In the following discussion we recommend that under certain circumstances one should consider switching to less expensive testing protocols in individual patients.

**Pre-test probability of CAD.** The diagnostic yield of exercise testing varies in different patient populations. The discriminate effectiveness of testing (i.e., the difference between pre- and post-test probability of CAD) is, in keeping with Bayesian probability analysis, relatively small in patients with low (<30%) or high (>70%) pre-test probability. Moreover, patients with a low probability of disease will have a relatively large number of false-positive results, whereas patients with high probability of disease might have false-negative results. Thus, it is important to consider the pre-test probability of disease (based on age, sex, and type of symptoms) when evaluating the clinical significance of test results.

It is well acknowledged that patients with a high probability of CAD should not undergo stress testing but, under appropriate clinical circumstances, should be referred directly for coronary angiography. Moreover, patients with a low probability of disease should not be tested at all. However, in clinical practice it might be difficult to categorize patients precisely in discreet pre-test probability categories. Particularly, the distinction between low and intermediate probability of CAD might be blurred.

The concordance between the results of exercise ECG and radionuclide MPI is also affected by the pre-test probability of disease. When the exercise ECG is normal in patients with low (<30%) pre-test probability of disease, MPI is generally normal as well (2). Thus, stress MPI does not add new information in these patients. However, in patients with the same pre-test probability but a positive exercise ECG, stress MPI might be abnormal in only one-half of these patients (2). One might anticipate that many patients in the low-probability category have normal stress results. Thus, a stepwise diagnostic approach might be cost-effective: if the symptom-limited exercise ECG (step 1) is normal, no further testing is needed; however, if the exercise ECG is positive, step 2 should consist of exercise MPI to resolve the issue of whether there is a false-positive exercise ECG. With this modification of the stress-testing algorithm, a substantial number of low-probability patients will not need radionuclide MPI.

**Duke treadmill score (DTS).** Exercise performance itself provides important information with regard to a patient’s risk of an adverse outcome. The DTS, which incorporates the presence or absence of angina, exercise ECG changes, and exercise capacity in METs, allows for post-test stratification of patients into low-, intermediate-, or high-risk categories for future cardiac events (3). Of note, maximal heart rate is not part of the DTS. Radionuclide MPI can further refine cardiac risk stratification within each DTS category. For example, although approximately 70% of the patients with a low-risk DTS indeed have normal MPI and a low annual cardiac event rate of 0.5%, approximately 30%
of patients might have abnormal radionuclide MPI and an intermediate cardiac annual cardiac event rate of approximately 3%.

**METs and prognosis.** There is a strong relationship between maximal exercise capacity and cardiac outcome. Patients who cannot achieve 7 METs (stage 2 of the Bruce protocol) are at very high risk of cardiac events. However, at such a low level of exercise one should attempt to distinguish between true cardiac limitation and decreased exercise capacity caused by lack of motivation, deconditioning, or orthopedic problems. This distinction is not always possible. Rather than chance nondiagnostic test results, patients who cannot complete stage 2 should be switched to pharmacological vasodilator stress testing.

In this issue of the *Journal*, Bourque et al. (4) focus on good exercise workload (≥10 METs, start of stage 4 of the Bruce protocol) and peak exercise heart rate as a means of identifying patients in whom radionuclide MPI does not provide incremental value. This is an important attempt to lower the cost of diagnostic testing for CAD by customizing stress testing in certain patient cohorts and foregoing the expense associated with radionuclide imaging. In this study, patients who achieved an exercise workload of ≥10 METs, reached 85% of their age-predicted maximal heart rate, and had no ischemic ECG changes (which constituted 31% of their patients) had no significant myocardial ischemia on exercise MPI. The authors propose that patients who meet these exercise characteristics should not be injected with radiopharmaceuticals, because cardiac imaging will not provide new information. If such customized exercise testing were to be applied widely, substantial cost savings could be achieved on a national level.

**Maximal exercise heart rate.** Patients who achieved a workload of ≥10 METs but did not achieve 85% of their age-predicted maximal heart rate had more ischemia than patients who achieved a similar workload but reached their target heart rate (4). At first glance this seems counterintuitive. One would suspect that the former group of patients were perhaps in better physical shape and might achieve a higher heart rate at a higher workload. However, exercise testing was symptom limited. These patients were more often taking beta-adrenergic receptor-blocking medication, had more known CAD, and might have had chronotropic incompetence.

Bourque et al. (4) assign great importance to achieving 85% of maximal age-predicted heart rate. This exercise parameter deserves commentary. As pointed out in the preceding text, peak exercise heart rate was never intended to be an exercise end point in itself, not in the original Bruce protocol (1), in the DTS (3), or in the American College of Cardiology/American Heart Association guidelines for exercise testing (5). In reviewing laboratories that applied for accreditation by the Intersocietal Commission for Accreditation of Nuclear Laboratories (6), it was noted that many clinical laboratories erroneously consider 85% of age-predicted heart rate as the primary exercise end point. Patients often were allowed—applying this criterion—to stop prematurely, before symptoms or fatigue occurred, resulting in inadequate stress testing.

In the early 1970s, Fox et al. (7) developed the concept of age-predicted maximal heart rate during exercise. The 85% heart rate threshold was arbitrarily defined for exercise prescription and assessment of cardiovascular fitness. Although there is a linear relationship between exercise workload and exercise heart rate, maximal achievable peak exercise heart rate decreases with age, and there is substantial variability in maximal heart rate among individuals of the same age. Tanaka et al. (8) prospectively revisited the validity of peak exercise heart rate in 514 healthy subjects. They observed that the customary equation (220 – age) significantly underestimated the maximal heart rate in subjects older than 40 years of age. Thus, with the conventional equation the true level of physical exercise might be significantly underestimated in the age group where CAD is most commonly suspected. Moreover, there is substantial scatter of data points around the regression line, which makes the use of a single target number very problematic (Fig. 1).

Thus, in the study by Bourque et al. (4) the importance of achieving a target heart rate seems overstated. Of greater importance might be the lack of achieving an adequate heart rate increase despite maximal effort, unmasking chronotropic incompetence, which is another predictor of adverse outcome.

**Customized exercise testing.** Customized stress testing seems very feasible. Adjusting the stress protocol to the individual patient might potentially affect the overall cost of national health care by substantially decreasing the expense of diagnostic cardiac stress testing while minimally impacting the detection of CAD. However, it...
cannot be overemphasized that this requires that cardiac stress tests are closely supervised and that one is prepared to modify the stress protocol at a moment’s notice.

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