Contrast-Enhanced Coronary 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 coronary computed tomography angiography (CCTA) 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 diagnostic alternative to current tests for cardiac ischemia (ie, non-invasive stress testing and/or coronary angiography).

A variety of noninvasive tests are used to diagnose coronary artery disease (CAD). They can be broadly classified as those that detect functional or hemodynamic consequences of obstruction and ischemia (exercise treadmill testing, myocardial perfusion imaging, stress echocardiography with or without contrast), and others that identify the anatomic obstruction itself (CCTA, coronary magnetic resonance imaging).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 CCTA.

Some tests will be unsuitable for particular patients. The presence of dense arterial calcification or an intracoronary stent can produce significant beam-hardening artifacts and may preclude a satisfactory imaging. 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.

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

Congenital coronary arterial anomalies (ie, abnormal origin 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 (eg, syncope). There is no specific clinical presentation to suggest a coronary artery anomaly.

Levels of radiation delivered with current generation scanners using reduction techniques (prospective gating and spiral acquisition) have declined substantially—typically to under 10 mSv. For example, an international registry developed to monitor CCTA radiation exposure recently reported a median of 2.4 mSv (interquartile range, 1.3-5.5).3 By comparison, radiation exposure accompanying rest-stress perfusion imaging ranges varies by isotope used—approximately 5 mSv for rubidium 82 (positron emission tomography [PET]), 14 mSv for fluorodeoxyglucose fluorine 18 (PET), 9 mSv for sestamibi (single-photon emission computed tomography), and 41 mSv for thallium; during diagnostic invasive coronary angiography, approximately 7 mSv is delivered.4 Electron beam computed tomography (EBCT) using electrocardiogram triggering delivers the lowest dose (0.7-1.1 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 sex (greater for women).5-7 Empirical data have suggested that every 10 mSv of exposure is associated with a 3% increase in cancer incidence over 5 years.8

The use of EBCT or helical CT to detect coronary artery calcification is addressed separately (evidence review 6.01.03).

**Regulatory Status**

Coronary computed tomography angiography (CCTA) is performed using multidetector-row computed tomography, and multiple devices have been cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process. Current machines are equipped with at least 64 detector rows. Intravenous iodinated contrast agents used for CCTA also have received FDA approval.
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 coronary computed tomography angiography for evaluation of patients without known coronary artery disease and acute chest pain in the emergency department setting is considered medically necessary.

Contrast-enhanced coronary computed tomography angiography for evaluation of patients with stable chest pain and meeting guideline criteria for a noninvasive test in the outpatient setting (see Policy Guidelines) is considered medically necessary.

Contrast-enhanced coronary computed tomography angiography for evaluation of anomalous (native) coronary arteries in patients in whom they are suspected may be considered medically necessary.

Contrast-enhanced coronary computed tomography angiography for coronary artery evaluation is considered not medically necessary for all other indications.

Policy Guidelines

The 2012 collaborative medical association guidelines for the diagnosis and management of patients with stable heart disease (Fihn et al, 2012) list several class I recommendations on use of noninvasive testing in patients with suspected stable ischemic heart disease. A class I recommendation indicates that a test should be performed. In general, patients with at least intermediate risk (10%-90% risk by standard risk prediction instruments) are recommended to have some type of test, the choice depending on interpretability of the electrocardiogram, capacity to exercise, and presence of comorbidity.

Rationale

Literature Search

This evidence review is based on a literature search of the MEDLINE database of literature reviews and 3 TEC Assessments.9-11

In 2016, the Agency for Healthcare Research and Quality (AHRQ) published a comparative effectiveness review on noninvasive testing for coronary artery disease (CAD).12 The review found that:

- After coronary computed tomography angiography (CCTA), clinical outcomes for patients with an intermediate pretest risk
Patients with Acute Chest Pain Presenting to the Emergency Setting

Diagnostic Accuracy

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.

Effect on Health Outcomes

A 2011 TEC Assessment examined evidence on the evaluation of patients with acute chest pain and without known coronary artery disease (CAD). Randomized controlled trials (RCTs) and prospective observational studies were identified. RCTs of CCTA procedures conducted in ED settings are described in Table 1.

A 2007 RCT by Goldstein et al randomized 197 patients from a single center without evidence of acute coronary syndromes to CCTA (n=99) or usual care (n=98). Over a 6-month follow-up, no cardiac events occurred in either arm. ICA rates were somewhat higher in the CCTA arm. Diagnosis was achieved more quickly after CCTA.

The CT-STAT RCT evaluated a similar sample of 699 patients from 16 centers. Over a 6-month follow-up, there were no deaths in either arm; there were 2 cardiac events in the CCTA arm and 1 in
the perfusion imaging arm. ICA rates were similar in both arms. A second noninvasive test was obtained more often after CCTA (10.2% vs 2.1%), but cumulative radiation exposure in the CCTA arm (using retrospective gating) was significantly lower (mean, 11.5 mSv vs 12.8 mSv). Time to diagnosis was shorter and estimated ED costs lower with CCTA.

A 2012 RCT (AC RIN-PA) by Litt et al also evaluated the safety of CCTA in patients in the ED.\(^{15}\) Although the trial was a randomized comparison with traditional care, the principal outcome was safety after negative CCTA examinations. No patients who had negative CCTA examinations (n=460) died or had a myocardial infarction (MI) within 30 days. Compared with traditional care, patients in the CCTA group had higher rates of discharge from the ED (49.6% vs 22.7%), shorter lengths of stay, and higher rates of detection of coronary disease.

A 2012 RCT (ROMICAT II) by Hoffmann et al compared length of stay and outcomes in patients evaluated with CCTA versus usual care.\(^{16}\) For patients in the CCTA arm, 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 or differences in adverse events at 28 days. However, in the CCTA arm, there was more subsequent diagnostic testing and higher cumulative radiation exposure. Cumulative costs of care were similar between groups.

A 2014 RCT (CT-COMPARE) by Hamilton-Craig et al assessed length of stay and patient costs in 562 patients presenting to the ED with low-to-intermediate risk chest pain who received CCTA or exercise stress testing.\(^{17}\) Costs within 30 days of presentation were significantly lower in the CCTA group (mean, $2193) than in the exercise testing group (mean, $2704; p<0.001). Length of stay was significantly reduced in the CCTA patients compared with the exercise testing patients. Clinical outcomes at 30 days and at 12 months did not differ.

In 2015, Linde et al reported long-term follow-up from the CATCH trial.\(^{18, 19}\) This trial randomized 600 patients to a CCTA-guided strategy or to standard of care (SOC). For the CCTA-guided strategy, referral for ICA required coronary stenosis greater than 70%. This trial differed in design from the other trials, because patients had been discharged from the ED, and if there was intermediate stenosis (50%-70%) on CCTA, a stress test was used. The referral rate for ICA was 17% for the CCTA strategy versus 12% with SOC (p=NS). At a median 18.7-month follow-up, a major cardiac event was observed in 5 patients in the CCTA-strategy arm compared to 14 in the SOC group (hazard ratio [HR], 0.36; 95% confidence interval [CI], 0.16 to 0.95; p=0.04). Three other follow-up studies reported no cardiac events after a negative CCTA in the ED after 12 (N=481),\(^{20}\) 24 (N=368),\(^{21}\) or 47 months (N=506).\(^{22}\)

| Table 1. RCTs Comparing CCTA to SOC in the Evaluation of Acute Chest Pain |
|-----------------------------|---|------------------|-----|----------------|-----------------|-----------------|
| Study (Year)                | N  | Study Design     | FU, mo | MI in Neg CCTA Arm | LOS, h (p) | ICA (CCTA vs Control) |
| Goldstein et al (2007) \(^{13}\) | 197 | CCTA vs SPECT   | 6     | 0              | 3.4 vs 15 | 12.1% vs 7.1%           |
| Goldstein et al (2011) \(^{14}\) | 699 | CCTA vs SPECT   | 6     | 0              | 2.9 vs 6.3 | 7.2% vs 6.5%           |
| Litt et al (2012) \(^{15}\)  | 1370| CCTA vs SPECT   | 1     | 0              | 18 vs 24 | 9.0% vs 3.5%            |
| Hoffmann et al (2012) \(^{16}\) | 1000| CCTA vs SOC    | 1     | 0              | 23.2 vs 30.8 | 11% vs 7%       |
| Hamilton-Craig et al (2014) \(^{17}\) | 562 | CCTA vs SOC    | 12    | 0              | 13.5 vs 20.7 | 8.0% vs 3.8%          |
Section Summary: Acute Chest Pain Presenting to the Emergency Setting

The high negative predictive value (NPV) of CCTA in patients presenting to the ED with chest pain permits ruling out coronary disease with high accuracy. The efficiency of the workup is improved, because patients are safely and quickly discharged from the ED with no adverse outcomes among patients with negative CCTA 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. Some studies have shown that subsequent invasive testing is more frequent in patients who received CCTA. Studies have differed over which treatment strategies result in higher overall radiation exposure. Incidental findings after CCTA 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 use of CCTA, 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 CAD. 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 CCTA alone is insufficient to establish clinical utility. A difficulty in evaluating a noninvasive diagnostic test for CAD is that patient outcomes depend not only on the test results, but also the management and treatment strategy. The most convincing evidence of clinical utility compares outcomes after anatomic-first (CCTA) 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

There is a fairly large body of evidence evaluating the diagnostic characteristics of CCTA for identifying coronary lesions. The best estimate of the diagnostic characteristics of CCTA can be obtained from recent meta-analyses and systematic reviews. Table 2 shows ranges of sensitivity and specificity for functional noninvasive tests from studies of the diagnosis and management of stable angina reviewed by Fihn et al.\textsuperscript{24} Sensitivities tended to range between 70% and 90%, depending on the test and study, and specificities ranged between 70% and 90%.

For CCTA, estimates of sensitivity from various systematic reviews are considerably higher (see Table 3). The guideline statement from Fihn cited studies reporting sensitivities between 93% and 97%.\textsuperscript{24} A meta-analysis by Ollendorf et al of 42 studies showed a summary sensitivity estimate of 98% and a specificity of 85%.\textsuperscript{25} 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%.\textsuperscript{26} In the meta-analysis by Nielsen et al, sensitivity of CCTA varied between 98% and 99% (depending on the analysis group).\textsuperscript{27}

Table 2: Summary of Estimates of Sensitivity and Specificity of Functional Noninvasive Tests From Recent Guideline Statement (24)

<table>
<thead>
<tr>
<th>Noninvasive Test</th>
<th>Sensitivity (Range or Single Estimates)</th>
<th>Specificity (Range or Single Estimates)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercise electrocardiography</td>
<td>61%</td>
<td>70%-77%</td>
</tr>
<tr>
<td>Pharmacologic stress echocardiography</td>
<td>85%-90%</td>
<td>79%-90%</td>
</tr>
<tr>
<td>Exercise stress echocardiography</td>
<td>70%-85%</td>
<td>77%-89%</td>
</tr>
<tr>
<td>Exercise myocardial perfusion imaging</td>
<td>82%-88%</td>
<td>70%-88%</td>
</tr>
<tr>
<td>Pharmacologic stress myocardial perfusion imaging</td>
<td>88%-91%</td>
<td>75%-90%</td>
</tr>
</tbody>
</table>

Table 3: Estimates of Sensitivity and Specificity of Coronary Computed Tomography Angiography From Guidelines and Meta-Analyses

<table>
<thead>
<tr>
<th>Study</th>
<th>Sensitivity (Range or Single Estimates)</th>
<th>Specificity (Range or Single Estimates)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fihn et al (2012) guideline statement\textsuperscript{24}</td>
<td>93%-97%</td>
<td>80%-90%</td>
</tr>
<tr>
<td>Ollendorf et al (2011) meta-analysis\textsuperscript{25}</td>
<td>98%</td>
<td>85%</td>
</tr>
<tr>
<td>Health Quality Ontario (2010) meta-analysis\textsuperscript{26}</td>
<td>97.7%</td>
<td>79%</td>
</tr>
<tr>
<td>Nielsen et al (2014) meta-analysis\textsuperscript{27}</td>
<td>98%-99%</td>
<td>82%-88%</td>
</tr>
</tbody>
</table>

Effect on Health Outcomes

Randomized Controlled Trials

For patients at intermediate risk of CAD, 3 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 CCTA or exercise electrocardiography, nuclear stress testing, or stress echocardiography (as determined by physician preference) as the initial diagnostic evaluation. For the composite end point of death, MI, hospitalization for unstable angina, or major procedural complication, the outcome rates between the 2 groups showed no statistically significant difference (HR=1.04; 95% CI, 0.83 to 1.29). CCTA also did not meet prespecified noninferiority criteria compared with alternative testing. Some clinical outcomes assessed at 12 months favored CCTA, but the differences were nonsignificant. Coronary catheterization rates and revascularization rates were higher in the CCTA group.

In the SCOT-HEART trial, 4146 patients were randomized to CCTA or SOC. 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 CCTA 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 rates of heart disease death and MI were lower with CCTA (1.3% vs 2.0%; HR=0.62; p=0.053), but results were of marginal statistical significance.

The CAPP trial randomized 500 patients with stable chest pain to CCTA 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 for further diagnostic tests and management. In the CCTA 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 CCTA arm than in the exercise stress testing arm.

Nonrandomized Studies

Nonrandomized studies comparing outcomes of patients following a CCTA strategy with outcomes following other noninvasive testing strategies were also identified. Some studies have emphasized downstream utilization of diagnostic testing and procedures rather than patient outcomes.

Nielsen et al conducted an observational trial comparing patients who underwent CCTA or 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 (eg, cardiac death, nonfatal MI). Subsequent utilization of cardiovascular tests and therapy were 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 of 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 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 CCTA, stress echocardiography, myocardial perfusion imaging (MPI), or exercise electrocardiography. In this study, patients undergoing CCTA had higher rates of several types of utilization subsequent to their tests than patients undergoing MPI. The study also presented outcomes for both stress echocardiography and exercise electrocardiography, but they tended not to differ from outcomes 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 CCTA than for MPI. There was no significant difference in all-cause mortality between CCTA and MPI. Although the mortality rate for CCTA (1.05%) was slightly lower than the mortality rate for MPI (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 CCTA were compared with patients undergoing initial MPI. The data source for this study was a proprietary claims database from 2 regional health plans. Utilization of medical care was lower after CCTA. Overall costs were lower, the proportion receiving ICA was lower, and the proportion receiving revascularization was lower after CCTA. In terms of clinical outcomes, the proportion with a hospitalization for angina was lower in the CCTA group. The CCTA 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 CCTA (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 rates of major cardiac events after MPI or CCTA were lower than after angiography; annual rates were 2.6%, 2.1%, and 7.0%, respectively. Revascularization rates were higher after CCTA than MPI (OR=1.6; 95% CI, 1.2 to 2.2).

**Incidental Findings**

A number of studies using scanners using 64 or more detector rows were identified. 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) 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. Three studies have estimated excess cancer risks due to radiation exposure from CCTA. Assuming a 16-mSv dose, Berrington de Gonzalez et al (2009) estimated that the 2.6 million CCTAs 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 CCTA with a 22-mSv dose. Einstein et al (2007) employed a standardized phantom to estimate organ dose from 64-slice CCTA.
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 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. 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.

**Section Summary: Stable Angina and Suspected CAD**

A number of studies have evaluated the diagnostic accuracy of CCTA for diagnosing CAD in an outpatient population. In general, these studies have reported high sensitivity and specificity, although there is some variability in these parameters across studies. Meta-analysis of these studies have shown that, for detection of anatomic disease, CCTA 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 CCTA.

Direct clinical trial evidence comparing CCTA and other strategies in the diagnostic management of stable patients with suspected CAD has not demonstrated the superiority of CCTA in any of the single clinical trials. Clinical trials have demonstrated greater utilization of ICA and subsequent revascularization procedures after CCTA. An important problem of interpreting the clinical trials is that the comparator strategies differ: in the PROMISE and the CAPP trials, CCTA was compared with an alternative noninvasive test; in other studies, CCTA was supplement to usual care (which may or may not have included a noninvasive test). These design differences in the clinical trials are likely to reflect how CCTA is used in clinical practice—either as a substitute for another noninvasive test or as an adjunct to other noninvasive tests. The PROMISE trial explicitly compared CCTA with an alternative functional test as the initial diagnostic test. Although the trial did not show the superiority of CCTA 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 the noninferiority of CCTA with other established noninvasive tests. Thus, the randomized studies indicate that outcomes of patients are likely to be similar with CCTA versus other noninvasive tests.

The nonrandomized studies of CCTA 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 CCTA, there is insufficient evidence that the magnitude of these effects is important for ascertaining the net benefit or risk of CCTA in this setting.

**Suspected 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 CCTA is able to delineate the course of these anomalous arteries, even when conventional angiography cannot. 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 CCTA could be completed.

**Other Diagnostic Uses of CCTA**

Given its ability to define coronary artery anatomy, there are many potential diagnostic uses of CCTA, 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). Other small studies have reported high sensitivity and specificity. 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. 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.

- Use for screening in a high-risk population was evaluated in the FACTOR-64 trial, which randomized 900 subjects with diabetes to screening with CCTA or SOC. Patients in this trial were asymptomatic, but 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).

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

Practice Guidelines and Position Statements

American College of Cardiology Foundation et al

The American College of Cardiology Foundation (ACCF) and several other medical societies issued joint guidelines for management of patients with stable ischemic heart disease in 2012 (see Table 4).24

Table 4. Joint Guidelines on Management of Stable Ischemic Heart Disease

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Recommendation</th>
<th>Class</th>
<th>LOE</th>
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<tr>
<td>Unknown</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Able to exercise</td>
<td>“CCTA might be reasonable for patients with an intermediate pretest probability of IHD who have at least moderate physical functioning or no disabling comorbidity.”</td>
<td>IIb</td>
<td>B</td>
</tr>
<tr>
<td>Unable to exercise</td>
<td>“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.”</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td>“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.”</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>Known coronary disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Able to exercise</td>
<td>“CCTA may be reasonable for risk assessment in patients with SIHD who are able to exercise to an adequate workload but have an uninterpretable ECG.”</td>
<td>IIb</td>
<td>B</td>
</tr>
<tr>
<td>Able to exercise</td>
<td>“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.”</td>
<td>III</td>
<td>C</td>
</tr>
<tr>
<td>Unable to exercise</td>
<td>“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.”</td>
<td>IIa</td>
<td>B</td>
</tr>
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<td></td>
<td>“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.”</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>Unable to exercise</td>
<td>“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.”</td>
<td>III</td>
<td>C</td>
</tr>
<tr>
<td>Regardless of patients’ ability to exercise</td>
<td>“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.”</td>
<td>IIb</td>
<td>C</td>
</tr>
</tbody>
</table>
Appropriate use criteria\textsuperscript{57,58} and expert consensus documents\textsuperscript{59} published jointly by ACCF and other medical societies have addressed CCTA 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 and other medical societies published appropriate use criteria for detection and risk assessment of stable ischemic heart disease.\textsuperscript{60} CCTA was considered appropriate for:

- Symptomatic patients with intermediate (10%-90%) pretest 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 CCTA 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%.\textsuperscript{61}

U.S. Preventive Services Task Force Recommendations

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

Summary of Evidence

For individuals who have acute chest pain and suspected coronary artery disease in the emergency setting, at intermediate to low risk, who receive coronary computed tomography angiography (CCTA), the evidence includes several randomized controlled trials. Relevant outcomes are overall survival, morbid events, and resource utilization. Trials have shown similar patient outcomes, with faster patient discharges from the emergency department, and lower short-term costs. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

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

For individuals who have suspected anomalous coronary arteries who receive CCTA, the evidence includes case series. Relevant outcomes are overall survival, test accuracy, morbid events, and resource utilization. Series have shown that CCTA can detect anomalous coronary arteries missed by other diagnostic modalities. Anomalous coronary arteries are rare, and formal studies to assess clinical utility are unlikely to be performed. In most situations, these case series alone would be insufficient to determine whether the test improves health outcomes. However, in situations where patient management will be affected by CCTA results (eg, with changes in surgical planning), an indirect chain of evidence indicates that health outcomes are improved. The evidence is sufficient to determine 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**


March 2017 Update Policy  Policy updated with literature review; references 12, and 18-19 added. Requirement for invasive angiography prior to computed tomography angiography removed from the policy statement on anomalous coronary arteries. Policy title changed to “Contrast-Enhanced Coronary Computed Tomography Angiography for Coronary Artery Evaluation”.

Keywords
Angiography, Computed Tomography Computed Tomography Angiography CTA CT Angiography

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 17, 2017 and is effective April 15, 2017.

Signature on file
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