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Trends in Noninvasive Testing for Coronary Artery Disease: Less Exercise, Less Information

Exercise testing, with or without imaging, has long been recognized as a safe and effective means for detecting obstructive coronary artery disease and providing important risk stratification in appropriately selected patients.

Pharmacologic stress tests were developed as an alternative to exercise testing for patients unable to perform exercise protocols. These tests increase heart rate and cardiac output or chemically induce coronary vasodilatation to unmask significant coronary stenosis. Patterns of stress testing (ie, exercise vs pharmacologic) may be related to the patient population, availability of specific resources in stress laboratories, and comorbidities.

Pharmacologic stress tests must be performed with imaging. Lucas et al[1] observed that in less than a decade, there has been a 3-fold increase in any stress imaging, averaging 6 tests per 1000 Medicare beneficiaries per year, despite no increase in prevalence of myocardial infarction over the same time period. With the aging population and obesity epidemic, stress testing may shift toward greater performance of pharmacologic studies as opposed to exercise; however, we opine that pharmacologic studies provide less information than exercise tests and may lead to inaccurate estimates of cardiovascular risk.

In our stress laboratory, we have maintained a longstanding policy to implement dynamic exercise as the standard stress test protocol. However, we have observed trends over time showing an increasing percentage of stress imaging tests have been performed pharmacologically rather than with exercise. Whereas 15 years ago, pharmacologic stress tests comprised one third of our stress imaging tests, these tests are now performed in nearly equal numbers to exercise tests. At our institution, pharmacologic stress testing initially became available for nuclear perfusion imaging in 1987 and for stress echocardiography in 1990. Initial growth in use may partly represent improved acceptance of new techniques. However, this does not account for the continued growth in use of pharmacologic stress testing.

Older adults may be more likely to be studied pharmacologically, although this may vary by testing modality. The mean age of patients undergoing pharmacologic nuclear tests at our institution increased between 1993 and 2008 at a rate of 0.7 ± 0.1 years per 5 calendar years. However, the age of patients undergoing dobutamine echocardiography declined over the same period (0.7 ± 0.2 years per 5 years). Thus, it would appear from these data that factors other than age account for the increase in use of pharmacologic stress testing.

The obesity epidemic may have influenced cardiovascular testing toward pharmacologic protocols. In our laboratory, the mean body mass index (BMI) of patients significantly increased for both pharmacologic nuclear studies (0.9 ± 0.2 kg/m^2 per 5 calendar years) and dobutamine echocardiograms (1.0 ± 0.1 kg/m^2 per 5 years) between 1993 and 2008 ($P < .001$ for both). One third of US adults are obese (BMI ≥30 kg/m^2), and obesity has been associated with comorbidities linked to cardiovascular disease.[2] Greater BMI has been associated with cause-specific mortality and lower survival, such that for each 5 kg/m^2 above a BMI of 25 kg/m^2, there is, on average, a 40% increased risk of cardiovascular mortality.[3] When we pooled pharmacologic nuclear and dobutamine echocardiogram studies from our institution from 1993 to 2008, trends reflected a slight decline in mean age but a significant increase in mean BMI among patients (**Figure 1**). Associated comorbidities, including musculoskeletal or neurologic conditions, may preclude the use of exercise testing because of an inability to achieve an adequate workload, and such patients should undergo pharmacologic methods for risk assessment.[4]

The preference of exercise testing over pharmacologic methods is based on numerous studies demonstrating the prognostic importance of information elucidated during symptom-limited exercise, including functional capacity and exercise duration,[5-7] heart rate[8-10] and rhythm,[11] and blood pressure responses.[12] Guidelines were developed on the basis of the pivotal assumption that able patients should be given an exercise test, optimally over an 8- to 10-minute interval, rather than receive pharmacologic testing.[13] A person's functional capacity, often estimated in units of oxygen uptake as metabolic units from treadmill speed and grade, is a powerful prognostic factor and at least as

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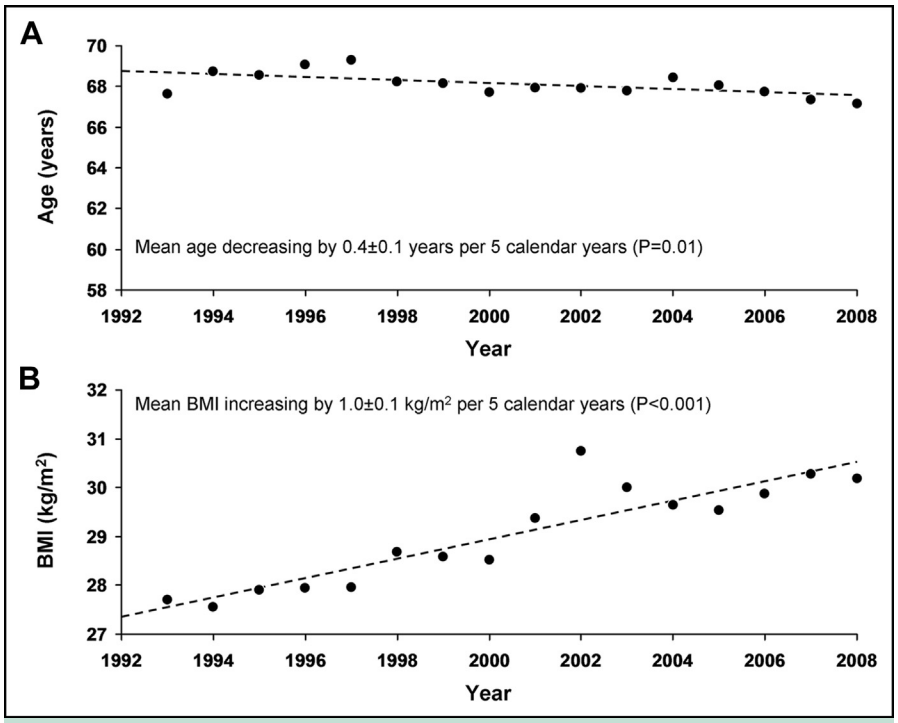

Figure 1 Linear regression showing change over time with respect to mean age (**A**) and mean BMI (**B**) in patients undergoing pharmacologic stress imaging (dobutamine echocardiography [n = 36,461] or pharmacologic nuclear [n = 7236]) at Mayo Clinic Rochester from 1993 to 2008. Age decreased by 0.4 ± 0.1 years per 5 calendar years ($P = .01$), and BMI increased by 1.0 ± 0.1 kg/m^2 per 5 years ($P < .001$). BMI = body mass index.

predictive of clinical events as myocardial perfusion abnormalities (ie, "positive" stress test). Prediction of cardiac events and mortality has been strongly associated with workload achieved, autonomically mediated heart rate changes such as heart rate recovery, and hemodynamic responses, information that is lacking from pharmacologic studies.

Reassurances given to patients after normal stress imaging studies should account for the type of testing performed (exercise vs pharmacologic). For example, cardiac event rates at 1 and 3 years were lower after a normal exercise echocardiogram compared with a normal dobutamine stress echocardiogram.[14,15] Patients with normal exercise studies who experienced clinical events were predicted on the basis of exercise-induced angina and low exercise capacity.[14] Adverse events in patients with normal dobutamine stress echocardiogram were predicted by comorbidities, such as diabetes and prior coronary disease.[15] Likewise, Rozanski et al[16] found that mortality was 2-fold higher in subjects with normal adenosine nuclear studies compared with normal nuclear exercise studies after matching subjects on baseline characteristics using propensity scores. The lowest annual mortality (<1%) was observed among patients with normal nuclear exercise study results, who were also in the highest quartile of exercise duration (≥9 minutes).[16] Assessment of myocardial viability with dobutamine stress echocardiography and assessment of the patient with left bundle branch block with nuclear perfusion imaging are situations in which pharmacologic stress testing is preferred, but they account for small numbers of tests.

Pharmacologic stress testing has an established track record for diagnostic accuracy, prognostic utility, and safety, and remains necessary in situations when exercise testing cannot be implemented. However, these studies deprive the provider of valuable test information, such as functional status, symptom status with exercise, and heart rate and blood pressure responses. Testing patterns that shift to drug provocation in lieu of exercise are less informative to clinicians who are interested in physiologic responses that convey the cardiovascular health status of their patients. Trends showing increasing use of pharmacologic stress protocols are concerning, because the lesser information available from these tests places the clinician in an increasingly precarious position of post-test management without having all of the important information.

S. Michael Gharacholou, MD, MSc
Patricia A. Pellikka, MD
Division of Cardiovascular Diseases
Department of Internal Medicine
Mayo Clinic
Rochester, Minn

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