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Exercise Capacity and Mortality in Older Men

A 20-Year Follow-Up Study

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***Background*—**Epidemiological findings, based largely on middle-aged populations, support an inverse and independent association between exercise capacity and mortality risk. The information available in older individuals is limited.

***Methods and Results*—**Between 1986 and 2008, we assessed the association between exercise capacity and all-cause mortality in 5314 male veterans aged 65 to 92 years (mean±SD, 71.4±5.0 years) who completed an exercise test at the Veterans Affairs Medical Centers in Washington, DC, and Palo Alto, Calif. We established fitness categories based on peak metabolic equivalents (METs) achieved. During a median 8.1 years of follow-up (range, 0.1 to 25.3), there were 2137 deaths. Baseline exercise capacity was 6.3±2.4 METs among survivors and 5.3±2.0 METs in those who died ($P<0.001$) and emerged as a strong predictor of mortality. For each 1-MET increase in exercise capacity, the adjusted hazard for death was 12% lower (hazard ratio=0.88; confidence interval, 0.86 to 0.90). Compared with the least fit individuals (≤4 METs), the mortality risk was 38% lower for those who achieved 5.1 to 6.0 METs (hazard ratio=0.62; confidence interval, 0.54 to 0.71) and progressively declined to 61% (hazard ratio=0.39; confidence interval, 0.32 to 0.49) for those who achieved >9 METs, regardless of age. Unfit individuals who improved their fitness status with serial testing had a 35% lower mortality risk (hazard ratio=0.65; confidence interval, 0.46 to 0.93) compared with those who remained unfit.

***Conclusions*—**Exercise capacity is an independent predictor of all-cause mortality in older men. The relationship is inverse and graded, with most survival benefits achieved in those with an exercise capacity >5 METs. Survival improved significantly when unfit individuals became fit. **(*Circulation*. 2010;122:790-797.)**

Key Words: aging ■ epidemiology ■ exercise ■ mortality

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An inverse, graded, independent, and robust association between fitness status and mortality is supported by large epidemiological studies in apparently healthy subjects[1–6] and in patients with documented cardiovascular disease (CVD).[1,5] These health risks are particularly apparent at relatively low fitness levels but decrease with higher physical activity patterns or fitness status.[1–5] Most of this evidence is based on studies conducted among middle-aged individuals. Relatively few studies have examined the health benefits of fitness in older populations,[7–13] and most of these studies used questionnaires to estimate either fitness or physical activity patterns in their cohort.[8,10–12] Although some studies used an exercise test to more objectively assess fitness,[7,9,13] they were composed of relatively small samples of older individuals individuals[7,9] or the cohort was relatively young.[13]

Clinical Perspective on p 797

According to a recent Centers for Disease Control and Prevention report, the proportion of Americans aged 65 years and older will double by 2030.[14] This, along with the high rates of poor physical health and activity limitations among the older individuals, will contribute to a projected 25% increase in the nation's overall healthcare costs during this time. Because regular physical activity contributes substantially to healthy aging by helping to prevent or control many of the health problems that often reduce the quality and length of life in older individuals (eg, low fitness, hypertension, obesity, and diabetes mellitus), the Centers for Disease Control and Prevention report states that a physically active lifestyle in older adults should be encouraged.[14]

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In light of the sparse data available on the relationship between fitness and mortality in older individuals, the present study was undertaken to assess the extent to which exercise capacity may predict all-cause mortality among older male veterans (aged >65 years) referred for an exercise tolerance test (ETT) for clinical reasons.

Methods

Study Design and Sample

We identified 5390 male veterans (age range, 65 to 92 years) from the Veterans Exercise Testing Study (VETS) who underwent a symptom-limited ETT between January 1986 and December 2008. The tests were administered at the Veterans Affairs Medical Center, Washington, DC (n=3128), or the Veterans Affairs Palo Alto Health Care System, Palo Alto, Calif (n=2186). All tests were performed either as a routine evaluation or to assess the possibility of exercise-induced ischemia. In addition to age (<65 years), we excluded the following subjects: (1) those with a history of an implanted pacemaker; (2) those who developed left bundle branch block during the test; (3) those with heart failure classified as New York Heart Association class II or higher and those unable to complete the test secondary to musculoskeletal or peripheral vascular issues; and (4) those who had a positive exercise test that was confirmed by additional diagnostic test (stress thallium or cardiac catheterization) or those who became unstable during the ETT or required emergent intervention.[15]

The final sample included 5314 men (3224 white and 2090 black). The mean age was 71.4±5.0 years, and the median age was 70.5 years. Participants were also divided into 2 age categories: 65 to 70 (n=2560) and >70 years (n=2754). All participants gave written consent before the ETT. The study was approved by the internal review boards at each institution.

All demographic, clinical, and medication information was obtained from patients' computerized medical records just before the ETT. Hypertension was defined as systolic blood pressure (BP) ≥140 mm Hg and or diastolic BP ≥90 mm Hg. Diabetes mellitus and dyslipidemia were defined on the basis of established criteria at the time the ETT was performed. Each individual was also asked to verify the computerized information with regard to history of chronic disease, current medications, and cigarette smoking habits. Body weight and height were recorded in the exercise stress laboratory before the test. Body mass index (BMI) was calculated as weight (kg) divided by height^2 (m^2). Individuals with CVD were defined as those with a history of myocardial infarction, angiographically documented coronary artery disease, coronary angioplasty, coronary artery bypass surgery, or chronic heart failure classified as New York Heart Association class I.

The Social Security Death Index was used to match all subjects to their record according to Social Security number and death dates from the Veterans Affairs Beneficiary Identification and Record Locator System File. This system is used to determine survivors among veterans and has been shown to be complete and accurate.[16] Vital status was evaluated annually and determined as of June 30, 2009; the outcome of interest was death from any cause.

Exercise Assessments

Exercise capacity for individuals tested at the Veterans Affairs Medical Center, Washington, DC, was assessed by the standard Bruce protocol. For the individuals assessed at the Veterans Affairs Palo Alto Health Care System, an individualized ramp protocol was used, as described elsewhere.[17] Peak exercise time was recorded in seconds. Peak workload was estimated in metabolic equivalents (METs). One MET is defined as the energy expended at rest, which is equivalent to an oxygen consumption of 3.5 mL per kilogram of body weight per minute.[18] Exercise capacity (in METs) was estimated on the basis of exercise time via a commonly used equation for the Bruce protocol[19] and based on American College of Sports Medicine equations for the ramp protocol.[18] Subjects were encouraged to exercise until the occurrence of volitional fatigue in the absence of symptoms or other clinical indications for stopping the test.[15] The use of handrails during the exercise test was discouraged. Age-predicted peak exercise heart rate (HR) was determined on the basis of standardized methods.[20] Medications were not changed or stopped before testing.

Supine resting HR and BP were assessed after 5 minutes of rest. Exercise BP was recorded at 2 minutes of each exercise stage, at peak exercise, and during recovery. Indirect arm-cuff sphygmomanometry was utilized for all BP assessments. ST-segment depression was measured visually. ST depression ≥1.0 mm that was horizontal or downsloping was considered to be suggestive of ischemia.

We also established fitness categories on the basis of the MET level achieved. For the formation of fitness categories, we chose the lowest 20th percentile of METs for the entire cohort (≤4 METs), a cutoff employed in previous studies,[2] to represent the lowest fit category. Thereafter, categories were established per 1-MET incremental increase in exercise capacity (eg, 4.1 to 5; 5.1 to 6; 6.1 to 7; 7.1 to 8; 8.1 to 9; and >9 METs). Those who achieved >9 METs comprised the highest fitness category. The establishment of fitness on the basis of MET level achieved is a more objective method of fitness than self-reported physical activity habits.[2]

Statistical Analysis

Continuous variables are presented as mean and SD, and categorical variables are expressed as absolute and relative frequencies (%). Associations between categorical variables were tested with the Pearson χ^2 test. One-way ANOVA was applied to determine age, BMI, resting and exercise HR and BP, and peak MET level differences between fitness categories and age groups. Normality of the tested variables was evaluated with the Shapiro-Wilk test. Equality of variances between groups was tested by the Levene test. The mortality rates were calculated for each fitness category. We considered individuals in the lowest fitness category (exercise capacity ≤4 METs) as the reference group and individuals with exercise capacity >9 METs as the highest fitness group. Log-rank tests were calculated to evaluate significance of fitness levels on all-cause mortality. Then Cox proportional hazards models were employed to determine the variables that were significantly associated with mortality. The models were adjusted for age in years, peak METs achieved, resting systolic BP (mm Hg), and BMI as continuous variables and for ethnicity, presence of CVD, cardiovascular medications (aspirin, angiotensin-converting enzyme inhibitors, calcium channel blockers, β-blockers, diuretics, vasodilators, and statins), and risk factors (hypertension, diabetes mellitus, dyslipidemia, and smoking) as categorical variables. The selection of these variables was based on their clinical relevance and their significant association with mortality observed in our cohort during the exploratory analyses. Cox proportional hazards models were also utilized to determine the variables that were associated with mortality in the subgroup of individuals with repeated exercise tests. The model was adjusted for all of the aforementioned variables. The proportional hazards assumption was evaluated with the use of Schoenfeld residuals and examined graphically. *P* values <0.05 with 2-sided tests were considered significant. All statistical analyses were performed with the use of SPSS software (SPSS version 18.1, SPSS Inc, Chicago, Ill).

Results

Demographic and Clinical Characteristics and Follow-Up Data

The median follow-up period was 8.1 years (47 170 person-years with a range of 0.1 to 25.3 years). There were 2137 deaths during the follow-up period, with an average annual mortality of 45 deaths per 1000 person-years. The annual mortality rates for the groups aged 65 to 70 and >70 years were 40.0 per 1000 and 49.6 per 1000 person-years, respectively (*P*<0.001). More than 80% of the participants (n=4266) achieved a peak HR that was at least 85% of the age-predicted value (34%; 358 of those who

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Table 1. Demographic and Clinical Characteristics of Study Participants

Demographic and Clinical Variables	Total (n=5314)	65–70 y (n=2560)	>70 y (n=2754)	*P**
Age, y	71.4±5.0	67.3±1.6	75.3±3.9	<0.001
BMI, kg/m^2	27.5±4.7	27.9±4.9	27.0±4.5	<0.001
Resting HR, bpm	72±14	72±14	71±13	<0.001
Resting systolic BP, mm Hg	139±21	137±20	140±22	<0.001
Resting diastolic BP, mm Hg	79±11	80±11	78±11	<0.001
CVD, %	36	36	36	0.84
Previous MI, %	24	24	24	0.87
Smoking, %	24	27	22	<0.001
Hypertension, %	56	54	57	0.07
Diabetes mellitus, %	20	20	19	0.53
Dyslipidemia, %	14.0	13.0	15.0	0.02
Treatment				
β-blocker, %	17	16	17	0.21
CCB, %	25	25	25	0.31
ACE-I, %	16	15	16	0.32
Diuretics, %	10	8	11	<0.001
Aspirin, %	5	5	6	0.003
Vasodilators, %	14	15	13	0.053
Statins, %	6	5	7	0.003
Exercise data				
Peak HR, bpm	128±23	131±23	125±22	<0.001
Peak systolic BP, mm Hg	179±31	182±31	176±30	<0.001
Peak diastolic BP, mm Hg	85±16	87±15	84±16	<0.001
Peak METs, 3.5 mL O_2/kg per minute	5.9±2.3	6.3±2.5	5.4±2.0	<0.001

MI indicates myocardial infarction; CCB, calcium channel blockers; and ACE-I, angiotensin-converting enzyme inhibitors.

*Comparisons between the 2 age groups.

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did not achieve this level were receiving β-blockers). Participant characteristics and exercise data for the entire cohort and the 2 age categories are presented in Table 1. Significant differences among the 2 age categories were noted in all variables examined except the prevalence of CVD, previous myocardial infarction, hypertension, diabetes mellitus, and use of β-blockers, calcium channel blockers, angiotensin-converting enzyme inhibitors, and vasodilators (Table 1). Peak exercise HR and systolic and diastolic BP were significantly different between the 3 groups. The peak MET level was progressively and significantly lower in the older age categories (Table 1). Comparisons between fitness categories also revealed significant differences in all variables examined except resting diastolic BP and the use of β-blockers. Significant differences were also noted in all exercise variables except peak diastolic BP (Table 2).

Predictors of All-Cause Mortality for the Entire Cohort

Hazard ratios for exercise capacity for the entire cohort and for each age category are presented in Table 3. With exercise capacity introduced in the model as a continuous variable, unadjusted data analysis revealed that mortality risk was ≈13% lower for each 1-MET increase in exercise capacity and 12% lower in the fully adjusted model for the entire cohort. Additional associations with all-cause mortality were noted with diabetes mellitus (hazard ratio=1.30; confidence interval [CI], 1.1 to 1.4; *P*<0.001); smoking (hazard ratio=1.29; CI, 1.2 to 1.4; *P*<0.001); CVD (hazard ratio=1.12; CI, 1.0 to 1.2); and BMI (hazard ratio=0.96; CI, 0.95 to 0.97; *P*<0.001).

Risk of Mortality Across Fitness Categories for the Entire Cohort

Relative mortality risks across fitness categories are presented in Table 4, and survival curves are presented in the Figure. Compared with those in the lowest 20th percentile of fitness (peak MET level ≤4), the adjusted hazard ratio for those who achieved 4.1 to 5.0 METs was not statistically significant. Thereafter, the hazard ratios for mortality were progressively lower as exercise capacity increased from 5.1 to 6.0 METs (hazard ratio=0.62; CI, 0.54 to 0.71; *P*<0.001); to 6.1 to 7.0 METs (hazard ratio=0.53; CI, 0.46 to 0.62; *P*<0.001); to 7.1 to 8.0 METs (hazard ratio=0.53; CI, 0.44 to 0.64; *P*<0.001); to 8.1 to 9.0 METs (hazard ratio=0.48; CI, 0.38 to 0.60; *P*<0.001); and >9 METs (hazard ratio=0.39; CI, 0.32 to 0.49; *P*<0.001). The trend for all fitness categories and all-cause mortality was highly significant (*P* for trend <0.001).

No significant colinearity was noted with any of the variables chosen for the Cox proportional hazards model

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Table 2. Demographic and Clinical Characteristics According to Fitness Categories

	Fitness Categories Based on Peak MET Level Achieved							
Variables	≤4	4.1–5.0	5.1–6.0	6.1–7.0	7.1–8.0	8.1–9.0	>9.0	*P* for Trend
n	1083	1226	866	835	486	355	463	
Age, y	72.4±5.3	72.1±5.1	71.6±5.0	70.8±4.5	70.7±5.0	70.4±4.7	69.4±4.0	<0.001
BMI, kg/m^2	27.4±5.0	27.7±5.0	28.0±4.8	27.7±4.6	27.0±4.1	27.0±4.0	26.4±3.5	<0.001
Resting HR, bpm	75±15	73±14	71±13	70±13	70±13	68±12	70±13	<0.001
Resting systolic BP, mm Hg	140±23	141±22	139±20	137±20	136±21	138±21	136±19	<0.001
Resting diastolic BP, mm Hg	79±12	78±12	79±11	80±10	79±11	79±11	80±11	0.3
CVD, %	44	41	36	34	29	29	19	<0.001
Previous MI, %	23	32	26	26	16	20	5	<0.001
Smoking, %	30	24	23	20	23	21	27	<0.001
Hypertension, %	55	57	61	55	52	54	48	<0.001
Diabetes mellitus, %	19	25	24	21	15	12	9	<0.001
Dyslipidemia, %	11	19	16	16	11	14	4	<0.001
Treatment								
β-blocker, %	17	15	19	18	14	15	19	0.09
CCB, %	29	24	26	24	24	25	21	0.02
ACE-I, %	14	16	18	17	13	16	13	0.04
Diuretics, %	8	11	12	13	7	6	4	0.02
Aspirin, %	5	7	6	6	5	5	2	0.004
Vasodilators, %	23	14	11	10	11	10	11	<0.001
Statins, %	3	5	8	8	8	5	7	<0.001
Exercise data								
Peak HR, bpm	119±23	121±25	128±21	132±19	136±19	137±18	143±20	<0.001
Peak systolic BP, mm Hg	169±33	173±33	181±29	184±28	184±28	188±27	187±24	<0.001
Peak diastolic BP, mm Hg	85±16	85±18	86±15	86±14	85±15	86±13	85±13	0.31
Peak METs, 3.5 mL O_2/kg per minute	3.2±0.7	4.7±0.3	5.6±0.3	6.6±0.3	7.6±0.3	8.6±0.3	11.0±1.8	<0.001

MI indicates myocardial infarction; CCB, calcium channel blockers; and ACE-I, angiotensin-converting enzyme inhibitors.

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(highest condition index <24). There were also no significant interactions relative to site by MET level ($P=0.16$), site by fitness category ($P=0.19$), race by MET level ($P=0.17$), or race by fitness category ($P=0.27$) on mortality risk. Therefore, the analyses were not stratified by these factors.

Risk of Mortality Across Fitness Categories According to Age Groups

Age-specific hazard ratios across fitness categories are also presented in Table 4. The findings were similar to those observed for the entire cohort. More specifically, compared with those in the lowest 20th percentile (peak MET level ≤4), the adjusted relative risks across fitness categories were 32% to 63% lower in those who achieved an exercise capacity >5 METs in the group aged 65 to 70 years and 45% to 60% lower for those older than 70 years.

Accounting for Reverse Causality

To account for the possibility that the higher mortality rates observed in the low-fitness categories were the result of underlying diseases (such as cachexia) or musculoskeletal or peripheral vascular issues and not low fitness per se (reverse causality), we undertook 3 approaches: (1) we excluded those who died within the initial 2 years of follow-up; (2) we excluded those who were not treated with β-blockers but did not achieve at least 85% of their age-predicted maximal HR (to account for factors that may have impaired exercise performance); and (3) we excluded those in the 2 lowest fitness categories (≤5 METs) with BMI <20. We then repeated the survival analyses separately (for each exclusion), as well as with all exclusions combined. In all 4 scenarios, the association between exercise capacity and mortality risk remained robust, and the risk reduction did not deviate substantially from that observed in the entire cohort (Table 5).

Finally, we examined the association between change in fitness and mortality in 867 individuals who had a second exercise evaluation (ETT) at least 6 months after the initial test (Table 6). On the basis of the significant reduction in risk for >5 METs noted in the entire cohort, we classified individuals as unfit if the MET level achieved during the initial exercise test was ≤5 METs and classified as fit those who achieved >5 METs. We then reclassified unfit individuals who also achieved ≤5 METs on the follow-up exercise test (remained unfit) as unfit-to-unfit (n=133; age=71±5 years; time between evaluations=3.3±2.6 years) and those who achieved >5 METs as unfit-to-fit (n=147; age=71±4 years; time between evaluations=3.9±3.3 years). Similarly, individuals classified as fit at baseline but who achieved ≤5 METs on

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Table 3. Mortality Risk Hazard Ratios for Exercise Capacity of Entire Cohort and the 2 Age Categories

Variables	No. of Deaths	Hazard Ratio	95% CI	*P*
All participants (n=5314)	2137			
Exercise capacity (for each 1-MET increment), unadjusted model		0.87	0.84–0.88	<0.001
Exercise capacity (for each 1-MET increment) adjusted for age, BMI, resting BP, race, cardiovascular risk factors,* cardiovascular medications,† and CVD‡		0.88	0.86–0.90	<0.001
Group aged 65–70 y (n=2560)	953			
Exercise capacity (for each 1-MET increment), unadjusted model		0.87	0.85–0.90	<0.001
Exercise capacity (for each 1-MET increment) adjusted for age, BMI, resting BP, race, cardiovascular risk factors, cardiovascular medications, and CVD		0.88	0.85–0.90	<0.001
Group aged >70 y (n=2754)	1184			
Exercise capacity (for each 1-MET increment), unadjusted model		0.86	0.83–89	<0.001
Exercise capacity (for each 1-MET increment) adjusted for age, BMI, resting BP, race, cardiovascular risk factors, cardiovascular medications, and CVD		0.88	0.85–0.91	<0.001

*Cardiovascular risk factors include hypertension, diabetes mellitus, dyslipidemia, and smoking.

†Cardiovascular medications include β-blockers, calcium channel blockers, angiotensin-converting enzyme inhibitors, diuretics, nitrates, vasodilators, aspirin, and statins.

‡CVD includes documented coronary artery disease, cardiac surgery for coronary artery disease, myocardial infarction, stroke, heart failure, and peripheral vascular disease.

the follow-up test were reclassified as fit-to-unfit (n=134; age=70±4 years; time between evaluations=4.1±2.9 years) and those who maintained a MET level >5 METs in both tests as fit-to-fit (n=449; age=70±4 years; time between evaluations=3.9±3.0 years).

In this subgroup, there were a total of 275 deaths during a mean follow-up period of 4.0 years (range, 6 months to 16.4 years; median, 3 years). The unadjusted mortality rate was 50% for the unfit-to-unfit; 42% for the unfit-to-fit; 37% for the fit-to-unfit; and 23% for the fit-to-fit. To assess the relative mortality risk among these categories, we performed a Cox proportional hazards analysis, adjusted for the same factors used in the primary analysis, using the unfit-to-unfit category as the reference group. The mortality risk was 61% lower in the fit-to-fit group (hazard ratio=0.39; CI, 0.28 to 0.54; $P<0.001$) and 41% lower in the fit-to-unfit group (hazard ratio=0.59; CI, 0.41 to 0.85; $P=0.005$). Individuals who were unfit during the initial test but became fit by the second test (unfit-to-fit) had a 35% lower mortality risk (hazard ratio=0.65; CI, 0.46 to 0.93; $P=0.019$) compared with subjects who were unfit at both examinations.

Discussion

In the present study, the association between exercise capacity and all-cause mortality in older male veterans (65 to 92 years) was assessed. Our findings support an inverse, graded, and independent association between impaired exercise capacity and all-cause mortality risk. For every 1-MET increase in exercise capacity, the mortality risk was 12% lower for the entire cohort and for the 2 age categories.

When fitness categories were considered, comparisons between the lowest fitness category (≤4 METs) and those who achieved 4.1 to 5.0 METs (next fitness category) revealed similar risk. Mortality risk then declined significantly for the remaining fitness categories, ranging from ≈40% for those who achieved 5.1 to 6 METs to 60% for those who achieved >9 METs. We observed similar results when the mortality and exercise capacity association was examined within each age category. Collectively, these findings suggest that an exercise capacity of >5 METs may be necessary for significant health benefits for those aged ≥65 years and confirm previous reports in broader age populations.[1,2,5,9]

Table 4. Adjusted* Hazard Ratios for Mortality Risk of Entire Cohort and Within the 2 Age Groups According to Fitness Categories*

MET Level Achieved	Entire Cohort (n=5314)	No. of Deaths (%)	Age 65–70 y (n=2560)	No. of Deaths (%)	Age >70 y (n=2754)	No. of Deaths (%)
≤4	1.0	615 (57)	1.0	246 (56)	1.0	369 (58)
4.1–5	0.93 (0.83–1.04)	622 (51)	0.92 (0.77–1.1)	244 (50)	0.92 (0.79–1.06)	378 (51)
5.1–6	0.62 (0.54–0.71)	298 (34)	0.68 (0.56–0.84)	145 (36)	0.55 (0.46–0.67)	153 (33)
6.1–7	0.53 (0.46–0.62)	260 (31)	0.53 (0.42–0.85)	128 (30)	0.54 (0.44–0.66)	132 (32)
7.1–8	0.53 (0.44–0.64)	146 (30)	0.53 (0.42–0.69)	82 (30)	0.50 (0.38–0.65)	64 (30)
8.1–9	0.48 (0.38–0.60)	95 (27)	0.45 (0.33–0.62)	47 (23)	0.50 (0.37–0.67)	48 (32)
>9	0.39 (0.32–0.49)	101 (22)	0.37 (0.28–0.49)	61 (19)	0.40 (0.28–0.55)	40 (29)

Values in parentheses represent 95% CIs unless indicated otherwise.

*Adjusted for age (in years), peak METs achieved, resting systolic BP (mm Hg), BMI, ethnicity, CVD, cardiovascular medications (aspirin, angiotensin-converting enzyme inhibitors, calcium channel blockers, β-blockers, diuretics, vasodilators, and statins), and risk factors (hypertension, diabetes mellitus, dyslipidemia, and smoking).

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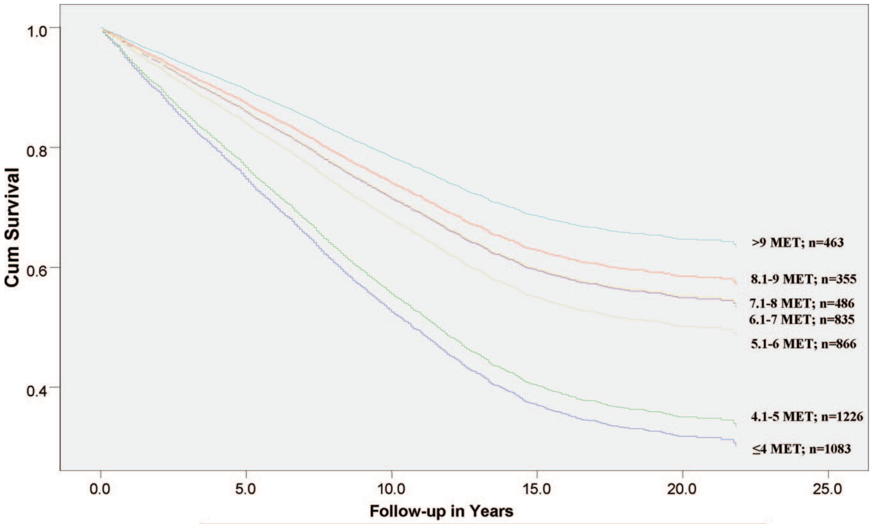

	Number of Cumulative Events/Number of Cases at Risk			
Fitness Categories	**5 years**	**10 years**	**15 years**	**20 years**
≤4 METs	337/724	535/379	608/186	615/63
4.1-5.0 METs	302/853	525/400	605/176	622/48
5.1-6 METs	121/656	233/330	289/122	298/36
6.1-7 METs	93/644	179/343	241/168	260/49
7.1-8.0 METs	51/386	108/180	140/72	146/22
8.1-9.0 METs	43/275	70/151	87/39	95/18
>9 METs	27/343	64/210	100/55	101/25

Figure. Cumulative (Cum) survival according to exercise capacity.

The inverse and graded association between exercise capacity and all-cause mortality is in accord with our previous reports among middle-aged individuals[1,5] and those from relatively small studies in older individuals.[9] However, the 12% reduction in risk for each 1-MET increase in exercise capacity is somewhat lower than the 18% reported in a smaller study among older subjects (n=514) from the Mayo Clinic.[7]

Several aspects of the present study make unique contributions to existing knowledge by providing information on the association between exercise capacity and mortality in older individuals. First, the 5314 subjects make it one of the largest studies to assess the association between fitness and mortality in a clinically referred cohort of older subjects, especially those aged 71 to 92 years (median age, 75 years; n=2754). Moreover, it allowed the formation of fitness categories per 1-MET increase in exercise capacity, which provided a more precise assessment of the association between fitness and mortality risk.

The size of our cohort also allowed us to consider the possibility that the higher mortality rates within the low fitness categories were influenced by subclinical disease and not exercise capacity per se (reverse causality). To account for this, we excluded those who died within the initial 2 years of follow-up, those who did not achieve at least 85% of age-predicted maximal HR, and those in the 2 lowest fitness categories with BMI <20. We then repeated the analysis after each exclusion and with all exclusions combined. The similarity in trends and magnitude of risk reduction observed between the findings of the entire cohort (Table 4) and these 4 separate analyses (Table 5) argue against the likelihood of reverse causality and support the validity of an association between fitness and mortality risk.

Further evidence against reverse causality is provided by the association between changes in exercise capacity over time and mortality risk in individuals with repeat exercise

Table 5. Adjusted* Hazard Ratios for Mortality Risk According to Fitness Categories (Conditional Exclusion of Study Participants)

MET Level Achieved	Excluding Deaths That Occurred During the First 2 y of Follow-Up (n=4889)	Excluding Those Who Did Not Achieve ≥85% of PMHR and Were Not Treated With β-Blockers (n=4624)	Excluding Those in the 2 Lowest Fitness Categories (≥5 METs) and BMI <20 (n=5186)	Excluding Those Who Met All 3 Conditions (n=4228)
≤4	1.0	1.0	1.0	1.0
4.1–5	0.93 (0.81–1.05)	0.88 (0.77–1.0)	0.92 (0.82–1.03)	0.86 (0.74–1.0)
5.1–6	0.67 (0.57–0.78)	0.54 (0.46–0.63)	0.62 (0.54–0.71)	0.58 (0.49–0.69)
6.1–7	0.60 (0.51–0.70)	0.51 (0.44–0.60)	0.54 (0.46–0.63)	0.57 (0.48–0.68)
7.1–8	0.55 (0.45–0.67)	0.51 (0.42–0.61)	0.53 (0.44–0.64)	0.52 (0.42–0.65)
8.1–9	0.52 (0.41–0.66)	0.45 (0.36–0.57)	0.48 (0.39–0.60)	0.49 (0.38–0.69)
>9	0.43 (0.34–0.54)	0.37 (0.30–0.46)	0.39 (0.31–0.48)	0.42 (0.33–0.54)

Values in parentheses represent 95% CIs. PMHR indicates predicted maximal HR.

*Adjusted for age (in years), peak METs achieved, resting systolic BP (mm Hg), BMI, ethnicity, CVD, cardiovascular medications (aspirin, angiotensin-converting enzyme inhibitors, calcium channel blockers, β-blockers, diuretics, vasodilators, and statins), and risk factors (hypertension, diabetes mellitus, dyslipidemia, and smoking).

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Table 6. Clinical Characteristics of Individuals With a Follow-Up Exercise Evaluation

Variables	Baseline	Follow-Up	*P*
n	867	867	
Age, y*	70.3±4.3	72.6±4.6	<0.001
BMI, kg/m^2	27.5±4.7	27.3±4.3	0.56
Resting HR, bpm	70±13	71±13	0.06
Resting systolic BP, mm Hg	140±20	139±20	0.2
Resting diastolic BP, mm Hg	81±11	77±11	0.001
CVD, %	53	57	<0.001
Previous MI	30	37	<0.001
Smoking, %	37	27	<0.001
Hypertension, %	54	65	<0.001
Diabetes mellitus, %	20	30	<0.001
Dyslipidemia, %	19	29	<0.001
Treatment			
β-blocker, %	13	25	<0.001
CCB, %	24	31	<0.001
ACE-I, %	13	23	<0.001
Diuretics, %	9	17	<0.001
Aspirin, %	6	7	0.7
Vasodilators, %	15	18	<0.03
Statins, %	4	16	<0.001

MI indicates myocardial infarction; CCB, calcium channel blockers; and ACE-I, angiotensin-converting enzyme inhibitors.

tests. Compared with unfit individuals in both tests (unfit-to-unfit), mortality risk was 61% lower in those who were physically fit in both tests (fit-to-fit). The mortality risk was 34% lower in individuals defined as unfit during the initial exercise test who became fit by the second test (unfit-to-fit). This finding suggests that advancing from a low-fit to a fit status yields significant health benefits even at an advanced age. Another clinically important finding is that the fitness-related health benefits are not ephemeral but are likely to endure for some years. This notion is supported by the observation that fit individuals who drifted into the unfit category by the second test maintained 41% lower risk compared with those who were unfit on both tests. Although these findings are based on a relatively small number of participants, they are strikingly similar to findings reported by Blair and coworkers[21] in a relatively young but larger cohort.

It is also noteworthy that the Veterans Affairs Health Care System is unique in that it ensures equal access to healthcare independent of a patient's financial status.[22] In addition, the Veterans Affairs electronic healthcare database is uniquely suited to determine mortality and other outcomes accurately and facilitates risk-adjustment models to study outcomes.[23] Thus, the system provides a unique opportunity to assess the association between mortality and exercise capacity while minimizing the influence of disparities in medical care.

Study Limitations

The inverse relationship between fitness and mortality may not demonstrate cause because residual confounding may still exist. Therefore, interventional studies are needed to confirm such a causal relationship. Although similar relationships have been demonstrated for CVD mortality, we only had information on all-cause mortality and did not have data on mortality related to cardiovascular interventions. In addition, we did not have information on physical activity patterns in all subjects; the extent to which exercise capacity reflects physical activity patterns in our sample is unknown. The onset of chronic diseases, their severity, and the duration of therapy were not evaluated because of incomplete records. Dietary information was also not available in our records. The fact that 2 different exercise protocols were used to assess fitness is also a potential limitation. Our previous work suggests that the ramp protocol is somewhat more accurate in predicting measured METs.[17] However, separate analyses from the 2 locations yielded similar results. Thus, the differences in protocols did not have a substantial impact. Finally, our findings are based on men only and cannot be extrapolated to women.

Clinical Implications

The present findings strongly support an inverse and graded association between exercise capacity and mortality risk in individuals aged 65 to 92 years. Similar to previous studies, significant reductions in mortality risk are evident beyond the fitness level represented by an exercise capacity of >5 METs. This level of fitness is likely achievable by most older individuals through 20 to 40 minutes of moderate daily exercise, such as walking.[24] The findings also suggest that the health benefits associated with improved fitness are likely to endure for some years.

The association between fitness and mortality in older individuals is of particular public health significance in light of the aging of the population. Importantly, our findings suggest that fitness-related health benefits are achieved regardless of age or fitness status. Thus, these results extend the public health message on the health benefits of fitness and physical activity to older individuals.[24] Collectively, these results support the concept that exercise capacity should be given as much attention by clinicians as other major risk factors. Thus, physicians and other healthcare professionals should encourage older individuals to initiate and maintain a physically active lifestyle consisting of moderate-intensity activities (brisk walking or similar activities) at any age. Such programs are likely to improve exercise capacity and lower the risk of mortality in older individuals.

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Disclosures

None.

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CLINICAL PERSPECTIVE

Our findings strongly support that increased exercise capacity is associated with significantly lower mortality risk in individuals aged 65 to 92 years. Most health benefits are evident at fitness levels reflected by an exercise capacity >5 METs. This level of fitness is likely achievable by most individuals regardless of age through 20 to 40 minutes of moderate daily exercise, such as brisk walking. In addition, improvement in fitness status even at this age appears to result in a significant reduction in mortality risk. The association between fitness and mortality in older individuals is of particular public health significance in light of the aging of the population. Our findings suggest that the fitness-related health benefits are achieved regardless of age or fitness status. Thus, these results extend the public health message on the health benefits of fitness and physical activity to older individuals. We urge that exercise capacity be given as much attention by clinicians as other major risk factors. Individuals should be encouraged by healthcare professionals to initiate and maintain a physically active lifestyle consisting of moderate-intensity activities (brisk walking or similar activities) at any age. Such programs are likely to improve exercise capacity and lower the risk of mortality in older individuals.

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