There is still a role for exercise testing in prognostic cardiology

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Stress echocardiography is a non-invasive test that is used to assess myocardial function and possible ischemic changes with increased cardiac workload; it can also assess the distribution of blood supply, as well as cardiac muscle viability and ability to perform normal function. Stress echocardiography is an established technique for the assessment of patients with suspected and established coronary artery disease (CAD). (1) It has been proposed that combining stress imaging may improve the accuracy of the exercise electrocardiogram (ECG) analysis. In the ischemic cascade, myocardial regional wall abnormalities occur even before significant ECG changes. (1, 2)

Exercise testing with echocardiography has been considered as an easily available examination modality for diagnosing coronary heart disease (CHD). However, false-positive exercise ECG tests are mostly observed in asymptomatic adults, especially among women. Therefore, the use of exercise ECG tests should focus on certain populations based on their pre-test probability and moreover, there is not enough evidence to recommend exercise ECG as a routine screening test.(3) Thus, current guidelines recommend against the use of exercise testing for risk assessment in asymptomatic subjects with a low (<10%) pre-test likelihood of CHD.(4) However, a number of recent studies have extended our knowledge on the prognostic significance of exercise testing and suggest that the prognostic value of exercise testing may have been underestimated. Cardiorespiratory fitness, an indicator of cardiopulmonary function and measured by maximal oxygen uptake during cardiopulmonary exercise testing, has been considered as a vital clinical sign and one of the most important prognostic measures.(5, 6)

We have demonstrated in one of our previous studies that myocardial ischemia during exercise and recovery, as indicated by ST depression in an ECG, is associated with acute coronary events and CHD death.(7) An important finding was that exercise-induced myocardial ischemia was a stronger predictor of CHD in those with an unfavorable coronary risk factor profile, i.e., in smokers and hypercholesterolemic and hypertensive men(7). Not only painful but also painless myocardial ischemia is quite commonly observed during the exercise. Indeed, we have found that painless myocardial ischemia during exercise, based on ST-segment depression in ECG, was present in 10.7% of a population-based sample of middle-aged males.(7) We have also shown that silent ischemic ECG findings that prolonged or developed during recovery were associated with an increased risk of both acute coronary events and CHD death.

In the current issue of the International Journal of Cardiology(8), Fitzgerald and colleagues using a sample of 3020 consecutive patients with mean age 58 years, investigated prospectively if ECG changes (ST-segment depression) during exercise testing can be prognostically important compared to echocardiographic stress imaging. The main objective of their study was to assess if exercise

induced ECG changes in the setting of a normal stress echocardiogram were associated with adverse outcomes. The study defined a prognostically significant level of ST depression based on patient outcomes using the cut of equal to or greater than 1.5mm depression in the ST segment of ECG findings. In this study(8), patients underwent standard Bruce protocol treadmill testing with digital gated echocardiography before and after exercise. The results confirm that non-ischemic stress echocardiography confers a good prognostic result. The study emphasizes the value of stress echocardiograms, with all non-ischemic stress echocardiograms indicating low adverse event rates, regardless of accompanying ECG changes.

Exercise ECG test can be performed without additional echocardiography devices. In the recent study, the echocardiogram was performed by cardiac sonographers, but all tests were supervised and read by cardiologists with subspecialty training in stress echocardiography.(8) Standard Bruce protocols were used to produce exercise stress test for all patients in a reproducible way. Diagnostic ST segment depression was defined as horizontal or downsloping ST depression 0.08 seconds from the J-point of at least 0.5mm.(8) While the definition for ST depression was set at 0.5mm, a predetermined evaluation was to assess the clinical value of degrees of ST depression (0.5mm, 1mm, 1.5mm, 2mm and greater than 3mm).

This study confirms that significant ST segment depression despite non-ischemic stress echocardiographic imaging carries a poorer prognosis compared to patients with normal exercise ECG analysis. The study results suggest that 1.5mm of ST depression during exercise testing appears to be the prognostically significant amount of change, but less ST depression than 1.5mm can be regarded as not prognostically significant. The results also suggest that high exercise capacity has a moderating effect and that those patients have low risk going forward despite the abnormal ECG finding.(8) Importantly, the study also suggests that all patients with a non-ischemic stress echocardiogram have low cardiac risk.(8) Exercise capacity has been consistently shown to be a strong predictor of mortality outcomes.(6) The recent study also demonstrated that exercise capacity had a modulating effect on the outcomes of exercise induced ST change, and exercise capacity of at least 13 METs was related to an excellent prognosis despite coexistent ECG changes. (8)

There are some issues which limits the wider use of stress echocardiography. First, it requires special skills for the operators whereas exercise ECG is an easily available in many hospitals. As an alternative to exercise stress testing, computer tomography coronary angiography (CCTA) is not possible for all patients in all ages. Second, it is possible that echocardiographic abnormalities may be due to other reasons such as left ventricular diastolic dysfunction or other cardiac diseases. More

studies in both genders would be needed to confirm that 1.5mm or other level of ST depression during exercise testing should be considered as a cut-off of ischemic ECG changes (instead of 1mm ST depression). Females have increased incidence of exercise induced ST depression and it is uncertain if the cut-offs for ST depression should be different based on gender and other characteristics. Age and an exaggerated exercise blood pressure response may also have an influence on ECG changes. Finally, repolarization and conduction abnormalities such as bundle branch block and pre-excitation can make interpretation ST-segment depression of ECG impossible.

Usefulness of exercise stress testing with cardiac imaging for the detection of myocardial ischemia has been documented.(1) CCTA has become more popular as a diagnostic tool for CAD. Compared with functional stress testing methods including exercise testing, CCTA imaging technique use is associated with a reduced incidence of myocardial infarction but an increased incidence of invasive coronary angiography, revascularization, CAD diagnoses, and the use of aspirin and statins.(3) However, it is usually recommended only for relatively low-risk populations to exclude CAD, because it may overestimate stenosis degrees and coronary calcifications in high-risk patient populations. CCTA does not provide data about the physiological importance of the observed stenosis without additional coronary flow measurement protocols which would be even more time-consuming and expensive. Therefore, there is still a need to use exercise testing, which provides the whole picture of the functional capacity, which is the main measure of prognosis. Exercise echocardiography could be used as an additional tool for diagnostics and assessing physiology when there are resources and skills to perform and interpret all provided data. Indeed, exercise testing has an important role in prognostic cardiology and its use should be widely encouraged - if clinicians should rely only on anatomic imaging data without functional aspects, treatment of chronic CAD would be challenging.(9, 10)

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