JACC Vol. 8, No. 3
September 1986:725–38

SPECIAL REPORT

Guidelines for Exercise Testing

A Report of the American College of Cardiology/American Heart Association Task Force on Assessment of Cardiovascular Procedures (Subcommittee on Exercise Testing)

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Preamble

It is becoming more apparent each day that despite a strong national commitment to excellence in health care, the resources and personnel are finite. It is, therefore, appropriate that the medical profession examine the impact of developing technology on the practice and cost of medical care. Such analysis, carefully conducted, could potentially impact on the cost of medical care without diminishing the effectiveness of that care.

To this end, the American College of Cardiology and the American Heart Association in 1980 established a Task Force on Assessment of Cardiovascular Procedures with the following charge:

> The Task Force of the American College of Cardiology and the American Heart Association shall define the role of specific noninvasive and invasive procedures in the diagnosis and management of cardiovascular disease.
>
> The Task Force shall address, when appropriate, the contribution, uniqueness, sensitivity, specificity, indications and contraindications and cost-effectiveness of such specific procedures.
>
> The Task Force shall include a Chairman and four members, two representatives from the American Heart Association and two representatives from the American College of Cardiology. The Task Force may select ad hoc members as needed upon the approval of the Presidents of both organizations.
>
> Recommendations of the Task Force are forwarded to the President of each organization.

The members of the Task Force are: Roman W. DeSanctis, MD, Harold T. Dodge, MD, T. Joseph Reeves, MD, Sylvan L. Weinberg, MD and Charles Fisch, MD, Chairman.

The Subcommittee on Exercise Testing was chaired by Robert C. Schlant, MD and included the following members: C. Gunnar Blomqvist, MD, Robert O. Brandenburg, MD, Robert DeBusk, MD, Myrvin H. Ellestad, MD, Gerald F. Fletcher, MD, Victor F. Froelicher, Jr., MD, Robert J. Hall, MD, Ben D. McCallister, MD, Paul L. McHenry, MD, Thomas J. Ryan, MD and L. Thomas Sheffield, MD.

This document was reviewed by the officers and other responsible individuals of the two organizations and re-

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0735-1097/86/$3.50

ceived final approval in February 1986. It is being published simultaneously in *Circulation* and *Journal of the American College of Cardiology*. The potential impact of this document on the practice of cardiology and some of its unavoidable shortcomings are clearly set out in the Introduction.

Charles Fisch, MD

Indications for Exercise Testing

The American College of Cardiology/American Heart Association Task Force on Assessment of Cardiovascular Procedures was formed to make recommendations regarding the appropriate use of technology in the diagnosis and treatment of patients with cardiovascular disease. One such important technique is exercise testing; its potential role has been emphasized through recent advances in the management of patients with a variety of heart diseases. The Subcommittee recommendations for current indications for exercise testing are consensus opinions and are based on current data on the natural history of various cardiovascular disorders and the potential value of exercise testing in answering specific clinical questions. The charge to this Subcommittee was specifically limited to standard exercise testing. A separate task force has been charged with reviewing the current indications for radionuclide testing, including techniques using exercise.

The Subcommittee has not offered recommendations about resources required to perform exercise testing, specific techniques of exercise testing, training of individuals to perform exercise testing or the appropriate management of patients with positive, equivocal or negative exercise tests.

Basic to the use of any diagnostic test is the identification of the specific clinical question that is to be asked. The most frequent indications for performing exercise tests in patients with known or suspected coronary artery disease (CAD) are (1) to determine the likelihood of CAD, (2) to estimate prognosis, (3) to determine functional capacity, and (4) to determine the effects of therapy. Additional considerations regarding any diagnostic test are whether the particular test is needed and whether the results will influence management, either currently or in the future.

Indications for exercise testing may be classified as follows:

Class I. Conditions for which there is general agreement that exercise testing is justified.

Class II. Conditions for which exercise testing is frequently used but in which there is a divergence of opinion with respect to value and appropriateness.

Class III. Conditions for which there is general agreement that exercise testing is of little or no value, inappropriate or contraindicated by risk.

General contraindications to exercise testing include unstable angina prior to a period of stabilization; the presence of untreated, life-threatening arrhythmias; uncompensated severe congestive heart failure; advanced atrioventricular heart block; acute myocarditis; and critical aortic stenosis.

Exercise Testing in Patients With Symptoms or Signs Suggestive of Coronary Artery Disease or With Known Coronary Artery Disease

Summary

Class I

1. To assist in the diagnosis of coronary artery disease in male patients with symptoms that are atypical for myocardial ischemia.
2. To assess functional capacity and to aid in assessing the prognosis of patients with known CAD.
3. To evaluate patients with symptoms consistent with recurrent, exercise-induced cardiac arrhythmias.

Class II

1. To assist in the diagnosis of CAD in women with a history of typical or atypical angina pectoris.
2. To assist in the diagnosis of CAD in patients taking digitalis.
3. To assist in the diagnosis of CAD in patients with complete right bundle branch block.
4. To evaluate the functional capacity and response to therapy with cardiovascular drugs in patients with CAD or heart failure.
5. To evaluate patients with variant angina.
6. To follow serially (at 1 year or longer intervals) patients with known CAD.

Class III

1. To evaluate patients with simple premature ventricular depolarizations on the resting ECG but no other evidence of CAD.
2. To evaluate functional capacity serially in the course of an exercise cardiac rehabilitation program.
3. To assist in the diagnosis of CAD in patients who demonstrate pre-excitation (Wolff-Parkinson-White) syndrome or complete left bundle branch block on the resting ECG.

Discussion

The four basic indications for obtaining an exercise stress test in patients with known or suspected CAD are the following:

1. As a *diagnostic test* in patients with suspected CAD.
2. To assist in identifying those patients with documented CAD who are potentially at *high risk* due to advanced coronary disease and/or left ventricular dysfunction.
3. To evaluate patients after coronary artery bypass surgery or percutaneous transluminal coronary angioplasty (see section on "Exercise Testing After Specific Procedures").

4. To quantify a patient's *functional capacity* or response to therapies, and to follow the natural course of disease at appropriate intervals.

Diagnostic testing

Sensitivity and specificity. In certain clinical settings the exercise test may serve as an appropriate, supplemental aid to the history and physical examination in helping the physician decide whether a patient has ischemic heart disease. Nonetheless, the exercise test has significant limitations as a diagnostic tool and there is no justification for obtaining a test on every patient who has chest pain or other abnormalities potentially related to ischemic heart disease. For instance, the male patient over age 40 with a history of typical exertional angina pectoris rarely needs an exercise test for *diagnostic* purposes. In men whose history indicates a very high probability of CAD, an abnormal exercise test merely confirms the clinical assessment (1). On the other hand, a negative exercise test, which occurs in at least 20% of patients with typical exertional angina and with a normal resting ECG, is not likely to sway the physician from his clinical impression. In this subset of patients, however, an exercise test may sometimes be used for the evaluation of exercise tolerance, prognosis and severity of underlying CAD, rather than for diagnostic purposes.

Male patients with a history consistent with typical angina pectoris have a 90% likelihood of having significant CAD as determined by coronary arteriography (1). In contrast, the prevalence of CAD in women with a history of typical angina pectoris is as low as 60 to 70% (1). A false positive exercise ST segment response is much more frequent in women than in men, and an abnormal response in women will not greatly enhance the predictive accuracy of the clinical diagnosis based on the history alone.

The prevalence of CAD decreases substantially as chest pain becomes less typical for angina pectoris. In men with atypical chest pain an abnormal exercise test may be helpful in arriving at a clinical diagnosis of CAD. This is especially true if the ST segment depression is marked ($\geq$ 2.0 mm), appears at low levels of exercise and persists for several minutes after exercise (2). Additional abnormalities such as negative U waves or an inappropriate blood pressure or heart rate response further enhance the predictive value of the test. In patients with atypical chest pain the prevalence of CAD in men is about 2.5 times greater than in women, while the prevalence of false positive exercise ST segment responses with atypical pain is about 4.5 times greater in women than in men (1). This combination of circumstances makes the exercise ECG test in women with atypical chest pain of very limited value.

Testing of patients with abnormal baseline electrocardiograms. If the patient has diagnostic ECG changes of a previous myocardial infarction (or a previous myocardial infarction has been clinically documented), there is no reason to perform an exercise test as a diagnostic procedure. As noted in a following section, "Evaluating Prognosis and Severity of Coronary Artery Disease," however, an exercise test in such patients may be of value for detecting remote ischemia or additional myocardium at jeopardy. One can also question the appropriateness of obtaining an exercise test for the purpose of establishing a diagnosis of ischemic heart disease in some patients with abnormal baseline ST-T changes. In individuals with typical angina pectoris, the presence of baseline ECG abnormalities at rest increases the probability of CAD, and an exercise test adds little diagnostic information. Patients with left ventricular hypertrophy with repolarization abnormalities may also have false positive ST segment changes during exercise.

The presence of left bundle branch block or other major intraventricular conduction defects or the pre-excitation (Wolff-Parkinson-White [WPW]) syndrome invalidates the interpretation of additional ST segment changes during exercise. One exception is complete right bundle branch block where exercise-induced abnormal ST segment depression in the lateral precordial leads (V_{4-6}) during exercise is a reliable indicator of myocardial ischemia.

Testing of patients receiving cardiovascular drugs. In the presence of a normal baseline ECG, the digitalis glycosides may still cause a false positive ST segment depression during and following exercise. In patients taking digoxin, it is best to discontinue the drug for at least 10 to 14 days, provided there is not strong clinical contraindication. In the absence of underlying cardiac disease, patients who are receiving cardiac glycosides will usually exhibit no greater than 1.0 mm of additional ST segment depression during or after exercise, although some have 2.0 mm depression. Cardiac abnormalities other than myocardial ischemia, such as left ventricular hypertrophy or mitral valve prolapse, may accentuate significantly the "digitalis ST segment effect" during exercise (3).

The beta-blocking agents present special problems in virtually every area of clinical exercise testing. In the area of *diagnostic* testing, these agents often prevent the patient from attaining the desired heart rate-blood pressure product and also increase the prevalence of false negative ST segment responses. To abruptly withdraw a beta-blocking agent from a patient prior to performing a diagnostic exercise test can be hazardous in the presence of advanced CAD. Initial diagnostic exercise testing is therefore usually performed without discontinuing the beta-blocking agent.

Calcium antagonists and nitrates may increase the exercise duration or work load required to produce limiting symptoms or abnormal ST segment depression, and in some cases may prevent the appearance of the abnormal ST segment changes. If the purpose of the exercise test is to establish a diagnosis of ischemic heart disease, these drugs should be withheld, if feasible, for at least 12 hours.

Ventricular arrhythmias and exercise testing. In an otherwise clinically healthy subject there is little or no correlation between the findings of isolated or occasional premature ventricular depolarizations (PVDs) at rest in the presence of CAD. Exercise testing of such individuals is not appropriate for the diagnosis of CAD unless major risk factors are also present.

Contrary to earlier beliefs, the suppression of PVDs during exercise testing does not exclude the presence of underlying CAD. PVDs that increase in frequency and/or complexity during exercise are not necessarily diagnostic of underlying ischemic heart disease (4). The appearance of PVDs during exercise in a patient who is apparently free of such arrhythmia at rest is a nondiagnostic finding (5). Multiform and consecutive PVDs are not uncommon during maximal exercise testing although ventricular tachycardia sustained for more than 3 to 4 beats is rare (5). The appearance of frequent PVDs during exercise in patients with recent myocardial infarction may have clinical significance.

Evaluation of functional capacity

In selected patients with CAD the evaluation of functional capacity is a valid indication for an exercise test. The estimate of functional capacity is useful for advice about safe work or recreational activities. It may also be used to evaluate the need for or the response to medical and surgical therapies.

Evaluating prognosis and severity of coronary artery disease

In patients who have an established diagnosis of CAD, the exercise test is a valuable tool for assessing the functional severity of underlying CAD and the prognosis or potential risk for future cardiac events. The test results may also aid in directing further diagnostic and therapeutic interventions. Several functional, hemodynamic and electrocardiographic parameters measured during and after exercise testing have been shown to correlate with severity of CAD (Table 1). Not all of these indicators, however, have been tested by appropriate clinical trials designed to determine their prognostic significance.

McNeer and colleagues (6) demonstrated that the duration of exercise, the maximal exercise heart rate and the ST segment response discriminated between patients with low and high survival rates, even when comparable anatomic CAD was present. A more recent report from the Coronary Artery Surgery Study confirmed these findings (7).

The study by McNeer and colleagues (6) did not address the prognostic significance of other parameters that have been correlated with significant, multiple vessel CAD, such as downsloping ST segment depression at low exercise heart rates or work loads (8), an inappropriate persistence of ST segment depression after exercise (8), an abnormal ST segment depression in multiple leads (2), and an abnormal systolic blood pressure response (9). A sustained decrease in systolic blood pressure following an initial, appropriate rise during submaximal exercise is a marker of severe myocardial ischemia. However, normal individuals may also exhibit a decrease in systolic blood pressure during maximal or near-maximal exercise. A failure of the systolic blood pressure to rise above 130 mm Hg during symptom-limiting exercise testing has been correlated with advanced left ventricular dysfunction (10). This finding in patients after recovery from myocardial infarction tends to define a group who have a higher morbidity and mortality during the subsequent year. Beta-blocking agents and combined alpha- and beta-blocking agents, such as labetalol, may also cause a delay in the normal rise of systolic blood pressure during exercise.

Table 1. Exercise Test Parameters Associated With Poor Prognosis and/or Increased Severity of CAD

Duration of symptom-limiting exercise
Failure to complete Stage II of Bruce protocol or equivalent work load (≤ 6.5 METS*) with other protocols
Exercise heart rate (HR) at onset of limiting symptoms
Failure to attain HR ≥ 120/min (off beta-blockers)
Time of onset, magnitude, morphology and postexercise duration of abnormal horizontal or downsloping ST segment depression
Onset at HR < 120/min or ≤ 6.5 METS
Magnitude ≥ 2.0 mm
Postexercise duration ≥ 6 min
Depression in multiple leads
Systolic BP response during or following progressive exercise
Sustained decrease of > 10 mm Hg or flat BP response (≤ 130 mm Hg) during progressive exercise
Other potentially important determinants
Exercise-induced ST segment elevation in leads other than aVR
Angina pectoris during exercise
Exercise-induced U wave inversion
Exercise-induced ventricular tachycardia

*Energy expenditure at rest, equivalent to an oxygen uptake of approximately 3.5 ml O_2 per kilogram body weight per minute.

Exercise-induced ST segment elevation appearing in leads with abnormal Q waves reflecting a previous myocardial infarction are usually associated with dyskinetic left ventricular wall motion (11). Exercise-induced ST segment elevation that develops in leads without abnormal Q waves or a history of variant angina is usually associated with a fixed, high-grade coronary artery stenosis. Exercise-induced negative U waves have been correlated with high grade stenosis in either the proximal left anterior descending or the left main coronary arteries (12).

Exercise-induced angina pectoris is an independent variable that identifies a cohort of subjects at higher risk of subsequent coronary events (13). The same is true of patients who demonstrate *chronotropic incompetence,* defined as a failure of the exercise heart rate to rise to within two standard deviations of the expected increase (14,15).

It is apparent that some of the parameters listed in Table 1 may be less reliable for estimating prognosis and severity of CAD if the patient is receiving a beta-blocking agent. On the other hand, almost half of the patients in McNeer's study (6) were receiving propranolol at the time of their exercise tests, and yet the significance of exercise duration and ST segment response remained valid.

Testing of patients unable to perform lower extremity exercise

Treadmill or bicycle testing is often impractical or suboptimal in individuals with vascular, neurologic or orthopedic impairment or the lower extremities. Dynamic upper extremity exercise testing is a useful alternative in these patients. While some investigators found arm ergometry less sensitive than treadmill testing in detecting CAD even when the same peak rate-pressure product is achieved (16), others have demonstrated no difference between tests (17). Assessment of tolerance to arm exercise may prove useful in evaluating patients whose occupations require primarily upper extremity work.

Conclusion

In general, the exercise test should be viewed as a potential adjunct to the initial clinical assessment of the patient. Optimal use of the exercise test requires that the physician observe the patient during the test and measure multiple responses, of which the exercise ECG is one. Exercise stress testing has marked limitations for the diagnosis of CAD, especially in certain subsets of patients. There is no indication for applying the test to all patients being evaluated for chest pain or other clinical manifestations potentially related to CAD. Even when an exercise stress test is obtained primarily for diagnostic purposes, valuable functional and prognostic information may also be obtained. Existing data support the concept that prognosis in patients with CAD is not entirely dependent on the extent and severity of anatomic lesions. Some patients who demonstrate a well preserved functional capacity with symptom-limited exercise have a relatively good prognosis with medical management alone, even in the presence of advanced CAD. In such patients, serial exercise tests at approximately 1 year intervals may be useful in guiding long-term management. Marked impairment of exercise tolerance, with or without other abnormal indicators of advanced CAD, warrants prompt consideration of further diagnostic studies.

Screening of Apparently Healthy Individuals

Summary

Class I — none

Class II

1. To evaluate asymptomatic male patients over age 40 in special occupations (pilots, firemen, police officers, bus or truck drivers and railroad engineers).
2. To evaluate asymptomatic male patients over the age of 40 with two or more of the following increased risk factors for CAD: serum cholesterol over 240 mg/dl, blood pressure $\geq 160/\geq 90$, cigarette smoking, diabetes mellitus or a family history of CAD with onset under the age of 55 years.
3. To evaluate male patients over the age of 40 who are sedentary and plan to enter a vigorous exercise program.

Class III

1. To evaluate asymptomatic, apparently healthy men or women with no risk factors for CAD.
2. To evaluate men or women with a history of chest discomfort not thought to be of cardiac origin.

Discussion

Table 2 summarizes nine follow-up studies that used maximal or near-maximal exercise testing to screen asymptomatic individuals for latent CAD and one study that evaluated men and women with atypical chest pain. The populations in these studies were tested and followed for the CAD end points of angina pectoris, acute myocardial infarction and sudden death.

There has been controversy over whether exercise testing provides additional prognostic information in normal men in the absence of conventional risk factors. In general, angiographic studies have confirmed the low predictive value of an abnormal exercise test response in men or women without conventional risk factors or symptoms. Similar results were also found in epidemiological studies of populations with a low prevalence of CAD. Thus, an exercise test is generally not appropriate in these patients.

Indications for screening apparently healthy individuals

Because it will be some time before CAD can be completely prevented, it is advisable to evaluate screening methods for diagnosing the earliest signs or symptoms of myocardial ischemia in individuals at increased risk for CAD. The use of exercise testing to induce myocardial ischemia not detectable at rest deserves consideration. The exercise ECG has a sensitivity of approximately 50% and a specificity of 90% in apparently healthy individuals (Table 2). The different reported predictive values are related to its use in populations with different prevalences of coronary disease (Appendix B). At present, it seems reasonable to screen men over the age of 40 years who have two or more strongly abnormal risk factors or a family history of premature cardiovascular disease. The potential iatrogenic problems resulting from screening should always be considered, and test results should be thought of as probability statements, not as absolutes.

It is difficult to choose a chronological age after which exercise testing is advisable as a screening technique prior to beginning an exercise program, since physiological age is important. In general, if the exercise is more strenuous than vigorous walking, most men over the age of 40 will benefit from such testing, especially in the presence of a

Table 2. Results of Exercise ECG Testing in Nine Prospective Studies Screening Asymptomatic Men for Latent CAD and One Study Evaluating Men and Women With Atypical Chest Pain Using Only ST Segment Depression as the Criterion for Abnormality

Principal Investigator	No. of Patients	Incidence of CAD (%)	Years of Follow-Up	Abnormal Exercise Test (%)	Sensitivity (%)	Specificity (%)	Predictive Value (%)	Relative Risk (×)
Bruce (18)	221	2.3	5.0	11.0	60	91	14	14.0
Aronow (19)	100	9.0	5.0	16.0	67	92	46	14.0
Cumming (20)	510	4.7	3.0	13.0	58	90	25	10.0
Froelicher (21)	1,390	3.3	6.3	10.0	61	92	20	14.0
Allen (22)	356	9.6	5.0	23.0	41	79	17	2.4
Bruce (23)	2,365	2.0	6.0	11.0	30	91	5	3.5
McHenry (24)	916							
Initial		7.1	12.7	2.5	14	98	39	6.0
Serial		...	...	6.7	32	95	34	6.4
MacIntyre (25)	578							
Men 47–57		6.9	8.0	4.0	16	97	26	4.0
Manca (26)								
Men	947	5.0	5.2	18.0	67	84	18	10.0
Women	508	1.6	5.2	28.0	88	73	5	15.0
Average								
Men only		5.4	5.4	13.0	50	90	21	9.0

× = -fold.

strong family history of premature coronary disease (i.e., family members aged less than 55 years with coronary event), two or more increased risk factors (serum cholesterol over 240 mg/dl, cigarette smoking, systemic hypertension ≥160/≥90, or diabetes mellitus), or a history suggestive of myocardial ischemia.

Screening of airline pilots. The character of the demanding work of airline pilots often makes it difficult for them to maintain a healthy life-style. As a result, many are overweight, deconditioned and smoke heavily. These pilots should avail themselves of the benefits of preventive medicine, including periodic assessment of their physical work capacity, their response to stress and the probability of their having underlying coronary atherosclerosis. Similar considerations apply to other individuals involved in work that may impact upon public safety, such as truck or bus drivers, railroad engineers, firemen and policemen.

Exercise Testing in Patients Soon After Myocardial Infarction

Summary

Class I

1. To evaluate the prognosis and functional capacity of patients with CAD soon after an uncomplicated myocardial infarction (predischarge or early postdischarge).

Class II

1. To evaluate patients who have a Class I indication but baseline electrocardiographic changes or coexisting medical problems that limit the value of the exercise test. In some of these patients, exercise testing may still yield clinically valuable information (duration of exercise, blood pressure response, production of chest discomfort, etc.).
2. To evaluate patients who have sustained a complicated myocardial infarction but who have subsequently "stabilized" (predischarge or early postdischarge).

Class III

1. To evaluate patients with acute ischemic heart syndrome (unstable angina pectoris, new onset angina pectoris or very recent acute myocardial infarction).
2. To evaluate patients with acute myocardial infarction who have uncompensated congestive heart failure, unstable cardiac arrhythmias or noncardiac conditions that severely limit their ability to exercise.

Discussion

The role of exercise testing performed within 3 weeks of uncomplicated myocardial infarction has emerged only during the past decade. The optimal timing for postinfarction exercise testing represents a compromise between the *risks* of precipitating recurrent infarction or death and the *benefits* of therapeutic interventions arising from early evaluation of prognosis and development of guidelines for physical activity. The risks of early exercise testing are related to three major factors: patient selection, timing of the test and exercise testing methods.

Patient selection

Patient selection, which is by far the most important single determinant of the risk of performing the test, can be properly judged only by the supervising physician through a careful history and physical examination prior to testing. Clinically significant abnormalities, especially congestive heart failure and unstable angina pectoris, are contraindications to early testing. Other patients are medically ineligible for early testing because of co-morbid conditions, including chronic obstructive pulmonary disease, peripheral vascular disease and orthopedic abnormalities. In other patients the interpretation of the electrocardiographic ST segment response to exercise is complicated by the existence of bundle branch block, left ventricular hypertrophy, digitalis effects or resting ST segment displacement.

Timing of the test

Some physicians prefer predischarge exercise testing 10 to 14 days after uncomplicated infarction rather than testing at 3 to 8 weeks. The risk of testing is low in properly selected patients at either time after myocardial infarction. Some physicians prefer to do both a predischarge test and a test at 6 to 8 weeks before allowing the patient with uncomplicated myocardial infarction to return to work or usual physical activities.

Exercise test methods

A variety of treadmill test protocols are suitable for early postinfarction testing. A convention that facilitates comparison of these protocols is the MET unit (see Appendix A). The protocol selected for early postinfarction testing should have a relatively low initial work load and small subsequent work load increments. Most patients can comfortably tolerate an initial work load of two to three METS with subsequent work load increments of one MET (27).

Test end points

Target heart rate. There is no evidence that a test that is limited by attainment of an arbitrary proportion of age-predicted heart rate is safer than one in which effort is discontinued because of the appearance of limiting symptoms, clinically significant signs or significant ventricular arrhythmias. Moreover, target heart rates are significantly diminished by beta-blockers, which are frequently prescribed for patients following myocardial infarction. The heart rate response during symptom-limited exercise testing may be more useful prognostically in patients *not* receiving beta-blockers (28). In *predischarge* exercise testing, five METS is a commonly used end point in the absence of prior end points. In general, a symptom-limited exercise test would identify more patients with ischemia either predischarge or at 6 weeks after infarction. In addition, a higher level exercise test (Bruce) will frequently be positive at 6 weeks when a low level exercise test (Naughton) is not.

Ventricular arrhythmias. It is prudent to stop an early postinfarction exercise test because of ventricular tachycardia (three or more consecutive premature ventricular depolarizations); however, significant ventricular arrhythmias may be more frequent during the recovery phase than during exercise.

Ischemic ST segment changes. It is prudent to stop an early postinfarction exercise test because of ischemic ST segment depression (≥ 2 mm). Exertional ST segment elevation is commonly noted in leads that demonstrate Q waves, and is not necessarily an indication for discontinuing the exercise test.

Exercise-induced hypotension. The frequent measurement of systolic blood pressure during early postinfarction exercise testing contributes importantly to the safety of the procedure, and the blood pressure should be measured at the end of every minute in these patients. A common convention in early postinfarction exercise testing is to discontinue the test when the patient develops a sustained systolic pressure drop of 10 mm Hg or greater in comparison to the highest value measured during a lower work load, even though hypotension by this criterion may occur in 15 to 20% of symptom-limited postinfarction tests (29).

Patients receiving beta-blocking agents may have a higher incidence of exertional hypotension, perhaps due in part to the blunted exercise heart rate response and impaired left ventricular function.

Limiting symptoms

- *Angina pectoris.* The incidence of exertional angina pectoris during early postinfarction exercise testing varies from 15 to 40% (30).
- *Dyspnea and fatigue.* These are the most frequent symptomatic end points for early postinfarction exercise testing. Together, they constitute between one-half and two-thirds of all test end points. Voluntary limitation by dyspnea and fatigue is a relatively reproducible end point. To determine whether a patient has attained a "clinically maximal" performance requires clinical judgment and experience.

Clinical application of postinfarction exercise testing

The prognosis after myocardial infarction is related to many factors, including the extent of myocardial ischemia and of left ventricular dysfunction (31,32). The prognostic value of exercise testing or of any diagnostic technique therefore cannot be considered apart from the clinical characteristics of the population to which it is applied. In general, exercise testing has been restricted to clinically low risk patients, i.e., those without congestive heart failure or unstable angina pectoris, who comprise approximately 40 to 60% of postinfarction patients.

The prognostic value of various exercise test parameters

Exercise-induced ischemic ST segment depression. This is the single most useful exercise test parameter for the evaluation of prognosis of patients soon after myocardial infarction. Patients who have ischemic ST segment depression of 1 mm or more during an exercise test performed 10

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to 21 days after an acute myocardial infarction have a risk of subsequent cardiac events which is 3 to 20 times higher than that of patients without this abnormality (28,29,33). Such patients, who comprise 30 to 40% of all patients undergoing early exercise testing, have a risk of death or recurrent infarction in the year after initial infarction of 5 to 15% (28,29,33). Conversely, in the 60 to 70% of patients who do not develop exercise-induced ischemic ST segment depression, the risk of death or recurrent infarction in the 12 months after initial infarction is as low as 2% (28,29,33). Much of the utility of exercise testing soon after infarction is related to its ability to identify *very low risk* patients, many of whom require no additional diagnostic procedures at that time, as well as *high risk* patients.

The prognostic value of exercise-induced ischemic ST segment depression is altered by the heart rate and work load at which the depression appears and by the clinical characteristics of the patient population. In general, patients with ischemic ST segment depression that appears at a low work load have a worse prognosis for a new coronary event or death than patients in whom a similar magnitude of ischemic ST segment depression occurs at a higher work load (28). In patient populations in which clinical heart failure and digitalis therapy are common, exercise-induced ischemic ST segment depression appears to be prognostically less useful than the finding of a low peak work load of less than four METS.

Peak work load. In general, patients who attain a high peak work load have clinically less advanced myocardial ischemia and left ventricular dysfunction than patients with low peak work loads.

Exercise induced angina pectoris. Exercise-induced angina pectoris is highly predictive of angina appearing during a later phase of convalescence. In general, patients with a low threshold for angina pectoris have a worse prognosis for a new coronary event or death and a lower functional capacity than patients with a high threshold (28).

Exercise induced ventricular arrhythmias. The frequency and complexity of exercise-induced ventricular arrhythmias are increased in early postmyocardial infarction patients with severe underlying myocardial ischemia, left ventricular dysfunction, and regional wall motion abnormalities (4,34).

Exercise induced ST segment elevation. This ubiquitous and nonspecific finding has less clinical utility than other cardiac abnormalities.

Exercise-induced hypotension. In patients with stable chronic ischemic heart disease, exertional hypotension is a relatively specific indicator of physiologically severe myocardial ischemia that often warrants further evaluation. In contrast, exertional hypotension in patients early after myocardial infarction appears to reflect a suboptimal increase in cardiac output arising from a transient suppression of the peak heart rate in combination with abnormal left ventricular function. The 10 to 20% incidence of exertional hypotension during symptom-limited testing performed 3 weeks after infarction decreases dramatically in the next 4 to 7 weeks (35). Patients with a recent inferior or posterior myocardial infarction often have well preserved left ventricular function but a markedly attenuated heart rate and blood pressure response to exercise, presumably caused by stimulation of left ventricular baroreceptors or deformation receptors. It is therefore important not to overinterpret exercise-induced hypotension appearing during early exercise testing, since this is a relatively common response, even in patients not receiving beta-blockers. While exercise-induced hypotension sometimes helps to identify a subgroup of patients with a higher incidence of severe CAD, it is relatively nonspecific and usually does not warrant further evaluation in the absence of other, more specific test abnormalities.

For exercise testing performed 21 days or more after infarction, symptom-limited testing appears as safe as "submaximal" exercise testing. In several large studies, patients with negative tests 2 to 3 weeks after myocardial infarction have a 12 month mortality of less than 2% (28,29,33). These patients appear to have a well preserved functional capacity, and it is probably safe for them gradually to resume most of their customary activities.

Occupational work clearance

Symptom-limited dynamic exercise testing provides an objective measure of *cardiovascular capacity.* If exercise-induced ischemic ST segment depression or angina pectoris are absent during symptom-limited dynamic exercise testing, they are also likely to be absent during customary activities, few of which involve an intensity of effort as great as that encountered during testing.

Most postinfarction patients whose exercise tests are "negative" with at least a seven MET work load 3 weeks after uncomplicated myocardial infarction are capable of resuming their usual occupational tasks within the next 2 to 3 weeks. In patients whose occupational activities involve heavy physical effort or extremes of temperature, a maximal or near-maximal exercise test performed approximately 6 to 8 weeks after infarction may be helpful in providing clearance to resume occupational activities. Patients with "positive" exercise tests may require further diagnostic testing and consideration of medical or surgical therapeutic interventions.

Exercise Testing After Specific Procedures

Summary

Class I

1. To evaluate patients after coronary artery revascularization by surgery or by coronary angioplasty.

Class II

1. To evaluate on a routine, yearly basis patients who remain asymptomatic after a revascularization procedure.

Discussion

Coronary artery bypass grafting

Testing prior to surgery. Preoperative treadmill exercise testing provides a baseline of exercise capacity for comparison following surgery. The primary indication for post-operative exercise testing is to document that the expected improvement has been obtained from the bypass procedure and to serve as a baseline for later comparisons.

Postoperative testing is often indicated in patients with one of the following circumstances: (1) suspected incomplete coronary revascularization (i.e., recurrent angina pectoris), (2) technical difficulties during or after the operation, (3) initial difficulties in being disconnected from the extracorporeal support system, (4) enzymatic or electrocardiographic evidence of intraoperative myocardial infarction, or (5) other evidence of perioperative complications. Exercise testing should be delayed for 3 months after surgery until chest pain and leg pain from the donor vessel site has subsided sufficiently to permit maximal or near-maximal exercise. Earlier testing can be performed at 3 to 6 weeks, but it is usually submaximal.

Even in patients with an abnormal resting ECG, much can be learned from the exercise stress test, such as time to maximal exercise, presence or absence of exertional angina pectoris, demonstration of stable rhythm and appropriate blood pressure and heart rate responses. The sensitivity of exercise testing for detecting two or more vessels left ungrafted has been reported to be 96 to 100% with a specificity of 91% (36).

Exercise testing for late complications or progression of disease after coronary artery bypass surgery. Repeat testing may be indicated in patients who have recurrent angina pectoris or a reduction in exercise capacity. The value of routine, periodic testing in patients who remain asymptomatic after coronary artery bypass surgery has not been documented.

Exercise testing of patients undergoing percutaneous transluminal coronary angioplasty (PTCA)

Pretreatment exercise testing provides a baseline for the evaluation of improvement following PTCA. The exercise ECG may fail to disclose ischemic abnormalities in some patients in whom PTCA is most clearly indicated, i.e., symptomatic individuals with proximal stenosis in a single vessel.

Post-treatment exercise testing can ordinarily be performed with safety on the day prior to hospital discharge, i.e., 2 to 5 days after the procedure. The presence of ECG abnormalities that may interfere with the interpretation of ischemic ST segment responses does not prevent the acquisition of other valuable data reflecting upon the adequacy of the coronary circulation. Evaluation of the adequacy of the coronary circulation by 201 Tl imaging in such patients is often very useful.

Late follow-up testing should be performed in patients who develop recurrence or worsening of angina pectoris or a deterioration of exercise tolerance. Exercise testing at 3 and 6 months helps to identify the 20 to 30% of patients who restenose in the first 6 months after the procedure. Thereafter, annual testing may be appropriate.

Exercise Testing in Patients With Valvular Heart Disease

Summary

Class II

1. To evaluate the functional capacity of selected patients with valvular heart disease.

Class III

1. To evaluate patients with symptomatic critical valvular aortic stenosis or hypertrophic obstructive cardiomyopathy.

Discussion

The principal indication for performing exercise tests on patients with valvular heart disease is to obtain objective data on exercise capacity, which is a measure of the overall functional capacity of the cardiovascular system. Evaluation of rhythm, heart rate and blood pressure responses during exercise can also contribute to better patient management, but the value of exercise-induced ST segment abnormalities as a sign of anatomical coronary artery disease is limited.

The functional classification of the New York Heart Association is often misleading (37,38). A significant negative relationship exists between exercise capacity and the severity of the valvular lesion as measured by cardiac catheterization and left ventriculography (37,39–41). Data obtained at rest from such tests or the medical history, however, often do not predict accurately the individual patient's response to exercise.

Current indications for surgery for valvular heart disease are largely based on a combination of symptoms, physical findings, chest roentgenographic, electrocardiographic, echocardiographic and catheterization data. Exercise test data may also be helpful in making decisions regarding catheterization and may provide a basis for advice about occupational and recreational physical activity. In selected patients serial exercise studies at 1 to 3 year intervals can be used to document progression of the disease and the effect of any therapeutic intervention. In general, exercise testing performed to evaluate the functional capacity of patients with valvular heart disease should be symptom-limited.

Mitral valve disease

Most patients with hemodynamically significant *mitral stenosis* have decreased exercise capacity (39–41). Relative tachycardia is an ineffective compensatory mechanism because the shorter period of diastolic filling further decreases left ventricular filling, particularly in patients with atrial fibrillation; therefore, control of the ventricular response by medication is essential (42,43). Exercise testing can provide an objective measure of functional capacity, particularly in patients who deny or minimize symptoms.

Patients with chronic *mitral regurgitation* often remain asymptomatic with well preserved exercise tolerance until the regurgitant volume becomes very large and is associated with high right-sided pressures. Abnormal ST responses to exercise may be found in patients with and without underlying CAD. Exercise testing is useful in establishing the degree of functional limitation in many patients with mitral regurgitation.

Patients with *mitral valve prolapse* form a heterogeneous subgroup. In the largest group of patients with primary or idiopathic prolapse, there is little evidence for exercise-induced myocardial ischemia despite the common history of chest pain and the common occurrence of exercise-induced ST segment abnormalities. The mechanism for ST segment abnormalities is unknown, but autonomic dysfunction may be an important factor (44).Exercise testing is not usually appropriate for patients with mitral valve prolapse unless there is evidence of marked mitral regurgitation or exertionally induced cardiac arrhythmias. Less frequently, mitral valve prolapse is secondary to CAD with papillary muscle dysfunction.

Aortic valve disease

Clinical evidence for critical aortic stenosis is generally regarded as a contraindication for exercise testing. Exercise-induced syncope, at times apparently caused by a depressor response with vasodilatation and bradycardia (45,46), is a feared complication. On the other hand, careful testing can be performed safely in patients with mild to moderate lesions (47). Angina and abnormal ST segment responses are likely to reflect myocardial ischemia, but these abnormalities provide little information about the presence or absence of significant CAD when left ventricular hypertrophy is present (48).

Limitations also apply to the evaluation of ST segment changes in patients with *aortic regurgitation*. Exercise capacity is often well maintained in the presence of significant regurgitation and left ventricular hypertrophy because of the increased heart rate, decrease in diastolic time and peripheral artery dilatation during exercise, despite severe left ventricular dysfunction in many patients. In some patients, however, a decrease in functional capacity may serve as an additional guide in timing cardiac surgery.

Exercise Testing in the Management of Patients With Hypertension or Cardiac Pacemakers

Summary

Class II

1. To evaluate the blood pressure response of patients being treated for systemic arterial hypertension who wish to engage in vigorous dynamic or static exercise.

Class III

1. To evaluate patients with severe, uncontrolled systemic hypertension.
2. To evaluate the blood pressure response to exercise in patients treated for hypertension who are not engaging in vigorous exercise.
3. To evaluate pacemaker function in patients with cardiac pacemakers.

Discussion

Exercise testing in patients with hypertension

Many investigators have used exercise testing for the diagnosis, categorization and treatment of patients with systemic hypertension (49–52). Exercise testing should not be performed in patients with uncontrolled severe hypertension. Exercise testing may be useful in helping to identify individuals with labile high blood pressure more likely to develop persistent hypertension, but it is not indicated in the routine management of patients with hypertension. It may be useful in patients who engage in vigorous dynamic or static exercise.

Exercise testing in patients with cardiac pacemakers

In general, exercise testing is not appropriate in most patients with cardiac pacemakers. In a few selected patients, however, such testing may occasionally help in the evaluation of overall cardiovascular performance during exercise.

Exercise Testing in Children

Summary

Class I

1. To evaluate the functional capacity of selected patients with congenital heart disease.

Class II

1. To evaluate the functional capacity of patients with valvular or congenital heart disease.

Discussion

In general, exercise testing in children is a safe (53–55) and useful noninvasive test for the management of selected children with suspected or asymptomatic cardiovascular disease.

Indications for exercise testing in children include (1) quantitation of the patient's exercise tolerance; (2) detection of electrophysiologic, hemodynamic or symptomatic responses that might indicate increased risk from underlying heart disease; (3) periodic evaluation of therapy or of the post surgical status; (4) detection of evidence of myocardial ischemia; and (5) detection of exercise-induced arrhythmia. Exercise testing has proven to be particularly useful in the evaluation of patients with congenital aortic stenosis, coarctation of the aorta, tetralogy of Fallot, arrhythmias, chest pain syndromes and adolescent hypertension (54). In selected patients, it may also help provide guidelines for participation in athletic activities (56).

Appendix A

The exercise test

The ECG, heart rate and blood pressure reponse should be carefully monitored and recorded by a physician during each stage of exercise (57) and at time of onset of ST segment abnormalities or chest pain. The physician should also observe for transient rhythm disturbances and other ECG manifestations of myocardial ischemia, such as intraventricular conduction disturbances and negative U waves.

End points for graded exercise testing

Many exercise laboratories employ submaximal tests, in which target heart rate end points correspond to 85 to 90% of the predicted maximal heart rate observed in normal subjects. The test is terminated short of the target heart rate if limiting symptoms such as increasing angina or severe dyspnea occur. The poor relationship between the maximal heart rate and age and the large scatter around the predicted regression line must be understood. Symptom-limited testing is preferable to submaximal testing when the test is used to evaluate a patient's functional capacity. The target heart rate approach has major limitations in patients receiving β-adrenergic blocking agents and in those with heart rate impairment or excess heart rate response.

Indications for terminating an exercise test, irrespective of the patient's symptomatic status or exercise heart rate, include a progressive and reproducible decrease in systolic blood pressure, a decreasing heart rate or the appearance of three consecutive PVDs. Excessive horizontal or downsloping ST segment depression ($\geq$ 2.0 mm) is often an indication for terminating a test.

Optimal lead systems

With few exceptions, a clinical exercise laboratory should monitor and record a minimum of three ECG leads corresponding to orthogonal X,Y and Z leads. Probably the most popular lead combination in use today consists of leads aVF, V_2 and V_5. The use of multiple (3 to 12) leads increases the sensitivity of the exercise ECG for detecting abnormal ST segment depression by 8 to 20% when compared with a single lateral precordial lead; a 12 lead system is preferable (58). The occurrence of abnormal ST segment depression in multiple leads may also be a useful marker of the severity of underlying CAD (2).

Causes of false positive ECG responses to exercise

Individuals with labile ST-T wave changes under various conditions have an increased incidence of false positive ST segment changes with exercise (59). These changes may be unmasked by recording the ECG after 20 to 30 seconds of voluntary hyperventilation in the standing position. If hyperventilation produces ST segment depression ($\geq$ 0.5 mm) or a reversal of polarity of the T wave, then abnormal ST segment depression during exercise must be interpreted with caution.

In individuals with left ventricular hypertrophy (hypertension, valvular heart disease or other causes), exercise-induced ST segment depression may result from hypertrophy alone, even when baseline ST-T segments are normal (3).

The incidence of false positive ST segment responses to exercise is higher in women than in men; the explanation for this phenomenon remains unclear. Patients with mitral valve prolapse also have a higher incidence of false positive ST segment responses, perhaps because they also have a predilection toward labile ST-T wave changes.

Baseline ST depression or T wave inversion, digitalis therapy, hypokalemia, anemia and hypoxemia increase the rate of false positive ST segment responses to exercise.

Appendix B

Definitions of terms commonly used in exercise testing

Sensitivity and specificity

The classic ECG response to ischemia on the exercise test is ST segment depression. Although many other exercise test variables are also correlated with coronary arteriographic findings, the ST segment response is still the accepted standard. The most commonly used definition for a positive ECG exercise test is $\geq$ 1 mm of horizontal or downward ST segment depression or elevation for at least

Table 3. Statistical Evaluation of Exercise Test Results

$$\text{Sensitivity (\%)} = \frac{TP}{TP + FN} \times 100$$

$$\text{Specificity (\%)} = \frac{TN}{TN + FP} \times 100$$

$$\text{Predictive value (\%) of a positive response} = \frac{TP}{TP + FP} \times 100$$

or

$$\text{Predictive value (\%) of a negative response} = \frac{TN}{TN + FN} \times 100$$

FN (false negative) = negative exercise ECG and positive angiogram; FP (false positive) = positive exercise ECG and negative angiogram; TN (true negative) = negative exercise ECG and negative angiogram; TP (true positive) = positive exercise ECG and positive angiogram.

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0.08 second after the end of the QRS complex, compared with the rest value (TP or PQ segment). When the rest ST segments are abnormal, an additional 1 to 2 mm of ST segment depression or elevation is accepted as a positive response. The specificity, however, may be considerably less than if the ECG at rest is normal. Correlations between an abnormal (positive) test and the presence of coronary disease, determined either angiographically or by clinical follow-up, are best expressed by the epidemiologic terms "sensitivity," "specificity" and "predictive value," which are defined in Table 3.

In general, sensitivity is an expression (in percent) of the ability of a test to identify individuals who have a given disorder, while specificity reflects the test's ability to identify individuals who do not have the disorder (Table 3). Thus, sensitivity reflects how reliably a positive test identifies disease, and specificity reflects how reliably a negative test identifies the absence of disease.

The most important determinant of sensitivity or specificity is the criterion or discriminant value used to define an abnormal test result. Thus, as the criteria required for a positive test result increase, the sensitivity decreases and the specificity increases. For example, if the amount of coronary stenosis used to define disease was placed at 70% diameter narrowing (91% decrease in cross-sectional area) rather than 50% diameter narrowing (75% decrease in cross-sectional area), the sensitivity of exercise testing decreases while the specificity increases. Conversely, when the criteria are made less stringent, the sensitivity increases but the specificity decreases. Another important determinant of sensitivity and specificity is the number of leads used to monitor the exercise electrocardiographic response. As the number of leads increases from 1 to 12, the sensitivity increases from 56 to 76%, while the specificity decreases from 94 to 82% (58).

The so-called *likelihood ratio* expresses the relative chance of observing a given test outcome among diseased and nondiseased patients. In the case of an abnormal test result, the likelihood ratio can be defined by the following equation: sensitivity/(1-specificity).

Predictive value and Bayes's theorem

The *predictive value* of a test is the likelihood that disease is present or absent depending on whether the test is positive or negative, respectively (Table 3). The sensitivity and specificity and corresponding likelihood ratios will determine how accurate certain test results will be (i.e., the test's *predictive value*).

A major determinant of the predictive accuracy of a test result is the prevalence of disease in the population under study, i.e., the likelihood of having disease before the test is undertaken or the pretest probability. This concept is referred to as Bayes's theorem, a statistical law of conditional probability that states that the likelihood of disease after a diagnostic test (the post-test risk) cannot be estimated from the test result alone but requires knowledge of the prevalence of disease (pretest risk) for the individual population group in question (60–62). Thus, the predictive accuracy of any test outcome that is less than a perfect diagnostic test (i.e., less than 100% specific) is influenced by the pretest likelihood of disease and by the criteria used to define a test result.

Definition of MET

A MET unit is the energy expenditure at rest, equivalent to an oxygen uptake of approximately 3.5 ml O_2 per kilogram body weight per minute. Exercise tests may be standardized in terms of the oxygen consumption (ml O_2/kg/min) associated with a specific work load. Exercise protocols have been developed so that each work load approximates a multiple of the oxygen consumption at rest, i.e., two or three times the oxygen consumption of rest in ml/kg/min, or 2 METS, 3 METS etc. Patients limited by symptoms usually have a work load capacity of about 6 METS or less, while asymptomatic patients may have performance capacities ranging from 7 to 10 METS or more. Regularly active healthy men may have capacities of 12 to 15 METS and endurance athletes 16 to 20 METS.

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