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Health Care Guideline

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- medical specialty and professional societies;
- researchers;
- federal, state and local government health care policy makers and specialists; and
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Health Care Guideline:
Cardiac Stress Test Supplement

INSTITUTE FOR CLINICAL SYSTEMS IMPROVEMENT

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The Cardiac Stress Test is a supplemental document that brings about consistency in recommendations that are common to the scope of the ICSI related cardiac guidelines: Stable Coronary Artery Disease, Inpatient Management of Heart Failure, Heart Failure in Adults, and Preoperative Evaluation.

1. General Principles and Philosophies Regarding Stress Testing

The following principles should always be considered when using stress testing in any clinical situation.

- Only order a test if the results will affect clinical management of the patient
- The likelihood of having coronary artery disease (CAD) should always be considered when applying the test results to the patient
- An important use of stress testing is to identify patients at high risk of cardiac death (those with left main or three-vessel CAD)
- A comprehensive stress test report includes information on several important diagnostic and prognostic variables and does not simply report the study as positive or negative on the basis of the exercise ECG or images result
- Most patients without prior revascularization with a normal or near-normal resting ECG and who are able to exercise adequately should undergo standard exercise treadmill testing rather than exercise or pharmacologic imaging (echo or nuclear imaging)
- These principles apply to both genders

2. Contraindications to Stress Testing

3. Deciding Which Stress Imaging Study to Order

4. Medications for Pharmacologic Stress Testing

Introduction

The primary aim of the Cardiac Stress Test Supplement is to aid the clinician in selecting the type of stress test for an individual patient in a specific clinical situation. Some basic principles concerning test use and interpretation are also reviewed. The supplement does not recommend when a stress test should be performed since this issue has already been addressed in the ICSI related cardiac guidelines. Once the clinician has decided to perform a stress test, the recommendations for test selection contained in the Cardiac Stress Test Supplement should be applicable to the various clinical situations addressed in these other guidelines.

The Cardiac Stress Test work group felt that the supplement would be more user friendly if arranged in the format of multiple tables instead of a decision-tree algorithm. This supplement is aimed at the primary care clinician. It is intended to function as a practical and concise aid for the busy practitioner. For this reason the rationale to support the recommendations made in the document and the number of references have intentionally been limited. This document is based on the American College of Cardiology/American Heart Association (ACC/AHA) Guideline: Guidelines for Exercise Testing.

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Foreword

Scope and Target Population

Please refer to related cardiac guidelines for specific target populations.

Clinical Highlights and Recommendations

The following principles apply to both genders and should always be considered when using stress testing in any clinical situation: *(Annotation #1A)*

- Only order a test if the results will affect clinical management of the patient. *(Annotation #1A)*
- The likelihood of having coronary artery disease (CAD) should always be considered when applying the test results to the patient. *(Annotation #1B)*
- An important use of stress testing is to identify patients at high risk of cardiac death (those with left main or three vessel CAD). *(Annotation #1C)*
- A comprehensive stress test report includes information on several important diagnostic and prognostic variables and does not simply report the study as positive or negative on the basis of the exercise ECG or images result. *(Annotation #1D)*
- Most patients without prior revascularization with a normal or near-normal resting ECG and who are able to exercise adequately should undergo standard exercise treadmill testing rather than exercise or pharmacologic imaging (echo or nuclear imaging). *(Annotation #1E)*
- Diagnostic goal and other ECG findings indicate which stress imaging study to order. *(Annotation #3)*
- Associated medical conditions determine which pharmacologic stress testing to use. *(Annotation #4)*

Related ICSI Scientific Documents

Related Guidelines

- Stable Coronary Artery Disease
- Heart Failure in Adults
- Diagnosis and Treatment of Chest Pain and Acute Coronary Syndrome (ACS)

Technology Assessment Reports

- Cardiac Rehabilitation (#12, 2002)
- Biochemical Markers for Cardiovascular Disease Risk (#66, 2003)

Patient and Family Guidelines

- Stable Coronary Artery Disease for Patients and Families
- Heart Failure in Adults for Patients and Families

Evidence Grading

Individual research reports are assigned a letter indicating the class of report based on design type: A, B, C, D, M, R, X.

A full explanation of these designators is found in the Discussion and References section of the guideline.

Disclosure of Potential Conflict of Interest

In the interest of full disclosure, ICSI has adopted the policy of revealing relationships work group members have with companies that sell products or services that are relevant to this guideline topic. The reader should not assume that these financial interests will have an adverse impact on the content of the guideline, but they are noted here to fully inform readers. Readers of the guideline may assume that only work group members listed below have potential conflicts of interest to disclose.

Todd Miller, MD, over the past 12 months, has received research grant support from Bristol/Myers Squibb.

No other work group members have potential conflicts of interest to disclose.

ICSI's conflict of interest policy and procedures are available for review on ICSI's Web site at http://www.icsi.org.

Algorithm Annotations

1. General Principles and Philosophies Regarding Stress Testing

- **Only order a test if the results will affect clinical management of the patient**

  Test results are unlikely to affect management decisions in certain clinical situations. For instance, patients at low probability of coronary artery disease (CAD) who are asymptomatic or have vague symptoms should ordinarily not undergo stress testing since the large majority of these patients will have normal test results. Of the small percentage of patients with a positive test, most will be false positives. At the other extreme, an 80-year-old patient with multiple risk factors who develops typical angina walking only a few feet also should not undergo stress testing. This patient's clinical characteristics alone place him at high risk of left main or three vessel CAD. The results of the exercise test in this case would not alter the clinician's diagnostic impression or the patient's risk classification. This patient should be either empirically treated with medical therapy or, if deemed a suitable candidate for revascularization, undergo coronary angiography *(Sox, 1986).*

- **The likelihood of having coronary artery disease (CAD) should always be considered when applying the test results to the patient**

  The posttest probability of disease is the product of the pretest probability of disease and the probability that the test results are accurate. The clinician can estimate the patient's pretest probability of disease from clinical variables. The variables that have been shown to be most predictive are age, gender and character of chest pain. Risk factors are not as strong predictors as these three variables, but the presence of risk factors, especially multiple risk factors, does increase the likelihood of coronary artery disease. Diabetes is the most important risk factor among the individual risk factors. The table below, "Pretest Probability of Coronary Artery Disease by Age, Gender, and Symptoms" was taken from the ACC/AHA Practice Guidelines: Guidelines for Exercise Testing.

Pretest Probability of Coronary Artery Disease by Age, Gender, and Symptoms*

Age (y)	Gender	Typical/Definite Angina Pectoris	Atypical/Probable Angina Pectoris	Nonanginal Chest Pain	Asymptomatic
30-39	Men Women	Intermediate Intermediate	Intermediate Very low	Low Very low	Very low Very low
40-49	Men Women	High Intermediate	Intermediate Low	Intermediate Very low	Low Very low
50-59	Men Women	High Intermediate	Intermediate Intermediate	Intermediate Low	Low Very low
60-69	Men Women	High High	Intermediate Intermediate	Intermediate Intermediate	Low Low

* No data exist for patients less than 30 or over 69 years of age, but it can be assumed that prevalence of CAD increases with age. In a few cases, patients with ages at the extremes of the decades listed may have probabilities slightly outside the high or low range. The above table considers only age, gender and symptoms.

The test is most useful for diagnostic purposes in patients whose pretest probability of disease is in the intermediate range of coronary disease (e.g., a middle-aged man with atypical chest pain or a middle-aged women with typical angina.) The results of a stress test do not provide a definitive answer as to whether CAD is present or absent but only alter the probability that CAD is present or absent *(Gibbons, 2002; Sox, 1986).*

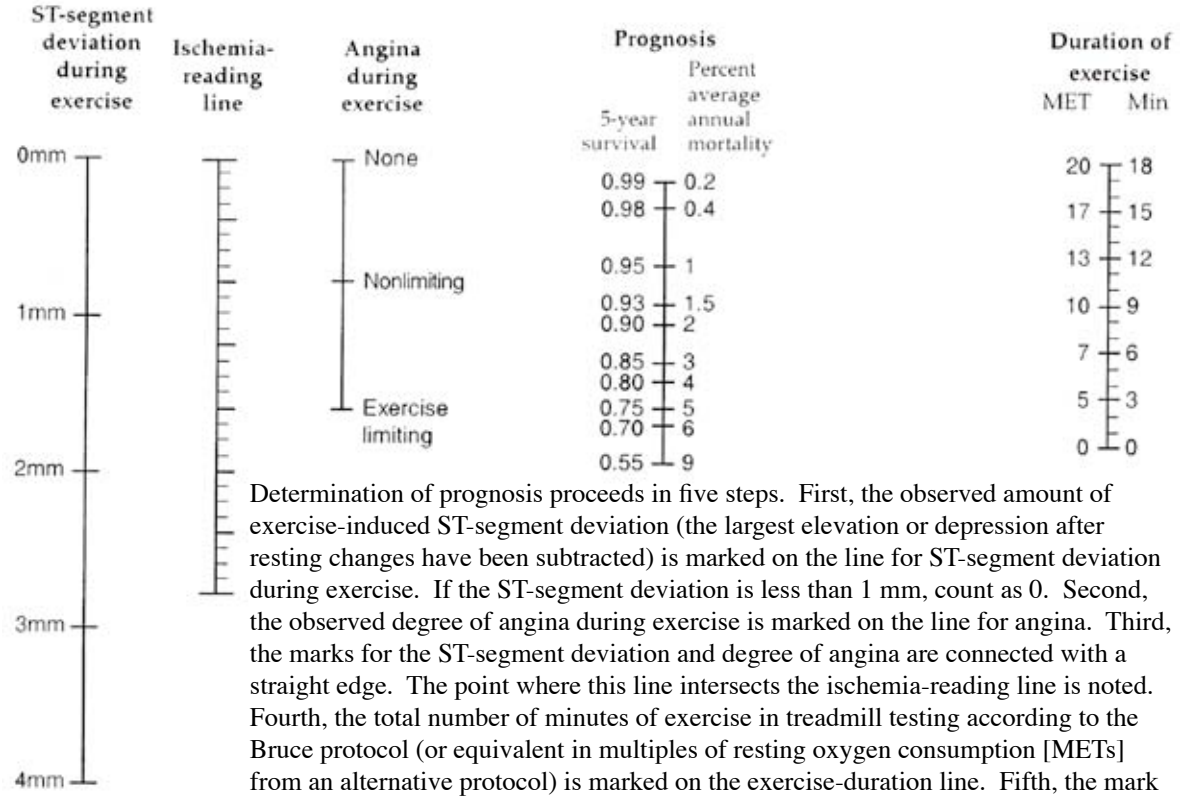
Supporting evidence is of class: R

- **An important use of stress testing is to identify patients at high risk of cardiac death (those with left main or three vessel CAD)**

  In the current era, the value of diagnostic modalities and therapeutic interventions is measured by their impact on patient prognosis. Although exercise testing is commonly performed for diagnostic purposes (i.e., to determine whether any CAD is present), a more important goal is to predict a patient's outcome. The Duke treadmill score is the most widely used method of prognostication. It may not apply to all patients being considered for stress testing (e.g., patients with recent infarction, previous cardiac surgery, or revascularization, or possibly asymptomatic patients). Nevertheless, the Duke treadmill score nomogram may be useful in estimating prognosis in other symptomatic patients *(Gibbons, 2002a; Gibbons, 2003; Mark, 1987; Mark, 1991).*

  The Duke Treadmill Scoring System can be determined by two methods:

  Nomogram



Determination of prognosis proceeds in five steps. First, the observed amount of exercise-induced ST-segment deviation (the largest elevation or depression after resting changes have been subtracted) is marked on the line for ST-segment deviation during exercise. If the ST-segment deviation is less than 1 mm, count as 0. Second, the observed degree of angina during exercise is marked on the line for angina. Third, the marks for the ST-segment deviation and degree of angina are connected with a straight edge. The point where this line intersects the ischemia-reading line is noted. Fourth, the total number of minutes of exercise in treadmill testing according to the Bruce protocol (or equivalent in multiples of resting oxygen consumption [METs] from an alternative protocol) is marked on the exercise-duration line. Fifth, the mark for ischemia is connected with that for exercise duration. The point at which this line intersects the line for prognosis indicates the five-year survival rate and the average annual mortality with these characteristics.

Equation

Treadmill score = duration of exercise in minutes on the Bruce protocol

– (minus) 5x maximal mm ST deviation

– (minus) 4x treadmill angina index

Treadmill Angina Index:

0 if no angina

1 if non-limiting angina

2 if limiting angina

High Risk =	treadmill score less than -10 79% four-year survival
Moderate Risk =	treadmill score -10 to +4 95% four-year survival
Low Risk =	treadmill score greater than or equal to +5 99% four-year survival

Patients categorized as high-risk have a poor prognosis and generally should undergo coronary angiography. Many of these patients will have severe (left main or three-vessel) CAD. The three large randomized trials (VA Study, European Cooperative Study, Coronary Artery Surgery Study) comparing medical therapy to coronary artery bypass surgery demonstrated that only patients with severe CAD demonstrated a survival benefit when treated with bypass surgery. On the other hand, patients categorized as low-risk have an excellent prognosis and are unlikely to benefit from an aggressive approach. These patients generally can be reassured and observed, or treated medically, if their chest pain is felt to be angina. Management of intermediate-risk patients is more problematic. Some of these patients may need to undergo further evaluation such as coronary angiography or stress imaging *(Gibbons, 2002a)*.

Several studies have demonstrated that myocardial perfusion imaging and stress echo are useful for prognostic purposes. Many studies have shown that the imaging results provide independent and/or incremental prognostic information to clinical and exercise variables. The most useful prognostic information from nuclear imaging is provided by the extent and severity of the perfusion defect on the stress images (a variable referred to as the summed stress score) *(Klocke, 2003)*. For echocardiography, important prognostic variables are an increase (or no change) in end-systolic volume or a decrease in ejection fraction with stress compared to rest and the number of segments with abnormal wall motion and the severity of the wall motion abnormality within those segments (for instance, dyskinesis is more severe than hypokinesis) on the stress images *(Cheitlin, 2003)*.

Supporting evidence is of classes: B, C, R

- **A comprehensive stress test report includes information on several important diagnostic and prognostic variables and does not simply report the study as positive or negative on the basis of the exercise ECG or images result**

The most widely used criteria to define an abnormal study include 1 mm horizontal or downsloping ST-segment depression 0.08 seconds after the J point by standard treadmill testing, a perfusion defect by myocardial perfusion imaging, and worsening regional wall motion by echocardiography. A test should not be viewed as simply positive or negative by these criteria.

Several parameters should be examined, both during exercise and in the recovery period, and included in the report:

EXERCISE	RECOVERY
• Duration	• Impaired heart rate recovery (persistently elevated heart rate)
• Time of onset of ST depression rate	• Impaired blood pressure recovery (persistently elevated systolic blood pressure)
• Magnitude of ST depression	• Frequent ventricular ectopy
• Impaired heart rate increase (chronotropic incompetence)	
• Frequent ventricular ectopy	
• Decrease in systolic blood pressure	

Several of these variables, including limited exercise capacity (less than 85% of predicted), chorontropic incompetence (less than or equal to 80% of predicted heart rate reserve for patients not taking beta-blockers), impaired heart rate recovery (less than or equal to 12 beats/minute one minute into recovery when performing cool-down), and complex ectopy (greater than 7 beats/minute or complex forms), have been reported to predict mortality *(Kligfield, 2006)*.

These variables should be considered along with the patient's clinical characteristics when using the test for diagnostic purposes and especially for risk stratification. For diagnostic purposes, the double product (systolic blood pressure X heart rate) and percent predicted maximum heart rate are helpful to assure that the patient has achieved an adequate level of myocardial "stress." For prognostic purposes, duration is more important, as applied in the Duke treadmill score. A common mistake when applying the results of stress imaging to patient management is to overrely on the imaging results at the expense of clinical and exercise data. Occasionally, patients with severe CAD will have normal or near-normal images. For instance, a diabetic patient with typical angina who develops ST-segment depression at a low workload, but whose perfusion or echo images are normal, should not be considered to be a low-risk patient. Such a patient still is at high risk of severe CAD despite the image results *(Cole, 1999; Frolkis, 2003; Gibbons, 2002b; Lauer, 1999; Kligfield, 2006)*.

Supporting evidence is of classes: B, R

- **Most patients without prior revascularization with a normal or near-normal resting ECG and who are able to exercise adequately should undergo standard exercise treadmill testing rather than exercise or pharmacologic imaging (echo or nuclear imaging)**

Standard exercise treadmill tests are currently underutilized in favor of more expensive imaging tests. Most patients with a normal or near-normal (less than 1 mm ST-segment depression) resting ECG who are able to exercise adequately (estimated five minutes or more of the Bruce protocol) should undergo standard exercise treadmill testing for the following reasons:

- Ninety-five percent of patients with a normal resting ECG have normal resting left ventricular ejection fraction. Therefore, most patients do not need to undergo an imaging procedure simply to measure ejection fraction.
- The exercise ECG has similar sensitivity and much higher specificity in patients with a normal resting ECG as opposed to those with resting ST-T abnormalities. Therefore, the exercise ECG

is highly accurate in patients with a normal resting ECG because there are fewer false positive results.

- In patients with a normal resting ECG, the standard exercise test is nearly as accurate as the imaging procedures for correctly identifying patients with left main or three-vessel CAD and for predicting outcomes. The higher sensitivity of the imaging procedures is due to the detection of more patients with one- or two-vessel CAD. However, the exercise ECG is nearly as accurate for correctly identifying the high-risk patients.

These recommendations are in agreement with other national guidelines to perform a standard treadmill test as the initial test in patients with a normal or near-normal resting ECG *(Gibbons, 2002b; Cheitlin, 2003; Klocke, 2003)*.

Preliminary data indicate that a small percentage of patients who are classified as low-risk by the Duke treadmill score are incorrectly classified and in fact, are at higher risk. These patients can be correctly classified as higher risk by nuclear imaging. These patients can be recognized on the basis of clinical variables before any stress testing is performed. The clinical variables that identify higher risk patients include a combination of advanced age, male gender, history of myocardial infarction, the presence of angina, and diabetes *(Poornima, 2004)*. If these findings can be confirmed in other studies, stress imaging may become the recommended initial stress test to evaluate patients with high risk clinical parameters.

The imaging procedures do have advantages over standard treadmill testing, which can be beneficial in selected patients, including higher sensitivity, direct measurement of left ventricular resting ejection fraction, greater accuracy when the resting ECG precludes accurate interpretation during exercise (LBBB, paced ventricular rhythm, WPW, LVH with strain, greater than 1 mm ST-segment depression), the ability to localize ischemia, and the provision of useful information when combined with pharmacologic stress. On the other hand, the standard exercise treadmill test is more widely available and can be performed at considerably lower cost.

Supporting evidence is of classes: B, C, D, R

- **These principles apply to both genders**

The exercise ECG has been shown to be useful for diagnostic and prognostic purposes in women but its accuracy is generally believed to be lower than that in men. The reported sensitivity and specificity in women from individual studies has been highly variable. Many studies have enrolled relatively few women. The major concern is the higher false positive rate in women versus men. However, at the present time there are insufficient data to recommend stress imaging as the initial study for evaluation of CAD in women with normal or near-normal resting ECG. The principles discussed above should be applicable to both genders *(Gibbons, 2002b; Morise, 2002; Berman, 2003; Mieres, 2005; Sanfilippo, 2005)*.

Supporting evidence is of classes: C, R

2. Contraindications to Stress Testing

- Absolute Contraindications
  - Acute myocardial infarction (within 48 hours)
  - Unstable angina not previously stabilized by medical therapy – appropriate timing of testing depends on level of risk of unstable angina. In the absence of definitive evidence but in keeping with local practice, the work group suggests a minimum of six hours after unstable angina is stabilized

- Uncontrolled cardiac arrhythmias causing symptoms or hemodynamic compromise
- Symptomatic severe aortic stenosis
- Uncontrolled symptomatic heart failure
- Acute pulmonary embolus or pulmonary infarction
- Acute myocarditis or pericarditis
- Acute aortic dissection

• Relative Contraindications

Relative contraindications can be superseded if the benefits of exercise outweigh the risks

- Left main coronary stenosis
- Moderate stenotic valvular heart disease
- Electrolyte abnormalities
- Severe arterial hypertension – in the absence of definitive evidence, the committee suggests systolic blood pressure of greater than 200 mm Hg and/or diastolic blood pressure of greater than 110 mm Hg
- Tachyarrhythmias or bradyarrhythmias
- Hypertrophic cardiomyopathy and other forms of outflow tract obstruction
- Mental or physical impairment leading to inability to exercise adequately
- High-degree atrioventricular block

(Gibbons, 2002b)

Supporting evidence is of class: R

3. Deciding Which Stress Imaging Study to Order

Expertise with the various imaging modalities should be the most important factor determining selection of a specific modality in an individual patient. All of the imaging modalities must be carefully performed and interpreted, preferably by personnel specifically trained in these techniques, to assure a high level of accuracy. If more than one technique is available in a given practice or institution, the technique that has been found to be most accurate should generally be the modality of choice.

Many factors may influence the selection of an imaging study in an individual patient. See Chart #1, "Benefits of Stress Test Selection." Cost is also a consideration. The charges for echocardiography are less than the charges for nuclear imaging in the Medicare population. Charges vary widely in the non-Medicare population. Chart #2, "Comparative Advantages of Stress Echocardiography and Nuclear Perfusion Imaging in Diagnosis of CAD," is intended to address the major factors that are considered in test selection and to indicate if the imaging modalities are of similar value for each factor or if one of the modalities is better validated or considered to be superior to the others for a given factor.

Chart 1:

Benefits of Stress Test Selection		
Most patients without prior revascularization with a normal or near-normal resting ECG and who are able to exercise adequately should undergo standard exercise treadmill testing rather than exercise or pharmacologic imaging (echo or nuclear imaging) for diagnostic and prognostic purposes. **Key:** **Yes = Useful** **No = Not Useful**		
Goal of Imaging Test	**Echo**	**Nuclear Perfusion Imaging**
Diagnosis CAD	Yes	Yes
Assess severe CAD/prognosis chronic CAD	Yes	Yes
Prognosis post-MI	Yes	Yes
Measure resting LVEF	Yes	Yes
Assess preoperative risk	Yes	Yes
Identify viable myocardium	Yes	Yes
Evaluate for cardiac etiology of exertional dyspnea	Yes	Yes
Evaluate post-CABG	Yes	Yes
Evaluate post-PCI*	Yes	Yes
Localize ischemia	Yes	Yes
Patient and ECG factors		
Resting ST-T, WPW, LVH strain	Yes	Yes
LBBB, ventricular pacing	Yes	Yes – with adenosine or dipyridamole
LVEF in atrial fibrillation	Yes	No
Unable to lie supine for 10 minutes	Yes	No
Severe COPD	Lower technical success rate; contrast enhancement may increase technical success	Yes
Severe obesity	Lower technical success rate; contrast enhancement may increase technical success	Yes. Lower specificity due to breast/diaphragm artifact. Consider two-day SPECT or PET if available.

*PCI = Percutaneous Coronary Intervention, which includes angioplasty, stents, etc.

Chart 2:

Comparative Advantages of Stress Echocardiography and Nuclear Perfusion Imaging in Diagnosis of CAD	
Advantages of Stress Echocardiography	**Advantages of Nuclear Perfusion Imaging**
1. Higher specificity	1. Higher technical success rate
2. Versatility – more extensive evaluation of cardiac anatomy and function	2. Higher sensitivity – especially for single-vessel coronary disease involving the left circumflex
3. Greater convenience/efficacy/availability	3. Better accuracy in evaluating possible ischemia when multiple resting LV wall motion abnormalities are present
4. Lower cost	4. More extensive published database – especially in evaluation of prognosis

This chart has been taken from the ACC/AHA/ACP-ASIM Guidelines for the Management of Patients with Chronic Stable Angina: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Patients with Chronic Stable Angina) *(Gibbons, 2002a).*

Supporting evidence is of classes: C, R

These charts can be used as a pocket card for quick references.

Diagnosis CAD

Several published studies demonstrate that the sensitivity of the imaging modalities is higher than that of standard exercise ECG and roughly equal between the modalities at 85%. Specificity for echo is 77%, versus 64% for perfusion imaging. There are very few direct comparison studies between the modalities performed in institutions with well-recognized laboratories in each of the modalities. The few published studies suggest similar accuracy *(Cheitlin, 2003; Fleischmann, 1998; Gibbons, 2002b, Klocke, 2003; Kim, 2001; Quinones, 1992).*

Supporting evidence is of classes: B, C, M, R

Assess severe CAD/prognosis chronic CAD

Both stress echocardiography and myocardial perfusion imaging have been well validated for identifying patients at increased risk of left main or three-vessel CAD and those with poor prognosis when treated medically *(Cheitlin, 2003; Gibbons, 2002a; Klocke, 2003).*

Supporting evidence is of classes: B, C, R

Prognosis post-MI

All modalities have been shown to be useful for risk assessment when performed shortly after MI. There are no published studies directly comparing the different modalities in this setting. The prognostic value of any modality will be less in lower-risk patients (those treated with thrombolytics). Echo and nuclear imaging provide measurement of left ventricular ejection fraction (LVEF), an important prognostic variable, which can be measured at the same time as the stress study. Nuclear imaging provides measurement of quantitated infarct size, which has been shown to be an important prognostic variable *(Cheitlin, 2003; Klocke, 2003; Shaw, 1996).*

Supporting evidence is of classes: B, M, R

Measure resting LVEF

Resting LVEF can be measured by echocardiography or by nuclear imaging *(Cheitlin, 2003; Klocke, 2003).*

Supporting evidence is of class: R

Assess preoperative risk

Patients at risk for CAD or with known CAD frequently undergo risk assessment before noncardiac surgery. Patients unable to adequately exercise are commonly evaluated by pharmacologic stress imaging. Echo and nuclear imaging are useful for identifying patients at increased risk of a perioperative cardiac event *(Eagle, 2002; Kerta, 2003).*

Supporting evidence is of classes: M, R

Identify viable myocardium

Assessment of myocardial viability is a complex clinical issue that generally is performed in patients with reduced LVEF who have coronary anatomy amenable to revascularization (PTCA or CABG). Thus, imaging is generally performed after coronary angiography. The gold standard has traditionally been positron emission tomography (PET), which is expensive and not readily available. Dobutamine echocardiography and resting and stress thallium and sestamibi perfusion imaging have been shown to be of value for identifying viable myocardium *(Cheitlin, 2003; Klocke, 2003).*

Supporting evidence is of class: R

Evaluate for cardiac etiology of exertional dyspnea

Exertional dyspnea can be due to lung disease, heart disease, systemic diseases (e.g., anemia), obesity, deconditioning, or a combination of conditions. Patients in whom a cardiac etiology cannot be confidently excluded on the basis of clinical assessment, (e.g., ECG and CXR) may require further evaluation. Potential cardiac causes include CAD (anginal equivalent), LV systolic dysfunction, LV diastolic dysfunction, valvular heart disease, pericardial disease, and cor pulmo-nale. Rest and stress echocardiography can address all of these potential etiologies with a one-time study. Myocardial perfusion imaging can be helpful if ischemia is present, if LV function is reduced (sestamibi), or if pulmonary uptake is increased (thallium) *(Cheitlin, 2003; Klocke, 2003; Abidov, 2005; Bergeron, 2004).*

Supporting evidence is of class: R

Evaluate post-CABG

Because of a high prevalence of resting ECG abnormalities in this population and the frequent need to localize ischemia, stress imaging is generally preferred over standard exercise ECG. Myocardial perfusion imaging and stress echo are more sensitive for detecting graft stenosis than standard exercise ECG. Perfusion imaging and stress echo have been shown to be useful for long-term prognosis *(Chin, 2003; Cheitlin, 2003; Gibbons, 2002b; Klocke, 2003).*

Supporting evidence is of classes: B, C, R

Evaluate post-PCI

Standard exercise ECG is an insensitive predictor of restenosis. Echo and perfusion imaging have been shown to be accurate for this purpose. There is limited data addressing long-term prognostic studies of either modality post-PCI *(Cheitlin, 2002; Gibbons, 2002b; Klocke, 2003).*

Supporting evidence is of classes: B, C, R

Localize ischemia

Occasionally there are patients who have multiple coronary stenoses in whom it is important to identify the "culprit" lesion before performing angioplasty. The standard exercise ECG cannot localize ischemia, whereas echo and myocardial perfusion imaging can *(Cheitlin, 2003; Klocke, 2003)*.

Supporting evidence is of class: R

Resting ST-T, WPW, LVH strain

The standard exercise ECG is known to be less specific in these settings, especially when there is greater than 1 mm ST depression on the resting ECG. Stress imaging is widely believed to be more accurate in these settings *(Cheitlin, 2003; Gibbons, 2002b; Klocke, 2003)*.

Supporting evidence is of class: R

LBBB, ventricular pacing

The standard exercise ECG is uninterpretable in the setting of LBBB and ventricular pacing. Exercise myocardial perfusion imaging frequently results in false positive perfusion defects (reversible or fixed), often involving the septum. These false positive perfusion defects are less often seen with adenosine or dipyridamole stress. Patients with LBBB frequently have abnormal wall motion involving the septum by echocardiography. Assessment of septal wall thickening rather than worsening wall motion (the traditional criterion of an abnormal study) during stress is more accurate for assessment of ischemia in these patients. The long-term prognostic value of both pharmacologic perfusion imaging and stress echocardiography in patients with LBBB has been demonstrated *(Cheitlin, 2003; Gibbons, 2002b; Klocke, 2003)*.

Supporting evidence is of classes: B, C, R

LVEF in atrial fibrillation

Stress echocardiography is the preferred technique. LVEF can be measured using sestamibi by either the 1st pass or gated technique, but accurate assessment requires the presence of a fairly regular heart rhythm.

Unable to lie supine for 10 minutes

Myocardial perfusion imaging requires that patients be able to lie supine for 10 minutes. Echocardiography can be performed with patients in the semirecumbent position and requires only a couple of minutes.

Severe COPD

Echocardiographic images may or may not be enhanced with contrast. COPD does not affect nuclear perfusion image quality.

Severe obesity

Echocardiographic images may or may not be enhanced with contrast. Diaphragm and/or breast artifacts are more common in obese patients and reduce the specificity of nuclear perfusion images. Image quality can be improved by performing a two-day versus one-day technetium SPECT protocol (higher doses of radioisotope can be administered with the two-day protocol) or by using PET imaging if available (PET imaging has built-in attenuation correction to reduce soft tissue imaging artifacts).

4. Medications for Pharmacologic Stress Testing

Details of the patient-related medical factors are addressed on the following pages.

	Medications for Pharmacologic Stress Testing		
Patient-Related Factors	**Dobutamine**	**Adenosine***	**Dipyridamole***
Associated Medical Conditions addressed in detail following this table			
a) Severe COPD or asthma	Indicated	Contraindicated	Contraindicated
b) Heart block (2º or 3º)	Indicated	Contraindicated	Contraindicated
c) Poorly controlled HTN	Contraindicated**	Indicated	Indicated
d) Relative hypotension	Contraindicated**	Indicated	Contraindicated
e) Unstable carotid cerebrovascular**** disease	Contraindicated**	Indicated	Contraindicated
f) Significant vent ectopy	Contraindicated**	Indicated	Indicated
g) Glaucoma***	Contraindicated	Indicated	Indicated
Medical Therapies			
h) Theophylline	Indicated	Contraindicated	Contraindicated
i) Dipyridamole by mouth	Indicated	Contraindicated	Indicated
j) Beta-blocker†	Indicated	Indicated	Indicated

* For adenosine/dipyridamole, withhold caffeinated products (e.g., chocolate, coffee) 24 hours
** These are not absolute contraindications but serious consideration of potential adverse effects should be given before ordering these tests.
*** Not a contraindication to dobutamine but a contraindication to atropine
**** Recent TIAs or stroke
† Beta-blockers
Beta-blockers are not contraindicated with dobutamine but they may require higher doses of dobutamine and/or earlier and higher doses of atropine.
Vasodilator testing has decreased sensitivity in patients taking beta blockers *(Taillefer, 2003)*.

This chart can be used as a pocket card for quick reference.

Associated Medical Conditions

Severe COPD or asthma

Adenosine and dipyridamole can precipitate an asthma attack in susceptible patients. These agents should not be used in the following patients:

- History of asthma
- Severe COPD (FEV_1 less than 30% of predicted for age)
- COPD with significant bronchodilator response (FEV_1 30%-39% of predicted with bronchodilator response greater than 15% or FEV_1 40%-100% of predicted with bronchodilator response greater than 30%)

Heart block (2° or 3°)

Adenosine and dipyridamole can cause transient block at the AV node and should not be given to patients with advanced heart block on the resting ECG.

Poorly controlled hypertension

Patients with hypertension generally should have their blood pressure well controlled before undergoing a stress test. In patients whose blood pressure is very labile or tends to run high despite efforts to control it, dobutamine should be used cautiously due to the occasional significant hypertensive response seen with this agent.

Relative hypotension

Patients with resting systolic BP less than 100 mmHg generally should not receive dobutamine or dipyridamole. Dobutamine causes an increase in systolic BP in the majority of patients but can also cause a significant decrease in systolic BP in a substantial minority of patients. Dipyridamole usually causes a modest decrease in systolic BP of 10-20 mmHg but occasionally causes a more severe decrease. Due to the prolonged duration of action (several minutes) of these agents, they generally should be avoided in patients with low resting systolic BP. The effects of adenosine on BP are similar to those of dipyridamole. However, in the patient who develops severe hypotension, this effect can be promptly reversed simply by discontinuing the medication due to its rapid half-life (less than 10 seconds).

Unstable carotid disease

See relative hypotension above. Patients with carotid artery disease scheduled for carotid endarterectomy commonly undergo cardiac screening preoperatively. Significant hypertension and prolonged hypotension should be avoided in these patients, making adenosine the agent of choice.

Significant ventricular ectopy

Patients with significant ventricular ectopy generally should be well stabilized before undergoing a stress test. In patients whose ectopy is difficult to control or whose history suggests a catecholamine-driven mechanism, dobutamine should be used cautiously due to its arrhythmogenic potential.

Glaucoma

Patients who do not achieve target heart rate with dobutamine alone are commonly administered atropine. The risk of atropine use in this setting is only for closed-angle glaucoma, which is in the minority of patients with glaucoma. This history may not be available. Should the patient need atropine, it would usually be safe to use. Should eye pain occur, an ophthamologist should be called promptly.

Medical Therapies

Theophylline

Theophylline blocks the effects of adenosine and dipyridamole. Patients ideally should be off theophylline-containing preparations for 48 to 72 hours.

Dipyridamole by mouth

Patients taking oral dipyridamole (Persantine® or Aggrenox®) should not receive intravenous adenosine due to the possibility of precipitating severe heart block. Patients taking oral dipyridamole can safely receive intravenous dipyridamole.

Beta-blocker

Beta-blockers decrease the effects of dobutamine. If the clinician feels the beta blocker can be safely withdrawn, the medication should be withheld for 48 to 72 hours to enhance the diagnostic accuracy of the test. Beta-blockers are not contraindicated with dobutamine but these patients may require higher doses of dobutamine and/or earlier and higher doses of atropine. Beta-blockers decrease the sensitivity of other vasodilator testing *(Taillefer, 2003)*.

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Evidence Grading System

I. CLASSES OF RESEARCH REPORTS

A. Primary Reports of New Data Collection:

Class A: Randomized, controlled trial

Class B: Cohort study

Class C: Non-randomized trial with concurrent or historical controls
Case-control study
Study of sensitivity and specificity of a diagnostic test
Population-based descriptive study

Class D: Cross-sectional study
Case series
Case report

B. Reports that Synthesize or Reflect upon Collections of Primary Reports:

Class M: Meta-analysis
Systematic review
Decision analysis
Cost-effectiveness analysis

Class R: Consensus statement
Consensus report
Narrative review

Class X: Medical opinion

References

Abidov A, Rozanski A, Hachamovitch R, et al. Prognostic significance of dyspnea in patients referred for cardiac stress testing. *N Engl J Med* 2005;353:1889-98. (Class D)

Bergeron S, Ommen SR, Bailey KR, et al. Exercise echocardiographic findings and outcome of patients referred for evaluation of dyspnea. *J Am Coll Cardiol* 2004;43:2242-46. (Class D)

Berman DS, Kang X, Hayes SW, et al. Adenosine myocardial perfusion single-photon emission computed tomography in women compared with men: impact of diabetes mellitus on incremental prognostic value and effect on patient management. *J Am Coll Cardiol* 2003;41:1125-33. (Class B)

Cheitlin MD, Armstrong WF, Aurigemma GP, et al. ACC/AHA/ASE 2003 guideline update for the clinical application of echocardiography: a report of the American college of cardiology/American heart association task force on practice guidelines (ACC/AHA/ASE committee to update the 1997 guidelines for the clinical application of echocardiography). 2003. American College of Cardiology Website. Available at: http://www.acc.org/clinical/guidelines/echo/index.pdf. (Class R)

Chin ASL, Goldman LE, Eisenberg MJ. Functional testing after coronary artery bypass graft surgery: a meta-analysis. *Can J Cardiol* 2003;19:802-08. (Class M)

Cole CR, Blackstone EH, Pashkow FJ, et al. Heart-rate recovery immediately after exercise as a predictor of mortality. *N Engl J of Med* 1999;341:1351-57. (Class B)

Eagle KA, Berger PB, Calkins H, et al. ACC/AHA guideline update on perioperative cardiovascular evaluation for noncardiac surgery: a report of the American college of cardiology/American heart association task force on practice guidelines (committee to update the 1996 guidelines on perioperative cardiovascular evaluation for noncardiac surgery). 2002. Available at: www.acc.org/clinical/guidelines/perio/dirindex.htm. (Class R)

Fleischmann KE, Hunink MGM, Kuntz KM, et al. Exercise echocardiography or exercise SPECT imaging: a meta-analysis of diagnostic test performance. *JAMA* 1998;280:913-20. (Class M)

Frolkis JP, Pothier CE, Blackstone EH, Lauer MS. Frequent ventricular ectopy after exercise as a predictor of death. *N Engl J Med* 2003;348:781-90. (Class B)

Gibbons RJ, Abrams J, Chatterjee K, et al. ACC/AHA 2002 guideline update for the management of patients with chronic stable angina: a report of the American college of cardiology/American heart association task force on practice guidelines (committee to update the 1999 guidelines for the management of patients with chronic stable angina). 2002a. Available at: www.acc.org/clinical/guidelines/stable/stable.pdf. (Class R)

Gibbons RJ, Balady GJ, Bricker JT, et al. ACC/AHA 2002 guideline update for exercise testing: a report of the American college of cardiology/American heart association task force on practice guidelines (committee on exercise testing). 2002b. Available at: www.acc.org/clinical/guidelines/exercise/dirindex.htm. Accessed on August 21, 2003. (Class R)

Kertai MD, Boersma E, Bax JJ, et al. A meta-analysis comparing the prognostic accuracy of six diagnostic tests for predicting perioperative cardiac risk in patients undergoing major vascular surgery. *Heart* 2003;89:1327-34. (Class M)

Kim C, Kwok YS, Heagerty P, et al. Pharmacologic stress testing for coronary disease diagnosis: a meta-analysis. *Am Heart J* 2001;142:934-44. (Class M)

References

Kligfield P, Lauer MS. Exercise electrocardiogram testing: beyond the ST segment. *Circulation* 2006;114:2070-82. (Class R)

Klocke FJ, Baird MG, Bateman TM, et al. ACC/AHA/ASNC guidelines for the clinical use of cardiac radionuclide imaging: a report of the American college of cardiology/American heart association task force on practice guidelines (ACC/AHA/ASNC committee to revise the 1995 guidelines for the clinical use of cardiac radionuclide imaging). 2003. American College of Cardiology Website. Available at: http://www.acc.org/clinical/guidelines/radio/rni_fulltext.pdf. (Class R)

Lauer MS, Francis GS, Okin PM, et al. Impaired chronotropic response to exercise stress testing as a predictor of mortality. *JAMA* 1999;281:524-29. (Class B)

Mark DB, Hlatky MA, Harrell FE Jr, et al. Exercise treadmill score for predicting prognosis in coronary artery disease. *Ann Intern Med* 1987;106:793-800. (Class C)

Mark DB, Shaw L, Harrell FE Jr, et al. Prognostic value of a treadmill exercise score in outpatients with suspected coronary artery disease. *N Engl J Med* 1991;325:849-53. (Class C)

Mieres JH, Shaw LJ, Arai A, et al. Role of noninvasive testing in the clinical evaluation of women with suspected coronary artery disease: consensus statement from the cardiac imaging committee, council on clinical cardiology, and the cardiovascular imaging and intervention committee, council on cardiovascular radiology and intervention, American Heart Association. *Circulation* 2005;111:682-96. (Class R)

Morise AP, Lauer MS, Froelicher VF. Development and validation of a simple exercise test score for use in women with symptoms of suspected coronary artery disease. *Am Heart J* 2002;144:818-25. (Class C)

Poornima IG, Miller TD, Christian TF, et al. Utility of myocardial perfusion imaging in patients with low-risk treadmill scores. *J Am Coll Cardiol* 2004;43:194-99. (Class B)

Quiñones MA, Verani MS, Haichia RM, et al. Exercise echocardiography versus ^{201}Tl single-photon emission computed tomography in evaluation of coronary artery disease: analysis of 292 patients. *Circulation* 1992;85:1026-31. (Class C)

Sanfilippo AJ, Abdollah H, Knott TC, et al. Stress echocardiography in the evaluation of women presenting with chest pain syndrome: a randomized, prospective comparison with electrocardiographic stress testing. *Can J Cardiol* 2005;21:405-12. (Class C)

Shaw LJ, Peterson ED, Kesler K, et al. A meta-analysis of predischarge risk stratification after acute myocardial infarction with stress electrocardiographic, myocardial perfusion, and ventricular function imaging. *Am J Cardiol* 1996;78:1327-37. (Class M)

Sox HC Jr. Probability theory in the use of diagnostic tests. An introduction to critical study of the literature. *Ann Intern Med* 1986;104:60-66. (Class not assignable)

Taillefer R, Ahlberg AW, Masood Y, et al. Acute beta-blockade reduces the extent and severity of myocardial perfusion defects with dipyridamole Tc-99m sestamibi SPECT imaging. *J Am Coll Cardiol* 2003;42:1475-83. (Class A)