Arm exercise as an alternative to pharmacologic stress testing: Arm exercise stress testing and outcome

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Background Treadmill exercise variables are powerful predictors of all-cause mortality but are unobtainable in at least 50% of patients because of disabilities precluding lower extremity exercise. Arm exercise stress testing is a potentially cost-effective alternative, but no long-term outcome data are available.

Methods We performed arm ergometer stress tests on 446 veterans aged 64.0 (11.1) years (mean [SD]) between 1997 and 2002 and investigated whether arm exercise capacity in resting metabolic equivalents, heart rate recovery (in beats per minute), delta (peak resting) heart rate (in beats per minute), and other exercise variables predict long-term all-cause mortality, myocardial infarction (MI), or coronary revascularization.

Results During follow-up of 12.0 (1.3) years, 255 patients died (57.2%), 70 had MI (15.7%), and 118 underwent coronary revascularization (26.4%). After adjustment for significant demographic and clinical variables, death was predicted by arm metabolic equivalents (hazard ratio/SD 0.59, 95% CI 0.46-0.75, $P < .001$), heart rate recovery (hazard ratio/SD 0.64, 95% CI 0.49-0.83, $P < .001$), and delta heart rate (hazard ratio/SD 0.75, 95% CI 0.63-0.91, $P < .001$). No exercise variables prognosticated MI, but coronary revascularization was predicted by stress-induced ST-segment deviations (hazard ratio 2.64, 95% CI 1.16-4.33, $P < .001$), limiting angina (hazard ratio 4.70, 95% CI 1.81-12.22, $P < .001$), and an abnormal perfusion imaging result (hazard ratio 2.0, 95% CI 1.14-3.51, $P < .02$).

Conclusions Arm exercise capacity, heart rate recovery, and delta heart rate predict 12-year all-cause mortality and arm exercise–induced ST changes, limiting angina, and an abnormal nuclear imaging result portend coronary revascularization in lower extremity disabled veterans. (Am Heart J 2014;167:169-77.)

Although treadmill exercise capacity and other exercise variables are powerful predictors of all-cause and cardiovascular mortality,[1–7] pharmacologic myocardial perfusion imaging (MPI) or echocardiographic stress tests are now performed in at least 50% of patients because of disabilities precluding lower extremity exercise.[8] These limitations, which include orthopedic conditions, peripheral arterial disease, diabetic foot ulcers, amputations, and gait disturbances, are becoming more prevalent in an aging and increasingly obese society. Pharmacologic MPI stress tests are several times more expensive than exercise electrocardiography (ECG), require administration of ionizing radiation, and do not provide powerful prognostic or clinically and functionally important information on exercise capacity or symptomatic, cardiovascular, and ECG responses to the relevant physiologic stress of exercise. Arm ergometer stress testing is a potentially useful alternative for these individuals but elicits different hemodynamic and metabolic responses[9,10] than leg exercise, and there are no data regarding its value for prediction of long-term outcome, despite the fact that many activities of daily living require arm exercise. Thus, the purpose of this investigation was to determine whether arm exercise capacity, heart rate recovery, delta (peak − rest) heart rate, and other traditionally measured exercise variables predict all-cause mortality, myocardial infarction (MI), or coronary revascularization over follow-up of at least 10 years in a high-risk population of veterans unable to perform lower extremity exercise.

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Methods

Setting and participants

Our population consisted of 446 consecutive patients (437 men, 9 women) aged 64.0 (11.1) years (mean [SD]) who were referred to the St Louis Veterans Administration Medical Center for stress testing from 1997 until 2002, were unable to perform treadmill or leg cycle ergometer exercise because of disabilities precluding lower extremity exercise, and were willing to complete an individualized arm ergometer protocol developed from earlier investigations.[11,12] There were no exclusions, but patients having upper extremity disabilities or medical conditions for which stress testing is contraindicated,[10] identified in a brief history, physical examination, and electronic medical record review, were not included. Participants were instructed to fast overnight and withhold ß-adrenergic blocking agents and one-half of their usual insulin dose but to ingest all other medications. The study was approved by the institutional review board of the St Louis Veterans Administration Medical Center. All patients provided voluntary written informed consent.

Arm exercise protocol

Patients exercised in the seated posture with a wall-mounted electronically braked cycle ergometer (Angio 2000; Lode BV, Groningen, the Netherlands) at a target cadence of 60 rpm to an end point of fatigue or symptom limitation. A progressive multistage protocol designed to elicit exhaustion or symptoms within 5 to 12 minutes was used with constant work rate increments of 50 to 200 kilo-pond-meters per minute every 2 minutes, based on pretest estimated exercise capacity.[11,12] Immediately after exercise, the ergometer resistance was eliminated and patients cycled gently with no resistance for 30 seconds. Exercise capacity in resting metabolic equivalents (METs) was determined from the duration of exercise at the peak arm ergometer work rate attained, using the standard relationship between oxygen uptake and cycle ergometer resistance, as described previously.[12,13]

After a brief clinical evaluation, a 12-lead ECG was recorded at baseline and every minute during and after exercise with continuous recording near-peak effort. Blood pressure was determined manually in the nondominant arm during seated rest and every 2 to 3 minutes during and after exercise. Peak heart rate and heart rate recovery (in beats per minute) were calculated from the ECG, and peak blood pressure values were those obtained nearest peak effort. Standard criteria were used for interpretation of the ECG response to arm exercise.[10,11]

Myocardial perfusion imaging protocol

Myocardial perfusion imaging also was performed, based on request by the referring physician, in 253 patients (56.7%). The procedure was performed as a single-day rest and stress imaging protocol in conjunction with arm exercise testing.[14]

Outcome and participant data

Occurrence and date of death, MI, and coronary revascularization (either coronary artery bypass grafting [CABG] or percutaneous coronary intervention [PCI]), demographic, medication, and resting ECG data and clinical diagnoses of study participants were determined by review of all Veterans Affairs electronic medical records preceding and after stress testing until the date of mortality or November 5, 2012. This information was supplemented by scanned reports of non–Veterans Affairs episodes of care, Missouri Department of Health and Senior Services, and Social Security Death Index data. Mortality and ascertainment reliability of these records are comparable with the National Death Index.[15] Research staff and investigators had no knowledge of stress test findings at the time of record review. The criteria for MI were elevated creatine kinase–MB or troponin above the 99th percentile and either ischemic ECG changes or symptoms. Patients were not censored after MI or coronary revascularization.

Data analysis

Data were carefully reviewed before analysis, and outliers were either corrected or removed. Missing data were not imputed, and analyses included only existing values for each variable. Student *t* tests were performed to evaluate differences between group means. χ^2 Statistics were used to examine associations among categorical variables. Univariate analyses were initially performed to determine which arm exercise and MPI variables were significant predictors of outcome and to identify demographic, resting hemodynamic and ECG variables, medications, and clinical diagnoses that were potentially confounding covariates. Significant variables by univariate analysis were tested for nonlinear associations and then entered into Cox regression models to determine relationships, measured as hazard ratios (HRs), for associations with mortality, MI, and coronary revascularization. Proportional hazards assumptions were confirmed with time-dependent variables by including interaction terms between covariates and the time to event variable in the model. Kaplan-Meier curves were generated to compare survival and other outcome events among various patient groups. Receiver operator characteristic curves (*C* statistics) were calculated to assess goodness of fit. The independent incremental value of significant demographic, clinical, and exercise variables for model improvement in prediction of survival was evaluated by χ^2 analysis. Absolute, relative, and incremental integrated discrimination improvements (IDIs) also were calculated for exercise variables. *P* values <.05 were considered statistically significant. All analyses were performed with SAS 9.3 (Cary, NC).[16]

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Results

Outcome events

The average (SD) follow-up interval for survivors in our population was 12.0 (1.3) years and 8.2 (3.4) years for the entire cohort. There were 255 deaths (57.2%), 70 patients had MI (15.7%), 43 underwent CABG (9.6%), 75 had PCI procedures (16.8%), and 320 experienced at least 1 of