Medical Policy

BlueCross BlueShield Kansas
An Independent licensee of the Blue Cross Blue Shield Association

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

Related Policies:	▪ *Computed Tomography to Detect Coronary Artery Calcification* ▪ *Coronary Computed Tomography Angiography with Selective Noninvasive Fractional Flow Reserve*

Professional / Institutional
Original Effective Date: November 1, 2001 / June 3, 2004
Latest Review Date: December 9, 2025
Current Effective Date: November 9, 2022

State and Federal mandates and health plan member contract language, including specific provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. To verify a member's benefits, contact Blue Cross and Blue Shield of Kansas Customer Service.

The BCBSKS Medical Policies contained herein are for informational purposes and apply only to members who have health insurance through BCBSKS or who are covered by a self-insured group plan administered by BCBSKS. Medical Policy for FEP members is subject to FEP medical policy which may differ from BCBSKS Medical Policy.

The medical policies do not constitute medical advice or medical care. Treating health care providers are independent contractors and are neither employees nor agents of Blue Cross and Blue Shield of Kansas and are solely responsible for diagnosis, treatment and medical advice.

If your patient is covered under a different Blue Cross and Blue Shield plan, please refer to the Medical Policies of that plan.

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,	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

Populations	Interventions	Comparators	Outcomes
meeting guideline criteria for noninvasive testing			• 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 machinery to obtain detailed volumetric images of blood vessels. It is a potential diagnostic alternative to current tests for cardiac ischemia (ie, noninvasive stress testing and/or coronary angiography).

OBJECTIVE

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

BACKGROUND

Coronary Artery Disease

Various noninvasive tests are used to diagnose coronary artery disease (CAD). These tests 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 the detection of 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 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 the 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,] Coronary computed tomographic angiography 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.[3,] 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

Exposure to ionizing radiation increases lifetime cancer risk.[4,] 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.[5,] 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.[6,] Einstein et al (2007) employed a standardized phantom to estimate organ dose from 64-slice CCTA.[7,] 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 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.[8,] 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.[9,]

Levels of radiation delivered with the 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 has reported a median of 2.4 mSv (interquartile range, 1.3 to 5.5).[10,] 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.[11,] Electron-beam computed tomography using electrocardiogram triggering delivers the lowest dose (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 sex (greater for women).[12,7,6,] Empirical data have suggested that every 10 mSv of exposure is associated with a 3% increase in cancer incidence over 5 years.[13,]

Incidental Findings

A number of studies using scanners with 64 or more detector rows were identified.[14,15,16,17,18,19,20,21,22,] 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.[14,] As expected, incidental findings were less frequent in the restricted field (clinically significant findings in 14% vs. 24% when the entire field was imaged).

REGULATORY STATUS

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

POLICY

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

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

C. Contrast-enhanced coronary computed tomography angiography for evaluation of individuals with suspected anomalous (native) coronary arteries is 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 collaborative medical association guidelines for the diagnosis and management of individuals with stable heart disease list several class I recommendations on the use of noninvasive testing in individuals with suspected stable ischemic heart disease. A class I recommendation indicates that a test should be performed. In general, individuals with at least intermediate risk (10% to 90% risk by standard risk prediction instruments) are recommended to have some type of test, the choice depending on interpretability of the electrocardiogram, capacity to exercise, and presence of comorbidity.

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.[65]

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.

RATIONALE

This evidence review was created using searches of the PubMed database. The most recent literature update was performed through August 4, 2025.

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 individuals with acute chest pain is to diagnose coronary artery obstruction and guide treatment decisions.

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

Populations

The relevant population of interest is individuals with acute chest pain and suspected coronary artery disease (CAD) who are at an intermediate- to low-risk presenting in the emergency setting.

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

Study Selection Criteria

For the evaluation of clinical validity of the CCTA for acute chest pain, studies that meet the following eligibility criteria were considered:

- Reported on the accuracy of the marketed version of the technology (including any algorithms used to calculate scores)
- Included a suitable reference standard
- Patient/sample clinical characteristics were described

- Patient/sample selection criteria were described.

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, 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).

Systematic Reviews
Barbosa et al (2023) published a living systematic review and meta-analysis that compared CCTA with the standard of care (SOC) in patients with acute chest pain.[23,] Twenty-two RCTs were included (n=4956 patients who underwent CCTA, n=4423 patients who received SOC). Revascularization was more common in the CCTA group (relative risk, 1.37; 95% confidence interval [CI], 1.08 to 1.74) than with SOC, but there was no difference in rates of referral for ICA, myocardial infarction (MI), all-cause mortality, or cardiovascular mortality. Length of stay was 14% lower (95% CI, 5 to 22) and costs were 17% lower (95% CI, 5 to 28) with CCTA than SOC.

Gongora et al (2018) published a meta-analysis of 10 RCTs (N=6285) comparing CCTA with the SOC in patients with acute chest pain in an ED or inpatient setting.[24,] 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 was 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 Coronary Computed Tomography Angiography in Emergency Department Settings

Study	Dates	Trials	Participants	N (Range)	Design	Duration, months
Barbosa et al (2023)[23,]	through October 2022	22	Acute chest pain	9379	RCT	1 to 60
Gongora et al (2018)[24,]	2007-2016	10	Acute chest pain in an ED or inpatient setting	6285	RCT	1 to 19

ED: emergency department; RCT: randomized controlled trial.

Table 2. Results of Systematic Reviews Comparing Coronary Computed Tomography Angiography With Standard of Care in Emergency Department 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)
Barbosa et al (2023)[23,]					
	No significant between-group difference	Higher incidence in CCTA	No significant between-group difference	No significant between-group difference	NR
RR (95% CI)	1.08 (0.8 to 1.30)	1.37 (1.08 to 1.74)	0.96 (0.59 to 1.58)	0.86 (0.66 to 1.12)	NR
Gongora et al (2018)[24,]					
	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	.01	<.001	.17	.47	.92

CCTA: coronary computed tomography angiography; CI: confidence interval; ICA: invasive coronary angiography; MACE: major adverse cardiac event; MI: myocardial infarction; NR: not reported; RR: relative risk; SOC: standard of care.

Skelly et al (2016) conducted a comparative effectiveness review for the Agency for Healthcare Research and Quality (AHRQ) that assessed noninvasive testing for CAD.[25,] 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. Of note, AHRQ archived this report since it is more 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 Randomized Controlled Trials Assessing Coronary Computed Tomography Angiography in Emergency Department Settings

Study; Trial	Countries	Sites	Dates	Participants	Interventions	
					Active	***Comparator(s)***
Gray et al (2021)[26]; RAPID-CTCA	UK	37	2015-2019	Adults with suspected ACS and at least 1 of: previous CHD, raised cardiac troponin levels, or abnormal ECG	877 to early CCTA + SOC	871 to SOC
Smulders et al (2019)[27]; 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)[28]	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)[29]; 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)

Study; Trial	Countries	Sites	Dates	Participants	Interventions	
Linde et al (2013)[30]; 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)[31]; 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)[32]; 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)[33]; 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)[34]	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; CHD: coronary heart disease; 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; SE: stress echocardiography; SOC: standard of care.

Gray et al (2021) published an open-label RCT comparing CCTA with SOC in intermediate-risk patients with suspected acute coronary syndrome (ACS).[26] Overall, the mean age was 61.6 years with 64% male patients. The primary endpoint was all cause death or subsequent type 1 or 4b MI at 1 year, and it occurred in 51 (5.8%) patients in the early CCTA group compared with 53 (6.1%) patients in the SOC group (hazard ratio [HR], 0.91; 95% CI, 0.62 to 1.35; p=.65). However, clinicians reported greater diagnostic certainty with CCTA (mean increase of 1.4), and fewer patients in the CCTA group underwent ICA (Table 4).

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 (ie, routine clinical care) in patients with non-ST-segment elevation myocardial infarction (NSTEMI).[27] 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=.001] and 66% CCTA [p<.001] as compared to routine clinical care [100%]). Significantly fewer ICAs were performed in the CCTA- than CMR-first strategy groups (p=.004). The reduction in ICA in the CMR- or CCTA-first strategy groups compared with routine clinical care was persistent after 1 year (88% CMR [p=.003], 70% CCTA [p<.001], and 100% routine clinical care). Similar clinical outcomes were seen: CMR versus routine (HR, 0.78; 95% CI, 0.37 to 1.61); CCTA versus routine (HR, 0.66; 95% CI, 0.31 to 1.42); and CMR versus CCTA (HR, 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<.001). A follow-up CMR led to a new MI diagnosis in 7 patients.

Levsky et al (2018) published an RCT comparing CCTA (n=201) to stress echocardiography (n=199) in low- to intermediate-risk patients presenting to the ED with acute chest pain. In the CCTA arm, 39 (19%) patients were hospitalized, compared with 22 (11%) patients in the stress echocardiography arm, resulting in a difference of 8% (95% CI, 1 to 15 ; p=.026).[28,] Median length of stay in the hospital was longer for the CCTA arm (58 hours vs. 34 hours; p=.002). There was no significant difference between the CCTA and stress echocardiography arms in terms of major adverse cardiac events (MACE, including death); MACE occurred in 11 CCTA patients and 7 stress echocardiography patients, respectively (p=.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 to 7.8 mSv), significantly more than that of stress echocardiography (0 mSv; p<.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 diagnostic performance and cost of CT angiography versus stress electrocardiogram (ECG) (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.[29,] Length of stay was significantly reduced in CCTA patients compared with exercise testing patients. Clinical outcomes at 30 days and 12 months did not differ.

Linde et al (2013) reported on the CArdiac cT in the treatment of acute CHest pain (CATCH) trial, which randomized 600 patients to a CCTA-guided strategy or to SOC.[30,] 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% to 70%) on CCTA, a stress test was performed.

Litt et al (2012) reported on the American College of Radiology Imaging Network of Pennsylvania (AC RIN-PA) trial, which also evaluated the safety of CCTA in patients in the ED.[31,] 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 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 Rule Out Myocardial Ischemia/Infarction by Computer Assisted Tomography (ROMICAT II) trial, which compared the length of stay with outcomes in 549 patients evaluated using CCTA or usual care.[32,] For the 50 patients in the CCTA arm, the 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 Coronary Computed Tomography for Systematic Triage of Acute Chest Pain Patients to Treatment (CT-STAT) trial, which evaluated a similar sample of 699 patients.[33,] Over a 6-month follow-up, there were no deaths in either arm; there were 2 cardiac

events in the CCTA arm and 1 in the perfusion imaging arm. 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 ACS to CCTA (n=99) or usual care (n=98).[34,] 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 Randomized Controlled Trials Assessing Coronary Computed Tomography Angiography in Emergency Department 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
Gray et al (2021)[26,]	54 vs. 60.8	NR	NR	2.2 vs. 2.0[d]	12
Smulders et al (2019)[27,]	66 vs. 100	NR	7	NR	1 and 12
Levsky et al (2018)[28,]	NR	NR	NR	5.4 vs. 4.7[c]	1 and 12
Hamilton-Craig et al (2014)[29,]	9.0 vs. 4.2	94%/99% vs. 83%/91%[d]	0	13.5 vs. 20.7[c]	1 and 12
Linde et al (2013)[30,]	17 vs. 12	71 vs. 36[e]	0	NR	4
Litt et al (2012)[31,]	5.1 vs. 4.2	NR	0	18.0 vs. 24.8	1
Hoffmann et al (2012)[32,]	12.0 vs. 21.0	NR	0	5.8 vs. 21.0	1
Goldstein et al (2011)[33,]	6.6 vs. 6.2	76.9 vs. 54.5	0	2.9 vs. 6.2	6
Goldstein et al (2007)[34,]	12.1 vs. 7.1	88.9 vs. 98.0	0	3.4 vs. 15.0	6

CCTA: coronary computed tomography angiography; FU: follow-up; ICA: invasive coronary angiography; MI: myocardial infarction; NR: not reported.
[a] Confirmed with angiographic and clinical results.
[b] Time from randomization to definitive diagnosis.
[c] Refers to length of stay rather than time to diagnosis.
[d] Reporting the sensitivity/specificity for CCTA versus exercise stress electrocardiogram for acute coronary syndrome with stenosis >70%.
[e] Positive predictive value for CCTA versus standard of care.

The purpose of the limitations tables (Tables 5 and 6) is to display notable limitations 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 Randomized Controlled Trials Assessing Coronary Computed Tomography Angiography in Emergency Department Settings

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Duration of Follow-Up[e]
Gray et al (2021)[26],					
Smulders et al (2019)[27],	2. Patients with a history of myocardial disease and/or severe noncardiac comorbidities were excluded				
Levsky et al (2018)[28],					
Hamilton-Craig et al (2014)[29],	4. Limited applicability to men <30 y and women <40 y				
Linde et al (2013)[30],					
Litt et al (2012)[31],	4. Limited to patients 40 to 74 y; may not be relevant for younger or older individuals				
Hoffmann et al (2012)[32],					
Goldstein et al (2011)[33],					
Goldstein et al (2007)[34],		3. Unequal rates of ICA/revascularization	3. Unequal rates of ICA/revascularization		

ICA: invasive coronary angiography.
The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[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 Randomized Controlled Trials Assessing Coronary Computed Tomography Angiography in Emergency Department Settings

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Gray et al (2021)[26,]		1,2. Patients and clinicians were not blinded				
Smulders et al (2019)[27,]		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)[28,]					2. Not powered to detect differences in MACE	
Hamilton-Craig et al (2014)[29,]					2. Not powered to compare outcomes	
Linde et al (2013)[30,]		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)[31,]					2. Due to low incidence of events, not powered for	

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
					primary outcome (safety)	
Hoffmann et al (2012)[32,]		1. No blinding to treatment				
Goldstein et al (2011)[33,]				1. 10.3% of patients lost to follow-up	2. Not powered for secondary outcome (safety)	
Goldstein et al (2007)[34,]					1. Power calculations not reported	4. No assessment of alternative noninvasive tests

ICA: invasive coronary angiography; MACE: major adverse cardiac event.
The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[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

Results from long-term follow-up studies are tabulated in Table 7.

Table 7. Results of Follow-Up Studies of Randomized Controlled Trials

Study	Initial Study Design (Trial)	Follow-Up Duration	Results
Linde et al (2015)[35,]	RCT (CATCH)	18.7 mo (IQR, 16.8 to 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=.04)
Schlett et al (2011)[36,]	RCT (ROMICAT)	2 y	Of 333 patients without CAD detected by CCTA, none had a MACE event during follow-up

CAD: coronary artery disease; CCTA: coronary computed tomography angiography; CI: confidence interval; HR: hazard ratio; IQR: interquartile range; MACE: major adverse cardiac event; RCT: randomized controlled trial; SOC: standard of care.

Nonrandomized Studies

Durand et al (2017) compared the diagnostic performance of dobutamine-stress echocardiography (DSE) with CCTA in 217 adults.[37,] Patients had normal measurements of troponin I or T, and electrocardiography results. All patients received DSE and CCTA, with only 75 (34.6%) patients receiving ICA, which served as the reference test. The primary endpoint 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 one patient presented with ACS whose diagnosis was initially missed. No limitations were identified. Tables 8 and 9 summarize the trial characteristics and results.

Table 8. Key Nonrandomized Trials Assessing Coronary Computed Tomography Angiography in Emergency Department Settings

Study	Study Type	Country	Dates	Participants	Treatment	Comparator	Follow-Up, mo
Durand et al (2017)[37,]	Prospective head-to-head multicenter	France	NR	Adults treated at the ED for chest pain <24 h after symptom onset	CCTA	DSE	6

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

Table 9. Results of Key Nonrandomized Trials Assessing Coronary Computed Tomography Angiography in Emergency Department Settings

Study	Diagnostic Accuracy		Incidence of MI	ICA, n (%)[a]
	CCTA[b]	***DSE***[b]		
Durand et al (2017)[37,]				
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 tomography angiography; CI: confidence interval; DSE: dobutamine-stress echocardiography; FU: follow-up; ICA: invasive coronary angiography; MI: myocardial infarction; NLR: negative likelihood ratio; PLR: positive likelihood ratio.
[a] Number of patients who received ICA.
[b] Of detected coronary stenosis >50%.

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 Coronary Artery Disease
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 an intermediate risk of CAD. The choice of the functional test is based on clinical factors such as the predicted risk of disease, ECG interpretability, and ability to exercise. When the 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 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 (eg, 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 versus alternative tests, and studies of incidental findings and radiation exposure.

Clinical Context and Test Purpose
The purpose of CCTA in individuals with stable chest pain and suspected CAD is to diagnose coronary artery obstruction and guide treatment decisions.

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

Populations
The relevant population of interest is individuals with stable chest pain and suspected CAD who are at an intermediate-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), 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.

Study Selection Criteria
For the evaluation of clinical validity of the CCTA for stable chest pain, studies that meet the following eligibility criteria were considered:

- Reported on the accuracy of the marketed version of the technology (including any algorithms used to calculate scores)
- Included a suitable reference standard
- Patient/sample clinical characteristics were described
- Patient/sample selection criteria were described.

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 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, systematic reviews, and guideline reports. Table 10 shows ranges of sensitivity and specificity for functional noninvasive tests as summarized in collaborative medical association guidelines for the diagnosis and management of stable angina by Fihn et al (2012).[38,] Sensitivities tended to range between 70% and 97%, 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).[38,]

Table 11. Systematic Review & Meta-analysis Characteristics of Clinical Validity for Coronary Computed Tomography Angiography in Stable Chest Pain and Suspected Coronary Artery Disease

Study	Study Population	Reference Standard	Threshold for Positive Index Test	Timing of Reference and Index Tests	Blinding of Assessors	Comment
Haase et al (2019)[39,]	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 N=5332 in 65 prospective diagnostic accuracy studies	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)[40,]	Studies examining the diagnostic accuracy of CCTA vs. functional testing in patients suspected of stable CAD	ICA	CCTA: NR	NR	NR	Details on blinding and timing were limited. Quality assessment results for bias risk in diagnostic

Study	Study Population	Reference Standard	Threshold for Positive Index Test	Timing of Reference and Index Tests	Blinding of Assessors	Comment
	N=1575 in 11 diagnostic accuracy studies					accuracy studies was predominantly low.
Ollendorf et al (2011)[41,]	42 diagnostic accuracy studies	ICA	CCTA: NR	NR	Blinded review of CCTA and ICA	
Health Quality Ontario (2010)[42,]	Individuals with intermediate pre-test probability of CAD	ICA	CCTA: • CAD: ≥50% stenosis	NR	NR	Analysis is limited by significant heterogeneity between studies.

CAD: coronary artery disease; CCTA: coronary computed tomography angiography; ICA: invasive coronary angiography; NR: not reported.

Table 12. Systematic Review & Meta-analysis Results for Coronary Computed Tomography Angiography in Stable Chest Pain and Suspected Coronary Artery Disease

Study; Subgroup	Clinical Validity, % (95% CI)			
	Sensitivity	***Specificity***	***PPV***	***NPV***
Haase et al (2019) (COME-CCT); Overall[39,]	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[39,] 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)[40,]	98 (93 to 99)	82 (63 to 93)	85 (71 to 93.5)	97.5 (87 to 99)
Ollendorf et al (2011)[41,]	98 (96 to 99)	85 (81 to 89)	NR	NR
Health Quality Ontario (2010)[42,]	96.1 (94 to 98.3)	81.5 (73.0 to 89.9)	NR	NR

CI: confidence interval; NPV: negative predictive value; NR: not reported; PPV: positive predictive value.

Clinically Useful
A test is clinically useful if the use of the results inform management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, 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
De Campos et al (2022) conducted a meta-analysis of long-term outcomes in patients receiving CCTA or functional testing for stable CAD.[43,] The composite primary outcome included the rate of death from any cause and nonfatal ACS. Follow-up ranged from 1 to 5 years; only 3 trials had follow-up periods longer than 1 year. The primary outcome occurred in 378 patients (2.6%) assigned to the CCTA group and in 397 (2.7%) of patients in the functional testing group (relative risk, 0.97; 95% CI, 0.76 to 1.22; p=.77; I^2=43%). Tables 13 and 14 summarize review characteristics and results.

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.[44,] 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. Coronary computed tomographic angiography 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 Review & Meta-analysis Assessing Coronary Computed Tomography Angiography for Stable Chest Pain

Study	Dates	Trials	Participants	N (Range)	Design	Duration
De Campos et al (2022)[43,]	2009-2019	8	Patients with stable CAD	29,579 (303 to 9102)	RCT	≥12 months follow-up
Foy et al (2017)[44,]	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 Review & Meta-analysis Assessing Coronary Computed Tomography Angiography for Stable Chest Pain

Study	Incidence of ICA, %	Revascularization, %	Adverse Events, %	New Diagnoses of CAD, %	Medication Use, %[a]
De Campos et al (2022)[43],					
CCTA vs. Functional stress testing	14.86 vs. 19.43[b]	NR	NR	NR	NR
OR (95% CI)	0.75 (0.6 to 0.96)	1.63 (0.97 to 2.74)			
Foy et al (2017)[44],					
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 tomography angiography; CI: confidence interval; ICA: invasive coronary angiography; MI: myocardial infarction; NR: not reported; OR: odds ratio; RR: relative risk.
[a] Proportion of patients who experienced a significant increase in medication use.
[b] This analysis excludes one study with a population deemed low-risk and another considered the main source of heterogeneity.

Randomized Controlled Trials

For patients at intermediate risk of CAD, 7 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 Randomized Controlled Trials Assessing Coronary Computed Tomography Angiography in Stable Chest Pain

Study; Trial	Countries	Sites	Dates	Participants	Interventions	
					Active	***Comparator***
Maurovich-Horvat et al (2022)[45,]; DISCHARGE	16 European countries	26	2015-2019	Patients with stable chest pain referred for ICA	1808 to CCTA	1753 to ICA
Stillman et al (2020)[46,]; RESCUE	U.S.	44	2011-2013	Patients with stable angina and suspected CAD	518 to CCTA	532 to SPECT-MPI
Newby et al (2019)[47,]; 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
Chang et al (2019)[48,]; CONSERVE	Various	22	2012-2016	Patients with suspected CAD referred to nonemergent ICA	823 to selective referral strategy with initial CCTA	808 to direct referral strategy with initial ICA
Rudzinski et al (2018)[49,]; CAT-CAD	Poland	1	2015-2016	Patients with stable angina and suspected CAD	60 to CCTA	60 to ICA
Douglas et al (2015)[50,]; PROMISE	U.S.	193	2010-2013	Symptomatic outpatients without diagnosed CAD	4996 to anatomic testing strategy with CCTA	5007 to functional testing strategy
SCOT-HEART Investigators (2015)[51,]; 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)[52,]; CAPP	U.K.	NR	2010-2011	Patients with symptoms of stable chest pain	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; SPECT-MPI: single photon emission computed tomography myocardial perfusion imaging.

Maurovich-Horvat et al (2022) reported results from the Diagnostic Imaging Strategies for Patients with Stable Chest Pain and Intermediate Risk of Coronary Artery Disease (DISCHARGE) trial.[45,] Patients were at least 30 years of age and randomized to CCTA or ICA. The primary outcome was a composite of cardiovascular death, nonfatal MI, or nonfatal stroke. After a median of 3.5 years of follow-up there was no difference in the primary outcome between the CCTA and ICA groups (HR, 0.70; 95% CI, 0.46 to 1.07; p=.1).

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.[46,] 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.

Newby et al (2019) 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 MI was found for patients undergoing CCTA with the SOC. Coronary computed tomographic angiography was not found to increase rates of revascularization or subsequent utilization of ICA at this time point.[47,] 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 [coronary heart disease] outcomes by enabling better targeting of preventative treatments to those with CAD."[53,]

Chang et al (2019) 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.[48,]

Rudzinski et al (2018) reported on results from the Coronary Artery Computed Tomography as the First-Choice Imaging Diagnostic in Patients With High Pre-Test Probability of Coronary Artery Disease (CAT-CAD) trial, which randomized 120 patients with suspected CAD to undergo CCTA versus direct ICA. Outcomes were evaluated during the diagnostic and therapeutic periods. Evaluation with CCTA was found to reduce the total number of ICAs performed.[49,]

Douglas et al (2015) reported on the PROspective Multicenter Imaging Study for Evaluation of Chest Pain (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.[50,] Coronary computed tomographic angiography 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.[54,] 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=.04). When the Framingham Risk Score was added to functional testing results, there was no significant difference in prognostic capability between the approaches (p=.29).

In the SCOT-HEART trial (2015), investigators randomized 4146 patients to CCTA plus SOC or SOC alone. The primary endpoint was the change in the proportion of patients with a more certain diagnosis (presence or absence) of angina pectoris.[51,] 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.[55,] 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. After 10 years of follow-up, death due to coronary heart disease and nonfatal MI were significantly less frequent with CCTA compared to SOC (6.6% vs. 8.2%; hazard ratio, 0.79; 95% CI, 0.63 to 0.99; p=.044).[56,] Rates of nonfatal MI (4.3% vs. 6.0%; HR, 0.72; 95% CI, 0.55 to 0.94; p=.017) and MACE (8.3% vs. 10.3%; HR, 0.80; 95% CI, 0.65 to 0.97; p=.026) were also significantly lower with CCTA than with SOC, respectively.

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.[52,] 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 Randomized Controlled Trials Assessing Coronary Computed Tomography Angiography in Stable Chest Pain

Study	Death or Nonfatal Myocardial Infarction	Incidence of ICA	Revascularization	Normal Findings on ICA	Angina Stability	Hospitalization
Maurovich-Horvat et al (2022)[45,]		NR		NR	NR	NR
CCTA, %	1.5		14.2			
ICA, %	1.7		18			
HR	0.87 (0.52 to 1.46)		0.76 (0.65 to 0.90)			
p	NR		NR			
Stillman et al (2020)[46,]		NR	NR	NR	NR	NR
CCTA, %	Negative test (1.2%); Positive test (20.5%)*					

Study	Death or Nonfatal Myocardial Infarction	Incidence of ICA	Revascularization	Normal Findings on ICA	Angina Stability	Hospitalization
SPECT-MPI, %	Negative test (3.2%); Positive test (34.8%)*					
HR	1.03 (0.61 to 1.75)*					
p	.19*					
Newby et al (2019)[47,]				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 to 1.13)	1.07 (0.91 to 1.27)			
p	.004	NR	NR			
Chang et al (2019)[48,]					NR	
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	.026 (1-sided noninferiority)	<.001	.007	<.001		NR
Rudzinski et al (2018)[49,]			NR		NR	
CCTA, n	0	21		5		25
ICA, n	0	59		42		73
p		<.0001		<.0001		<.0001
Douglas et al (2015)[50,]		NR	NR	NR	NR	
CCTA group	104					61

Study	Death or Nonfatal Myocardial Infarction	Incidence of ICA	Revascularization	Normal Findings on ICA	Angina Stability	Hospitalization
Functional testing group	112					41
HR (95% CI)	0.88 (0.67 to 1.15)					
p	.35					
SCOT-HEART Investigators (2015)[51,]		NR	NR	NR	NR	
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	.527					.399
McKavanagh et al (2015)[52,]	NR	NR	NR	NR		NR
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					.028	

CI: confidence interval; CCTA: coronary computed tomography angiography; HR: hazard ratio; ICA: invasive coronary angiography; MD: mean difference; NR: not reported; SPECT-MPI: single photon emission computed tomography myocardial perfusion imaging.
*In the Stillman et al (2020) study, the primary endpoint included cardiovascular death, nonfatal myocardial infarction, or revascularization.

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

Table 17. Study Relevance Limitations of Randomized Controlled Trials Assessing Coronary Computed Tomography Angiography in Stable Chest Pain

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Duration of Follow-Up[e]
Maurovich-Horvat et al (2022)[45,]	4. Conducted only in European population				
Stillman et al (2020)[46,]				1. Key health outcomes not addressed	2. Not sufficient duration for harms
Newby et al (2019)[47,]	4. Patients >75 y excluded				
Chang et al (2019)[48,]	4. Population included >84% Asian patients in each treatment arm				
Rudzinski et al (2018)[49,]					2. Not sufficient duration for harms
Douglas et al (2015)[50,]				1. Test performance and utility not addressed	
SCOT-HEART Investigators (2015)[51,]	4. Patients >75 y excluded				
McKavanagh et al (2015)[52,]	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 gaps assessment.
[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 Randomized Controlled Trials Assessing Coronary Computed Tomography Angiography for Stable Chest Pain

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Maurovich-Horvat et al (2022)[45,]		1. Not blinded to treatment assignment.				
Stillman et al (2020)[46,]		1. Not blinded to treatment assignment.		1. High loss to follow-up or missing data (ie, low adherence).		
Newby et al (2019)[47,]		1-3. Treatments and outcomes not blinded and potential bias among attending clinicians was present.				
Chang et al (2019)[48,]	2. Allocation not concealed.	1. Not blinded to treatment assignment.		1. High loss to follow-up or missing data.		
Rudzinski et al (2018)[49,]	2. Allocation not concealed.			2. Unclear handling of missing data.	1. Power calculation not reported.	3. Confidence intervals not reported.
Douglas et al (2015)[50,]						
SCOT-HEART Investigators (2015)[51,]		1-3. Treatments and outcomes not blinded and potential bias among attending clinicians was present.				
McKavanagh et al (2015)[52,]					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 gaps assessment.
CAD: coronary artery disease.
[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 Coronary Artery Disease
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 the 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. Recent clinical trials have demonstrated similar or lower rates of ICA and subsequent revascularization procedures with CCTA versus standard care or ICA, respectively. An important problem when interpreting the clinical trials is that the comparator strategies differ: in the PROMISE and 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, an examination of some secondary clinical outcomes supports a conclusion of noninferiority. The results of the other randomized trials are consistent with the noninferiority of CCTA compared with other established noninvasive tests and ICA. Thus, the randomized studies suggest that outcomes of patients are likely to be similar to CCTA versus 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 individuals who have suspected anomalous coronary arteries is to provide a treatment option that is an alternative to or an improvement on existing therapies.

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

Populations
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. 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.

Study Selection Criteria
For the evaluation of clinical validity of the CCTA for anomalous coronary arteries, studies that meet the following eligibility criteria were considered:

- Reported on the accuracy of the marketed version of the technology (including any algorithms used to calculate scores)
- Included a suitable reference standard
- Patient/sample clinical characteristics were described
- Patient/sample selection criteria were described.

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 inform management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, 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; however, 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.[57,58,59,60,]

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 Coronary Computed Tomography Angiography
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. In 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).[61,] Other small studies have reported high sensitivity and specificity.[62,63,] 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 patients undergoing CCTA (n=1000) or a control intervention (n=1000).[64,] 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 Screening For Asymptomatic Obstructive Coronary Artery Disease Among High-Risk Diabetic Patients Using CT Angiography (FACTOR-64) trial, which randomized 900 subjects with diabetes to screening with CCTA or SOC.[65,] 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=.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).[66,] 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. Occurrence of MACE was 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<.001). Obstructive multivessel CAD predicted the highest risk of MACE (odds ratio, 8.9; 95% CI, 5.1 to 15.3; p<.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.

SUPPLEMENTAL INFORMATION

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American College of Cardiology Foundation et al

The American College of Cardiology along with several other organizations (2021) published guidelines for evaluation and diagnosis of chest pain that include recommendations for coronary computed tomography angiography (CCTA).[67,]

For intermediate-risk patients with no known coronary artery disease (CAD) the guidelines pertinent to CCTA state:

- "For intermediate-risk patients with acute chest pain and no known CAD eligible for diagnostic testing after a negative or inconclusive evaluation for ACS [acute coronary syndrome], CCTA is useful for exclusion of atherosclerotic plaque and obstructive CAD."
- "For intermediate-risk patients with acute chest pain with evidence of previous mildly abnormal stress test results (≤1 year), CCTA is reasonable for diagnosing obstructive CAD."
- "For intermediate-risk patients with acute chest pain and no known CAD, as well as an inconclusive prior stress test, CCTA can be useful for excluding the presence of atherosclerotic plaque and obstructive CAD."

For intermediate-risk patients with known CAD the guidelines pertinent to CCTA state:

- "For intermediate-risk patients with acute chest pain and known nonobstructive CAD, CCTA can be useful to determine progression of atherosclerotic plaque and obstructive CAD."

The American College of Cardiology Foundation and several other medical societies (2012) issued joint guidelines for the management of patients with stable ischemic heart disease (Table 19).[38,]

Table 19. 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 a 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
	"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
	"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	IIb	C

Diagnosis	Recommendation	Class	LOE
	high-risk result and knowledge of angiographic coronary anatomy is unknown."		

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.

The American College of Cardiology Foundation and other medical societies (2013) published appropriate use criteria for detection and risk assessment of stable ischemic heart disease.[68,] Coronary computed tomography angiography was considered appropriate for:

- Symptomatic patients with intermediate (10% to 90%) pretest probability of 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.

In 2023, the American College of Cardiology published a guideline on management of patients with chronic coronary disease.[69,] The recommendation related to CCTA was modified from the aforementioned 2021 guideline on evaluation and diagnosis of chest pain. Patients who may be appropriate for CCTA include those with chronic coronary disease, prior coronary revascularization, and a change in functional capacity despite optimal medical therapy. The role of CCTA in these patients is to evaluate bypass graft or stent patency. A separate statement recommends against CCTA in patients who do not have a change in clinical or functional status.

National Institute for Health and Care Excellence

The National Institute for Health and Care Excellence (2016) has recommended CCTA as first-line testing for patients with stable angina if the clinical assessment indicates typical or atypical angina, or if the clinical assessment indicates non anginal chest pain but 12-lead resting electrocardiography has been done and indicates ST-T changes or Q waves.[70,]

Society of Cardiovascular Computed Tomography

The Society of Cardiovascular Computed Tomography (SCCT, 2021) published an expert consensus document on CCTA.[71,] Recommendations on use of CCTA in select patients are included in Table 20. In addition to the recommendations listed below, the expert consensus included additional recommendations in several patient populations, including patients with known CAD.

Table 20. Society of Cardiovascular Computed Tomography Guidelines on Coronary Computed Tomography Angiography

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).

Diagnosis	Recommendation
	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.

In 2022, SCCT published an expert consensus document on use of CCTA for patients presenting to the emergency department with acute chest pain.[72,] Relevant recommendations from the consensus document are listed in Table 21.

Table 21. Society of Cardiovascular Computed Tomography Guidelines on Coronary Computed Tomography Angiography for Acute Chest Pain in the Emergency Department

Scenario	Recommendation
Patient with no known CAD	
ECG diagnostic for STEMI	CCTA is usually not appropriate (door-to-balloon time <90 minutes should be prioritized).
NSTE-ACS is leading diagnosis (evidence of myocardial ischemia on ECG without ST-segment elevation, elevated troponin)	CCTA may be appropriate (eg, to determine if invasive evaluation is appropriate).
High risk for ACS (no definite evidence of myocardial ischemia on ECG, normal or equivocal troponin)	CCTA may be appropriate as an alternative to functional testing or invasive evaluation.
Low to intermediate risk for ACS (no definite evidence of myocardial ischemia on ECG, normal or equivocal troponin, and/or inadequate or mildly abnormal functional testing during index ED visit or within previous year)	CCTA is appropriate and is most effective to rule out ACS.
Very low risk for ACS (no definite evidence of myocardial ischemia on ECG, normal or equivocal troponin, and/or non-cardiac chest pain is leading diagnosis)	CCTA may be appropriate (eg, to confidently exclude CAD and provide risk stratification).
Patient with documented CAD, post-revascularization	

Scenario	Recommendation
Prior PCI with stent ≥3 mm within a proximal coronary segment (no definite evidence of myocardial ischemia on ECG, normal or equivocal troponin)	CCTA is appropriate for early triage.
Prior CABG (no definite evidence of myocardial ischemia on ECG, normal or equivocal troponin)	CCTA is appropriate, particularly for evaluating graft patency.

ACS: acute coronary syndrome; CABG: coronary artery bypass grafting; CAD: coronary artery disease; CCTA: coronary computed tomography angiography; ECG: electrocardiography; ED: emergency department; NSTE-ACS: non-ST-segment-elevation myocardial infarction acute coronary syndrome; PCI: percutaneous coronary intervention; STEMI: ST-segment-elevation myocardial infarction.

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 ongoing trials that might influence this review are listed in Table 22.

Table 22. Summary of Key Trials

NCT Number	Title	Enrollment	Completion Date
Ongoing			
NCT06552663	The Diagnostic Power Of Coronary Ct Angiography In Patients With Chest Pain And Zero Calcium Score	75	Dec 2025
NCT04748237	Randomized Evaluation of Coronary Computed Tomographic Angiography in Intermediate-risk Patients Presenting to the Emergency Department With Chest Pain	1600	Dec 2025
NCT02099019	Usefulness of Coronary Computed Tomography Angiography for Therapeutic Decision-Making; Revascularization	3000	Feb 2025 (unknown status)
NCT05677386	Prevention of Heart Disease in Adult Danes Using Computed Tomography Coronary Angiography - The DANE-HEART Trial	6000	Jun 2033
NCT06101862	Team-based Interventional Triage in Acute Coronary Syndrome Based on Non-Invasive Computed Tomography Coronary Angiography - a Randomized Trial	2300	Oct 2036

NCT: national clinical trial.

CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. This may not be a comprehensive list of procedure codes applicable to this policy.

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.

The code(s) listed below are medically necessary ONLY if the procedure is performed according to the "Policy" section of this document.

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

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 Effective 01-01-2007	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.

Revisions	
	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.
	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:

Revisions	
	• 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.
	Updated Revisions and References sections.
Effective 08-11-2009	In Header: • Added policy reference of Cardiac Computed Tomography (CT)
	In Rationale section:

Revisions	
	• 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 inductions: 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.
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

Revisions	
	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

Revisions	
	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 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 References section.
November 5, 2019	Updated Description section.
	Updated Rationale section.
	In Coding section: • Added ICD-10 code: I20.8.
	Updated References section.
05-22-2020	Updated Policy Guidelines: • Replaced chart in policy guidelines that was omitted in error- Pretest Probability of CAD by age, gender, and symptoms
11-05-2021	In related policies the following policies are archived Deleted: *CTA and MRA of the Head, Neck, Abdomen, Pelvis, and Lower Extremities* *Cardiac Computed Tomography (CT)*
	Updated Description section
	Updated Rationale section
	Updated Reference section
11-09-2022	Updated Description Section
	Updated Policy Section ▪ Section C: Re-worded statement to read " Contrast-enhanced coronary computed tomography angiography for evaluation of individuals with suspected anomalous (native) coronary arteries is considered medically necessary."
	Updated Rationale Section
	Updated References Section
10-24-2023	Updated Description Section
	Updated Rationale Section
	Updated Coding Section ▪ Removed ICD-10 Codes
	Updated References Section
11-20-2024	Updated Description Section

Revisions	
	Updated Rationale Section
	Updated References Section
12-09-2025	Updated Description Section
	Updated Rationale Section
	Updated Reference Section

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. Kochar A, Kiefer T. Coronary Artery Anomalies: When You Need to Worry. Curr Cardiol Rep. May 2017; 19(5): 39. PMID 28374180
4. 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.
5. Berrington de González 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
6. 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
7. 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
8. 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
9. 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
10. 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.
11. 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
12. 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

13. 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
14. 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
15. 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
16. 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
17. 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
18. 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
19. 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. 2010; 11(1): 60-8. PMID 20046496
20. 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
21. 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
22. 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. 2010; 34(2): 296-301. PMID 20351524
23. Barbosa MF, Canan A, Xi Y, et al. Comparative Effectiveness of Coronary CT Angiography and Standard of Care for Evaluating Acute Chest Pain: A Living Systematic Review and Meta-Analysis. Radiol Cardiothorac Imaging. Aug 2023; 5(4): e230022. PMID 37693194
24. 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
25. 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.
26. Gray AJ, Roobottom C, Smith JE, et al. Early computed tomography coronary angiography in patients with suspected acute coronary syndrome: randomised controlled trial. BMJ. Sep 29 2021; 374: n2106. PMID 34588162
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, Sørgaard 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, Sørgaard 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, Nørgaard 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. De Campos D, Teixeira R, Saleiro C, et al. Computed tomography coronary angiography as the noninvasive in stable coronary artery disease? Long-term outcomes meta-analysis. Future Cardiol. May 2022; 18(5): 407-416. PMID 35119305
44. 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
45. Maurovich-Horvat P, Bosserdt M, Kofoed KF, et al. CT or Invasive Coronary Angiography in Stable Chest Pain. N Engl J Med. Apr 28 2022; 386(17): 1591-1602. PMID 35240010
46. 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
47. 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
48. 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
49. Rudziński PN, Kruk M, Kępka 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. 2018; 12(6): 472-479. PMID 30201310
50. 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
51. 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
52. 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
53. 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
54. 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

55. 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
56. Williams MC, Wereski R, Tuck C, et al. Coronary CT angiography-guided management of patients with stable chest pain: 10-year outcomes from the SCOT-HEART randomised controlled trial in Scotland. Lancet. Jan 25 2025; 405(10475): 329-337. PMID 39863372
57. 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
58. 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
59. 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
60. 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
61. 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
62. 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
63. 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
64. 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
65. Muhlestein JB, Lappé 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
66. 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
67. Gulati M, Levy PD, Mukherjee D, et al. 2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR Guideline for the Evaluation and Diagnosis of Chest Pain: Executive Summary: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. J Am Coll Cardiol. Nov 30 2021; 78(22): 2218-2261. PMID 34756652
68. 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
69. Virani SS, Newby LK, Arnold SV, et al. 2023 AHA/ACC/ACCP/ASPC/NLA/PCNA Guideline for the Management of Patients With Chronic Coronary Disease: A Report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines. Circulation. Aug 29 2023; 148(9): e9-e119. PMID 37471501
70. 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 August 4, 2025.
71. 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. 2021; 15(3): 192-217. PMID 33303384
72. Maroules CD, Rybicki FJ, Ghoshhajra BB, et al. 2022 use of coronary computed tomographic angiography for patients presenting with acute chest pain to the emergency department: An expert consensus document of the Society of cardiovascular computed tomography (SCCT): Endorsed by the American College of Radiology (ACR) and North American Society for cardiovascular Imaging (NASCI). J Cardiovasc Comput Tomogr. 2023; 17(2): 146-163. PMID 36253281

OTHER REFERENCES

1. Blue Cross and Blue Shield of Kansas Cardiology Liaison Committee: May 2007; May 2008; April 2009; April 2010; May 2011; May 2012; July 2016; January 2017.
2. MCMC, Medical Care Ombudsman Program (MCOP), May 22, 2007, MCOP ID 1074-6539.
3. Blue Cross and Blue Shield of Kansas Radiology Liaison Committee: February 2008; February 2009; February 2010; February 2011; February 2012.
4. Blue Cross and Blue Shield of Kansas Medical Advisory Committee: April 2009; April 2010; April 2011; April 2012.