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Noninvasive Assessment of Coronary Artery Disease

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KEYWORDS

• Coronary artery disease • Exercise treadmill testing
• Cardiac single-photon emission computed tomography
• Cardiac positron emission tomography • Stress echocardiography
• Myocardial perfusion imaging • Cardiac computed tomography
• Cardiac magnetic resonance imaging

HOSPITAL MEDICINE CLINICS CHECKLIST

1. Multiple noninvasive stress-testing and imaging modalities are available for the assessment of coronary artery disease in both symptomatic and asymptomatic individuals, with the most common forms involving exercise tolerance testing or pharmacologic stress with either echocardiographic or nuclear perfusion imaging.
2. Exercise testing is ideal and should always be considered first in the setting of risk stratification for low-risk to intermediate-risk chest pain for those with normal electrocardiogram (ECG) findings, with pharmacologic stress being reserved for patients who cannot exercise or have uninterpretable ECG findings.
3. The major types of pharmacologic stressor agents include dobutamine, adenosine, dipyridamole, and regadenoson.
4. Exercise duration and functional capacity are a powerful prognostic indicator of survival and future cardiac events.

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Conflicts of Interest: The authors have no conflicts of interests to disclose.
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5. The strengths of nuclear myocardial perfusion imaging, cardiac positron emission tomography (PET), and cardiac magnetic resonance (CMR) imaging are the ability to provide functional data on myocardial blood flow and to evaluate for stress-induced ischemia and infarction in areas of significant coronary artery disease.
6. Cardiac PET and CMR imaging can also provide information on viability in dysfunctional myocardium, which may initially appear as infarcted tissue on either standard myocardial perfusion or echocardiographic imaging.
7. The strengths of stress echocardiography are the ability to assess for stress-induced ischemia with inducible wall motion abnormalities or areas of infarction, and to assess the effects of exercise/dobutamine on valvular function, transvalvular gradients, and pulmonary artery pressures.
8. Cardiac computed tomographic angiography (CCTA) can provide coronary anatomic data with a superior negative predictive value to conventional stress testing to exclude significant coronary artery disease in symptomatic patients.
9. For primary prevention purposes, coronary artery calcium scoring can provide long-term prognostic data on cardiac events in selected asymptomatic patients with an intermediate Framingham Risk Score of 10% to 20% of a 10-year risk of a cardiac event.
10. Radiation exposure occurs with myocardial perfusion testing, cardiac PET, and CCTA testing, and does not occur with echocardiography or CMR imaging.

1. What are the benefits of exercise tolerance testing compared with pharmacologic stress?

An exercise tolerance test (ETT) is a cardiovascular examination using either a treadmill or bicycle exercise with serial electrocardiography (ECG) and blood pressure monitoring. It was first developed in the late 1920s and subsequently validated in numerous studies as a way to assess for inducible coronary ischemia. Most widely used in the United States is the treadmill exercise stress test, which incorporates incremental increases in speed and incline of the treadmill settings to evaluate for functional capacity, symptoms with stress, and ECG changes, which may indicate underlying inducible coronary ischemia. The value of the evaluation of the natural state of human physical stress in detection of underlying coronary artery ischemia cannot be understated.[1]

Many advances in modern medicine have created pharmacologic agents that can simulate the body to behave as if under maximal physical stress or by inducing maximal coronary artery hyperemia through coronary vasodilation; however, they do not replace the physiologic data derived from exercise testing that provide an abundance of physiologic information of clinical importance in overall assessment of the patient. In addition to ischemia assessment, the ETT provides data on the patient's functional capacity, which has been shown to be a significant prognostic indicator of future events. The Duke treadmill score is widely used to predict long term outcomes based on exercise time, ST segment deviation, and the degree of angina during the ETT.[2,3] Blood pressure trends and correlation with exercise can also be monitored during ETT (**Fig. 1**). ETT testing can provoke symptoms or arrhythmia with exercise to suggest underlying coronary ischemia.

2. Which patients should be referred for a pharmacologic stress test as opposed to ETT?

- Inability to exercise (eg., musculoskeletal/joint pain, frailty)
- Inability to achieve an appropriate peak heart rate response during exercise (sinus node dysfunction, chronotropic incompetence, deconditioning)
- Marked ST-T abnormalities on resting ECG
- ECG changes secondary to digoxin
- Left bundle branch block (LBBB)
- Paced rhythm

3. What types of exercise protocols are commonly used? What do they consist of?

The Bruce protocol is the most widely used treadmill exercise test. It consists of 2 changing variables: speed and angle of incline. The test starts at a low speed (2.73 km/h [1.7 miles/h]) and a 10% incline, and every 3 minutes the speed and angle of incline are increased (**Fig. 2**, **Table 1**). The maximum time of the test is 27 minutes, which is usually reached only by well-conditioned individuals. The duration of exercise correlates to functional capacity or oxygen uptake during exercise, which is measured in metabolic equivalents (METs): 1 MET = 3.5 mL O_2/kg/min.

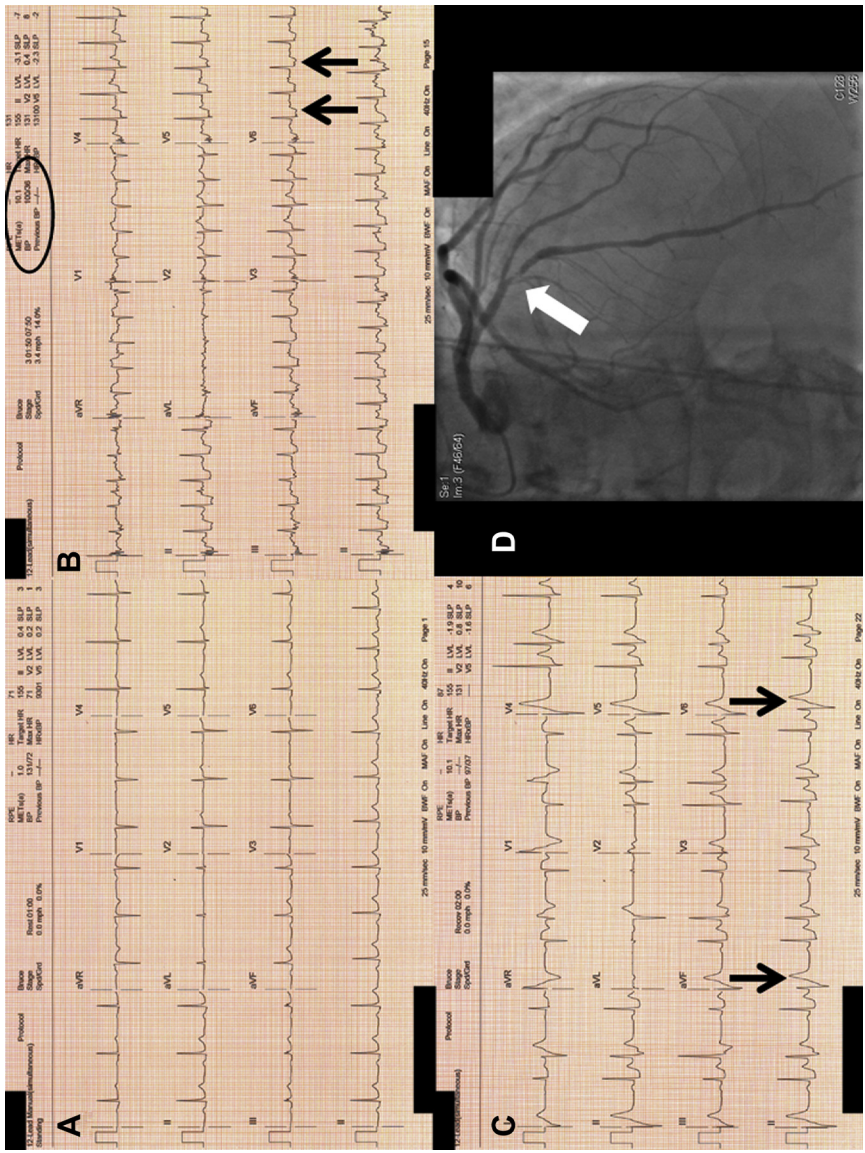
A modified form of the Bruce protocol is available, which has lower speeds and slower increases in incline, which may allow an appropriate heart rate response (see below for further details) to be achieved by less physically capable patients, who may not be able to tolerate the rapid and strenuous standard Bruce protocol.

Other protocols exist, but are used less frequently: the Balke protocol (which starts at 0% slope and 4.82 to 5.31 km/h [3 to 3.3 miles/h] depending on gender, with slower increases in incline and speed), and Naughton (which starts at 0% slope and 1.61 km/h [1 miles/h], with slower increases of both variables at 2-minute intervals).[4]

4. When should an imaging component be added to exercise testing? Which imaging modality should be selected?

Exercise stress testing should be conducted when the patient is clinically gauged to have the ability to exercise to a level that produces meaningful results ($\geq$85% of the patient's predicted maximal heart rate without symptoms/ECG changes or a double product [peak systolic blood pressure and heart rate] $\geq$20,000). This allows for evaluation of functional capacity, the effect of stress on hemodynamic parameters, and the evaluation of stress-induced symptoms. However, standard exercise testing does not localize the area or the size of tissue at risk. Therefore, imaging should be added to patients with previous revascularization. Furthermore, baseline ECG abnormalities can interfere with accurate interpretation of a treadmill test. Thus, patients with preexcitation (Wolff-Parkinson-White syndrome) or more than 1 mm ST depression at rest who can exercise are recommended to undergo exercise imaging stress testing for diagnosis. Patients with a LBBB pattern or right ventricular pacing should not undergo exercise stress testing alone because the results on ECG can be uninterpretable, unless the goal of ETT testing is to assess functional capacity. Patients with a LBBB pattern on ECG should undergo pharmacologic stress testing as exercise stress testing can potentially show septal perfusion abnormalities that are nonspecific for obstructive coronary artery disease.[5,6]

According to the 2007 American College of Cardiology (ACC)/American Heart Association (AHA) Task Force on Chronic Stable Angina recommendations, the choice of imaging modality should be based on local expertise and availability. Traditional


A
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imaging modalities include radionuclide myocardial perfusion imaging (rMPI) and stress echocardiography. Both types of imaging modalities may be completed with either exercise or a pharmacologic stressor. rMPI can be further subdivided into planar myocardial perfusion imaging, single-photon emission computed tomography (SPECT) and positron emission tomography (PET) imaging. Planar imaging is rarely used because it provides a two-dimensional image. On the other hand, SPECT provides three-dimensional images via 180° acquisition with computer processing of the acquired data and is considered state-of-the art in myocardial perfusion imaging.[7]

Stress echocardiography can be completed with exercise or with pharmacologic stressors. Rest images should be obtained before institution of exercise/stress. Stress images are obtained immediately after exercise. Care must be taken to image the patient immediately because stress-induced wall motion abnormalities may quickly resolve on completion of exercise. Furthermore, the images must be obtained in the supine position; therefore, the patient must be able to quickly maneuver from the treadmill on to the examination table. In both exercise and pharmacologic stress echocardiography, ischemia/infarction is predicted by fixed wall motion abnormalities and new or worsening wall abnormalities, as well as stress-induced changes in left ventricle (LV) shape, cavity size, and global contractility (**Fig. 3**).[8]

SPECT involves the visualization of myocardial perfusion via the introduction of a specifically tagged radiopharmaceutical, typically thallium-201 (Tl-201), technetium 99m-tetrofosmin (Myoview, GE Healthcare, Waukesha, WI), or technetium 99m-sestamibi (Cardiolite, Lantheus Medical Imaging, North Bellerica, MA). These radiopharmaceuticals are taken up by the myocardium in proportion to the amount of coronary blood flow (**Figs. 4** and **5**).

Tl-201 is a potassium analogue with a 73-hour half-life, which limits the amount that can be administered to the patient, thereby decreasing image quality. It quickly redistributes and is renally cleared. Myoview and Cardiolite are similar in their pharmacodynamics. Their half-life is approximately 6 hours, which allows for larger doses and thereby better image quality. They are both cleared through the hepatobiliary system.

PET involves the visualization of myocardial perfusion as well as metabolic activity via the introduction of tagged tracer. Rubidium 82 chloride and nitrogen 13 ammonia are tracers, which are used to document coronary blood flow. The addition of fluorine 18–labeled deoxyglucose allows for assessment of not only perfusion but also metabolic activity. Correction for attenuation artifact is performed, thus reducing the amount of artifacts that can be seen with SPECT (**Figs. 6** and **7**). Furthermore, PET images can be acquired more rapidly, have better spatial resolution, and require a lower radiation dose. However, access to PET scanning is limited because of cost and availability of the scanner at most institutions.[9,10]

Fig. 1. An abnormal exercise treadmill test. A 65-year-old man with a family history of premature coronary artery disease and recent onset of chest pain was referred for exercise echocardiography testing. (*A*) ECG at rest showing normal sinus rhythm with no ST-T segment abnormalities or axis deviation. (*B*) ECG at peak exercise, which shows 2.5-mm to 3-mm flat ST segment depression seen in the inferolateral leads (*arrows*) along with symptoms of chest pain and hypotension (*circle*). (*C*) ECG in recovery, showing atrial and ventricular bigeminy (*arrows*) caused by an atypical right bundle branch block pattern seen with the wider complexes. Features of ST depressions, symptoms, hypotension, and postrecovery ventricular ectopy are concerning for high-risk, poor prognostic features. (*D*) Coronary angiography, showing 95% stenosis of the midleft anterior descending artery (*arrow*).

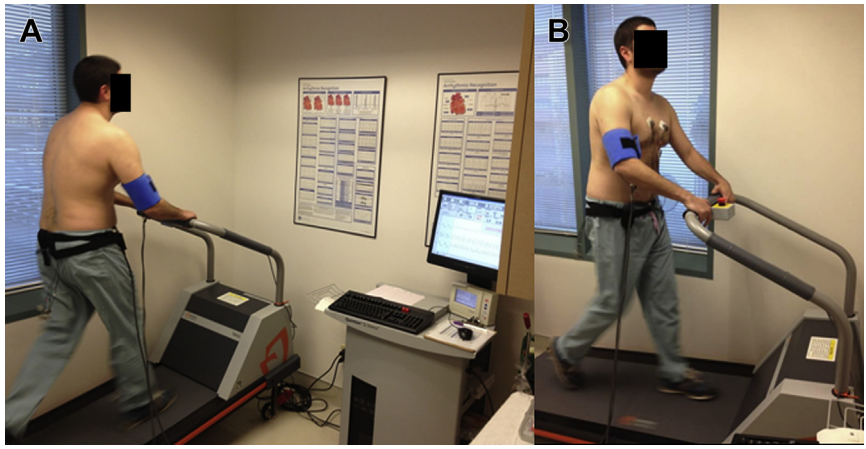

Fig. 2. Exercise treadmill testing with Quinton Q stress treadmill system (Cardiac Science, Waukesha, WI). (*A*) General setup of a treadmill machine connected to continuous blood pressure and 12-lead ECG monitoring with continuous printouts of rhythm strips. The speed and the incline of the treadmill can be programmed to increase per protocol. (*B*) Patient hooked up with ECG and blood pressure monitoring.

5. What are the potential benefits of echocardiographic imaging over rMPI?

In addition to data on myocardial ischemia, stress echocardiography can show evidence of pulmonary hypertension, abnormal ventricular relaxation, pericardial abnormalities, and valvular disease. Stress echocardiography is also particularly useful in evaluating for symptoms related to valve disease, such as mitral regurgitation, mitral stenosis, or pulmonary hypertension, which may be moderate in severity but may be exacerbated with exercise. In addition, there is no radiation exposure to the patient.[8]

6. When should pharmacologic stress testing be used?

Exercise testing provides a greater physiologic stressor than can be produced with pharmacologic testing, and more relevant clinical information. Exercise capacity alone is a strong prognostic indicator of cardiac mortality in both healthy individuals and in those with cardiovascular disease. Patients with a lower exercise capacity have a higher risk of death. Peak exercise capacity achieved is a stronger predictor of increased mortality than other well-established risk factors.[2] Furthermore, maximal

Table 1
Bruce exercise treadmill protocol showing the exercise duration, incline grade, miles per hour, and metabolic equivalent of each stage

Stage	Min	% Grade	MPH (km/h)	METs
1	3	10	1.7 (2.7)	4
2	6	12	2.5 (4.0)	6.6
3	9	14	3.4 (5.5)	9.1
4	12	16	4.2 (6.8)	12.9
5	15	18	5.0 (8.0)	15.0
6	18	20	5.5 (8.9)	16.9
7	21	22	6.0 (9.7)	19.1

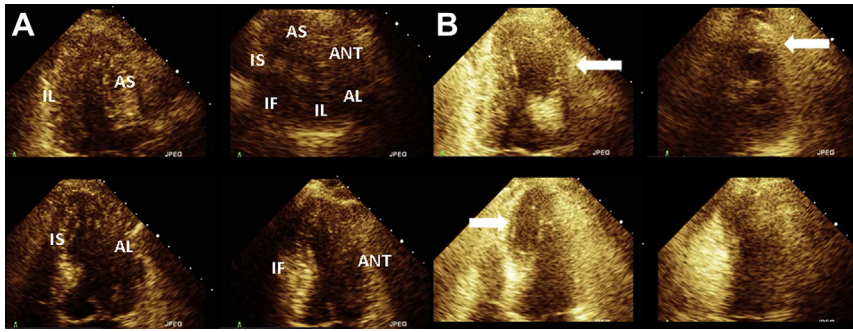

Fig. 3. Echocardiographic portion of **Fig. 1**. Simultaneous 4-view presentation showing all wall segments, including 3-chamber apical (*upper left*), parasternal short axis view (*upper right*), 4-chamber apical view (*lower left*), and 2-chamber apical view (*lower right*). (*A*) Wall segments at rest before exercise. There are no wall motion abnormalities at rest, with an ejection fraction of 60% to 65%. (*B*) Wall segments seen at peak exercise. The anterior and midseptum to distal septum (*arrows*) become severely hypokinetic, suggestive of exercise-induced ischemia in the left anterior descending artery. This finding correlates with the angiogram seen in **Fig. 1**D. AL, anterolateral; ANT, anterior; AS, anteroseptal; IL, inferolateral; INF, inferior; IS, inferoseptal.

heart rate seems to affect both the sensitivity and the specificity of exercise testing.[11] Therefore, pharmacologic agents should be used only in patients who cannot exercise or in whom exercise stress testing is contraindicated.

7. What are the pharmacologic agents used in stress testing?

There are 2 main categories of pharmacologic stress agents: vasodilators and inotropes/chronotropes.

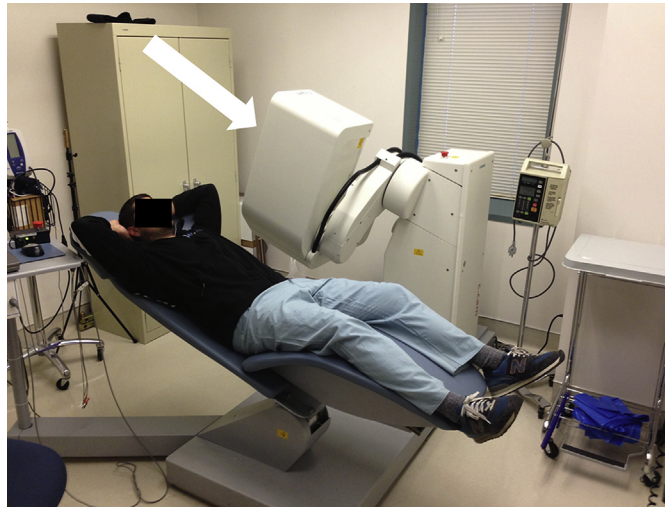

Fig. 4. Image acquisition for SPECT, showing a Siemens c.cam (Siemens Medical Solutions, Malvern, PA), with its γ camera (*arrow*) for image acquisition of γ radiation-emitting radioisotopes, which can be used in office settings because of its compact size.

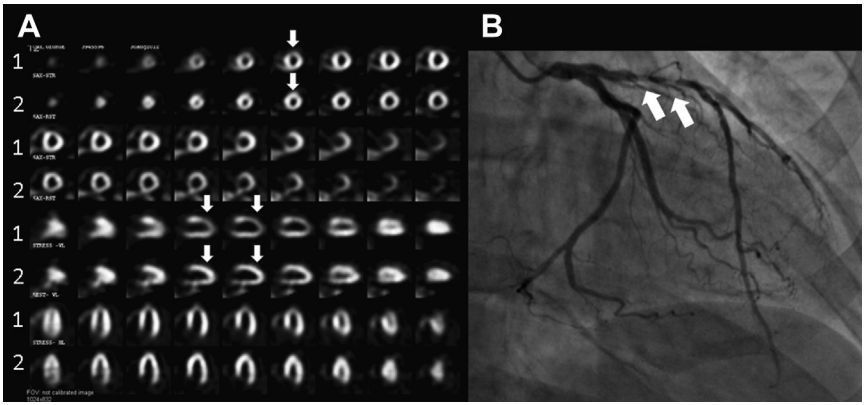

Fig. 5. Exercise myocardial perfusion SPECT and corresponding invasive coronary angiogram in a 64-year-old man with a history of prehypertension and hyperlipidemia with a history of exertional chest discomfort. During the exercise stress treadmill portion, the patient had chest pain at 108 beats per minute (69% maximum predicted heart rate) with up to 3.5-mm ST depressions in his inferolateral leads. Pharmacologic stress with regadenoson was then administered, given his inability to reach his target heart rate. (*A*) Myocardial perfusion imaging with various projections of the LV. Images obtained during stress (*row 1*) and their corresponding resting images (*row 2*) are shown. During stress, decreased tracer uptake is noted in the anterior and apical wall (*arrows*), which completely reverse at rest, which is consistent with stress-induced ischemia in the left anterior descending artery territory. The LV was also noted to be dilated. (*B*) Coronary angiogram showing 2 sequential calcified high-grade lesions in the midportion of the left anterior descending artery (*arrows*).

Vasodilators include adenosine, dipyridamole (Persantine), and regadenoson (Lexiscan). They primarily function via the A2A receptors, producing coronary vasodilatation and hyperemia. In areas of stenosis, coronary blood flow is already augmented via compensatory mechanisms; therefore, tracer uptake in stenotic areas after induction of hyperemia are lower than nonstenotic areas. Vasodilators are typically used in

Fig. 6. A cardiac PET scanner (Siemens Biograph PET-CT scanner [Siemens Medical Solutions, Malvern, PA]).

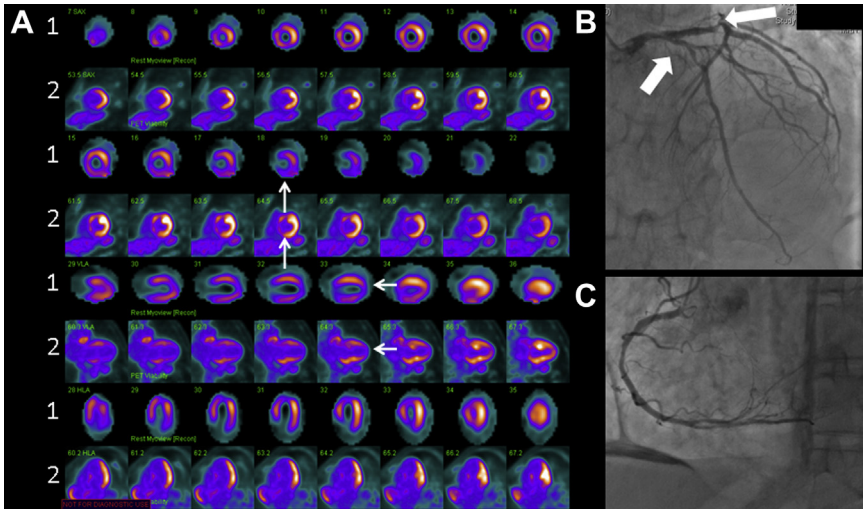

Fig. 7. Correlation of SPECT and PET with coronary angiography. Images are obtained from the diagnostic workup of a 91-year-old man with new-onset congestive heart failure and an ejection fraction of 30%. (*A*) Comparison of rest SPECT images (*row 1*) and PET images (*row 2*) with evidence of [^{18}F]fluoro-2-deoxyglucose uptake seen in the inferior wall (*vertical arrow*) on PET, which was shown as a perfusion defect on SPECT imaging (likely because of attenuation artifact). There is also an apical defect seen both on SPECT and PET that is fixed, likely representing an apical infarct without viability (*horizontal arrows*). (*B*) Coronary angiography of the left coronary artery system, showing significant stenoses of the midleft anterior descending artery and midleft circumflex artery (*arrows*), but evidence of viability within the inferior and lateral walls and most of the anterior wall. (*C*) Coronary angiography of the right coronary artery, which shows diffuse intermediate appearing lesions.

conjunction with rMPI. Specifically, they may be more effective in patients who require β-blocker therapy, as β-blockers can attenuate the effects of dobutamine.[12]

Dobutamine is the only ionotrope/chronotrope used as a stress agent. It functions primarily by stimulating β_1 receptors which increases myocardial contractility, heart rate, and cardiac output, resulting in increased oxygen demand and secondary coronary vasodilation. Atropine is used when heart rate response to maximum dose dobutamine is inadequate to evaluate for an ischemic response.[13] Dobutamine as a stress agent is typically used in patients undergoing stress echocardiography. However, patients who have had recent theophylline intake, caffeine intake, or have reactive airway disease and are likely to have suboptimal echocardiographic windows (such as those with high body mass index) can undergo dobutamine rMPI.[10,12,14]

8. How do the pharmacologic agents compare?

Table 2 presents a comparison of the pharmacologic agents.

9. What is the pooled sensitivity and specificity of exercise ECG, rMPI, and ECG stress testing?

In a meta-analysis looking at the accuracy of noninvasive tests in assessing for coronary artery disease (CAD), which was conducted independent of type of stressor, PET had the highest sensitivity, whereas echocardiography had the highest specificity. In

Table 2
Comparison of pharmacologic stress agents and exercise

Stressor	Mechanism of Action	Mechanism of Stress	Hemodynamic Effects	Indications	Contraindications	Limitations	Combined with Exercise?	Side Effects	Indications for Early Termination/ Reversal	Reversal Agent
Exercise	Physiologic response to exercise, which results in increased heart rate, stroke volume, and cardiac output	Vagal withdrawal and sympathetic stimulation	Increase heart rate, and myocardial contractility Peripheral vasocon-striction, with coronary vasodi-latation Gradual increase in SBP, with stable or decrease in DBP	The preferred and first-line test for stress in a patient who is able to exercise, and does not have a contraindi-cation	LBBB Baseline ST depression Ventricular preexcitation Chronotropic incompetence	Potential for artifact limiting interpretation while exercising Potential for false-positive result, especially in female patients	N/A	Fatigue Shortness of breath Risk of fall and injury with exercise	Drop in SBP greater than 10 mm Hg from baseline Moderate-severe angina Sustained VT ST increase >1 mm	None
Adenosine	Activation of adenosine receptors	Hyperemia in normal vessels with an attenuated response in stenotic vessels	Increased heart rate Decreased DBP and SBP	Inability to perform adequate exercise LBBB Ventricular preexcitation	Absolute Asthmatics with ongoing wheezing Second-degree and third-degree AV block without a pacemaker SBP <90 Recent dipyridamole use, sensitivity Unstable ACS Relative Sinus bradycardia <40 bpm	Anti-ischemics lead to a decreased diagnostic accuracy and it is recommended that they be discontinued for 48 h before testing Hold methylxanthines for 12 h before study Hold dipyridamole for 48 h before study	Yes, noted to have decreased SE and improved image quality except for those patients with LBBB	Major AV block 7.6% MI is extremely rare Minor Flushing 35%–40% Chest pain 25%–30% Dyspnea 20%	SBP <80 Symptomatic second-degree HB Wheezing Severe chest Pain with ST depression >2 mm Signs of poor perfusion problem Patient request	Amiophylline, rarely used because of short half-life

Dipyridamole	Prevents intracellular reuptake and deamination leading to increased tissue levels	Similar to adenosine	Similar to adenosine	Similar to adenosine	Similar to adenosine	Similar to adenosine	Similar to adenosine	Major AV block 2% Minor Flushing Chest pain	Similar to adenosine	Amiophylline, often required because of prolonged half-life compared with adenosine
Regadenoson	Activation of adenosine A_2 receptors	Similar to adenosine	Similar to adenosine	Similar to adenosine	Absolute Bronchospasm, although current studies suggest a better safety profile in reactive airway disease Otherwise, similar to adenosine	Similar to adenosine	Similar to adenosine	Common Shortness of breath Headache Flushing Rare Chest discomfort Angina Dizziness Nausea Heart block significantly less common than in adenosine	Similar to adenosine	Amiophylline
Dobutamine	Activation of B_1 and B_2 receptors	Dose-related increase in heart rate, blood pressure, contractility, and increases in regional blood flow	Increases in heart rate and blood pressure	Recommended only in patients who have contra-indications to pharma-cologic stressors, primarily reactive airway disease	Absolute MI within 1 wk Unstable angina Significant LVOT Severe AS Atrial tachyarrhythmias with uncontrolled ventricular response History of VT Uncontrolled hypertension Aortic dissection or large aneurysm	Given the mechanism of stress is similar to exercise, achieving >85% of predicted heart rate is desirable Atropine can be added to augment heart rate response	No	Major Ischemic ST depression 33% Significant arrhythmia 8%–10% Minor Palpitations 29% Chest Pain 31% Headache 14% Dyspnea 14%	Similar to exercise Termination for ventricular arrhythmias and ST segment depression is more common than with other stressors	β-Blockers

Abbreviations: ACS, acute coronary syndrome; AS, aortic stenosis; AV, atrioventricular node; bpm, beats per minute; DBP, diastolic blood pressure; HB, heart block; LVOT, left ventricular outflow tract; MI, myocardial infarction; N/A, not applicable; SBP, systolic blood pressure; VT, ventricular tachycardia.

Data from Refs.[10,13–19]

these studies, the prevalence of CAD ranged from 64% to 70%. Exercise testing had both lower specificity and sensitivity compared with other stress imaging modalities; however, its ability to document that workload at which ischemia occurs, exercise capacity, hemodynamic response to exercise, and its prognostic value still make it the initial test of choice in patients who can achieve the required peak heart rate.[20] In comparing modalities, it is important to determine pretest probability of CA, because it can aid in determining which modality to choose. Tests with higher sensitivity minimize false-negative tests that exclude significant CAD reliably. Tests with higher specificity minimize false-positive results, but may lead to misdiagnoses and further testing of patients with such results. Therefore, these tests have the best positive and negative predictive value in a patient population with an intermediate pretest probability of CAD (**Table 3**).[23]

10. What are the sensitivities/specificities of each individual stress modality?

A meta-analysis of multiple stress modalities showed that the diagnostic performance was similar between the tests. However, stress SPECT and electron-beam computed tomography (EBCT) tended to be more sensitive, whereas dipyridamole echocardiography tended to be more specific. Because EBCT has a low specificity for significant CAD, it is not recommended as a testing modality because it may increase the number of patients referred for further unnecessary testing (**Table 4**).[24,25] However, it does have an indication for primary prevention screening in asymptomatic patients, which is further discussed later.

11. What are the evidence-based recommendations regarding stress testing choice for patients who can exercise?

According to the 2012 American College of Cardiology Foundation (ACCF)/AHA/American College of Physicians (ACP)/American Association for Thoracic Surgery (AATS)/Preventive Cardiovascular Nurses Association (PCNA)/Society for Cardiovascular Angiography and Interventions (SCAI)/Society of Thoracic Surgeons (STS) guideline for the diagnosis and management of patients with stable ischemic heart disease, standard exercise testing is recommended for patients with an intermediate pretest probability of ischemic heart disease who have an interpretable ECG, moderate physical functioning, and no disabling comorbidity; whereas in those with an uninterpretable ECG, exercise stress with imaging is recommended (class I). For patients with low pretest probability who require testing, standard exercise ECG testing is reasonable. For patients with an intermediate or high pretest probability of ischemic heart disease with an interpretable ECG, exercise or pharmacologic stress rMPI or echocardiography is reasonable. For patients with an intermediate or high pretest probability of ischemic heart disease with an uninterpretable ECG, pharmacologic stress cardiac magnetic resonance imaging (CMRI) is reasonable (class IIa).[26]

12. What are the evidence-based recommendations regarding stress testing choice for patients who are incapable of moderate physical function or have disabling comorbidity?

According to the 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease, pharmacologic stress with either rMPI or echocardiography is recommended for patients with intermediate to high pretest probability for ischemic heart disease (class I). For patients

Table 3
Sensitivity and specificity of noninvasive tests for the detection of CAD

Diagnostic Test	Sensitivity (Range)	Specificity (Range)	Studies	Patients	Patients with Coronary Disease	Sensitivity for Left Main or Three-Vessel Disease	Studies	Patients
			n		%		*n*	
Planar thallium imaging	0.79 (0.70–0.94)	0.73 (0.43–0.97)	6	510	66	0.93	2	72
SPECT	0.88 (0.73–0.98)	0.77 (0.53–0.96)	8	628	70	0.98	3	92
Echocardiography	0.76 (0.40–1.00)	0.88 (0.80–0.95)	10	1174	64	0.94	4	115
PET	0.91 (0.69–1.00)	0.82 (0.73–0.88)	3	206	68	Not available		
Exercise ECG	0.68	0.77	132	24,074	66	0.86	48	

Data from Garber AM, Solomon NA. Cost-effectiveness of alternative test strategies for the diagnosis of coronary artery disease. Ann Intern Med 1999;130:719–28.

Table 4
Pooled sensitivity, specificity, and log of the diagnostic odds ratio and corresponding 95% confidence intervals per type of stress testing modality using a random effects meta-analysis

Test	No. of Studies	Sensitivity % (95% CI)	Specificity % (95% CI)	lnDOR (95% CI)
Exercise echo	55	82.7 (80.2–85.2)	84.0 (80.4–87.6)[a]	3.0 (2.7–3.3)
Adenosine echo	11	79.2 (72.1–86.3)	91.5 (87.3–95.7)	3.0 (2.5–3.5)
Dipyridamole echo	58	71.9 (68.6–75.2)	94.6 (92.9–96.3)[a]	3.0 (2.8–3.2)
Dobutamine echo	102	81.0 (79.1–82.9)	84.1 (82.0–86.1)[a]	2.9 (2.7–3.0)
Combined echo	226	79.1 (77.6–80.5)	87.1 (85.7–88.5)[a]	2.9 (2.8–3.0)
Exercise SPECT	48	88.1 (85.8–90.3)[b]	68.8 (62.8–74.8)	2.7 (2.6–3.0)
Adenosine SPECT	14	90.5 (89.0–91.9)[c]	81.0 (73.5–88.6)	3.4 (3.0–3.8)[d]
Dipyridamole SPECT	23	90.4 (87.3–93.5)[c]	75.4 (66.2–84.6)	2.7 (2.3–3.1)
Dobutamine SPECT	16	83.6 (78.4–88.8)	75.1 (71.1–79.0)	2.5 (2.1–2.9)
Combined SPECT	103	88.1 (86.6–89.6)[c]	73.0 (69.1–76.9)	2.8 (2.6–3.0)
EBCT	21	93.1 (90.7–95.6)[c]	54.5 (45.3–63.8)[c]	2.6 (2.2–3.0)

Abbreviations: CI, confidence interval; lnDOR, natural logarithm of the diagnostic odds ratio.
[a] Nonoverlapping CIs, indicating a statistically higher specificity than the corresponding SPECT test.
[b] Nonoverlapping CIs, indicating a statistically higher sensitivity than the corresponding echocardiography test.
[c] Nonoverlapping CIs, indicating a statistically higher sensitivity than all other tests, except for adenosine and dipyridamole SPECT and a statistically lower specificity than all other tests except for exercise SPECT.
[d] Nonoverlapping CIs, indicating a statistically higher lnDOR than exercise and dobutamine SPECT and EBCT.
Data from Heijenbrok-Kal MH, Fleischmann KE, Hunink MG. Stress echocardiography, stress single-photon-emission computed tomography and electron beam computed tomography for the assessment of coronary artery disease: a meta-analysis of diagnostic performance. Am Heart J 2007;154:415–23.

with a low pretest probability of ischemic heart disease who require testing, pharmacologic stress echocardiography is reasonable. For patients with low to intermediate pretest probability, coronary computed tomographic angiography (CCTA) is acceptable. For patients with intermediate to high pretest probability, pharmacologic stress CMR imaging is reasonable (class IIa) (**Table 5**).[26]

13. How do the different stress modalities compare?

Table 6 presents a comparison of the different stress modalities.

14. What is the role for cardiac imaging in recognition of acute coronary syndrome in the setting of ongoing chest pain?

Acute coronary syndrome (ACS) has a varied presentation and is typically diagnosed by ECG findings and biomarker increases in concert with the characteristic clinical picture. However, patients can present atypically or data may be nondiagnostic, leading to erroneous discharge from the hospital. Previous studies have shown that 1% to 10% of patients with ACS are discharged home from the emergency room.[16,29] Rest myocardial imaging tests may be useful for evaluating patients with ongoing or recently resolved chest pain who have nondiagnostic or normal ECGs and negative

biomarkers.[29] According to the ACC/AHA/American Society of Nuclear Cardiology 2003 guidelines, rest rMPI has a class I recommendation to assess myocardial risk in patients with possible ACS who have nondiagnostic ECGs and negative cardiac biomarkers. Patients who have normal resting perfusion scans in this setting are considered to be low risk and may be discharged from the emergency department.[30] Multiple studies have shown that resting rMPI can accurately risk stratify patients who present with chest pain. The advantages of rest rMPI were confirmed by a large, prospective multicenter trial, which showed that with implementation there was a 10% absolute reduction of admissions for noncardiac chest pain.[30–33] Furthermore, multiple studies have shown that the negative predictive value of rest rMPI for ACS is 99% to 100%, which confirms that rest rMPI has the potential to safely reduce admissions for noncardiac chest pain.[34]

Because perfusion defects on rMPI do not distinguish between acute ischemia, acute infarction, or previous infarction, there are several limitations to the usage of rest rMPI for the evaluation of ACS. Rest rMPI is nondiagnostic in patients with a history of myocardial infarction, resolution of chest pain more than 3 hours before injection, and in cases in which a small area of the myocardium is affected.

15. What is the clinical usefulness of cardiac PET testing?

Cardiac PET imaging relies on positron-emitting radiopharmaceuticals (rubidium 82, nitrogen 13 ammonia, and oxygen 15 water) as myocardial perfusion tracers. [^{18}F]Fluorodeoxyglucose is used for metabolic assessment. PET imaging has superior imaging aspects to SPECT imaging, by providing higher temporal and spatial resolution, and has attenuation correction protocols in place, which can affect the accuracy of traditional SPECT testing. Oxygen-15 is not used in clinical practice and is used in the experimental setting. Absolute quantification of myocardial blood flow is assessed with cardiac PET and it is used to assess for stress-induced ischemia, and for viability in ischemic and dysfunctional myocardium (see **Fig. 7**).

16. What is the diagnostic accuracy of cardiac PET testing and when is it appropriate to perform it?

A large meta-analysis by Jaarsma and colleagues[27] evaluated 166 articles comparing the diagnostic accuracy of SPECT, CMR imaging, and PET for the diagnosis of obstructive CAD, showing a pooled sensitivity of 84% and specificity of 81% for PET, and a pooled sensitivity of 88% and specificity of 61% for SPECT. CMR imaging also had a pooled sensitivity of 89%, and specificity of 76%, and PET was believed to have an overall higher diagnostic accuracy than SPECT, including for women and obese patients.

As per the 2009 Appropriate Use Criteria for Cardiac Radionuclide Imaging, it is considered appropriate to perform PET stress testing in the following situations[35]:

For symptomatic patients:

- Patients with nonacute symptoms with a low pretest probability of CAD who either have an uninterpretable ECG or are unable to exercise
- Patients with nonacute symptoms with an intermediate probability of CAD who have an interpretable ECG and are able to exercise
- Patients with nonacute symptoms with an intermediate probability of CAD who have an uninterpretable ECG or are unable to exercise
- Patients with nonacute symptoms with a high pretest probability of CAD regardless of ECG interpretability and ability to exercise

Table 5
Stress testing and advanced imaging for initial diagnosis in patients with suspected stable ischemic heart disease who require noninvasive testing

	Exercise Status		ECG Interpretable		Pretest Probability of IHD				
Test	Able	Unable	Yes	No	Low	Intermediate	High	COR	LOE
Patients able to exercise[a]									
Exercise ECG	X		X			X		I	A
Exercise with nuclear MPI or Echo	X			X		X	X	I	B
Exercise ECG	X		X		X			IIa	C
Exercise with nuclear MPI or Echo	X		X			X	X	IIa	B
Pharmacologic stress CMR imaging	X			X		X	X	IIa	B
CCTA	X		Any			X		IIb	B
Exercise Echo	X		X			X		IIb	C
Pharmacologic stress with nuclear MPI, Echo, or CMR imaging	X		X			Any		III: No Benefit	C
Exercise stress with nuclear MPI	X		X		X			III: No Benefit	C
Patients unable to exercise									
Pharmacologic stress with nuclear MPI or Echo		X	Any			X	X	I	B

Pharmacologic stress Echo		X	Any		X				IIa	C
CCTA		X	Any		X	X			IIa	B
Pharmacologic stress CMR imaging		X	Any			X	X		IIa	B
Exercise ECG		X		X		Any			III: No Benefit	C
Other										
CCTA If patient has any of the following: 1. Continued symptoms with prior normal test, or 2. Inconclusive exercise or pharmacologic stress, or 3. Unable to undergo stress with MPI or Echo	Any		Any			X			IIa	C
CAC score	Any		Any		X				IIb	C

Abbreviations: CAC, coronary artery calcium; CCTA, cardiac computed tomography angiography; COR, class of recommendation; Echo, echocardiography; IHD, ischemic heart disease; LOE, level of evidence; MPI, myocardial perfusion imaging; N/A, not available.

[a] Patients are candidates for exercise testing if they are capable of performing at least moderate physical functioning (ie, moderate household, yard, or recreational work and most activities of daily living) and have no disabling comorbidity. Patients should be able to achieve 85% of age-predicted maximum heart rate.

From Fihn SD, Gardin JM, Abrams J, et al. 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology Foundation/American Heart Association Task Force on, American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. J Am Coll Cardiol 2012;60:2579; with permission.

Table 6
Comparison of different stress testing modalities

Test	Advantages	Disadvantages	Side Effects	Contraindications	Limitations	Radiation Exposure	Cost	Indications
Exercise treadmill	Widely available, and easy to perform and interpret. No IV line is needed	Patient must be able to exercise and have adequate chronotropic response to reach 85% target heart rate	Only what is expected from routine exercise, possible ischemic symptoms if underlying coronary artery disease is present, arrhythmias	Inability to exercise or significantly abnormal baseline ECG	Must achieve 85% predicted heart rate for diagnostic accuracy	None	$	Basic ischemia evaluation with the added benefit of functional and hemodynamic response to exercise is sought Normal/near-normal baseline ECG
Exercise SPECT	Higher sensitivity/specificity of the common stress modalities used Assessment of function status, wall motion, coronary perfusion, and viability	Attenuation caused by soft tissue leading to artifact Relative blood flow based on tracer uptake in the area May underestimate ischemic area in patients with left main disease Radiation	Same as above exercise stress tests	Inability to exercise. LBBB	Same as above exercise stress tests	High	$$$	Patients who are able to exercise, who may have abnormal baseline ECG, equivocal treadmill stress, or higher sensitivity/specificity is indicated
Exercise echocardiography	Assess functional status, BP response to exercise, wall motion, LVEF with exercise, and valvular function in response to routine exercise	Subjective image interpretation Can be nondiagnostic because of image quality-COPD, obesity Cannot assess functional capacity Labor intensive	Same as above exercise stress tests	Poor acoustic windows/large body habitus	Same as above exercise stress tests	None	$$	Patients who are able to exercise, who may have abnormal baseline ECG, equivocal treadmill stress, or higher sensitivity/specificity is indicated

Dobutamine echocardiography	Assesses multiple parameters: wall motion, LVEF, wall thickness, valvular function	Subjective image interpretation Can be nondiagnostic because of image quality-COPD, obesity Cannot assess functional capacity Labor intensive	Ventricular arrhythmias	Symptomatic aortic aneurysm Recent MI Hemodynamically significant LVOT obstruction Severe aortic stenosis (can be used in low-output aortic stenosis to differentiate between severe vs pseudosevere)	Must achieve 85% predicted heart rate for diagnostic accuracy	None	$$	Patients in whom adequate exercise cannot be achieved who have contraindications to vasodilatory agents
Vasodilatory SPECT	Safe Indicated in LBBB Computer-aided interpretation	Cannot assess functional capacity Attenuation because of soft tissue leading to artifact Relative blood flow based on tracer uptake in the area May underestimate severity of ischemia in patients with left main disease/ multivessel CAD Radiation	Heart block	Bronchospastic disease (although some evidence for use of regadenoson) Hypotension Severe bradycardia	Interaction with methylxanthines	High	$$$	Patients in whom adequate exercise cannot be achieved

(*continued on next page*)

Table 6
(*continued*)

Test	Advantages	Disadvantages	Side Effects	Contraindications	Limitations	Radiation Exposure	Cost	Indications
Vasodilatory PET	Absolute coronary blood flow quantification Myocardial function Myocardial metabolism High spatial resolution Decreased attenuation Shorter acquisition time Higher diagnostic accuracy and decreased radiation than SPECT Accurate attenuation correction Compare metabolic activity and flow	Not widely available Cannot assess functional capacity In patients with multivessel disease, metabolic images may be falsely negative Reimbursement limited for first-line usage Radiation	Similar to pharmacologic-mediated SPECT	Similar to pharmacologic-mediated SPECT	Similar to pharmacologic-mediated SPECT Cyclotron required onsite for perfusion tracers	Moderate	$$$$	Patients in whom adequate exercise cannot be achieved

Vasodilatory MRI	Identifies a higher proportion of patients with left main disease No radiation Superior temporal and spatial resolution Concurrent valvular evaluation and right ventricular/LV volumetric analysis Assess for viability	Expensive Long acquisition times Not widely available Limited accuracy in coronary anatomy evaluation, inferior to CCTA	Reaction to gadolinium Adverse effects can be experienced with pharmacologic stress agents (vasodilators, dobutamine)	Claustrophobia (relative) Advanced renal disease Medical devices/foreign bodies that are not safe for MRI	Foreign metallic bodies can cause artifact	None	$$$$	Patients presenting with chest pain with intermediate to high pretest probability of CAD who are incapable of at least moderate physical function or have disabling comorbidities
CCTA	High negative predictive value for negative studies Calcium scoring highly predictive of future cardiac events Coronary anatomy variants can also be assessed (ie, anomalous takeoff, myocardial bridging)	Radiation (in retrospective ECG gated studies) Moderate to heavy coronary calcium can cause overestimation of stenosis severity Poor correlation with functional significance of coronary stenoses	Iodinated contrast reaction Reactions to rate control agents (ie, β-blockers)	Contrast allergy (relative) Advanced renal disease (relative) Cardiac arrhythmias (relative)	Image quality can be degraded by increased heart rate and protocols Atrial arrhythmias can interfere with image acquisition Heavy coronary calcification can limit accuracy of estimated stenosis severity Foreign metallic bodies can cause artifact	Low (prospective ECG gating) to high (retrospective ECG gating)	$$$$	Patients presenting with chest pain with low to intermediate pretest probability of CAD who are unable to perform at least moderate physical functioning or have disabling comorbidity Patients with persistent symptoms with previous equivocal or normal stress testing

Vasodilatory = adenosine/dipyridamole/regadenoson.

Abbreviations: COPD, chronic obstructive pulmonary disease; IV, intravenous; LVEF, left ventricular ejection fraction; LVOT, left ventricular outflow tract.

Data from Refs.[9,10,12,14,16,26–28]

- Patients with acute chest pain concerning for ACS who have an ECG with no ischemic changes or with LBBB pattern or with an electronically ventricular paced rhythm, with negative or borderline, equivocal, or minimally increased troponin levels
- Rest imaging alone is considered appropriate for acute chest pain concerning for ACS with an initially negative troponin level, with an ECG showing no ischemic changes or with LBBB pattern or electronically ventricular paced rhythm with recent or ongoing chest pain

For asymptomatic patients:

- Asymptomatic but have high risk of coronary heart disease (CHD) (risk criteria of the Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults)
- Asymptomatic but have an Agatston coronary calcium score (CCS) between 100 and 400 with a high CHD risk
- Asymptomatic but have an Agatston CCS greater than 400

In the setting of preoperative cardiac risk assessment:

- Patients without active cardiac conditions with greater than or equal to 1 clinical risk factor presenting for noncardiac intermediate or high-risk surgery
- Patients without active cardiac conditions with poor or unknown functional capacity (<4 METs) presenting for noncardiac intermediate-risk or high-risk surgery

For other clinical indications (including previous testing):

- Patients who have increased troponin levels without additional evidence of ACS
- Patients who have had previous noninvasive evaluation with equivocal, borderline, or discordant results
- Patients who have had previous exercise treadmill testing with intermediate-risk or high-risk Duke treadmill scores

As per 2009 ACCF/AHA guidelines, in the preoperative setting before noncardiac surgery, noninvasive stress testing meets a class I indication for patients with active cardiac conditions in whom noncardiac surgery is planned and should be treated per ACC/AHA guidelines. It is a class IIa indication for patients with 3 or more clinical risk factors and poor functional capacity (<4 METs) who require vascular surgery, which is reasonable if it changes management. For intermediate-risk or vascular surgery, it is a class IIb indication for noninvasive stress testing to be considered in patients with at least 1 to 2 clinical risk factors and poor functional capacity (less than 4 METs) if it changes management.[36]

As per 2012 ACCF/AHA guidelines, the indications for cardiac PET in assessment of suspected CAD are the same as that of nuclear myocardial perfusion imaging (MPI).[26]

Although PET stress testing has the advantages of decreased radiation and higher diagnostic accuracy compared with traditional nuclear imaging, it is limited by the requirement of possessing a generator capable of producing radiopharmaceutical tracers for imaging, its high costs, and limited reimbursement.

17. What is the role for cardiac computed tomography?

The evolution of computed tomography (CT) technology has now made noninvasive imaging of the coronary arteries a feasible option with comparable results to the gold standard of invasive coronary angiography in selected patients. The use of multidetector CT (MDCT) systems (with most studies validating the accuracy of 64-channel

or slice systems) is directed at imaging during contrast enhancement of the coronary arteries with synchronization of the patient's cardiac cycle by ECG gating, CT imaging can accurately evaluate cardiac structures and the presence of CAD, with high spatial and temporal resolution with short acquisition times. There are 2 major applications of cardiac CT in evaluating for CAD: CCS assessment in primary prevention and MDCT assessment for chest pain.

18. What is the clinical usefulness in performing CCS testing and its prognostic significance?

CCS measurement is performed either by EBCT or by MDCT to evaluate for calcification (without contrast). Coronary artery calcification (CAC) occurs almost exclusively in atherosclerotic arteries and is absent in the normal vessel wall. CAC is seen frequently in older persons, as is advanced plaque. On CT, CAC is defined as a lesion above a threshold of 130 Hounsfield units with an area of 3 or more adjacent pixels of at least 1 mm^2. Typically, a score of 1 to 10 is considered minimal, 11 to 100 mild, 101 to 400 moderate, and more than 400 severe (**Fig. 8**). There is a positive but nonlinear correlation between the amount of CAC and the degree of coronary artery stenosis seen,[37] and there is no clear relationship between vulnerable and calcified plaque.[38] However, there are studies showing the valuable additional prognostic information that CCS provides along with traditional methods of cardiovascular risk assessment for 10-year risk of CHD events, such as Framingham risk assessment.

Although the downside to this testing modality is that noncalcified plaque is not seen, the cardiac event of a CCS of 0 in asymptomatic patients has been found in many studies to be associated with a low annual event rate. The St Francis Heart Study reported that a CCS of 0 was associated with a 0.12% annual event rate over 4.3 years,[39] and in MESA (Multi-Ethnic Study of Atherosclerosis), a CCS of 0 was associated with

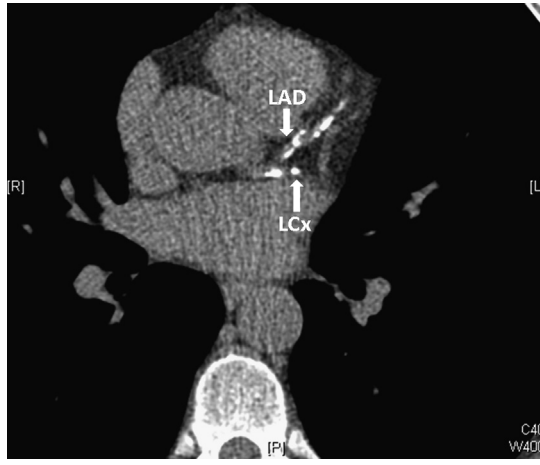

Fig. 8. CCS with cardiac CT in an asymptomatic 66-year-old man with a history of prehypertension and hyperlipidemia who had a Framingham risk score of 13% at 10 years (intermediate risk). CCS was performed for primary prevention screening. This axial view shows extensive calcium in the left anterior descending artery (LAD) and left circumflex artery (LCx). His total calcium score was 926.8, which as per the Multi-Ethnic Study of Atherosclerosis (MESA) database is at the 90th percentile for age, race, and gender (MESA calculator, http://www.mesa-nhlbi.org/Calcium/input.aspx).

an annual 0.11% event rate at 3.8 years. However, MESA reported that the presence of coronary calcium was associated with a higher coronary event rate, with a hazard ratio of 7.73 for a CAC score of 101 to 300, and 9.67 amongst people with a CAC score of more than 300 ($P<.001$).[40] Extremely high CAC scores of more than 1000 in a study of 98 asymptomatic patients resulted in a cardiac event (myocardial infarction or cardiac death) in 36% of the patients studied at 17 months.[41] CAC scoring has also been shown to be an independent predictor of risk after adjusting for all Framingham risk factors[42] and can also be used to more accurately risk stratify annual cardiac event rates in conjunction with traditional Framingham risk assessment.[39]

19. What is the indication to perform calcium score assessment?

As per 2010 ACCF/AHA guidelines, CCS screening holds a class IIa indication for cardiovascular risk assessment for primary prevention in asymptomatic adults at intermediate risk (10%–20% 10-year risk), and a class IIb indication for persons at low to intermediate risk (6%–10% 10-year risk). Persons at low risk (<6% 10-year risk) have a class III indication for CAC measurement.[43] As per 2010 ACCF/Society of Cardiovascular Computed Tomography/American College of Radiology/AHA appropriate use criteria guidelines, it is considered appropriate to perform noncontrast CT for CCS in asymptomatic patients without known CAD who have an intermediate global risk estimate for CAD, or in patients with a family history of premature CAD and low global CAD risk estimate.[28]

In symptomatic patients, as per 2012 ACCF/AHA guidelines, noncontrast cardiac CT to determine CCS has a class IIb indication and may be considered in patients with a low to intermediate pretest probability of obstructive CAD.[26]

20. What is the diagnostic accuracy of CCTA?

Coronary CT using MDCT technology involves timed contrast administration with ECG gated image acquisition while the coronary arteries are opacified. Because of cardiac motion affecting the quality of images, slow heart rates are typically achieved with periprocedural β-blockade (**Fig. 9**). Most studies focus on the accuracy of 64-slice CT, which has been shown to have high accuracy in multiple studies in excluding obstructive CAD.[44,45] However, because of the blooming effect of calcium that can be seen in heavy coronary calcium burden, it can result in overestimation in severity of stenoses. The ACCURACY (Assessment by Coronary Computed Tomographic Angiography of Individuals Undergoing Invasive Coronary Angiography) trial studied 230 patients with a prevalence of 25%, and the sensitivity and specificity for detecting patients with at least 1 stenosis of 50% or greater was 95% and 83%, respectively. The negative predictive value was 99%, but with a positive predictive value of 64%, because of the low prevalence of disease.[44] Meijboom and colleagues[45] showed a sensitivity of 99% in 360 symptomatic patients. As with all diagnostic testing, appropriate selection of symptomatic patients with low to intermediate pretest likelihood of CAD optimizes the performance and accuracy of CCTA in excluding patients with CAD. Several studies have also shown the role of CCTA in the emergency room setting with low cardiac event in patients with negative studies and faster discharge times.[21,22,46] CCTA can also be used to evaluate for myocardial bridging (in which segments of the coronary artery can have an intramyocardial course) and anomalous coronary arteries. Although the test can be performed quickly, its downsides include contrast administration and increased radiation exposure (more prominently in retrospective protocols when image acquisition occurs at all phases of the cardiac cycle), which can vary from institution to institution.

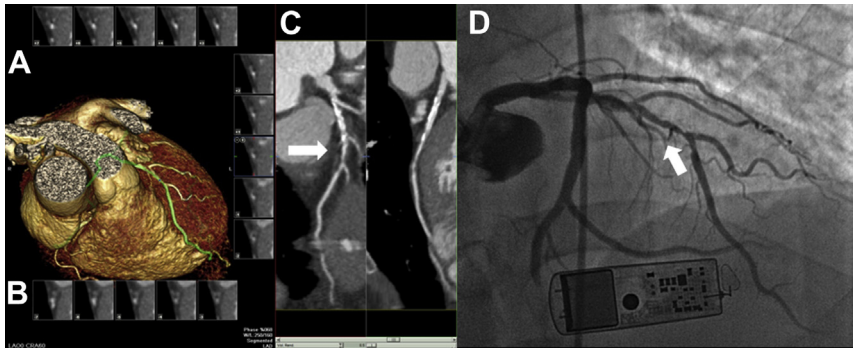

Fig. 9. 64-Slice CCTA and corresponding invasive coronary angiogram in a 64-year-old man with a history of hypertension and hyperlipidemia with a history of chest pain and occasional palpitations. (*A*) Volume rendering with three-dimensional reconstruction of the heart showing the course of the left anterior descending (LAD) artery (*green*). (*B*) Multiplanar format view of the LAD artery showing multiple cross-sectional views of each segment of the LAD artery, showing varying degrees of significant calcified and noncalcified stenosis. (*C*) Curved multiplanar reconstruction showing significant mixed noncalcified and calcified plaque in the proximal LAD to mid-LAD artery (*arrow*). (*D*) Invasive coronary angiography showing a diffusely calcified proximal LAD to mid-LAD artery (*arrow*), which was found to be functionally significant on invasive fractional flow reserve testing.

21. What are the indications for CCTA?

As per 2010 Appropriate Use Criteria for Cardiac Computed Tomography, the use of CCTA is deemed appropriate in the following clinical scenarios[28]:

- Patients with acute symptoms concerning for ACS who either have: (1) have a normal ECG and cardiac biomarkers, (2) have an uninterpretable or nondiagnostic ECG, or (3) equivocal biomarkers who have a low or intermediate pretest probability of CAD
- Patients with nonacute symptoms possibly representing an ischemic equivalent who have an interpretable ECG and are able to exercise with an intermediate pretest probability of CAD
- Patients with nonacute symptoms possibly representing an ischemic equivalent who have an interpretable ECG and are not able to exercise with a low or intermediate pretest probability of CAD
- Patients who have had previous stress imaging with discordant ECG exercise and imaging results, or equivocal stress imaging results
- Patients who had have normal previous stress imaging studies but with new or worsening symptoms
- Patients who have undergone ECG exercise testing alone and have intermediate-risk findings, or normal exercise testing findings with continued symptoms
- Patients with new-onset or newly diagnosed clinical heart failure and no previous CAD with a low/intermediate pretest probability of CAD
- Patients undergoing preoperative coronary assessment before noncoronary cardiac surgery with an intermediate pretest probability of CAD

As per 2012 ACCF/AHA guidelines, for patients who have at least moderate physical functioning or no disabling comorbidity, CCTA holds a class IIb indication for risk assessment in patients for suspected CAD who have an intermediate pretest

probability of CAD. For patients who cannot exercise, CCTA holds a class IIa indication to assess for suspected CAD in patients with a low to intermediate pretest probability of CAD who are unable to perform at least moderate physical functioning or have disabling comorbidity.

It also holds a class IIa indication for patients with an intermediate pretest probability of CAD who have (1) continued symptoms with previous normal test findings, (2) inconclusive results from previous exercise or pharmacologic stress testing, or (3) are unable to undergo stress with nuclear MPI or echocardiography.[26]

22. What are the clinical applications of CMR imaging and its strengths and weaknesses?

CMR imaging has been increasingly used in structural, volumetric, and valvular assessment of cardiac function, and can be used in assessing for ischemia and infarction. It has appealing aspects given its superior temporal resolution, and lack of radiation ionizing exposure. It uses the principles of MRI in imaging cardiac tissue by using magnetization to align atomic nuclei in the body, which can be used to construct an ECG gated image in the scanned area. Heart muscles can be visualized for fat or scar through a spin echo sequence, in which blood appears black. ECG gated cinematic images over several cardiac cycles can evaluate for wall motion abnormalities through balanced steady-state free precession. When adding gadolinium to assess for scar, in a sequence known as inversion recovery, normal cardiac myocardium appears dark, whereas areas of infarction can appear white. Perfusion studies with pharmacologic agents or exercise can also be used to assess for ischemia/infarction, which results in wall motion abnormalities and delayed uptake of contrast. The absence of significant late gadolinium enhancement in thinned, hypokinetic myocardium can also imply viability (**Fig. 10**).[47,48] Its accuracy in assessing coronary anatomy is limited compared with that of CCTA. It can also pose logistical challenges given its long acquisition times, and it may be uncomfortable for patients who are claustrophobic or who have medical devices such as pacemakers and implantable defibrillators, which are not safe for MRI. Also, advanced renal disease can pose as a contraindication to gadolinium administration given its propensity to cause nephrogenic systemic fibrosis.

23. What is the diagnostic accuracy of CMR imaging?

IMPACT-II (Magnetic Resonance Imaging for Myocardial Perfusion Assessment in Coronary Artery Disease Trial)[49] compared diagnostic accuracy of pharmacologic stress (adenosine) CMR imaging with SPECT in 533 patients, with a CAD prevalence of 49%. CMR imaging and SPECT were found to have a sensitivity of 75% and 59%, respectively, and specificities were 59% and 72%, respectively. Positive and negative predictive values for CMR imaging were 70% and 65%, respectively, and 73% and 65%, respectively, for SPECT. Although specificity of CMR imaging was believed to be inferior to SPECT in this study, Jaarsma and colleagues[27] showed in their meta-analysis that SPECT had a pooled sensitivity of 88% and specificity of 61% with SPECT, and CMR imaging had a pooled sensitivity of 89% and specificity of 76%. Meta-analyses[50] have shown a sensitivity and specificity of dobutamine CMR imaging of 83% and 86% respectively, and sensitivity and specificity of vasodilator stress-induced CMR imaging was 91% and 81%.

CMR angiography showed an 81% negative predictive value for excluding CAD in a multicenter controlled clinical trial, and meta-analyses[51,52] have shown diagnostic

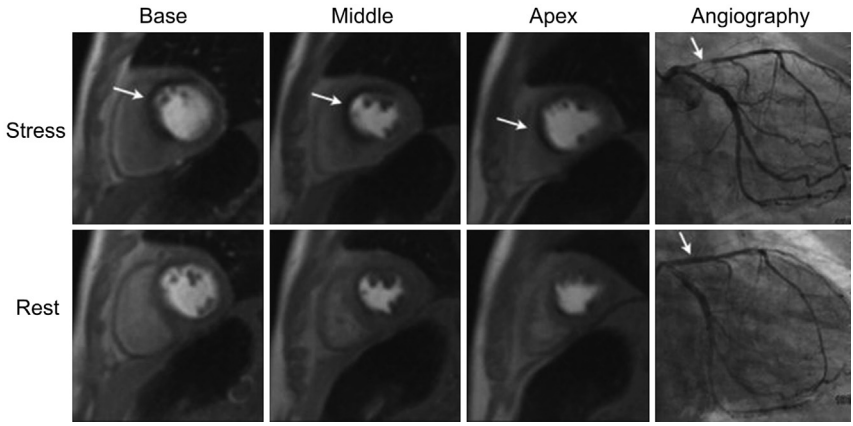

Fig. 10. Stress CMRI. Myocardial perfusion analysis during vasodilator infusion in a 74-year-old man with chest pain at mild exertion, known 2-vessel CAD, and no wall motion abnormalities. The top row shows 3 short axis views (basal, midventricular, and apical) during contrast-enhanced first-pass perfusion CMR imaging during adenosine stress. A large perfusion defect of the anterior and septal wall is obvious (*white arrows*). The bottom row shows the same slices during contrast-enhanced first-pass perfusion CMR imaging at rest, with clearly less extensive perfusion defect. On the right side, the coronary angiography is depicted. A severe stenosis of the proximal left anterior descending artery, which supplies the anterior and septal wall, is seen (*white arrow in the top image*). It is treated by stent implantation (*white arrow in the bottom image*). (*From* von Knobelsdorff-Brenkenhoff F, Schulz-Menger J. Cardiovascular magnetic resonance imaging in ischemic heart disease. J Magn Reson Imaging 2012;36:24; with permission.)

sensitivity and specificity ranging from 87% to 88% and 56% to 70%, respectively, which in general is lower than the diagnostic accuracy of CCTA.

24. When is it appropriate to use CMR imaging for assessing for CAD?

As per 2006 Appropriateness Criteria for Cardiac Magnetic Resonance Imaging, it is considered appropriate to perform vasodilator perfusion CMR imaging or dobutamine stress function CMR imaging in patients presenting with chest pain who have either an uninterpretable ECG or are unable to exercise, and have an intermediate pretest probability of CAD.[53]

As per 2012 ACCF/AHA guidelines, for patients with suspected CAD, CMR imaging with pharmacologic stress has a class IIa indication for risk assessment in patients with an intermediate to high pretest probability of obstructive CAD who are able to exercise to at least moderate adequate workload but have an uninterpretable ECG. For patients unable to exercise, pharmacologic stress CMR imaging has a class IIa indication for testing of patients with an intermediate to high pretest probability of CAD who are incapable of at least moderate physical function or have disabling comorbidities.[26]

25. What are the average radiation doses associated with cardiac imaging modalities compared with other conventional imaging tests?

The most commonly used term that quantifies radiation exposure in diagnostic imaging is effective dose, which is a single-dose parameter that estimates whole-body

Table 7
Mean effective radiation doses

	Dose (mSV)
Natural environmental exposure (yearly)	2–3
Commercial flight	0.005/h
Chest radiography (posteroanterior, lateral)	0.04–0.06
Diagnostic cardiac catheterization	2–10
Percutaneous coronary intervention	25
Tl-Tl stress redistribution SPECT	22
Tl-Tc SPECT MPI	23–41
Tc-Tc SPECT MPI	15
Rubidium Rb 82 PET	12–13
Ammonia N 13 PET	2
FDG F 18 PET	7
Head CT	5
Chest CT	12
Pelvis CT	15
CCS (EBCT)	0.8–1.3
CCS (64-slide MDCT)	2–3
Cardiac MDCT (8 slice)	12–24
Cardiac MDCT (64 slice)	9–24
Cardiac MDCT (320 slice)	6
Prospective MDCT (64 slice)	2–3

Abbreviations: FDG, fluorodeoxyglucose; Tc, technetium.
Adapted from Vorobiof G, Achenbach S, Narula J. Minimizing radiation dose for coronary CT angiography. Cardiol Clin 2012;30:9–17.

radiation risk from ionizing radiation. It factors in the type of radiation and the specific organ being exposed, and is defined in milliSieverts (mSv) (**Table 7**).

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