The Exercise Test as Gatekeeper*
Limiting Access or Appropriately Directing Resources?

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The evaluation of a patient with a history suggestive of coronary artery disease is familiar to any internist. After a careful history and physical examination, the internist often turns to exercise testing to provide further diagnostic information. If the patient has an abnormal test result, the physician is faced with deciding whether to refer the patient for more invasive testing and therapy. There should be specific reasons to send a patient with stable angina to cardiac catheterization. Cardiac catheterization is a procedure that provides anatomic rather than functional information. Thus, the major reason to catheterize a patient is to assess whether the patient has the appropriate anatomy for invasive therapy, including coronary artery bypass surgery and percutaneous transluminal coronary angioplasty. In deciding which patient to refer for catheterization, the internist should evaluate whether the patient has a higher risk of mortality from the invasive procedures than from medical management. If the answer to this question is no, then the catheterization can lead to improved survival. Remember that this relates only to the issue of quantity of life and not quality of life.

The decision-making process becomes more difficult when catheterization is looked at as a tool to decide whether angioplasty is an appropriate course of therapy. Unfortunately, there are little comparative data regarding angioplasty as an alternative to medical therapy. Coronary artery bypass surgery is the current standard of care for patients with three-vessel or left main disease, the only coronary anatomy that has been associated with improved survival after revascularization compared with medical therapy.¹ Percutaneous transluminal coronary angioplasty, another form of revascularization, is not likely to make a difference in terms of mortality reduction, and there have been little data to support its use in this role. Therefore, percutaneous transluminal coronary angioplasty should currently be viewed as an alternative to medical therapy when patients have angina refractory to medical treatment. The ACME trial showed that patients randomized to percutaneous transluminal coronary angioplasty, as opposed to medical therapy, had more relief of angina and greater increase in exercise performance, although these differences were not clinically meaningful.² Those randomized to angioplasty also had double the risk of serious morbidity, with increased frequencies of both nonfatal myocardial infarction and emergency bypass surgery. In deciding to refer a patient to catheterization for possible percutaneous transluminal coronary angioplasty, the internist must therefore be fully cognizant of the risk of morbidity that would be incurred without the promise of increased longevity.

Overuse of Invasive Procedures

Given that the average annual mortality rate of patients with stable coronary artery disease is not only low, but in fact decreasing, it is interesting to note the rapidly increasing number of invasive procedures performed every year. Over the past decade, the number of coronary angiograms has more than doubled from 410,000 procedures in 1981 to 1 million in 1991. Parallel trends in the number of procedures indicate similarly aggressive approaches to therapy for ischemia. More than 265,000 patients underwent coronary bypass surgery in 1991 in the United States compared with 158,000 in 1981, and the use of percutaneous transluminal coronary angioplasty has increased from 60,000 procedures in 1986 to greater than 300,000 in 1991.³

This increase in use of invasive procedures is a concern since they are often performed on patients who have an inherently low risk of cardiac mortality.⁴ ⁵ These patients may, in fact, have coronary artery disease, but may additionally fall into a category

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of patient whose likelihood of being harmed by an invasive procedure significantly outweighs the potential benefit of performing it.

The overuse of cardiac catheterization may be due to a number of different factors. Financial motives and fear of litigation offer easy and popular explanations. It is likely, however, that internists and patients are also driven by two misconceptions: (1) that any ischemia is ominous, necessitating other than symptomatic treatment, and (2) that cardiac catheterization is the “gold standard” for diagnosis. In this era of medical cost-containment, physicians’ decisions to request expensive and perhaps unnecessary invasive procedures will be increasingly scrutinized. Is there a way in which the practitioner can better assess data from noninvasive testing to decide which patients are at higher risk for cardiac events to more judiciously and appropriately use invasive cardiac procedures?

**Prognostic Scores to Predict Cardiac Mortality**

Two recent studies have shown that patients with coronary artery disease can be effectively stratified as to risk of cardiovascular death by using scores derived from clinical and exercise test variables. At both Duke University and the Long Beach VA Medical Center, researchers developed equations using variables that had been determined by a Cox proportional hazard model to predict cardiac mortality.

<table>
<thead>
<tr>
<th>Table 1—Prognostic Score*</th>
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<tr>
<td>Duke Score: (MET−5 [mm exercise-induced ST depression]−4 (treadmill angina index])</td>
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<tr>
<td>VA Score: (5 [CHF and/or digoxin use]+mm exercise-induced ST depression+change in SBP score−METs)</td>
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*Prognostic scores derived from studies at Duke University and the Long Beach Veterans Affairs Medical Center (VA). The Duke score is based on three exercise variables: exercise tolerance in metabolic equivalents (METs); the largest measured ST segment depression during exercise; and a treadmill angina pectoris score (0 for no angina during exercise, 1 for typical angina, and 2 for angina leading to discontinuation of exercise). The VA score incorporates heart failure, based on congestive heart failure (CHF) or digoxin use, or both, in addition to three exercise variables. These are exercise-induced ST segment depression, a “change in systolic blood pressure” (SBP score) (values ranging from 0 for an increase in blood pressure >40 mm Hg to 5 for a decrease below the level of blood pressure at rest) and exercise capacity in METs.

<table>
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<tr>
<th>Table 2—Mortality Rate by Risk Group*</th>
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<tr>
<td>Duke Risk Category</td>
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<tr>
<td>---------------------</td>
</tr>
<tr>
<td>Low (≥5)</td>
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<tr>
<td>Moderate (−10 to +4)</td>
</tr>
<tr>
<td>High (≤−11)</td>
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*Mortality rate of risk categories determined by the Duke and Veterans Affairs prognostic scores. Data from the initial studies of the Duke inpatient population and the Veterans Administration population that had been referred for cardiac catheterization are reported.

<table>
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<th>Table 3—Projected Annual Mortality From Prognostic Score</th>
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<tr>
<td>Annual cardiovascular mortality=−0.00018 (Duke score)2−0.0071 (Duke score)2+0.143 (Duke score)+1.60</td>
</tr>
<tr>
<td>Annual cardiovascular mortality=0.0026 (VA score)2+0.105 (VA score)+1.37 (VA score)+6</td>
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*Polynomial equations derived from survival curves of the Duke and VA study populations. Equations can be used to calculate a given patient’s annual cardiovascular mortality based on their Duke or VA prognostic score. (Table 1). Variables found to be independently associated with time to cardiovascular death were weighted, according to their power, to create an equation that calculates a numeric score. Annual mortality for 4 years of follow-up was determined in each population. The derived equations allow stratification of patients into low-, moderate-, and high-risk groups (Table 2). Additionally, polynomial equations were calculated from the plots of mortality vs prognostic score that allows for individualized calculation of estimated mortality for a specific score (Table 3). Such a protocol allowed the investigators to assess more accurately which patients warranted referral for cardiac catheterization; namely, those patients whose risk of mortality from coronary artery disease was higher than that from coronary artery bypass surgery.

The VA study additionally provided further evidence of overuse of invasive cardiac procedures, even in a “non-fee for service” setting. Of the 588 patients selected for cardiac catheterization, 53% had a projected 4-year cardiovascular mortality of less than 2%. Of those selected for bypass surgery, 35% had a 4-year cardiovascular mortality of less than 2%. The Parsonnet scoring system, which estimates operative mortality from case-mix data, yields a minimum 2% mortality from coronary artery bypass surgery, even in patients of the lowest risk profile. Therefore, these patients would usually do better with medical management and do not require invasive procedures.

It appears that physicians have an exaggerated perception of the risk of ischemia in patients with stable coronary artery disease. Therefore, the studies concluded that the use of such equations permits a better understanding of the risk of ischemia and helps internists to restrict cardiac catheterization and by-
pass surgery to those patients who truly have an increased risk of cardiac mortality.

**Applicability of the Duke and VA Scores to the General Population**

Is it reasonable to assume that the equations constructed for these two specific study populations generate data that are valid for the patients of any practicing internist? Both studies attempted to address this question through their study design. Although the equations were each generated from populations with a relatively high prevalence of disease, each group reaffirmed their findings by further evaluating an outpatient population.\(^7\)\(^8\)\(^10\)\(^11\) Additionally, the researchers at the VA analyzed the VA population with the Duke score, and found that the resultant risk stratification was very similar to that generated by the VA score\(^11\) (Fig 1). This similarity suggests that the scores are applicable to a broad patient population. Nevertheless, the Duke score is more applicable to women and nonveterans, since the VA population had no women, and the Duke score has been independently validated. The VA score should be used for veterans and also for patients who have a history of congestive heart failure or perhaps exertional hypotension since the Duke score does not consider these indicators.

**Defense of Natural History Studies**

Critics of this approach to evaluation of risk in patients with coronary artery disease would question the ability of the Duke and VA studies to assess accurately outcome. It is true that attempts to delineate the natural history of coronary artery disease are plagued by the necessity of intervention if a patient presents with an unstable clinical picture. In other words, if a patient were to present with unstable angina, it would not be medicolegally feasible to allow the patient to continue without treatment to observe outcome, given high clinical suspicion of an adverse result. Therefore, the sickest patients may be removed from the data and lessen the ability of certain variables to predict outcome.

On further consideration, however, natural history studies can be defended on several grounds. The above concerns would prove significant if the rate of intervention in these studies was high. In nine natural history studies that attempted to determine the independent predictive value of clinical and exercise test variables, the annual rate of cardiac catheterization in the populations that were not initially selected for catheterization was only 2% over a 5-year follow-up.\(^12\)\(^13\)\(^14\)\(^15\)\(^16\)\(^17\)\(^18\)\(^19\) Thus, few patients were removed from follow-up analysis. In the populations that were selected for study because they underwent cardiac catheterization, the intervention rate was much higher, approaching 25% over 5 years. This higher rate of intervention is mitigated by the fact that low-to-moderate risk patients represent a high percentage of those selected for both further catheterization and therapeutic intervention. Lastly, the process of censoring, while it potentially removes patients selected for intervention, should remove these patients from both the numerator and the denominator in risk calculations. While true natural history studies cannot be ethically accomplished for coronary artery disease, the available studies do offer a reasonable approximation of outcomes and certainly are more scientifically based than empirical assumptions.

**Practical Implications for the Internist**

The time-honored approach to the evaluation of coronary artery disease can benefit from the addition of these decision-making scores. After the initial assessment by the internist, patients with suspected coronary artery disease can undergo exercise testing. Using the above equations, the internist can decide which patients to refer to a cardiologist for invasive testing based on the patient’s risk stratification. The internist will additionally be able to rapidly and accurately counsel patients as to their risk of mortality from coronary artery disease. This model is overly simplistic in that it does not address those patients in whom exercise testing is contraindicated and those patients for whom invasive procedures might produce valuable symptomatic relief rather than increased longevity. As a practical tool for many patients, however, it will allow the internist to more judiciously use invasive cardiac procedures.
ESTIMATED PROGNOSIS

The age expected annual mortality from any cause is 5.4% (National Center for Health Statistics, 1990). The VA score (METs, CHF, SBP rise, and ST depression) estimates an annual cardiovascular mortality of 4.4% (not greater than two times the age expected mortality). The Duke Score (METs, ST depression, and treadmill angina) estimates an annual cardiovascular mortality of 3.7% (not greater than two times the age expected mortality). The estimated operative mortalities for bypass surgery are 16% (Parsonnet, 1989), 3% (NY State Dept. of Health, 1992) and 3% (VA, 1993). The posttest probability for coronary artery disease is 97% (Morise, 1992). The probabilities of having severe coronary artery disease are 41% (Duke, 1993), 56% (Detrano, 1992) and 96% (Morise, 1992).

FIGURE 2. Computer-generated estimates of prognosis and disease severity. The Expert System (EXTRA) calculates the VA and Duke scores from the clinical and exercise test data, in addition to the National Center for Health Statistics' age expected annual mortality, and the estimated operative mortality calculated with the Parsonnet, the New York State Health Department, and the VA Surgical Study scores. Disease probability (pretest and posttest) and disease severity are predicted by the Morise, Duke, and Detrano algorithms.

IMPLICATIONS OF COMPUTERIZED CALCULATION FOR UTILITY OF SCORE

To use the equations to help decide which patients to refer for catheterization, the internist must calculate the mortality risk from coronary bypass surgery for each patient as well as the Duke or VA score. Risk of bypass is highly dependent on patient profile. While this process is straightforward, the internist may have concerns about the cost in time needed to calculate risks.

At the PAVAMC, we have developed a computerized expert system called EXTRA (Exercise Test Reporting Aide) that has simplified the process of generating risk profiles. The internist enters pertinent patient information into a computer, including age, race, medications, cardiac history, risk factors, ECG data, and results of the exercise treadmill test. The computer then analyzes the data and at the bottom of the printout calculates both the VA and Duke scores, as well as the age-expected annual mortality from any cause, and the estimated operative mortality for bypass surgery. (Fig 2). The immediately printed report, therefore, quickly provides the data that the internist needs to assess the need for invasive cardiac procedures.

FOLLOW-UP OF LOW-RISK PATIENTS

While the VA and Duke equations are based on 4-year survival data for patients in a given risk group, coronary artery disease is a progressive disease, and a patient may change risk group after this time. How should the low-risk patients that are not referred for catheterization be managed?

Prevention

The first approach for the internist is to promote prevention of progressive disease. Recent data have supported the role of risk factor modification not only in the role of disease prevention, but also in actual regression of atherosclerotic disease. Therefore, patients should be advised to stop smoking, exercise, lose weight, and modify dietary habits to lower fat and sodium intake as necessary. In addition, stress management skills should be taught.

Medical Management

For patients in whom hyperlipidemia or hypertension is refractory to dietary or behavioral modification, appropriate lipid-lowering agents or antihypertensives should be used. Diabetics should attempt to keep blood glucose levels under good control, in light of recent studies that show decreased microvascular sequelae of diabetes in patients who maintain tight control of blood glucose levels. While to our knowledge no prospective data are available for the impact of tight control of diabetes on cardiac morbidity and mortality, it is reasonable to infer a similar reduction in cardiac risk.

Antiangina drugs, while ameliorating symptoms and increasing exercise tolerance, do not have a curative or preventive role in coronary artery disease. To the extent to which they improve quality of life, and thereby facilitate other risk factor modification, their role cannot be understated. Aggravating medical conditions should be monitored and controlled, including dysrhythmias, anemia, and thyrotoxicosis.

Reassessment

The patient with “low-risk” angina should have routine follow-up visits once a year or more frequently if risk-factor modification requires more frequent evaluation. Unless the patient manifests signs of worsening disease, the patient is not in need of further testing. If the patient does exhibit symptoms that imply progression of ischemia or myocardial damage, such as clinical congestive heart failure,
reduced exercise tolerance, or unstable angina, it is reasonable to assume that the calculated risk will have changed. Therefore, such patients should undergo repeated exercise testing with repeated risk calculation. If the patient is still at a lower risk of cardiac death than risk of operative mortality, the patient should continue to be medically managed.

In summary, current medical practice has taken a very aggressive approach to managing coronary artery disease in terms of both diagnosis and therapy. The number of invasive cardiac procedures performed is increasing, despite decreasing cardiac mortality. Given that this aggressive approach has now become the "standard of care," it is difficult for practitioners to decide against these invasive procedures. Additionally, this aggressive approach fosters an exaggerated notion of the risk of ischemia. Therefore, invasive cardiac procedures are often performed in low-risk patients whose disease severity does not warrant such intervention.

Due to overwhelming public concern over the expense of medical services, rationing of health-care dollars is an increasing priority. Inherent to the process of rationing is the fact that money spent for one patient is de facto being "taken away" from another. Currently, money that could be channeled into AIDS or used to vaccinate children is being spent on unnecessary cardiac procedures. There exist ways, however, to allow the internist to decide which patients require invasive measures using noninvasive parameters. After a history, physical examination, and a treadmill test, the Duke and VA scoring systems allow internists to provide information regarding the patient's status and to help make recommendations for optimal management. With advances in computerized data gathering, these scoring systems will become progressively easier to use. The internist will thus be able to rapidly determine both a diagnostic and therapeutic plan and provide the patient with prognostic information. Ultimately, this will lead to a more cost-effective and appropriate use of invasive cardiac procedures.

REFERENCES