Exercise testing and disease risk: individualized medicine without the “omics”?

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EXERCISE TESTING is a powerful physiological tool that can provide insights into cardiopulmonary fitness, all-cause mortality, and the risk of death from cardiovascular disease (1, 9). It can also be combined with a variety of other technologies to provide specific insight into a variety of pathophysiological conditions in selected groups of patients. Perhaps most well-known of these combinations is graded treadmill exercise testing along with a 12-lead electrocardiogram (ECG) to detect evidence of myocardial ischemia during exercise. As heart rate and blood pressure rise, myocardial oxygen demand increases and if this is not accompanied by a parallel rise in myocardial blood flow due to a flow-limiting lesion in the coronary arteries, evidence of myocardial ischemia is seen on the ECG (1, 3). Additionally, when this information is combined with demographic data, measures of exercise capacity, hemodynamic responses to exercise, and various forms of cardiovascular imaging, even more insight about the risk profile of a specific patient can be obtained. Information from these tests can be useful to guide therapeutic decision making and to assess the cardiovascular risks associated with other medical interventions like surgery (1).

In the 1960s and 1970s, as the data on exercise testing as a powerful diagnostic tool for ischemic heart disease emerged, the “average” patient was frequently a middle-aged male with a number of risk factors who was capable of performing a treadmill test. However, the question of how to evaluate patients who are unable to complete an exercise test for orthopedic or other reasons has always been problematic. This challenge seems to be increasing with the aging of the population, along with the combined effects of the obesity, diabetes, and peripheral artery disease epidemics, which all operate to limit the ability of many individuals to simply walk on the treadmill. Additionally, individuals with spinal cord injuries are living longer and coronary artery disease is now an issue for these patients.

One alternative is arm exercise testing. This can usually be performed by individuals not able to perform leg exercise, and although exercise capacity is lower with the arms than the legs, even mild levels of arm exercise can evoke robust heart rate and blood pressure responses to exercise (1). This is important because of the well-known linkage between heart rate, blood pressure, and myocardial oxygen demand, which can normally evoke large increases in coronary flow as described above (3).

In the study by Chan and colleagues (1) in this issue of the Journal of Applied Physiology, a population of older patients unable to perform treadmill exercise testing was subjected to a rigorous arm exercise protocol. The main findings are that low exercise capacity with arm exercise, ECG changes during arm exercise, and defects in myocardial perfusion imaging were all associated with either mortality or the likelihood of a future myocardial infarction. In this context, the ability of exercise capacity and exercise ECG results to provide substantial insight about future risk was especially impressive and shows the continuing utility of what might be called “low tech” physiologically based diagnostic testing.

In addition to the physiological data, the authors took advantage of the sophisticated electronic medical record system available to investigators at the U.S. Veterans Affairs Health System to track the patients and ascertain long term outcome data. In this context, the study of Chan et al. (1) shows the potential power of what might be called high-resolution, physiologically based phenotyping along with an integrated medical record system to provide insight about individual patients. While there has been much discussion about so-called individualized or personalized medicine based on “omic” markers of disease risk, results so far have been disappointing (2, 4, 6–8). That physiologically based testing can play such a central role in determining disease risk for both individuals and groups of patients is continuing evidence of the importance of physiology in clinical medicine (5). Perhaps the revolution in individualized medicine is already here but has been ignored or is hiding in clinical physiology labs.

DISCLOSURES
No conflicts of interest, financial or otherwise, are declared by the author.

REFERENCES