Exercise Capacity and All-cause Mortality in African-American and Caucasian Men with Type 2 Diabetes Mellitus

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**Objective:** Assess the association between exercise capacity and mortality in African-Americans and Caucasians with type 2 diabetes and explore racial differences regarding this relationship.

**Research design and methods:** African-American (n=1,703; age=60±10) and Caucasian (n=1,445; age=62±10) men with type 2 diabetes completed a maximal exercise test between 1986 and 2007 at the Veterans Affairs Medical Centers in Washington, DC and Palo Alto, California. Three fitness categories were established (Low, Moderate and High-Fit) based on peak metabolic equivalents (METs) achieved. They were followed for all-cause mortality for 7.3±4.7 years.

**Results:** The adjusted mortality risk was 23% higher in African-Americans compared to Caucasians (hazard ratio=1.23; CI: 1.1-1.4). A graded reduction in mortality risk was noted with increased exercise capacity for both races. There was a significant interaction between race and METs (p<0.001), and among race and fitness categories (p<0.001). The association was stronger for Caucasians. Each 1-MET increase in exercise capacity yielded 19% lower risk for Caucasians and 14% for African-Americans (p<0.001). Similarly, the risk was 43% lower (hazard ratio=0.57; CI: 0.44-0.73) for Moderate-Fit and 67% lower (hazard ratio=0.33; CI: 0.22-0.48) for High-Fit Caucasians. The comparable reductions in African-Americans were 34% (hazard ratio=0.66; CI: 0.55-0.80), and 46% (hazard ratio=0.54; CI: 0.39-0.73) respectively.

**Conclusion:** Exercise capacity is a strong predictor of all-cause mortality in African-American and Caucasian men with type 2 diabetes. The exercise capacity-related reduction in mortality appears to be stronger and more graded for Caucasians than for African-Americans.
Poor exercise capacity is a well established independent predictor of cardiovascular and overall mortality among healthy subjects, and patients with diabetes mellitus and/or cardiovascular disease (CVD) (1-5), whereas increased physical activity and higher cardiorespiratory fitness confer health benefits in proportion to the level of fitness (1,2,6), independent of body mass index (BMI) (3,4). Increases in physical activity patterns, have thus emerged as an integral part of the prevention and management of type 2 diabetes mellitus (5-7).

African-Americans have a 2- to 6-fold higher risk for developing diabetes mellitus (8), and approximately double the diabetes death rate (9), than do Caucasians. Socioeconomic and quality of health care differences have been cited as possible reasons for this apparent racial disparity (10-12). When access to health care is comparable, significantly lower overall mortality rates were reported among a National population of African-American veterans versus Caucasians with diabetes mellitus (10).

An intriguing finding is that African-American diabetics exhibit significantly lower exercise capacity than do Caucasian diabetics (13). The relationship between exercise capacity and mortality risk in African-American diabetics has not been previously reported, and possible racial differences regarding this relationship have not been explored.

The Veterans Health Administration in the US Department of Veterans Affairs Health Care System ensures equal access to high quality health care independent of a patient’s financial status (14). In addition, the Veterans Affairs Medical Center (VAMC) electronic health information database is well suited to determine mortality accurately (15), thus providing an opportunity to assess the association between exercise capacity and mortality under comparable medical care.

In the present study, we assessed the relationship between exercise capacity and all-cause mortality in diabetics and possible racial differences regarding this relationship.

RESEARCH DESIGN AND METHODS

Between July 1986 and November 30, 2007, a symptom-limited exercise tolerance tests (ETT) has been administered to veterans with type 2 diabetes mellitus at the VAMC in Washington, DC and Palo Alto, California, either as part of routine evaluations or to assess exercise-induced ischemia. This information along with the individual’s medical history has been electronically stored.

From this database we excluded females and those with any of the following: 1) history of an implanted pacemaker; 2) left bundle branch block; 3) unstable symptoms; and 4) impaired chronotropic response. After these exclusions, the participant group was comprised of 1,703 African-Americans and 1,445 Caucasians. The study was approved by the Institutional Review Board at each institution, and all subjects gave written informed consent prior to undergoing ETT.

All demographic, clinical and medication information was obtained from individual’s computerized medical records just prior to ETT. Each individual was asked to verify the computerized information, including history of chronic disease, current medications and smoking habits. Body weight and height were assessed by a standardized scale and recorded prior to the test. BMI was calculated as weight (kg) divided by height$^2$ (m$^2$). Demographic data are included in Table 1.

Dates of death were verified from the Veterans Affairs Beneficiary Identification and Record Locator System File. This system is used to determine benefits to survivors of veterans and is has been shown to be
complete and accurate (95%) (16). Vital status was determined as of February 28, 2008.

Exercise testing was performed using the Bruce protocol at the VAMC, Washington DC, and an individualized ramp protocol as described elsewhere (17) for men assessed at the VAMC, Palo Alto CA. Peak exercise capacity (metabolic equivalents-METs) was estimated using standardized equations based on peak speed and grade for the ramp protocol (17) and on peak exercise time for the Bruce protocol (18). Subjects were encouraged to exercise until volitional fatigue in the absence of symptoms or other indications for stopping (19). The use of handrails was discouraged, but allowed when necessary for balance and safety. Age-predicted peak exercise heart rate (HR) was determined based on a population-specific equation (20). Medications were not altered before testing.

Three fitness categories were established based on the MET level achieved. Those who achieved a peak MET level ≤5 METs (lowest 25%) of the METs achieved by the cohort comprised the low fitness category (Low-Fit; n=934); those whose MET level was >75% (≥8 METs) comprised the highest fit category (High-Fit; n=762). The remaining (5.1-7.9 MET level) comprised the moderate fitness category (Moderate-Fit; n=1,452).

**Statistical Analysis:** Follow-up time is presented as mean± standard deviation (SD) and median of years. Mortality rate was calculated as the ratio of events by the number of persons or by the person years of observation. Continuous variables are presented as mean values ± SD and categorical variables as relative frequencies (%). Associations between categorical variables were tested using chi-square analysis. One-way analysis of variance was applied to determine age and BMI differences between races and fitness categories. Because of racial differences in age, ANCOVA was utilized to assess whether racial difference existed in exercise test variables, using age as a covariate. Age and BMI were used as covariates when comparisons among fitness categories were made. Post-hoc procedures were performed (Bonferroni) for multiple comparisons. Equality of variances between groups was tested by Levene’s test.

The relative risk for mortality was calculated for each fitness category. Kaplan-Meier survival curves were generated for the three fitness categories. Cox proportional hazard models were used to determine the variables that were significantly associated with mortality among fitness categories. The analyses were adjusted for age, BMI, history of CVD, cardiovascular medications (ACE-I, beta-blockers, CCB, diuretics, statins) and risk factors (hypertension, dyslipidemia, smoking). Racial difference regarding the effect of exercise capacity on mortality risk was tested using a dummy-variable that combined the exercise data with race. P-values <0.05 using two sided tests were considered statistically significant. All statistical analyses were performed using SPSS software version 15.0 (SPSS Inc., Chicago, IL, USA).

**RESULTS**

The mean (±SD) follow-up period was 7.3±5 years, (median 6.4 years), and 23,137 person-years. There were 823 deaths (26.1%), resulting in an average annual mortality of 3.56%. Of those who died, 509 (29.9%) were African-Americans and 314 (21.7%) were Caucasians.

Approximately 79% of subjects achieved a peak HR of ≥85% of the age-predicted value. Approximately 44% of those who did not achieve this level were receiving beta-blockers.

Participants’ characteristics and exercise data are presented in Table 1. African-Americans were younger than Caucasians (p<0.001). After controlling for
age, African-Americans had higher resting diastolic BP, and were more likely to have CVD, hypertension, dyslipidemia, and be treated with diuretics and insulin. Caucasians were more likely to smoke, have a family history of coronary heart disease (CHD), and be treated with beta-blockers, ACE-I, statins and oral glycemic agents. After adjusting for age and resting diastolic BP, the peak exercise systolic and diastolic BP and HR were significantly higher in African-Americans versus Caucasians, while peak MET level was higher in Caucasians.

Adjusted mortality for age, CVD, risk factors, resting diastolic BP, CV medication, insulin and oral glycemic agents, and METs, revealed that all cause mortality was 23% higher (hazard ratio=1.23; CI=1.02-1.47; p=0.02) in African-Americans than Caucasians. This relationship was consistent within Moderate (hazard ratio=1.31; CI: 1.04-1.64) and High-Fit categories (hazard ratio=2.31; CI: 1.44-3.70) with no significant racial differences in mortality rates within the Low-Fit category (hazard ratio=1.16; CI: 0.94-1.44).

African-Americans who died were significantly older (64±10 versus 59±9 yrs; p<0.001) and had higher resting systolic BP (143±23 versus 133±21 mmHg; p<0.001) when compared with those still alive. They also had lower BMI (28.7±5.4 versus 30.7±5.5; p<0.001), and were more likely to smoke and have a higher prevalence of CVD.

Similarly, Caucasians who died were older (66±9 versus 61±9 yrs; p<0.001), and had higher resting systolic BP (139±23 versus 133±20 mmHg; p<0.001) than those alive. In addition, they had significantly lower BMI (28.4±4.8 versus 30.9±5.8; p<0.001), diastolic BP (77±12 versus 79±11 mmHg; p<0.001) and were more likely to have CVD.

Comparisons among fitness categories revealed that age was significantly lower (p<0.001) for the High-Fit versus Moderate and Low-Fit categories (56±9.2; 61±10; 65±9 yrs, respectively). Similar findings were observed for both races. BMI was lower (p<0.05) in the High-Fit compared with the Moderate and Low-Fit categories (30.3±5.9 versus 30.6±5.6 versus 29.5±5.1 for Low, Moderate and High-Fit, respectively). Thus, age and BMI were used as covariates when assessing differences in resting and exercise HR, BP and MET levels among the fitness categories.

Exercise capacity and other clinical predictors of total mortality for the entire group and for each race are presented in Table 2. Survival analysis revealed a 16% reduction in mortality risk for every 1-MET increase in exercise capacity in the entire cohort (p<0.001), 14% in African-Americans (p<0.001) and 19% in Caucasians (p<0.001).

There were 394 (42.2%) deaths in the Low-Fit category, 339 (23.3%) in the Moderate-Fit, and 90 (11.8%) in the High-Fit category (Figure 1). Among African-Americans, there were 230 (46.4%) deaths in the Low-Fit, 224 (26.7%) in the Moderate-Fit and 55 (14.9%) in the High-Fit category. In Caucasians, there were 164 (37.4%) deaths in the Low-Fit category, 115 (18.8%) in the Moderate-Fit; and 35 (8.9%) in the High-Fit category.

To assess total mortality risk associated with exercise capacity, we compared the Moderate and High-Fit categories to the Low-Fit (Cox proportional hazard). The adjusted relative risks of these comparisons are presented in Table 3. The risk of mortality was 37% lower for those with an exercise capacity between 5.1 to 7.9 METs (p<0.001) and 67% lower for those who achieved ≥ 8 METs (p<0.001). The findings did not change substantially when deaths that occurred within the first year of follow up were excluded.

To assess racial differences in mortality risk, we probed for interaction between race and fitness. A significant interaction was noted between race and METs
(p<0.001), and among race and fitness categories (p<0.001). Thus, we examined mortality rates among fitness categories for each race (Table 3). The Low-Fit category was used as the referent.

In African-Americans, the relative risk was 34% lower for those achieving 5.1 to 7.9 METs (p<0.001), and 46% lower for those achieving 8 or more METs (p<0.001). In Caucasians, the relative risk was 43% lower (p<0.001) for those achieving 5.1 to 7.9 METs and 67% lower (p<0.001) for those achieving ≥8 METs.

Finally, we addressed the effects of exercise capacity on mortality risk when expressed as a percentage of age-predicted values, calculated based on an equation derived from a large cohort of veterans referred for exercise testing (2). These analyses resulted in no significant differences relative to the findings when exercise capacity was expressed as an absolute value.

CONCLUSIONS

The findings of the current study support a strong inverse and graded association between exercise capacity and risk for all cause mortality in middle-aged and older African-American and Caucasian male Veterans with type 2 diabetes mellitus. After adjusting for age, BMI, cardiovascular risk factors and cardiac medications total mortality risk was progressively lower as exercise capacity increased beyond 5 METs (Table 3). Our findings support previous reports of an inverse relationship between aerobic fitness and total mortality in both healthy and diseased populations (1-5). They also confirm a previous report in predominantly male Caucasian diabetics that the largest proportional reduction in risk occurs between the least fit and the moderate fit categories (4).

The current study is unique because it is the first to provide information on the association between exercise capacity and mortality risk in African-American men with type 2 diabetes mellitus and to compare these relationships with a similar group of Caucasians. In this regard, it is important to emphasize that a strong, inverse and dose-response reduction in the mortality risk for both African-Americans and Caucasians was observed. Equally important is the finding of racial disparities in this relationship. More specifically, we noted that the exercise-related reduction in mortality may be stronger and more graded for Caucasians than for African-Americans. For example, the adjusted mortality risk reduction per each 1-MET increase in exercise capacity was significantly greater for Caucasians (19%) when compared to African-Americans (14%). Furthermore, comparisons between fitness categories revealed significant and clinically relevant differences in the mortality risk reduction between races. When compared to Low-Fit (≤5 METs), the mortality risk reduction for those achieving 5.1-7.9 METs was 43% for Caucasians and 34% for African-Americans. In the high fitness category (≥8 METs), the risk was lowered by 67% (an additional 24% reduction) in Caucasians and only 46% (an additional 12% reduction) in African-Americans (Table 3).

It is noteworthy that in our previous work of over 15,600 veterans with multiple risk factors (1), a close scrutiny of the database revealed that racial disparities were evident only in diabetics.

The mechanism(s) responsible for the racial disparity in the association of exercise capacity and mortality risk in diabetic men are not readily evident and are beyond the scope of this study. Nevertheless, because obesity has been identified as a risk factor for impaired exercise capacity (21) and is more common among African-Americans (22), we examined possible racial differences in the prevalence of obesity as one likely explanation. However, the prevalence of overweight for both African-Americans and
Caucasians was 49.8% and 49.0% versus 50.7% for obese, respectively (p=0.35). We also noted no significant racial differences in waist circumference on 182 diabetics with available waist circumference data (p=0.116).

Another possible mechanism may be racial differences in vascular reactivity. Endothelium-dependent vasodilatation is significantly impaired in healthy African-American adults (23) and diabetics (24) when compared with that in the corresponding groups of Caucasians. In the current study, impaired vascular reactivity may have been more prevalent or more severe in African-Americans than Caucasians.

It is also possible that the racial differences on the impact of exercise capacity on mortality risk may be due to racial differences on adherence to medical therapy or socioeconomic factors that we were not able to account for in this study. We also probed for racial differences between the two sites regarding fitness, but found no interactions. Finally, genetic differences between the two races can not be discounted.

Another notable aspect of our study relates to the socioeconomic strata of our cohort. Most information on the association between exercise capacity and total mortality in diabetics has been derived from predominantly, middle to upper socioeconomic status Caucasians (3-5). Socioeconomic factors for such individuals may be more favorable and allow for a more optimal management of their diabetes mellitus. Thus, the reported benefits of exercise in such populations may be exaggerated when compared with individuals in relatively low socioeconomic strata. Our cohort consists of Caucasian and African-American veterans who mostly represent relatively lower socioeconomic strata. Thus, our findings support the notion that higher exercise capacity is associated with lower all-cause mortality in men with type 2 diabetes mellitus, independent of socioeconomic status.

Finally, the equal access to high quality health care provided by the Veterans Health Administration in the US Department of Veterans Affairs Health Care System, independent of a patient’s financial status strengthens the contention that increased exercise capacity provides protection against premature mortality in diabetic men.

Our study has some limitations. The inverse association between cardiorespiratory fitness and mortality does not prove cause and effect relationships. Although similar reciprocal relationships have been demonstrated between fitness and CVD mortality, we only had information on all-cause mortality, and did not have data on cardiovascular mortality. However, using all-cause mortality as an end point in clinical investigations is viewed as an objective, unbiased and accurate while cardiovascular mortality has been criticized as highly inaccurate (25). The onset of diabetes mellitus and other chronic diseases, their severity and duration of therapy and their status of physical activity could not be evaluated due to incomplete records. This may explain part of the racial disparity noted. Finally, our findings are based on men only and can not be extrapolated to women.

In conclusion, our findings support the concept that exercise capacity is a strong predictor of all-cause mortality in African-American and Caucasian men with type 2 diabetes mellitus. The reduction is graded and more pronounced in Caucasians than African-Americans. It is important to emphasize that the inherent limitations of any epidemiologic study do not permit definitive statements and that the finding regarding racial differences should be confirmed by future studies. Despite these limitations, our findings raise the intriguing possibility that racial differences in the fitness-related health benefits may exist and that research on racial disparities should be pursued.
Our findings extend the public health message regarding the health benefits of cardiorespiratory fitness to men with diabetes mellitus and support the concept that exercise capacity should be given as much attention by clinicians as other major risk factors and health care professionals should encourage diabetics to initiate and maintain a physically active lifestyle consisting of moderate-intensity activities.

ACKNOWLEDGMENTS:
We wish to acknowledge Monica Aiken, MA and Chris McManus, MS for their invaluable work over the years in data collection, management, and retrieval.
REFERENCES
## Table 1  
Demographic and Clinical Characteristics for African-Americans and Caucasians with Type 2 Diabetes

<table>
<thead>
<tr>
<th>Variables</th>
<th>Total</th>
<th>African-American</th>
<th>Caucasian</th>
<th>p-value *</th>
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<tbody>
<tr>
<td>n</td>
<td>3,148</td>
<td>1,703</td>
<td>1,445</td>
<td>-</td>
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<tr>
<td>Age (yrs)</td>
<td>61±10</td>
<td>60 ±10</td>
<td>62±10</td>
<td>&lt;0.001</td>
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<tr>
<td>BMI (kg/m²)</td>
<td>30±5.6</td>
<td>30±5.5</td>
<td>30±5.7</td>
<td>0.27</td>
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<tr>
<td>Resting HR (beats/min)</td>
<td>76±14</td>
<td>76±14</td>
<td>76±14</td>
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<td>Resting Systolic BP (mmHg)</td>
<td>135±21</td>
<td>136±22</td>
<td>134±21</td>
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<tr>
<td>Resting Diastolic BP (mmHg)</td>
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<td>81±12</td>
<td>78±12</td>
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<td>CVD (%)</td>
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<td>51.7</td>
<td>47.3</td>
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<td>Smoking (%)</td>
<td>42</td>
<td>35.1</td>
<td>50.2</td>
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<td>Hypertension (%)</td>
<td>73.6</td>
<td>75.6</td>
<td>71.3</td>
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<td>Family History of CHD</td>
<td>14.8</td>
<td>12.3</td>
<td>18.8</td>
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<td>Dyslipidemia (%)</td>
<td>26.9</td>
<td>34.6</td>
<td>17.9</td>
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<td>Beta-Blocker (%)</td>
<td>18.3</td>
<td>13.1</td>
<td>24.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CCB (%)</td>
<td>21.4</td>
<td>20.6</td>
<td>22.4</td>
<td>0.23</td>
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<tr>
<td>ACE-I (%)</td>
<td>37.5</td>
<td>34.6</td>
<td>40.9</td>
<td>&lt;0.001</td>
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<tr>
<td>Diuretics (%)</td>
<td>15.7</td>
<td>18.6</td>
<td>12.3</td>
<td>&lt;0.001</td>
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<tr>
<td>Aspirin (%)</td>
<td>5.9</td>
<td>5.9</td>
<td>5.8</td>
<td>0.511</td>
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<td>Statins (%)</td>
<td>14.6</td>
<td>9.4</td>
<td>20.7</td>
<td>&lt;0.001</td>
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<tr>
<td>Insulin (%)</td>
<td>30.7</td>
<td>33.7</td>
<td>22.8</td>
<td>&lt;0.001</td>
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<tr>
<td>Oral glycemic agents (%)</td>
<td>34.2</td>
<td>33.2</td>
<td>36.8</td>
<td>0.13</td>
</tr>
<tr>
<td><strong>Exercise Data</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Peak HR (beats/min)</td>
<td>135±25</td>
<td>138±25</td>
<td>131±25</td>
<td>&lt;0.001</td>
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<tr>
<td>Peak Systolic BP (mmHg)</td>
<td>183±32</td>
<td>188±33</td>
<td>176±31</td>
<td>&lt;0.001</td>
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<tr>
<td>Peak Diastolic BP (mmHg)</td>
<td>86±16</td>
<td>89±16</td>
<td>82±15</td>
<td>&lt;0.001</td>
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<tr>
<td>Peak METs (3.5 ml O₂/kg/min)</td>
<td>6.4±2.3</td>
<td>6.3±2.0</td>
<td>6.5±2.6</td>
<td>0.001</td>
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</table>

* P-values represent comparisons between AA and Caucasians
Table 2. Hazard Ratios for All-Cause Mortality According to Exercise Capacity

<table>
<thead>
<tr>
<th>VARIABLES</th>
<th>Hazard ratio</th>
<th>95% CI</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>All (n=3,148)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Peak Exercise Capacity (For each 1-MET increment)</td>
<td>0.79</td>
<td>0.76-0.82</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Adjusted for Age and BMI</td>
<td>0.82</td>
<td>0.79-0.86</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Adjusted Age, BMI, CV Risk Factors, CVD and CV Medications</td>
<td>0.84</td>
<td>0.81-0.87</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>African-Americans (n=1,703)</td>
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<tr>
<td>Peak Exercise Capacity (For each 1-MET increment)</td>
<td>0.80</td>
<td>0.76-0.84</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Adjusted for Age and BMI</td>
<td>0.85</td>
<td>0.93-0.96</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Adjusted Age, BMI, CV Risk Factors, CVD, and CV Medications†</td>
<td>0.86</td>
<td>0.82-0.90</td>
<td>&lt;0.001</td>
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<tr>
<td>Caucasians (n=1,445)</td>
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<tr>
<td>Peak Exercise Capacity (For each 1-MET increment)</td>
<td>0.77</td>
<td>0.73-0.82</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Adjusted for Age and BMI</td>
<td>0.81</td>
<td>0.76-0.85</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Adjusted Age, BMI, CV Risk Factors CVD, and CV Medications†</td>
<td>0.81</td>
<td>0.77-0.86</td>
<td>&lt;0.001</td>
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</table>

* CV Risk Factors include: hypertension, dyslipidemia and smoking
† CV Medications include: ACE, beta-blockers, CCB, diuretics, insulin, aspirin and Statins.

Table 3. Relative Risk for All-Cause Mortality According to Fitness Categories

<table>
<thead>
<tr>
<th>Entire Cohort (n=3,148)</th>
<th>Low-Fit</th>
<th>Moderate-Fit</th>
<th>High-Fit</th>
<th>p-value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>MET Level Achieved</td>
<td>≤5 METs</td>
<td>5.1-7.9 METs</td>
<td>≥8 METs</td>
<td></td>
</tr>
<tr>
<td>Age-adjusted</td>
<td>Referent</td>
<td>0.62 (0.53-0.71)</td>
<td>0.41 (0.32-0.52)</td>
<td>&lt;0.001</td>
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<tr>
<td>Multi-adjusted†</td>
<td>Referent</td>
<td>0.63 (0.55-0.73)</td>
<td>0.41 (0.33-0.53)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Excluding deaths that occurred during the 1st year of follow-up</td>
<td>Referent</td>
<td>0.63 (0.53-0.73)</td>
<td>0.43 (0.14-0.55)</td>
<td>&lt;0.001</td>
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<tr>
<td>African-Americans (n=1,703)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age-adjusted</td>
<td>Referent</td>
<td>0.65 (0.54-0.78)</td>
<td>0.54 (0.39-0.73)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Multi-adjusted†</td>
<td>Referent</td>
<td>0.66 (0.55-0.80)</td>
<td>0.54 (0.39-0.73)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Excluding deaths that occurred during the 1st year of follow-up</td>
<td>Referent</td>
<td>0.65 (0.53-0.79)</td>
<td>0.56 (0.40-0.77)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Caucasians (n=1,445)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age-adjusted</td>
<td>Referent</td>
<td>0.55 (0.43-0.70)</td>
<td>0.32 (0.22-0.47)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Multi-adjusted†</td>
<td>Referent</td>
<td>0.57 (0.44-0.73)</td>
<td>0.33 (0.22-0.48)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Excluding deaths that occurred during the 1st year of follow-up</td>
<td>Referent</td>
<td>0.57 (0.43-0.72)</td>
<td>0.34 (0.23-0.51)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

* Adjusted for: age, BMI, ACE-I, b-blockers, CCB, diuretics, statins, hypertension, dyslipidemia and smoking.
† P-values are for both the Moderate-Fit and High-Fit categories compared to the Low-Fit category (referent), and for linear trend.
Figure 1  Cumulative Survival for the Entire Cohort According to Fitness Categories

<table>
<thead>
<tr>
<th>Years of Follow-up</th>
<th>No. of Cumulative Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤5 METs</td>
<td>218 340 386 394</td>
</tr>
<tr>
<td>5.1-7.9 METs</td>
<td>156 270 325 339</td>
</tr>
<tr>
<td>≥8 METs</td>
<td>37 71 87 90</td>
</tr>
</tbody>
</table>