Brief report

Cardiorespiratory fitness and mortality in diabetic men with and without cardiovascular disease

Paul McAuleya,*, Jonathan Myersb, Brian Emersona, Ricardo B. Oliveirab, Carolyn L. Bluec, Jesse Pittsleya, Victor F. Froelicherb

a Department of Human Performance and Sport Sciences, Winston-Salem State University, Winston-Salem, NC, USA
b Division of Cardiology, VA Palo Alto Health Care System/Stanford University, Palo Alto, CA, USA
c Department of Community Practice, School of Nursing, University of North Carolina Greensboro, Greensboro, NC, USA

1. Introduction

The lifetime risk of cardiovascular disease (CVD) is higher for individuals with diabetes [1,2]. Higher cardiorespiratory fitness (fitness) attenuates the mortality risk associated with CVD and diabetes [4,5]. Yet information on the influence of fitness on mortality in patients having both diabetes and CVD remains largely unexplored.

A previous report from the Veterans Exercise Testing Study (VETS) provided compelling evidence that moderate to high levels of fitness can reduce all-cause mortality risk in diabetes (P < 0.001) and halved risk of death in diabetes/CVD (P < 0.001). Fitness was a potent effect modifier in the association of diabetes and CVD to mortality.

2. Research design and methods

The Veterans Exercise Testing Study (VETS) is a prospective epidemiologic investigation of more than 9000 veteran diabetes research and clinical practice xxx (2009) xxx–xxx

Keywords:
Cardiorespiratory fitness
Cardiovascular diseases
Diabetes mellitus
Exercise testing
Mortality

© 2009 Published by Elsevier Ireland Ltd.

patients (3% women) referred to two university-affiliated
Veterans Affairs medical centers (Long Beach, from 1987 to
1991; Palo Alto, from 1992 to the present). From this database, a
total of 7775 men were evaluated for inclusion into this study.
We excluded 175 subjects because of missing data on height,
weight or exercise capacity; and another 51 underweight
patients (BMI < 18.5 kg/m²). Therefore, participants for the
present analysis were 7549 men who completed a baseline
medical examination and maximal exercise test during 1987–
2003. All subjects gave informed written consent for participa-
tion in the study. Additional information on study methods
and subject characteristics of this cohort has been published
elsewhere [7].

Height and weight were measured using standard proce-
dures and body mass index (BMI) was calculated as weight in
kilograms divided by the square of height in meters. Maximal
exercise testing was performed using an individualized ramp
test as previously described [8]. We estimated maximal
metabolic equivalents (METs, 1 MET = 3.5 ml O₂ uptake
kg⁻¹ min⁻¹) from final treadmill speed and grade using
standard equations [9]. Subjects with diabetes included those
with type 1 or type 2 diabetes determined according to the
American Diabetes Association diagnosis and classification
criteria [10]. Patients classified as having CVD included those
with a history of myocardial infarction, angiographically
documented coronary artery disease, coronary angioplasty,
coronary bypass surgery, chronic heart failure, stroke, and/or
peripheral vascular disease. We defined low, moderate, and
high-fitness as <5, 5–10, and >10 METs, respectively, as in
previous VETS reports [3,7]. Subjects were also classified
according to diabetes/CVD status (either, diabetes, CVD, and
both), resulting in 12 combined disease status/fitness groups.
The statistical software Number Crunching Statistical Soft-
ware (Kaysville, UT) was used for all statistical analyses.

Participants were followed for at least 1 year from their
baseline examination until their death or until 30 December,
2004. The California Health Department Service and Social
Security Death Indices were used to ascertain the vital status
of each subject. Cox proportional hazards analyses were used
to assess the joint effects of fitness and diabetes and CVD
status at baseline with the risk of all-cause mortality. We
selected no diabetes/no CVD and high-fitness (N = 1229) as the
reference group and calculated hazard ratios (HRs) of all-cause
mortality for the remaining 11 disease status-fitness groups.
Covariates included: age (years), ethnicity (non-Hispanic
White, African-American, Hispanic, Asian-Pacific Islander,
or unknown), currently smoking (yes or no), hypertension (yes
or no), hypercholesterolemia (yes or no) and BMI (kg/m²). We
used ANOVA to compare means for continuous variables and
X² for categorical variables. All P values are 2-sided and
P < 0.05 was regarded as statistically significant.

3. Results

We recorded 1637 deaths during a mean follow-up of 8.1 ± 4.7
years. The study population consisted of 74% non-Hispanic
Whites, 9.2% Hispanics and 11.5% African-Americans, who
ranged in age from 21 to 93 years (mean [SD] 59 [±11]). In
general, subjects with neither diabetes nor CVD were younger,
more likely to have high-fitness, less likely to have hyperten-
sion, but as likely to have hypercholesterolemia as those
patients with diabetes, CVD or both (Table 1). Compared to
the reference group, adjusted hazard ratios (HRs) (95% confidence
intervals) for low-, moderate-, and high-fitness, respectively,
were: 3.79 (2.08–6.90), 2.42 (1.54–3.82), and 0.95 (0.35–2.61) in
diabetes; 4.62 (3.53–6.05), 2.83 (2.20–3.64), and 1.36 (1.00–1.85) in
CVD; and 5.17 (3.62–7.39), 3.72 (2.68–5.16), and 2.60 (1.34–5.05)
in diabetes/CVD.

Table 1 – Baseline characteristics according to disease status among 7549 men in the Veterans Exercise Testing Study,

<table>
<thead>
<tr>
<th>Diabetes/CVD status</th>
<th>Neither (N = 3121)</th>
<th>Diabetes (N = 434)</th>
<th>CVD (N = 3496)</th>
<th>Both (N = 498)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>55.8 ± 11.9</td>
<td>58.5 ± 9.7</td>
<td>61.2 ± 10.3</td>
<td>62.4 ± 9.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Non-Hispanic White (%)</td>
<td>72.6</td>
<td>55.5</td>
<td>77.5</td>
<td>67.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>28.5 ± 4.9</td>
<td>30.6 ± 5.7</td>
<td>27.8 ± 4.8</td>
<td>29.5 ± 5.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fitness groups (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low-fit (&lt;5 METs)</td>
<td>9.1</td>
<td>14.7</td>
<td>21.5</td>
<td>28.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Moderate-fit (5–10 METs)</td>
<td>51.5</td>
<td>66.1</td>
<td>58.9</td>
<td>58.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>High-fit (&gt;10 METs)</td>
<td>39.4</td>
<td>19.1</td>
<td>19.7</td>
<td>13.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fitness, METs</td>
<td>9.5 ± 3.6</td>
<td>7.6 ± 2.9</td>
<td>7.6 ± 3.4</td>
<td>6.6 ± 3.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Blood pressure (mmHg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>131.7 ± 18.8</td>
<td>134.7 ± 20.1</td>
<td>133.7 ± 21.1</td>
<td>136.9 ± 20.7</td>
<td>0.001</td>
</tr>
<tr>
<td>Diastolic</td>
<td>82.8 ± 11.4</td>
<td>80.1 ± 10.8</td>
<td>81.5 ± 11.2</td>
<td>79.8 ± 11.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>42.6</td>
<td>71.7</td>
<td>51.0</td>
<td>68.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Currently smoking (%)</td>
<td>29.6</td>
<td>23.7</td>
<td>30.5</td>
<td>19.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypercholesterolemia (%)</td>
<td>30.2</td>
<td>39.6</td>
<td>30.9</td>
<td>38.2</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Data shown are mean ± SD unless otherwise specified. BMI, body mass index; METs, maximal metabolic equivalents achieved during the
treadmill test; CVD, cardiovascular disease.

* History of physician diagnosed high cholesterol or measured fasting total cholesterol ≥ 220 mg/dL (5.70 mmol/L).
* History of physician diagnosed hypertension or measured resting systolic blood pressure ≥ 140 or resting diastolic blood pressure ≥ 90 mmHg.

in diabetes/CVD (Table 2). Within disease group comparisons revealed that, relative to low-fit, mortality risks for high-fit patients were 50% lower for diabetes, CVD, nearly nullified (92%) for CVD, and completely nullified (100%) for diabetes and CVD with mortality.

**Table 2 – Fitness level and diabetes/CVD status stratified HRs (95% CI) for all-cause mortality among 7549 men in the Veterans Exercise Testing Study, 1987–2003.**

<table>
<thead>
<tr>
<th>Fitness level</th>
<th>CVD/diabetes status</th>
<th>N</th>
<th>Deaths, N (%)</th>
<th>Age-adjusted HR (95% CI)</th>
<th>Multivariate HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High (&gt;10 METs)</td>
<td>Neither</td>
<td>1229</td>
<td>71 (6)</td>
<td>1 [Ref.]</td>
<td>1 [Ref.]</td>
</tr>
<tr>
<td></td>
<td>Diabetes</td>
<td>83</td>
<td>4 (5)</td>
<td>0.93 (0.34–2.56)</td>
<td>0.95 (0.35–2.61)</td>
</tr>
<tr>
<td></td>
<td>CVD</td>
<td>688</td>
<td>97 (14)</td>
<td>1.40 (1.03–1.90)</td>
<td>1.36 (1.00–1.85)</td>
</tr>
<tr>
<td></td>
<td>Both</td>
<td>65</td>
<td>10 (15)</td>
<td>2.49 (1.28–4.83)</td>
<td>2.60 (1.34–5.05)</td>
</tr>
<tr>
<td>Moderate (5–10 METs)</td>
<td>Neither</td>
<td>1607</td>
<td>214 (13)</td>
<td>1.73 (1.32–2.28)</td>
<td>1.80 (1.37–2.37)</td>
</tr>
<tr>
<td></td>
<td>Diabetes</td>
<td>287</td>
<td>26 (9)</td>
<td>2.13 (1.36–3.34)</td>
<td>2.42 (1.54–3.82)</td>
</tr>
<tr>
<td></td>
<td>CVD</td>
<td>2058</td>
<td>652 (32)</td>
<td>2.81 (2.19–3.62)</td>
<td>2.83 (2.20–3.64)</td>
</tr>
<tr>
<td></td>
<td>Both</td>
<td>290</td>
<td>79 (27)</td>
<td>3.49 (2.52–4.83)</td>
<td>3.72 (2.68–5.16)</td>
</tr>
<tr>
<td>Low (&lt;5 METs)</td>
<td>Neither</td>
<td>285</td>
<td>69 (25)</td>
<td>3.17 (2.26–4.46)</td>
<td>3.25 (2.31–4.59)</td>
</tr>
<tr>
<td></td>
<td>Diabetes</td>
<td>64</td>
<td>13 (20)</td>
<td>3.53 (1.94–6.41)</td>
<td>3.79 (2.08–6.90)</td>
</tr>
<tr>
<td></td>
<td>CVD</td>
<td>750</td>
<td>343 (46)</td>
<td>4.55 (3.48–5.95)</td>
<td>4.62 (3.53–6.05)</td>
</tr>
<tr>
<td></td>
<td>Both</td>
<td>143</td>
<td>59 (41)</td>
<td>4.92 (3.66–6.99)</td>
<td>5.17 (3.62–7.39)</td>
</tr>
</tbody>
</table>

BMI, body mass index; METs, maximal metabolic equivalents; CVD, cardiovascular disease.

The multivariate hazard ratio (HR) was calculated using Cox proportional hazards models adjusted for age, ethnicity, smoking, hypertension, hypercholesterolemia and BMI (entered as a continuous variable).

**Conflict of interest**

There are no conflicts of interest.

**Contributions**

All authors had access to the data and a role in writing the manuscript.

**References**


