
Medical Policy



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***Current Policy Effective Date: 5/1/24**
(See policy history boxes for previous effective dates)

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

Description/Background

Contrast-enhanced coronary computed tomography angiography (CCTA) is a noninvasive imaging test that requires the use of intravenously administered contrast material and high-resolution, high-speed computed tomography (CT) machinery to obtain detailed volumetric images of blood vessels. It is a potential diagnostic alternative to current tests for cardiac ischemia (i.e., noninvasive stress testing and/or coronary angiography).

CORONARY ARTERY DISEASE

Various noninvasive tests are used in the diagnosis of coronary artery disease. These tests can be broadly classified as those that detect functional or hemodynamic consequences of obstruction and ischemia (exercise treadmill testing, myocardial perfusion imaging [MPI], stress echo with or without contrast), and others identifying the anatomic obstruction itself (CCTA and coronary magnetic resonance imaging [MRI]).¹ Functional testing involves inducing ischemia by exercise or pharmacologic stress and detecting its consequences. However, not all patients are candidates. For example, obesity or obstructive lung disease can make obtaining echocardiographic images of sufficient quality difficult. Conversely, the presence of coronary calcifications can impede detecting coronary anatomy with coronary CCTA.

Diagnostic Testing

Some tests will be unsuitable for particular patients. The presence of dense arterial calcification or an intracoronary stent can produce significant beam-hardening artifacts and may preclude a satisfactory imaging. The presence of an uncontrolled rapid heart rate or arrhythmia hinders the ability to obtain diagnostically satisfactory images. Evaluation of the distal coronary arteries is more difficult than visualization of the proximal and mid-segment coronary arteries due to greater cardiac motion and the smaller caliber of coronary vessels in distal locations.

Evaluation of obstructive CAD involves quantifying arterial stenoses to determine whether significant narrowing is present. Lesions with stenosis more than 50% to 70% in diameter accompanied by symptoms are considered significant.

CCTA is a noninvasive imaging test that requires the use of intravenously administered contrast material and high-resolution, high-speed computed tomography machinery to obtain detailed volumetric images of blood vessels. It has been suggested that CCTA may help rule out CAD and avoid invasive coronary angiography in patients with a low clinical likelihood of significant CAD. Also, of interest is the potentially important role of nonobstructive plaques (i.e., those associated with <50% stenosis) because their presence is associated with increased cardiac event rates.² CCTA also can visualize the presence and composition of these plaques and quantify plaque burden better than conventional angiography, which only visualizes the vascular lumen. Plaque presence has been shown to have prognostic importance.

Coronary Arterial Anomalies

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

Radiation Exposure

Exposure to ionizing radiation increases lifetime cancer risk.⁵² Three studies have estimated excess cancer risks due to radiation exposure from CCTA. Assuming a 16-mSv dose, Berrington de Gonzalez et al (2009) estimated the 2.6 million CCTAs performed in 2007 would result in 2700 cancers or approximately 1 per 1000.⁵³ Smith-Bindman et al (2009) estimated that cancer would develop in 1 of 270 women and 1 of 600 men, age 40 undergoing CCTA with a 22-mSv dose.⁷ Einstein et al (2007) employed a standardized phantom to estimate organ dose from 64-slice CCTA.⁶ With modulation and exposures of 15 mSv in men and 19 mSv in women, calculated lifetime cancer risk at age 40 was 7 per 1000 men (1/143) and 23 per 1000 women (1/43). However, estimated radiation exposure used in these studies was considerably higher than received with current scanners—now typically under 10 mSv and often less than 5 mSv with contemporary machines and radiation reduction techniques. For example, in the 47-center Prospective Multicenter Study on Radiation Dose Estimates of Cardiac CT Angiography I (PROTECTION I) study enrolling 685 patients, the mean radiation dose was 3.6 mSv, using a sequential scanning technique.⁵⁴ In a study of patients undergoing an axial scanning protocol, Hausleiter et al (2012) reported on a mean radiation dose of 3.5 mSv and produced equivalent ratings of image quality compared with helical scan protocols, which had much higher mean radiation doses of 11.2 mSv.⁵⁵

Levels of radiation delivered with current generation scanners utilizing reduction techniques (prospective gating and spiral acquisition) has declined substantially—typically to under 10 mSv. For example, an international registry developed to monitor coronary CTA radiation recently reported a median 2.4 mSv (interquartile range, [IQR]: 1.3 to 5.5) exposure.³ By comparison, radiation exposure accompanying rest-stress perfusion imaging ranges varies according to isotope used—approximately 5 mSv for rubidium-82 (positron emission tomography, PET), 9 mSv for sestamibi (single-photon emission computed tomography, SPECT), 14 mSv for F-18 FDG (fludeoxyglucose) (PET), and 41 mSv for thallium; during

diagnostic invasive coronary angiography, approximately 7 mSv will be delivered.⁴ EBCT using electrocardiogram (ECG) triggering delivers the lowest dose (approximately 0.7 to 1.1 mSv with 3-mm sections). Any cancer risk due to radiation exposure from a single cardiac imaging test depends on age (higher with younger age at exposure) and gender (greater for women).⁵⁻⁷ Empirical data suggest that every 10 mSv of exposure is associated with a 3% increase in cancer incidence over 5 years.⁸

Incidental Findings

A number of studies using scanners with 64 or more detector rows were identified.^{43, 44, 45, 46, 47, 48, 49, 50, 51} Incidental findings were frequent (26.6% to 68.7%) with pulmonary nodules typically the most common and cancers typically more rare (>5/1000 or less). Aglan et al (2010) compared the prevalence of incidental findings when the field of view was narrowly confined to the cardiac structures with that when the entire thorax was imaged.⁴³ As expected, incidental findings were less frequent in the restricted field (clinically significant findings in 14% versus 24% when the entire field was imaged).

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

Regulatory Status:

CCTA is performed using multidetector-row CT (MDCT), and multiple manufacturers have received U.S. Food and Drug Administration (FDA) 510(k) clearance to market machines. Current machines are equipped with at least 64 detector rows. Intravenous iodinated contrast agents used for coronary CTA also have received FDA approval.

Medical Policy Statement

Coronary computed tomography-angiography (CCTA) and CT angiography (CTA) are **considered established procedures**. They are useful diagnostic procedures when indicated for individuals meeting selection criteria.

Inclusionary and Exclusionary Guidelines

Inclusions:

Note: CCTA may be done in an inpatient, outpatient or emergency department setting.

The following patients are considered appropriate candidates for CT angiography:

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

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

The following patients are considered appropriate candidates for coronary computed tomography-angiography (CCTA).

Suspected CAD in symptomatic patients who have not had evaluation for CAD within the preceding 60 days

CCTA is considered established in **ANY** of the following scenarios:

- Chest pain with or without other symptoms of myocardial ischemia
 - With pretest probability of CAD > 15%
- Patients without chest pain whose predominant symptom is dyspnea
 - With pretest probability of CAD > 15%
- Patients with any cardiac symptom who have diseases/conditions with which CAD commonly coexists, such as **ANY** of the following:
 - Abdominal aortic aneurysm
 - Established and symptomatic peripheral vascular disease
 - Prior history of stroke, transient ischemic attack (TIA), carotid endarterectomy (CEA), or high-grade carotid stenosis (> 70%)
 - Chronic kidney disease

Established flow-limiting CAD in patients who have new or worsening symptoms

CCTA is considered established in the following scenario:

- Patients whose symptoms persist despite maximal anti-ischemic medical therapy or contraindication thereto
 - Patients with established CAD and typical angina pectoris despite maximal anti-ischemic therapy maybe better served with invasive coronary angiography

Established or suspected CAD

CCTA is considered established in **ANY** of the following scenarios:

Patients who have undergone cardiac transplantation

- With new or worsening cardiac symptoms

- With new or worsening physical examination abnormalities
- Clinically stable patients who have not had evaluation for CAD in the preceding year

Patients (symptomatic or asymptomatic) with ANY of the following new onset arrhythmias who have not had evaluation for CAD since the arrhythmia was recognized

- Sustained (lasting more than 30 seconds) or nonsustained (more than 3 beats but terminating within 30seconds) ventricular tachycardia
- Atrial fibrillation or flutter and high or intermediate risk of CAD (using ASCVD Pooled Cohort Equations*)
- Atrial fibrillation or flutter and established CAD
- Frequent premature ventricular contractions (PVC) defined as more than 30 PVCs per hour on ambulatory EKG (Holter) monitoring
 - CCTA is not clinically indicated for evaluation of infrequent premature atrial or ventricular depolarizations

Patients (symptomatic or asymptomatic) with new onset congestive heart failure (CHF) or recently recognized LV systolic dysfunction who have not had evaluation for CAD since the onset of LV dysfunction/CHF

- For patients in this category with established CAD, or those with suspected CAD whose CAD risk (using ASCVD Pooled Cohort Equations*) is high, coronary angiography may be more appropriate than noninvasive evaluation

Abnormal resting EKG

- Patients with **ANY** of the following newly recognized and not previously evaluated resting EKG changes:
 - Left bundle branch block
 - ST depression ≥ 1 mm
 - Left ventricular (LV) hypertrophy with repolarization abnormality
- Patients who would otherwise undergo exercise EKG testing (without imaging) but have **ANY** of the following resting EKG findings that would render the interpretation of an exercise EKG test difficult or impossible:
 - Left bundle branch block
 - Ventricular paced rhythm
 - Left ventricular hypertrophy with repolarization abnormality
 - Digoxin effect
 - ST depression ≥ 1 mm on a recent EKG (within the past 30 days)
 - Pre-excitation syndromes (e.g., Wolff-Parkinson-White syndrome)

Patients with abnormal exercise treadmill test (performed without imaging) who have not undergone evaluation for CAD since the treadmill test

- Abnormal findings on an exercise treadmill test include chest pain, ST segment change, abnormal blood pressure response, or complex ventricular arrhythmias

Patients who have undergone recent (within the past 60 days) stress testing with adjunctive imaging (MPI, SE, perfusion PET, stress MRI)

- When the stress imaging test is technically suboptimal, technically limited, inconclusive, indeterminate, or equivocal, such that myocardial ischemia cannot be adequately excluded

- A stress imaging test is deemed to be abnormal when there are abnormalities on the imaging portion of the test. Electrocardiographic abnormalities without imaging evidence of ischemia do not render a stress imaging test abnormal.
- When the stress imaging test is abnormal and **ALL** of the following apply:
 - The stress test demonstrates moderate or severe ischemia
 - CCTA is requested to exclude left main CAD
 - In the absence of left main CAD GDMT will be instituted
 - Invasive coronary angiography will be reserved for persistent symptoms on GDMT

Preoperative evaluation of patients undergoing non-coronary cardiac valve surgery

- Patients undergoing evaluation for transcatheter aortic valve implantation/replacement (TAVI or TAVR) at low risk for CAD (using ASCVD Pooled Cohort Equations*) to avoid invasive angiography, where all the necessary preoperative information can be obtained using cardiac CT
- Patients undergoing evaluation for valve surgery (not including TAVR) at low or intermediate risk for CAD (using ASCVD Pooled Cohort Equations*)

* Factors included in ASCVD Pooled Cohort Equations

Age	Sex	Race	Lipid profile	Diabetes mellitus	Hypertension	Antihypertensive medication use	Tobacco use
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The atherosclerotic cardiovascular disease (ASCVD) Pooled Cohort Equations risk calculation tool is used to estimate risk of atherosclerotic cardiovascular disease. This tool, which is endorsed by several professional societies, incorporates age, gender, race, several clinical conditions known to affect ASCVD risk (including diabetes, dyslipidemia, hypertension), and tobacco use.

Preoperative cardiac evaluation of patients undergoing non-emergency non-cardiac surgery (includes surveillance for CAD in those awaiting solid organ transplant)

Prior to considering elective surgery, patients with active cardiac conditions such as unstable coronary syndromes (unstable angina), decompensated heart failure (NYHA class IV, worsening or new onset heart failure), significant arrhythmias (third degree AV block Mobitz II AV block, uncontrolled supraventricular arrhythmia, symptomatic ventricular arrhythmias, ventricular tachycardia), symptomatic bradycardia or severe stenotic valvular lesions should be evaluated and managed per ACC/AHA guidelines. That evaluation may include CCTA.

- **Low-risk surgery** (endoscopic procedures, superficial procedures, cataract surgery, breast surgery, ambulatory surgery)
 - Provided that there are no active cardiac conditions (as outlined above), CCTA prior to low-risk surgery is considered **not medically necessary**
- **Intermediate-risk surgery (including but not limited to intraperitoneal and intrathoracic surgery, carotid endarterectomy, head and neck surgery, orthopedic surgery, prostate surgery, gastric bypass surgery) or high-risk surgery** (including but not limited to aortic and other major vascular surgery, peripheral vascular surgery) when **BOTH** of the following apply:
 - Patient has not had a negative evaluation for CAD or a coronary revascularization procedure within the previous one (1) year

- At least **ONE** of the following applies:
 - Patient has established CAD (prior MI, prior PCI or CABG) or presumed CAD (Q waves on EKG, abnormal MPI, SE, or cardiac PET)
 - Patient has compensated heart failure or prior history of CHF
 - Patient has diabetes mellitus
 - Patient has chronic kidney disease
 - Patient has a history of cerebrovascular disease (TIA, stroke, or documented carotid stenosis requiring carotid endarterectomy)
 - Patient is unable to walk on a treadmill for reasons other than obesity
- **Patients awaiting solid organ transplant**
 - Asymptomatic patients who have not undergone evaluation for CAD within the preceding one (1) year
 - Patients with symptoms consistent with myocardial ischemia

Miscellaneous indications for CCTA

CCTA is considered established in **ANY** of the following scenarios:

Inability to perform exercise EKG test

- Patients who would otherwise undergo exercise EKG testing (without imaging) but are unable (for reasons other than obesity) to perform exercise to a degree that would yield a diagnostic test. This provision includes patients with musculoskeletal, neurological or pulmonary limitation.

Established Kawasaki disease

- Periodic surveillance up to one year following diagnosis when previous imaging study reveals **ANY** of the following: Coronary abnormalities
 - Left ventricular dysfunction
 - Pericardial effusion
 - Valvular regurgitation (other than trace or trivial regurgitation)
 - Aortic dilation
 - Annual evaluation in patients who have small or medium-sized coronary artery aneurysms
 - Semiannual evaluation (every 6 months) in patients who have large or giant coronary artery aneurysms, or coronary artery obstruction

Congenital coronary artery anomalies

- Evaluation of suspected congenital anomalies of the coronary arteries in **ANY** of the following scenarios:
 - Exertional syncope
 - History of anomalous coronary artery in a first-degree relative
 - Following coronary angiography which failed to adequately define the origin or course of a coronary artery
 - Coronary ostia appear to be abnormally positioned on echocardiography

CCTA is also established for the evaluation of intra- and extra-cardiac structures, including but not limited to:

- Evaluation of cardiac mass (suspected tumor or thrombus) and patients with technically limited images from echocardiogram, MRI or TEE.

- Evaluation of pericardial conditions (pericardial mass, constrictive pericarditis, or complications of cardiac surgery) and patients with technically limited images from echocardiogram, MRI or TEE.
- Evaluation of pulmonary vein anatomy prior to invasive radiofrequency ablation for atrial fibrillation (e.g., pulmonary vein isolation).
- Non-invasive coronary arterial mapping, including internal mammary artery prior to repeat cardiac surgical revascularization.
- Evaluation of suspected aortic dissection or thoracic aortic aneurysm.
- Evaluation of suspected pulmonary embolism.

The following patients are considered appropriate candidates for cardiac CT.

Congenital heart disease

Cardiac CT is considered established in **ANY** of the following scenarios:

- Evaluation of suspected or established congenital heart disease in patients whose echocardiogram is technically limited or non-diagnostic
- Further evaluation of patients whose echocardiogram suggests a new diagnosis of complex congenital heart disease
- Evaluation of complex congenital heart disease in patients who are less than one year post-surgical correction
- Consideration for surgical repair of congenital heart disease
- Evaluation of complex congenital heart disease in patients who have new or worsening symptoms and/or a change in physical examination
- Assist in surgical planning for patients with complex congenital heart disease
- Surveillance in asymptomatic patients with complex congenital heart disease who have not had cardiac MRI or cardiac CT within the preceding year
 - Cardiac MRI or transesophageal echocardiography may be preferable to cardiac CT in order to avoid radiation exposure.

Cardiomyopathy

Cardiac CT is considered established in **ANY** of the following scenarios:

- Evaluation of patients with suspected arrhythmogenic right ventricular dysplasia (ARVD) who have **ANY** of the following:
 - Severe right ventricular dysfunction on another cardiac imaging study
 - Precordial T wave inversion not associated with RBBB
 - First-degree relative with established ARVD or unexplained sudden cardiac death at age younger than 35 years
 - Ventricular tachycardia or frequent PVCs (> 500 in 24 hours or > 30 per hour)
- To assess left ventricular (LV) function in patients with suspected or established cardiomyopathy when all other noninvasive imaging is not feasible or technically suboptimal
 - Other modalities providing noninvasive evaluation of LV function include transthoracic and transesophageal echocardiography, blood pool imaging (MUGA or First pass), and cardiac MRI
- To assess right ventricular function in patients with suspected right ventricular dysfunction when all other noninvasive imaging is not feasible or technically suboptimal
 - Other modalities providing noninvasive evaluation of right ventricular function include transthoracic and transesophageal echocardiography, blood pool imaging (MUGA or First pass), and cardiac MRI

Valvular heart disease

Cardiac CT is considered established in **EITHER** of the following scenarios:

- Evaluation of suspected dysfunction of native or prosthetic cardiac valves when all other cardiac imaging options are not feasible or technically suboptimal
 - Other modalities providing noninvasive evaluation of native or prosthetic valves include transthoracic and transesophageal echocardiography, and cardiac MRI
- Evaluation of established dysfunction of native or prosthetic cardiac valves when all other cardiac imaging options are not feasible or technically suboptimal
 - Other modalities providing noninvasive evaluation of native or prosthetic valves include transthoracic and transesophageal echocardiography, and cardiac MR

Evaluation of patients with established coronary artery disease (CAD)

Cardiac CT is considered established for the following:

- Noninvasive localization of coronary bypass grafts or potential grafts (including internal mammary artery) and/or evaluation of retrosternal anatomy in patients undergoing repeat surgical revascularization

Intra-cardiac and para-cardiac masses and tumors

Cardiac CT is considered established in **ANY** of the following scenarios:

- Patients with a suspected cardiac or para-cardiac mass (thrombus, tumor, etc.) suggested by transthoracic echocardiography, transesophageal echocardiography, blood pool imaging or contrast ventriculography who have not undergone cardiac CT or cardiac MRI within the preceding 60 days
- Patients with established cardiac or para-cardiac mass (thrombus, tumor, etc.) who are clinically unstable
- Patients with established cardiac or para-cardiac mass (thrombus, tumor, etc.) who are clinically stable and have not undergone cardiac CT or cardiac MRI within the preceding year
- Patients with established cardiac or para-cardiac mass (thrombus, tumor, etc.) who have undergone treatment (chemotherapy, radiation therapy, thrombolysis, anticoagulation or surgery) within the preceding year and have not had cardiac CT or cardiac MRI within the preceding 60 days

Left atrial appendage closure device

Cardiac CT is considered established in **EITHER** of the following scenarios:

- Evaluation of cardiac anatomy prior to implantation of a left atrial appendage closure device
- Following placement of a left atrial appendage closure device, a single study may be performed as an alternative to TEE to assess for intracardiac thrombus

Cardiac aneurysm and pseudoaneurysm

Cardiac CT is considered established for evaluation of cardiac aneurysm or pseudoaneurysm.

Evaluation of pericardial conditions (pericardial effusion, constrictive pericarditis, or congenital pericardial diseases)

Cardiac CT is considered established in **ANY** of the following scenarios:

- Patients with suspected pericardial constriction
- Patients with suspected congenital pericardial disease
- Patients with suspected pericardial effusion who have undergone echocardiography deemed to be technically suboptimal in evaluation of the effusion
- Patients whose echocardiogram shows a complex pericardial effusion (loculated, containing solid material)

Evaluation of cardiac venous anatomy

Cardiac CT is considered established in **EITHER** of the following scenarios:

- For localization of the pulmonary veins in patients with chronic or paroxysmal atrial fibrillation/flutter who are being considered for ablation
- Coronary venous localization prior to implantation of a biventricular pacemaker

Evaluation of the thoracic aorta

Cardiac CT is considered established in **ANY** of the following scenarios:

- Patients with suspected thoracic aortic aneurysm/dilation who have not undergone CT or MRI of the thoracic aorta within the preceding 60 days
- Patients with confirmed thoracic aortic aneurysm/dilation with new or worsening signs/symptoms
- Ongoing surveillance of stable patients with confirmed thoracic aortic aneurysm/dilation who have not undergone surgical repair and have not had imaging of the thoracic aorta within the preceding 6 months
- Patients with suspected aortic dissection
- Patients with confirmed aortic dissection who have new or worsening symptoms
- Patients with confirmed aortic dissection in whom surgical repair is anticipated (to assist in preoperative planning)
- Ongoing surveillance of stable patients with confirmed aortic dissection who have not undergone imaging of the thoracic aorta within the preceding year
- Patients with confirmed aortic dissection or thoracic aortic aneurysm/dilation who have undergone surgical repair within the preceding year and have not undergone imaging of the thoracic aorta within the preceding 6 months
- Patients who have sustained blunt chest trauma, penetrating aortic trauma or iatrogenic trauma as a result of aortic instrumentation
- Patients being evaluated for potential transcatheter aortic valve implantation/replacement (TAVI or TAVR) provided that the patient has not undergone cardiac CT or cardiac MRI within the preceding 60 days

Exclusions:

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

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

Established codes:

75572

75573

75574

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

75571

Rationale

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

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

PATIENTS WITH ACUTE CHEST PAIN PRESENTING TO THE EMERGENCY SETTING

Clinical Context and Test Purpose

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

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

Populations

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

Interventions

The intervention of interest is CCTA.

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. 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.

Clinically Valid

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

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

Clinically Useful

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

Direct Evidence

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

Systematic Reviews

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

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

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

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

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

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

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

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

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

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

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

Randomized Controlled Trials

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

Table 3. Characteristics of RCTs Assessing CCTA in ED Settings

Study; Trial	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator(s)
Smulders et al (2019) ⁶⁶ CARMENTA	Netherlands	1	2012-2016	Patients with acute chest pain, normal or inconclusive ECG, and elevated cardiac troponin levels presenting to the ED	70 to CCTA	68 to CMR; 69 to routine clinical care
Levsky et al (2018) ¹⁴	U.S.	1	2011-2016	Patients with acute chest pain or pressure for whom noninvasive testing is requested	201 to CCTA	199 to SE
Hamilton-Craig et al (2014) ¹⁵ ; CT-COMPARE	Australia	1	2010-2011	Men ≥30 y or women ≥40 y presenting to the ED with acute undifferentiated chest pain	322 to CCTA	240 to SOC (exercise treadmill testing)
Linde et al (2013) ¹⁶ ; CATCH	Denmark	1	2010-2013	Patients with suspected NSTEMI-ACS but normal ECG and troponins; discharged within 24 h needing further risk stratification	299 to CCTA (285 had FU available)	301 to SOC (291 had FU available)
Litt et al (2012) ¹⁷ ; AC RIN-PA	U.S.	5	2009-2011	Symptoms consistent with possible ACS; >30 y; low risk of MI	908 to CCTA	462 to traditional care

Hoffmann et al (2012) ¹⁸ ; ROMICAT II	U.S.	9	2010-2012	Chest pain or angina equivalent <24 h before ED presentation; 40-74 y; sinus rhythm; warranting further risk stratification	50 to CCTA	499 to SOC
Goldstein et al (2011) ¹⁹ ; CT-STAT	U.S.	16	2007-2008	Chest pain <12 h; ≥25 y; low risk of complications; no sign of ischemia at enrollment	361 to CCTA	338 to MPI
Goldstein et al (2007) ²⁰	U.S.	1	2005	Chest pain or angina-like symptoms <12 h; ≥25 y; low risk of complications	99 to MSCT	98 to SOC

ACS: acute coronary syndrome; CCTA: coronary computed tomography angiography; CMR; cardiovascular magnetic resonance imaging; ECG: electrocardiogram; ED: emergency department; FU: follow-up; MI: myocardial infarction; MPI: myocardial perfusion imaging; MSCT: multislice computed tomography; NSTEMI-ACS: non-ST-elevation acute coronary syndrome; RCT: randomized controlled trial; 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).⁶⁸ 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 myocardial infarction (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% confidence interval [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 invasive coronary angiography (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 (i.e., routine clinical care) in patients with non-ST-segment elevation myocardial infarction (NSTEMI).⁶⁶ Results revealed that CMR or CCTA as an initial test was associated with a reduced proportion of patients referred to ICA during initial hospitalization [87% CMR ($p=.001$) and 66% CCTA ($p<.001$) as compared to routine clinical care (100%)]. Significantly fewer ICAs were performed in the CCTA- than CMR-first strategy ($p=.004$). The reduction in ICA in the CMR- or CCTA-first strategy compared with routine clinical care was persistent after 1 year [88% CMR ($p=.003$), 70% CCTA ($p<.001$) and 100% routine clinical care]. Similar clinical outcomes were seen: CMR versus routine, hazard ratio (HR) 0.78; 95% confidence interval (CI), 0.37 to 1.61; CCTA versus routine, HR 0.66; 95% CI, 0.31 to 1.42; and CMR versus CCTA, (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 myocardial infarction (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 of the stress echocardiography arm, resulting in a difference of 8% (95% CI, 1% to 15%; $p=0.026$).¹⁴ Median length of stay in the hospital was longer for the CCTA arm (58 hours vs. 34 hours; $p=.002$). 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, 5.3-7.8 mSv), significantly more than that of stress echocardiography (0 mSv; $p < 0.001$) The trial had a number of limitations, including the single-center design and omission of high sensitivity troponin assays.

Hamilton-Craig et al (2014) reported on the 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.¹⁵ 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 CATCH trial, which randomized 600 patients to a CCTA-guided strategy or to SOC.¹⁶ For the CCTA-guided strategy, referral for ICA required coronary stenosis greater than 70%. This trial differed in design from the others because patients had been discharged from the ED, and if there was intermediate stenosis (50%-70%) on CCTA, a stress test was performed.

Litt et al (2012) reported on the AC RIN-PA trial, which also evaluated the safety of CCTA in patients in the ED.¹⁷ Although the trial was a randomized comparison with traditional care, the principal outcome was safety after negative CCTA examinations. No patients who had negative CCTA examinations ($n=460$) died or had a myocardial infarction (MI) within 30 days. Compared with traditional care, patients in the CCTA group had higher rates of discharge from the ED (49.6% vs. 22.7%) and higher rates of detection of coronary disease.

Hoffmann et al (2012) reported on the ROMICAT II trial, which compared the length of stay with outcomes in 549 patients evaluated using CCTA or usual care.¹⁸ For the 50 patients in the CCTA arm, mean hospital length of stay was reduced by 7.6 hours, and more patients were discharged directly from the ED (47% vs. 12%). There were no undetected coronary syndromes or differences in adverse events at 28 days. However, in the CCTA arm, there was more subsequent diagnostic testing and higher cumulative radiation exposure.

Goldstein et al (2011) reported on the CT-STAT trial, which evaluated a similar sample of 699 patients.¹⁹ Over a 6-month follow-up, there were no deaths in either arm; there were 2 cardiac events in the CCTA arm and one in the perfusion imaging arm. A second noninvasive test was obtained more often after CCTA (10.2% vs. 2.1%), but cumulative radiation exposure in the CCTA arm (using retrospective gating) was significantly lower (mean, 11.5 mSv vs. 12.8 mSv).

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

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

Study	ICA (CCTA vs Control), %	Diagnostic Accuracy (CCTA vs Control), % ^a	MI in Negative CCTA Arm	Median Diagnostic Time (CCTA vs Control), hr ^b	FU, mo
Gray et al (2021)	54 vs 60.8	NR	NR	2.2 vs 2.0 ^d	12
Smulders et al (2019) ⁶⁶	66 vs 100	NR	7	NR	1 and 12
Levsky et al (2018) ¹⁴	NR	NR	NR	5.4 vs 4.7 ^d	1 and 12

Hamilton-Craig et al (2014) ¹⁵	9.0 vs 4.2	94%/99% vs 83%/91% ^c	0	13.5 vs 20.7 ^d	1 and 12
Linde et al (2013) ¹⁶	17 vs 12	71 vs 36 ^e	0	NR	4
Litt et al (2012) ¹⁷	5.1 vs 4.2	NR	0	18.0 vs 24.8	1
Hoffmann et al (2012) ¹⁸	12.0 vs 21.0	NR	0	5.8 vs 21.0	1
Goldstein et al (2011) ¹⁹	6.6 vs 6.2	76.9 vs 54.5	0	2.9 vs 6.2	6
Goldstein et al (2007) ²⁰	12.1 vs 7.1	88.9 vs 98.0	0	3.4 vs 15.0	6

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

^a Confirmed with angiographic and clinical results.

^b Time from randomization to definitive diagnosis.

^c 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 vs standard of care.

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

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

Study	Population ^a	Intervention ^b	Comparator ^c	Outcomes ^d	Duration of Follow-Up ^e
Smulders et al (2019) ⁶⁶	2. Patients with a history of myocardial disease and/or severe noncardiac comorbidities were excluded				
Levsky et al (2018) ¹⁴					
Hamilton-Craig et al (2014) ¹⁵	4. Limited applicability to men <30 y and women <40 y				
Linde et al (2013) ¹⁶					
Litt et al (2012) ¹⁷	4. Limited to patients 40 to 74 y; may not be relevant for				

	younger or older individuals				
Hoffmann et al (2012) ¹⁸					
Goldstein et al (2011) ¹⁹					
Goldstein et al (2007) ²⁰		3. Unequal rates of ICA/revascularization	3. Unequal rates of ICA/revascularization		

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

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

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

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

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

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

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

Study	Allocation ^a	Blinding ^b	Selective Reporting ^c	Data Completeness ^d	Power ^e	Statistical ^f
Smulders et al (2019) ⁶⁶		1, 2.			3. Sample size calculation based on an estimated 75% ICA referral rate; however, all patients (100%) in the routine clinical care arm eventually underwent ICA	
Levsky et al (2018) ¹⁴					2. Not powered to detect differences in MACE	
Hamilton-Craig et al (2014) ¹⁵					2. Not powered to compare outcomes	
Linde et al (2013) ¹⁶		1. Only patients and clinicians blinded to treatment allocation			2. Not powered to detect differences in secondary outcomes (intermediate cardiac events)	

Litt et al (2012) ¹⁷					2. Due to low incidence of events, not powered for primary outcome (safety)	
Hoffmann et al (2012) ¹⁸		1. No blinding to treatment				
Goldstein et al (2011) ¹⁹				1. 10.3% of patients lost to follow-up	2. Not powered for secondary outcome (safety)	
Goldstein et al (2007) ²⁰					1. Power calculations not reported	4. No assessment of alternative noninvasive tests

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

CCTA: coronary computed tomography angiography; ED: emergency department; ICA: invasive coronary angiography; MACE: major adverse cardiac event; RCT: randomized controlled trial:

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

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

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

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

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

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

Long-Term Follow-Up Studies

Table 7. Results of Follow-Up Studies of RCTs

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

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

Nonrandomized Studies

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

initially missed. No limitations were identified. Tables 8 and 9 summarize the trial characteristics and results.

Table 8. Key Nonrandomized Trials Assessing CCTA in ED Settings

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

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

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

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

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

^a Of detected coronary stenosis >50%.

^b Number of patients who received ICA.

Section Summary: Acute Chest Pain Presenting to the Emergency Setting

The high negative predictive value of CCTA in patients presenting to the ED with chest pain permits ruling out coronary disease with high accuracy. The efficiency of the workup is improved, as patients are safely and quickly discharged from the ED with no adverse outcomes among patients who have negative CTA examinations.

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

PATIENTS WITH STABLE CHEST PAIN AND SUSPECTED CAD

Before the use of CCTA, the initial noninvasive test in a diagnostic strategy was always a functional test. Current practice guidelines recommend a noninvasive test be performed in patients with intermediate risk of CAD. The choice of functional test is based on clinical factors such the predicted risk of disease, electrocardiogram interpretability, and ability to exercise. When disease is detected, treatment alternatives include medical therapy or revascularization (percutaneous coronary intervention or coronary artery bypass graft surgery). If revascularization is indicated, patients undergo ICA to confirm the presence of stenosis. Which approach to adopt is based on the extent of anatomic disease, symptom severity, evidence of ischemia from functional testing, and, more recently, fractional flow reserve obtained during invasive angiography. Many studies have shown that only a subset of anatomically defined coronary lesions are clinically significant and benefit from revascularization. Other studies have shown only limited benefits for treating coronary stenoses in stable patients. Thus, an

assessment of the diagnostic characteristics of CCTA alone is insufficient to establish clinical utility. A difficulty in evaluating a noninvasive diagnostic test for CAD is that patient outcomes depend not only on test results but also on the management and treatment strategy. The most convincing evidence of clinical utility compares outcomes after anatomic-first (CCTA) and functional-first (e.g., perfusion imaging, stress echocardiography) strategies.

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

Clinical Context and Test Purpose

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

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

Populations

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

Interventions

The intervention of interest is CCTA.

Comparators

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

Outcomes

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

Clinically Valid

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

Review of Evidence

There is a large body of evidence evaluating the diagnostic characteristics of CCTA for identifying coronary lesions. The best estimate of the diagnostic characteristics of CCTA can be obtained from recent meta-analyses and systematic reviews. Table 10 shows ranges of sensitivity and specificity for functional noninvasive tests from studies of the diagnosis and management of stable angina reviewed by Fihn et al (2012).²⁴ Sensitivities tended to range between 70% and 90%, depending on the test and study, and specificities ranged between 70% and 90%.

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

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

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

Adapted from Fihn et al (2012).²⁴

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

Study	Study Population	Reference Standard	Threshold for Positive Index Test	Timing of Reference and Index Tests	Blinding of Assessors	Comment
Haase et al (2019) ²⁵	Individuals with a clinical indication for coronary angiography due to suspected CAD because of stable chest pain. Individual patient data sufficient to calculate pre-test clinical risk. N = 5332 in 65 prospective diagnostic accuracy studies	ICA	CCTA: Obstructive CAD: \geq 50% stenosis Pre-test Clinical Risk: CAD Consortium prediction tool	NR	NR	Acceptable thresholds for index and reference tests were unclear. Calculation of pre-test clinical risk assessment not clearly described. Timing of tests not reported.

Nielsen et al (2014) ²⁶	Studies examining the diagnostic accuracy of CCTA vs functional testing in patients suspected of stable CAD N = 1575 in 17 diagnostic accuracy studies		ICA	CCTA: NR	NR	NR	Details on blinding and timing were limited. Quality assessment results for bias risk in diagnostic accuracy studies was predominantly low.
Ollendorf et al (2011) ²⁷	42 diagnostic accuracy studies		ICA	CCTA: NR	NR	Blinded review of CCTA and ICA	
Health Quality Ontario (2010) ²⁸	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; MA: meta-analysis; NR: not reported; SR: systematic review.

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

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

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

Clinically Useful

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

Direct Evidence

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

Systematic Reviews

De Campos et al (2022) conducted a meta-analysis of long-term outcomes in patients receiving CCTA or functional testing for stable CAD.⁶⁹ 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; I² =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.²⁹ In the CCTA arm, there were 10,315 patients, and in the functional stress testing arm, there were 9777 patients; both CCTA and functional stress testing strategies varied among the 13 trials. Overall mortality and cardiac hospitalization did not differ between CCTA and functional stress testing groups. There were fewer cases of MI in the CCTA group than in the functional stress testing group; however, the incidence of ICA and revascularization were higher in the CCTA group. CCTA was associated with an increase in new diagnoses of CAD as well as increased prescription of aspirin and statin therapy. All trials reported a lack of blinding, both of patients and personnel, and the overall quality of evidence was moderate, despite a high risk of bias in several studies included. Additional limitations included the lack of available patient-level data, the absence of assessment of time to hospital discharge, and differences in radiation exposure. Tables 13 and 14 summarize review characteristics and results.

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

Study	Dates	Trials	Participants	N (Range)	Design	Duration
De Campos et al (2022)	2009-2019	8	Patients with stable CAD	29,579 (303 to 9102)	RCT	≥ 12 months follow-up
Foy et al (2017)²⁹	2000-2016	13	Patients with suspected CAD	20,092 (CCTA arm: n=10,315; functional stress testing arm: n=9777)	RCT	NR

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

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

Study	Incidence of ICA, %	Revascularization, %	Adverse Events, %	New Diagnosis of CAD, %	Medication Use, % ^a

De Campos et al (2022)					
CCTA vs. Functional stress testing	14.86 vs 19.43 ^b	NR	NR	NR	NR
PR (95% CI)	0.75 (0.6 to 0.96)	1.63 (0.97 to 2.74)			
Foy et al (2017)²⁹					
CCTA vs. Functional stress testing	11.7 vs. 9.1	7.2 vs. 9.1	•Mortality: 1.0 vs. 1.1 •Hospitalization: 2.7 vs. 2.7 •MI: 0.7 vs. 1.1	18.3 vs. 8.3	Aspirin: 21.6 vs. 8.2 Statins: 20.0 vs. 7.3
RR (95% CI)	1.33 (1.12 to 1.59)	1.86 (1.43 to 2.43)	•Mortality: 0.93 (0.71 to 1.21) •Hospitalization: 0.98 (0.79 to 1.21) •MI: 0.71 (0.53 to 0.96)	2.80 (2.03 to 3.87)	Aspirin: 2.21 (1.21-4.04) Statins: 2.03 (1.09-3.76)

CAD: coronary artery disease; CCTA: coronary computed tomography angiography; CI: confidence interval; ICA: invasive coronary angiography; MI: myocardial infarction; NR: not reported; OR: odds ratio; RR: relative risk; SR: systematic review.

^a Proportion of patients who experienced a significant increase in medication use.

^b This analysis excludes 1 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 RCTs Assessing CCTA in Stable Chest Pain

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
Maurovich-Horvat et al (2022) 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)	U.S.	44	2011-2013	Patients with stable angina and suspected CAD	518 to CCTA	532 to SPECT-MPI
Rudzinski et al (2018); CAT-CAD	Poland	1	2015-2016	Patients with stable angina and suspected CAD	60 to CCTA	60 to ICA
Newby et al (2018); SCOT-HEART	U.K	12	2010-2019	Patients referred for assessment of angina due to suspected CHD	2073 to standard of care plus CCTA	2073 to standard of care
Chang et al (2018)	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
Douglas et al (2015); PROMISE	U.S	193	2010-2013	Systematic outpatients without diagnosed CAD	4996 to anatomic testing strategy with CCTA	5007 to functional testing strategy

SCOT-HEART Investigators (2015) ; SCOT-HEART	U.K.	12	2010-2014	Patients referred for assessment of angina due to suspected CHD	2073 to standard of care plus CCTA	2073 to standard of care
McKavanagh et al (2015) ;CAPP	U.K.	NR	2010-2011	Patients with symptoms of stable chest pain to EST or cardiac CT	250 to EST	250 to cardiac CT

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

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.⁷⁰ 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.⁴⁴ The primary endpoint was first MACE (cardiac death or MI), or revascularization. Over a mean follow-up period of 16.2 months, there was a similar rate of MACE or revascularization in patients with CCTA compared to SPECT-MPI (p=.19). The authors did not report separate rates of MACE and revascularization.

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

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

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

Douglas et al (2015) reported on the PROMISE trial, which randomized 10,003 patients to CCTA or exercise electrocardiography, nuclear stress testing, or stress echocardiography (as determined by physician preference) as the initial diagnostic evaluation.⁴⁸ CCTA also did not meet prespecified noninferiority criteria compared with alternative testing. Some clinical outcomes assessed at 12 months favored CCTA, but the differences were nonsignificant. Coronary catheterization and revascularization rates were higher in the CCTA group. In a

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

In the SCOT-HEART trial (2015), investigators randomized 4146 patients to CCTA plus SOC or SOC alone. The primary end point was the change in the proportion of patients with a more certain diagnosis (presence or absence) of angina pectoris.⁴⁹ Secondary outcomes included death, MI, revascularization procedures, and hospitalizations for chest pain. Analysis of the primary outcome showed that patients who underwent CCTA had an increase in the certainty of their diagnosis relative to those in usual care (relative risk, 1.79; 95% CI, 1.62 to 1.96). Williams et al (2017) reported on symptoms and quality of life for participants in the SCOT-HEART trial.⁵³ Symptoms improved in both groups; however, improvements in symptoms and quality of life at 6 months were lower in patients in the CCTA arm than the functional testing arm. This outcome was due primarily to patients who were diagnosed with moderate CAD or had a new prescription of preventative therapy compared with patients diagnosed with normal coronary arteries or who had their preventative therapy discontinued.

In the comparison of cardiac computerized tomography and exercise stress electrocardiogram test for the investigation of stable chest pain CAPP trial, McKavanagh et al (2015) randomized 500 patients with stable chest pain to CCTA or exercise stress testing.⁵⁰ The primary outcome was the change difference in scores of Seattle Angina Questionnaire domains at 3 months. Patients were also followed for further diagnostic tests and management. In the CCTA arm, 15.2% of subjects underwent revascularization. In the exercise stress testing arm, 7.7% underwent revascularization. For the primary outcome, angina stability and quality of life showed significantly greater improvement in the CCTA arm than in the exercise stress testing arm.

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

Study	Death or Nonfatal Myocardial Infarction	Incidence of ICA	Revascularization	Normal Findings on ICA	Angina Stability	Hospitalization
Maurovich-Horvat et al (2022)		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)		NR	NR	NR	NR	NR

CCTA, %	Negative test (1.2%); positive test (20.5%)					
SPECT-MPI, %	Negative test (3.2%); Positive test (34.8%)*					
HR	1.03 (0.61 to 1.75)*					
P	.19					
Rudzinski et al (2018)						
CCTA, n	0	21		5		25
ICA, n	0	59		42		73
P		<0.0001		<0.0001		<0.0001
Newby et al (2018)						
CCTA + standard care, n (%)	48 (2.3)	491 (23.7)	279 (13.5)			
Standard care, n (%)	81 (3.9)	502 (24.2)	267 (12.9)			
HR at 5 yr (95% CI)	0.59 (0.41 to 0.84)	1.00 (0.88-1.13)	1.07 (0.91 to 1.27)			
P	0.004	NR	NR			
Chang et al (2018)						
Selective Referral to CCTA, n (%)	36 (4.6)	179 (23%)	98 (13%)	24.6%		33 (4.2%)
Direct Referral to ICA, n (%)	33 (4.6)	719 (89%)	127 (18%)	61.1%		31 (4.3%)
HR (95% CI)	0.99 (0.66 to 1.47)	NR	NR			NR
P	0.99 .026 (1-sided noninferiority)	<0.001	0.007	<0.001		NR
Douglas et al (2015)						
CCTA group	104					61
Functional testing group	112					41
HR (95% CI)	0.88 (0.67 to 1.15)					
P	0.35					
SCOT-HEART Investigators (2015)						
CCTA, n (%)	26					511 (12.3)
Standard care, n (%)	42					247 (11.9)
HR (95% CI)	0.616 (0.378-1.006)					0.928 (0.780-1.104)
P	0.527					0.399
McKavanagh et al (2015)						
MD at 3 mo (95% CI)					-11.1 (-17.4 to -4.8)	
P						
MD at 12 mo (95% CI)					-6.8 (-12.8 to -0.7)	
P					0.028	

CI: confidence interval; CCTA: coronary computed tomography angiography; HR: hazard ratio; ICA: invasive coronary angiography; MD: mean difference; NR: not reported; RCT: randomized controlled trial; 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. Relevance Limitations of RCTs Assessing CCTA in Stable Chest Pain

Study	Population ^a	Intervention ^b	Comparator ^c	Outcomes ^d	Duration of FU ^e
Maurovich-Horvat et al (2022)	4. Conducted only in European population				
Stillman et al (2020)				1. Key health outcomes not addressed	2. Not sufficient duration for harms
Rudzinski et al (2018)					2. Not sufficient duration for harms.
Newby et al (2018)	4. Patients >75 y excluded.				
Chang et al (2018)	4. Population included >84% Asian patients in each treatment arm.				
Douglas et al (2015)				1. Test performance and utility not addressed	
SCOT-HEART Investigators (2015)	4. Patients >75 y excluded.				
McKavanagh et al (2015)	4. Low number of diabetics included due to exclusion criteria		1, 2. Noted difficulty in contrasting the results of anatomic and functional tests		

The study limitations stated in this table are those notable in the current review; this is not a comprehensive limitations assessment.

CCTA: coronary computed tomography angiography; RCT: randomized controlled trial.

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

^b Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest.

^c Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.

^d Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.

^e Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

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

Study	Allocation ^a	Blinding ^b	Selective Reporting ^c	Data Completeness ^d	Power ^e	Statistical ^f
Maurovich-Horvat et al (2022)		1. Not blinded to treatment assignment.				

Stillman et al (2020)		1. Not blinded to treatment assignment.		1. High loss to follow-up or missing data (ie, low adherence)		
Rudzinski et al (2018)	2. Allocation not concealed.			2. Unclear handling of missing data.	1. Power calculation not reported.	3. Confidence intervals not reported.
Newby et al (2018)		1-3. Treatments and outcomes not blinded and potential bias among attending clinicians was present.				
Chang et al (2019)	2. Allocation not concealed.	1. Not blinded to treatment assignment.		1. High loss to follow-up or missing data.		
Douglas et al (2015)						
SCOT-HEART Investigators (2015)		1-3. Treatments and outcomes not blinded and potential bias among attending clinicians was present.				
McKavanagh et al (2015)					3. Study not powered to evaluate prognosis or adverse CAD events	

The study limitations stated in this table are those notable in the current review; this is not a comprehensive limitations assessment.

CAD: coronary artery disease; CCTA: coronary computed tomography angiography; RCT: randomized controlled trial.

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

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

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

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

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

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

Section Summary: Stable Angina and Suspected CAD

A number of studies have evaluated the diagnostic accuracy of CCTA for diagnosing CAD in an outpatient population. In general, these studies have reported high sensitivity and specificity, although there is some variability in these parameters across studies. Meta-analyses of these studies have shown that, for detection of anatomic disease, CCTA has a sensitivity greater than 95%, which is superior to all other functional noninvasive tests. Specificity is at least as good as other noninvasive tests. However, the link between improved

diagnosis and health outcomes is not as clear, and thus outcome studies are necessary to demonstrate the clinical utility of CCTA.

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

SUSPECTED ANOMALOUS CORONARY ARTERIES

Anomalous coronary arteries are an uncommon finding during angiography, occurring in approximately 1% of coronary angiograms completed for evaluation of chest pain. However, these congenital anomalies can be clinically important depending on the course of the anomalous arteries.

Clinical Context and Test Purpose

The purpose of CCTA in 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 are 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.

Clinically Valid

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

Clinically Useful

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

Direct Evidence

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

Case Series

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

Section Summary: Suspected Anomalous Coronary Arteries

Results from case series have shown that CCTA delineates the course of anomalous coronary arteries, even when conventional angiography cannot. However, none of the studies reported results when the initial reason for the study was to identify these anomalies, nor did any of the studies discuss the impact on therapeutic decisions. Given the uncommon occurrence of these symptomatic anomalies, it is unlikely that a prospective trial of CCTA could be completed.

Other Diagnostic Uses of CCTA

Given its ability to define coronary artery anatomy, there are many potential diagnostic uses of CCTA, including patency of coronary artery bypass grafts, in-stent restenosis, screening, and preoperative evaluation.

Patency

Evaluating patency of vein grafts is generally less of a technical challenge due to vein size and lesser motion during imaging. In contrast, internal mammary grafts may be more difficult to image due to their small size and presence of surgical clips. Finally, assessing native vessels distal to grafts presents difficulties, especially when calcifications are present, due to their small size. For example, a 2008 meta-analysis including results from 64-slice scanners, reported high sensitivity 98% (95% CI, 95 to 99; 740 segments) and specificity 97% (95% CI, 94 to 97).⁵⁸ Other small studies have reported high sensitivity and specificity.^{59,60} Lacking are multicenter studies demonstrating likely clinical benefit, particularly given the reasonably high disease prevalence in patients evaluated.

In-Stent Restenosis

Use of CCTA for evaluation of in-stent restenosis presents other technical challenges – motion, beam hardening, and partial volume averaging. Whether these challenges can be sufficiently overcome to obtain sufficient accuracy and impact outcomes has not been demonstrated.

Screening

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

Preoperative Evaluation

Use for screening in a high-risk population was evaluated in the FACTOR-64 trial, which randomized 900 subjects with diabetes to screening with CCTA or SOC.⁶² Patients in this trial were asymptomatic but considered to be at high risk for CAD due to long-standing diabetes. The primary outcome was a composite of mortality, nonfatal MI, or unstable angina requiring hospitalization. At a median follow-up of 4 years, there was no significant difference between the groups for the primary outcome (CTA, 6.2%; control, 7.6%; HR=.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).⁶³ While current guidelines recommend stress testing in individuals at intermediate- to high-risk, over one-third of perioperative MACE occur among those with negative test results. MACE were reported in 7.2% of 3480 patients. Risk of perioperative MACE was found to increase with the severity of CAD on CCTA findings (no CAD, 2.0%; non-obstructive CAD, 4.1%; obstructive single-vessel, 7.1%; obstructive multivessel, 23.1%; p <.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.

SUMMARY OF EVIDENCE

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

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

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

Ongoing and Unpublished Clinical Trials

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

Table 19. Summary of Key Trials

NCT Number	Title	Enrollment	Completion Date
Ongoing			
NCT04748237	Randomized Evaluation of Coronary Computed Tomographic Angiography in Intermediate-risk Patients Presenting to the Emergency Department With Chest Pain	3500	Dec 2025
NCT02099019	Usefulness of Coronary Computed Tomography Angiography for Therapeutic Decision-Making; Revascularization	3000	Feb 2025
NCT05677386	Prevention of Heart Disease in Adult Danes Using Computed Tomography Coronary Angiography - The DANE-HEART Trial	6000	Dec 2025
Unpublished			
NCT03129659	Coronary CT Angiography for Improved Assessment of Suspected Acute Coronary Syndrome With Inconclusive Diagnostic Work-up	230	Sep 2022

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

SUPPLEMENTAL INFORMATION

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 Foundation (ACCF) and several other medical societies issued joint guidelines for management of patients with stable ischemic heart disease in 2012 (Table 20).³⁸

Table 20. Guidelines on Management of Stable IHD

Diagnosis	Recommendation	Class	LOE
Unknown	Able to exercise		
	“CCTA might be reasonable for patients with an intermediate pretest probability of IHD who have at least moderate physical functioning or no disabling comorbidity.”	IIb	B
	Unable to exercise		
Known CAD	“CCTA is reasonable for patients with a low to intermediate pretest probability of IHD who are incapable of at least moderate physical functioning or have disabling comorbidity.”	IIa	B
	“CCTA is reasonable for patients with an intermediate pretest probability of IHD who a) have continued symptoms with prior normal test findings, or b) have inconclusive results from prior exercise or pharmacological stress testing, or c) are unable to undergo stress with nuclear MPI or echocardiography.”	IIa	C
	Able to exercise		
Known CAD	“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
	Unable to exercise		
	“Pharmacological stress imaging (nuclear MPI, echocardiography, or CMR) or CCTA is not recommended for risk assessment in patients with SIHD who are able to exercise to an adequate workload and have an interpretable ECG.”	III	C
	“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	III	C

	time is not recommended for risk assessment in patients with SIHD.”		
	Regardless of patients’ ability to exercise		
	“CCTA might be considered for risk assessment in patients with SIHD unable to undergo stress imaging or as an alternative to invasive coronary angiography when functional testing indicates a moderate- to high-risk result and knowledge of angiographic coronary anatomy is unknown.”	IIb	C

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

In 2013, ACCF and other medical societies published appropriate use criteria for detection and risk assessment of stable ischemic heart disease.⁶² CCTA was considered appropriate for:

- Symptomatic patients with intermediate (10%-90%) pretest probability of coronary artery disease (CAD) and uninterpretable ECG or inability to exercise
- Patients with newly diagnosed systolic heart failure
- Patients who have had a prior exercise ECG or stress imaging study with abnormal or unknown results
- Patients with new or worsening symptoms and normal exercise ECG

National Institute for Health and Care Excellence

The National Institute for Health and Care Excellence has recommended CCTA as first-line testing for patients with stable angina if the clinical assessment indicates typical or atypical angina, or if clinical assessment indicates nonanginal chest pain but 12-lead resting electrocardiography (ECG) has been done and indicates ST-T changes or Q waves.⁶⁵

Society of Cardiovascular Computed Tomography

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

Table 21. Society of Cardiovascular Computed Tomography Guidelines on Coronary Computed Tomography 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).
	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.⁶⁹ Relevant recommendations from the consensus document are listed in Table 22.

Table 22. 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).
NSTEMI-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	
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; NSTEMI: non-ST-segment-elevation myocardial infarction; ST-segment-elevation myocardial infarction.

Government Regulations

National:

There is no national coverage determination.

Local:

Wisconsin Physicians Service Insurance Corporation

L35121 Coronary Computed Tomography Angiography (CCTA)

Original effective date 10/01/2015; Revision effective date 11/30/2023

Coverage Indications, Limitations, and/or Medical Necessity

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

stenotic lesions noted on diagnostic cardiac catheterization but more importantly, with atheromas on intracoronary ultrasound.

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

Indications:

1. CCTA used as an alternative to invasive angiography and stress testing. For patients with anginal symptoms, patients with unclear stress test results, patients in whom the stress test result contradicts the clinical assessment, patients with low risk of CAD who cannot exercise, to determine the patency of coronary artery bypass grafts, as an alternative when cardiac catheterization is impossible or carries a high risk, to rule out stenosis before non-coronary cardiac surgery such as valve replacement or resection of tumors, and clarifying unclear finding after invasive angiography.
2. CCTA used to assess patient suspected of having a congenital coronary anomaly of great vessels, cardiac chambers and valves. It is often used after an anomaly has been identified following a different test such as prior invasive coronary angiogram. CCTA is used to decide if surgery is indicated and for surgical planning.
3. CCTA used to evaluate acute chest pain in the emergency department (ED). The rationale is to quickly triage patients in order to rule out coronary artery disease as a possible cause of symptoms. Many will present with a normal electrocardiogram and myocardial enzymes.
4. CCTA used to assess coronary or pulmonary venous anatomy. Coronary mapping is primarily for pre-surgical planning such as pacemaker lead placement in the lateral coronary vein to resynchronize cardiac contraction in patients with heart failure or guiding biventricular pacemaker placement. Pulmonary vein anatomy can vary from patient to patient. Pulmonary vein mapping is primarily for catheter ablation which can isolate electrical activity from the pulmonary veins and allow for the elimination of recurrent atrial fibrillation or help eliminate procedural complications.
5. CCTA used to assess etiology with new onset heart failure for evaluation of coronary arteries.

Limitations:

1. The test is never covered for screening, i.e., in the absence of signs, symptoms or disease.
2. The test will be considered not medically necessary if the anticipated results are not expected to provide new, additional information to that already previously obtained from other tests (such as stress myocardial perfusion images or cardiac ultrasound). New or additional information should facilitate the management decision, not merely add a new layer of testing.
3. The test will be considered not medically necessary if pretest evaluation indicates that the patient would require invasive cardiac angiography for further diagnosis or for therapeutic intervention.

4. The test may be denied, on post-pay review, as not medically necessary when used for cardiac evaluation if there were pre-test knowledge of sufficiently extensive calcification of the suspect coronary segment that would diminish the interpretive value. (e.g., angina decubitus, unstable angina, Prinzmetal angina, etc.)
5. Coverage is limited to devices that process thin, high resolution slices (1mm or less). The multi-detector scanners must have at least 64 slices per rotation capability.
6. The administration of beta blockers and the monitoring of the patient during MDCT/CCTA by a physician experienced in the use of cardiovascular drugs is included as part of the test and is not a separately payable service.
7. All studies must be ordered by the physician/qualified non-physician practitioner treating the patient and who will use the results of the test in the management of the patient.
8. The test must be performed under the direct supervision of a physician, similar to the stress myocardial perfusion imaging.
9. This LCD does not address electron beam tomography (EBT) technology or Ultrafast CT for coronary artery examination. There is no extension of coverage of EBT based on this policy.
10. Quantitative calcium scoring is not a covered service and will be denied as not medically necessary. Calcium scoring reported in isolation is considered a screening service. When performed in association with CT angiography, there is neither separate nor additional included reimbursement for the calcium scoring.
11. Atrial fibrillation or atrial flutter alone is not an indication; atrial fibrillation or atrial flutter with planned ablation therapy is allowed.

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

Related Policies

Computed Tomography to Detect Coronary Artery Calcification

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The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through December, 2023, the date the research was completed.

Joint BCBSM/BCN Medical Policy History

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

5/1/19	2/19/19		Routine policy maintenance. References # 12, 14 and 21-23 added. No change in policy status.
5/1/20	2/18/20		Rationale updated, reference # 25, 31-33 and 63 were added. No change in policy status.
5/1/21	2/16/21		Routine policy maintenance. References # 66 and 67 added. No change in policy status.
5/1/22	2/15/22		Routine policy maintenance, references # 44 and 66 added. No change in policy status.
5/1/23	2/21/23		Routine policy maintenance, references 68, 69, 70 added. No change in policy status. Vendor managed codes by AIM. (ky)
5/1/24	2/20/24		Routine maintenance Updated Medical Policy Statement with addition of CT angiography (CTA). Aligned JUMP policy with Carelon policy Imaging of the Heart 4/14/2024. Moved: Consideration for surgical repair of congenital heart disease under Inclusions section Congenital heart disease: Cardiac CT is considered established 4th bullet. Vendor: Carelon (ky)

Next Review Date: 1st Qtr. 2025

BLUE CARE NETWORK BENEFIT COVERAGE

POLICY: CONTRAST-ENHANCED COMPUTED TOMOGRAPHY ANGIOGRAPHY (CTA, CCTA, MDCT, MSCT) OF THE HEART AND/OR CORONARY ARTERIES

I. Coverage Determination:

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

II. Administrative Guidelines:

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