ACR Appropriateness Criteria® Chronic Chest Pain—High Probability of Coronary Artery Disease

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Abstract

In patients with chronic chest pain in the setting of high probability of coronary artery disease (CAD), imaging has major and diverse roles. First, imaging is valuable in determining and documenting the presence, extent, and severity of myocardial ischemia, hibernation, scarring, and/or the presence, site, and severity of obstructive coronary lesions. Second, imaging findings are important in determining the course of management of patients with suspected chronic myocardial ischemia and better defining those patients best suited for medical therapy, angioplasty/stenting, or surgery. Third, imaging is also necessary to determine the long-term prognosis and likely benefit from various therapeutic options by evaluating ventricular function, diastolic relaxation, and end-systolic volume. Imaging studies are also required to demonstrate other abnormalities, such as congenital/acquired coronary anomalies and severe left ventricular hypertrophy, that can produce angina in the absence of symptomatic coronary obstructive disease due to atherosclerosis. Clinical risk assessment is necessary to determine the pretest probability of CAD. Multiple methods are available to categorize patients as low, medium, or high risk for developing CAD.

The American College of Radiology Appropriateness Criteria are evidence-based guidelines for specific clinical conditions that are reviewed annually by a multidisciplinary expert panel. The guideline development and revision include an extensive analysis of current medical literature from peer reviewed journals and the application of well-established methodologies (RAND/UCLA Appropriateness Method and Grading of Recommendations Assessment, Development, and Evaluation or GRADE) to rate the appropriateness of imaging and treatment procedures for specific clinical scenarios. In those instances where evidence is lacking or equivocal, expert opinion may supplement the available evidence to recommend imaging or treatment.

Key Words: Appropriateness Criteria, Appropriate Use Criteria, AUC, chronic chest pain, coronary artery, coronary artery disease, high-risk cardiac disease, high probability of coronary artery disease, myocardial ischemia

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ACR Appropriateness Criteria® Chronic Chest Pain—High Probability of Coronary Artery Disease. Variant 1 and Table 1.

Variant 1. Chronic chest pain; high probability of coronary artery disease.

Radiologic Procedure	Rating	Comments	RRL
X-ray chest	9		☢
Tc-99m SPECT MPI rest and stress	9		☢☢☢☢
MRI heart with function and vasodilator stress perfusion without and with IV contrast	9		○
Arteriography coronary	9		☢☢☢
Rb-82 PET heart stress	8		☢☢☢
US echocardiography transthoracic stress	8		○
CTA coronary arteries with IV contrast	8		☢☢☢
MRI heart with function and inotropic stress without and with IV contrast	7		○
MRI heart with function and inotropic stress without IV contrast	7		○
MRI heart function and morphology without and with IV contrast	7		○
MRA coronary arteries without and with IV contrast	5		○
US echocardiography transthoracic resting	4		○
MRI heart function and morphology without IV contrast	4		○
MRA coronary arteries without IV contrast	4		○
CT chest with IV contrast	4		☢☢☢
CT chest without IV contrast	4		☢☢☢
CT chest without and with IV contrast	4		☢☢☢
US abdomen	3		○
CT coronary calcium	3		☢☢☢
Tc-99m ventriculography	3		☢☢☢

Note: Rating scale: 1, 2, 3 = usually not appropriate; 4, 5, 6 = may be appropriate; 7, 8, 9 = usually appropriate. CTA = CT angiography; IV = intravenous; MPI = myocardial perfusion imaging; MRA = MR angiography; RRL = relative radiation level; SPECT = single-photon emission computed tomography; US = ultrasound.

Table 1. Relative radiation level designations

RRL	Adult Effective Dose Estimate Range (mSv)	Pediatric Effective Dose Estimate Range (mSv)
○	0	0
☢	<0.1	<0.03
☢☢	0.1-1	0.03-0.3
☢☢☢	1-10	0.3-3
☢☢☢☢	10-30	3-10
☢☢☢☢☢	30-100	10-30

Note: Relative radiation level (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."

SUMMARY OF LITERATURE REVIEW

Introduction/Background

Chronic chest pain of suspected cardiac origin is usually a consequence of myocardial ischemia, representing an imbalance between myocardial oxygen demand and coronary blood flow. This is usually caused by fixed, hemodynamically significant coronary stenosis due to atherosclerotic plaque formation leading to reduced myocardial perfusion. Less common causes of chronic chest pain include coronary spasm, microvascular disease, or a combination of both. In the setting of high probability of coronary artery disease (CAD), flow-limiting epicardial coronary artery narrowing is most likely. However, chest pain of myocardial ischemic origin can also occur in patients with relatively normal coronary arterial caliber but with conditions resulting in increased demand for oxygenation (eg, increased myocardial mass and workload due to systemic arterial hypertension or

aortic stenosis). Although the syndrome of exertional angina pectoris is nearly always diagnostic of chronic CAD, nonischemic cardiac (eg, myocarditis, pericarditis) and extracardiac (eg, esophageal reflux/spasm) etiologies and costochondritis should also be considered in the setting of nonexertional or atypical chest pain [1].

In patients with chronic chest pain in the setting of high probability of CAD (variant 1), imaging has major and diverse roles. First, imaging is valuable in determining and documenting the presence, extent, and severity of myocardial ischemia, hibernation, scarring, and/or the presence, site, and severity of obstructive coronary lesions. Second, imaging findings are important in determining the course of management of patients with suspected chronic myocardial ischemia and better defining those patients best suited for medical therapy, angioplasty/stenting, or surgery. Third, imaging is also necessary to determine the long-term prognosis and likely benefit from various therapeutic options by evaluating ventricular function, diastolic relaxation, and end-systolic volume. Imaging studies are also required to demonstrate abnormalities (eg, congenital or acquired coronary anomalies, severe left ventricular [LV] hypertrophy) that can produce angina in the absence of symptomatic coronary obstructive disease due to atherosclerosis.

Clinical risk assessment is necessary to determine the pretest probability of CAD. Multiple methods are available to categorize patients as at low, medium, or high risk for developing CAD. Existing methods, including the Diamond and Forrester method, Framingham risk score, coronary calcium score (CCS), and Duke clinical score, are based on different criteria, such as age, gender, family history of CAD, type of chest pain, lipid levels, and previous cardiovascular events. One study suggests that the Diamond and Forrester method overestimates the prevalence of obstructive CAD and the Duke clinical score performs better in low-risk patients [2-4]. McKavanagh et al [2] suggested that stable CAD would be more accurately risk stratified using the CCS rather than the Diamond and Forrester method. In conclusion, risk assessment for CAD using various existing methods can lead to variable pretest probability and may stratify patients in different risk categories [4].

The imaging modalities historically used in evaluating suspected chronic myocardial ischemia are (1) chest radiography, (2) stress and rest radionuclide single-photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI), (3) catheter-based selective coronary angiography with or without left ventriculography, and (4) radionuclide ventriculography with and without stress. Stress echocardiography, PET, cardiac MRI, and cardiac multidetector MDCT have all been more recently shown to be valuable in the evaluation of ischemic heart disease. In those patients who do not present with signs classic for angina pectoris or in those patients who do not respond as expected to standard management, the exclusion of noncardiac causes of chronic chest pain requires the use of additional studies (eg, esophagography, upper gastrointestinal series, and biliary ultrasound).

Chest Radiography. The chest radiograph is an inexpensive test that can rapidly demonstrate many noncardiac causes of chronic chest pain, including a variety of diseases of the mediastinum, pleura, or lung. It may also provide qualitative indirect information about LV function as reflected in cardiac size and pulmonary vascular patterns (eg, pulmonary venous hypertension) [5]. However, chest radiographs can neither establish nor exclude chronic ischemic heart disease. In addition, radiographs (including fluoroscopy) are insensitive for detecting coronary arterial calcification [6]. Chest radiography, therefore, is of limited value in symptomatic patients with a high risk for CAD.

Imaging of Myocardium

SPECT. Stress SPECT MPI demonstrates relative myocardial perfusion defects, indicating the presence of myocardial ischemia. For this reason, it is considered an important first-line study in the evaluation of patients with chronic chest pain and a high likelihood of CAD. By acquiring rest and stress perfusion scans, it is possible to demonstrate reversibility (ischemia) or irreversibility (infarction) of a myocardial perfusion defect. The territory of the perfusion defect identifies the likely coronary artery involved and can usually distinguish between significant single-vessel and multivessel coronary arterial obstructions [7-16]. The magnitude of the abnormality and the presence of high-risk findings also assist in clinical decision making [17,18].

Presently, SPECT perfusion agents labeled with technetium-99m (Tc-99m), such as Tc-99m sestamibi and Tc-99m tetrofosmin, are used most commonly because of improved image resolution, higher count density, and more favorable dosimetry. The sensitivity and specificity of Tc-99m-agent SPECT in detecting CAD are equal to and usually superior to those of thallium-201 (^{201}Tl) [19]. With the use of electrocardiogram gating and with improved imaging protocols and image quality, the diagnostic accuracy of stress SPECT MPI for detecting angiographically significant CAD is high (sensitivity of

87%-89% and specificity of 73%-75%) [20]. More important, a normal stress SPECT MPI examination in patients with intermediate to high likelihood of CAD predicts a very low rate of cardiac death or nonfatal myocardial infarction (≤1% per year) [21]. Furthermore, SPECT MPI may be used for risk stratification in scenarios such as follow-up after percutaneous coronary intervention (PCI) and coronary artery bypass graft or evaluation before noncardiac surgery. Limitations of stress SPECT MPI are its relatively high cost and relatively high radiation dose.

Software algorithms such as iterative reconstruction, maximum a posteriori noise regularization and resolution-recovery, and new hardware and detector materials continue to be refined, allowing image acquisitions at significantly shorter acquisition times or, alternatively, at lower doses of radiation compared with conventional algorithms [22,23].

Stress radionuclide ventriculography consists of measurement of the ejection fraction and assessment of regional wall motion at rest and during stress. However, radionuclide ventriculography is rarely used as SPECT MPI has largely replaced it; hence availability of and expertise with this method are very limited. In patients with typical angina (high pretest likelihood of disease), stress SPECT MPI is useful for estimating the extent (single-vessel versus multivessel disease) and severity of coronary stenosis, which has relevance for prognosis, choice among therapeutic options, and advisability of performing coronary arteriography.

Hybrid SPECT/coronary CT angiography (CCTA) combines the anatomic information provided by CT with the functional perfusion evidence of SPECT, resulting in enhanced diagnostic accuracy for detecting significant CAD compared with SPECT and CCTA alone [24]. Schaap et al [24] found that the sensitivity and specificity of hybrid SPECT/CCTA were 96% and 95%, respectively, compared with SPECT (93% and 79%) and CCTA (98% and 62%) alone. There was 92% agreement on the necessity of revascularization in the treatment decisions on the basis of hybrid SPECT/CCTA versus SPECT and coronary angiography alone [25]. Thus, the combination of SPECT and CCTA provides excellent diagnostic performance and compensates for the drawbacks of each technique as a stand-alone imaging procedure.

PET. Myocardial PET imaging using rubidium-82 (^{82}Rb) or nitrogen ^{13}N ammonia for assessing perfusion, and fluorine-18-2-fluoro-2-deoxy-D-glucose for evaluating metabolism, are now recognized as useful methods for the evaluation of ischemic heart disease [26]. PET perfusion imaging has several advantages over SPECT, including higher spatial and temporal resolution, superior attenuation and scatter correction, and the capability to perform quantitative measurements [27,28]. In a meta-analysis of eight studies with 791 patients evaluated for CAD by PET perfusion imaging, the overall sensitivity and specificity were determined to be 93% and 92%, respectively [29]. In the same article, three studies comparing ^{201}Tl SPECT with ^{82}Rb or ^{13}N ammonia PET were analyzed, and the overall accuracy of PET was 91%, compared with 81% for ^{201}Tl SPECT. Gated PET also provides assessment of LV function and overall provides important diagnostic and prognostic data [30].

Hybrid PET scanners use CT for attenuation correction (PET/CT) after completion of the PET study. By coupling the PET perfusion examination findings to a CCTA, PET/CT permits the fusion of anatomic coronary arterial and functional (perfusion) myocardial information and enhances diagnostic accuracy [26,31]. The fused examinations can accurately measure the atherosclerotic burden and identify the hemodynamic functional significance of coronary stenoses [32,33]. The results of the combined examinations can more accurately identify patients for revascularization [33]. In a study of 110 consecutive patients with combined stress ^{82}Rb PET perfusion imaging and CCTA, nearly half of significant angiographic stenoses (47%) occurred without evidence of ischemia, whereas 50% of normal PET studies were associated with some CCTA abnormality [32].

Echocardiography. Stress 2-D echocardiography for myocardial contractility assessment is increasingly used for patients with suspected regional wall motion abnormalities secondary to regional ischemia, in part because of the ubiquity of 2-D echocardiography. In patients for whom exercise is not feasible, pharmacologic stress echocardiography is performed. A meta-analysis of 44 studies indicated that stress echocardiography has similar sensitivity to stress SPECT MPI (85% and 87%, respectively), with higher specificity (77% versus 64%) [34-36]. A study that compared dobutamine-atropine stress echocardiography and dipyridamole Tc-99m sestamibi SPECT found that SPECT had similar sensitivity for detection of CAD, with dobutamine-atropine stress echocardiography being more specific (91% versus 73%) [37]. Marwick et al [38] also showed that dobutamine stress echocardiography and perfusion scintigraphy have equivalent accuracy for

diagnosing obstructive CAD. Stress echocardiography includes rest as well as stress images.

In a meta-analysis of 435 patients, dipyridamole and dobutamine stress contractility echocardiography had similar accuracy (87% versus 84%), specificity (89% versus 86%), and sensitivity (85% versus 86%) for detecting CAD [38,39]. The pharmacologic stress echocardiography techniques are limited by the fact that they sometimes yield nondiagnostic results and that suboptimal definition of some regions of the left ventricle can lead to subjective interpretation.

Administration of an echocardiography contrast agent (ie, microbubbles) improves endocardial visualization at rest and more so during stress, leading to a more precise interpretation with greater accuracy in evaluating CAD in patients with two or more nonvisualized segments and low confidence of interpretation [39,40].

Rest transthoracic echocardiography can be useful if pericardial effusion or valvular or chamber abnormalities are suspected. Transesophageal echocardiography is generally not indicated for evaluating chronic angina and the feasibility of this study does not justify its use in this setting. However, it is sometimes used for assessing aortic pathology (eg, dissection, aneurysm, and penetrating ulcer) in patients with chronic chest pain, although CT and MRI are less invasive and simpler to perform.

MRI. Use of MRI for evaluating general cardiac anatomy and function and specific aspects of valvular disease, cardiomyopathies, and myocardial viability is well established.

MRI myocardial perfusion techniques can be used to assess for significant CAD. The diagnostic accuracy of stress perfusion MRI has been evaluated by many studies and has been found to be equivalent, and in many cases superior, to stress SPECT MPI [41-52]. The CE-MARC trial, the largest prospective evaluation of MRI, revealed that MRI and SPECT had similar specificity and positive predictive value (PPV), with the sensitivity and negative predictive value (NPV) of MRI significantly better than SPECT (sensitivity, 86.5% versus 66.5%; NPV, 90.5% versus 79.1%) [53]. A meta-analysis from pooled studies found that perfusion stress MRI has sensitivity of 89.1% and specificity of 84.9% on a patient-based analysis using fractional flow reserve (FFR) as a reference, suggesting that stress perfusion MRI remains an accurate test for the detection of flow-limiting stenosis. Hamon et al [54] also reported that MRI is highly sensitive for the detection of CAD with moderate specificity. De Jong et al [55] concluded that MRI perfusion diagnoses CAD better than echocardiography and SPECT.

Clinically, MRI with function and vasodilator stress perfusion has been used to diagnose hemodynamically significant CAD in patients with intermediate to high likelihood of having significant stenosis. The technique is commonly used in patients with poor acoustic windows in whom stress echocardiography imaging would be difficult to visualize [56]. It has also been shown to have a higher diagnostic accuracy than dobutamine stress echocardiography [55-57]. In patients with poor echocardiography examinations, dobutamine stress MRI can be used to predict myocardial infarction or cardiac death [58].

Despite its superior diagnostic performance, MRI is generally not appropriate for evaluating the individual chronic chest pain patient with a high probability of CAD in the setting of implanted electronic devices (eg, permanent pacemaker, an implantable cardioverter defibrillator). In addition, general reliance on MRI in assessing chronic chest pain is hindered by the limited availability of advanced facilities and experienced personnel.

Imaging of Coronary Arteries

CT. MDCT as well as electron-beam CT (less commonly used) are used for detecting the presence and severity of calcification, a sign of coronary atherosclerosis [59-69]. In a large study of 10,377 patients, Shaw et al [70] showed that CCS provides independent incremental information in the prediction of all-cause mortality.

In a prospective study, Kim et al [71] found that even in patients with a CCS of 0, there was a 4.3% prevalence of CAD. Thus, a CCS of 0 does not reliably exclude obstructive CAD among patients with a high suspicion of CAD. On the other hand, patients who do present with chronic chest pain of suspected cardiac origin are typically older, with a significant proportion older than 60 years of age. Because coronary calcium is so prevalent in this population, a "positive" CCS, even in the upper quartiles, cannot be used as strong evidence of myocardial ischemia.

CCTA uses iodinated contrast and electrocardiographically gated MDCT to evaluate for CAD. Studies using 64-slice CCTA have shown a high sensitivity and high NPV for treatable stenoses of the coronary arteries [72-75]. A recent meta-analysis to evaluate the diagnostic accuracy of 64-slice CCTA compared with conventional selective coronary angiography included 27 studies and 1,740 patients and found that the sensitivity, specificity, PPV, and NPV were 86%, 96%, 83%, and 96.5%, respectively, by per segment analysis and 97.5%, 91%,

93%, and 96.5%, respectively, by per patient analysis [76-78]. The CCTA ACCURACY trial found 95% sensitivity, 83% specificity, 64% PPV, and 99% NPV for detection of CAD, suggesting that CCTA possesses high diagnostic accuracy for detecting coronary stenosis at thresholds of 50%. The high NPV (99%) also establishes CCTA as an effective noninvasive alternative to invasive coronary angiography (ICA) to exclude CAD in low-risk patients [79].

However, the pretest probability of CAD does affect the diagnostic performance of CCTA in high-risk patients, the population under consideration in this document. In CORE-64 (Coronary Artery Evaluation Using 64-Row Multidetector Computed Tomography Angiography), the pretest probability and CCS significantly affect NPV for detecting obstructive CAD by CCTA. Therefore, both pretest probability for CAD and coronary artery calcium scoring should be considered before using CCTA for excluding obstructive CAD [80]. The NPV of CCTA is significantly lower in patients with a high prevalence of CAD, and a negative CCTA reduces the estimated posttest probability of having obstructive disease only to approximately 17% [81,82]. Because of this high residual posttest probability despite a negative CCTA, many symptomatic high-probability patients are likely to still require invasive selective coronary angiography. CCTA, therefore, may be of limited clinical value in the evaluation of the high-estimated-pretest-probability group.

There are two additional special considerations for CCTA. The first is a stress perfusion CT that can be performed as an additional data acquisition, but during the same imaging session as CCTA. CT myocardial perfusion adds a functional estimate of myocardial perfusion to the CCTA data, using iodinated contrast as a perfusion agent [78,83-85]. CT perfusion improves the diagnostic value for detecting CAD compared with CCA alone, particularly in patients with severe calcification [86,87]. CT perfusion imaging was shown when combined with CTA to accurately predict atherosclerotic perfusion abnormalities when compared with coronary angiography and SPECT [88]. In addition, CT perfusion was demonstrated to be highly accurate in determining the presence or absence of myocardial ischemia in patients with obstructive CAD when compared with SPECT MPI in the presence of stenosis ($\geq$50% of CTA) with sensitivity, specificity, PPV, and NPV of 100%, 81%, 50%, and 100%, respectively, and an area under the curve of 0.92 [89].

The second special consideration is the emergence of methods applied to CCTA data after image acquisition to estimate FFR. For example, the NXT trial (Analysis of Coronary Blood Flow Using CT Angiography: Next Steps) concluded that FFR estimates from postprocessed CT images provide high diagnostic accuracy for the diagnosis of hemodynamically significant CAD with ICA as a reference [90,91]. Other studies [92-94] have supported this emerging technology. Neither CT perfusion (where separate data are acquired in addition to the CCTA) nor FFR estimates (image analysis steps applied to CCTA images) were independently considered in the panel ratings.

MR Angiography. Although MR angiography (MRA) of the pulmonary and systemic vessels has matured significantly over the past decade, MRA of the coronary arteries is still problematic because of their small size and incessant motion tied to the respiratory and cardiac cycles. At this time, coronary MRA should be limited to sites with extensive experience and appropriate capabilities to exclude disease in the proximal coronary arteries. At present, only CCTA can noninvasively visualize coronary arteries on a routine basis; in direct comparison, coronary MRA had similar sensitivity but significantly lower specificity and accuracy as compared with CCTA [95].

Selective Coronary Angiography. Catheter-based selective coronary angiography remains the coronary imaging modality of choice with the highest spatial and temporal resolution. Although only projection images are obtained (as opposed to 3-D volumes in CCTA), selective coronary angiography is considered to be the gold standard for depicting the anatomy and the severity of obstructive CAD and other coronary abnormalities (eg, coronary spasm) [96]. In addition to visualizing the coronary arteries, the procedure is used to guide stents to the site of blockage.

FFR measurement accurately estimates the functional severity of stenosis in obstructive CAD. In the FAME 2 trial (Fractional Flow Reserve Versus Angiography for Multivessel Evaluation 2), the authors concluded that performing FFR in addition to PCI resulted in a lower end point composite death rate at 1 year (13.2% versus 18.3%) compared with performing PCI alone. FAME 2 trial findings suggest that in patients with stable CAD with functionally significant stenosis, FFR-guided PCI with optimal medical therapy reduced revascularization rates (1.6% versus 11.1%) compared with optimal medical therapy alone. Thus, FFR has been validated to be an essential component of ICA to diagnose CAD [97-99].

There is conclusive evidence that selective coronary angiography is indicated in patients in whom angina is not adequately managed by aggressive medical therapy and in those in whom left coronary artery stenosis or severe multivessel CAD is suggested by results of stress SPECT MPI or stress echocardiography or CCTA.

LV catheterization and left ventriculography are generally indicated, but not always necessary, to define ventricular function in patients with angina. Currently, noninvasive imaging techniques like MRI and echocardiography are used more frequently to define LV function.

Other noncardiac diagnostic studies, such as abdominal ultrasound and chest CT, should be considered only after a cardiac etiology has been accurately excluded using the appropriate imaging modalities and clinical evaluation described above.

SUMMARY OF RECOMMENDATIONS

- The chest radiograph is a good initial assessment of the overall thorax in a patient with chronic chest pain.
- Coronary angiography is the current gold standard for evaluating CAD, allowing immediate intervention, although it is an invasive procedure with associated risks.
- CTA of the coronary arteries provides not only coronary artery stenosis evaluation similar to that of catheterization but plaque analysis as well as morphologic and, if desired, functional information.
- Stress MRI, SPECT MPI, PET, and TTE are first-line modalities in noninvasively identifying ischemia and indirectly assessing CAD. In addition, these procedures provide functional and morphologic cardiac information.

SUMMARY OF EVIDENCE

Of the 100 references cited in the ACR Appropriateness Criteria® Chronic Chest Pain—High Probability of Coronary Artery Disease document, 84 are categorized as diagnostic references, including 8 well-designed studies, 36 good-quality studies, and 29 quality studies that may have design limitations. Additionally, 5 references are categorized as therapeutic references, including 4 well-designed studies. There are 13 references that may not be useful as primary evidence. There are 10 references that are meta-analysis studies.

The 100 references cited in the ACR Appropriateness Criteria® Chronic Chest Pain—High Probability of Coronary Artery Disease document were published from 1980 to 2015.

While there are references that report on studies with design limitations, 48 well-designed or good-quality studies provide good evidence.

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, both because of 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 compared to those specified for adults (see Table 1). Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® Radiation Dose Assessment Introduction document [100].

SUPPORTING DOCUMENTS

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

REFERENCES

1. Di Fiore DP, Beltrame JF. Chest pain in patients with "normal angiography": could it be cardiac? Int J Evid Based Healthc 2013;11:56-68.
2. McKavanagh P, Lusk L, Ball PA, et al. A comparison of Diamond Forrester and coronary calcium scores as gatekeepers for investigations of stable chest pain. Int J Cardiovasc Imaging 2013;29:1547-55.
3. Versteylen MO, Joosen IA, Shaw LJ, Narula J, Hofstra L. Comparison of Framingham, PROCAM, SCORE, and Diamond Forrester to predict coronary atherosclerosis and cardiovascular events. J Nucl Cardiol 2011;18:904-11.
4. Wasfy MM, Brady TJ, Abbara S, et al. Comparison of the Diamond-Forrester method and Duke clinical score to predict obstructive coronary artery disease by computed tomographic angiography. Am J Cardiol 2012;109:998-1004.
5. Margolis JR, Chen JT, Kong Y, Peter RH, Behar VS, Kisslo JA. The diagnostic and prognostic significance of coronary artery calcification. A report of 800 cases. Radiology 1980;137:609-16.
6. Milne EN, Pistolesi M, Miniati M, Giuntini C. The radiologic distinction of cardiogenic and noncardiogenic edema. AJR Am J Roentgenol 1985;144:879-94.

7. Basu S, Senior R, Dore C, Lahiri A. Value of thallium-201 imaging in detecting adverse cardiac events after myocardial infarction and thrombolysis: a follow up of 100 consecutive patients. Bmj 1996;313:844-8.
8. Bax JJ, Poldermans D, Elhendy A, Boersma E, Rahimtoola SH. Sensitivity, specificity, and predictive accuracies of various noninvasive techniques for detecting hibernating myocardium. Curr Probl Cardiol 2001;26:147-86.
9. Beller GA. Diagnostic accuracy of thallium-201 myocardial perfusion imaging. Circulation 1991;84(3 Suppl):I1-6.
10. Christian TF, Miller TD, Bailey KR, Gibbons RJ. Noninvasive identification of severe coronary artery disease using exercise tomographic thallium-201 imaging. Am J Cardiol 1992;70:14-20.
11. Gibbons RJ. Rest and exercise radionuclide angiography for diagnosis in chronic ischemic heart disease. Circulation 1991;84(3 Suppl):I93-9.
12. Giri S, Shaw LJ, Murthy DR, et al. Impact of diabetes on the risk stratification using stress single-photon emission computed tomography myocardial perfusion imaging in patients with symptoms suggestive of coronary artery disease. Circulation 2002;105:32-40.
13. Meine TJ, Hanson MW, Borges-Neto S. The additive value of combined assessment of myocardial perfusion and ventricular function studies. J Nucl Med 2004;45:1721-4.
14. Soman P, Taillefer R, DePuey EG, Udelson JE, Lahiri A. Enhanced detection of reversible perfusion defects by Tc-99m sestamibi compared to Tc-99m tetrofosmin during vasodilator stress SPECT imaging in mild-to-moderate coronary artery disease. J Am Coll Cardiol 2001;37:458-62.
15. Taillefer R, DePuey EG, Udelson JE, Beller GA, Latour Y, Reeves F. Comparative diagnostic accuracy of Tl-201 and Tc-99m sestamibi SPECT imaging (perfusion and ECG-gated SPECT) in detecting coronary artery disease in women. J Am Coll Cardiol 1997;29:69-77.
16. Vanzetto G, Ormezzano O, Fagret D, Comet M, Denis B, Machecourt J. Long-term additive prognostic value of thallium-201 myocardial perfusion imaging over clinical and exercise stress test in low to intermediate risk patients: study in 1137 patients with 6-year follow-up. Circulation 1999;100:1521-7.
17. Baghdasarian SB, Noble GL, Ahlberg AW, Katten D, Heller GV. Risk stratification with attenuation corrected stress Tc-99m sestamibi SPECT myocardial perfusion imaging in the absence of ECG-gating due to arrhythmias. J Nucl Cardiol 2009;16:533-9.
18. Emmett L, Iwanochko RM, Freeman MR, Barolet A, Lee DS, Husain M. Reversible regional wall motion abnormalities on exercise technetium-99m-gated cardiac single photon emission computed tomography predict high-grade angiographic stenoses. J Am Coll Cardiol 2002;39:991-8.
19. Maddahi J, Kiat H, Van Train KF, et al. Myocardial perfusion imaging with technetium-99m sestamibi SPECT in the evaluation of coronary artery disease. Am J Cardiol 1990;66:55E-62E.
20. Saraste A, Nekolla S, Schwaiger M. Nuclear cardiology needs new "blood." J Nucl Cardiol 2009;16:180-3.
21. Hachamovitch R, Rozanski A, Hayes SW, et al. Predicting therapeutic benefit from myocardial revascularization procedures: are measurements of both resting left ventricular ejection fraction and stress-induced myocardial ischemia necessary? J Nucl Cardiol 2006;13:768-78.
22. Ali I, Ruddy TD, Almgrahi A, Anstett FG, Wells RG. Half-time SPECT myocardial perfusion imaging with attenuation correction. J Nucl Med 2009;50:554-62.
23. Sharir T, Ben-Haim S, Merzon K, Prochorov V, Dickman D, Berman DS. High-speed myocardial perfusion imaging initial clinical comparison with conventional dual detector anger camera imaging. JACC Cardiovasc Imaging 2008;1:156-63.
24. Schaap J, Kauling RM, Boekholdt SM, et al. Incremental diagnostic accuracy of hybrid SPECT/CT coronary angiography in a population with an intermediate to high pre-test likelihood of coronary artery disease. Eur Heart J Cardiovasc Imaging 2013;14:642-9.
25. Schaap J, de Groot JA, Nieman K, et al. Hybrid myocardial perfusion SPECT/CT coronary angiography and invasive coronary angiography in patients with stable angina pectoris lead to similar treatment decisions. Heart 2013;99:188-94.
26. Danad I, Raijmakers PG, Knaapen P. Diagnosing coronary artery disease with hybrid PET/CT: it takes two to tango. J Nucl Cardiol 2013;20:874-90.
27. Jaarsma C, Leiner T, Bekkers SC, et al. Diagnostic performance of noninvasive myocardial perfusion imaging using single-photon emission computed tomography, cardiac magnetic resonance, and positron emission tomography imaging for the detection of obstructive coronary artery disease: a meta-analysis. J Am Coll Cardiol 2012;59:1719-28.
28. Bateman TM, Heller GV, McGhie AI, et al. Diagnostic accuracy of rest/stress ECG-gated Rb-82 myocardial perfusion PET: comparison with ECG-gated Tc-99m sestamibi SPECT. J Nucl Cardiol 2006;13:24-33.
29. Machac J. Cardiac positron emission tomography imaging. Semin Nucl Med 2005;35:17-36.
30. Lertsburapa K, Ahlberg AW, Bateman TM, et al. Independent and incremental prognostic value of left ventricular ejection fraction determined by stress gated rubidium 82 PET imaging in patients with known or suspected coronary artery disease. J Nucl Cardiol 2008;15:745-53.
31. Sampson UK, Dorbala S, Limaye A, Kwong R, Di Carli MF. Diagnostic accuracy of rubidium-82 myocardial perfusion imaging with hybrid positron emission tomography/computed tomography in the detection of coronary artery disease. J Am Coll Cardiol 2007;49:1052-8.
32. Di Carli MF, Dorbala S, Curillova Z, et al. Relationship between CT coronary angiography and stress perfusion imaging in patients with suspected ischemic heart disease assessed by integrated PET-CT imaging. J Nucl Cardiol 2007;14:799-809.
33. Namdar M, Hany TF, Koepfli P, et al. Integrated PET/CT for the assessment of coronary artery disease: a feasibility study. J Nucl Med 2005;46:930-5.
34. Fleischmann KE, Hunink MG, Kuntz KM, Douglas PS. Exercise echocardiography or exercise SPECT imaging? A meta-analysis of diagnostic test performance. JAMA 1998;280:913-20.
35. Quinones MA, Verani MS, Haichin RM, Mahmarian JJ, Suarez J, Zoghbi WA. Exercise echocardiography versus 201Tl single-photon emission computed tomography in evaluation of coronary artery disease. Analysis of 292 patients. Circulation 1992;85:1026-31.
36. Schinkel AF, Bax JJ, Geleijnse ML, et al. Noninvasive evaluation of ischaemic heart disease: myocardial perfusion imaging or stress echocardiography? Eur Heart J 2003;24:789-800.
37. Smart SC, Bhatia A, Hellman R, et al. Dobutamine-atropine stress echocardiography and dipyridamole sestamibi scintigraphy for the detection of coronary artery disease: limitations and concordance. J Am Coll Cardiol 2000;36:1265-73.
38. Marwick T, D'Hondt AM, Baudhuin T, et al. Optimal use of dobutamine stress for the detection and evaluation of coronary artery disease: combination with echocardiography or scintigraphy, or both? J Am Coll Cardiol 1993;22:159-67.
39. Picano E, Molinaro S, Pasanisi E. The diagnostic accuracy of pharmacological stress echocardiography for the assessment of coronary artery disease: a meta-analysis. Cardiovasc Ultrasound 2008;6:30.
40. Plana JC, Mikati IA, Dokainish H, et al. A randomized cross-over study for evaluation of the effect of image optimization with contrast on the diagnostic accuracy of dobutamine echocardiography in coronary artery disease the OPTIMIZE trial. JACC Cardiovasc Imaging 2008;1:145-52.
41. Al Sayari S, Kopp S, Bremerich J. Stress cardiac MR imaging: the role of stress functional assessment and perfusion imaging in the evaluation of ischemic heart disease. Radiol Clin North Am 2015;53:355-67.
42. al-Saadi N, Gross M, Paetsch I, et al. Dobutamine induced myocardial perfusion reserve index with cardiovascular MR in patients with coronary artery disease. J Cardiovasc Magn Reson 2002;4:471-80.

43. Al-Saadi N, Nagel E, Gross M, et al. Noninvasive detection of myocardial ischemia from perfusion reserve based on cardiovascular magnetic resonance. Circulation 2000;101:1379-83.
44. Bettencourt N, Chiribiri A, Schuster A, et al. Direct comparison of cardiac magnetic resonance and multidetector computed tomography stress-rest perfusion imaging for detection of coronary artery disease. J Am Coll Cardiol 2013;61:1099-107.
45. Ishida N, Sakuma H, Motoyasu M, et al. Noninfarcted myocardium: correlation between dynamic first-pass contrast-enhanced myocardial MR imaging and quantitative coronary angiography. Radiology 2003;229:209-16.
46. Keijer JT, van Rossum AC, van Eenige MJ, et al. Magnetic resonance imaging of regional myocardial perfusion in patients with single-vessel coronary artery disease: quantitative comparison with (201)thallium-SPECT and coronary angiography. J Magn Reson Imaging 2000;11:607-15.
47. Kwong RY, Schussheim AE, Rekhraj S, et al. Detecting acute coronary syndrome in the emergency department with cardiac magnetic resonance imaging. Circulation 2003;107:531-7.
48. Nagel E, Klein C, Paetsch I, et al. Magnetic resonance perfusion measurements for the noninvasive detection of coronary artery disease. Circulation 2003;108:432-7.
49. Paetsch I, Jahnke C, Wahl A, et al. Comparison of dobutamine stress magnetic resonance, adenosine stress magnetic resonance, and adenosine stress magnetic resonance perfusion. Circulation 2004;110:835-42.
50. Schwitter J, DeMarco T, Kneifel S, et al. Magnetic resonance-based assessment of global coronary flow and flow reserve and its relation to left ventricular functional parameters: a comparison with positron emission tomography. Circulation 2000;101:2696-702.
51. Schwitter J, Nanz D, Kneifel S, et al. Assessment of myocardial perfusion in coronary artery disease by magnetic resonance: a comparison with positron emission tomography and coronary angiography. Circulation 2001;103:2230-5.
52. Wilke NM, Jerosch-Herold M, Zenovich A, Stillman AE. Magnetic resonance first-pass myocardial perfusion imaging: clinical validation and future applications. J Magn Reson Imaging 1999;10:676-85.
53. Greenwood JP, Maredia N, Younger JF, et al. Cardiovascular magnetic resonance and single-photon emission computed tomography for diagnosis of coronary heart disease (CE-MARC): a prospective trial. Lancet 2012;379:453-60.
54. Hamon M, Fau G, Nee G, Ehtisham J, Morello R. Meta-analysis of the diagnostic performance of stress perfusion cardiovascular magnetic resonance for detection of coronary artery disease. J Cardiovasc Magn Reson 2010;12:29.
55. de Jong MC, Genders TS, van Geuns RJ, Moelker A, Hunink MG. Diagnostic performance of stress myocardial perfusion imaging for coronary artery disease: a systematic review and meta-analysis. Eur Radiol 2012;22:1881-95.
56. Hundley WG, Hamilton CA, Thomas MS, et al. Utility of fast cine magnetic resonance imaging and display for the detection of myocardial ischemia in patients not well suited for second harmonic stress echocardiography. Circulation 1999;100:1697-702.
57. Nagel E, Lehmkuhl HB, Bocksch W, et al. Noninvasive diagnosis of ischemia-induced wall motion abnormalities with the use of high-dose dobutamine stress MRI: comparison with dobutamine stress echocardiography. Circulation 1999;99:763-70.
58. Hundley WG, Morgan TM, Neagle CM, Hamilton CA, Rerkpattanapipat P, Link KM. Magnetic resonance imaging determination of cardiac prognosis. Circulation 2002;106:2328-33.
59. Agatston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte M Jr, Detrano R. Quantification of coronary artery calcium using ultrafast computed tomography. J Am Coll Cardiol 1990;15:827-32.
60. Agatston AS, Janowitz WR, Kaplan G, Gasso J, Hildner F, Viamonte M Jr. Ultrafast computed tomography-detected coronary calcium reflects the angiographic extent of coronary arterial atherosclerosis. Am J Cardiol 1994;74:1272-4.
61. Breen JF, Sheedy PF II, Schwartz RS, et al. Coronary artery calcification detected with ultrafast CT as an indication of coronary artery disease. Radiology 1992;185:435-9.
62. Carr JJ, Crouse JR III, Goff DC Jr, D'Agostino RB Jr, Peterson NP, Burke GL. Evaluation of subsecond gated helical CT for quantification of coronary artery calcium and comparison with electron beam CT. AJR Am J Roentgenol 2000;174:915-21.
63. de Agustin JA, Marcos-Alberca P, Fernandez-Golfin C, et al. Should computed tomography coronary angiography be aborted when the calcium score exceeds a certain threshold in patients with chest pain? Int J Cardiol 2013;167:2013-7.
64. Detrano RC, Anderson M, Nelson J, et al. Coronary calcium measurements: effect of CT scanner type and calcium measure on rescan reproducibility—MESA study. Radiology 2005;236:477-84.
65. Fallavollita JA, Brody AS, Bunnell IL, Kumar K, Canty JM Jr. Fast computed tomography detection of coronary calcification in the diagnosis of coronary artery disease. Comparison with angiography in patients < 50 years old. Circulation 1994;89:285-90.
66. Nasir K, Clouse M. Role of nonenhanced multidetector CT coronary artery calcium testing in asymptomatic and symptomatic individuals. Radiology 2012;264:637-49.
67. Stanford W, Thompson BH, Burns TL, Heery SD, Burr MC. Coronary artery calcium quantification at multi-detector row helical CT versus electron-beam CT. Radiology 2004;230:397-402.
68. Wong ND, Vo A, Abrahamson D, Tobis JM, Eisenberg H, Detrano RC. Detection of coronary artery calcium by ultrafast computed tomography and its relation to clinical evidence of coronary artery disease. Am J Cardiol 1994;73:223-7.
69. Yerramasu A, Lahiri A, Venuraju S, et al. Diagnostic role of coronary calcium scoring in the rapid access chest pain clinic: prospective evaluation of NICE guidance. Eur Heart J Cardiovasc Imaging 2014;15:886-92.
70. Shaw LJ, Raggi P, Schisterman E, Berman DS, Callister TQ. Prognostic value of cardiac risk factors and coronary artery calcium screening for all-cause mortality. Radiology 2003;228:826-33.
71. Kim YJ, Hur J, Lee HJ, et al. Meaning of zero coronary calcium score in symptomatic patients referred for coronary computed tomographic angiography. Eur Heart J Cardiovasc Imaging 2012;13:776-85.
72. Mollet NR, Cademartiri F, van Mieghem CA, et al. High-resolution spiral computed tomography coronary angiography in patients referred for diagnostic conventional coronary angiography. Circulation 2005;112:2318-23.
73. Pugliese F, Mollet NR, Runza G, et al. Diagnostic accuracy of non-invasive 64-slice CT coronary angiography in patients with stable angina pectoris. Eur Radiol 2006;16:575-82.
74. Ropers D, Rixe J, Anders K, et al. Usefulness of multidetector row spiral computed tomography with 64- × 0.6-mm collimation and 330-ms rotation for the noninvasive detection of significant coronary artery stenoses. Am J Cardiol 2006;97:343-8.
75. Schlattmann P, Schuetz GM, Dewey M. Influence of coronary artery disease prevalence on predictive values of coronary CT angiography: a meta-regression analysis. Eur Radiol 2011;21:1904-13.
76. Abdulla J, Abildstrom SZ, Gotzsche O, Christensen E, Kober L, Torp-Pedersen C. 64-multislice detector computed tomography coronary angiography as potential alternative to conventional coronary angiography: a systematic review and meta-analysis. Eur Heart J 2007;28:3042-50.
77. Abdulla J, Pedersen KS, Budoff M, Kofoed KF. Influence of coronary calcification on the diagnostic accuracy of 64-slice computed tomography coronary angiography: a systematic review and meta-analysis. Int J Cardiovasc Imaging 2012;28:943-53.
78. Carrascosa PM, Deviggiano A, Capunay C, et al. Incremental value of myocardial perfusion over coronary angiography by spectral computed tomography in patients with intermediate to high likelihood of coronary artery disease. Eur J Radiol 2015;84:637-42.
79. Budoff MJ, Dowe D, Jollis JG, et al. Diagnostic performance of 64-multidetector row coronary computed tomographic angiography

for evaluation of coronary artery stenosis in individuals without known coronary artery disease: results from the prospective multicenter ACCURACY (Assessment by Coronary Computed Tomographic Angiography of Individuals Undergoing Invasive Coronary Angiography) trial. J Am Coll Cardiol 2008;52:1724-32.
80. Arbab-Zadeh A, Miller JM, Rochitte CE, et al. Diagnostic accuracy of computed tomography coronary angiography according to pre-test probability of coronary artery disease and severity of coronary arterial calcification. The CORE-64 (Coronary Artery Evaluation Using 64-Row Multidetector Computed Tomography Angiography) International Multicenter Study. J Am Coll Cardiol 2012;59:379-87.
81. Husmann L, Schepis T, Scheffel H, et al. Comparison of diagnostic accuracy of 64-slice computed tomography coronary angiography in patients with low, intermediate, and high cardiovascular risk. Acad Radiol 2008;15:452-61.
82. Meijboom WB, van Mieghem CA, Mollet NR, et al. 64-Slice computed tomography coronary angiography in patients with high, intermediate, or low pretest probability of significant coronary artery disease. J Am Coll Cardiol 2007;50:1469-75.
83. Magalhaes TA, Kishi S, George RT, et al. Combined coronary angiography and myocardial perfusion by computed tomography in the identification of flow-limiting stenosis—the CORE320 study: an integrated analysis of CT coronary angiography and myocardial perfusion. J Cardiovasc Comput Tomogr 2015;9:438-45.
84. Pontone G, Andreini D, Baggiano A, et al. Functional relevance of coronary artery disease by cardiac magnetic resonance and cardiac computed tomography: myocardial perfusion and fractional flow reserve. Biomed Res Int 2015;2015:297696.
85. Varga-Szemes A, Meinel FG, De Cecco CN, Fuller SR, Bayer RR II, Schoepf UJ. CT myocardial perfusion imaging. AJR Am J Roentgenol 2015;204:487-97.
86. Osawa K, Miyoshi T, Koyama Y, et al. Additional diagnostic value of first-pass myocardial perfusion imaging without stress when combined with 64-row detector coronary CT angiography in patients with coronary artery disease. Heart 2014;100:1008-15.
87. Rochitte CE, George RT, Chen MY, et al. Computed tomography angiography and perfusion to assess coronary artery stenosis causing perfusion defects by single photon emission computed tomography: the CORE320 study. Eur Heart J 2014;35:1120-30.
88. George RT, Arbab-Zadeh A, Miller JM, et al. Adenosine stress 64- and 256-row detector computed tomography angiography and perfusion imaging: a pilot study evaluating the transmural extent of perfusion abnormalities to predict atherosclerosis causing myocardial ischemia. Circ Cardiovasc Imaging 2009;2:174-82.
89. George RT, Arbab-Zadeh A, Miller JM, et al. Computed tomography myocardial perfusion imaging with 320-row detector computed tomography accurately detects myocardial ischemia in patients with obstructive coronary artery disease. Circ Cardiovasc Imaging 2012;5:333-40.
90. Koo BK, Erglis A, Doh JH, et al. Diagnosis of ischemia-causing coronary stenoses by noninvasive fractional flow reserve computed from coronary computed tomographic angiograms. Results from the prospective multicenter DISCOVER-FLOW (Diagnosis of Ischemia-Causing Stenoses Obtained Via Noninvasive Fractional Flow Reserve) study. J Am Coll Cardiol 2011;58:1989-97.
91. Norgaard BL, Leipsic J, Gaur S, et al. Diagnostic performance of noninvasive fractional flow reserve derived from coronary computed tomography angiography in suspected coronary artery disease: the NXT trial (Analysis of Coronary Blood Flow Using CT Angiography: Next Steps). J Am Coll Cardiol 2014;63:1145-55.
92. Min JK, Koo BK, Erglis A, et al. Effect of image quality on diagnostic accuracy of noninvasive fractional flow reserve: results from the prospective multicenter international DISCOVER-FLOW study. J Cardiovasc Comput Tomogr 2012;6:191-9.
93. Norgaard BL, Gaur S, Leipsic J, et al. Influence of coronary calcification on the diagnostic performance of CT angiography derived FFR in coronary artery disease: a substudy of the NXT trial. JACC Cardiovasc Imaging 2015;8:1045-55.
94. Douglas PS, Pontone G, Hlatky MA, et al. Clinical outcomes of fractional flow reserve by computed tomographic angiography-guided diagnostic strategies vs. usual care in patients with suspected coronary artery disease: the prospective longitudinal trial of FFR(CT): outcome and resource impacts study. Eur Heart J 2015;36:3359-67.
95. Pouleur AC, le Polain de Waroux JB, Kefer J, Pasquet A, Vanoverschelde JL, Gerber BL. Direct comparison of whole-heart navigator-gated magnetic resonance coronary angiography and 40- and 64-slice multidetector row computed tomography to detect the coronary artery stenosis in patients scheduled for conventional coronary angiography. Circ Cardiovasc Imaging 2008;1:114-21.
96. Alderman EL, Corley SD, Fisher LD, et al. Five-year angiographic follow-up of factors associated with progression of coronary artery disease in the Coronary Artery Surgery Study (CASS). CASS Participating Investigators and Staff. J Am Coll Cardiol 1993;22:1141-54.
97. De Bruyne B, Pijls NH, Kalesan B, et al. Fractional flow reserve-guided PCI versus medical therapy in stable coronary disease. N Engl J Med 2012;367:991-1001.
98. Fearon WF, Shilane D, Pijls NH, et al. Cost-effectiveness of percutaneous coronary intervention in patients with stable coronary artery disease and abnormal fractional flow reserve. Circulation 2013;128:1335-40.
99. Tonino PA, De Bruyne B, Pijls NH, et al. Fractional flow reserve versus angiography for guiding percutaneous coronary intervention. N Engl J Med 2009;360:213-24.
100. American College of Radiology. ACR Appropriateness Criteria® Radiation Dose Assessment Introduction. Available at: http://www.acr.org/~/media/ACR/Documents/AppCriteria/RadiationDoseAssessmentIntro.pdf. Accessed May 1, 2016.