Medical Policy

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Title: **Contrast-Enhanced Coronary Computed Tomography Angiography (CCTA) for Coronary Artery Evaluation**

See also: *Computed Tomography to Detect Coronary Artery Calcification*
CTA and MRA of the Head, Neck, Abdomen, Pelvis, and Lower Extremities
Cardiac Computed Tomography (CT)

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Populations	Interventions	Comparators	Outcomes
Individuals: • With acute chest pain and suspected coronary artery disease in the emergency setting, at intermediate to low risk	Interventions of interest are: • Coronary computed tomography angiography	Comparators of interest are: • Standard emergency department care • Alternative noninvasive testing and standard emergency department care	Relevant outcomes include: • Overall survival • Morbid events • Resource utilization
Individuals: • With stable chest pain, intermediate risk of coronary artery disease, meeting guideline criteria for noninvasive testing	Interventions of interest are: • Coronary computed tomography angiography	Comparators of interest are: • Alternative noninvasive testing and standard care	Relevant outcomes include: • Overall survival • Test accuracy • Morbid events • Resource utilization
Individuals: • With suspected anomalous coronary arteries	Interventions of interest are: • Coronary computed tomography angiography	Comparators of interest are: • Standard of care	Relevant outcomes include: • Overall survival • Test accuracy • Morbid events • Resource utilization

DESCRIPTION

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 alternative to current diagnostic tests for cardiac ischemia (ie, non-invasive stress testing and/or coronary angiography).

OBJECTIVE

The objective of this policy is to evaluate whether coronary computed tomography angiography (CCTA) improves health outcomes compared to alternative testing strategies. Three major indications for cardiac or coronary computed tomography angiography are considered: (1) evaluation of patients with acute chest pain without known coronary disease presenting in the emergency department (ED) setting, (2) evaluation of stable patients with signs and symptoms of coronary artery disease in the non-ED setting, and (3) evaluation of anomalous coronary arteries.

BACKGROUND

Coronary Artery Disease

Various noninvasive tests are used to diagnose coronary artery disease (CAD). They can be broadly classified as those that detect functional or hemodynamic consequences of obstruction and ischemia (exercise treadmill testing, myocardial perfusion imaging, stress echocardiography with or without contrast), and others that identify the anatomic obstruction itself (coronary computed tomography angiography [CCTA], coronary magnetic resonance imaging).[1] Functional testing involves inducing ischemia by exercise or pharmacologic stress and detecting its consequences. However, not all patients are candidates. For example, obesity or obstructive lung disease can make obtaining

echocardiographic images of sufficient quality difficult. Conversely, the presence of coronary calcifications can impede detecting coronary anatomy with CCTA.

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.

Contrast-enhanced 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 (ie, those associated with <50% stenosis) because their presence is associated with increased cardiac event rates.[2] CCTA also can visualize the presence and composition of these plaques and quantify plaque burden better than conventional angiography, which only visualizes the vascular lumen. Plaque presence has been shown to have prognostic importance.

Coronary Arterial Anomalies

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

Radiation Exposure

Levels of radiation delivered with current generation scanners using reduction techniques (prospective gating and spiral acquisition) have declined substantially—typically to under 10 mSv. For example, an international registry developed to monitor CCTA radiation exposure recently reported a median of 2.4 mSv (interquartile range, 1.3-5.5).[3] By comparison, radiation exposure accompanying rest-stress perfusion imaging varies by isotope used—approximately 5 mSv for rubidium 82 (positron emission tomography), 14

mSv for fluorine 18 fluorodeoxyglucose, 9 mSv for sestamibi (single-photon emission computed tomography), and 41 mSv for thallium; during diagnostic invasive coronary angiography, approximately 7 mSv is delivered.[4] Electron-beam computed tomography using electrocardiogram triggering delivers the lowest dose (0.7-1.1 mSv with 3-mm sections). Any cancer risk due to radiation exposure from a single cardiac imaging test depends on age (higher with younger age at exposure) and sex (greater for women).[5-7] Empirical data have suggested that every 10 mSv of exposure is associated with a 3% increase in cancer incidence over 5 years.[8]

The use of electron-beam computed tomography or helical computed tomography to detect coronary artery calcification is not addressed in this policy.

REGULATORY STATUS

Coronary computed tomography angiography (CCTA) is performed using multidetector-row computed tomography, and multiple devices have been cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) clearance process. Current machines are equipped with at least 64 detector rows. Intravenous iodinated contrast agents used for CCTA also have received FDA approval.

POLICY

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

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

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

D.   Contrast-enhanced coronary computed tomography angiography for coronary artery evaluation is considered **experimental / investigational** for all other indications.

Policy Guidelines

The 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS guidelines for the diagnosis and management of patients with stable heart disease have several class I recommendations regarding the use of noninvasive testing in patients with suspected stable ischemic heart disease. A class I recommendation indicates that a test should be performed. In general, patients with at least intermediate risk (10-90% risk by standard risk prediction

instruments) are recommended to have some kind of test, the choice of test depending on interpretability of the ECG, capability to exercise, and presence of comorbidity.

Pretest Probability of CAD by age, gender, and symptoms*

Age (yrs)	Gender	Typical / Definite Angina Pectoris	Atypical / Probable Angina Pectoris	Nonanginal Chest Pain	Asymptomatic
< 39	Men	Intermediate	Intermediate	Low	Very Low
	Women	Intermediate	Very Low	Very Low	Very Low
40-49	Men	High	Intermediate	Intermediate	Low
	Women	Intermediate	Low	Very Low	Very Low
50-59	Men	High	Intermediate	Intermediate	Low
	Women	Intermediate	Intermediate	Low	Very Low
> 60	Men	High	Intermediate	Intermediate	Low
	Women	High	Intermediate	Intermediate	Low

High: >90% pretest probability. Intermediate: between 10% and 90% pretest probability. Low: between 5% and 10% pretest probability. Very low: <5% pretest probability. CAD: coronary artery disease. *Modified from the ACC/AHA Exercise Testing Guidelines to reflect all age ranges.[60]

RATIONALE

This policy was originally based on a literature search of the MEDLINE database and updated with subsequent literature review and/or repeat TEC Assessments.[9-11] The most recent literature review covers the period through July 10, 2018.

This review has been informed by several TEC Assessment (2005, 2006, 2011).[9-11]

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 in 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 the use of CCTA improve the net health outcome of patients with acute chest pain?

The following PICOTS were used to select literature to inform this review.

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

Interventions
The intervention of interest is CCTA.

Comparators
The following tests and practices are currently being used to make decisions about managing acute chest pain and suspected CAD: 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 (ICA).

Timing
The time of interest is in the first few days after admission to an ED and after several years or more after CCTA to evaluate event rates.

Setting
CCTA is administered in hospital ED setting.

Technically Reliable
Assessment of technical reliability focuses on specific tests and operators and requires review of unpublished and often proprietary information. Review of specific tests, operators, and unpublished data are outside the scope of this evidence review and alternative sources exist. This evidence review focuses on the clinical validity and clinical utility.

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).

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

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 avoid unnecessary 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).

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 results in 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. See Tables 1 and 2 for 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 for the Agency for Healthcare Research and Quality that assessed noninvasive testing for CAD.[13] Reviewers 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 (low strength of evidence).
- After CCTA, referral for ICA and revascularization
  - was more common than after functional testing (high strength of evidence).
  - was similar compared with single-photon emission computed tomography and usual care (low strength of evidence).
- After CCTA, additional testing in the ED setting
  - was less common compared with usual care (moderate strength of evidence).
  - was more common than after single-photon emission computed tomography (high strength of evidence).

- After CCTA, hospitalization
  - was less common compared with 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.

A TEC Assessment (2011) examined evidence on patients with acute chest pain and without known CAD.[11]

Randomized Controlled Trials: RCTs and prospective observational studies were identified. 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
Levsky et al (2018)[14]	U.S.	1	2011-2016	Patients with acute chest pain or pressure for whom noninvasive testing 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 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 (n=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 tomographic angiography; 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.

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.

Hamilton-Craig et al (2014) reported on the CT-COMPARE trial, which assessed the length of stay and patient costs in 562 patients presenting to the ED with low-to-intermediate risk chest pain who received CCTA or exercise stress testing.[15] Length of stay was significantly reduced in the CCTA patients compared with the exercise testing patients. Clinical outcomes at 30 days and at 12 months did not differ.

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), h[b]	FU, mo
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 tomographic angiography; ED: emergency department; FU: follow-up; HR: hazard ratio; 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 acute coronary syndrome 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 gaps tables (see 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. Relevance Gaps for RCTs Assessing CCTA in ED Settings

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Duration of Follow-Up[e]
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 40-74 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 evidence gaps stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
CCTA: coronary computed tomographic 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 Gaps of RCTs Assessing CCTA in ED Settings

Study	Selection[a]	Blinding[b]	Delivery of Test[c]	Selective Reporting[d]	Data Completeness[e]	Statistical[f]
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 evidence gaps stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
CCTA: coronary computed tomographic angiography; ED: emergency department; MACE: major adverse cardiac event; RCT: randomized controlled trial:
[a] Selection key: 1. Selection not described; 2. Selection not random or consecutive (ie, convenience).
[b] Blinding key: 1. Not blinded to results of reference or other comparator tests.
[c] Test Delivery key: 1. Timing of delivery of index or reference test not described; 2. Timing of index and comparator tests not same; 3. Procedure for interpreting tests not described; 4. Expertise of evaluators not described.
[d] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[e] Data Completeness key: 1. Inadequate description of indeterminate and missing samples; 2. High number of samples excluded; 3. High loss to follow-up or missing data.
[f] Statistical key: 1. Confidence intervals and/or p values not reported; 2. Comparison to other tests not reported.

Follow-Up Studies: Linde et al (2015) reported long-term follow-up[21] from the CATCH trial.[16] Results from long-term follow-up studies are tabulated in Table 7.

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 in 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 because patients are safely and quickly discharged from the ED with no adverse outcomes among patients with negative CCTA examinations.

Other important outcomes that require consideration when comparing technologies include ICA rates, use of a second noninvasive test, radiation exposure, and follow-up of any incidental findings. Some studies have shown that subsequent invasive testing is more frequent in patients who received CCTA. Studies have differed over which treatment strategies result in higher overall radiation exposure. Incidental findings after CCTA are common and lead to further testing, but the impact of these findings on subsequent health outcomes is uncertain.

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 the 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 (eg, 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 the use of CCTA improve the net health outcome of patients with stable chest pain?

The following PICOTS were used to select literature to inform this review.

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

Interventions
The intervention of interest is 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.

Timing
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.

Setting
CCTA is administered in a cardiology clinic setting equipped with standard noninvasive testing for CAD and CCTA.

Technically Reliable
Assessment of technical reliability focuses on specific tests and operators and requires review of unpublished and often proprietary information. Review of specific tests, operators, and unpublished data are outside the scope of this evidence review and alternative sources exist. This evidence review focuses on the clinical validity and clinical utility.

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).

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%.

For CCTA, estimates of sensitivity from various systematic reviews are considerably higher (see Table 11). The guideline statement from Fihn et al (2012) cited studies reporting sensitivities between 93% and 97%.[24] A systematic review by Ollendorf et al (2011) of 42 studies showed a summary sensitivity estimate of 98% and a specificity of 85%.[25] A meta-analysis of 8 studies conducted by the Health Quality Ontario (2010) showed a summary sensitivity estimate of 97.7%

and a specificity of 79%.[26] In the meta-analysis by Nielsen et al (2014), sensitivity rates for CCTA varied between 98% and 99% (depending on the analysis group).[27]

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	70-77
Pharmacologic stress echocardiography	85-90	79-90
Exercise stress echocardiography	70-85	77-89
Exercise myocardial perfusion imaging	82-88	70-88
Pharmacologic stress myocardial perfusion imaging	88-91	75-90

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

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Table 11. Sensitivity and Specificity Estimates for CCTA From Guidelines and Meta-Analyses

Study	Study Type	Sensitivity (Range or Single Estimates), %	Specificity (Range or Single Estimates), %
Nielsen et al (2014)[27]	Meta-analysis	98-99	82-88
Fihn et al (2012)[24]	Guideline	93-97	80-90
Ollendorf et al (2011)[25]	Meta-analysis	98	85
Health Quality Ontario (2010)[26]	Meta-analysis	97.7	79

CCTA: coronary computed tomography angiography.

Case Series: Sandstedt et al (2018) published a case series evaluating 1205 patients with suspected CAD who underwent CCTA at a single center.[28] Most patients had normal findings (n=668 [55.4%]). Of the 218 patients who underwent ICA, 149 patients had obstructive stenosis, 49 patients had nonobstructive stenosis, and 20 patients did not have evidence of stenosis. The study had several limitations, including a high number of exclusions because of poor image quality, a single-reader clinical evaluation, and limitations inherent of a single-center study. Tables 12 and 13 summarize series characteristics and results.

Table 12. Characteristics of Key Case Series

Study	Country	Participants	Treatment Delivery	Follow-Up
Sandstedt et al (2018)[28]	Sweden	Suspected CAD without previous CAD	CCTA	7.5 y (median 3.1 y; IQR, 425-1793 d)

IQR: interquartile range; CAD: coronary artery disease; CCTA: coronary computed tomographic angiography.

Table 13. Results of Key Case Series

Study	Treatment	Incidence of CAD	Incidence of MACE	Predictors of MACE
Sandstedt et al (2018)[28]	1205 consecutive patients underwent CCTA at a single center	360 (29.9%) had nonobstructive CAD; 177 (14.7%) had obstructive CAD	1.0% of patients with normal coronary arteries experienced ≥1 MACE; 4.6% of those with nonobstructive CAD; 20.7% of those with obstructive CAD	• Nonobstructive CAD predicted MACE (HR=3.48; 95% CI, 1.13 to 10.67; p=0.029) • Obstructive CAD predicted MACE (HR=29.26; 95% CI, 10.86 to 78.83; p<0.001)

CAD: coronary artery disease; CCTA: coronary computed tomographic angiography; CI: confidence interval; HR: hazard ratio; MACE: major adverse cardiac event.

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 avoid unnecessary 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 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 14 and 15 summarize review characteristics and results.

Table 14. 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 tomographic angiography; NR: not reported; RCT: randomized controlled trial.

Table 15. Results of Systematic Reviews Assessing CCTA for Stable Chest Pain

Study	Incidence of ICA, %	Revascularization, %	Adverse Events, %	New Diagnoses 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 to 4.04) Statins: 2.03 (1.09 to 3.76)

CAD: coronary artery disease; CCTA: coronary computed tomographic 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 16 and 17 summarize trial characteristics and results.

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

Study; Trial	Countries	Sites	Dates	Participants	Interventions	
					Active	**Comparator**
Douglas et al (2015)[30]; 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)[31]; SCOT-HEART	U.K.	12	2010-2014	Patients referred for assessment of suspected angina due to CHD	2073 to standard of care plus CCTA	2073 to standard of care
McKavanagh et al (2015)[32]; 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 tomographic angiography; EST: exercise stress electrocardiogram test; NR: not reported; RCT: randomized controlled trial.

Douglas et al (2014) 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.[30] CCTA also did not meet prespecified noninferiority criteria compared with alternative testing. Some clinical outcomes assessed at 12 months favored CCTA, but the differences were nonsignificant. Coronary catheterization rates and revascularization rates were higher in the CCTA group. In 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.[33] However, CCTA had better discriminatory ability than functional testing to predict events (eg, 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.[31] 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.[34] 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 CAPP trial, McKavanagh et al (2015) randomized 500 patients with stable chest pain to CCTA or exercise stress testing.[32] 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 17. Results of Key RCTs Assessing CCTA in Stable Chest Pain

Study	Death or Nonfatal Myocardial Infarction	Angina Stability	Hospitalization
Douglas et al (2015)[30]			
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)[31]			
CCTA, n (%)	26		511 (12.3)
Standard care, n (%)	42		247 (11.9)
HR (95% CI)	0.616 (0.378 to 1.006)		0.928 (0.780 to 1.104)
p	0.527		0.399
McKavanagh et al (2015)[32]			
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 tomographic angiography; HR: hazard ratio; MD: mean difference; RCT: randomized controlled trial.
Tables 18 and 19 display notable the gaps identified in each trial.

Table 18. Relevance Gaps of RCTs Assessing CCTA in Stable Chest Pain

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Duration of Follow-Up[e]
Douglas et al (2015)[30]				1. Test performance and utility not addressed	
SCOT-HEART Investigators (2015)[31]	4. Patients >75 y excluded				
McKavanagh et al (2015)[32]	4. Low number of diabetics included due to exclusion criteria		1, 2. Noted difficulty in contrasting the results of anatomic and functional tests		

The evidence gaps stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
CCTA: coronary computed tomographic 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 19. Study Design and Conduct Gaps of RCTs Assessing CCTA for Stable Chest Pain

Study	Selection[a]	Blinding[b]	Delivery of Test[c]	Selective Reporting[d]	Data Completeness[e]	Statistical[f]
Douglas et al (2015)[30]						
SCOT-HEART Investigators (2015)[31]		1.-3. Treatments and outcomes not blinded and potential bias among attending clinicians was present				
McKavanagh et al (2015)[32]					3. Study not powered to evaluate prognosis or adverse CAD events	

The evidence gaps stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
CAD: coronary artery disease; CCTA: coronary computed tomographic angiography; RCT: randomized controlled trial.
[a] Selection key: 1. Selection not described; 2. Selection not random or consecutive (ie, convenience).
[b] Blinding key: 1. Not blinded to results of reference or other comparator tests.
[c] Test Delivery key: 1. Timing of delivery of index or reference test not described; 2. Timing of index and comparator tests not same; 3. Procedure for interpreting tests not described; 4. Expertise of evaluators not described.
[d] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[e] Data Completeness key: 1. Inadequate description of indeterminate and missing samples; 2. High number of samples excluded; 3. High loss to follow-up or missing data.
[f] Statistical key: 1. Confidence intervals and/or p values not reported; 2. Comparison to other tests not reported.

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

Nielsen et al (2013) conducted an observational trial comparing patients who underwent CCTA with those having exercise stress testing.[35] Patients had a low-to-intermediate pretest probability of CAD and presented with suspected angina. Patients were followed for 12 months after the initial test and assessed for occurrence of major adverse events (eg, cardiac death, nonfatal MI). Subsequent utilization of cardiovascular tests and therapy were also compared between groups. Clinical outcomes were not formally compared because there were few clinical events. No deaths were reported during the follow-up period. Three patients in the exercise testing group had MIs within 12 months. For downstream test utilization, the exercise test group had greater subsequent use of perfusion imaging (9% vs 4%, p=0.03). Rates of ICA and revascularization did not differ significantly between groups.

In 2825 patients evaluated for stable angina and suspected CAD in Japan, Yamauchi et al (2012) examined outcomes after initial CCTA (n=625), MPI (n=1205), and angiography (n=950).[36] Average follow-up was 1.4 years. In a Cox proportional hazards model adjusted for potential confounders, the relative hazard rates of major cardiac events after MPI or CCTA were lower than after angiography; annual rates were 2.6%, 2.1%, and 7.0%, respectively. Revascularization rates were higher after CCTA than MPI (OR=1.6; 95% CI, 1.2 to 2.2).

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.

The nonrandomized studies of CCTA have several methodologic shortcomings, including reliance on administrative data and inability to assess and adjust fully for potential confounding. The findings have shown little difference in patient outcomes between diagnostic strategies. Downstream utilization of medical care showed variable findings.

Suspected Anomalous Coronary Arteries
Anomalous coronary arteries are an uncommon finding during angiography, occurring in approximately 1% of coronary angiograms completed for evaluation of chest pain. However, these congenital anomalies can be clinically important depending on the course of the anomalous arteries. A number of case series have consistently reported that CCTA can delineate the course of these anomalous arteries, even when conventional angiography cannot.[37-40] 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.

Clinical Context and Therapy 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 PICOTS were used to select literature to inform this review.

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

Interventions
The therapy being considered is CCTA.

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.

Timing
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.

Setting
CCTA is administered in cardiology clinic setting equipped with standard noninvasive testing for CAD and CCTA.

Technically Reliable
Assessment of technical reliability focuses on specific tests and operators and requires review of unpublished and often proprietary information. Review of specific tests, operators, and unpublished data are outside the scope of this evidence review and alternative sources exist. This evidence review focuses on the clinical validity and clinical utility.

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).

Incidental Findings and Radiation Exposure
A number of studies using scanners with 64 or more detector rows were identified.[41-49] Incidental findings were frequent (26.6%-68.7%) with pulmonary nodules typically the most common and cancers typically more rare ($\approx$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.[41] As expected, incidental findings were less frequent in

the restricted field (clinically significant findings in 14% vs 24% when the entire field was imaged).

Exposure to ionizing radiation increases lifetime cancer risk.[50] Three studies have estimated excess cancer risks due to radiation exposure from CCTA.[6,7,51] 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.[51] Smith-Bindman et al (2009) estimated that cancer would develop in 1 of 270 women and 1 of 600 men age 40 undergoing CCTA with a 22-mSv dose.[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 per 1000 men (1/143) and 23 per 1000 women (1/43). However, estimated radiation exposure used in these studies was considerably higher than received with current scanners—now typically under 10 mSv and often less than 5 mSv with contemporary machines and radiation reduction techniques. For example, in the 47-center PROTECTION I study enrolling 685 patients, the mean radiation dose was 3.6 mSv, using a sequential scanning technique.[52] In a study of patients undergoing an axial scanning protocol, Hausleiter et al (2012) reported on 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.[53]

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 avoid unnecessary 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.

Chain of Evidence
Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.

Because the clinical validity of CCTA for suspected anomalous coronary arteries has not been established, a chain of evidence cannot be constructed.

Subsection Summary: Incidental Findings and Radiation Exposure
Although studies of incidental findings and radiation exposure raise issues regarding the potential for adverse effects of CCTA, there is insufficient evidence that the magnitude of these effects is important for ascertaining the net benefit or risk of CCTA in this setting.

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 less technically challenging 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 systematic review, including results from 64-slice scanners, Stein et al (2008) reported high sensitivity (98%; 95% CI, 95% to 99%; 740 segments) and specificity (97%; 95% CI, 94% to 97%).[54] Other small studies have reported high sensitivity and specificity.[55,56] 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 evaluating in-stent restenosis presents other technical challenges—motion, beam-hardening, and partial volume averaging. Whether these challenges can be 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 1000 patients undergoing CCTA or control intervention of 1000 similar patients.[57] Findings reported in this study were abnormal in 215 screened patients. Over 18 months of follow-up, screening was associated with more invasive testing, 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.[58] 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 (CCTA, 6.2% vs control, 7.6%; HR=0.80; p=0.38).

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

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 randomized controlled trials, a systematic review, and a prospective head-to-head study comparing CCTA with an alternative noninvasive test. Relevant outcomes are overall survival, morbid events, and resource utilization. Trials have shown similar patient outcomes, with faster patient discharges from the emergency department, and lower short-term costs. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

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

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

PRACTICE GUIDELINES AND POSITION STATEMENTS

<u>American College of Cardiology Foundation et al</u>
The American College of Cardiology Foundation (ACCF) and several other medical societies issued joint guidelines for management of patients with stable ischemic heart disease in 2012 (see Table 20).[24]

Table 20. Joint Guidelines on Management of Stable Ischemic Heart Disease

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 coronary disease			
	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		

Diagnosis	Recommendation	Class	LOE
	"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.[59] 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.[60]

U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATIONS
No U.S. Preventive Services Task Force recommendations for CCTA have been identified.

ONGOING AND UNPUBLISHED CLINICAL TRIALS
Some currently unpublished trials that might influence this review are listed in Table 21.

Table 21. Summary of Key Trials

NCT Number	Title	Enrollment	Completion Date
Ongoing			
NCT01283659	IMAGE-HF Project I-C: Computed Tomographic Coronary Angiography for Heart Failure Patients (CTA-HF)	253	Dec 2018
NCT02400229	Diagnostic Imaging Strategies for Patients With Stable Chest Pain and Intermediate Risk of Coronary Artery Disease (DISCHARGE)	3546	Sep 2019
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	2500	Dec 2019
Unpublished			

NCT Number	Title	Enrollment	Completion Date
NCT02291484	Comprehensive Cardiac CT Versus Exercise Testing in Suspected Coronary Artery Disease (2) (CRESCENT2)	250	May 2016 (completed)
NCT01384448	Stress Echocardiography and Heart Computed Tomography (CT) Scan in Emergency Department Patients With Chest Pain	400	Feb 2017 (completed)
NCT01559467	The Supplementary Role of Non-invasive Imaging to Routine Clinical Practice in Suspected Non-ST-elevation Myocardial Infarction (CARMENTA)	300	June 2017 (completed)

NCT: national clinical trial; ISRCTN: International Standard Registered Clinical/soCial sTudy Number.

CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

CPT/HCPCS

75574　　Computed tomographic angiography, heart, coronary arteries and bypass grafts (when present), with contrast material, including 3D image postprocessing (including evaluation of cardiac structure and morphology, assessment of cardiac function, and evaluation of venous structures, if performed)

ICD-10 Diagnoses

I20.8　　Other forms of angina pectoris
I25.10　　Atherosclerotic heart disease of native coronary artery without angina pectoris
I25.110　　Atherosclerotic heart disease of native coronary artery with unstable angina pectoris
I25.111　　Atherosclerotic heart disease of native coronary artery with angina pectoris with documented spasm
I25.118　　Atherosclerotic heart disease of native coronary artery with other forms of angina pectoris
I25.119　　Atherosclerotic heart disease of native coronary artery with unspecified angina pectoris
I25.700　　Atherosclerosis of coronary artery bypass graft(s), unspecified, with unstable angina pectoris
I25.701　　Atherosclerosis of coronary artery bypass graft(s), unspecified, with angina pectoris with documented spasm
I25.708　　Atherosclerosis of coronary artery bypass graft(s), unspecified, with other forms of angina pectoris
I25.709　　Atherosclerosis of coronary artery bypass graft(s), unspecified, with unspecified angina pectoris
I25.710　　Atherosclerosis of autologous vein coronary artery bypass graft(s) with unstable angina pectoris
I25.711　　Atherosclerosis of autologous vein coronary artery bypass graft(s) with angina pectoris with documented spasm
I25.718　　Atherosclerosis of autologous vein coronary artery bypass graft(s) with other forms of angina pectoris

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I25.719	Atherosclerosis of autologous vein coronary artery bypass graft(s) with unspecified angina pectoris
I25.720	Atherosclerosis of autologous artery coronary artery bypass graft(s) with unstable angina pectoris
I25.721	Atherosclerosis of autologous artery coronary artery bypass graft(s) with angina pectoris with documented spasm
I25.728	Atherosclerosis of autologous artery coronary artery bypass graft(s) with other forms of angina pectoris
I25.729	Atherosclerosis of autologous artery coronary artery bypass graft(s) with unspecified angina pectoris
I25.730	Atherosclerosis of nonautologous biological coronary artery bypass graft(s) with unstable angina pectoris
I25.731	Atherosclerosis of nonautologous biological coronary artery bypass graft(s) with angina pectoris with documented spasm
I25.738	Atherosclerosis of nonautologous biological coronary artery bypass graft(s) with other forms of angina pectoris
I25.739	Atherosclerosis of nonautologous biological coronary artery bypass graft(s) with unspecified angina pectoris
I25.790	Atherosclerosis of other coronary artery bypass graft(s) with unstable angina pectoris
I25.791	Atherosclerosis of other coronary artery bypass graft(s) with angina pectoris with documented spasm
I25.798	Atherosclerosis of other coronary artery bypass graft(s) with other forms of angina pectoris
I25.799	Atherosclerosis of other coronary artery bypass graft(s) with unspecified angina pectoris
I25.810	Atherosclerosis of coronary artery bypass graft(s) without angina pectoris

REVISIONS

01-10-2006	In "Policy" section, deleted old policy and added "Computed tomographic angiography (CTA) is considered experimental/investigational for the evaluation of coronary arteries including but not limited to the following: 1. Screening for coronary artery disease (CAD), either in asymptomatic subjects or as part of a preoperative evaluation 2. Diagnosis of CAD, in patients with acute or non-acute symptoms, or after a coronary intervention 3. Delineation of a coronary artery anatomy or anomaly Computed tomographic angiography (CTA) of other arteries may be indicated when medically necessity is properly documented."
	In "Coding", Covered Diagnosis section added "Note: The use of any diagnosis code does not guarantee reimbursement. Medical necessity will be based on documentation in the medical record."
	In "Reference" Government Agency; Medical Society; and Other Authoritative Publications section added #3 – BCBSA, #4 - BCBSKS Medical Consultant (401) and #5 – BCBSKS Medical Consultant (MCMC).
Effective 09-01-2006	In "Policy" section added "Note: As of June 14, 2006, per updated review by consultant, coronary CT angiography remains experimental / investigational because of lack of adequate repeated studies. Further investigation is needed. Consultant (MCMC – S087, Board certified in Internal Medicine, Cardiovascular Disease and Clinical Cardiac

	Electrophysiology) stated "There are, however, rare, highly specialized cases where a patient is at high risk of complications from coronary angiography, a properly performed SPECT nuclear stress imaging study has been somewhat positive but not definitive, where the noninvasive detection of a significant coronary lesion would lead to an invasive evaluation, in which case multislice CT angiography procedure is medically appropriate and necessary in order to exclude a lesion and prevent a high risk invasive procedure."
	In "Coding" CPT section added CPT codes 0145T, 0150T, and 0151T as directed by the Medical Director.
	In "Reference" Government Agency; Medical Society; and Other Authoritative Publications section added #6, MCMC, Medical Care Ombudsman Program (MCOP), June 14, 2006, MCOP ID 1070-1753.
Effective 01-01-2007	In "Coding" CPT section, CPT code 72175 revised for 2007, the term 'noncoronary' has been added.
Effective 04-01-2007	In "Policy" section, deleted "Consultant (MCMC – S087, Board certified in Internal Medicine, Cardiovascular Disease and Clinical Cardiac Electrophysiology) stated "There are, however, rare, highly specialized cases where a patient is at high risk of complications from coronary angiography, a properly performed SPECT nuclear stress imaging study has been somewhat positive but not definitive, where the noninvasive detection of a significant coronary lesion would lead to an invasive evaluation, in which case multislice CT angiography procedure is medically appropriate and necessary in order to exclude a lesion and prevent a high risk invasive procedure" per Medical Director.
	In "Coding" CPT section, deleted CPT codes 0145T, 0150T, and 0151T per Medical Director.
	In "Coding" section, Covered Diagnosis, deleted "Note: The use of any diagnosis code does not guarantee reimbursement. Medical necessity will be based on documentation in the medical record. Services performed for any other diagnosis requires review with medical records" per Medical Director.

Effective 07-30-2007	• Description section was updated to provide more detail about CTA technology.
	• Policy was liberalized to consider CTA medically necessary for evaluation of anomalous (native) coronary arteries in symptomatic patients when conventional angiography is unsuccessful or equivocal and when results will impact treatment. CTA remains experimental / investigational for all other indications.
	• Policy section was revised deleting: "Computed tomographic angiography (CTA) is considered experimental/investigational for the evaluation of coronary arteries including but not limited to the following:
	  1. Screening for coronary artery disease (CAD), either in asymptomatic subjects or as part of a preoperative evaluation
	  2. Diagnosis of CAD, in patients with acute or non-acute symptoms, or after a coronary intervention
	  3. Delineation of a coronary artery anatomy or anomaly"
	AND
	"Note: As of June 14, 2006, per updated review by consultant, coronary CT angiography remains experimental / investigational because of lack of adequate repeated studies. Further investigation is needed."
	• Policy section was revised adding the first two paragraphs.
	• Documentation section was added.

	• CPT codes 0146T, 0147T, 0148T, and 0149T were added for coronary anomalies. • Diagnosis codes 746.85 and 746.87 were added for coronary anomalies. Codes 747, 747.10, 747.11, 747.21, 747.22, and 747.3 were deleted.
	• References were updated.
Effective 01-25-2008	• Changed the name of the Policy to "Coronary CT Angiography and Calcium Scoring" from "Computed Tomographic Angiography (CTA)"

	In Description section: • • Added "coronary" to the second paragraph, fifth sentence, "…suggested that coronary CTA may be…" • Added "coronary" to the third paragraph, first sentence, "Coronary CTA has several..."
	In Policy section: • Removed the third paragraph, "Computed tomographic angiography (CTA) of other arteries may be indicated when medical necessity is properly documented." • Under "Documentation" added "coronary", "All coronary CTA studies will be..." • Under "Utilization" added "coronary", "Coronary CTA studies will be…"
	In Coding section: • Removed CPT codes 70496, 70498, 71275, 72191 73206, 73706, 74175. • Removed Diagnosis codes 093.0, 414.10, 415.0, 415.11, 417.0, 417.1, 417.8, 441.02, 444.1, 447.0, 447.2, 453.2, 745.0, 745.10, 745.11, 745.12, 745.19, 745.2, 745.3, 746.87, 747.20, 747.29, 747.40, 794.2, 996.1, 996.74, V12.59 • Removed Revenue Codes 32X, 34X, 35X, 40X.
Effective 01-30-2008	In Description section: • Added "The available evidence does not provide sufficient information to permit conclusions on the effect of coronary CT angiography on health outcomes." • "Electron beam computed tomography (EBCT) and multi detector computed tomography (MDCT) are methods used for measurement of coronary artery calcification. Calcium scores have been investigated both as a diagnostic technique in symptomatic patients to determine the necessity of coronary angiography or in asymptomatic patients as a screening technique for coronary artery disease. Published studies do not establish a clear role for detection of coronary artery calcification by computed tomography in coronary disease risk stratification in asymptomatic or symptomatic patients, nor have any studies shown that clinical outcomes can be favorably altered by the use of computed tomography based determination of coronary artery calcification in screening for coronary artery disease"
	In Policy section: • Added "The use of computed tomography to detect coronary artery calcification is considered investigational."
	In Coding section added: • Added CPT/HCPCS codes 0144T S8092. • Added Diagnosis codes 414.01, V81.1
Effective 12-15-2008	In Heading: • Revised title from Coronary CT Angiography and Calcium Scoring to Contrast-Enhanced Computed Tomography Angiography (CTA) for Coronary Artery Evaluation. • Added a "See also" reference to other pertinent policies.
	In Description section: • Updated terminology and discussion.
	In Policy section: • Removed "The use of computed tomography to detect coronary artery calcification is considered investigational." See Computed Tomography to Detect Coronary Artery Calcification policy.
	Added Rationale section.
	In Coding section: • Removed CPT / HCPCS codes: 0144T, S8092. • Removed Diagnosis codes: 414.11, 414.19, 441.01, 441.03, 441.1, 441.2, 441.5, 441.3, 441.7, 441.9, 442.82, 446.7, 746.85, V81.0. • Added Diagnosis codes: 414.02, 414.03, 414.04, 414.05.

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	Updated Revisions and References sections.
Effective 08-11-2009	In Header: • Added policy reference of Cardiac Computed Tomography (CT)
	In Rationale section: • Added 2009 Update
01-01-2010	In Coding Section: • Added CPT Code: 75574 • Removed CPT Codes: 0146T, 0147T, 0148T, 0149T

08-19-2011	In the Policy Language section:
	• In Item #1, added "using 64 slices or greater may be considered medically necessary for the following indictions:
	   a. For the evaluation of chest pain syndrome in patients with intermediate pre-test probability of CAD by Framingham risk scoring (10-20%)* or by American College of Cardiology criteria ** (see policy guidelines) and ECG is uninterpretable of patient is unable to exercise or have contraindications to exercise and pharmacologic stress testing.
	   b. For the evaluation of acute chest pain in patients with intermediate pre-test probability of CAD by Framingham risk scoring (10-20%)* or by American College of Cardiology criteria** (see policy guidelines) and no ECG changes and serial enzymes are negative.
	   c. For the evaluation of chest pain syndrome in patients with uninterpretable or equivocal stress test (exercise, perfusion, or stress echo).
	   d. For the assessment of complex congenital heart disease including anomalies of coronary circulation, great vessels, and cardiac chambers and valves."
	• Added Item #3, "Contrast-enhanced computed tomographic angiography is considered experimental / investigational for any of the following Body mass index (BMI) greater than 40.
	   a. Inability to image at desired heart rate (under 80 beats per minute).
	   b. Persons in atrial fibrillation or with other significant arrhythmia.
	   c. Persons with extensive coronary calcification by plain film or with prior contraindications to the procedure:
	   d. Angston score greater than 1700."

	Added Policy Guidelines.
	Updated Other References.
12-09-2011	Updated Description section.
	In the Policy section: • Added "Contrast–enhanced computed tomographic angiography for the emergency evaluation of patients without known coronary artery disease and acute chest pain is considered medically necessary."
	Updated Rationale section.
	Updated Reference section.
02-26-2013	Updated Description section.
	Updated Rationale section.
	Updated Reference section.
12-31-2013	In Coding section: ▪ Added ICD-10 Diagnosis *(Effective October 1, 2014)*
02-04-2015	Updated Description section.
	Updated Rationale section.
	Updated Coding section: ▪ Changed effective date for ICD-10 Diagnoses to *October 1, 2015*.
	Updated References section.

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03-02-2016	Updated Description section.
	In Policy section:
	▪ Removed Item 1, "Contrast-enhanced computed tomographic angiography using 64 slices or greater may be considered medically necessary for the following indications: a. For the evaluation of chest pain syndrome in patients with intermediate pre-test probability of CAD by Framingham risk scoring (10-20%)* or by American College of Cardiology criteria**(see Policy Guidelines) and ECG is uninterpretable or patient is unable to exercise or have contraindications to exercise and pharmacologic stress testing. b. For the evaluation of acute chest pain in patients with intermediate pre-test probability of CAD by Framingham risk scoring (10-20%)* or by American College of Cardiology criteria**(see Policy Guidelines) and no ECG changes and serial enzymes are negative. c. for the evaluation of chest pain syndrome in patients with uninterpretable or equivocal stress test (exercise, perfusion, or stress echo). d. For the assessment of complex congenital heart disease including anomalies of coronary circulation, great vessels, and cardiac chambers and valves" and revised to read, "Contrast-enhanced computed tomography angiography for evaluation of patients with stable chest pain and meet guideline criteria (see Policy Guidelines) for requiring a noninvasive test in the outpatient setting is considered medically necessary."
	▪ In Item 2, removed "emergency" and added "in the emergency room/emergency department setting" to read, "Contrast-enhanced computed tomographic angiography for the evaluation of patients without known coronary artery disease and acute chest pain in the emergency room/emergency department setting is considered medically necessary.
	▪ Added Item 3.
	▪ Removed previous Item 4, "Contrast-enhanced computed tomographic angiography is considered experimental / investigational for any of the following contraindications to the procedure: a. Body mass index (BMI) greater than 40. b. Inability to image at desired heart rate (under 80 beats per minute). c. Persons in atrial fibrillation or with other significant arrhythmia. d. Persons with extensive coronary calcification by plain film or with prior Angston score greater than 1700."
	▪ In Policy Guidelines, replaced all previous verbiage with 2012 ACCF/AHA/ACP/AATS/ PCNA, SCAI/STS guidelines.
	Updated Rationale section.
	Updated References section.
	Added Appendix section.
05-25-2016	In Policy section:
	▪ In Policy Guidelines, added Pretest Probability table.
	Updated References section.
12-21-2016	Policy title changed from "Contrast-Enhanced Computed Tomography Angiography (CTA) for Coronary Artery Evaluation."
	Updated Description section.
	In Policy section:
	▪ In Item A, added "coronary", "symptoms of", "ischemic heart disease", "ing", and removed "chest pain" and "requiring" to read, "Contrast-enhanced coronary computed tomography angiography for evaluation of patients with symptoms of stable ischemic heart disease and meeting guideline criteria (see Policy Guidelines) for a noninvasive test in the outpatient setting is considered medically necessary."

	▪ In Item B, added "coronary" and removed "the" to read, "Contrast-enhanced coronary computed tomography angiography for evaluation of patients without known coronary artery disease and acute chest pain in the emergency room/emergency department setting is considered medically necessary." ▪ In Item C, added "coronary" and removed "[when conventional angiography is unsuccessful or equivocal and when the results will impact treatment]" to read, "Contrast-enhanced coronary computed tomography angiography for the evaluation of anomalous (native) coronary arteries in patients in whom they are suspected may be considered medically necessary." ▪ In Item D, added "coronary" to read, "Contrast-enhanced coronary computed tomography angiography for coronary artery evaluation is considered experimental / investigational for all other indications."	
	Updated Rationale section.	
	Updated References section.	
	Removed Appendix.	
10-25-2017	Updated Description section.	
	Updated Rationale section.	
	Updated References section.	
04-25-2018	Updated title page; removed (see also): "CTA and MRA of the Chest (excluding the heart)"	
	In Coding section: ▪ Removed ICD-9 codes.	
	Updated References section.	
11-07-2018	Updated Description section.	
	In Policy section: ▪ In Item B, removed "emergency room/" to read, "Contrast-enhanced coronary computed tomography angiography for evaluation of patients without known coronary artery disease and acute chest pain in the emergency room/emergency department setting is considered medically necessary."	
	Updated Rationale section.	
	In Coding section: ▪ Added ICD-10 code: I20.8.	
	Updated References section.	

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