretest disease probability were not reported except by Chow et al.(29) but given that all patients were referred to ICA, pretest probability was presumably at least in the upper intermediate range. With these caveats, the studies supported the conclusion that coronary CTA is sensitive for detecting stenoses in samples with varying disease prevalences. Sensitivities are at least as good those cited for other noninvasive tests; false positives are not uncommon, but the rate is similar to other noninvasive tests. However, as suggested by Chow et al (29) sensitivity and specificity achieved in the real world are likely lower than those reported under more carefully controlled conditions. These results are, however, subject to verification bias,(32) because all patients were referred for ICA. Performance characteristics reported from these studies, as well as for noninvasive tests among patients selectively referred to ICA, might differ in practice when the test is used in patients not referred. In comparison, a recent meta-analysis including smaller single-center studies (42 total) estimated pooled sensitivity and specificity of 98% and 85%, respectively. (33) Finally, radiation exposure reported in these studies was consistent with others using retrospective gating. Current prospective gating techniques result in lower radiation doses.

Incidental Findings

Nine studies using 64+ slice scanners were identified. (34-42) Incidental findings were frequent (26.6% to 68.7%) with pulmonary nodules typically the most common and cancers rare (approximately 5/1,000 or less). Aglan et al. (34) compared the prevalence of incidental findings when the field of view was narrowly confined to the cardiac structures seen when the entire thorax was imaged. As expected, incidental findings were less frequent in the restricted field (clinically significant findings in 14% versus 24% when the entire field was imaged).

Prognosis

Hulten et al. (43) performed a meta-analysis of 18 studies (n=9,592) with 3 or more months’ follow-up (median 20 months) enrolling patients with suspected CAD (mean age 59 years, 58% male). Annualized death or myocardial infarction (MI) rates after a normal coronary CTA (no identified stenosis >50%) was 0.15%. The pooled rate included 2 studies of EBCT and 4 that utilized 16 slice scanners; most events in the normal group occurred in one of the EBCT studies. Bamberg et al. (44) pooled results from 9 studies (n=3,670) enrolling ≥100 patients with ≥1 year follow-up enrolling patients with suspected CAD (mean age 59.1±2.6 years, 63% male). The pooled annualized event rate (all-cause and cardiac death, MI, unstable angina, revascularization) was 1.1% following a coronary CTA without evidence of significant stenosis; in the 38% of patients without evidence of any atherosclerotic plaque, the annual event rate 0.4%. In comparison, Metz et al. (45) performed a meta-analysis of event rates following a negative MPI and stress echocardiography. The pooled annual cardiac death and MI rates following negative MPI (17 studies; 8,008 patients) and stress echocardiography (4 studies; 3,021 patients) were 0.45% and 0.51%, respectively.
Subsequent or Downstream Testing

Whether tests are used to replace, or added to, others currently in use is relevant. Few studies have addressed this issue. In an analysis of 2006 data from patients without CAD as recorded in claims, Min et al. (46) found that following MPI, 11.6% of 6,588 patients underwent subsequent MPI, coronary CTA, or invasive angiography; following coronary CTA, 14.6% of 1,647 patients underwent one of those tests. More recently, a study of Medicare claims from 2005-2008 showed different results. (47) Compared with MPI, patients undergoing CTA had a higher likelihood of subsequent cardiac catheterization (22.9% vs. 12.1%), and higher rates of percutaneous coronary procedures and bypass surgery. Aggregate healthcare spending was higher in subjects who had CTA. Cheezum et al. (48) retrospectively identified 241 symptomatic patients without known CAD undergoing coronary CTA and matched them by age and gender to 252 also symptomatic patients undergoing MPI. Downstream testing was less frequent following coronary CTA than MPI (11.5% vs. 17.0%), as well as ICA (3.3% vs. 8.1%). Finally, coronary CTA and ICA in Ontario are centralized to a single academic center in Ottawa, which allowed investigators to examine coronary CTA accuracy concurrent with the impact on ICA referrals. (49) Consecutive patients (n=3,538) were evaluated by ICA during 14 months before and in the 12 months after (n=3,479) coronary CTA introduction. The rate of normal ICA decreased from 31.5% before to 26.8% after coronary CTA introduction (p=0.003). During the same period at 3 other centers without coronary CTA programs, normal ICA rates increased from 30.0% to 31.0%. The 2012 Study of Myocardial Perfusion and Coronary Anatomy Imaging Roles in Coronary Artery Disease (SPARC), is a prospective multicenter registry study of imaging modalities.50 In 1703 patients with no history of CAD, angiography was more frequent within 90 days after coronary CTA (13.2%) compared with SPECT (4.3%) or positron emission tomography (PET) (11.1%). Although study results vary and all are observational with the attendant potential for selection bias (in effect, confounding by test selection), angiography rates appear higher after coronary CTA.

Outcome Studies

In 2825 patients evaluated for stable angina and suspected CAD in Japan, Yamauchi et al. (51) examined outcomes after initial coronary CTA (n=625), MPI (n=1205), or angiography (n=950). Average follow-up was 1.4 years. In a Cox proportional hazards model adjusted for potential confounders, the relative hazard of major cardiac events following MPI or coronary CTA were lower than following angiography; annual rates of 2.6%, 2.1%, and 7.0% respectively. Revascularization rates were higher following coronary CTA than MPI (OR 1.6; 95% CI: 1.2 to 2.2). However, the results are limited by the observational nature of the data and difficulty controlling for selection bias in a conventional analysis.

Radiation Exposure

Exposure to ionizing radiation increases lifetime cancer risk. (BEIR VII, 52) Three studies have estimated excess cancer risks due to radiation exposure from coronary CTA. (6, 7, 53) Assuming a 16-mSv dose, Berrington de Gonzalez et al. (53) estimated that the 2.6 million coronary CTAs performed in 2007 would result in 2,700 cancers or approximately 1 per 1,000. Smith- Bindman et al. (7) estimated cancer would develop in 1 of 270 women and 1 of 600 men age 40 undergoing coronary CTA with a
22-mSv dose. Einstein et al. (6) employed a standardized phantom to estimate organ dose from 64-slice coronary CTA. With modulation and exposures of 15 mSv in men and 19 mSv in women, the calculated lifetime cancer risk at age 40 was 7 per 1,000 men (1 in 143) and 23 per 1,000 women (1 in 43). However, estimated radiation exposure used in these studies is considerably higher than received with current scanners—now typically under 10 mSv and often less than 5 mSv with 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. (54) In a study of patients undergoing an axial scanning protocol, mean radiation dose was 3.5 mSv, and produced equivalent ratings of image quality compared to helical scan protocols, which had much higher mean radiation doses of 11.2 mSv. (55)

Although indirectly related to coronary CTA, Eisenberg et al. (8) analyzed administrative data from 82,861 patients undergoing imaging or procedure accompanied by radiation between April 1996 and March 2006 with 12,020 incident cancers identified. Based on estimated radiation exposures accompanying various cardiac imaging and procedures, over 5 years, there was an increased relative hazard for cancer of 1.003 per mSv (95% confidence interval [CI]: 1.002-1.004).

Section Summary. A number of multicenter studies have evaluated the diagnostic accuracy of CTA for diagnosing coronary ischemia in an outpatient population. In general, these studies report high sensitivity and specificity, but there is some variability in these parameters across studies. Use of CTA in this situation does not have the same advantage of improving the efficiency of diagnosis as it does in the emergency setting. There is evidence that angiography rates are higher following coronary CTA. Evidence defining comparative outcomes outside the emergency room setting is limited. Lacking direct comparative outcome evidence, the risk/benefit ratio in patients with stable angina and suspected CAD depends on the diagnostic accuracy, downstream testing, impact of incidental findings, and the amount of radiation exposure. Given the uncertainty in these factors, it is not possible to conclude that the use of CTA in this setting leads to improved outcomes compared to alternative strategies. Therefore CTA is considered investigational when used in the outpatient setting to evaluate patients with suspected cardiac ischemia.

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 their 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 due to their small size and when calcifications are present. 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). (56) Other small studies have reported high sensitivity and specificity. (57-58) 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 those challenges can be sufficiently overcome to obtain sufficient accuracy and impact outcomes has not been demonstrated.

• The use for screening a low-risk population was recently evaluated in 1,000 patients undergoing coronary CTA compared to a control group of 1,000 similar patients. (59) Findings were abnormal in 215 screened patients. Over 18 months’ follow-up, screening was associated with more invasive testing, statin use, but without difference in cardiac event rates.

• Coronary CTA for preoperative evaluation before non-cardiac surgery has been suggested, evaluated in only small studies, and lacking demonstrable clinical benefit.

Ongoing and Unpublished Clinical Trials

An online search of ClinicalTrials.gov identified 6 RCTs and 3 observational studies of coronary CTA (see Table 1). Five RCTs and 1 observational study (NCT01635309) are enrolling patients with suspected coronary artery disease. One RCT (NCT01283659) evaluates patients with heart failure. One observational study (NCT00991835) prospectively evaluates coronary plaque progression and outcomes (cardiovascular events and death). The third observational study (NCT01635309) evaluates preoperative coronary CTA in noncardiac surgery patients.

Table 1. Ongoing Studies of Coronary CTA Listed at ClinicalTrials.gov

<table>
<thead>
<tr>
<th>NCT Number</th>
<th>Title</th>
<th>Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCT01174550</td>
<td>PROspective Multicenter Imaging Study for Evaluation of Chest Pain (PROMISE)</td>
<td>10,000</td>
<td>December 2014</td>
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<tr>
<td>NCT00705458</td>
<td>Study Comparing CT Scan and Stress Test in Diagnosing Coronary Artery Disease in Patients Hospitalized for Chest Pain (PROSPECT)</td>
<td>400</td>
<td>December 2013a</td>
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<tr>
<td>NCT01368770</td>
<td>Stress Testing Compared to Coronary Computed Tomographic Angiography in Patients With Suspected Coronary Artery Disease</td>
<td>500</td>
<td>December 2014</td>
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<tr>
<td>NCT01384448</td>
<td>Stress Echocardiography and Heart Computed Tomography (CT) Scan in Emergency Department Patients With Chest Pain</td>
<td>400</td>
<td>June 2015</td>
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<tr>
<td>NCT01559467</td>
<td>The Supplementary Role of Non-invasive Imaging to Routine Clinical Practice in Suspected Non-ST-elevation Myocardial Infarction (CARMEN Ta)</td>
<td>300</td>
<td>April 2015</td>
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<tr>
<td>NCT01283659</td>
<td>Angiography for Heart IMAGE-HF Project I-C: Computed Tomographic Coronary Failure Patients (CTA-HF)</td>
<td>250</td>
<td>June 2016</td>
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</tbody>
</table>

a Expected  
b Estimated  
c ClinicalTrials.gov indicates this trial is still ongoing.
### 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. (60) 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)

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<tr>
<th>NCT Number</th>
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<th>Completion Date</th>
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<tr>
<td>NCT01083134</td>
<td>The Correlation of Heart Hemodynamic Status Between 320Multidetector Computed Tomography, Echocardiography and Cardiac Catheterization in Patients With Coronary Artery Disease</td>
<td>100</td>
<td>March 2020</td>
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<tr>
<td>NCT00991835</td>
<td>Plaque Registration and Event Detection In Computed Tomography (PREDICT)</td>
<td>3015</td>
<td>December 2014</td>
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<tr>
<td>NCT01635309</td>
<td>Coronary CT Angiography to Predict Vascular Events In Noncardiac Surgery patients cOhort evaluatioN (CTA -VISION) Study</td>
<td>1200</td>
<td>November 2014</td>
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</tbody>
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* Expected  
* Estimated
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 (61,62) and expert consensus documents (63) 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.(64) 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%.(65)

U.S. Preventive Services Task Force Recommendations

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

Summary

In patients presenting to emergency settings with acute chest pain that is possibly cardiac in origin and no known history of CAD, the net health outcome following coronary CTA appears at least as good as that obtained following other noninvasive testing strategies. CTA can rule out active coronary disease with a high rate of certainty in patients with low-to-moderate pre-test probabilities of CAD. In addition, it is an efficient strategy in the emergency setting compared to alternative approaches. Therefore, CTA may be considered medically necessary for use in this patient population.

When anomalous coronary arteries require evaluation in symptomatic patients, coronary CTA also is likely to be beneficial in the setting of equivocal or unsuccessful invasive angiography. It has been demonstrated that CTA can define the anatomy of anomalous vessels when angiography is equivocal. Thus, CTA may be considered medically necessary for evaluating anomalous coronary arteries.

For other indications such as evaluation of patients with stable chest pain, the balance of potential benefits and harms remains uncertain owing largely to the lack of direct comparative evidence. A fundamental difficulty with current, albeit substantial indirect evidence surrounding coronary CTA is that decision making has historically relied on a strategy of functional non-invasive testing followed by
invasive angiography to define anatomy. There is observational evidence that angiography rates are higher following coronary CTA than MPI. The individual studies and systematic reviews of coronary CTA accuracy for anatomic obstruction indicate sensitivity, specificity, PPV, and NPV as good as or better than with other noninvasive tests. There is limited evidence that coronary CTA may decrease the rate of normal ICAs in the diagnostic evaluation of CAD. Studies in representative populations that examined the frequency of repeated testing are lacking. Noncardiac findings are frequent, but the consequences as benefits and harms have received limited scrutiny. Evidence indicates radiation exposure with current scanners utilizing reduction techniques is lower than with MPI. Because of the uncertainty regarding whether outcomes are improved with CTA compared to alternative tests, the use of CTA for this patient population is considered not medically necessary.

**Medicare National Coverage**

No national coverage determination.

**References**


Association journal = *journal de l’Association medicale canadienne.* Mar 8 2011;183(4):430-436. PMID 21324846


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<thead>
<tr>
<th>Page</th>
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<tr>
<td>32</td>
<td>Diamond GA, Kaul S. Gone fishing!: on the &quot;real-world&quot; accuracy of computed tomographic coronary angiography: Comment on the &quot;Ontario multidetector computed tomographic coronary angiography study&quot;. <em>Archives of internal medicine.</em> Jun 13 2011;171(11):1029-1031. PMID 21403008</td>
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Policy History

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<tr>
<th>Date</th>
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<tr>
<td>September 2012</td>
<td>New Policy</td>
<td></td>
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<tr>
<td>March 2014</td>
<td>Update 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 2015</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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</table>

Keywords

Angiography, Computed Tomography
Computed Tomography Angiography
CTA
CT Angiography

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 20, 2015 and is effective April 15, 2015.

Signature on file

Deborah M. Smith, MD, MPH