American College of Radiology
ACR Appropriateness Criteria®

Asymptomatic Patient at Risk for Coronary Artery Disease

Variant: 1 Asymptomatic patient. Low risk for coronary artery disease. Initial imaging.

Procedure	Appropriateness Category	Relative Radiation Level
US echocardiography transthoracic resting	Usually Not Appropriate	O
US echocardiography transthoracic stress	Usually Not Appropriate	O
Radiography chest	Usually Not Appropriate	☢
MRA coronary arteries without and with IV contrast	Usually Not Appropriate	O
MRA coronary arteries without IV contrast	Usually Not Appropriate	O
MRI heart function and morphology without and with IV contrast	Usually Not Appropriate	O
MRI heart function and morphology without IV contrast	Usually Not Appropriate	O
MRI heart function with stress without and with IV contrast	Usually Not Appropriate	O
MRI heart function with stress without IV contrast	Usually Not Appropriate	O
CT coronary calcium	Usually Not Appropriate	☢☢☢
CTA coronary arteries with IV contrast	Usually Not Appropriate	☢☢☢
SPECT or SPECT/CT MPI rest and stress	Usually Not Appropriate	☢☢☢☢

Variant: 2 Asymptomatic patient. Intermediate risk for coronary artery disease. Initial imaging.

Procedure	Appropriateness Category	Relative Radiation Level
CT coronary calcium	Usually Appropriate	☢☢☢
CTA coronary arteries with IV contrast	May Be Appropriate	☢☢☢
US echocardiography transthoracic resting	Usually Not Appropriate	O
US echocardiography transthoracic stress	Usually Not Appropriate	O
Radiography chest	Usually Not Appropriate	☢
MRA coronary arteries without and with IV contrast	Usually Not Appropriate	O
MRA coronary arteries without IV contrast	Usually Not Appropriate	O
MRI heart function and morphology without and with IV contrast	Usually Not Appropriate	O
MRI heart function and morphology without IV contrast	Usually Not Appropriate	O
MRI heart function with stress without and with IV contrast	Usually Not Appropriate	O
MRI heart function with stress without IV contrast	Usually Not Appropriate	O
SPECT or SPECT/CT MPI rest and stress	Usually Not Appropriate	☢☢☢☢

Variant: 3 Asymptomatic patient. High risk for coronary artery disease. Initial imaging.

Procedure	Appropriateness Category	Relative Radiation Level
CT coronary calcium	May Be Appropriate	☢☢☢
CTA coronary arteries with IV contrast	May Be Appropriate	☢☢☢
US echocardiography transthoracic resting	Usually Not Appropriate	O
US echocardiography transthoracic stress	Usually Not Appropriate	O
Radiography chest	Usually Not Appropriate	☢
MRA coronary arteries without and with IV contrast	Usually Not Appropriate	O

MRA coronary arteries without IV contrast	Usually Not Appropriate	O
MRI heart function and morphology without and with IV contrast	Usually Not Appropriate	O
MRI heart function and morphology without IV contrast	Usually Not Appropriate	O
MRI heart function with stress without and with IV contrast	Usually Not Appropriate	O
MRI heart function with stress without IV contrast	Usually Not Appropriate	O
SPECT or SPECT/CT MPI rest and stress	Usually Not Appropriate	☢☢☢☢

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Summary of Literature Review

Introduction/Background

In the United States, atherosclerotic cardiovascular disease (ASCVD) remains 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]. Identification of patients who may benefit from early intervention prior to development of symptoms has been shown to reduce mortality and morbidity [3].

Cardiovascular disease 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 [4]. Risk assessment for ASCVD is intended to aid in determining the appropriate lifestyle changes and pharmacological interventions to reduce a patient's risk of adverse cardiovascular outcomes (eg, myocardial infarction, stroke, cardiovascular death). A global risk score, such as the Framingham Risk Score (FRS), Reynolds risk score, or Systematic Coronary Risk Evaluation, is used to categorize a patient's risk as low, intermediate, or high risk. These risk factors are strong population-based markers but poor individual discriminators of coronary atherosclerotic disease (CAD), and many individuals with one or more risk factors do not experience a cardiac event [4]. Risk calculators are also bound by the underlying prior data that informs them, and as population health and lifestyle changes, risk calculators become less accurate [5]. More recently, the 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol, suggested the use of a pooled cohort risk calculator in patients to categorize their 10-year risk of ASCVD as low risk (<5%), borderline risk (5% to <7.5%), intermediate risk (7.5% to <20%), or high risk (>20%) [3].

There is a well-established discordance between the prognostic accuracy of current risk estimation scores versus imaging when directly measuring the burden of atherosclerosis for the assessment of individual ASCVD risk as a guide to optimally manage preventive therapies [6]. Imaging allows for the detection of subclinical coronary atherosclerosis. Patients with familial hyperlipidemia in particular have a high prevalence of subclinical coronary atherosclerosis that is independently

associated with cardiovascular risk [7]. The coronary artery calcium (CAC) score is a validated measure of overall coronary atherosclerotic burden, the strongest known imaging measure of risk in asymptomatic individuals. Individual data derived from this and other imaging tests provide useful prognostic information for patient management and can complement current risk prediction models [8].

The purpose of this document is to discuss the use of diagnostic imaging tests in asymptomatic patients who are at elevated risk of future cardiovascular events related to atherosclerosis. The tests are to improve targeted preventive efforts based on patient risk and are aimed at identification of CAD.

Appropriate imaging tests 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. See the ACR Appropriateness Criteria® topics on "Acute Nonspecific Chest Pain—Low Probability of Coronary Artery Disease" [9], "Chronic Chest Pain-Noncardiac Etiology Unlikely; Low to Intermediate Probability of Coronary Artery Disease" [10], and "Chronic Chest Pain—High Probability of Coronary Artery Disease" [11] for further information and to guide imaging. Please note that the topic of preoperative cardiac evaluation is a distinct and evolving topic, and there is not a current ACR Appropriateness Criteria concerning preoperative evaluations (regarding cardiac or noncardiac surgery); this topic is not considered to be within the scope of this document.

Special Imaging Considerations

Imaging findings in CAD range from direct visualization of plaque and perfusion deficits to ventricular dilatation and infarct [12]. Radiographs depict static findings of late CAD, such as severe coronary artery calcification and heart size, whereas multidetector CT (MDCT) can directly visualize plaque in the coronary arteries. MDCT of the heart is performed with electrocardiogram (ECG) synchronization and can be performed without or with intravenous (IV) contrast—the former defined as CT CAC score—and can assess overall calcific burden of the coronary arteries only; the latter is CT angiography (CTA) coronaries with IV contrast that allows assessment of both noncalcified and calcified plaque and any resultant visualized nonobstructive or obstructive coronary stenosis.

Resting image modalities (ultrasound [US], scintigraphy, CT, and MRI) depict late findings of CAD, such as ventricular dilatation and wall-motion abnormalities, and can directly visualize the morphology of infarcted myocardial segments. Intravascular US, an invasive technique, can detect both calcified and noncalcified plaque. Myocardial perfusion can be assessed by stress, rest, and/or delayed imaging, which can be accomplished by US (via assessment of wall-motion changes at stress versus rest, or with contrast echocardiography); cardiac perfusion scintigraphy (via comparison of first-pass radiotracer perfusion to the ventricle at stress versus rest, or measurement of coronary blood flow); and MRI (via comparison of wall-motion or first-pass gadolinium enhancement of the ventricle during stress versus rest). Cardiac MRI is performed with ECG synchronization and may be performed without and with IV contrast and before and after vasodilators or inotropes if stress myocardial perfusion assessment is desired. MR angiography (MRA) of the coronary arteries is possible without or with IV contrast, but it only depicts luminal blood and cannot depict calcified plaque. Myocardial scarring, infarction, and viability can be assessed by cardiac MRI or cardiac PET.

For the purposes of distinguishing between CT and CTA, ACR Appropriateness Criteria topics use the definition in the ACR–NASCI–SIR–SPR Practice Parameter for the Performance and Interpretation of Body Computed Tomography Angiography (CTA) [13]:

> "*CTA uses a thin-section CT acquisition that is timed to coincide with peak arterial or venous enhancement. The resultant volumetric dataset is interpreted using primary transverse reconstructions as well as multiplanar reformations and 3-D renderings."*

All elements are essential: 1) timing, 2) reconstructions/reformats, and 3) 3-D renderings. Standard CTs with contrast also include timing issues and reconstructions/reformats. Only in CTA, however, is 3-D rendering a **required** element. This corresponds to the definitions that the CMS has applied to the Current Procedural Terminology codes.

Initial Imaging Definition

Initial imaging is defined as imaging at the beginning of the care episode for the medical condition defined by the variant. More than one procedure can be considered usually appropriate in the initial imaging evaluation when:

- There are procedures that are equivalent alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care)

OR

- There are complementary procedures (ie, more than one procedure is ordered as a set or simultaneously where each procedure provides unique clinical information to effectively manage the patient's care).

Discussion of Procedures by Variant

Variant 1: Asymptomatic patient. Low risk for coronary artery disease. Initial imaging.

Variant 1: Asymptomatic patient. Low risk for coronary artery disease. Initial imaging.
A. CT Coronary Calcium

The CAC score first became available and validated with electron beam CT, and in the modern era, MDCT is used to acquire this data. Several multicenter trials have assessed the use of CAC in asymptomatic patients at intermediate risk for CAD. In the Multi-Ethnic Study of Atherosclerosis (MESA), Joshi et al [14] followed 6,814 participants including 13% with a CAC score >100 and 34% with a nonzero CAC score with low risk over a period of 10.4 years and found an event rate of 2.4% (33 events). CAC was present in 76% of participants with an event. In the multivariate analysis, only CAC >100 was predictive of coronary heart disease [14]. Recently, in a large cohort of 14,169 low-risk patients with a family history of CAD, Dudum et al showed that a calcium score of >100 had a 2.2 times higher risk for all-cause mortality, 4.3 times higher cardiovascular specific mortality, and 10.4 times higher risk of coronary heart disease, than patients with a zero calcium score [15,16]. Mitchell et al [17] evaluated 23,637 subjects with a mean age of 50.0 ± 8.5 years and low burden of traditional risk factors, they noted relative adjusted subhazard ratio for CAC 1 to 100, 101 to 400, and >400 was 2.2, 3.8, and 5.9 for myocardial infarction; 1.2, 1.4, and 1.9 for stroke; 1.4, 2.0, and 2.8 for major adverse cardiovascular events (MACE); and 1.2, 1.5 and 2.1 for death (P < .0001) over a

median follow-up period of 11.4 years. Among subjects without traditional risk factors (n = 6,208; mean age 43.8 ± 4.4 years), the presence of any CAC (>0; n = 848) was associated with an increased risk of MACE (adjusted subhazard ratio: 1.67; 95% confidence interval [CI], 1.16 to 2.39) noting the fact that young individuals without traditional risk factors are typically not offered preventive therapy with statins. Carr et al [18] prospectively enrolled a much younger cohort of 3,043 patients with mean [SD] age 40.3 [3.6] years in the Coronary Artery Risk Development in Young Adults (CARDIA) study and noted that 10.2% of patients had CAC, with a geometric mean Agatston score of 21.6 (interquartile range, 17.3–26.8). During 12.5 years of follow-up, 57 coronary heart disease events and 108 cardiovascular events were observed. After adjusting for demographics, risk factors, and treatments, patients with any CAC experienced a 5-fold increase in coronary heart disease events (hazard ratio [HR], 5.0; 95% CI, 2.8–8.7) and 3-fold increase in cardiovascular events (HR, 3.0; 95% CI, 1.9–4.7), and those with a CAC score of ³100 had an incidence of 22.4 deaths per 100 participants (HR, 3.7; 95% CI, 1.5–10.0).

Variant 1: Asymptomatic patient. Low risk for coronary artery disease. Initial imaging.
B. CTA Coronary Arteries

There is no relevant literature supporting the use of coronary CTA (CCTA) in asymptomatic patients at low risk of CAD. Choi et al [19] identified atherosclerotic plaques in 215 of 1,000 middle-aged asymptomatic patients with 2% prevalence of plaque in the low-risk group.

Variant 1: Asymptomatic patient. Low risk for coronary artery disease. Initial imaging.
C. US Echocardiography Transthoracic Resting

There is no relevant literature supporting the use of transthoracic echocardiography (TTE) resting in asymptomatic patients at low risk of CAD.

Variant 1: Asymptomatic patient. Low risk for coronary artery disease. Initial imaging.
D. US Echocardiography Transthoracic Stress

There is no relevant literature supporting the use of TTE stress in asymptomatic patients at low risk of CAD. The sensitivity and specificity of the test is 72% to 83% and 84% to 95%, respectively, for identification of ischemic myocardium and has been validated only in elevated risk populations [20].

Variant 1: Asymptomatic patient. Low risk for coronary artery disease. Initial imaging.
E. MRA Coronary Arteries

There are very limited data on the utility of MRA in asymptomatic patients, which demonstrated a low yield in a small cohort of nonrandomized asymptomatic self-referred patients. In this cohort of 341 patients, 3.8% were found to have significant CAD ³50% stenosis in a protocol that also included MRA, MRI perfusion, and delayed-enhancement imaging; 0.9% of the cohort underwent percutaneous coronary intervention after CAD was detected by cardiac MRI and MRA and was found to have good correlation with stress perfusion MRI in the 13 positive patients, 3 of which were confirmed with invasive angiography [21].

Variant 1: Asymptomatic patient. Low risk for coronary artery disease. Initial imaging.
F. MRI Heart Function with Stress

There is no relevant literature supporting the use of MRI heart function with stress in asymptomatic patients at low risk of CAD.

Variant 1: Asymptomatic patient. Low risk for coronary artery disease. Initial imaging.
G. MRI Heart Function and Morphology

Weir-McCall et al [22] demonstrated an overall low utility of resting MRI via abnormal late gadolinium enhancement in asymptomatic low-risk volunteers (0.67% of whom were found to have abnormalities, including myocardial infarction), with only 0.2% of volunteers having a previously unrecognized myocardial infarction.

Variant 1: Asymptomatic patient. Low risk for coronary artery disease. Initial imaging.
H. Radiography Chest

There is no relevant literature to support the use of chest radiographs to evaluate asymptomatic patients at low risk of CAD.

Variant 1: Asymptomatic patient. Low risk for coronary artery disease. Initial imaging.
I. SPECT/CT MPI Rest and Stress

There is no relevant literature supporting the use of single-photon emission computed tomography (SPECT)/CT myocardial perfusion imaging (MPI) rest and stress in asymptomatic patients at low risk of CAD. Stress SPECT sensitivity and specificity for detection of obstructive CAD (≥50% diameter stenosis) are 74% and 79%, respectively, in symptomatic patients [23].

Variant 2: Asymptomatic patient. Intermediate risk for coronary artery disease. Initial imaging.

Variant 2: Asymptomatic patient. Intermediate risk for coronary artery disease. Initial imaging.
A. CT Coronary Calcium

Kondos et al [24] found that any measurable coronary calcium was independently related to hard (death and myocardial infarction) and soft (revascularization procedure) events in men and women at low to intermediate pretest risk; this finding provided incremental prognostic information over conventional risk factors.

Many trials have found evidence of the prognostic use of a CAC score. Shaw et al [25] followed 10,377 asymptomatic patients for 5 ± 3.5 years and found a CAC score 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 CAC scores of 11 to 100, 101 to 400, 401 to 1,000, and >1,000, respectively. Budoff et al [26] 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 CAC score of 0, and 87.8% for a score >1,000. In the CARDIA study, of the 2,831 participants, the CAC score and prevalence increased, and an increase in FRS with a score >0 was observed in 7.3%, 20.2%, 19.1%, and 44.8% of individuals with FRSs of 0% to 2.5%, 2.6% to 5%, 5.1% to 10%, and >10%, respectively. A CAC score of ≥100 was observed in 1.3%, 2.4%, and 3.5% of those with FRSs of 0% to 2.5%, 2.6% to 5%, and 5.1% to 10%, respectively, without significant change in stratification according to sex and race. The yield of CAC was deemed considerable in the intermediate-risk group [27]. Additionally, the MESA of 6,779 initially asymptomatic individuals also showed CAC as an independent predictor of cerebrovascular events when CAC analysis was stratified by sex or race or ethnicity and improved discrimination for a cerebrovascular event when added to the full model (C-statistic: 0.744 versus 0.755) [28]. Although the authors of the study do not specify the pretest risk of the overall patient population, the presence of hypertension and treated hypertension as well as the degree of coronary calcification was higher in the group containing individuals who had cerebrovascular events.

In the MESA, Polonsky et al [29] used the CAC score, in conjunction with their conventional FRS, to evaluate 5,878 asymptomatic men and women. In that study, the net reclassification index 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 [29]. The Heinz Nixdorf Recall study, a large population-based study with nearly 5,000 participants and a 5-year follow-up, demonstrated a net reclassification index of 24% and 19% as high- and low-risk groups, respectively [30]. The recent AHA/ACC/AACVPR/AAPA/ABC/ACPM/ ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol also suggests patients with a 10-year risk of 5% to 7.5% (borderline risk) in the presence of risk-enhancing factors, such as family history, of premature ASCVD; persistently elevated LDL-C levels ^{3}160 mg/dL; metabolic syndrome; chronic kidney disease; history of preeclampsia; or premature menopause (age <40 years); chronic inflammatory disorders (eg, rheumatoid arthritis, psoriasis, or chronic HIV); high-risk ethnic groups (eg, South Asian); and persistent elevations of triglycerides ^{3}175 mg/dL may benefit from a CAC score prior to initiating a statin therapy [3]. These studies have shown that CAC score predicts future mortality and major cardiac events and aids in improved risk stratification beyond the conventional risk factor–based scores alone. A positive calcium score can restratify asymptomatic patients with a family history of premature CAD to a high-risk category and can even reclassify those individuals without risk factors as higher risk than those with multiple risk factors but no coronary artery calcification [31,32].

Variant 2: Asymptomatic patient. Intermediate risk for coronary artery disease. Initial imaging.

B. CTA Coronary Arteries

In a recent study, Di Cesare et al [33] showed utility of CCTA in asymptomatic patients at intermediate risk of stenosis detection in 112 out of 185 (60.5%) patients: 56 patients (30.2%) had mild stenosis, 49 patients (26.5%) had moderate stenosis, only 3 patients (1.6%) had severe stenosis, and in 4 patients (2.2%) evaluation could not be determined.

Variant 2: Asymptomatic patient. Intermediate risk for coronary artery disease. Initial imaging.

C. US Echocardiography Transthoracic Resting

There is no relevant literature supporting the use of TTE resting in asymptomatic patients at intermediate risk of CAD.

Variant 2: Asymptomatic patient. Intermediate risk for coronary artery disease. Initial imaging.

D. US Echocardiography Transthoracic Stress

The sensitivity and specificity of stress TTE is 85% and 89%, respectively, has been validated only in populations at elevated risk, and is best utilized to search for obstructive major epicardial coronary stenosis [34]. There is no relevant literature to support the use of stress TTE in asymptomatic patients at intermediate risk of CAD.

Variant 2: Asymptomatic patient. Intermediate risk for coronary artery disease. Initial imaging.

E. MRA Coronary Arteries

MRA of the coronary arteries can assess for arterial patency and pathologic wall thickening but not calcific burden, and it cannot reliably assess small distal vessels [35,36]. There is no relevant literature to support the use of MRA of the coronary arteries in asymptomatic patients at

intermediate risk of CAD.

Variant 2: Asymptomatic patient. Intermediate risk for coronary artery disease. Initial imaging.
F. MRI Heart Function and Morphology

There is no relevant literature to support the use of MRI heart function and morphology to evaluate asymptomatic patients at intermediate risk of CAD.

Variant 2: Asymptomatic patient. Intermediate risk for coronary artery disease. Initial imaging.
G. MRI Heart Function with Stress

The IMPACT II study demonstrated a sensitivity of 67% and specificity of 61% for detection of ischemic heart disease, including 533 patients in the intermediate-risk population [37]. The vast majority of the patients in this study were symptomatic, with angina pectoris. The sensitivity and specificity of the test in the asymptomatic intermediate-risk population has not been validated.

Variant 2: Asymptomatic patient. Intermediate risk for coronary artery disease. Initial imaging.
H. Radiography Chest

There is no relevant literature to support the use of chest radiographs alone as a test to evaluate asymptomatic patients at intermediate risk of CAD.

Variant 2: Asymptomatic patient. Intermediate risk for coronary artery disease. Initial imaging.
I. SPECT/CT MPI Rest and Stress

Stress SPECT MPI is the most commonly used stress-imaging technique for patients with suspected or known CAD but has been primarily validated in symptomatic patients, and no studies have examined SPECT MPI alone in asymptomatic intermediate-risk patients. However, in combination with a calcium score of ≥400, expert consensus has speculated that the test may be used for intermediate-risk patients [38]. However, there is no relevant literature to support the use of SPECT MPI in asymptomatic patients at intermediate risk of CAD, except in diabetic patients or those about to undertake a vigorous exercise program [39].

Variant 3: Asymptomatic patient. High risk for coronary artery disease. Initial imaging.

Variant 3: Asymptomatic patient. High risk for coronary artery disease. Initial imaging.
A. CT Coronary Calcium

Studies to date indicate the high prevalence of calcific plaque burden in a high-risk patient, and further testing may be warranted to exclude epicardial stenosis. Data from a large study with 29,312 high-risk patients support the rationale of the "power of zero"; in absence of coronary calcification, only 0.56% participants developed a cardiovascular event during a mean follow-up period of 51 months [40]. A similar observation was also noted in the JUPITER population study in the MESA cohort in which event rates were 0.8 per 1,000 person years with zero calcium score versus 20.2 per 1,000 person years and a calcium score >100. The estimated number needed to treat for 5 years was at 549 in the zero calcium score group versus 42 in the nonzero calcium score group [41].

Variant 3: Asymptomatic patient. High risk for coronary artery disease. Initial imaging.
B. CTA Coronary Arteries

There is an added value of coronary atherosclerotic plaque burden as a prognostic benefit in addition to the assessment for epicardial stenosis, such that in high-risk asymptomatic patients, CCTA examinations can be useful. Cho et al [42], in their study of 3,217 asymptomatic patients from the CONFIRM registry stratified according to the magnitude of their CAC score, found that CCTA did provide incremental value in patients with a CAC score >100. The incremental value of CCTA over FRS was demonstrated in individuals with CAC scores >100 (likelihood ratio χ^2, 25.34; increment in C-statistic, 0.24; net reclassification index, 0.62; all $P < .001$) but not with CAC scores ≤100 (all $P > .05$). For subgroups with CAC score >100, the utility of CCTA for predicting the study end point was evident among individuals whose CAC score ranged from 101 to 400; the observed predictive benefit attenuated with increasing CAC score. In a high-risk population of 665 asymptomatic patients, the multivariate analysis, adjusted for age, gender, and CAC score, obstructive CAD on CCTA (≥50% luminal stenosis) was a significant predictor of adverse events (HR, 5.9; CI, 1.3–26.1). Dedic et al [43] also showed that the addition of CCTA to age and gender, plus a CAC score, increased the C-statistic from 0.81 to 0.84 and resulted in a total net reclassification index of 0.19 ($P < .01$). Incremental value of the CCTA was also demonstrated by Plank et al [44] in a series of 711 patients, where prevalence of a zero calcium score was 306 (43%); out of those, 100 (32.7%) had noncalcified plaque only seen on CTA. With a mean follow-up period of 2.65 years, MACE rate was 0% in CAD negative and higher (1.2%) in CAD positive by CTA.

In a large multicenter registry of 27,125 patients (which included both symptomatic and asymptomatic patients), Min et al [45] found that CCTA improved discrimination by maximal stenosis, number of obstructive vessels, and segment stenosis score (C-index 0.77, 0.77, and 0.78, respectively) beyond age, gender, and CAC score (C-index 0.64) in a small subset of 400 asymptomatic patients. Similarly, CCTA findings improved risk reclassification by per patient maximal stenosis (integrated discrimination improvement [IDI] index, 0.03; $P = .03$) and number of obstructive vessels (IDI index, 0.06; $P = .002$), and by trend for segment stenosis score (IDI, 0.03; $P = .06$).

In the FACTOR-64 study of 900 asymptomatic patients with both type 1 and 2 diabetes, with a mean follow-up time of 4.0 years, the primary outcome event rates were not significantly different between the CCTA and the control groups (6.2% [28 events] versus 7.6% [34 events]; HR, 0.80 [95% CI, 0.49–1.32]; $P = .38$) [46]. A study of 517 asymptomatic subjects also showed that CAD- and plaque-positive remodeling increased MACE prediction compared with a model based on 10-year FRS, carotid disease, and CAC score estimation. In the diabetes subgroup, the percentage of segments with remodeled plaque was the only predictor of MACE [47].

In the asymptomatic diabetic population in patients between the ages of 55 and 74, Halon et al [48] demonstrated 2,242 plaques in 499 subjects with 24 patients with acute coronary syndromes during median follow-up of 9.2 years. Additional imaging parameters, like plaque volume (upper versus lower quartile HR, 6.9; 95% CI, 1.6–30.8; $P = .011$), percentage of low-density plaque content <50 Hounsfield units (HR, 14.2; 95% CI, 1.9–108; $P = .010$), and mild plaque calcification (HR versus all other plaques, 3.3; 95% CI, 1.5–7.3; $P = .004$), predicted plaque events univariately after adjustment by clinical risk score. In this series, a culprit plaque event occurred in 13 of 376 (3.5%) high-risk plaques (plaques with ≥2 risk predictors) versus 11 of 1,866 (0.6%) in non–high-risk plaques ($P < .0001$), at 12 of 343 (3.5%) stenotic sites (≥50%) versus 12 of 1,899 (0.6%) nonstenotic sites ($P < .0001$), and in 7 of 131 (5.3%) high-risk plaques with stenosis ($P < .0001$ versus all others) [48]. A systemic review and meta-analysis composed of 10 studies, including 5,012 asymptomatic

participants with diabetes who underwent CCTA, found that presence of obstructive CAD on CCTA (versus nonobstructive or no CAD) was associated with a significantly elevated risk of adverse events (summary HR, 4.07; 95% CI, 2.30–7.21). Beller et al [49] observed estimated HR for nonobstructive plaque (versus no CAD) was 2.17 (95% CI, 1.11–4.25). The pooled HRs per unit for segment stenosis score and segment involvement score were 1.44 (95% CI, 0.98–2.12) and 1.73 (95% CI, 1.07–2.80) respectively. The authors concluded that the presence and extent of CAD on CCTA were strong, independent predictors of cardiovascular events in asymptomatic individuals with diabetes.

Variant 3: Asymptomatic patient. High risk for coronary artery disease. Initial imaging. C. US Echocardiography Transthoracic Resting

There is no relevant literature supporting the use of resting TTE in asymptomatic patients at high risk of CAD.

Variant 3: Asymptomatic patient. High risk for coronary artery disease. Initial imaging. D. US Echocardiography Transthoracic Stress

TTE performed at rest and stress can assess for inducible wall-motion abnormalities, thus revealing ischemic heart disease. The sensitivity and specificity of the test is 72% to 83% and 84% to 95%, respectively, and has been validated only in symptomatic elevated risk populations and is best utilized to identify obstructive major epicardial coronary stenosis [20]. There is no relevant literature to support the use of stress TTE in asymptomatic patients at high risk of CAD.

Variant 3: Asymptomatic patient. High risk for coronary artery disease. Initial imaging. E. MRA Coronary Arteries

MRA of the coronary arteries can assess for arterial patency and pathologic wall thickening but not calcific burden, and it cannot reliably assess small, distal vessels [35,36]. There is no relevant literature to support the use of MRA of the coronary arteries in asymptomatic patients at high risk of CAD.

Variant 3: Asymptomatic patient. High risk for coronary artery disease. Initial imaging. F. MRI Heart Function with Stress

There is no relevant literature supporting the use of MRI heart function with stress in asymptomatic patients at high risk of CAD.

Variant 3: Asymptomatic patient. High risk for coronary artery disease. Initial imaging. G. MRI Heart Function and Morphology

Cardiac MRI can assess resting left ventricular function and potential ischemic scar burden. There is no relevant literature supporting the use of cardiac MRI as a screening test in asymptomatic patients at high risk of CAD.

Variant 3: Asymptomatic patient. High risk for coronary artery disease. Initial imaging. H. Radiography Chest

There is no relevant literature supporting the use of chest radiographs over other modalities as a screening test in asymptomatic patients at high risk of CAD.

Variant 3: Asymptomatic patient. High risk for coronary artery disease. Initial imaging. I. SPECT/CT MPI Rest and Stress

Stress SPECT MPI is the most commonly used stress-imaging technique for patients with suspected or known CAD but has been primarily validated in symptomatic patients. Stress SPECT pooled

sensitivity and specificity for detection of obstructive CAD (≥50% diameter stenosis) was 74% and 79%, respectively, as validated chiefly in symptomatic patients [50]. Young et al [51], in their study Detection of Ischemia in Asymptomatic Diabetics (DIAD), a randomized controlled trial, enrolled and randomized 1,123 asymptomatic participants with type 2 diabetes to either an adenosine-stress radionuclide MPI or no screening imaging, showed the positive predictive value of having moderate or large MPI defects was only 12% with 7 nonfatal myocardial ischemia's and 8 cardiac deaths (2.7%) in the screened MPI group and 10 nonfatal myocardial ischemia's and 7 cardiac deaths (3.0%) among the not-screened group (HR, 0.88; 95% CI, 0.44–1.88; *P* = .73). Overall, cardiac event rates were not significantly reduced by MPI screening for myocardial ischemia over 4.8 years. In a prospective multicenter BARDOT trial, 22% of asymptomatic high-risk patients with diabetes had abnormal SPECT, but those with abnormal SPECT randomized to medical versus invasive-medical strategies had similar event rates (*P* = .215) [52]. For a selected subgroup of asymptomatic patients with diabetes, data suggest routine use of SPECT as a screening test is likely to have a lower yield as well as limited effect on clinical outcomes [53]. However, the most recent ACC/AHA/ASNC Appropriate Use Criteria for SPECT MPI states SPECT would be useful when the calcium score is >400 or 100 to 400 if the patient is at high risk of CAD [38].

Summary of Recommendations

- **Variant 1**: Imaging is usually not appropriate for the initial evaluation of an asymptomatic patient with low risk of coronary artery disease.
- **Variant 2**: CT coronary calcium is usually appropriate for the initial imaging of an asymptomatic patient with intermediate risk of coronary artery disease.
- **Variant 3**: CT coronary calcium or CTA coronary arteries with IV contrast may be appropriate for the initial imaging of an asymptomatic patient with high risk of coronary artery disease.

Supporting Documents

The evidence table, literature search, and appendix for this topic are available at https://acsearch.acr.org/list. The appendix includes the strength of evidence assessment and the final rating round tabulations for each recommendation.

For additional information on the Appropriateness Criteria methodology and other supporting documents, please go to the ACR website at https://www.acr.org/Clinical-Resources/Clinical-Tools-and-Reference/Appropriateness-Criteria.

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 [54].

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."		

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Disclaimer

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.

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