Epidemiology/Population

Exercise Capacity and All-Cause Mortality in Male Veterans With Hypertension Aged $\geq$70 Years

Charles Faselis, Michael Doumas, Andreas Pittaras, Puneet Narayan, Jonathan Myers, Apostolos Tsimploulis, Peter Kokkinos

Abstract—Aging, even in otherwise healthy subjects, is associated with declines in muscle mass, strength, and aerobic capacity. Older individuals respond favorably to exercise, suggesting that physical inactivity plays an important role in age-related functional decline. Conversely, physical activity and improved exercise capacity are associated with lower mortality risk in hypertensive individuals. However, the effect of exercise capacity in older hypertensive individuals has not been investigated extensively. A total of 2153 men with hypertension, aged $\geq$70 years (mean, 75±4) from the Washington, DC, and Palo Alto Veterans Affairs Medical Centers, underwent routine exercise tolerance testing. Peak workload was estimated in metabolic equivalents (METs). Fitness categories were established based on peak METs achieved, adjusted for age: very-low-fit, 2.0 to 4.0 METs (n=386); low-fit, 4.1 to 6.0 METs (n=1058); moderate-fit, 6.1 to 8.0 METs (n=495); high-fit $>8$ METs (n=214). Cox proportional hazard models were applied after adjusting for age, body mass index, race, cardiovascular disease, cardiovascular medications, and risk factors. All-cause mortality was quantified during a mean follow-up period of 9.0±5.5 years. There were a total of 1039 deaths or 51.2 deaths per 1000 person-years of follow-up. Mortality risk was 11% lower (hazard ratio, 0.89; 95% confidence interval, 0.86–0.93; P<0.001) for every 1-MET increase in exercise capacity. When compared with those achieving $\leq$4.0 METs, mortality risk was 18% lower (hazard ratio, 0.82; 95% confidence interval, 0.70–0.95; P=0.011) for the low-fit, 36% for the moderate-fit (hazard ratio, 0.64; 95% confidence interval, 0.52–0.78; P<0.001), and 48% for the high-fit individuals (hazard ratio, 0.52; 95% confidence interval, 0.39–0.69; P<0.001). These findings suggest that exercise capacity is associated with lower mortality risk in elderly men with hypertension. (Hypertension. 2014;64:30-35.)

Key Words: hypertension ■ mortality

Hypertension represents a major public health problem, affecting more than 1 billion persons worldwide, a number that is expected to increase to $\approx$1.5 billion during the next decade.1 The prevalence of hypertension rises with increasing age; in fact, the majority of elderly individuals have high blood pressure (BP).2 On the basis of Framingham data, the probability of an individual with normal BP at 55 years of age to become hypertensive during the next 2 decades is $\approx$90%,3 with 7.6 million premature deaths ($\approx$13.5% of the total global mortality) attributed to high BP.4 Given that advances in medical therapy and living conditions have prolonged life expectancy, the number of older individuals is expected to double over the next 2 decades, with 1 of 5 individuals being $\geq$65 years by 2030.5 Thus, the prevalence of hypertension is expected to continue to be a major public health problem worldwide.

Although cardiorespiratory fitness (CRF) is influenced by many factors, regular physical activity develops CRF.6,7 Low-to-moderate intensity exercise training has been shown to improve CRF significantly in middle-aged and older hypertensive veterans.8 Increased physical activity leading to improved CRF status is now a part of standard lifestyle recommendations for hypertensive individuals by itself or as an adjunct to pharmaceutical therapy to manage hypertension and lower mortality risk.9 Increased CRF is associated with a lower rate of progression to hypertension10 and a lower mortality risk in relatively healthy individuals and those with comorbidities, including hypertension.11–15 Significant reductions is mortality risk are noted in middle-aged individuals when peak exercise capacity exceeds $\approx$5 to 7 metabolic equivalents (METs).11–15 However, it is not known whether this fitness threshold applies to the elderly. The proportion of individuals achieving the minimum amount of recommended physical activity decreases with age and is estimated to be as low as 15.9% in adults $\geq$65 years of age.16 Furthermore, chronic health conditions known to be associated with aging might limit the ability of older individuals to exercise or to achieve an exercise capacity necessary for health benefits. Moreover, medical costs increase substantially with aging, which coupled with life prolongation, dramatically increase healthcare costs during subsequent decades.9 Because regular physical activity is associated with better health

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outcomes, medical costs may be substantially reduced by improvements in physical activity, especially in the elderly.17

Physical inactivity is currently considered an established cardiovascular risk factor.18 A plethora of evidence demonstrates an inverse and graded association between increased fitness status and mortality risk in the general population and in a wide variety of chronic health conditions, including coronary artery disease, heart failure, diabetes mellitus, hypertension, and prehypertension.11–15,19–22 However, most of these studies included a limited number of older individuals, limiting the ability to generalize these findings to the elderly. The fitness–mortality risk association in elderly hypertensive individuals has not been addressed to our knowledge. This is important clinically because of our aging population and concomitant heightened prevalence of hypertension. Thus, we sought to assess the effects of exercise capacity on all-cause mortality in a large cohort of elderly male veterans with hypertension.

Methods

Study Population

In the Veterans Exercise Testing Study (VETS), there were 2153 male veterans with hypertension aged ≥70 years, who underwent an exercise test between 1986 and December 2012. Of those, 1065 (49.5%) were black, 971 (45.1%) were white, and 117 (5.4%) were other or unknown races. Exercise testing was performed either at the Veterans Affairs Medical Center, Washington, DC (n=1448) or at the Veterans Affairs Palo Alto Healthcare System, Palo Alto, CA (n=705). Exercise tests were conducted as a part of routine evaluation or for the clinical suspicion of coronary artery disease. Our study population consisted of elderly (≥70 years) individuals with hypertension, excluding individuals (1) with a positive exercise test that was subsequently confirmed by a stress thallium test or cardiac catheterization, (2) who became unstable during the test or required emergent intervention, (3) who developed left bundle branch block during the exercise test, (4) with heart failure (New York Heart Association class ≥II), (5) with an implanted pacemaker, (6) unable to complete the test because of musculoskeletal or peripheral vascular disease20 or achieve a peak exercise capacity of ≥2 METs, and (7) those with body mass index (BMI) <18.5 kg/m². Written informed consent was granted by all study participants before conducting the exercise test. The study was approved by the Internal Review Boards at each institution (Washington, DC, and Palo Alto, CA).

Demographic, clinical information, and medications were extracted from electronic medical records just before the exercise test. Comorbidities were defined by International Classification of Diseases—Ninth Revision codes. Individuals were asked to verify the computerized information on the history of chronic diseases, current medications, and cigarette smoking habits. Cardiovascular disease was defined as a history of myocardial infarction, angiographically documented coronary artery disease, coronary angioplasty, coronary artery bypass surgery, or chronic heart failure New York Heart Association class I (patients with higher New York Heart Association classes were excluded). Body weight and height were recorded before the test; BMI was calculated as weight (kg) divided by height² (m²).

The Social Security Death Index was used to match all subjects to 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.30 Vital status was evaluated annually and determined as of December 31, 2012. The outcome for this study was all-cause mortality.

Exercise Assessments

Exercise capacity was assessed by the standard Bruce protocol at the Veterans Affairs Medical Center, Washington, DC. An individualized ramp protocol was used at the Veterans Affairs Palo Alto Healthcare System, as described previously.31 Subjects were encouraged to exercise until the occurrence of volitional fatigue in the absence of symptoms or other clinical indications for stopping the test.29 Peak exercise time was recorded in seconds. Peak workload was estimated in METs. One MET is defined as the energy expended at rest, which is approximately equivalent to an oxygen consumption of 3.5 mL/kg of body weight per minute.32 Exercise capacity (in METs) was estimated on the basis of exercise time via a commonly used equation for the Bruce protocol29 and based on American College of Sports Medicine equations for the ramp protocol.32 Administration of medications remained unchanged for the exercise testing.

Supine resting heart rate and BP were assessed after 5 minutes of rest in a quiet room. Indirect arm-cuff sphygmomanometry was used for all BP assessments following standard methodology. ST-segment depression was measured visually. ST depression ≥1.0 mm that was horizontal or downsloping was considered to be suggestive of ischemia.

Fitness Categories

We established 4 fitness categories on the basis of the MET level achieved. When forming fitness categories, a cutoff of ≤4 METs was chosen to represent the very-low-fit category (n=386) as in previous studies.21–23 Thereafter, categories were established per 2-MET incremental increases in exercise capacity. Individuals with exercise capacity from 4.1 to 6.0 METs constituted the low-fit category (n=1058); those with exercise capacity between 6.1 and 8.0 METs constituted the moderate-fit category (n=495); and those who achieved >8 METs constituted the high-fit category (n=214).

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 χ² test. One-way ANOVA was applied to determine age, BMI, resting and exercise heart rate and BP, and peak MET level differences between fitness categories and age groups. Normality of the tested variables was evaluated with the Shapiro–Wilks 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 very-low-fit category (exercise capacity, ≤4 METs) as the reference group. Log-rank tests were calculated to evaluate significance of fitness levels on all-cause mortality. Cox proportional hazards models were then used 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, the presence of cardiovascular disease, cardiovascular medications (aspirin, angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, calcium channel blockers, β-blockers, diuretics, vasodilators, and statins), muscle-wasting disease (cancer, kidney failure, and HIV/AIDS), and cardiovascular 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 (univariate) analysis. The proportional hazards assumption was evaluated with the use of Schoenfeld residuals. P<0.05 with 2-sided tests were considered significant. All statistical analyses were performed with the use of SPSS software (SPSS version 19; SPSS Inc, Chicago, IL).

Results

Baseline Demographic and Clinical Characteristics

The mean follow-up period was 9.3±5.7 years (20120.6 person-years; range, 6 months to 26.9 years). There were 1039 deaths during the follow-up period, with an average annual mortality of 51.6 deaths per 1000 person-years.

The baseline and clinical characteristics for the entire cohort and according to the 4 fitness categories are presented...
in Table 1. There were significant differences between fitness categories in nearly all baseline characteristics, except resting diastolic BP, the prevalence of diabetes mellitus, cardiovascular disease, and smoking habits. In particular, patients with lower compared to those with higher exercise capacity were older; had higher BMI levels, resting heart rate, and systolic BP values; had lower prevalence of dyslipidemia and the use of lipid-lowering agents; and had more common use of antihypertensive medications.

Predictors of All-Cause Mortality

Cox proportional hazards analyses revealed that the strongest predictors of mortality were age (hazard ratio, 1.03; 95% confidence interval [CI], 1.01–1.03; P<0.001), BMI (hazard ratio, 0.98; 95% CI, 0.96–0.99; P=0.002), muscle-wasting disease (hazard ratio, 1.77; 95% CI, 1.53–2.05; P<0.001), diabetes mellitus (hazard ratio, 1.35; 95% CI, 1.18–1.56; P<0.001), cardiovascular disease (hazard ratio, 1.33; 95% CI, 1.18–1.51; P<0.001), statins (hazard ratio, 0.55; 95% CI, 0.47–0.64; P<0.001), cardiac/antihypertensive medications (hazard ratio, 0.73; 95% CI, 0.62–0.85; P<0.001), and exercise capacity (METs). Mortality risk was 11% lower for each 1-MET increase in exercise capacity (hazard ratio, 0.89; 95% CI, 0.86–0.93; P<0.001).

Mortality Risk According to Fitness Categories

Relative mortality risks across the 4 fitness categories are presented in Table 2. With the very-low-fit group (peak MET level, ≤4) as the reference group and adjustments for age, BMI, and resting BP, the adjusted mortality hazard ratios were progressively lower because exercise capacity increased from 4.1 to 6.0 METs (hazard ratio, 0.79; 95% CI, 0.68–0.92; P<0.001), from 6.1 to 8.0 METs (hazard ratio, 0.55; 95% CI, 0.45–0.67; P<0.001), and >8 METs (hazard ratio, 0.44; 95% CI, 0.34–0.59; P<0.001). The trend for all fitness categories and all-cause mortality was highly significant (P for trend<0.001).

When the model was fully adjusted for all significant variables, the hazard ratios were slightly reduced but remained highly significant. In comparison with the low-fit category, individuals in the moderate-fit category had an 18% lower mortality risk (hazard ratio, 0.82; 95% CI, 0.70–0.95; P=0.011); the mortality risk was lower by 36% in the high-fit category (hazard ratio, 0.64; 95% CI, 0.52–0.78; P<0.001) and 48% lower in the very-high-fit category (hazard ratio, 0.52; 95% CI, 0.39–0.69; P<0.001).

No significant collinearity was noted for any of the variables chosen for the Cox proportional hazards model (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.

To minimize the likelihood that reverse causality might have accounted for the association between low exercise capacity and increased all-cause mortality, we excluded 184 individuals who died within the initial 2 years of follow-up. Reanalysis of the data revealed that the exercise capacity–mortality risk association remained robust, and risk did not deviate substantially from that for the entire cohort (hazard ratio, 0.77; 95% CI, 0.85–0.92; hazard ratio, 0.67; 95% CI, 0.54–0.82; hazard...
These findings suggest that health benefits of fitness are apparent even in older cohorts. To account for this, in our cohort, the exercise capacity–mortality risk association remained robust, and risk did not deviate substantially from that presented for the entire cohort. Further support for the exercise capacity–mortality risk association concept is provided by the findings of previous studies in older veterans and a younger nonveteran cohort in whom exercise capacity was tracked over time. In these studies, changes in exercise capacity reflected concomitant changes in mortality risk. Collectively, these findings argue against the likelihood of reverse causality and support the validity of the exercise capacity–mortality risk association.

Discussion

The current findings support an inverse, independent, and graded association between exercise capacity and mortality risk in hypertensive individuals aged ≥70 years. For each 1-MET increase in exercise capacity, the mortality risk was lowered by 11%. When fitness categories were considered, mortality risk was 18% for the low-fit (4.1–6 METs), 36% for the moderate-fit (6.1–8.0 METs), and 46% lower for the high-fit (>8.0 METs) category when compared with individuals in the lowest fitness category (≤4.0 METs).

Although similar relationships have been shown in other populations, including veterans, to our knowledge, this is the first study to assess the effect of fitness on mortality risk in a relatively large and clinically referred cohort of elderly hypertensive individuals (n=2153), approximately 50% of whom were black. It is also noteworthy that the exercise capacity–mortality risk association was graded with a significantly lower mortality observed ≥4 METs and a magnitude similar to that reported in much younger populations, including veterans. These findings suggest that health benefits of fitness are apparent regardless of age.

The possibility that the higher mortality rates observed in the low-fitness categories were the result of pre-existing, underlying illness (such as cachexia) or musculoskeletal or peripheral vascular issues and not low fitness per se (reverse causality) remains a consideration in epidemiological data, especially in older cohorts. To account for this, in our cohort, we did not include those with BMI <18.5 kg/m², those unable to complete the test because of musculoskeletal or peripheral vascular disease, or those unable to achieve a peak exercise capacity of ≥2 METs. In addition, we excluded those who died within the initial 2 years of follow-up. Reanalysis of the data revealed that the exercise capacity–mortality risk association remained robust, and risk did not deviate substantially from that presented for the entire cohort. Further support for the exercise capacity–mortality risk association concept is provided by the findings of previous studies in older veterans and a younger nonveteran cohort in whom exercise capacity was tracked over time. In these studies, changes in exercise capacity reflected concomitant changes in mortality risk. Collectively, these findings argue against the likelihood of reverse causality and support the validity of the exercise capacity–mortality risk association.

Physical activity is essential for healthy aging, and elderly individuals should strive to be as physically active as their ability allows, in accordance with the American College of Sports Medicine recommendations. Improved physical fitness is likely to improve muscular function and balance, leading to fewer musculoskeletal injuries and falls that the elderly are prone to and will ultimately lead to an improvement in quality of life. The findings of the current study strengthen the contention that the health benefits of increased physical activity are similar among elderly hypertensive individuals as they are in younger populations. The peak exercise capacity associated with significantly lower mortality risk (>4 METs) is relatively easy to achieve even for individuals aged ≥70 years, generally requiring moderate levels of activity, such as brisk walking for 20 to 30 minutes per day, 3 to 6 days a week. Therefore, efforts to increase physical activity for the public regardless of age should be emphasized.

The equal access to care independent of a patient’s financial status provided by the Veterans Health Administration is also noteworthy. This permits epidemiological evaluations while minimizing the influence of disparities in medical care. Along with the existence of electronic health records within the Veterans Affairs Healthcare System, this enables detailed observation of history and alterations in health status. These attributes, coupled with the consideration for individuals diagnosed with muscle wasting disease, minimize the likelihood of reverse causality and support the validity of exercise capacity–mortality risk association for subjects >70 years.

Limitations

This study has several limitations inherent to prospective follow-up evaluations. We only had information on all-cause mortality and did not have data on cardiovascular mortality. The onset of chronic diseases, their severity, and duration of therapy were not evaluated. Dietary information was also not available in our records. The 2 different exercise protocols 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. However, separate analyses from the 2 locations yielded similar results, suggesting that the differences in protocols had minimal effect.

### Table 2. Hazard Ratios for Mortality Risk of the Entire Cohort and According to Fitness Categories

<table>
<thead>
<tr>
<th>Fitness Categories According to Peak METs Achieved</th>
<th>No. of Deaths (%)</th>
<th>Hazard Ratio (Age Adjusted)</th>
<th>Hazard Ratio (Adjusted for Age, BMI, and Resting BP)</th>
<th>Hazard Ratio (Fully Adjusted)*</th>
<th>P Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤4 MET (n=386)</td>
<td>243 (63.0)</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>...</td>
</tr>
<tr>
<td>4.1–6.0 MET (n=1058)</td>
<td>540 (51.0)</td>
<td>0.78 (0.67–0.90)</td>
<td>0.79 (0.68–0.92)</td>
<td>0.82 (0.70–0.95)</td>
<td>0.011</td>
</tr>
<tr>
<td>6.1–8.0 MET (n=495)</td>
<td>191 (36.8)</td>
<td>0.54 (0.45–0.65)</td>
<td>0.55 (0.45–0.67)</td>
<td>0.64 (0.52–0.78)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&gt;8.0 MET (n=214)</td>
<td>65 (30.4)</td>
<td>0.47 (0.35–0.62)</td>
<td>0.44 (0.34–0.59)</td>
<td>0.52 (0.39–0.69)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

BMI indicates body mass index; BP, blood pressure; and MET, metabolic equivalent.
*Adjusted for age, resting BP, BMI, ethnicity, β-blockers, calcium channel blockers, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, diuretics, hypoglycemic and lipid-lowering agents, history of smoking, cardiovascular disease, dyslipidemia, muscle-wasting disease, sleep apnea, alcohol/drug abuse, and diabetes mellitus.
†For fully adjusted model.
Fitness levels are based on METs achieved from work rate and not a direct assessment of oxygen uptake. In addition, fitness was assessed only at baseline, and follow-up data on the fitness status of the participants were not available. Finally, only male Veterans were included, which limits the ability to generalize the findings to women.

Perspectives

Our findings have a significant clinical and public health effect for the following reasons. First, relatively moderate increases in exercise capacity (>4.0 METs) lower mortality risk in men with hypertension aged 270 years. Second, this level of exercise capacity is achievable by most elderly individuals engaging in a brisk walk of 20 to 40 minutes most days of the week. Because walking requires virtually no instructions, it has a relatively low cost, carries a low risk of injury, and can be easily implemented to large populations, it may constitute an effective intervention to mitigate the deleterious effects of hypertension in the elderly.

Disclosures
None.

References


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**Novelty and Significance**

**What Is New?**

- To the best of our knowledge, this is the first large prospective cohort study to assess the effect of exercise capacity in hypertensive individuals aged ≥70 years.

**What Is Relevant?**

- Our findings support the concept that health benefits of increased physical activity are evident in elderly hypertensive individuals that are similar to other populations. Thus, hypertensive individuals aged ≥70 years can lower their risk of mortality by engaging in brisk walking most days of the week. The peak exercise capacity of >4 metabolic equivalents associated with significantly lower mortality risk is achievable for most individuals aged ≥70 years, requiring only moderate levels of activity, such as a brisk walk of 20 to 30 minutes per day, 3 to 6 days a week. Because the number of older individuals is expected to double over the next 2 decades and the prevalence of hypertension rises with increasing age, the current findings have significant public health relevance.

**Summary**

Our findings support that increased exercise capacity is associated with lower mortality risk in men with hypertension aged ≥70 years. Thus, fitness-related health benefits are independent of age.
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