A nomogram of exercise capacity for age predicted mortality in women with cardiovascular symptoms

Gulati M, Black HR, Shaw LJ, et al. **The prognostic value of a nomogram for exercise capacity in women.** N Engl J Med. 2005;353:468-75.

Clinical impact ratings: GIM/FP/GP ★★★★★★☆ Cardiology ★★★★☆☆☆ Geriatrics ★★★★★★☆

Question

In women with cardiovascular symptoms and in asymptomatic women, does the percentage of predicted exercise capacity for age predict all-cause and cardiac mortality?

Methods

Design: 2 cohort studies, 1 for derivation of a nomogram (St. James Women Take Heart Project [SJWTHP]) and 1 for validation (Economics of Noninvasive Diagnosis Study [ENDS]).

Setting: Metropolitan Chicago (SJWTHP) and 6 medical centers in the United States (ENDS).

Patients: The derivation cohort included 5721 women ≥ 35 years of age (mean age 52 y) with the ability to walk on a treadmill at a moderate pace, weight ≤ 148 kg, and blood pressure < 170/110 mm Hg. Exclusion criteria included pregnancy, typical angina symptoms, history of cardiac disease, and incomplete data on cardiac risk factors. The validation cohort included 4471 women (mean age 61 y) with cardiovascular symptoms. Women who were recently hospitalized for unstable angina, myocardial infarction, or coronary revascularization were excluded.

Description of prediction guide: For all participants, exercise capacity (measured in metabolic equivalents [METs]) was estimated based on the speed and grade of a treadmill according to the Bruce protocol. Through use of the derivation cohort, a linear regression of exercise capacity on age was calculated as MET = 14.7 – 0.13 × age. For a given age, the percentage of predicted exercise capacity was obtained from (observed METs ÷ age-predicted METs) × 100. A nomogram to determine the percentage of predicted exercise capacity for age was constructed using the linear regression equation for the deviation cohort. The association between exercise capacity and mortality was assessed using Cox proportional-hazards models.

Outcome: All-cause and cardiac mortality.

Main results

In both derivation and validation cohorts, the rates of all-cause and cardiac mortality were greater in women with exercise capacity < 85% of the age-predicted value than in women with exercise capacity ≥ 85% of the age-predicted value (Table). Both rates were also greater in women whose exercise capacity was less than that predicted for age than in women whose exercise capacity exceeded the age-predicted value by more than 3 METs (Table).

Conclusion

In women with cardiovascular symptoms and asymptomatic women, the percentage of predicted exercise capacity for age predicted all-cause and cardiac mortality.

Sources of funding: AstraZeneca; DuPont Pharmaceuticals; Irwin Foundation; Merck; Pfizer/Pharmacia; Siemans Gamasonics; St. James Hospital and Health Centers.

For correspondence: Dr. M. Gulati, Northwestern University, Chicago, IL, USA. E-mail m-gulati@northwestern.edu.

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Associations between exercise capacity and all-cause and cardiac mortality in women*

Exercise capacity	Hazard ratios (95%)			
	All-cause mortality		Cardiac mortality	
	Derivation cohort	Validation cohort	Derivation cohort	Validation cohort
< 85% of predicted value for age†	2.03 (1.51 to 2.71)	2.37 (1.90 to 2.97)	2.44 (1.46 to 4.09)	2.02 (1.43 to 2.85)
Observed minus predicted value < 0 vs > 3 METs	2.63 (1.33 to 5.19)	3.28 (2.47 to 4.35)	4.27 (1.03 to 17.6)	3.80 (2.26 to 6.38)

*METs = metabolic equivalents; CI defined in Glossary.
†The reference group was women whose predicted exercise capacity was ≥ 85% for age.

Commentary

The study by Gulati and colleagues provides important information about predicting age-adjusted exercise capacity in women. Moreover, it reemphasizes the prognostic importance of functional status, specifically the percentage of predicted exercise capacity. Beyond these results, the implications are less clear.

Previous studies have shown independent prognostic significance of exercise capacity in suspected coronary heart disease (1), and this has led guidelines to call for exercise as the preferred provocative stimulus for stress testing and exercise capacity as a key variable for prognostication. The study by Gulati and colleagues further calls into question the increasing infatuation, especially in the United States, with pharmacologic stress testing, even in patients who can exercise. While it is tempting to use this study to underscore the clinical importance of encouraging physical fitness, the study simply reports an association and does not address causality or the effect of interventions to improve exercise capacity.

Should we use this nomogram to risk-stratify in practice? Probably not, at least not yet. The nomogram was developed in a sample of asymptomatic women (85% white) with "the ability to walk on a treadmill at a moderate pace," thus almost certainly overestimating exercise capacity compared with a truly representative sample. Surprisingly, Gulati and colleagues did not report what proportion of the symptomatic sample achieved predicated exercise capacity, thus we have little information about the comparability of the samples. The authors did not provide adequate information on how well the predictive model discriminates risk. The exercise capacity threshold of 85% of the age-predicted value, and more important, categories according to an absolute difference in expected compared with observed METs, provide some information. But we need to know the relation between capacity as a continuous measure and outcome, since that would provide the most useful predictive value. Exercise capacity data are routinely collected during exercise stress testing, and further prospective quantification is warranted.

Christopher Granger, MD, FACC
Duke University Medical Center
Durham, North Carolina, USA

Reference

1. **Mark DB, Shaw L, Harrell FE Jr., et al.** Prognostic value of a treadmill exercise score in outpatients with suspected coronary artery disease. N Engl J Med. 1991;325:849-53.