The Prognostic Value of Exercise Testing in Elderly Men

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PURPOSE: Our purposes were to compare the responses to exercise testing in elderly (≥65 years of age) and younger men, and to investigate whether exercise testing has similar prognostic value in the two age groups.

METHODS: We included all elderly (n = 1185) and younger (n = 2789) male veterans without established coronary heart disease who underwent routine clinical exercise testing between 1987 and 2000 at two academically affiliated Veteran's Affairs medical center laboratories. Measurements included a standardized medical history, exercise testing, and all-cause mortality.

RESULTS: Compared with younger patients, elderly patients achieved a lower workload (a mean [± SD] of 7 ± 3 vs.10 ± 4 metabolic equivalents [METs], $P < 0.001$) and were more likely to have abnormal ST depression (27% [n = 324] vs. 16% [n = 436], $P < 0.001$). During the mean follow-up of 6 years, annual mortality was twice as high among elderly patients as among younger patients (4% vs. 2%, $P < 0.001$). The only exercise test variable that was associated significantly with time to death in both age groups was maximal METs achieved: each 1 MET increase in exercise capacity was associated with an 11% reduction in annual mortality. Exercise-induced ST depression was more common in those who subsequently died, but was not an independent predictor of mortality.

CONCLUSION: In elderly men, exercise testing provided prognostic information incremental to clinical data. Achieved workload (in METs) was the major exercise testing variable associated with all-cause mortality. Its prognostic importance was the same in elderly as in younger men. **Am J Med. 2002;112: 453–459.** ©2002 by Excerpta Medica, Inc.

The standard exercise treadmill test is widely used to evaluate heart disease in elderly persons; more than 800 000 tests are performed annually in U.S. adults over the age of 65 years. Despite its widespread use, the prognostic value of exercise testing has not been fully characterized in the elderly. In a recent study of 514 elderly patients, the value of exercise-induced ST depression to predict prognosis was questioned (1). Few elderly patients have been included in most prognostic studies of exercise testing. The studies that did include elderly patients were relatively small and did not use multivariate analysis to identify independent prognostic variables (2,3). There have also been studies of selected elderly populations, such as symptomatic patients selected for coronary angiography. Others included healthy persons, whereas some did not evaluate the incremental value of exercise testing over clinical data.

A greater prevalence and severity of coronary disease and the presence of more comorbid conditions in elderly persons may alter the ability of exercise testing to predict outcomes (4). People tend to be more sedentary with aging, and differences in physiological responses to exercise may contribute to differing interpretations of exercise test results (5,6). Exercise testing guidelines have recommended that more data be obtained regarding exercise testing in elderly persons (7,8). We therefore studied patient outcomes following exercise testing in male veterans, and compared the results in elderly and younger men.

METHODS

Sample

There were 6213 consecutive men referred to two clinical exercise laboratories (Long Beach VA, 1987–1991, and Palo Alto VA, 1992–2000) that were directed in consistent fashion by two of the authors (VFF and JM). Patients who were subjects in research protocols, or who had a history of congestive heart failure, myocardial infarction, or coronary bypass surgery, were also excluded. The final study sample after exclusions included 3974 patients.

Data Collection

Both laboratories had university affiliations, with academic medical staffs, house officers, and fellows. All tests were supervised directly by these physicians or by nurse practitioners; all tests were also read by two of the investigators (VFF and JM). A thorough clinical history, a list of medications, and cardiac risk factors were recorded at the time of exercise treadmill testing using computerized forms that included standard definitions of clinical conditions and exercise responses (9,10).

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Exercise Testing

Patients underwent symptom-limited treadmill testing using the United States Air Force School of Aerospace Medicine protocol (11) or an individualized ramp treadmill protocol (12). Before ramp testing, the patients were given a questionnaire to estimate their exercise capacity; this allowed most patients to reach maximal exercise within the recommended range of 8 to 12 minutes (13). Heart rate targets were not used as an endpoint or to judge the adequacy of the test. Patients did not perform a cool-down walk; they were placed supine immediately after exercise (14). Medications were not changed or stopped before testing.

Visual ST-segment depression was measured at the J junction; ST slope was measured during the following 60 ms and classified as upsloping, horizontal, or downsloping. The ST response considered was the most horizontal or downsloping ST-segment depression in any lead, except aVR during exercise or recovery. An abnormal response was defined as ≥1 mm of horizontal or downsloping ST-segment depression. Ventricular tachycardia was defined as a run of ≥3 consecutive premature ventricular contractions (15). Blood pressure was taken manually, and metabolic equivalents (METs) were estimated from treadmill speed and grade. Exertional hypotension consisted of either a 10-mm Hg drop in systolic blood pressure after a rise, or a drop of 10 mm Hg below standing pretest. An exercise systolic blood pressure code was recorded (0 = increase greater than 40 mm Hg; 1 = increase 31 to 40 mm Hg; 2 = increase 21 to 30 mm Hg; 3 = increase 11 to 20 mm Hg; 4 = increase 0 to 10 mm Hg; 5 = drop below standing pretest) (16). Pressure rate product (or double product) pretest and at maximal exercise was calculated as the product of systolic blood pressure and heart rate. Delta pressure rate product was calculated as (pressure rate product at maximal exercise minus the pressure rate product at rest)/1000.

No test was classified as indeterminate (17). The exercise tests were performed, analyzed, and reported per standard protocol and utilizing a computerized database (EXTRA, Mosby Publishers, Chicago, IL) (18).

Follow-up

The Social Security Death Index was used to match all patients using name and social security number. The index is updated weekly, and current information was used. Vital status was determined as of July 2000. Data on cardiac interventions or nonfatal cardiovascular events were not available.

Statistical Methods

The sample was divided into those aged ≥65 years (elderly) and <65 years. Number Crunching System Software (Salt Lake City, UT) was used for all statistical analyses. Unpaired *t* tests were used to compare the mean values in the two groups, and chi-squared tests were used to compare proportions. Total (all-cause) mortality was used as the endpoint for survival analysis using Kaplan-Meier curves, and Cox proportional hazards regression was used to identify variables that were independently associated with time to death. All variables that were significant in univariate analysis ($P < 0.001$) were included in the multivariable analysis. Age was included as a continuous variable within the two age groups.

RESULTS

The elderly men (age ≥65 years) had a mean body mass index that was 2 kg/m^2 lower than that of the younger men (Table 1). The average resting heart rate was about 3 beats/min lower in elderly men, and the mean systolic blood pressure was 8 mm Hg higher. Overall, 74% (n = 2940) were white, 9% (n = 357) were Hispanic, and 12% (n = 477) were black. There were no significant differences in the use of beta-blockers, angiotensin-converting enzyme inhibitors, or antiarrhythmic agents between the groups, but elderly patients more commonly used other cardiovascular medications. Elderly subjects were significantly more likely to have a history of pulmonary disease, typical angina, and stroke. Hypertension was the only cardiac risk factor that was more common in elderly men; however, smoking, obesity, and family history of coronary disease were less prevalent in this group. Rest electrocardiogram (ECG) abnormalities, including atrial fibrillation and ST depression, were more common in the older age group (Table 2). No differences between the age groups were detected in ECG signs of left ventricular hypertrophy or QRS prolongation.

Exercise Test Responses

No major complications occurred during testing. The average resting hemodynamic values differed statistically, but not clinically, in both groups (Table 3). Angina occurred during testing in 10% of both groups. All the major exercise ECG abnormalities were significantly more prevalent in elderly subjects, occurring about twice as often ($P < 0.001$). ST elevation was rare (less than 2% of patients).

Exercise hemodynamic values revealed many differences between the age groups. Average maximum heart rate, maximum pressure rate product, Delta pressure rate product, and METs achieved were all significantly lower in older patients ($P < 0.001$). Failure to reach age-predicted heart rate target occurred in nearly half of those tested, and was significantly more common in the older age group. Older patients more frequently had an exercise capacity <5 METs (28% in the elderly patients vs. 9% in the younger patients).

Table 1. Clinical Characteristics of the Sample, Stratified by Age and by Survival during Follow-up*

Characteristic	Age <65 Years Survived (n = 2520)	Age <65 Years Died (n = 269)	P Value	Age ≥65 Years Survived (n = 909)	Age ≥65 Years Died (n = 276)	P Value	P Value for Comparison of Age Groups
	Number (%) or Mean ± SD			Number (%) or Mean ± SD			
Age (years)	51 ± 9	56 ± 7	<0.001	71 ± 5	71 ± 5	0.97	<0.001
Body mass index (kg/m^2)	29 ± 5	28 ± 5	0.002	27 ± 4	26 ± 4	<0.001	<0.001
Medication use							
Beta-blockers	339 (13)	35 (13)	0.84	140 (15)	46 (17)	0.61	0.06
Calcium antagonists	454 (18)	76 (28)	<0.001	241 (26)	84 (30)	0.20	<0.001
Nitrates	285 (11)	70 (26)	<0.001	140 (15)	61 (22)	0.009	<0.001
ACE inhibitors	201 (8)	4 (2)	<0.001	98 (11)	9 (3)	<0.001	0.07
Antihypertensive agents	429 (17)	81 (30)	<0.001	253 (28)	95 (34)	0.04	<0.001
Antiarrhythmic agents	20 (1)	3 (1)	0.58	11 (1)	3 (1)	0.87	0.28
Anticoagulant agents	405 (16)	8 (3)	<0.001	199 (22)	12 (4)	<0.001	0.02
Medical history							
Atrial fibrillation	34 (1)	3 (1)	0.75	18 (2)	6 (2)	0.84	0.10
Claudication	87 (3)	10 (4)	0.82	41 (4)	25 (9)	0.004	0.002
Stroke	50 (2)	9 (3)	0.14	34 (4)	13 (5)	0.47	<0.001
Pulmonary disease	107 (4)	24 (9)	<0.001	77 (8)	29 (10)	0.30	<0.001
Typical angina	299 (12)	51 (19)	<0.001	136 (15)	63 (23)	0.002	<0.001
Cardiac risk factors							
Diabetes	234 (9)	32 (12)	0.17	89 (10)	29 (10)	0.73	0.68
Hyperlipidemia	794 (32)	80 (30)	0.55	273 (30)	67 (24)	0.06	0.10
Family history of coronary disease	704 (28)	48 (18)	<0.001	115 (13)	37 (13)	0.74	<0.001
Hypertension	1062 (42)	123 (46)	0.27	512 (56)	144 (52)	0.24	<0.001
Smoking							
Current	915 (36)	110 (41)	0.14	154 (17)	69 (25)	0.003	<0.001
Ever	1550 (62)	126 (47)	<0.001	486 (54)	118 (43)	0.009	<0.001
Obesity (body mass index >27 kg/m^2)	1466 (58)	135 (50)	0.01	420 (46)	100 (36)	0.003	<0.001

* Of those aged <65 years at the time of exercise testing, 90% survived during follow-up, compared with 77% of those aged ≥65 years (P <0.001).
ACE = angiotensin-converting enzyme.

Survival

All-cause mortality was 23% in the older age group, compared with 10% in the younger age group. The average annual mortality was 4% in elderly patients and 2% in the younger veterans. The average maximum heart rate, maximum pressure rate product, Delta pressure rate product, and METs achieved were all significantly lower in patients from both age groups who died as compared

Table 2. Resting Electrocardiogram Abnormalities, Stratified by Age and Survival during Follow-up

Abnormality	Age <65 Years Survived (n = 2520)	Age <65 Years Died (n = 269)	P Value	Age ≥65 Years Survived (n = 909)	Age ≥65 Years Died (n = 276)	P Value	P Value for Comparison of Age Groups
	Number (%)			Number (%)			
Abnormal ECG	469 (19)	86 (32)	<0.001	265 (29)	98 (36)	0.05	<0.001
Intraventricular conduction delay	75 (3)	12 (4)	0.18	42 (5)	10 (4)	0.48	0.05
Left ventricular hypertrophy	96 (4)	21 (8)	0.002	43 (5)	23 (8)	0.02	0.06
Atrial fibrillation	14 (1)	1 (0.4)	0.70	11 (1)	8 (3)	0.05	<0.001
ST depression	106 (4)	29 (11)	<0.001	77 (8)	38 (14)	0.009	<0.001

ECG = electrocardiogram.

Table 3. Exercise Test Responses, Stratified by Age and by Survival during Follow-up

	Age <65 Years			Age ≥65 Years			
	Survived (n = 2520)	Died (n = 269)		Survived (n = 909)	Died (n = 276)		
Measurement	Number (%) or Mean ± SD		*P* Value	Number (%) or Mean ± SD		*P* Value	*P* Value for Comparison of Age Groups
Exercise-induced ST depression	376 (15)	60 (22)	0.002	236 (26)	88 (32)	0.05	<0.001
Silent ischemia	258 (10)	29 (11)	0.78	156 (17)	50 (18)	0.71	<0.001
Intraventricular conduction delay	55 (2)	16 (6)	<0.001	41 (4)	20 (7)	0.07	<0.001
Ventricular arrhythmia	113 (4)	15 (6)	0.42	90 (10)	38 (14)	0.07	<0.001
Exercise-induced hypotension	40 (2)	12 (4)	<0.001	37 (4)	9 (3)	0.54	<0.001
Resting							
Heart rate (beats/minute)	79 ± 18	83 ± 15	<0.001	76 ± 32	78 ± 17	0.18	<0.001
Systolic blood pressure (mm Hg)	132 ± 20	135 ± 21	0.008	141 ± 23	138 ± 26	0.17	<0.001
Maximum							
Heart rate (beats per minute)	147 ± 23	136 ± 25	<0.001	132 ± 23	127 ± 21	<0.001	<0.001
Exercise heart rate <85% age predicted	1031 (41)	142 (53)	<0.001	407 (45)	161 (58)	<0.001	<0.001
Maximum double product (× 1000)	27 ± 6	25 ± 7	<0.001	24 ± 6	23 ± 6	<0.001	<0.001
Difference double product (×1000)	17 ± 6	14 ± 6	<0.001	14 ± 6	12 ± 6	<0.001	<0.001
METs	10 ± 4	8 ± 4	<0.001	7 ± 3	6 ± 3	<0.001	<0.001
Predicted METs <5	190 (8)	56 (21)	<0.001	241 (26)	91 (33)	0.04	<0.001

METs = metabolic equivalents.

with survivors (Table 3, *P* <0.001). In younger patients, rate-dependent QRS prolongation was more prevalent in those who died. Exercise-induced hypotension (2% vs. 4%) also occurred more frequently in those from the younger age group who died. In both age groups, those who died were significantly more likely to fail to reach their age-predicted heart rate target.

In multivariable analyses, age and resting heart rate were associated with mortality (Table 4) only in the younger veterans. Of the exercise test–related measurements, only MET exercise capacity, but not exercise-induced ECG abnormalities, was associated with mortality (Figure). Each 1 MET increase in exercise capacity was associated with an 11% reduction in mortality in both age groups.

DISCUSSION

Exercise testing is widely used in elderly patients. All official statements about ischemic heart disease recommend standard exercise testing as the first diagnostic test to evaluate chest pain in elderly patients who do not have resting ECG abnormalities that would affect the interpretation of the exercise ECG response (19,20). Previous multicenter studies have presented treadmill results from large samples of patients, but with only a small proportion of elderly patients (21,22). Series have often targeted younger patients or asymptomatic persons (23–28).

Our results help to define the clinical utility of the exercise test and its prognostic applications in elderly men.

Table 4. Clinical and Exercise Test Variables Independently Associated with Mortality

Variable (Unit)	Hazard Ratio (95% Confidence Interval)	*P* Value
Age <65 years		
Age (per 5 years)	1.27 (1.16–1.39)	<0.001
Exercise capacity (per 1 MET increase)	0.89 (0.85–0.93)	<0.001
Resting heart rate (per 5 beats per minute increase)	1.10 (1.05-1.15)	<0.001
Age ≥65 years		
Exercise capacity (per 1 MET increase)	0.89 (0.84–0.94)	<0.001

MET = metabolic equivalent.

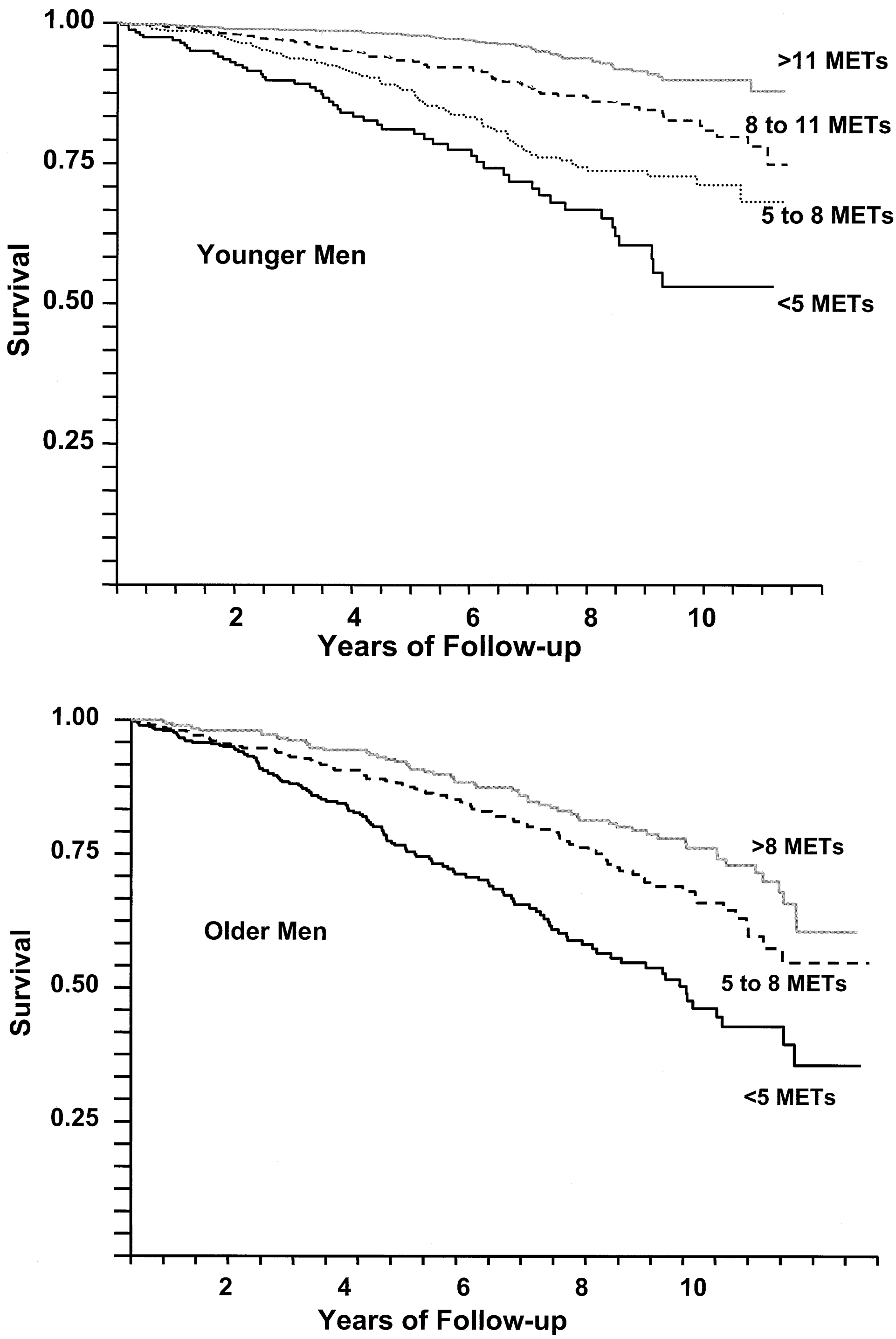

Figure. Kaplan-Meier survival curves, stratified by metabolic equivalents (METs) with age-specific cutpoints, for younger (<65 years) and older (>65 years) male veterans.

Strengths of this study include a large sample size, a long follow-up, the inclusion of consecutive referrals of elderly patients, exclusion of patients with known heart disease, and the application of standardized methodology for "symptom and sign" limited maximal exercise testing. Trained physicians or nurses were always in attendance, and senior physicians were always available for consultation.

The elderly men in our study had a greater prevalence of comorbid conditions than did the younger veterans. One exception was obesity, which was less common in the older age group, which may explain the similar prevalence of diabetes in both groups (10%). Fewer older veterans were current smokers. Resting ECG abnormalities, including atrial fibrillation and ST depression, were more common in the elderly patients. The greater prevalence of exercise-induced abnormalities, including silent ischemia, is consistent with a previous study in veterans (29). However, our study could not address the value of exercise testing in women because of the low prevalence of female veterans.

The largest previous study of elderly patients was the Rochester Epidemiology Project (1), which used treadmill testing records from physician offices to identify a retrospective cohort of Olmsted County residents who had been tested between 1987 and 1989. Initial treadmill tests were performed in 3107 persons (514 aged ≥65 years). In contrast with our study, 32% of younger persons and 48% of elderly persons were women. Compared with younger patients, elderly patients achieved a lower workload (6 vs. 11 METs, $P < 0.001$) and had a greater prevalence of abnormal exercise-induced ST depression (28% vs. 9%, $P < 0.001$). These findings were similar to those in our study. With a mean follow-up of 6 years, all-cause mortality was higher among elderly persons (37%) than among younger persons (8%; $P < 0.001$), which was somewhat different than the mortality rates that we observed (23% vs. 10%). METs and angina with exercise testing were associated with cardiac events in both age groups, whereas exercise-induced ST depression was associated with cardiac events only in younger persons. As in our study, METs was the only exercise-testing variable that was independently associated with all-cause mortality in both age groups ($P < 0.001$).

In our studies, variables indicating the presence of exercise-induced ischemia were significantly more prevalent in those from both age groups who died, but were not independently associated with mortality. This may be because we used all-cause mortality (30) instead of cardiovascular mortality. Our results could also be due to the more effective methods of treatment that are available for coronary disease. Alternatively, it may represent our inability to censor patients from follow-up after cardiac interventions. In contrast, the Duke score—which includes two variables associated with ischemia—was generated using the endpoints of myocardial infarction and cardiovascular death (31). In addition, patients who underwent revascularization were removed from follow-up (censored) in the calculation of the Duke score. Such censoring would likely increase the association of ischemic variables with outcomes.

In summary, our findings demonstrate the prognostic importance of exercise testing in elderly men. The exercise test offers incremental value over clinical variables alone. Exercise capacity is the most important prognostic measurement and has the same association with mortality in elderly as in younger patients.

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