Safety and Utility of Exercise Testing in Emergency Room Chest Pain Centers

An Advisory From the Committee on Exercise, Rehabilitation, and Prevention, Council on Clinical Cardiology, American Heart Association

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Rapid triage and management of patients with an acute chest pain syndrome is an integral part of routine emergency room clinical activities. Specialized chest pain centers have been developed to better risk stratify patients in the emergency department setting using noninvasive test protocols to cost-effectively identify those patients who can be safely discharged with an acceptably low risk of cardiac events.1–16 The aim of this report is to summarize and interpret the evidence regarding the safety and utility of exercise testing in the evaluation of patients with chest pain who present to the emergency department. The rationale for implementation of a chest pain unit in the emergency department, use of different noninvasive test procedures and serum markers, and patient treatment will not be reviewed in detail except as they pertain to the use of exercise testing.

Historical Perspective

The role of exercise testing after stabilization of hospitalized patients with unstable angina has been extensively described.17–28 Swahn et al23 reported on 400 patients <65 years of age who underwent symptom-limited predischarge exercise testing after stabilization of unstable angina using an electrically braked bicycle ergometer starting at 10 W with continuous load increases of 10 W/min. The incidence of exercise-induced ST-segment depression ≥1 mm was 33% in 272 men and 116 women. An abnormal exercise electrocardiogram (ECG) was recorded in 51% to 53% of patients with an abnormal ECG at rest versus 16% to 19% when the resting ECG was normal. Peak workload achieved was greater in men than in women, although the peak rate-pressure product was similar. After 1 year, there were 49 cardiac events in the 276 men who performed the exercise test compared with only 5 cardiac events in the 118 women.24 Exercise-induced ST-segment depression and low peak rate-pressure product independently identified risk of myocardial infarction or cardiac death. Exercise test variables were not predictive of cardiac events for the women enrolled in this study. Madsen et al25 reported on 257 patients stabilized for unstable angina, 26 of whom had a cardiac death or nonfatal myocardial infarction over a median 14-month follow-up. The presence of ST depression or negative T waves on the resting ECG or exercise-induced ST depression or angina during the exercise test was predictive of cardiac events. Severi et al26 reported on 374 patients who had an exercise stress test and underwent coronary angiography during the same admission. In the 54 patients with a normal rest and normal exercise ECG, only 4% of patients had 3-vessel coronary disease, and no patient had left main disease; 8-year survival was 100%. In the 86 patients with a normal resting ECG but abnormal exercise ECG, 3-vessel or left main coronary disease was present in 22% and 9%, respectively; 8-year survival was 97%. In the 59 patients with an abnormal resting ECG and normal exercise ergometry study, 3-vessel or left main coronary disease was noted in 19% of patients; 8-year survival was 88%. In the 175 patients with an abnormal rest and abnormal exercise ECG, only 2% of patients had normal vessels; 3-vessel or left main coronary disease was noted in 41% and 12%, respectively; 8-year survival was 70%. Similar prognostic findings were reported by Frueergaard et al.27

The incidence of myocardial infarction or death within 24 hours of exercise testing in 632 hospitalized subjects stabilized for unstable angina symptoms is 0.5% (range, 0.2% to 0.9%) (Table 1). The absence of exercise-induced angina or ECG abnormalities in patients with a normal resting ECG identifies a low-risk patient subset. The relative risk of abnormal resting ECG or exercise test findings is different in men and women. There are few data on patients >75 years of age. The relative safety of exercise ECG in risk stratification of hospitalized patients with unstable angina has led to a broader use of exercise testing in the emergency department setting. Various clinical algorithms are now available that allow patients who present to the emergency department with chest pain to be stratified into low-, intermediate-, and high-risk subgroups.

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identify patients with a low to intermediate pretest risk of an acute coronary ischemic syndrome. This protocol, which incorporates selective historical, physical examination, and ECG variables into the concomitant use of serum markers of myocardial cell death (usually creatine kinase-MB [CK-MB] or troponin I or T), has been commonly used by emergency departments in their chest pain centers. It is used to identify those patients who are at low risk of having an acute coronary ischemic syndrome. The risk stratification process takes into account that some patients with chest pain have no known history of coronary disease and have atypical symptoms and hence a relatively low probability of coronary artery disease, whereas other patients have documented coronary disease and more typical symptoms of an acute coronary syndrome. Thus, with the use of such an algorithm, it is possible to identify patients with a low to intermediate pretest risk of an acute coronary syndrome before exercise testing.

**Exercise ECG Testing in Emergency Department Chest Pain Centers**

A limited number of studies address the safety and efficacy of exercise ECG testing within the context of a chest pain center. In an early study, Tsakonis et al. performed exercise ECG testing using a symptom-limited modified Bruce treadmill protocol without complications or adverse associated events in 28 patients with a normal ECG and chest pain that was “consistent with” but “not characteristic of” angina. Of the 28 patients, 5 had a positive exercise ECG examination (≥1-mm ST-segment depression) and were admitted. The remainder (23 of 28) were discharged and had no adverse cardiac events when followed up for a mean of 6.1 months. Similar results were reported by Kerns et al., who noted lower patient charges and substantially shortened lengths of stay by using exercise ECG testing for low-risk subjects with a normal ECG as part of their emergency department chest pain center protocol.

The largest reported study of exercise ECG testing as part of a chest pain center protocol was a retrospective analysis that included 1010 patients (498 women and 512 men). This protocol was unique in that it initially used 9 hours of continuous ST-segment monitoring, clinical findings, serum CK-MB, serial ECGs, and resting echocardiogram. In the absence of relevant pathology, ie, sustained or recurrent ST-segment depression, new Q waves, wall motion abnormalities, or elevations in serum CK-MB, symptom-limited exercise ECG testing was subsequently performed by 791 patients (78%). This study supports the safety of symptom-limited exercise ECG testing among chest pain center patients with a 5% prevalence of disease as defined by diagnosis at hospital discharge for admitted patients and a very low 30-day cardiac event rate in discharged patients. A high specificity and negative predictive value for the exercise ECG examination are noted in Table 2, as are the low to intermediate sensitivity and positive predictive values.

The Rapid Rule-Out of Myocardial Ischemia Observation (ROMIO) study prospectively evaluated 100 patients with chest pain who were randomly assigned to regular care (admission) or chest pain center protocol. The latter used a 12-hour clinical, ECG, and CK-MB algorithm that included continuous ST-segment analysis and symptom-limited exercise ECG testing. There were no adverse effects during exercise testing in either group. Coronary artery disease was detected in 6 patients (6% disease prevalence) and was not significantly different between the 2 groups. Length of stay (11.9 versus 22.8 hours) and total costs (a 30-day savings of $624 per patient) were significantly lower in the chest pain center group.

In a comprehensive seminal study, Zalenski and colleagues prospectively evaluated 317 patients who presented to the emergency department with chest pain. Excluded were patients who had a confirmed diagnosis of heart disease, cardiac complications before enrollment, significant arrhythmia, an inability to perform an exercise ECG examination, or a significant noncardiac diagnosis that required admission (eg, stroke). The study group represented 26% of all patients presenting with chest pain to the emergency department during the enrollment period. The chest pain protocol used the Goldman et al. algorithm and exercise ECG testing (symptom-limited Bruce or modified Bruce treadmill protocol) for patients who had not been identified as having acute coronary ischemia during the clinical observation period. Seventy-one percent (224 patients) of the study group underwent exercise ECG testing. All patients, including those with protocol-negative and negative exercise ECG results and patients with positive findings, were then admitted to establish a reference diagnosis by clinical presentation, exercise or pharmacological stress nuclear perfusion studies, or coronary angiography. Thirty patients in this low-risk group (9.5%) met the criteria for the reference outcomes of acute coronary ischemia. When performance of the protocol, including exercise ECG, was considered against the reference diagnosis of acute coronary ischemia, sensitivity was 90%, specificity was 51%, positive predictive value of the protocol was 16%, and negative predictive value was 98%. When sensitivity and specificity were examined for each component of the protocol, the best values were obtained when CK-MB, resting ECG, and exercise ECG testing were all used. Of particular interest was the incremental diagnostic value (as analyzed by receiver-operating curve) of the exercise ECG test when added to serial CK-MB and serial ECG testing: 148 (66%) had negative tests and reached 85% of the age-predicted

**TABLE 1. Safety of Exercise Testing in Patients Stabilized for Unstable Angina**

<table>
<thead>
<tr>
<th>Patients Who Performed an Exercise Test, n</th>
<th>Death or Myocardial Infarction Within 24 h, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Butman et al (1984) 125</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Swahn et al (1986) 400</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Wilcox et al (1991) 107</td>
<td>1 (0.9)</td>
</tr>
<tr>
<td>Total 632</td>
<td>3 (0.5)</td>
</tr>
</tbody>
</table>
maximum heart rate. Seventy-six patients had either negative or inconclusive tests, failing to reach 85% of the age-predicted maximum heart rate. The positive predictive value was 24% but was only 8% in the inconclusive tests. There were no adverse events related to the exercise. A cost analysis on a randomly selected subset of 165 patients in this study demonstrated a savings of $567 per patient treated with the chest pain center protocol incorporating exercise ECG testing.

In a recent report, Polanczyk et al.\textsuperscript{6} presented in-hospital and 6-month outcome data of 276 chest pain patients determined to be at low risk by the Goldman\textsuperscript{2} algorithm. Patients underwent symptom-limited exercise tests within 48 hours of presentation with chest pain. There were no adverse events relating to the exercise ECG tests. These investigators, in contrast to Gibler et al.,\textsuperscript{5} did not use continuous ST-segment monitoring or 2-dimensional echocardiography and extended their follow-up period to 6 months. Exercise tests that were negative for ischemia at a peak work rate <3 metabolic equivalents (METs) were classified as equivocal. The 6-month event rate in the 195 patients with a negative test was 2% (negative predictive value, 98%) in contrast to an event rate of 15% in patients with positive or equivocal tests. Sensitivity and specificity were 73% and 74%, respectively.

A recent, randomized, controlled trial of 424 unstable angina patients at intermediate risk for short-term cardiovascular events\textsuperscript{9} compared the safety, effectiveness, and cost of those admitted to a chest pain center versus those admitted to the hospital. After 6 hours of observation in the chest pain center, patients who did not manifest clinical changes, ECG changes, or CK-MB elevations performed a functional stress study. An exercise ECG test was performed in those patients who were able to walk and who had no confounding resting ECG abnormalities. The remaining patients underwent nuclear or echocardiographic exercise or pharmacological stress studies. There were no adverse clinical events associated with stress testing. Patients with negative tests were discharged home, and patients with other results (equivocal or positive) were subsequently admitted to the hospital. No significant difference in event rate was found between the hospital and the chest pain center patients. Patients assigned to hospital admission had a significantly higher resource utilization during the first 6 months compared with those assigned to the chest pain center.

Table 3 illustrates indications and contraindications for exercise ECG testing in the emergency department setting based on the above information.

<table>
<thead>
<tr>
<th>Investigators</th>
<th>No. of Subjects</th>
<th>Follow-Up Period</th>
<th>Exercise ECG Test</th>
<th>Adverse Events, n*</th>
<th>% Disease Prevalence</th>
<th>Clinical Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tsakonis et al\textsuperscript{4}</td>
<td>28</td>
<td>6.1 mo</td>
<td>Modified Bruce (SLM)</td>
<td>0</td>
<td>0</td>
<td>Exercise testing was safe</td>
</tr>
<tr>
<td>Kerns et al\textsuperscript{7}</td>
<td>32</td>
<td>6 mo</td>
<td>Bruce (APMHR)</td>
<td>0</td>
<td>0</td>
<td>Exercise testing was safe; reduced cost vs admission</td>
</tr>
<tr>
<td>Gibler et al\textsuperscript{5}</td>
<td>1010</td>
<td>30 d</td>
<td>Bruce (SLM)</td>
<td>0</td>
<td>5</td>
<td>Sensitivity=29%, specificity=99.4%, positive predictive value=44%, negative predictive value=98.7%†</td>
</tr>
<tr>
<td>Gomez et al\textsuperscript{3}</td>
<td>50</td>
<td>None</td>
<td>Cornell (SLM)</td>
<td>0</td>
<td>6</td>
<td>No difference in clinical outcome; reduced cost vs admitted control</td>
</tr>
<tr>
<td>Zalenski et al\textsuperscript{1}</td>
<td>317</td>
<td>None; patients admitted for reference diagnosis</td>
<td>Modified Bruce</td>
<td>0</td>
<td>9.5</td>
<td>Sensitivity=90%, specificity=50%, negative predictive value=98%‡</td>
</tr>
<tr>
<td>Polanczyk et al\textsuperscript{6}</td>
<td>276§</td>
<td>6 mo</td>
<td>Modified Bruce</td>
<td>0</td>
<td>25</td>
<td>Sensitivity=73%, specificity=74%, negative predictive value=98%</td>
</tr>
<tr>
<td>Farkouh et al\textsuperscript{9}</td>
<td>424</td>
<td>6 mo</td>
<td>Not specified</td>
<td>0</td>
<td></td>
<td>Intermediate-risk patients were studied; no difference in clinical outcomes; reduced cost vs admitted control</td>
</tr>
</tbody>
</table>

SLM indicates symptom-limited maximum end point; APMHR, age-predicted maximum heart rate end point.

*Death or myocardial infarction.
†With respect to diagnosis if admitted, and 30-day follow-up on all patients.
‡With respect to reference diagnosis from admission of all patients.
§Included 70 patients (25%) with a history of CHD.
| TABLE 3. Indications and Contraindications for Exercise ECG Testing in the Emergency Department Setting |

Requirements before exercise ECG testing that should be considered in the emergency department setting
- 2 Sets of cardiac enzymes at 4-h intervals should be normal
- ECG at the time of presentation, and preexercise 12-lead ECG shows no significant change
- Absence of rest ECG abnormalities that would preclude accurate assessment of the exercise ECG
- From admission to the time results are available from the second set of cardiac enzymes: patient asymptomatic, lessening chest pain symptoms, or persistent atypical symptoms
- Absence of ischemic chest pain at the time of exercise testing

Contraindications to exercise ECG testing in the emergency department setting
- New or evolving ECG abnormalities on the rest tracing
- Abnormal cardiac enzymes
- Inability to perform exercise
- Worsening or persistent ischemic chest pain symptoms from admission to the time of exercise testing
- Clinical risk profiling indicating imminent coronary angiography is likely
Imaging Modalities

Cardiac imaging modalities increase the sensitivity to detect coronary disease and cardiac events compared with exercise ECG alone. The test provides the ability to quantify the extent of jeopardized myocardium and localized ischemic territories and provides important diagnostic information in patients with a noninterpretable exercise ECG. Patients with a high-risk $^{99m}$Tc sestamibi rest perfusion scan are at increased risk of developing myocardial infarction, dying, or requiring coronary revascularization, whereas patients with a low-risk scan have a low 30-day cardiac event rate (<1% to 2%). The presence and magnitude of new or presumed-new regional wall motion abnormalities detected with 2-dimensional echocardiography in patients with chest pain are correlated to subsequent risk of cardiac death or myocardial infarction. The incidence of abnormal resting sestamibi single-photon emission computed tomography in patients presenting with chest pain to the emergency department ranges from 22% to 47%. Few data evaluate the cost-effectiveness of myocardial perfusion imaging versus echocardiography in the routine evaluation of patients presenting with chest pain to the emergency department. In patients able to perform an exercise test in this setting, the incremental prognostic and cost-effective value of imaging technologies over the posttest likelihood of subsequent cardiac events using clinical history and resting and exercise ECGs requires further study.

Summary

When reviewed together, the studies summarized here confirm the safety of symptom-limited treadmill exercise ECG testing after 8 to 12 hours of evaluation in patients who have been identified as being at low to intermediate risk by a clinical algorithm that uses serum markers of myocardial necrosis and resting ECGs. This is consistent with similar safety data reported in patient groups with a higher disease prevalence, such as patients presenting with unstable angina, Utility, expressed as the incremental clinical value of exercise ECG testing when added to a chest pain center clinical algorithm, serial serum markers of myocardial necrosis, and serial ECG testing, has been demonstrated in at least 2 well-designed studies.

Key Points and Recommendations

- Symptom-limited treadmill exercise ECG testing is acceptably safe in chest pain center patients when they have been identified as having “low risk/low likelihood” (<7% by Goldman criteria) of having an acute coronary ischemic syndrome by use of an appropriate clinical protocol.
- The protocol must include serial clinical assessment, resting ECGs, and serum markers of myocardial necrosis. In most instances, this would require 8 to 12 hours of monitoring and assessment. Exercise ECG testing increases the diagnostic value of the chest pain center protocol when added to serial CK-MB/troponin testing and the resting ECG.
- The exercise ECG testing facility should conform to the American Heart Association (AHA) guidelines for clinical exercise ECG testing laboratories. The American College of Physicians/AHA/American College of Cardiology (ACC) task force statement on clinical competence in exercise testing recommends that exercise testing in selected patients can be safely performed by properly trained nurses, exercise physiologists, physical therapists, or medical technicians working directly under the supervision of a physician who should be in the immediate vicinity and available for emergencies. In higher-risk patients, exercise testing should be supervised by an appropriately trained physician. The exercise ECG laboratory should conform to the AHA guidelines for exercise testing ECG laboratories.
  - Exercise ECG testing should be used in most chest pain centers as the first-line noninvasive stress test for ambulatory patients when the resting ECG is normal and the patient is not on digoxin therapy. In patients who do not meet these criteria, stress imaging should be considered.
  - Chest pain center exercise ECG testing can effectively incorporate a variety of treadmill protocols. Most clinical studies have used the Bruce or modified Bruce treadmill protocol. The use of protocols that have lower work rate increments per stage, eg, ramp, Naughton, ACIP, or Balke treadmill protocols, would be appropriate in those patients who are elderly or whose recent activity levels suggest significant deconditioning. Bicycle ergometer exercise testing is probably equally safe and predictive compared with treadmill exercise testing.32
  - Chest pain center exercise ECG testing should use a symptom-limited maximum end point as opposed to predetermined work rate or heart rate end point. Symptom-limited maximum testing was used in most of the reported clinical studies of chest pain center exercise ECG outcomes and has a very low incidence of adverse events.
  - Interpretation of chest pain center exercise ECG tests and consequent decisions regarding immediate hospital admission for further evaluation should be based on the ACC/AHA Guidelines for Exercise Testing. Use of logistic regression equations, such as the Duke Treadmill Score, has been demonstrated to be of prognostic value in evaluating inpatients and ambulatory patients in an outpatient setting but has not been tested in emergency department chest pain centers. Exercise tests without ischemic responses in patients who fail to achieve 6 METs (for patients >75 years of age, a 4- to 5-MET exertion expectation is appropriate) or who fail to achieve 85% of age-predicted maximum heart rate should be considered inconclusive; such patients should be further evaluated.
  - Within the context of a chest pain protocol, patients referred for exercise testing should be selected to represent a low disease prevalence group (Table 3). Accordingly, exercise ECG testing will have a high negative predictive value for both a reference diagnosis and 30-day event-free clinical outcome in a population with a low pretest probability of disease and a low positive predictive value with regard to the same end points.
  - A small number of patients identified as being at low to intermediate risk through the use of a chest pain algorithm and who have a negative exercise ECG will present with acute myocardial infarction or will require coronary revas-
cularization during the immediate or 6-month period after the evaluation. This fact reflects the clinical reality that the protocols define a very-low-risk group but not a zero-risk group.

- Patients who require stress imaging studies because of an inability to exercise, uninterpretable ECGs at rest or during exercise, or inconclusive or equivocal exercise ECG findings ideally should remain at the hospital until the study is completed. When patients are discharged from the emergency department with a return follow-up visit for such testing, compliance has been suboptimal. This patient subgroup is often elderly and has a higher coronary artery disease prevalence compared with patients with a negative exercise ECG.

Future Directions

Exercise ECG in the emergency department setting is safe and cost-effective in diagnostic risk stratification of selected low-risk patients with chest pain. More studies are needed to determine cost-effectiveness in clinical patient subsets with a higher pretest risk of disease, in women, and in elderly patients. Additional research is required to determine optimal clinical patient subsets for the concomitant use of cardiac imaging techniques.

References


Key words: AHA Science Advisory ■ exercise ■ tests ■ angina ■ coronary disease
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