American College of Radiology
ACR Appropriateness Criteria®
Chronic Chest Pain-Noncardiac Etiology Unlikely: Low to Intermediate Probability of Coronary Artery Disease

Variant 1: **Chronic chest pain, noncardiac etiology unlikely: low to intermediate probability of coronary artery disease. Initial imaging.**

Procedure	Appropriateness Category	Relative Radiation Level
CTA coronary arteries with IV contrast	Usually Appropriate	☢☢☢
US echocardiography transthoracic stress	Usually Appropriate	O
MRI heart with function and vasodilator stress perfusion without and with IV contrast	Usually Appropriate	O
Rb-82 PET/CT heart	Usually Appropriate	☢☢☢☢
SPECT or SPECT/CT MPI rest and stress	Usually Appropriate	☢☢☢☢
SPECT or SPECT/CT MPI stress only	Usually Appropriate	☢☢☢
MRI heart with function and inotropic stress without and with IV contrast	May Be Appropriate	O
MRI heart with function and inotropic stress without IV contrast	May Be Appropriate	O
US echocardiography transthoracic resting	May Be Appropriate	O
CT coronary calcium	May Be Appropriate	☢☢☢
MRI heart function and morphology without IV contrast	May Be Appropriate	O
CT chest with IV contrast	May Be Appropriate	☢☢☢
MRA coronary arteries without and with IV contrast	May Be Appropriate	O
Arteriography coronary	Usually Not Appropriate	☢☢☢
CT chest without and with IV contrast	Usually Not Appropriate	☢☢☢
CT chest without IV contrast	Usually Not Appropriate	☢☢☢
SPECT or SPECT/CT MPI rest only	Usually Not Appropriate	☢☢☢

CHRONIC CHEST PAIN-NONCARDIAC ETIOLOGY UNLIKELY: LOW TO INTERMEDIATE PROBABILITY OF CORONARY ARTERY DISEASE

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Summary of Literature Review

Introduction/Background

Chronic chest pain (CCP) with low to intermediate probability of coronary artery disease (CAD) can arise from cardiac and noncardiac etiologies. While there are multiple potential noncardiac causes of CCP, such as costochondritis, arthritic or degenerative diseases, prior trauma, primary or metastatic tumors, pleural disease, or gastrointestinal causes, the scope of this document is focused on evaluating chest pain when a cardiac etiology is the concern.

When CCP with a cardiac origin is suspected, it is helpful to estimate the patient's probability of CAD. A clinical risk assessment can stratify the patients into low probability, intermediate probability, and high probability of CAD. Multiple clinical risk assessment tools are available, including the Framingham risk score, Diamond Forrester method, and Duke Clinical Score. While these tools are helpful in asymptomatic patients, they may not best stratify a patient's risk, particularly in patients who are symptomatic [1,2]. Coronary calcium score (CCS), although traditionally applied to asymptomatic patients, may better stratify patients at risk [3].

Multiple imaging tools can be used to evaluate CCP in symptomatic patients with low to intermediate probability for CAD. The imaging modalities available include: (1) multidetector coronary computed tomography angiography (CCTA); (2) stress and rest radionuclide single-photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI); (3) catheter-based invasive coronary angiography (ICA) with or without ventriculography; (4) chest radiography; (5) stress echocardiography; (6) PET; and (7) cardiac MRI and MR angiography (MRA).

Special Imaging Considerations

Advances in cardiac CT imaging technology have further reduced radiation dose in CCTA examinations [4]. New and available dose-reducing techniques include prospective triggering [5-7], iterative reconstruction algorithms [8], long z-axis coverage, and high-pitch spiral acquisition [9]. However, these newer low-dose techniques may not be available or appropriate for all patients. Although these techniques can reduce patient radiation dose, there may be patients for whom these radiation dose techniques are not optimal. In all cases, the imaging physician must select the appropriate combination of imaging parameters to acquire a diagnostic examination at a radiation dose that is as low as reasonably achievable.

Variant 1: Chronic chest pain, noncardiac etiology unlikely: low to intermediate probability of coronary artery disease. Initial imaging.

CTA Coronary Arteries

In patients with low to intermediate probability of CAD, multidetector CCTA can be performed for direct coronary artery evaluation. CCTA has been shown to be of value when evaluating patients with CAD because of its high negative predictive value. The use of CCTA has advantages when compared to other testing modalities. CCTA has superior diagnostic accuracy compared to other examinations, may identify high-probability patients

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based on plaque morphology, and allow for more appropriate selection of patients for downstream testing, including ICA, compared to other noninvasive strategies. The use of CCTA may decrease health care use and improve outcomes, including a decreased risk of myocardial infarction [10-17]. CCTA has also shown promise in directing appropriate patients for ICA compared to noninvasive strategies, may reduce downstream noninvasive testing, identify high-probability patients based on plaque morphology, and have superior diagnostic accuracy compared to other diagnostic tests [18,19].

Specifically, recent trials from the Computed Tomography versus Exercise Testing in Suspected Coronary Artery Disease (CRESCENT), the Scottish COmputed Tomography of the HEART (SCOT-HEART), the Prospective Multicenter Imaging Study for Evaluation of Chest Pain trial (PROMISE trial), the Cardiac CT for the Assessment of Chest Pain and Plaque (CAPP) study, and COronary CT Angiography EvaluatioN For Clinical Outcomes: An InteRnational Multicenter Registry (CONFIRM) registry provide additional support for the use of CCTA into the diagnostic algorithm when evaluating patients with chest pain.

The CRESCENT investigators suggest that the use of CCTA in combination with calcium scoring may allow for a structured protocol that allows a diagnosis to be reached faster with no increase in the referral rate for ICA [20]. The CCTA can also reduce the time to diagnosis and determine which patients need invasive testing [12,13,21-23]. Specifically in patients in whom angina that is due to CAD was suspected, the SCOT-HEART investigators showed that CCTA clarified the diagnosis by providing added certainty, enabling targeted interventions, and potentially reducing the risk of future myocardial infarction [24].

The PROMISE investigators evaluated patients with stable chest pain to either CCTA or functional testing. Their work has shown that patients who underwent CCTA had a lower risk of death and lower risk of myocardial infarction (not leading to a fatality) compared to patients who underwent conventional functional testing. The investigators suggest that CCTA can be a safe alternative to functional testing in a low-risk population [25,26].

CCTA has also provided prognostic information beyond that of clinical risk scores [27]. Data from the CAPP and CONFIRM investigators have provided additional information. The CAPP investigators have shown that patients undergoing CCTA identified significant disease, underwent more revascularizations, less diagnostic testing, and fewer admissions for chest pain [28]. The CONFIRM investigators have also shown that CCTA better predicted risk compared to well-established clinical risk scores and reclassified approximately one [29].

CCTA has the potential to characterize plaque and has the potential to identify "high-risk" plaque potentially allowing for patient risk stratification [30-32]. New technology may allow for noninvasive assessment of lesion-specific ischemia (CT fractional flow reserve) [33-36] with the added promise to better determine the functional significance of coronary lesions and determine which lesions are suited for downstream ICA [37]. Recent work from the Prospective LongitudinAl Trial of FFR_{CT}: Outcome and Resource Impacts (PLATFORM) investigators and others suggests that CCTA integrated with a noninvasive CT fractional flow reserve assessment may better select patients for ICA without negatively impacting mortality and appropriately select patients who need revascularization [38-40].

CT Chest

When CAD and other cardiac etiologies of chest pain, such as aortic disease pericardial disease, are suspected, a chest CT may be appropriate.

SPECT or SPECT/CT MPI

Stress SPECT MPI [41] is a central part of the diagnostic pathway when evaluating patients with CCP. A SPECT MPI scan is performed with either exercise-induced or pharmacologically induced stress to demonstrate myocardial perfusion or contraction abnormalities.

Use of stress imaging can be performed rapidly and increasingly through protocol optimization, with lower radiation doses [42]. Patients who undergo SPECT imaging have outcomes similar to CCTA in terms of outcomes [25,43]. In addition, the use of stress MPI improved clinical decision making for chest pain patients [44].

CT Coronary Calcium

CCS can be used as a diagnostic tool when evaluating patients with chest pain [45]. In patients presenting with stable angina, a positive CCS score is more accurate than clinical risk stratification tools, such as the Diamond Forrester risk stratification tool, for determining which patients have CAD [46]. CCS is also predictive of which patients may have significant stenosis and can be used to determine which patients need additional diagnostic testing and may benefit from initiation of medical treatment [46,47]. However, a CCS of "zero," showing no calcified coronary plaque, does not exclude acute coronary syndrome, significant coronary plaque burden, or plaque, which suggests that additional testing beyond CCS may be needed [48-50].

US Echocardiography Transthoracic Stress
When echocardiography is performed, stress contraction abnormalities are induced by either exercise or inotropic stimulation. In any situation where a SPECT MPI study cannot be performed, an exercise-stress or dobutamine-stress echocardiogram may be substituted [51,52]. Stress echocardiography is used to evaluate for wall motion abnormalities and can provide data regarding flow reserve, which can aid in patient risk stratification [53].

US Echocardiography Transthoracic Resting
In certain cases, if valvular heart disease, hypertrophic cardiomyopathy, or pericardial disease is the primary diagnostic concern, an echocardiogram at rest may be the preferred examination. The use of nonstress echocardiography in patients with stable chest pain when coronary artery disease is suspected may not reveal additional diagnostic information [54].

MRI Heart
MRI is an emerging technology, and its clinical applications to cardiac imaging continue to develop. Currently, stress cardiac MRI and coronary MRA are available to diagnose CAD.

Cardiac MRI without stress can be performed to evaluate valvular heart disease, nonischemic etiologies of chest pain, such as hypertrophic cardiomyopathy, or evaluate for pericardial disease.

Stress cardiac MRI can be performed with dobutamine, adenosine, or dipyridamole. Dobutamine-stress functional cardiac MRI may also play a role in the assessment of chronic CCP [55]. This is especially true when the echocardiographic examination is nondiagnostic. In settings where the study may be adequately monitored, dobutamine-stress functional cardiac MRI provides high sensitivity and specificity for ischemia by the induction of wall motion abnormality [56]. However, adenosine-stress cardiac MRI perfusion imaging is easier to perform and also has been shown to have relatively high sensitivity and specificity for the presence of CAD [56-59]. Dipyridamole-stress MRI can also show ischemia-related wall motion abnormalities, perfusion defects and scar and can help direct revascularization [60].

MRA Coronary Arteries
Coronary MRA is a developing modality to evaluate the coronary arteries. Coronary MRA has been shown to identify severe stenosis, but its sensitivity and specificity for moderate or mild lesions is lower [61,62]. Technological developments may make the use of coronary MRA more widespread and result in shorter acquisition times and improved spatial resolution [63].

Arteriography Coronary
ICA may be used if less-invasive imaging was consistent with the presence of significant CAD. However, the use of ICA as a first-line tool to evaluate for CAD in patients who are low to intermediate probability will not have a high diagnostic yield [64], and utilizing noninvasive testing prior to ICA increases the yield of positive ICA [64].

Exercise Treadmill Testing
Exercise treadmill testing can be of value in the assessment of patients with low to intermediate probability for CAD. Among patients who are low to intermediate probability, exercise treadmill testing in the acute setting showed a high specificity for detecting CAD with a greater than 50% stenosis [65]. This procedure is not included on the variant table because generally only imaging procedures are assessed for appropriateness in the ACR Appropriateness Criteria documents.

Rb-82 PET/CT Heart
PET/CT performed with perfusion agents (rubidium-82 or nitrogen-13-ammonia) may play a role in assessing patients with chronic indeterminate chest pain and who are at low probability to intermediate probability for CAD. Cardiac PET/CT has been shown to provide incremental prognostic value to historical and clinical variables [66], and may be of particular use in patients with equivocal or suboptimal SPECT MPI or echocardiographic results. Compared to SPECT MPI, PET offers higher spatial and contrast resolution and can be used to quantify myocardial blood flow, increasing the specificity of PET compared to SPECT [67].

Summary of Recommendations

- **Variant 1:** In the evaluation of CCP, noncardiac etiology unlikely, low to intermediate probability of CAD, CTA coronary arteries with IV contrast, or US echocardiography transthoracic stress, or MRI heart with function and vasodilator stress perfusion without and with IV contrast, or Rb-82 PET/CT heart, or SPECT or SPECT/CT MPI rest and stress, or Tc-99m SPECT/CT stress only is usually appropriate. These procedures are equivalent alternatives.

Summary of Evidence

Of the 68 references cited in the *ACR Appropriateness Criteria® Chronic Chest Pain-Noncardiac Etiology Unlikely: Low to Intermediate Probability of Coronary Artery Disease* document, 3 are categorized as therapeutic. Additionally, 63 references are categorized as diagnostic references including 11 well-designed studies, 18 good-quality studies, and 17 quality studies that may have design limitations. There are 20 references that may not be useful as primary evidence. There are 2 references that are meta-analysis studies.

The 68 references cited in the ACR Appropriateness Criteria® *Chronic Chest Pain-Noncardiac Etiology Unlikely: Low to Intermediate Probability of Coronary Artery Disease* document were published from 2000 to 2018.

Although there are references that report on studies with design limitations, 29 well-designed or good-quality studies provide good evidence.

Appropriateness Category Names and Definitions

Appropriateness Category Name	Appropriateness Rating	Appropriateness Category Definition
Usually Appropriate	7, 8, or 9	The imaging procedure or treatment is indicated in the specified clinical scenarios at a favorable risk-benefit ratio for patients.
May Be Appropriate	4, 5, or 6	The imaging procedure or treatment may be indicated in the specified clinical scenarios as an alternative to imaging procedures or treatments with a more favorable risk-benefit ratio, or the risk-benefit ratio for patients is equivocal.
May Be Appropriate (Disagreement)	5	The individual ratings are too dispersed from the panel median. The different label provides transparency regarding the panel's recommendation. "May be appropriate" is the rating category and a rating of 5 is assigned.
Usually Not Appropriate	1, 2, or 3	The imaging procedure or treatment is unlikely to be indicated in the specified clinical scenarios, or the risk-benefit ratio for patients is likely to be unfavorable.

Relative Radiation Level Information

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, because of both organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared with those specified for adults (see Table below). Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® Radiation Dose Assessment Introduction document [68].

Relative Radiation Level Designations		
Relative Radiation Level*	**Adult Effective Dose Estimate Range**	**Pediatric Effective Dose Estimate Range**
O	0 mSv	0 mSv
☢	<0.1 mSv	<0.03 mSv
☢☢	0.1-1 mSv	0.03-0.3 mSv
☢☢☢	1-10 mSv	0.3-3 mSv
☢☢☢☢	10-30 mSv	3-10 mSv
☢☢☢☢☢	30-100 mSv	10-30 mSv

*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (eg, region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as "Varies."

Supporting Documents

For additional information on the Appropriateness Criteria methodology and other supporting documents go to www.acr.org/ac.

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