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**American College of Radiology
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Clinical Condition: Asymptomatic Patient at Risk for Coronary Artery Disease

Variant 1: Low risk.

Radiologic Procedure	Rating	Comments	RRL*
CT coronary calcium	3	In patients with strong family history, this study may be of value.	☼☼☼
Fluoroscopy heart	2		☼☼
US echocardiography transthoracic resting	2		O
X-ray chest	1		☼
CTA coronary arteries with IV contrast	1		☼☼☼
MRI heart with stress without and with IV contrast	1		O
MRI heart with stress without IV contrast	1		O
MRI heart function and morphology without and with IV contrast	1		O
MRI heart function and morphology without IV contrast	1		O
MRA coronary arteries without IV contrast	1		O
MRA coronary arteries without and with IV contrast	1		O
Tc-99m SPECT MPI rest and stress	1		☼☼☼☼
US echocardiography transthoracic stress	1		O
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation Level

Clinical Condition: Asymptomatic Patient at Risk for Coronary Artery Disease

Variant 2: Intermediate risk.

Radiologic Procedure	Rating	Comments	RRL*
CT coronary calcium	8		☼☼☼
CTA coronary arteries with IV contrast	3		☼☼☼
US echocardiography transthoracic stress	3		O
X-ray chest	2		☼
Fluoroscopy heart	2		☼☼
MRI heart with stress without and with IV contrast	2		O
MRI heart with stress without IV contrast	2		O
MRI heart function and morphology without and with IV contrast	2		O
MRI heart function and morphology without IV contrast	2		O
MRA coronary arteries without IV contrast	2		O
MRA coronary arteries without and with IV contrast	2		O
Tc-99m SPECT MPI rest and stress	2		☼☼☼☼
US echocardiography transthoracic resting	2		O
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation Level

Clinical Condition: Asymptomatic Patient at Risk for Coronary Artery Disease

Variant 3: High risk.

Radiologic Procedure	Rating	Comments	RRL*
MRI heart with stress without and with IV contrast	5		O
US echocardiography transthoracic stress	5		O
Tc-99m SPECT MPI rest and stress	5		☼☼☼☼
CTA coronary arteries with IV contrast	4		☼☼☼
MRI heart with stress without IV contrast	4		O
CT coronary calcium	3		☼☼☼
US echocardiography transthoracic resting	3		O
MRI heart function and morphology without and with IV contrast	3		O
MRI heart function and morphology without IV contrast	3		O
MRA coronary arteries without and with IV contrast	3		O
MRA coronary arteries without IV contrast	2		O
X-ray chest	2		☼
Fluoroscopy heart	2		☼☼
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation Level

ASYMPTOMATIC PATIENT AT RISK FOR CORONARY ARTERY DISEASE

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Summary of Literature Review

Introduction/Background

In the United States, atherosclerotic cardiovascular disease (CVD) is the leading cause of death for both men and women [1]. Although improvements in awareness, knowledge, and medications have led to a decrease in death rates, the burden of disease remains very high [1,2]. Because atherosclerotic coronary artery disease (CAD) has a long and asymptomatic latent period, it is believed that early targeted preventive measures would be a great benefit to reducing mortality and morbidity. To identify patients who might benefit from early intervention, it is essential to accurately classify individuals who are asymptomatic but at elevated risk.

CVD prevention has traditionally been based on the assessment of a patient's conventional risk-factor profile, a combined evaluation based on genetic, social, physiological, and environmental factors [3]. Risk assessment for CAD is intended to aid in determining the appropriate lifestyle changes and pharmacological interventions to reduce a patient's risk of cardiac death. A global risk score, such as Framingham, Reynolds, Systematic Coronary Risk Evaluation, or Prospective Cardiovascular Munster, is used to categorize patient risk as low, intermediate, or high. However, these risk factors are strong population-based markers but poor individual discriminators of CAD disease, and many individuals with 1 or more risk factors do not experience a cardiac event [3].

There is a growing discordance between the recognized ability of current risk estimation tools to predict outcomes versus that of actual measured outcomes [4]. Recent imaging advances have made it possible to detect subclinical coronary atherosclerosis. The coronary artery calcium score (CACS) is a marker of vascular injury that correlates closely with the overall atherosclerotic burden. Individual data derived from this and other imaging tests provide useful prognostic information for patient management and can complement current risk prediction models.

Non-imaging-based diagnostics, such as exercise treadmill testing, are also used for assessing asymptomatic patients who have an elevated risk for CVD. The added value of imaging-based tests has been previously established; therefore, a discussion of the use of non-imaging-based tests is beyond the scope of this document. Our purpose is to discuss the use of diagnostic imaging tests in asymptomatic patients who are at elevated risk for future cardiovascular events. The assessment goal for these patients is to further refine targeted preventative efforts based on patient risk. Diagnostic imaging tests are used only in asymptomatic patients at elevated cardiovascular risk. (Imaging use in patients who have a known diagnosis of CAD, cardiac symptoms, history of a coronary event, or prior intervention can be found in other ACR Appropriateness Criteria[®].)

The following imaging modalities are available for evaluating asymptomatic patients at elevated risk for CAD: chest radiography, chest fluoroscopy, multidetector computed tomography CT (MDCT), ultrasound (US), magnetic resonance imaging (MRI), cardiac perfusion scintigraphy, echocardiography, and positron emission tomography (PET).

Chest Radiography

A chest radiograph is commonly used in asymptomatic individuals as part of a routine physical examination or presurgical testing. A routine chest radiograph can detect unsuspected abnormalities of the lungs and thorax, assess for cardiomegaly, detect coronary calcium, or serve as a baseline for future measurement. Radiographs of the chest can depict the presence of coronary artery calcifications, which are indicative of CAD. Radiographic

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analyses of living and autopsied patients have demonstrated that coronary calcification is easily detected, occurs frequently, increases with age, and can indicate severe underlying lesions [5-8]. There is also an association between aortic arch calcification depicted on chest radiography and CAD [9].

Chest Fluoroscopy

Fluoroscopic visualization of coronary calcification is a noninvasive method used mainly in the past as a screening technique for CAD. The prevalence of CAD in patients with fluoroscopically detected coronary artery calcifications is significantly greater than in those without calcifications [10]. When compared with coronary angiography, chest fluoroscopy of an asymptomatic military flight crew demonstrated an overall sensitivity and specificity of 66.3% and 77.6%, respectively, for detecting significant CAD [11]. Patients who have calcification detected by chest fluoroscopy also have a significantly poorer survival [12].

Computed Tomography: Coronary Artery Calcium Scoring

CACS, performed on either an electron-beam CT or MDCT is a proven marker for the presence of coronary atherosclerosis and risk of future cardiovascular events [13,14]. CACS is useful in risk stratification and reclassification, as a strong association has been found between the calcium score and future mortality and/or adverse cardiac events [15-17]. Many trials have found evidence of the prognostic use of CACS. Shaw et al [18] followed 10,377 asymptomatic patients for 5 ± 3.5 years and found CACS to be an independent predictor of death that increased proportionally relative to baseline, with an adjusted relative risk of 1.6, 1.7, 2.5, and 4 for CACS 11 to 100, 101 to 400, 401 to 1,000, and $>1,000$, respectively.

CACS provides incremental prognostic information beyond traditional risk factor evaluation. In the St. Francis Heart Study, a CACS >100 predicted CAD events independently of standard risk factors [15]. Kondos et al [19] found that any measurable coronary calcium was independently related to hard (death and myocardial infarction [MI]) and soft (revascularization procedure) events in men and women; this finding provided incremental prognostic information over conventional risk factors. Budoff et al [20] also demonstrated incremental risk beyond age, gender, ethnicity, and cardiac risk factors in evaluating data from 25,253 asymptomatic patients who had a 10-year adjusted survival rate of 99.4% for a CACS of 0 and 87.8% for a score $>1,000$.

CACS can be used to stratify and reclassify patient risk more accurately than traditional methods. In 2 recent large-population-based studies, CACS demonstrated a high reclassification rate in the intermediate-risk cohort. This finding further supports the benefit of imaging of subclinical coronary atherosclerosis when compared with traditional risk categorization. These 2 independent observational and prospective studies showed a high net reclassification index (NRI) based on a CACS approach. In the Multi-Ethnic Study of Atherosclerosis, Polonsky et al [13] used CACS, in conjunction with their conventional Framingham Risk Score, to evaluate 5,878 asymptomatic men and women. In that study, the NRI was 25%, an additional 23% of subjects with events were reclassified to the high-risk category, and 13% of subjects without events were reclassified to the low-risk category. The Heinz Nixdorf Recall Study, a large population-based study with nearly 5,000 participants and a 5-year follow-up, demonstrated a NRI of 24% and 19% as high- and low-risk groups, respectively [21].

Several guidelines on imaging of asymptomatic CAD included recommendations for using CACS [22]. The *2010 Appropriate Use Criteria for Cardiac Computed Tomography* found that CACS use was appropriate in asymptomatic, intermediate-risk patients and in low-risk patients who had a family history of premature CAD [23]. Other guidelines concluded there was sufficient evidence to consider recommending CACS [24-28], and one guideline recommended its use [29]. These guidelines recommended CACS exclusively in patients at intermediate risk for CAD. For patients at low and high risk for CAD, the guidelines were unanimous in not advocating CT calcium scoring [22].

Computed Tomography: Coronary Angiography

Coronary CT angiography (CCTA) noninvasively assesses patency of the coronary lumen, the arterial wall, calcified and noncalcified plaques, and ventricular function [30,31]. In addition to many single-center studies, 3 multicenter trials evaluated the diagnostic use of 64-slice CCTA and reported sensitivities for detecting a 50% stenosis from 85% to 99%, with negative predictive values from 83% to 99% [32-34]. It is not known, however, whether CCTA can be used as a prognostic tool, independent of CACS and clinical risk models, to stratify asymptomatic patients and predict future cardiac events.

Several studies examined CAD in asymptomatic patients and reported a relatively high prevalence of occult atherosclerosis; this discovery could have a significant impact on therapeutic decision-making and management

[35-39]. One relatively large study of 1,000 asymptomatic patients reported using CCTA to evaluate the prevalence of occult CAD and its ability to predict future adverse coronary events [36]. Among asymptomatic patients, Choi et al [36] found atherosclerotic plaques in 22%, stenoses of $\geq 50\%$ in 5%, and stenosis of $\geq 75\%$ in 2%. Of those who had significant stenosis, 25% were initially classified as low-risk according to National Cholesterol Education Program criteria, and 58% had CACS < 100 . At midterm follow-up (17 ± 2 months) all coronary events occurred in individuals for whom CCTA had depicted CAD. In another study using CCTA, two-thirds of asymptomatic diabetics were found to have occult CAD, including 26% with obstructive disease [38]. Hadamitzky et al [40] retrospectively assessed the value of CCTA in predicting cardiac events in 451 asymptomatic patients, with a median follow-up of 27.5 months. In 48% of patients, CCTA could be used to reclassify the clinically assessed cardiovascular risk from intermediate- or high- to low-risk.

In patients who had suspected but undocumented CAD, Russo et al [41] evaluated the incremental prognostic value of CCTA against both a traditional clinical-risk model and calcium scoring. While CACS again had significant incremental prognostic value compared with a baseline clinical-risk model, CCTA provided an additional incremental prognostic value, compared with a baseline clinical-risk model plus CACS. The presence of noncalcified or mixed plaques, regardless of lesion severity, was found to be the strongest predictor of events ($P < .0001$) as a potential marker of plaque vulnerability.

Results from both CACS and CCTA studies have demonstrated that patients who have occult CAD could be misclassified when conventional risk-stratification algorithms are used. In symptomatic patients, CT can independently predict future events, and data suggest it can yield improved risk stratification beyond traditional scoring methods. In asymptomatic patients, CACS can also be used to stratify and reclassify patient risk more accurately than traditional methods. Using CCTA in asymptomatic patients remains controversial, primarily because of the higher radiation dose, added cost, and use of nephrotoxic contrast, but it has the potential to identify useful data beyond what is derived from CACS. As detailed in the *2010 ACCF/AHA Guideline for Assessment of Cardiovascular Risk in Asymptomatic Adults: Executive Summary*, CCTA is not recommended for cardiovascular risk assessment in asymptomatic adults [2].

Recent advances in cardiac CT imaging technology allow for further radiation dose reduction in CCTA examinations [42]; new and available dose-reducing techniques include prospective triggering [43-45], adaptive statistical iterative reconstruction [46], and high-pitch spiral acquisition [47]. However, these newer low-dose techniques may not be appropriate in all patients due to their dependency on a combination of factors, including heart rate, rhythm, and large body size. Thus, although these techniques are promising in terms of reducing patient radiation dose, there may be patients for whom these radiation dose techniques are not optimal, such as an obese, elderly patient with an arrhythmia who might best benefit from retrospective gating in order to allow assessment of the coronary arteries at multiple phases of the cardiac cycle. In addition, not all scanners are capable of all radiation dose reduction techniques. 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 (ALARA).

Magnetic Resonance Imaging

Cardiac MRI is an accurate and reliable means for evaluating cardiac anatomy and ventricular function [48]. Recent progress has shown it to be an excellent method for evaluating myocardial ischemia and infarction. Stress first-pass contrast-enhanced myocardial perfusion MRI detects subendocardial ischemia with high diagnostic accuracy in patients with significant CAD [49-51]. Wall motion abnormalities identified during dobutamine stress MRI accurately identify patients at increased risk for cardiac death and myocardial infarction (MI); patients with normal findings have very low risk for future cardiac events [52,53].

Assessment of myocardial viability is important in predicting functional recovery after revascularization and in risk stratification of patients who have CAD [54]. Although coronary MRA does not expose patients to radiation, like CACS or CCTA, noninvasive MRI of the coronary artery is technically demanding due to the small size and tortuous course of the coronary arteries and the complex motion caused by cardiac contraction and respiration.

In asymptomatic patients, MRI of the coronary wall may enhance risk stratification by quantifying the subclinical coronary atherosclerotic plaque burden [55,56]. In a subset of asymptomatic patients in the Multi-Ethnic Study of Atherosclerosis, coronary arterial remodeling was evaluated using coronary wall MRI as a marker of subclinical atherosclerosis. MRI detected positive arterial remodeling in asymptomatic men and women who had subclinical atherosclerosis [57]. Recently, the presence of unrecognized MI in asymptomatic patients, as detected by contrast-

enhanced MR, was associated with increased mortality risk and more strongly associated with mortality than electrocardiogram; the presence of unrecognized MI improved risk stratification for mortality over recognized MI [58]. Currently, no consensus guideline recommends the use of MRI for risk stratification in asymptomatic patients [30].

Cardiac Perfusion Scintigraphy

Myocardial perfusion scintigraphy (MPS) can detect silent myocardial ischemia but is limited in its ability to detect early or subclinical atherosclerosis. Patients undergoing MPS who do not show inducible ischemia have a very low (<1% per year) cardiac event rate during the following 2 to 3 years [59,60]. The prevalence of silent myocardial ischemia in asymptomatic populations varies significantly [61,62]. In nondiabetic patients, evidence of silent ischemia increases from 2% in the fifth and sixth decades to 15% in the ninth decade [61].

A positive MPS is an independent predictor of future coronary events, and it is independent of conventional risk factors [61]. Use of MPS in asymptomatic individuals who have intermediate risk is effective for CAD detection and risk stratification. In asymptomatic patients at moderate risk for CAD, Khandaker et al [62] showed that the annual mortality was 4.0% in patients with a positive MPS versus 1.6% in those who had normal scans. Zellweger et al [63] evaluated 3,664 consecutive asymptomatic patients with no prior diagnosis of CAD who were undergoing MPS and followed them for 1 year or more. They reported that patients with $\geq 7.5\%$ myocardium ischemia had a significantly greater risk (3.1% major event rate per year) than those with less ischemia (0.4% major event rate).

Asymptomatic patients who have type 2 diabetes have a higher cardiac risk than nondiabetic patients [64]. The average annual hard event rate (cardiac death or MI) in diabetic patients with a normal MPS was 0.85%, as opposed to 5.9% in those with a moderately to severely abnormal MPS [60]. However, for any degree of perfusion abnormality, the risk in diabetic patients is higher compared with nondiabetic patients [64]. Recently, Wackers et al [65] reported a prevalence of 21% abnormal MPS using gated ^{99m}Tc -sestamibi in the Detection of Silent Myocardial Ischemia in Asymptomatic Diabetics study. The presence of moderate to large ischemic defects was associated with a significantly higher event rate (2.4% per year) compared with patients who had normal perfusion or small perfusion abnormalities (0.4% per year) [66].

As detailed in the *2010 ACCF/AHA Guideline for Assessment of Cardiovascular Risk in Asymptomatic Adults: Executive Summary*, stress magnetic perfusion imaging (MPI) is indicated for risk assessment in asymptomatic adults who have diabetes or asymptomatic adults who have a strong family history of congenital heart disease; it is also indicated when previous risk-assessment testing has suggested a high risk of CHD, such as a CACS >400 [2]. Stress MPI is not indicated for cardiovascular risk assessment in low- or intermediate-risk asymptomatic adults.

Echocardiography

Stress echocardiography can be used for screening high-risk asymptomatic patients. It is most commonly used before major noncardiac surgery. A number of studies have demonstrated that the yearly event rate following a normal exercise or dobutamine stress echocardiography (DSE) is only 0.4% to 0.9%, a value similar to that following a normal MPS [67,68]. Prognostic data from stress echocardiography can be used to risk-stratify patients. Following a normal stress echocardiogram, the cardiac event-free survival rates at 1, 2, and 3 years are 99.2%, 97.8%, and 97.4%, respectively [69]. Subgroups with an intermediate or high pretest probability of CAD also had low cardiac event rates.

Poldermans et al [70] showed that the rate of cardiac death or MI in patients who had a new abnormal stress echocardiogram increased 3.6- and 2.5-fold, respectively. They also reported that DSE can assess the risk for future cardiac events by distinguishing subgroups of patient with high ($>30\%$ in 5 years), median (12% in 5 years), and low (8% in 5 years) risk. Importantly, patients with normal DSE have a good prognosis. In symptomatic patients who have new onset of chest pain and no previously known CAD, stress echocardiography is an independent and incremental predictor of hard cardiac events beyond that provided by electrocardiogram and clinical data alone [71].

Despite these results, stress echocardiography is not indicated for cardiovascular risk assessment in low- or intermediate-risk asymptomatic adults [3].

Summary

- Recent imaging advances have made it possible to detect subclinical coronary atherosclerosis. A number of imaging modalities may be used for evaluating asymptomatic patients at elevated risk for future cardiovascular events.
- The goal of assessment in asymptomatic patients is to refine targeted preventative efforts based on patient risk.
- In low-risk patients, all modalities were considered “usually not appropriate”, but the panel did comment that CACS may be useful in low-risk patients who have a strong family history of coronary risk.
- In intermediate-risk patients, CACS was determined to be “usually appropriate”, as it can be used to stratify and reclassify patient risk more accurately than traditional methods.
- In high-risk patients, it was determined that CCTA and stress-and-rest studies using MRI, single-photon emission CT, MPI, and ultrasound “may be appropriate.”

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 as compared to 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.

Relative Radiation Level Designations		
Relative Radiation Level*	Adult Effective Dose Estimate Range	Pediatric Effective Dose Estimate Range
○	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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The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.