Medical Policy

Blue Cross Blue Shield Blue Care Network of Michigan

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***Current Policy Effective Date: 5/1/22**
(See policy history boxes for previous effective dates)

Title: Contrast-Enhanced Computed Tomography Angiography (CTA, CCTA, MDCT, MSCT) of the Heart and/or Coronary Arteries

Description/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 (i.e., noninvasive stress testing and/or coronary angiography).

CORONARY ARTERY DISEASE

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 identifying the anatomic obstruction itself (CCTA 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 CCTA.

Diagnostic Testing

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 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 considered significant.

CCTA is a noninvasive imaging test that requires the use of intravenously administered contrast material and high-resolution, high-speed computed tomography machinery to obtain detailed volumetric images of blood vessels. 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 potentially important role of nonobstructive plaques (i.e., 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.

Coronary Arterial Anomalies

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.

Radiation Exposure

Exposure to ionizing radiation increases lifetime cancer risk.[52] 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 the 2.6 million CCTAs performed in 2007 would result in 2700 cancers or approximately 1 per 1000.[53] 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-mSvdose.[7] Einstein et al (2007) employed a standardized phantom to estimate organ dose from 64-slice CCTA.[6] With modulation and exposures of 15 mSv in men and 19 mSv in women, calculated lifetime cancer risk at age 40 was 7 per1000 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 Prospective Multicenter Study on Radiation Dose Estimates of Cardiac CT Angiography I (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, Hausleiter et al (2012) reported on a mean radiation dose of 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.[55]

Levels of 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] By comparison, radiation exposure accompanying rest-stress perfusion imaging ranges varies according to isotope used—approximately 5 mSv for rubidium-82 (positron emission tomography, PET), 9 mSv for sestamibi (single-photon emission computed tomography, SPECT), 14 mSv for F-18 FDG (fludeoxyglucose) (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 suggest that every 10 mSv of exposure is associated with a 3% increase in cancer incidence over 5 years.[8]

Incidental Findings
A number of studies using scanners with 64 or more detector rows were identified. [43, 44, 45, 46, 47, 48, 49, 50, 51] Incidental findings were frequent (26.6% to 68.7%) with pulmonary nodules typically the most common and cancers typically more 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.[43] As expected, incidental findings were less frequent in the restricted field (clinically significant findings in 14% versus 24% when the entire field was imaged).

The use of electron beam CT or helical CT to detect coronary artery calcification is addressed in a separate policy, "Computed Tomography to Detect Coronary Artery Calcification."

Regulatory Status:

CCTA 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.

Medical Policy Statement

Coronary computed tomography-angiography (CCTA) is an established procedure. It is a useful diagnostic procedure when indicated for patients meeting selection criteria.

Inclusionary and Exclusionary Guidelines (Clinically based guidelines that may support individual consideration and pre-authorization decisions)

Inclusions:
Note: CCTA may be done in an inpatient, outpatient or emergency room setting.
The following patients are considered appropriate candidates for CT angiography by the American College of Cardiology:

- Those with stress test results that are equivocal or discordant with other clinical evidence, in lieu of invasive coronary angiography
- Those with low-intermediate risk acute chest pain in order to exclude coronary artery disease in the emergency department or inpatient setting
- Those with new onset chest pain in low-intermediate risk patients in the outpatient setting
- Symptomatic patients for the evaluation of coronary bypass graft or coronary stent patency, in order to facilitate decision making for invasive angiography
- Those with suspected coronary anomalies

- Patients scheduled for cardiac or major thoracic surgery, such as aortic valve replacement or aortic aneurysm repair, in order to exclude coronary artery disease, as an alternative to invasive coronary angiography
- Patients with incomplete invasive catheterization results as an alternative to repeat invasive catheterization
- Patients anticipating cardiac surgery who require an assessment of coronary or pulmonary venous anatomy: This application of CTA for the coronary and pulmonary veins is primarily for pre-surgical planning. Evaluation of coronary venous anatomy can be useful for the cardiologist who needs to place a pacemaker lead in the lateral coronary vein in order to resynchronize cardiac contraction in patients with heart failure. This may be helpful to guide biventricular pacemaker placement. Pulmonary vein anatomy can vary from patient to patient. Pulmonary vein catheter ablation can isolate electrical activity from the pulmonary veins and allow for the elimination of recurrent atrial fibrillation. The presence of a pulmonary venous anatomic map may help eliminate procedural complications and allow for the successful completion of the intracardiac catheter ablation of an arrhythmogenic focus.

An additional indication for cardiac CT is for the assessment of complex congenital heart disease including anomalies of coronary circulation, great vessels, and cardiac chambers and valves. Examples of these conditions include, but are not limited to:
- Anomalous pulmonary venous drainage
- Other complex congenital heart diseases
- Sinus venosum atrial septal defect
- Kawasaki's disease
- Consideration for surgical repair of tetralogy of Fallot or other congenital heart disease.
- Pulmonary outflow tract obstruction

CCTA is also established for the evaluation of intra- and extra-cardiac structures, including but not limited to:
- Evaluation of cardiac mass (suspected tumor or thrombus) and patients with technically limited images from echocardiogram, MRI or TEE.
- Evaluation of pericardial conditions (pericardial mass, constrictive pericarditis, or complications of cardiac surgery) and patients with technically limited images from echocardiogram, MRI or TEE.
- Evaluation of pulmonary vein anatomy prior to invasive radiofrequency ablation for atrial fibrillation (e.g., pulmonary vein isolation).
- Non-invasive coronary arterial mapping, including internal mammary artery prior to repeat cardiac surgical revascularization.
- Evaluation of suspected aortic dissection or thoracic aortic aneurysm.
- Evaluation of suspected pulmonary embolism.

<u>Exclusions:</u>
- Those individuals who do not meet the criteria stated above.
- For screening purposes
- Multidetector CT scanners that have fewer than 64 detectors
- Computed tomography of the heart, without contrast material, with quantitative evaluation of coronary calcium. Calcium scoring reported in isolation is considered a screening service. See JUMP policy "Computed Tomography to Detect Coronary Artery Calcification."

CPT/HCPCS Level II Codes *(Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure)*

Established codes:

75572 75573 75574

Other codes (investigational, not medically necessary, etc.):

75571

Rationale

Evidence reviews assess whether a medical test is clinically useful. A useful test provides information to make a clinical management decision that improves the net health outcome. That is, the balance of benefits and harms is better when the test is used to manage the condition than when another test or no test is used to manage the condition.

The first step in assessing a medical test is to formulate the clinical context and purpose of the test. The test must be technically reliable, clinically valid, and clinically useful for that purpose. Evidence reviews assess the evidence on whether a test is clinically valid and clinically useful. Technical reliability is outside the scope of these reviews, and credible information on technical reliability is available from other sources.

PATIENTS WITH ACUTE CHEST PAIN PRESENTING TO THE EMERGENCY SETTING

Clinical Context and Test Purpose
The purpose of coronary computed tomography angiography (CCTA) imaging in patients with acute chest pain is to diagnose coronary artery obstruction and guide treatment decisions.

The question addressed in this evidence review is: Does CCTA improve the net health outcome of patients with acute chest pain?

The specific clinical context of each test is described briefly in the following sections. The following **PICO** was used to select literature to inform this review.

Populations
The relevant population of interest are patients with acute chest pain and suspected coronary artery disease (CAD) who are at intermediate to low risk.

Interventions
The intervention of interest is CCTA. CCTA is administered in a hospital emergency department (ED) setting.

Comparators
The comparator of interest is standard emergency department (ED) care and alternative noninvasive testing including stress tests.

Outcomes

The outcomes of interest are mortality, diagnostic accuracy, and utilization of invasive coronary artery angiography.

Clinically Useful

A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, or more effective therapy, or avoid unnecessary therapy or testing.

Direct Evidence

Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from randomized controlled trials (RCTs).

Review of Evidence

Systematic Reviews

Gongora et al (2018) published a meta-analysis of 10 RCTs (total N=6285 patients) comparing CCTA with the standard of care (SOC) in patients with acute chest pain in an ED setting or an inpatient setting.[12] Pooled results suggested that CCTA is associated with more frequent revascularization and ICA, without reducing the risk of adverse cardiac events. Among the limitations of the review were the heterogeneity of SOC across assessed studies, the possibility of publication bias due to the small number of trials available, and the presence of only a few studies that prespecified downstream testing criteria following CCTA results. Tables 1 and 2 summarize review characteristics and results.

Table 1. Characteristics of Systematic Reviews Assessing CCTA in ED Settings

Study	Dates	Trials	Participants	N (Range)	Design	Duration, mo
Gongora et al (2018)[12]	2007-2016	10	Acute chest pain in ED or inpatient setting	6285	RCT	1-19

ED: emergency department; CCTA: coronary computed tomographic angiography; RCT: randomized controlled trial.

Table 2. Results of Systematic Reviews Comparing CCTA With SOC in ED Settings

Study	ICA (CCTA vs SOC)	Revascularization (CCTA vs SOC)	All-Cause Mortality (CCTA vs SOC)	All-Cause MI (CCTA vs SOC)	All-Cause MACE (CCTA vs SOC)
Gongora et al (2018)[12]					
	Higher incidence in CCTA	Higher incidence in CCTA	No significant between-group difference	No significant between-group difference	No significant between-group difference
RR (95% CI)	1.32 (1.07 to 1.63)	1.77 (1.35 to 2.31)	0.48 (0.17 to 1.36)	0.82 (0.49 to 1.39)	0.98 (0.67 to 1.43)
p	0.01	<0.001	0.17	0.47	0.92

CCTA: coronary computed tomographic angiography; CI: confidence interval; ED: emergency department; ICA: invasive coronary angiography; MACE: major adverse cardiac event; MI: myocardial infarction; RR: relative risk; SOC: standard of care.

Skelly et al (2016), conducted a comparative effectiveness review on noninvasive testing for coronary artery disease (CAD).[13] The review found that:

- After CCTA, clinical outcomes for patients with an intermediate pretest risk
  - were similar when compared with usual care or functional testing (low-to-moderate strength of evidence).
  - were similar when compared with single-photon emission computed tomography (SPECT) (low strength of evidence).
- After CCTA, referral for invasive coronary angiography (ICA) and revascularization
  - was more common than after functional testing (high strength of evidence)
  - was similar compared with SPECT and usual care (low strength of evidence).

- After CCTA, additional testing in the emergency department (ED) setting
  - was less common compared with usual care (moderate strength of evidence).
  - was more common than after SPECT (high strength of evidence)
- After CCTA, hospitalization
  - was less common compared to usual care in the ED setting (moderate to low strength of evidence)
  - was similar to functional testing in the outpatient setting (moderate strength of evidence).

Overall, reviewers found no clear differences between strategies for clinical or management outcomes, although CCTA could lead to a higher frequency of referral for ICA and revascularization. Of note, AHRQ archived this report since it is greater than 3 years old. The findings of the report may be used for research purposes, but should not be considered current

Randomized Controlled Trials

Tables 3 and 4 summarize the characteristics and results of RCTs assessing CCTA procedures conducted in ED settings.

Table 3. Characteristics of RCTs Assessing CCTA in ED Settings

Study; Trial	Countries	Sites	Dates	Participants	Interventions	
					Active	***Comparator(s)***
Smulders et al (2019)[66] CARMENTA	Netherlands	1	2012-2016	Patients with acute chest pain, normal or inconclusive ECG, and elevated cardiac troponin levels presenting to the ED	70 to CCTA	68 to CMR; 69 to routine clinical care
Levsky et al (2018)[14]	U.S.	1	2011-2016	Patients with acute chest pain or pressure for whom noninvasive testing is requested	201 to CCTA	199 to SE
Hamilton-Craig et al (2014)[15]; CT-COMPARE	Australia	1	2010-2011	Men ≥30 y or women ≥40 y presenting to the ED with acute undifferentiated chest pain	322 to CCTA	240 to SOC (exercise treadmill testing)
Linde et al (2013)[16]; CATCH	Denmark	1	2010-2013	Patients with suspected NSTE- ACS but normal ECG and troponins; discharged within 24 h needing further risk stratification	299 to CCTA (285 had FU available)	301 to SOC (291 had FU available)
Litt et al (2012)[17]; AC RIN-PA	U.S.	5	2009-2011	Symptoms consistent with possible ACS; >30 y; low risk of MI	908 to CCTA	462 to traditional care
Hoffmann et al (2012)[18]; ROMICAT II	U.S.	9	2010-2012	Chest pain or angina equivalent <24 h before ED presentation; 40-74 y; sinus rhythm; warranting further risk stratification	50 to CCTA	499 to SOC
Goldstein et al (2011)[19]; CT-STAT	U.S.	16	2007-2008	Chest pain <12 h; ≥25 y; low risk of complications; no sign of ischemia at enrollment	361 to CCTA	338 to MPI

Goldstein et al (2007)[20]	U.S.	1	2005	Chest pain or angina-like symptoms <12 h; ≥25 y; low risk of complications	99 to MSCT	98 to SOC

ACS: acute coronary syndrome; CCTA: coronary computed tomography angiography; CMR; cardiovascular magnetic resonance imaging; ECG: electrocardiogram; ED: emergency department; FU: follow-up; MI: myocardial infarction; MPI: myocardial perfusion imaging; MSCT: multislice computed tomography; NSTE-ACS: non-ST-elevation acute coronary syndrome; RCT: randomized controlled trial; SE: stress echocardiography; SOC: standard of care.

Smulders et al (2020) published a 3-arm, prospective, open-label RCT that compared a diagnostic strategy incorporating cardiovascular magnetic resonance imaging (CMR) or CCTA as a gatekeeper for ICA with a control strategy (i.e., routine clinical care) in patients with non-ST-segment elevation myocardial infarction (NSTEMI).[66] Results revealed that CMR or CCTA as an initial test was associated with a reduced proportion of patients referred to ICA during initial hospitalization[87% CMR (p=0.001) and 66% CCTA (p<0.001) as compared to routine clinical care (100%)]. Significantly fewer ICAs were performed in the CCTA- than CMR-first strategy (p=0.004). The reduction in ICA in the CMR- or CCTA-first strategy compared with routine clinical care was persistent after 1 year [88% CMR (p=0.003), 70% CCTA (p<0.001) and 100%routine clinical care]. Similar clinical outcomes were seen: CMR versus routine, hazard ratio (HR) 0.78; 95% confidence interval (CI), 0.37 to 1.61; CCTA versus routine, HR 0.66; 95% CI, 0.31 to 1.42; and CMR versus CCTA, 1.19; 95% CI,0.53 to 2.66. In the non-CMR and non-CCTA arms, follow-up CMR and CCTA were performed in 67% and 13% of patients and led to a new diagnosis in 33% and 3%, respectively (p<0.001). A follow-up CMR led to a new myocardial infarction (MI) diagnosis in 7 patients.

Levsky et al (2018) published an RCT: in the CCTA arm, 39 (19%) patients were hospitalized, compared with 22 (11%) patients of the stress echocardiography arm, resulting in a difference of 8% (95% CI, 1% to 15%; p=0.026).[14] Median length of stay in the hospital was longer for the CCTA arm (58 hours vs. 34 hours; p=0.002, respectively). There was no significant difference between the CCTA and stress echocardiography arms in terms of major adverse cardiac events (MACE; including death): respectively, MACE occurred in 11 CCTA patients and 7 stress echocardiography patients (p=0.47) over a median follow-up of 24 months. The median complete initial work-up radiation exposure for the CCTA arm was 6.4 mSv (interquartile range, 5.3-7.8 mSv), significantly more than that of stress echocardiography (0 mSv; p<0.001) The trial had a number of limitations, including the single-center design and omission of high sensitivity troponin assays.

A 2014 RCT (CT-COMPARE) 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.[15] Costs within 30 days of presentation were significantly lower in the CTA group than the exercise testing group (mean $2193 vs. $2704 p<0.001). Length of stay was significantly reduced in the CTA patients compared to the exercise testing group (mean 13.5 hours vs. 20.7 hours, p<0.0001). Clinical outcomes at 30 days and at 12 months were not different.

Linde et al (2013) reported on the CATCH trial, which randomized 600 patients to a CCTA-guided strategy or to SOC.[16] For the CCTA-guided strategy, referral for ICA required coronary stenosis greater than 70%. This trial differed in design from the others because patients had been discharged from the ED, and if there was intermediate stenosis (50%-70%) on CCTA, a stress test was performed.

Litt et al (2012) reported on the AC RIN-PA trial, which also evaluated the safety of CCTA in patients in the ED.[17] 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%) and higher rates of detection of coronary disease.

Hoffmann et al (2012) reported on the ROMICAT II trial, which compared the length of stay with outcomes in 549 patients evaluated using CCTA or usual care.[18] For the 50 patients in the CCTA arm, mean hospital length of 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.

Goldstein et al (2011) reported on the CT-STAT trial, which evaluated a similar sample of 699 patients.[19] Over a 6-month follow-up, there were no deaths in either arm; there were 2 cardiac events in the CCTA arm and one in the perfusion imaging arm. 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).

Goldstein et al (2007) randomized 197 patients without evidence of acute coronary syndromes to CCTA (n=99) or usual care (n=98).[20] Over a 6-month follow-up, no cardiac events occurred in either arm. Diagnosis was achieved more quickly after CCTA.

Table 4. Summary of Results of RCTs Assessing CCTA in ED Settings

Study	ICA (CCTA vs Control), %	Diagnostic Accuracy (CCTA vs Control), %[a]	MI in Negative CCTA Arm	Median Diagnostic Time (CCTA vs Control), hr[b]	FU, mo
Smulders et al (2019)[66]	66 vs 100	NR	7	NR	1 and 12
Levsky et al (2018)[14]	NR	NR	NR	5.4 vs 4.7[d]	1 and 12
Hamilton-Craig et al (2014)[15]	9.0 vs 4.2	94%/99% vs 83%/91%[c]	0	13.5 vs 20.7[d]	1 and 12
Linde et al (2013)[16]	17 vs 12	71 vs 36[e]	0	NR	4
Litt et al (2012)[17]	5.1 vs 4.2	NR	0	18.0 vs 24.8	1
Hoffmann et al (2012)[18]	12.0 vs 21.0	NR	0	5.8 vs 21.0	1
Goldstein et al (2011)[19]	6.6 vs 6.2	76.9 vs 54.5	0	2.9 vs 6.2	6
Goldstein et al (2007)[20]	12.1 vs 7.1	88.9 vs 98.0	0	3.4 vs 15.0	6

CCTA: coronary computed tomography angiography; ED: emergency department; FU: follow-up; ICA: invasive coronary angiography; MI: myocardial infarction; NR: not reported; RCT: randomized controlled trial.

[a] Confirmed with angiographic and clinical results.

[b] Time from randomization to definitive diagnosis.

[c] Reporting the sensitivity/specificity for CCTA vs exercise stress electrocardiogram for ACS with stenosis >70%.

[d] Refers to length of stay rather than time to diagnosis.

[e] Positive predictive value for CCTA vs standard of care.

The purpose of the limitations tables (Tables 5 and 6) is to display notable gaps identified in each study. This information is synthesized as a summary of the body of evidence following each table and provides the conclusions on the sufficiency of the evidence supporting the position statement.

Table 5. Study Relevance Limitations for RCTs Assessing CCTA in ED Settings

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Duration of Follow-Up[e]
Smulders et al (2019)[66]	2. Patients with a history of myocardial disease and/or severe noncardiac comorbidities were excluded				
Levsky et al (2018)[14]					
Hamilton-Craig et al (2014)[15]	4. Limited applicability to men <30 y and women <40 y				
Linde et al (2013)[16]					
Litt et al (2012)[17]	4. Limited to patients 40 to 74 y; may not be relevant for younger or older individuals				
Hoffmann et al (2012)[18]					
Goldstein et al (2011)[19]					
Goldstein et al (2007)[20]		3. Unequal rates of ICA/revascularization	3. Unequal rates of ICA/revascularization		

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
CCTA: coronary computed tomography angiography; ED: emergency department; ICA: invasive coronary angiography; RCT: randomized controlled trial.

[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.

[b] Intervention key: 1. Classification thresholds not defined; 2. Version used unclear; 3. Not intervention of interest.

[c] Comparator key: 1. Classification thresholds not defined; 2. Not compared to credible reference standard; 3. Not compared to other tests in use for same purpose.

[d] Outcomes key: 1. Study does not directly assess a key health outcome; 2. Evidence chain or decision model not explicated; 3. Key clinical validity outcomes not reported (sensitivity, specificity, and predictive values); 4. Reclassification of diagnostic or risk categories not reported; 5. Adverse events of the test not described (excluding minor discomforts and inconvenience of venipuncture or noninvasive tests).

[e] Follow-Up key: 1. Follow-up duration not sufficient with respect to natural history of disease (true-positives, true-negatives, false-positives, false-negatives cannot be determined).

Table 6. Study Design and Conduct Limitations of RCTs Assessing CCTA in ED Settings

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]

Smulders et al (2019)[66]		1, 2.			3. Sample size calculation based on an estimated 75% ICA referral rate; however, all patients (100%) in the routine clinical care arm eventually underwent ICA	
Levsky et al (2018)[14]					2. Not powered to detect differences in MACE	
Hamilton-Craig et al (2014)[15]					2. Not powered to compare outcomes	
Linde et al (2013)[16]		1. Only patients and clinicians blinded to treatment allocation			2. Not powered to detect differences in secondary outcomes (intermediate cardiac events)	
Litt et al (2012)[17]					2. Due to low incidence of events, not powered for primary outcome (safety)	
Hoffmann et al (2012)[18]		1. No blinding to treatment				
Goldstein et al (2011)[19]				1. 10.3% of patients lost to follow-up	2. Not powered for secondary outcome (safety)	
Goldstein et al (2007)[20]					1. Power calculations not reported	4. No assessment of alternative noninvasive tests

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
CCTA: coronary computed tomography angiography; ED: emergency department; ICA: invasive coronary angiography; MACE: major adverse cardiac event; RCT: randomized controlled trial:

[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.

[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.

[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.

[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).

[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.

[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

Long-Term Follow-Up Studies

Table 7. Results of Follow-Up Studies of RCTs

Study	Initial Study Design	Follow-Up Duration	Results
Linde et al (2015)[21]	RCT (CATCH)	18.7 mo (IQR, 16.8-20.1)	In the CCTA group (n=285), there were 5 MACE vs 14 MACE in the SOC group (n=291) (HR=0.36; 95% CI, 0.16 to 0.95; p=0.04)
Schlett et al (2011)[22]	RCT (ROMICAT)	2 y	Of 333 patients without CAD detected by CCTA, none had a MACE event during follow-up

ACS: acute coronary syndrome; AMI: acute myocardial infarction; CAD: coronary artery disease; CCTA: coronary computed tomographic angiography; CI: confidence interval; ED: emergency department; HR: hazard ratio; IQR: interquartile range; MACE: major adverse cardiac event; SOC: standard of care.

Nonrandomized Studies

Durand et al (2017) compared the diagnostic performance of dobutamine-stress echocardiography (DSE) with CCTA in 217 adults.[23] Patients had normal measurements of troponin I or T, and electrocardiograph results. All patients received DSE and CCTA, with only 75 (34.6%) patients receiving ICA, which served as the reference test. The primary end point was the diagnostic accuracy of the tests for detecting coronary stenosis greater than 50%. Forty-nine (22.6%) patients had a positive CCTA while 33 (15.2%) patients had a positive DSE. A negative CCTA result was reported in 144 (66.4%) patients, and 146 (67.3%) had a negative DSE result. Overall, CCTA was more sensitive than DSE in detecting CAD, while specificity was similar between tests. At 6 months, no patients had died or received a diagnosis of MI, but 1 patient presented with acute coronary syndrome whose diagnosed was initially missed. No limitations were identified. Tables 8 and 9 summarize the trial characteristics and results.

Table 8. Key Nonrandomized Trials Assessing CCTA in ED Settings

Study	Study Type	Country	Dates	Participants	Treatment	Comparator	Follow-Up
Durand et al (2017)[23]	Prospective head-to-head multicenter	France	NR	Adults treated at ED for chest pain <24 h after symptom onset	CCTA	DSE	6 mo

CCTA: coronary computed tomographic angiography; DSE: dobutamine-stress echocardiography; ED: emergency department; NR: not reported

Table 9. Results of Key Nonrandomized Trials Assessing CCTA in ED Settings

Study	Diagnostic Accuracy		Incidence of MI	ICA, n (%)[b]
	CCTA[a]	DSE[a]		
Durand et al (2017)[23]				
N	217	217	None during FU	75 (34.6)
Sensitivity, %	96.9	51.6		
Specificity, %	48.3	46.7		
PLR (95% CI)	2.09 (1.36 to 3.11)	1.03 (0.62 to 1.72)		
NLR (95% CI)	0.07 (0.01 to 0.52)	1.10 (0.63 to 1.96)		

CCTA: coronary computed tomographic angiography; CI: confidence interval; DSE: dobutamine-stress echocardiography; ED: emergency department; FU: follow-up; ICA: invasive coronary angiography; MI: myocardial infarction; NLR: negative likelihood ratio; PLR: positive likelihood ratio.

[a] Of detected coronary stenosis >50%.

[b] Number of patients who received ICA.

Section Summary: Acute Chest Pain Presenting to the Emergency Setting

The high negative predictive value 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, 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 invasive coronary angiography 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.

PATIENTS WITH STABLE CHEST PAIN AND SUSPECTED CAD

Before the 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 for 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 test results but also on the management and treatment strategy. The most convincing evidence of clinical utility compares outcomes after anatomic-first (CCTA) and functional-first (e.g., perfusion imaging, stress echocardiography) strategies.

Relevant studies reviewed here include those comparing the diagnostic performance of CCTA with angiography, studies of outcomes of patients undergoing CCTA vs. alternative tests, and studies of incidental findings and radiation exposure.

Clinical Context and Test Purpose

The purpose of CCTA in patients with stable chest pain and suspected CAD is to diagnose coronary artery obstruction and guide treatment decisions.

The question addressed in this evidence review is: Does CCTA improve the net health outcome of patients with stable chest pain?

The specific clinical context of each test is described briefly in the following sections. The following **PICO** was used to select literature to inform this review.

Populations

The relevant population of interest is patients with stable chest pain and suspected CAD who are at intermediate – risk and meet guideline criteria for noninvasive testing.

Interventions

The intervention of interest is CCTA. CCTA is administered in a cardiology clinic setting equipped with standard noninvasive testing for CAD and CCTA.

Comparators

The following tests and practices are currently being used to make decisions about managing stable chest pain: noninvasive testing including exercise electrocardiography, myocardial perfusion imaging (MPI), and stress echocardiography, and standard care.

Outcomes

The outcomes of interest are mortality, sensitivity and specificity, MI, hospitalization, and utilization of ICA. The time of interest is in the short-term to evaluate follow-up procedures after imaging and for several years or more after CCTA to determine event rates.

Clinically Valid

A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

Review of Evidence

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 10 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 (2012).[24] Sensitivities tended to range between 70% and 90%, depending on the test and study, and specificities ranged between 70% and 90%.

Characteristics and results of reviews are summarized in Tables 11 and 12. For CCTA, estimates of sensitivity from various systematic reviews are considerably higher (Table 12).

Table 10. Sensitivity and Specificity Estimates for Functional Noninvasive Tests From Guidelines

Noninvasive Test	Sensitivity (Range or Single Estimates), %	Specificity (Range or Single Estimates), %
Exercise electrocardiography	61	70 to 77
Pharmacologic stress echocardiography	85 to 90	79 to 90
Exercise stress echocardiography	70 to 85	77 to 89
Exercise myocardial perfusion imaging	82 to 88	70 to 88
Pharmacologic stress myocardial perfusion imaging	88 to 91	75 to 90
Coronary computed tomography angiography	93 to 97	80 to 90

Adapted from Fihn et al (2012). [24]

Table 11. SR & MA Characteristics of Clinical Validity for CCTA in Stable Chest Pain and Suspected CAD

Study	Study Population	Design[a]	Reference Standard	Threshold for Positive Index Test	Timing of Reference and Index Tests	Blinding of Assessors	Comment

Haase et al (2019)[25]	Individuals with a clinical indication for coronary angiography due to suspected CAD because of stable chest pain. Individual patient data sufficient to calculate pre-test clinical risk. Studies comparing CCTA with ICA. N = 533,265 prospective diagnostic accuracy studies	MA	ICA	CCTA: Obstructive CAD: ≥ 50% stenosis Pre-test Clinical Risk: CAD Consortium prediction tool	NR	NR	Acceptable thresholds for index and reference tests were unclear. Calculation of pre-test clinical risk assessment not clearly described. Timing of tests not reported.
Nielsen et al (2014)[26]	Studies examining the diagnostic accuracy of CCTA vs functional testing in patients suspected of stable CAD where ICA is used as a reference standard. N = 157,517 diagnostic accuracy and nonrandomized studies	MA	ICA	CCTA: NR	NR	NR	Details on blinding and timing were limited. Quality assessment results for bias risk in diagnostic accuracy studies was predominantly low.
Ollendorf et al (2011)[27]	Diagnostic accuracy studies of CCTA vs ICA as the reference standard. 42 diagnostic accuracy studies	MA	ICA	CCTA: NR	NR	Blinded review of CCTA and ICA	
Health Quality Ontario (2010)[28]	Diagnostic accuracy studies of CCTA in suspected CAD with ICA as reference standard. Individuals with intermediate pre-test probability	MA	ICA	CCTA: CAD: ≥ 50% stenosis	NR	NR	Analysis is limited by significant heterogeneity between studies.

	of CAD. N = 1178 studies						

CAD: coronary artery disease; CCTA: coronary computed tomography angiography; ICA: invasive coronary angiography; MA: meta-analysis; NR: not reported; SR: systematic review. 1 Key eligibility criteria.

Table 12. SR & MA Results for CCTA in Stable Chest Pain and Suspected CAD

Study; Subgroup	Clinical Validity, % (95% CI)			
	Sensitivity	***Specificity***	***PPV***	***NPV***
Haase et al (2019) (COME-CCT); Overall[25]	95.2 (92.6 to 96.9)	79.2 (74.9 to 82.9)	75.6 (NR)	86.3 (NR)
Haase et al (2019) (COME-CCT); Pre-test Clinical Risk Subgroup[25] 7%	NR	NR	50.9 (43.3 to 57.7)	97.8 (96.4 to 98.7)
15%	NR	NR	55.8 (48.6 to 62.3)	97.1 (95.4 to 98.2)
50%	NR	NR	75.4 (70.5 to 79.5)	90.9 (87.5 to 93.4)
67%	NR	NR	82.7 (78.3 to 86.2)	85.0 (80.2 to 88.9)
Nielsen et al (2014)[26]	98 (93 to 99)	82 (63 to 93)	85 (71 to 93.5)	97.5 (87 to 99)
Ollendorf et al (2011)[27]	98 (96 to 99)	85 (81 to 89)	NR	NR
Health Quality Ontario (2010)[28]	96.1 (94 to 98.3)	81.5 (73.0 to 89.9)	NR	NR

CAD: coronary artery disease; CCTA: coronary computed tomography angiography; CI: confidence interval; MA: meta-analysis; NPV: negative predictive value; NR: not reported; PPV: positive predictive value; SR: systematic review.

Clinically Useful

A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, or more effective therapy, or avoid unnecessary therapy, or testing.

Direct Evidence

Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from RCTs.

Systematic Reviews

Foy et al (2017) conducted a systematic review comparing CCTA with functional stress testing for patients with suspected CAD and stable or acute chest pain.[29] In the CCTA arm, there were 10,315 patients, and in the functional stress testing arm, there were 9777 patients; both CCTA and functional stress testing strategies varied among the 13 trials. Overall mortality and cardiac hospitalization did not differ between CCTA and functional stress testing groups. There were fewer cases of MI in the CCTA group than in the functional stress testing group; however, the incidence of ICA and revascularization were higher in the CCTA group. CCTA was associated with an increase in new diagnoses of CAD as well as increased prescription of aspirin and statin therapy. All trials reported a lack of blinding, both of patients and personnel,

and the overall quality of evidence was moderate, despite a high risk of bias in several studies included. Additional limitations included the lack of available patient-level data, the absence of assessment of time to hospital discharge, and differences in radiation exposure. Tables 13 and 14 summarize review characteristics and results.

Table 13. Characteristics of Systematic Reviews Assessing CCTA for Stable Chest Pain

Study	Dates	Trials	Participants	N (Range)	Design	Duration
Foy et al (2017)[29]	2000-2016	13	Patients with suspected CAD	20,092 (CCTA arm: n=10,315; functional stress testing arm: n=9777)	RCT	NR

CAD: coronary artery disease; CCTA: coronary computed tomography angiography; NR: not reported; RCT: randomized controlled trial.

Table 14. Results of Systematic Reviews Assessing CCTA for Stable Chest Pain

Study	Incidence of ICA, %	Revascularization, %	Adverse Events, %	New Diagnosis of CAD, %	Medication Use, %[a]
Foy et al (2017)[29]					
CCTA vs. Functional stress testing	11.7 vs. 9.1	7.2 vs. 9.1	•Mortality: 1.0 vs. 1.1 •Hospitalization: 2.7 vs. 2.7 •MI: 0.7 vs. 1.1	18.3 vs. 8.3	Aspirin: 21.6 vs. 8.2 Statins: 20.0 vs. 7.3
RR (95% CI)	1.33 (1.12 to 1.59)	1.86 (1.43 to 2.43)	•Mortality: 0.93 (0.71 to 1.21) •Hospitalization: 0.98 (0.79 to 1.21) •MI: 0.71 (0.53 to 0.96)	2.80 (2.03 to 3.87)	Aspirin: 2.21 (1.21-4.04) Statins: 2.03 (1.09-3.76)

CAD: coronary artery disease; CCTA: coronary computed tomography angiography; CI: confidence interval; ICA: invasive coronary angiography; MI: myocardial infarction; RR: relative risk.
[a] Proportion of patients who experienced a significant increase in medication use.

Randomized Controlled Trials

For patients at intermediate risk of CAD, 3 major RCTs were identified by comparing outcomes after a CCTA strategy with outcomes after other noninvasive testing strategies. Tables 15 and 16 summarize trial characteristics and results.

Table 15. Characteristics of Key RCTs Assessing CCTA in Stable Chest Pain

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	**Comparator**
Stillman et al (2020)	U.S.	44	2011-2013	Patients with stable angina and suspected CAD	518 to CCTA	532 to SPECT-MPI
Rudzinski et al (2018); CAT-CAD	Poland	1	2015-2016	Patients with stable angina and suspected CAD	60 to CCTA	60 to ICA
Newby et al (2018); SCOT-HEART	U.K	12	2010-2019	Patients referred for assessment of angina due to suspected CHD	2073 to standard of care plus CCTA	2073 to standard of care
Chang et al	Various	22	2012-	Patients with suspected	823 to selective	808 to direct

(2018			2016	CAD referred to nonemergent ICA	referral strategy with initial CCTA	referral strategy with initial ICA
Douglas et al (2015) ; PROMISE	U.S	193	2010-2013	Systematic outpatients without diagnosed CAD	4996 to anatomic testing strategy with CCTA	5007 to functional testing strategy
SCOT-HEART Investigators (2015) ; SCOT-HEART	U.K.	12	2010-2014	Patients referred for assessment of angina due to suspected CHD	2073 to standard of care plus CCTA	2073 to standard of care
McKavanagh et al (2015) ;CAPP	U.K.	NR	2010-2011	Patients with symptoms of stable chest pain to EST or cardiac CT	250 to EST	250 to cardiac CT

CAD: coronary artery disease; CHD: coronary heart disease; CT: computed tomography; CCTA: coronary computed tomography angiography; EST: exercise stress electrocardiogram test; ICA: invasive coronary angiography; NR: not reported; RCT: randomized controlled trial.

Stillman et al (2020) reported results from the Randomized Evaluation of Patients with Stable Angina Comparing Utilization of Noninvasive Examinations (RESCUE) trial, which randomized 1050 patients with stable angina and suspected CAD to CCTA or single photon emission CT myocardial perfusion imaging (SPECT-MPI) to direct patients to optimal medical therapy alone or optimal medical therapy with revascularization.[44,] The primary endpoint was first MACE (cardiac death or MI), or revascularization. Over a mean follow-up period of 16.2 months, there was a similar rate of MACE or revascularization in patients with CCTA compared to SPECT-MPI (p=.19). The authors did not report separate rates of MACE and revascularization.

Rudzinski et al (2018) reported on results from the Coronary Artery Computed Tomography as the First-Choice Imaging Diagnostics in Patients With High Pre-Test Probability of Coronary Artery Disease (CAT-CAD) trial, which randomized 120 patients with suspected CAD to undergo CCTA vs. direct ICA. Outcomes were evaluated during the diagnostic and therapeutic periods. Evaluation with CCTA was found to reduce the total number of ICAs performed.[47]

Newby et al (2018) published updated 5-year outcomes from the CT coronary angiography in patients with suspected angina due to coronary heart disease (SCOT-HEART) trial. A significantly lower rate of death or nonfatal myocardial infarction was found for patients undergoing CCTA with the SOC. CCTA was not found to increase rates of revascularization or subsequent utilization of ICA at this time point. [45] The authors of a post-hoc analysis of the 5 year SCOT-HEART data concluded that "the beneficial effect of CCTA on outcomes is consistent across subgroups with plausible underlying mechanisms" and that CCTA "improves CHD outcomes by enabling better targeting of preventative treatments to those with CAD."[67]

Chang et al (2018) randomized 1611 patients to different referral strategies, where initial assessment for CAD was performed by CCTA or ICA. Downstream clinical decision-making and testing were left to the discretion of treating physicians. The primary outcome measure was noninferiority of CCTA in regard to MACE.[46]

Douglas et al (2015) reported on the PROMISE trial, which 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.[48] 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 and revascularization rates were higher in the CCTA group. In a

further prespecified analysis of PROMISE trial data, Hoffmann et al (2017) found that there was no difference in event rates (death, MI, or angina) between the groups at a median of 26 months follow-up.[52] However, CCTA had better discriminatory ability than functional testing to predict events (e.g., in categories of normal, mildly abnormal, moderately abnormal, and severely abnormal) in patients who had nonobstructive CAD (p=0.04). When the Framingham Risk Score was added to functional testing results, there was no significant difference in prognostic capability between the approaches (p=0.29).

In the SCOT-HEART trial (2015), investigators randomized 4146 patients to CCTA plus SOC or SOC alone. The primary end point was the change in the proportion of patients with a more certain diagnosis (presence or absence) of angina pectoris.[49] 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). Williams et al (2017) reported on symptoms and quality of life for participants in the SCOT-HEART trial.[53] Symptoms improved in both groups; however, improvements in symptoms and quality of life at 6 months were lower in patients in the CCTA arm than the functional testing arm. This outcome was due primarily to patients who were diagnosed with moderate CAD or had a new prescription of preventative therapy compared with patients diagnosed with normal coronary arteries or who had their preventative therapy discontinued.
In the comparison of cardiac computerized tomography and exercise stress electrocardiogram test for the investigation of stable chest pain CAPP trial, McKavanagh et al (2015) randomized 500 patients with stable chest pain to CCTA or exercise stress testing.[50] 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.

Table 16. Results of Key RCTs Assessing CCTA in Stable Chest Pain

Study	Death or Nonfatal Myocardial Infarction	Incidence of ICA	Revascularization	Normal Findings on ICA	Angina Stability	Hospitalization
Stillman et al (2020)		NR	NR	NR	NR	NR
CCTA, %	Negative test (1.2%); positive test (20.5%)					
SPECT-MPI, %	Negative test (3.2%); Positive test (34.8%)*					
HR	1.03 (0.61 to 1.75)*					
P	.19					
Rudzinski et al (2018)						
CCTA, n	0	21		5		25
ICA, n	0	59		42		73
P		<0.0001		<0.0001		<0.0001
Newby et al (2018)				NR	NR	NR

CCTA + standard care, n (%)	48 (2.3)	491 (23.7)	279 (13.5)			
Standard care, n (%)	81 (3.9)	502 (24.2)	267 (12.9)			
HR at 5 yr (95% CI)	0.59 (0.41 to 0.84)	1.00 (0.88-1.13)	1.07 (0.91 to 1.27)			
P	0.004	NR	NR			
Chang et al (2018)						
Selective Referral to CCTA, n (%)	36 (4.6)	179 (23%)	98 (13%)	24.6%		33 (4.2%)
Direct Referral to ICA, n (%)	33 (4.6)	719 (89%)	127 (18%)	61.1%		31 (4.3%)
HR (95% CI)	0.99 (0.66 to 1.47)	NR	NR			NR
P	0.99 0.026 (1-sided noninferiority)	<0.001	0.007	<0.001		NR
Douglas et al (2015)						
CCTA group	104					61
Functional testing group	112					41
HR (95% CI)	0.88 (0.67 to 1.15)					
P	0.35					
SCOT-HEART Investigators (2015)						
CCTA, n (%)	26					511 (12.3)
Standard care, n (%)	42					247 (11.9)
HR (95% CI)	0.616 (0.378-1.006)					0.928 (0.780-1.104)
P	0.527					0.399
McKavanagh et al (2015)						
MD at 3 mo (95% CI)					-11.1 (-17.4 to -4.8)	
P						
MD at 12 mo (95% CI)					-6.8 (-12.8 to -0.7)	
P					0.028	

CI: confidence interval; CCTA: coronary computed tomography angiography; HR: hazard ratio; ICA: invasive coronary angiography; MD: mean difference; NR: not reported; RCT: randomized controlled trial.

Tables 17 and 18 display notable relevance, design, and conduct limitations identified in each trial.

Table 17. Relevance Limitations of RCTs Assessing CCTA in Stable Chest Pain

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Duration of FU[e]
Stillman et al (2020)				1. Key health outcomes not addressed	2. Not sufficient duration for harms
Rudzinski et al (2018)					2. Not sufficient duration for harms.

Newby et al (2018)	4. Patients >75 y excluded.				
Chang et al (2018)	4. Population included >84% Asian patients in each treatment arm.				
Douglas et al (2015)				1. Test performance and utility not addressed	
SCOT-HEART Investigators (2015)	4.Patients >75 y excluded.				
McKavanagh et al (2015)	4. Low number of diabetics included due to exclusion criteria		1, 2. Noted difficulty in contrasting the results of anatomic and functional tests		

The study limitations stated in this table are those notable in the current review; this is not a comprehensive limitations assessment.
CCTA: coronary computed tomography angiography; RCT: randomized controlled trial.
[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.Not the intervention of interest.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 18. Study Design and Conduct Limitations of RCTs Assessing CCTA for Stable Chest Pain

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Stillman et al (2020)		1. Not blinded to treatment assignment.		1. High loss to follow-up or missing data (ie, low adherence)		
Rudzinski et al (2018)	2. Allocation not concealed.			2. Unclear handling of missing data.	1. Power calculation not reported.	3. Confidence intervals not reported.
Newby et al (2018)		1-3. Treatments and outcomes not blinded and potential bias among attending clinicians was present.				
Chang et al (2019)	2. Allocation not concealed.	1. Not blinded to treatment assignment.		1. High loss to follow-up or missing data.		
Douglas et al						

(2015)						
SCOT-HEART Investigators (2015)		1-3. Treatments and outcomes not blinded and potential bias among attending clinicians was present.				
McKavanagh et al (2015)					3. Study not powered to evaluate prognosis or adverse CAD events	

The study limitations stated in this table are those notable in the current review; this is not a comprehensive limitations assessment.
CAD: coronary artery disease; CCTA: coronary computed tomography angiography; RCT: randomized controlled trial.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

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-analyses 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 when 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 supplemented usual care (which may or may not have included a noninvasive test). These trial design differences 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 compared with other established noninvasive tests. Thus, the randomized studies suggest that outcomes of patients are likely to be similar to CCTA vs other noninvasive tests.

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.

Clinical Context and Test Purpose

The purpose of CCTA in patients who have suspected anomalous coronary arteries is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of CCTA improve net health outcomes in patients with suspected anomalous coronary arteries?

The following **PICO** was used to select literature to inform this review.

Populations

The relevant population of interest are individuals with suspected anomalous coronary arteries.

Interventions

The therapy being considered is CCTA. CCTA is administered in a cardiology clinic setting equipped with standard noninvasive testing for CAD.

Comparators

The following practice is currently being used to make decisions about managing suspected anomalous coronary arteries: SOC without CCTA.

Outcomes

The general outcomes of interest are overall survival, test accuracy, morbid events, and resource utilization. The time of interest is in the short-term to evaluate follow-up procedures after imaging and for several years or more after CCTA to determine event rates.

Clinically Valid

A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

Clinically Useful

A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, or more effective therapy, or avoid unnecessary therapy, or testing.

Direct Evidence

Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from RCTs. No RCTs were identified assessing the clinical utility of CCTA for suspected anomalous coronary arteries; case series exist.

Case Series

A number of case series have consistently reported that CCTA can delineate the course of these anomalous arteries, even when conventional angiography cannot.[39,40,41,42]

Section Summary: Suspected Anomalous Coronary Arteries
Results from case series have shown that CCTA delineates the course of anomalous coronary 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 the 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.

Patency
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).[58] Other small studies have reported high sensitivity and specificity.[59,60] Lacking are multicenter studies demonstrating likely clinical benefit, particularly given the reasonably high disease prevalence in patients evaluated.

In-Stent Restenosis
Use of CCTA 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.

Screening
Use for screening a low-risk population was evaluated by McEvoy et al (2011) in patients undergoing CCTA (n=1000) or a control intervention (n=1000).[61] Findings reported in this study were abnormal in 215 screened patients. Over 18 months of follow-up, screening was associated with more invasive testing and statin use, but no difference in cardiac event rates.

Preoperative Evaluation
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.[62] 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).

The utility of CCTA for the pre-operative screening of patients undergoing noncardiac surgery with an intermediate- to high-risk of CAD was assessed by Koshy et al (2019).[63] While current guidelines recommend stress testing in individuals at intermediate- to high-risk, over one-third of perioperative MACE occur among those with negative test results. MACE were reported in 7.2% of 3480 patients. Risk of perioperative MACE was found to increase with the severity of CAD on CCTA findings (no CAD, 2.0%; non-obstructive CAD, 4.1%; obstructive single-vessel, 7.1%; obstructive multivessel, 23.1%; $p < 0.001$). Obstructive multivessel CAD predicted the

highest risk of MACE (odds ratio 8.9, 95% CI 5.1 to 15.3; p < 0.001). In a high-risk subgroup, absence of multivessel disease demonstrated a high negative predictive value of 96% (95% CI, 92.8 to 98.4). The investigators acknowledge that the prognostic value of these findings has unclear clinical utility, as it is not known how non-obstructive or single-vessel CAD findings would change the clinical management of patients. Additionally, prior studies have not demonstrated a benefit of preoperative medical therapy or revascularization in lowering the incidence of MACE.

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 CCTA, the evidence includes several RCTs. Relevant outcomes include overall survival, morbid events, and resource utilization. The studies showed similar patient outcomes, with faster patient discharges from the ED, 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.

For individuals who have stable chest pain, intermediate risk of coronary artery disease, meeting guideline criteria for noninvasive testing (i.e., intermediate risk) who receive CCTA, the evidence includes studies of diagnostic accuracy of CCTA, RCTs comparing CCTA with alternative diagnostic strategies, and observational studies comparing CCTA with alternative diagnostic strategies. Relevant outcomes include overall survival, test accuracy, morbid events, and resource utilization. Studies of diagnostic accuracy show that CCTA has higher sensitivity and similar specificity to alternative noninvasive tests. Although randomized trials do not show superiority of CCTA to other diagnostic strategies, they are consistent with noninferiority, which has 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.

For individuals who have suspected anomalous coronary arteries who receive CCTA, the evidence includes case series. Relevant outcomes include overall survival, test accuracy, morbid events, and resource utilization. The studies show that CCTA 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.

Ongoing and Unpublished Clinical Trials

Some currently unpublished trials that might influence this review are listed in Table 19.

Table 19. Summary of Key Trials

NCT Number	Title	Enrollment	Completion Date
Ongoing			
NCT02400229	Diagnostic Imaging Strategies for Patients With Stable Chest Pain and Intermediate Risk of Coronary Artery Disease: Comparative Effectiveness Research of Existing Technologies - A Pragmatic Randomised Controlled Trial of CT Versus ICA	3546	Mar 2022

NCT02284191	The Role of Early CT Coronary Angiography in the Evaluation, Intervention and Outcome of Patients Presenting to the Emergency Department With Suspected or Confirmed Acute Coronary Syndrome	1749	Dec 2020
NCT03129659	Coronary CT Angiography for Improved Assessment of Suspected Acute Coronary Syndrome With Inconclusive Diagnostic Work-up	230	Sep 2021
NCT02099019	Usefulness of Coronary Computed Tomography Angiography for Therapeutic Decision-Making; Revascularization	3000	Feb 2025

NCT: national clinical trial; ISRCTN: international standard registered clinical/so

SUPPLEMENTAL INFORMATION

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 (Table 20).[38]

Table 20. Guidelines on Management of Stable IHD

Diagnosis	Recommendation	Class	LOE
Unknown			
	Able to exercise		
	"CCTA might be reasonable for patients with an intermediate pretest probability of IHD who have at least moderate physical functioning or no disabling comorbidity."	IIb	B
	Unable to exercise		
	"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."	IIa	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."	IIa	C
Known CAD			
	Able to exercise		
	"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."	IIb	B
	Able to exercise		
	"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."	III	C
	Unable to exercise		
	"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."	IIa	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."	IIa	C
	Unable to exercise		
	"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."	III	C
	Regardless of patients' ability to exercise		
	"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."	IIb	C

CCTA: coronary computed tomography angiography; CMR: cardiac magnetic resonance; ECG: electrocardiography; IHD: ischemic heart disease; LOE: level of evidence; MPI: myocardial perfusion imaging; SIHD: stable ischemic heart disease.

In 2013, ACCF and other medical societies published appropriate use criteria for detection and risk assessment of stable ischemic heart disease.[62] 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 has recommended CCTA as first-line testing for patients with stable angina if the clinical assessment indicates typical or atypical angina, or if clinical assessment indicates nonanginal chest pain but 12-lead resting ECG has been done and indicates ST-T changes or Q waves.[65]

Society of Cardiovascular Computed Tomography

The Society of Cardiovascular Computed Tomography (2021) published an expert consensus document on CCTA.[66,] Recommendations on use of CCTA in select patients are included in Table 22. In addition to the recommendations listed below, the expert consensus included additional recommendations in several patient populations, including patients with known coronary artery disease.

Table 21. Society of Cardiovascular Computed Tomography Guidelines on Coronary Computed Tomography Agniography

Diagnosis	Recommendation
Stable chest pain with no known CAD	It is appropriate to perform CTA as the first line test for evaluating patients with no known CAD who present with stable typical or atypical chest pain, or other symptoms which are thought to represent a possible anginal equivalent (eg, dyspnea on exertion, jaw pain). It is appropriate to perform coronary CTA following a nonconclusive functional test, in order to obtain more precision regarding diagnosis and prognosis, if such information will influence subsequent patient management. Coronary CTA is rarely appropriate in very low risk symptomatic patients,

	such as those <40 years of age who have noncardiac symptoms (eg, chest wall pain, pleuritic chest pain).
Noncardiac surgery	It is appropriate to perform CTA as an alternative to other noninvasive tests for evaluation of selected patients prior to noncardiac surgery.
Coronary anomalies	It is appropriate to perform CTA for the evaluation of coronary anomalies.

CAD: coronary artery disease; CTA: cardiac computed tomography angiography.

Government Regulations

National:

There is no national coverage determination.

Local:

Wisconsin Physicians Service Insurance Corporation
L35121 Coronary Computed Tomography Angiography (CCTA)
Original effective date 10/01/2015; Revision effective date 10/28/2021

Coverage Indications, Limitations, and/or Medical Necessity

The multi-detector helical computed tomography (MDCT) technology requires thin (up to 1 mm) slices, 0.5 to 0.75 mm reconstructions, multiple simultaneous images (e.g. 16, 32, 64 or more slices), and cardiac gating (often requiring beta blockers for ideal heart rate). There is significant post-processing, depending on the number of slices per second for image generation. For coronary artery imaging, the resulting images show a high correlation with stenotic lesions noted on diagnostic cardiac catheterization but more importantly, with atheromas on intracoronary ultrasound.

Current available body of evidence demonstrates that CCTA can reliably rule out the presence of significant coronary artery disease (CAD) in patients with a low to intermediate probability of having CAD and can reliably achieve a high degree of diagnostic accuracy and technical performance necessary to replace conventional angiography.

Indications:

1. CCTA used as an alternative to invasive angiography and stress testing. For patients with anginal symptoms, patients with unclear stress tests results, patients in whom the stress test result contradicts the clinical assessment, patients with low risk of CAD who cannot exercise, to determine the patency of coronary artery bypass grafts, as an alternative when cardiac catheterization is impossible or carries a high risk, to rule out stenosis before non-coronary cardiac surgery such as valve replacement or resection of tumors, and clarifying unclear finding after invasive angiography.
2. CCTA used to assess patient suspected of having a congenital coronary anomaly of great vessels, cardiac chambers and valves. It is often used after an anomaly has been identified following a different test such as prior invasive coronary angiogram. CCTA is used to decide if surgery is indicated and for surgical planning.
3. CCTA used to evaluate acute chest pain in the emergency department (ED). The rationale is to quickly triage patients in order to rule out coronary artery disease as a possible cause of symptoms. Many will present with a normal electrocardiogram and myocardial enzymes.

4. CCTA used to assess coronary or pulmonary venous anatomy. Coronary mapping is primarily for pre-surgical planning such as pacemaker lead placement in the lateral coronary vein to resynchronize cardiac contraction in patients with heart failure or guiding biventricular pacemaker placement. Pulmonary vein anatomy can vary from patient to patient. Pulmonary vein mapping is primarily for catheter ablation which can isolate electrical activity from the pulmonary veins and allow for the elimination of recurrent atrial fibrillation or help eliminate procedural complications.
5. CCTA used to assess etiology with new onset heart failure for evaluation of coronary arteries.

Limitations:

1. The test is never covered for screening, i.e., in the absence of signs, symptoms or disease.
2. The test will be considered not medically necessary if the anticipated results are not expected to provide new, additional information to that already previously obtained from other tests (such as stress myocardial perfusion images or cardiac ultrasound). New or additional information should facilitate the management decision, not merely add a new layer of testing.
3. The test will be considered not medically necessary if pretest evaluation indicates that the patient would require invasive cardiac angiography for further diagnosis or for therapeutic intervention.
4. The test may be denied, on post-pay review, as not medically necessary when used for cardiac evaluation if there were pre-test knowledge of sufficiently extensive calcification of the suspect coronary segment that would diminish the interpretive value. (e.g., angina decubitus, unstable angina, Prinzmetal angina, etc.)
5. Coverage is limited to devices that process thin, high resolution slices (1mm or less). The multi-detector scanners must have at least 64 slices per rotation capability.
6. The administration of beta blockers and the monitoring of the patient during MDCT/CCTA by a physician experienced in the use of cardiovascular drugs is included as part of the test and is not a separately payable service.
7. All studies must be ordered by the physician/qualified non-physician practitioner treating the patient and who will use the results of the test in the management of the patient.
8. The test must be performed under the direct supervision of a physician, similar to the stress myocardial perfusion imaging.
9. This LCD does not address electron beam tomography (EBT) technology or Ultrafast CT for coronary artery examination. There is no extension of coverage of EBT based on this policy.
10. Quantitative calcium scoring is not a covered service and will be denied as not medically necessary. Calcium scoring reported in isolation is considered a screening service. When performed in association with CT angiography, there is neither separate nor additional included reimbursement for the calcium scoring.
11. Atrial fibrillation or atrial flutter alone is not an indication; atrial fibrillation or atrial flutter with planned ablation therapy is allowed.

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [CMS, formerly HCFA] are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

Related Policies

Computed Tomography to Detect Coronary Artery Calcification

References

1. Mastouri R, Sawada SG, Mahenthiran J. Current noninvasive imaging techniques for detection of coronary artery disease. Expert Rev Cardiovasc Ther. Jan 2010; 8(1): 77-91. PMID 20030023
2. Chow BJ, Small G, Yam Y, et al. Incremental prognostic value of cardiac computed tomography in coronary artery disease using CONFIRM: COroNary computed tomography angiography evaluation for clinical outcomes: an InteRnational Multicenter registry. Circ Cardiovasc Imaging. Sep 2011; 4(5): 463-72. PMID 21730027
3. National Research Council, Committee to Assess Health Risks from Exposure to Low Level of Ionizing Radiation. Health risks from exposure to low levels of ionizing radiation: BEIR VII Phase 2. Washington, D.C.: National Academies Press; 2006.
4. Berrington de Gonzalez A, Mahesh M, Kim KP, et al. Projected cancer risks from computed tomographic scans performed in the United States in 2007. Arch Intern Med. Dec 14 2009; 169(22): 2071-7. PMID 20008689
5. Smith-Bindman R, Lipson J, Marcus R, et al. Radiation dose associated with common computed tomography examinations and the associated lifetime attributable risk of cancer. Arch Intern Med. Dec 14 2009; 169(22): 2078-86. PMID 20008690
6. Einstein AJ, Henzlova MJ, Rajagopalan S. Estimating risk of cancer associated with radiation exposure from 64-slice computed tomography coronary angiography. JAMA. Jul 18 2007; 298(3): 317-23. PMID 17635892
7. Bischoff B, Hein F, Meyer T, et al. Comparison of sequential and helical scanning for radiation dose and image quality: results of the Prospective Multicenter Study on Radiation Dose Estimates of Cardiac CT Angiography (PROTECTION) I Study. AJR Am J Roentgenol. Jun 2010; 194(6): 1495-9. PMID 20489088
8. Hausleiter J, Meyer TS, Martuscelli E, et al. Image quality and radiation exposure with prospectively ECG-triggered axial scanning for coronary CT angiography: the multicenter, multivendor, randomized PROTECTION-III study. JACC Cardiovasc Imaging. May 2012; 5(5): 484-93. PMID 22595156
9. Hadamitzky M, Achenbach S, Malhotra V, et al. Update on an International Registry for monitoring cardiac CT radiation dose [abstract]. J Cardiovasc Comput Tomogr. 2011;5(4S):S48.
10. Gerber TC, Carr JJ, Arai AE, et al. Ionizing radiation in cardiac imaging: a science advisory from the American Heart Association Committee on Cardiac Imaging of the Council on Clinical Cardiology and Committee on Cardiovascular Imaging and Intervention of the Council on Cardiovascular Radiology and Intervention. Circulation. Feb 24 2009; 119(7): 1056-65. PMID 19188512
11. Hausleiter J, Meyer T, Hermann F, et al. Estimated radiation dose associated with cardiac CT angiography. JAMA. Feb 04 2009; 301(5): 500-7. PMID 19190314
12. Eisenberg MJ, Afilalo J, Lawler PR, et al. Cancer risk related to low-dose ionizing radiation from cardiac imaging in patients after acute myocardial infarction. CMAJ. Mar 08 2011; 183(4): 430-6. PMID 21324846

13. Aglan I, Jodocy D, Hiehs S, et al. Clinical relevance and scope of accidental extracoronary findings in coronary computed tomography angiography: a cardiac versus thoracic FOV study. Eur J Radiol. Apr 2010; 74(1): 166-74. PMID 19268514
14. Husmann L, Tatsugami F, Aepli U, et al. Prevalence of noncardiac findings on low dose 64-slice computed tomography used for attenuation correction in myocardial perfusion imaging with SPECT. Int J Cardiovasc Imaging. Dec 2009; 25(8): 859-65. PMID 19662511
15. Kawano Y, Tamura A, Goto Y, et al. Incidental detection of cancers and other non-cardiac abnormalities on coronary multislice computed tomography. Am J Cardiol. Jun 01 2007; 99(11): 1608-9. PMID 17531590
16. Kirsch J, Araoz PA, Steinberg FB, et al. Prevalence and significance of incidental extracardiac findings at 64-multidetector coronary CTA. J Thorac Imaging. Nov 2007; 22(4): 330-4. PMID 18043387
17. Koonce J, Schoepf JU, Nguyen SA, et al. Extra-cardiac findings at cardiac CT: experience with 1,764 patients. Eur Radiol. Mar 2009; 19(3): 570-6. PMID 18925400
18. Lazoura O, Vassiou K, Kanavou T, et al. Incidental non-cardiac findings of a coronary angiography with a 128-slice multi-detector CT scanner: should we only concentrate on the heart?. Korean J Radiol. Jan-Feb 2010; 11(1): 60-8. PMID 20046496
19. Lehman SJ, Abbara S, Cury RC, et al. Significance of cardiac computed tomography incidental findings in acute chest pain. Am J Med. Jun 2009; 122(6): 543-9. PMID 19486717
20. Machaalany J, Yam Y, Ruddy TD, et al. Potential clinical and economic consequences of noncardiac incidental findings on cardiac computed tomography. J Am Coll Cardiol. Oct 13 2009; 54(16): 1533-41. PMID 19815125
21. Yorgun H, Kaya EB, Hazirolan T, et al. Prevalence of incidental pulmonary findings and early follow-up results in patients undergoing dual-source 64-slice computed tomography coronary angiography. J Comput Assist Tomogr. Mar-Apr 2010; 34(2): 296-301. PMID 20351524
22. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Contract Enhanced Cardiac Computed Tomographic Angiography for Coronary Artery Evaluation. TEC Assessments. 2005;Volume 20:Tab 4.
23. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Contrast-Enhanced Cardiac Computed Tomographic Angiography in the Diagnosis of Coronary Artery Stenosis or for Evaluation of Acute Chest Pain. TEC Assessments. 2006;Volume 21:Tab 5.
24. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Coronary Computed Tomographic Angiography in the Evaluation of Patients with Acute Chest Pain. TEC Assessments. 2011;Volume 26:Tab 9.
25. Gongora CA, Bavishi C, Uretsky S, et al. Acute chest pain evaluation using coronary computed tomography angiography compared with standard of care: a meta-analysis of randomised clinical trials. Heart. Feb 2018; 104(3): 215-221. PMID 28855273
26. Skelly AC, Hashimoto R, Buckley DI, et al. Noninvasive testing for coronary artery disease (Comparative Effectiveness Review No. 171). Rockville, MD: Agency for Healthcare Research and Quality; 2016.
27. Smulders MW, Kietselaer BLJH, Wildberger JE, et al. Initial Imaging-Guided Strategy Versus Routine Care in Patients With Non-ST-Segment Elevation Myocardial Infarction. J Am Coll Cardiol. Nov 19 2019; 74(20): 2466-2477. PMID 31727284
28. Levsky JM, Haramati LB, Spevack DM, et al. Coronary Computed Tomography Angiography Versus Stress Echocardiography in Acute Chest Pain: A Randomized Controlled Trial. JACC Cardiovasc Imaging. Sep 2018; 11(9): 1288-1297. PMID 29909113
29. Hamilton-Craig C, Fifoot A, Hansen M, et al. Diagnostic performance and cost of CT angiography versus stress ECG--a randomized prospective study of suspected acute

coronary syndrome chest pain in the emergency department (CT-COMPARE). Int J Cardiol. Dec 20 2014; 177(3): 867-73. PMID 25466568
30. Linde JJ, Kofoed KF, Sorgaard M, et al. Cardiac computed tomography guided treatment strategy in patients with recent acute-onset chest pain: results from the randomised, controlled trial: CArdiac cT in the treatment of acute CHest pain (CATCH). Int J Cardiol. Oct 15 2013; 168(6): 5257-62. PMID 23998546
31. Litt HI, Gatsonis C, Snyder B, et al. CT angiography for safe discharge of patients with possible acute coronary syndromes. N Engl J Med. Apr 12 2012; 366(15): 1393-403. PMID 22449295
32. Hoffmann U, Truong QA, Schoenfeld DA, et al. Coronary CT angiography versus standard evaluation in acute chest pain. N Engl J Med. Jul 26 2012; 367(4): 299-308. PMID 22830462
33. Goldstein JA, Chinnaiyan KM, Abidov A, et al. The CT-STAT (Coronary Computed Tomographic Angiography for Systematic Triage of Acute Chest Pain Patients to Treatment) trial. J Am Coll Cardiol. Sep 27 2011; 58(14): 1414-22. PMID 21939822
34. Goldstein JA, Gallagher MJ, O'Neill WW, et al. A randomized controlled trial of multi-slice coronary computed tomography for evaluation of acute chest pain. J Am Coll Cardiol. Feb 27 2007; 49(8): 863-71. PMID 17320744
35. Linde JJ, Hove JD, Sorgaard M, et al. Long-Term Clinical Impact of Coronary CT Angiography in Patients With Recent Acute-Onset Chest Pain: The Randomized Controlled CATCH Trial. JACC Cardiovasc Imaging. Dec 2015; 8(12): 1404-1413. PMID 26577263
36. Schlett CL, Banerji D, Siegel E, et al. Prognostic value of CT angiography for major adverse cardiac events in patients with acute chest pain from the emergency department: 2-year outcomes of the ROMICAT trial. JACC Cardiovasc Imaging. May 2011; 4(5): 481-91. PMID 21565735
37. Durand E, Bauer F, Mansencal N, et al. Head-to-head comparison of the diagnostic performance of coronary computed tomography angiography and dobutamine-stress echocardiography in the evaluation of acute chest pain with normal ECG findings and negative troponin tests: A prospective multicenter study. Int J Cardiol. Aug 15 2017; 241: 463-469. PMID 28325613
38. Fihn SD, Gardin JM, Abrams J, et al. 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS Guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, and the American College of Physicians, American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. J Am Coll Cardiol. Dec 18 2012; 60(24): e44-e164. PMID 23182125
39. Haase R, Schlattmann P, Gueret P, et al. Diagnosis of obstructive coronary artery disease using computed tomography angiography in patients with stable chest pain depending on clinical probability and in clinically important subgroups: meta-analysis of individual patient data. BMJ. Jun 12 2019; 365: l1945. PMID 31189617
40. Nielsen LH, Ortner N, Norgaard BL, et al. The diagnostic accuracy and outcomes after coronary computed tomography angiography vs. conventional functional testing in patients with stable angina pectoris: a systematic review and meta-analysis. Eur Heart J Cardiovasc Imaging. Sep 2014; 15(9): 961-71. PMID 24618659
41. Ollendorf DA, Kuba M, Pearson SD. The diagnostic performance of multi-slice coronary computed tomographic angiography: a systematic review. J Gen Intern Med. Mar 2011; 26(3): 307-16. PMID 21063800

42. Medical Advisory Secretariat. Non-invasive cardiac imaging technologies for the diagnosis of coronary artery disease: a summary of evidence-based analyses. Ont Health Technol Assess Ser. 2010; 10(7): 1-40. PMID 23074410
43. Foy AJ, Dhruva SS, Peterson B, et al. Coronary Computed Tomography Angiography vs Functional Stress Testing for Patients With Suspected Coronary Artery Disease: A Systematic Review and Meta-analysis. JAMA Intern Med. Nov 01 2017; 177(11): 1623-1631. PMID 28973101
44. Stillman AE, Gatsonis C, Lima JAC, et al. Coronary Computed Tomography Angiography Compared With Single Photon Emission Computed Tomography Myocardial Perfusion Imaging as a Guide to Optimal Medical Therapy in Patients Presenting With Stable Angina: The RESCUE Trial. J Am Heart Assoc. Dec 15 2020; 9(24): e017993. PMID 33283579
45. Newby DE, Adamson PD, Berry C, et al. Coronary CT Angiography and 5-Year Risk of Myocardial Infarction. N Engl J Med. Sep 06 2018; 379(10): 924-933. PMID 30145934
46. Chang HJ, Lin FY, Gebow D, et al. Selective Referral Using CCTA Versus Direct Referral for Individuals Referred to Invasive Coronary Angiography for Suspected CAD: A Randomized, Controlled, Open-Label Trial. JACC Cardiovasc Imaging. Jul 2019; 12(7 Pt 2): 1303-1312. PMID 30553687
47. Rudzinski PN, Kruk M, Kepka C, et al. The value of Coronary Artery computed Tomography as the first-line anatomical test for stable patients with indications for invasive angiography due to suspected Coronary Artery Disease: CAT-CAD randomized trial. J Cardiovasc Comput Tomogr. Nov 2018; 12(6): 472-479. PMID 30201310
48. Douglas PS, Hoffmann U, Patel MR, et al. Outcomes of anatomical versus functional testing for coronary artery disease. N Engl J Med. Apr 02 2015; 372(14): 1291-300. PMID 25773919
49. Newby D, Williams M, Hunter A, et al. CT coronary angiography in patients with suspected angina due to coronary heart disease (SCOT-HEART): an open-label, parallel-group, multicentre trial. Lancet. Jun 13 2015; 385(9985): 2383-91. PMID 25788230
50. McKavanagh P, Lusk L, Ball PA, et al. A comparison of cardiac computerized tomography and exercise stress electrocardiogram test for the investigation of stable chest pain: the clinical results of the CAPP randomized prospective trial. Eur Heart J Cardiovasc Imaging. Apr 2015; 16(4): 441-8. PMID 25473041
51. Adamson PD, Williams MC, Dweck MR, et al. Guiding Therapy by Coronary CT Angiography Improves Outcomes in Patients With Stable Chest Pain. J Am Coll Cardiol. Oct 22 2019; 74(16): 2058-2070. PMID 31623764
52. Hoffmann U, Ferencik M, Udelson JE, et al. Prognostic Value of Noninvasive Cardiovascular Testing in Patients With Stable Chest Pain: Insights From the PROMISE Trial (Prospective Multicenter Imaging Study for Evaluation of Chest Pain). Circulation. Jun 13 2017; 135(24): 2320-2332. PMID 28389572
53. Williams MC, Hunter A, Shah A, et al. Symptoms and quality of life in patients with suspected angina undergoing CT coronary angiography: a randomised controlled trial. Heart. Jul 2017; 103(13): 995-1001. PMID 28246175
54. Berbarie RF, Dockery WD, Johnson KB, et al. Use of multislice computed tomographic coronary angiography for the diagnosis of anomalous coronary arteries. Am J Cardiol. Aug 01 2006; 98(3): 402-6. PMID 16860032
55. Datta J, White CS, Gilkeson RC, et al. Anomalous coronary arteries in adults: depiction at multi-detector row CT angiography. Radiology. Jun 2005; 235(3): 812-8. PMID 15833984
56. Romano S, Morra A, Del Borrello M, et al. Multi-slice computed tomography and the detection of anomalies of coronary arteries. J Cardiovasc Med (Hagerstown). Feb 2008; 9(2): 187-94. PMID 18192814

57. Schmitt R, Froehner S, Brunn J, et al. Congenital anomalies of the coronary arteries: imaging with contrast-enhanced, multidetector computed tomography. Eur Radiol. Jun 2005; 15(6): 1110-21. PMID 15756551
58. Stein PD, Yaekoub AY, Matta F, et al. 64-slice CT for diagnosis of coronary artery disease: a systematic review. Am J Med. Aug 2008; 121(8): 715-25. PMID 18691486
59. Auguadro C, Manfredi M, Scalise F, et al. Multislice computed tomography for the evaluation of coronary bypass grafts and native coronary arteries: comparison with traditional angiography. J Cardiovasc Med (Hagerstown). Jun 2009; 10(6): 454-60. PMID 19395978
60. Tochii M, Takagi Y, Anno H, et al. Accuracy of 64-slice multidetector computed tomography for diseased coronary artery graft detection. Ann Thorac Surg. Jun 2010; 89(6): 1906-11. PMID 20494047
61. McEvoy JW, Blaha MJ, Nasir K, et al. Impact of coronary computed tomographic angiography results on patient and physician behavior in a low-risk population. Arch Intern Med. Jul 25 2011; 171(14): 1260-8. PMID 21606093
62. Muhlestein JB, Lappe DL, Lima JA, et al. Effect of screening for coronary artery disease using CT angiography on mortality and cardiac events in high-risk patients with diabetes: the FACTOR-64 randomized clinical trial. JAMA. Dec 03 2014; 312(21): 2234-43. PMID 25402757
63. Koshy AN, Ha FJ, Gow PJ, et al. Computed tomographic coronary angiography in risk stratification prior to non-cardiac surgery: a systematic review and meta-analysis. Heart. Sep 2019; 105(17): 1335-1342. PMID 31018953
64. Wolk MJ, Bailey SR, Doherty JU, et al. ACCF/AHA/ASE/ASNC/HFSA/HRS/SCAI/SCCT/SCMR/STS 2013 multimodality appropriate use criteria for the detection and risk assessment of stable ischemic heart disease: a report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, American Heart Association, American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Failure Society of America, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance, and Society of Thoracic Surgeons. J Am Coll Cardiol. Feb 04 2014; 63(4): 380-406. PMID 24355759
65. National Institute for Health and Care Excellence (NICE). Chest pain of recent onset: assessment and diagnosis [CG95]. 2016; https://www.nice.org.uk/guidance/CG95. Accessed January 2022
66. Narula J, Chandrashekhar Y, Ahmadi A, et al. SCCT 2021 Expert Consensus Document on Coronary Computed Tomographic Angiography: A Report of the Society of Cardiovascular Computed Tomography. J Cardiovasc Comput Tomogr. May-Jun 2021; 15(3): 192-217. PMID 33303384
64. Blue Cross Blue Shield Association. Contrast-Enhanced Coronary Computed Tomography Angiography for Coronary Artery Evaluation. Medical Policy Reference Manual. MPRM 6.01.43. Last updated October 2021.
65. HAYES Medical Technology Directory. Multislice Computed Tomography for Detection of Coronary Artery Disease. Lansdale, PA: HAYES, Inc., Published July 2007. Last updated July 2011. Archived August 2012; Outdated.
66. Smulders MW, Kietselaer BLJH, Wildberger JE, et al. Initial Imaging-Guided Strategy Versus Routine Care in Patients With Non-ST-Segment Elevation Myocardial Infarction. J Am Coll Cardiol. Nov 19 2019; 74(20): 2466-2477. PMID 31727284
67. Adamson PD, Williams MC, Dweck MR, et al. Guiding Therapy by Coronary CT Angiography Improves Outcomes in Patients With Stable Chest Pain. J Am Coll Cardiol. Oct 22 2019; 74(16): 2058-2070. PMID 31623764

The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through January, 2022, the date the research was completed.

Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
1/19/06	1/19/06	1/17/06	Joint medical policy established
7/1/07	6/19/07	5/27/07	Routine maintenance with review of new literature.
11/1/08	8/19/08	10/30/08	Routine maintenance
3/1/11	2/8/11	1/4/11	Deleted "T" codes, added new LCD codes. Changed status of 0144T (new code 75571) from established to experimental/investigational. Updated references. Changed title from "Multi-Slice CT Angiography of Coronary Vessels (CCTA)" to "Contrast-Enhanced Computed Tomography Angiography (CTA, CCTA, MDCT, MSCT) of the Heart and/or Coronary Arteries" as multi-slice CTA is only one form of coronary CTA.
11/1/12	8/21/12	8/21/12	Policy reformatted to mirror LCD. Added additional information regarding uses for cardiac CT for morphology.
7/1/13	4/16/13	4/22/13	Inclusionary guidelines updated to indicate that CCTA does not have to be done in a Consortium-approved facility if the services were done in an Emergency Room setting. References updated.
2/1/14	8/20/13	9/3/13	Deleted language stating that CCTA must be done in a facility that participates in the BCBSM/BCN collaborative Quality Initiative for Emerging Non-Invasive Cardiovascular Imaging, as this testing is being opened up to other facilities. Effective date set for 2/1/14 for administrative purposes. No other changes.
5/1/15	2/17/15	2/27/15	Routine maintenance References and rationale updated. Added new Medicare LCD to Government Regulations section.
5/1/16	2/16/16	2/16/16	Routine maintenance, references and rationale updated. Updated LCD LCD information.
5/1/17	2/21/17	2/21/17	Routine maintenance. References and rationale updated.
5/1/18	2/20/18	2/20/18	Routine maintenance. Rationale updated; references 29 & 31 added. No change in policy status.

5/1/19	2/19/19		Routine policy maintenance. References # 12, 14 and 21-23 added. No change in policy status.
5/1/20	2/18/20		Rationale updated, reference # 25, 31-33 and 63 were added. No change in policy status.
5/1/21	2/16/21		Routine policy maintenance. References # 66 and 67 added. No change in policy status.
5/1/22	2/15/22		Routine policy maintenance, references # 44 and 66 added. No change in policy status.

Next Review Date: 1st Qtr. 2023

BLUE CARE NETWORK BENEFIT COVERAGE
POLICY: CONTRAST-ENHANCED COMPUTED TOMOGRAPHY ANGIOGRAPHY OF THE HEART AND/OR CORONARY ARTERIES (CTA, CCTA)

I. Coverage Determination:

Commercial HMO (includes Self-Funded groups unless otherwise specified)	Covered, policy guidelines apply. 75571 is non-covered.
BCNA (Medicare Advantage)	See government section.
BCN65 (Medicare Complementary)	Coinsurance covered if primary Medicare covers the service. Must be performed at a Medicare approved facility.

II. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Payment is based on BCN payment rules, individual certificate and certificate riders.
- Appropriate copayments will apply. Refer to certificate and applicable riders for detailed information.
- CPT - HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.