CME Feature

Choosing a Stress Test

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The Association of Black Cardiologists (ABC), Inc. is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to sponsor continuing medical education for physicians.

The Need:
Cardiologists need to stay current on the latest noninvasive techniques for detecting coronary heart disease and for determining appropriate therapeutic approaches based on the assessment of risk. Non-cardiologists also need to understand when cardiovascular diagnostic tests are indicated and what each specific test type is relevant for assessing which conditions and determining appropriate triage. There is evidence that stress testing is underappreciated by non-cardiologists as a risk-assessment tool. As such, referrals to cardiologists for such testing is no doubt underutilized.

Learning Objectives:
The goals of this article are 1) to provide the clinician with knowledge and understanding of the appropriate use of noninvasive techniques for detecting CHD, 2) to have the clinician distinguish between the various types of stress testing, and 3) to enable the clinician to weigh the incremental diagnostic value of each type of technique relative to the cost and risk to the patient. .

After reading this article, the physician reader should be able to:
- understand the validity of noninvasive diagnostic test data in answering clinical questions being investigated;
- know the pretest likelihood of the CHD condition being assessed;
- know the incremental diagnostic value of each test type;
- appreciate the relative cost of each test; and,
- understand the availability/reliability of each testing modality in the broad community and within different types of institutions.

CME Material:
On page 23 of this publication is a combined Self-Test and Answer Sheet. To receive CME credit, please follow the instructions detailed on the test form. This activity was planned and produced in accordance with the ACCME Essentials. The ABC designates this continuing medical education activity for two (2) credit hours in Category 1 of the Physician's Recognition Award of the American Medical Association.

INTRODUCTION

Choosing the correct method of noninvasive assessment in the context of coronary artery disease involves several important cognitive steps, both in choice of stress modality and technique. These decisions ultimately have significant bearing on the clinical relevance of the reported results. These cognitive steps can be easily divided into:

1. the validity of data derived from the test in answering the clinical question being investigated,
2. the pretest likelihood of the condition in the patient being tested,
3. the incremental prognostic value of the test being ordered over existing clinical data,
4. the cost of the test, and finally,
5. the availability and reliability of a testing modality within the particular institution in which the test is being ordered.

After the initial decision is made to proceed with a particular noninvasive modality for assessing the patient with coronary artery disease, the assessment strategy is further refined based on patient factors such as exercise status, likelihood of presence of recent coronary plaque rupture, body habitus, and presence or absence of active bronchoconstriction. To use a noninvasive test in the management of specific clinical groups of patients with coronary artery disease, there has to be established validity in the literature for use in this setting. Fortunately, in ischemic heart disease, all the commonly available non-invasive testing modalities

have been widely applied to disparate clinical situations across the spectrum of ischemic heart disease presentations.

The clinical question, therefore, is not whether stress tests should be used to assist in diagnosis and risk assessment, but rather what *type of test* should be used in the context of *which* clinical settings. This paper addresses this critical question.

CLINICAL SETTINGS

Initial Assessment of Coronary Artery Disease

Testing asymptomatic patients for coronary artery disease relies heavily on the presence of cardiac risk factors increasing the pre-test likelihood of the condition. Generally, testing in asymptomatic low-likelihood populations generates a majority of false positives, rendering the test of no clinical utility. In particular, an expensive test such as an echocardiographic stress test or myocardial perfusion imaging study should not be performed in asymptomatic patients with a low pre-test likelihood of coronary artery disease.

In the symptomatic patient, the pre-test likelihood of coronary disease should be calculated from patient data. These include the following:

- age
- total cholesterol
- HDL cholesterol
- smoking status
- systolic blood pressure
- presence or absence of diabetes mellitus
- presence or absence of electrocardiographic criteria for left ventricular hypertrophy.

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Patients with intermediate (20 - 80%) pre-test likelihood of disease are most likely to benefit from performance of a non-invasive stress test. If a simple diagnosis is all that is required, then standard exercise treadmill testing is generally the first step. If further information on prognosis and extent of coronary disease is required, there may be a place for a stress-imaging procedure as a first step.[1]

Chronic Stable Angina

Patients with chronic stable angina represent an exceedingly difficult group to follow. A fair number of these patients do very well over the long term, but morbid and mortal events are not easily predicted. A study by Norwegian investigators in 1993 followed 50 patients with chronic stable angina over 15 years. The mortality rate was 28%, all of which were cardiac deaths.[2] All the patients in the study had regular yearly exercise treadmill testing. However, review of the data demonstrated that neither clinical nor exercise test variables predicted mortality in the majority of patients. Studies such as this one, and the fact that approximately one-third of coronary artery disease patients initially present with sudden cardiac death, crystallize the clinical difficulties in managing this group of patients.

Asymptomatic progression of coronary artery disease is common. The warranty period of a myocardial perfusion study is only two years. Very active patients (exercise capacity >5 METS), with stable angina pectoris, should be observed closely for changes in exercise tolerance. Sequential symptom-limited exercise treadmill tests can be used to document changes in exercise tolerance over time and also to determine any new markers of disease progression, such as ST segment depression, exercise-induced arrhythmias, or heart failure. In sedentary patients with exercise capacity <5 METS, a baseline imaging study should be done. If the coronary anatomy is known and disease is very limited, then these patients can be followed with a repeat imaging study in three to five years. If the baseline coronary anatomy is not known, or, if multivessel nonobstructive coronary disease is present, then an imaging study should be performed every two to three years.[3]

Unstable Angina

The United States Agency for Health Care Policy and Research (AHCPR) has set a goal of reduced annual mortality <1%, as the threshold for continuing medical therapy without further testing in patients with unstable angina.[4] Myocardial perfusion imaging is the only noninvasive prognostic tool that achieves this level. A normal perfusion scan, with or without the presence of coronary artery disease, confers a less than 1% yearly mortality.

Studies with stress echocardiography are promising but show a much wider range of mortal and morbid events of between 0.85% and 3% per year. Based on current AHCPR guidelines, a normal stress echocardiogram would not necessarily preclude further testing. It is anticipated that as further information becomes

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available, the medium-term prognostic value of this imaging modality will become much better defined. In the presence of an unstable coronary artery plaque, cardiac stress testing should not be performed, as it could lead to exacerbation of the clinical course. Cardiac stress testing includes regular treadmill exercise testing and possibly dobutamine stress testing. Adenosine and dipyridamole are intravenous vasodilator agents used in conjunction with myocardial perfusion imaging that do not require the provocation of myocardial ischemia for detection of coronary stenoses. These agents have been safely used at 48 hours post-admission in unstable angina patients.[5]

Post-myocardial Infarction Patients

Post-myocardial infarction patients with known coronary artery disease should only be triaged to cardiac catheterization if they have markers of high risk. High-risk markers for post-MI patients are listed in Table 1 below. All other patients should undergo risk stratification with the goal of identifying patients with severe residual stenosis in the culprit vessel or, with significant ischemia at a distance from the culprit vessel, necessitating a revascularization strategy to improve patient longevity.

MARKETS FOR HIGH RISK IN POST-MI

- Recurrent Ischemia
- Depressed LV Function
- Widespread ECG Changes
- Prior MI

In this setting, a low-level exercise treadmill test can be performed pre-discharge at four to seven days post-myocardial infarction, followed by a symptom-limited test at three weeks. Alternatively, myocardial perfusion imaging or a stress echocardiogram may be performed to obtain the same clinical data with improved sensitivity and greater prognostic information.

Pre- and Post-revascularization Assessment

With the advent of percutaneous transluminal coronary angioplasty (PTCA) and the attendant uncertainty regarding the effectiveness of this therapy, there has probably been redundant noninvasive testing to assess for efficacy of treatment or lack thereof. It has become clear that myocardial perfusion defects will persist even after clinically successful angioplasty for relief of symptoms. It does appear, however, that stenting improves coronary flow reserve to a greater extent than does angioplasty alone. As a result, myocardial perfusion defects are significantly less post-stenting than after balloon-only angioplasty procedures.

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The most recent recommendations for cardiac stress testing are essentially geared toward patients who redevelop symptoms. However, if patients are sedentary or have the additional risk of a rapidly progressive disease such as diabetes, post-transplant arteriopathy, or end-stage renal disease, the approach outlined under chronic stable angina should be followed. Exercise treadmill testing is often sufficient, since any provocation of ischemia in this group is usually considered enough reason to proceed to angiography if initially rendered asymptomatic post-revascularization.

In institutions that utilize a strategy of early aggressive use of coronary angiography prior to functional testing, apparent intermediate coronary stenoses noted in multiple vessels creates a conundrum in terms of which, if any, vessels to revascularize. In this setting, myocardial perfusion imaging has proven exceedingly useful in determining the functional significance of angiographically intermediate stenoses.[6]

Left Ventricular Dysfunction

Noninvasive cardiac testing in patients with left ventricular dysfunction centers around etiology and focuses on the viability of hypokinetic and akinetic left ventricular segments. This group of patients has limited exercise tolerance. Thus, they are unlikely to achieve an adequate workload for assessment during an exercise treadmill test. Frequently, resting electrocardiographic abnormalities are also present, which further confound this methodology.

Use of stress echocardiogram and myocardial perfusion imaging is also problematic in this group of patients. Using the echocardiogram, it is difficult to assess either improvement or worsening in a ventricular segment that is already hypokinetic at rest. Patchy non-segmental defects may be seen on the myocardial perfusion study in this group of patients even in the absence of epicardial stenoses. This finding is most likely due to coronary flow reserve abnormalities. If, however, large segmental confluent defects are found, these usually indicate the presence of ischemic heart disease.

Both stress echocardiogram and myocardial perfusion imaging are of equivalent value in assessing myocardial viability. The stress echocardiogram techniques tend to be somewhat more specific and the perfusion imaging techniques tend to be somewhat more sensitive.

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Preoperative Assessment

In March 1996, an American College of Cardiology/American Heart Association taskforce published a report on guidelines for perioperative cardiovascular evaluation for non-cardiac surgery.[7] These guidelines combine the presence of major and intermediate clinical predictors with the surgery-specific risks to determine which patients should undergo noninvasive testing. Detailed review is outside the scope of this paper.

Since most of the patients who will be referred for noninvasive testing will be those incapable of achieving a workload of 4 METS, exercise treadmill testing is not recommended. Dobutamine stress echocardiogram and myocardial perfusion imaging appear to have equivalent clinical utility in this group of patients. Test selection will be based on other factors, such as the availability and reliability of a particular technique, and any other ancillary information that may be required.

Evaluation of Chest Pain in the Emergency Department

With the current emphasis on cost containment within the healthcare system, attention has focused on patients presenting to the emergency department with chest pain. It is estimated that $10-13 billion is spent each year in the U.S. on evaluating patients in coronary care units for possible myocardial infarction, who do not have an acute coronary syndrome. The appropriate methodology for chest pain triage in the emergency room is still in a state of flux. However, large-scale clinical trials are presently being embarked upon, which, in due course, will anchor our clinical approach to this important group of patients. What *is* obvious at this point in time is that a well-trained interdisciplinary team approach obtains the best results.

Most research data to date in chest pain triage, has been with myocardial perfusion imaging, which appears to appropriately triage patients so that only those patients with significant coronary artery disease are admitted. Appropriate use of myocardial perfusion imaging also helps to prevent the inadvertent discharge home of those patients with atypical presentation but significant coronary disease. Only patients determined to be at mild to moderate risk of myocardial infarction or those with unstable coronary ischemic syndromes need to undergo cardiac imaging protocols. Patients determined to be at high risk should be admitted. There may be a place for immediate exercise treadmill testing in very low-risk patients, but this approach remains to be subjected to multi-center prospective trials to establish its efficacy and safety.

Although myocardial perfusion imaging is an "immobile" subspecialty, certain factors favor its utility as the imaging test of choice in the emergency room. These are: 1) interpretable studies in all patients regardless of physical characteristics, 2) less dependency on individual operator competence in acquiring diagnostic quality studies, and 3) the ability to obtain an immediate "freeze-frame" snapshot of myocardial perfusion as soon as the radioisotope is injected acutely with a broad time window for subsequent image acquisition (~ 2.5 hrs) while the patient is being stabilized. Several single institution and multi-institution studies have suggested a drastic reduction in inappropriate discharge from the emergency room when the judicious use of perfusion imaging is incorporated into a well-defined

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emergency room assessment protocol. Reports using resting echocardiography in the emergency department are also encouraging, but there is less available data at the present time.[8]

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Determining Pre-test Likelihood

In a universe of imperfect medical tests, Bayes' theorem is particularly pertinent in our understanding of which patient requires a particular test. When such a test is applied to a patient with low likelihood of disease (for example, less than 5% pre-test likelihood), the chances of a positive test representing true disease is markedly diminished, and the positive predictive value of the test is significantly reduced. Even in a patient with high pre-test likelihood of the disease, performance of the test does not significantly improve the positive predictive value and in such an instance, the test could be considered unnecessary, at least for diagnostic purposes.

Physicians should not view this situation as an unfriendly quasi-statistical invasion on medical prerogatives. On the contrary, a major physician task now becomes determining the appropriate patients to be subjected to expensive and potentially risky testing procedures. In general, for diagnostic purposes, the pre-test likelihood of coronary artery disease should be in the intermediate 20 - 80% range to attain meaningful changes in probability of disease with testing. Several nomograms for both men and women are commonly used for estimating pre-test likelihood of disease in the setting of ischemic heart disease.[1]

Incremental Diagnostic and Prognostic Value of Additional Tests

By requesting an additional test, the physician is hoping for greater diagnostic certainty or prognostic power. Myocardial perfusion imaging and stress echocardiography techniques provide both. Because myocardial perfusion imaging has been widely available longer than stress echocardiography, the literature related to the former is more voluminous and more broadly accepted. There are several studies documenting the incremental diagnostic and prognostic value of myocardial perfusion imaging over clinical and exercise variables. In one study by Hachamovitch et al., there was clearly additional significant risk stratification within each Duke treadmill group based on semi-quantitative myocardial perfusion scores, even after prognostic stratification by the Duke exercise treadmill score.[9] Interestingly enough, individuals with the highest risk perfusion studies in all three groups of Duke treadmill scores had similar rates of hard events such as death and myocardial infarction (approximately 8%). The converse was also true. A normal myocardial perfusion study, even in the presence of known coronary atherosclerosis, had a low event rate equivalent to that of age-matched normal controls.

There is always a strong clinical need to assess the cardiac patient's response to symptom-limited exercise testing. This provides important information for quality of life and exercise prescription determination. It precisely defines, by direct observation, the actual limiting symptoms with exertion. Exercise testing also affords the opportunity to reveal other non-atherosclerotic diagnoses such as asthma, chronic obstructive lung diseases, or exercise-induced hypertension.

Formal cardiopulmonary exercise testing is often needed to separate cardiac, pulmonary, and musculoskeletal causes of exercise limitation. Generally, noninvasive myocardial perfusion imaging and stress echocardiography are expensive and should only be performed if the incremental information is needed for clinical decision-making and prognostication.

NON-CLINICAL FACTORS

Cost of the Test

Standard exercise treadmill testing is significantly less expensive than either stress echocardiography or myocardial perfusion imaging, the latter two being of similar cost to the patient. Since there are infinitely more atherosclerotic plaques present in the general population than require intervention, overall healthcare

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costs can be reduced with judicious use of non-invasive imaging. Despite the costs incurred with non-invasive testing, a significant number of cardiac catheterizations and coronary interventions can be prevented using these testing modalities. Preliminary data in

nuclear cardiology suggest that this is the case for myocardial perfusion imaging.[10] A recent multicenter collaboration proved that the use of perfusion techniques prevents cardiac catheterization and intervention costs downstream, resulting in lower per capita costs for management of ischemic heart disease.

Availability and Reliability of the Tests

Generally, because of its low cost and moderate diagnostic and prognostic utility, the exercise treadmill test will be the test of first choice in ischemic heart disease. There are, however, specific patient groups who would not benefit from this type of testing and these patients should be triaged directly to an imaging study (See Table 2).

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When considering whether to proceed to an cardiac imaging study for incremental clinical information, it is imperative that the physician have data on sensitivity and specificity of that imaging study for the particular institution in which the test is being performed. It is important that the echocardiography or nuclear cardiology laboratory enters all patients undergoing cardiac catheterization into a database so that figures for sensitivity and specificity can be generated from these total numbers. In cases where a test is already well established and used routinely to decide whether or not to proceed to cardiac catheterization, specificity in the total group of low-likelihood patients (those with < 5% likelihood of coronary artery disease) presenting to that laboratory should be assessed. This is known as the normalcy rate. This figure does not

TABLE 2
Selecting Stress Type based on Exercise Status

Exercise Status	Choice of Stress Protocol	Patient Characteristics
Good exercise tolerance	TXT	• Expected to achieve > 85% MPHR; > 5 METS workload • Normal baseline EKG
	TXT + MPI or Stress Echo	• Abnormal baseline EKG • High pre-test likelihood needing prognostic/risk stratification information
Limited exercise capacity	TXT + MPI + vasodilator agent (Aden* or Dip) DSE **	• Unsure of ability to achieve 7-10 METS or 85% MPHR • On antianginal medications with negative chronotropic action and DO NOT WISH to stop medications for 48 hrs.
No exercise indicated	Rest MPI + vasodilator agent (Aden* or Dip) DSE **	• Unable to exercise • Close to acute plaque rupture (AMI; unstable angina) • LBBB
	Rest MPI Rest Echo (+ low-dose dobutamine for viability)	• Viability only testing • Emergency department triage of chest pain
Unrelated to exercise status	MPI using Tc-99m radiotracers ± vasodilator agents	• Very large body habitus, especially with markedly increased torso adiposity

** Symptams with DSE are not necessarily related to exercise symptoms in daily life. DSE not advised for patients on ß-blockers and is not likely to be as safe in potentially unstable patients.

* For severe bronchospastic patients with limited ventilatory reserve, dobutamine is the preferred pharmacologic agent. Inhaled bronchodilator pretreatment increases tolerability of adenosine in this patient group.

Abbreviations: TXT = treadmill stress test; MPHR = maximum predicted heart rate; MPI = myocardial perfusion imaging; Aden = adenosine; Dip = dipyridamole; DSE = dobutamine stress echocardiography; AMI = acute myocardial infarction; LBBB = left bundle branch block

have the benefit of cardiac catheterization validation, but the expected incidence of disease in this group, and hence, the number of positive studies, should be appropriately low. When evaluating competing imaging techniques, there is no substitute for these values. A single institution is generally more proficient in one or the other technique. Thus, this becomes the preferred technique unless inapplicable in a particular patient because of physical or clinical characteristics.

Regular review of abnormal studies with the imaging expert to provide feedback to the imager on apparently false positive or negative studies will go a long way to improving your ability to utilize the non-invasive imaging approach for management of coronary artery disease. It is only with this type of relationship that an appreciation of the reliability and significance of an imaging finding can really develop between imager and clinician. The answer will never be to submit all patients to cardiac catheterization, especially in this era of cost containment. Furthermore, present imaging techniques give us the ability to avoid cardiac catheterization in a significant number of patients.

Choice of Test Based on Patient Characteristics

The main patient characteristic that affects utilization of treadmill testing and myocardial perfusion imaging is the exercise capacity. Table 2 provides an algorithm outlining the choice of stress protocol based on different levels of exercise capacity. Multicenter trial data presents strong evidence for the safety of vasodilator stress (adenosine and dipyridamole) early post myocardial infarction.[11] Safety data is not as strong for dobutamine stress echocardiography.

Vasodilator stress is generally combined with exercise, even in patients with limited exercise capacity, since any degree of exercise improves the quality of the study for interpretation.[12] Our own preliminary observations suggest that pre-exercise and starting the adenosine infusion after exercise is begun, induces redistribution of blood flow away from the splanchnic and other nonexercising areas.[13] This results in even better target-to-background ratios and improved normal segment washout profiles. It should be emphasized that patients who have brochoconstriction, especially when this is evident on arrival at the cardiac stress laboratory, are not candidates for either adenosine or dipyridamole.

Summary

In summary, this paper discusses the important factors in choosing a stress test in the setting of manifest or probable coronary atherosclerosis. These factors, both clinical and non-clinical, are enumerated and discussed. In general, exercise testing is usually the test of first choice. The exception is for those patients unlikely to tolerate a sufficient workload to result in adequate testing. An example of his type is the patient with left ventricular dysfunction. As for cost-efficiency, the physician is encouraged to consider each test's specificity and sensitivity, based on usage in his/her institution. Further, testing patients with low-likelihood (<5%) of cardiac disease, should be avoided.

These recommendations represent one institution's approach and attempts to cover most, if not all, of the common clinical scenarios.

About the Authors

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Dr. Robinson is Co-Director of Nuclear Cardiology, Medical College of Georgia. He earned his medical degree from the University of the West Indies, Kingston, Jamaica in 1976, followed by Internal Medicine Residency, Dalhousie University, Halifax, N.S., Canada. Dr. Robinson completed his cardiology fellowship and one year of Clinical Nuclear Cardiology at the University of Calgary, Foothills Hospital, Alberta, Canada. In 1985-88 Dr. Robinson was awarded the Alberta Heritage Clinical Research Fellowship at the University of Calgary. He subsequently became Director of Nuclear Cardiology and consultant cardiologist at The Moncton Hospital, N.B., Canada. Since 1994, Dr. Robinson has been Co-director of Nuclear Cardiology at the Medical College of Georgia. Additionally, he was formerly Chief of Cardiology Services, Veterans Administration Medical Center, Augusta, Georgia. Dr. Robinson's research interests include capacitance physiology, assessment of coronary flow reserve in coronary artery disease, and assessment of myocardial viability. His research on transient ischemic dilation in myocardial perfusion studies was abstracted by Practical Reviews in Nuclear Medicine 2000 for dissemination to physicians in the field.

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