Prognostic Value of Exercise Capacity in Patients With Coronary Artery Disease: The FIT (Henry Ford Exercise Testing) Project

Rupert K. Hung, BA; Mouaz H. Al-Mallah, MD; John W. McEvoy, MB, BCh; Seamus P. Whelton, MD; Roger S. Blumenthal, MD; Khurram Nasir, MD; John R. Schairer, DO; Clinton Brawner, PhD; Mohsen Alam, MD; Steven J. Keteyian, PhD; and Michael J. Blaha, MD, MPH

Abstract

Objective: To examine the prognostic value of exercise capacity in patients with nonrevascularized and revascularized coronary artery disease (CAD) seen in routine clinical practice.

Patients and Methods: We analyzed 9852 adults with known CAD (mean ± SD age, 61±12 years; 69% men [n=6836], 31% black race [n=3005]) from The Henry Ford Exercise Testing (FIT) Project, a retrospective cohort study of patients who underwent physician-referred stress testing at a single health care system between January 1, 1991, and May 31, 2009. Patients were categorized by revascularization status (nonrevascularized, percutaneous coronary intervention [PCI], or coronary artery bypass graft [CABG] surgery) and by metabolic equivalents (METs) achieved on stress testing. Using Cox regression models, hazard ratios for mortality, myocardial infarction (MI), and downstream revascularizations were calculated after adjusting for potential confounders, including cardiac risk factors, pertinent medications, and stress testing indication.

Results: There were 3824 all-cause deaths during median follow-up of 11.5 years. In addition, 1880 MIs, and 1930 revascularizations were ascertained. Each 1-MET increment in exercise capacity was associated with a hazard ratio (95% CI) of 0.87 (0.85-0.89), 0.87 (0.85-0.90), and 0.86 (0.84-0.89) for mortality; 0.98 (0.96-1.01), 0.88 (0.84-0.92), and 0.93 (0.90-0.97) for MI; and 0.94 (0.92-0.96), 0.91 (0.88-0.95), and 0.96 (0.92-0.99) for downstream revascularizations in the nonrevascularized, PCI, and CABG groups, respectively. In each MET category, the nonrevascularized group had similar mortality risk as and higher MI and downstream revascularization risk than the PCI and CABG surgery groups (P<.05).

Conclusion: Exercise capacity was a strong predictor of mortality, MI, and downstream revascularizations in this cohort. Furthermore, patients with similar exercise capacities had an equivalent mortality risk, irrespective of baseline revascularization status.
benefits beyond that of OMT alone.²⁶⁻²⁹ Given its prognostic value in other patient populations, the degree to which exercise capacity can help predict outcomes in nonrevascularized and revascularized patients with CAD remains an important area of uncertainty.

We sought to examine the potential interactive effect of exercise capacity and revascularization status on mortality, myocardial infarction (MI), and revascularization risk in a diverse cohort of patients with CAD referred for exercise testing in routine clinical practice.

PATIENTS AND METHODS

Study Design
This study was based on data from the Henry Ford ExercIse Testing (FIT) Project, a retrospective cohort study aimed at investigating the implications of exercise capacity on cardiovascular outcomes and total mortality.³⁰ The FIT Project is unique in its combined use of (1) directly measured exercise data, (2) collected medical history and medication treatment data taken at the time of the stress test, (3) retrospective verification and supplementation of supporting clinical data using the electronic medical record (EMR) and administrative databases, and (4) follow-up for all-cause mortality and select nonfatal outcomes via linkage with the death registry and medical claims files.

The FIT Project cohort is a registry of 69,885 consecutive patients who underwent physician-referred treadmill stress testing at a Henry Ford Health System facility in metropolitan Detroit, Michigan, between January 1, 1991, and May 31, 2009. These medical centers are part of a large, vertically integrated organization that provides health care and offers a managed care insurance plan. Exercise data, medical history, and current medications were collected by exercise physiologists and nurses at the time of testing into a common clinical reporting tool that directly populated the EMR. Supporting clinical data and follow-up for cardiovascular outcomes were derived from the EMR and administrative databases shared across Henry Ford Health System. Patients younger than 18 years at the time of stress testing and patients undergoing modified Bruce and non-Bruce protocol tests were not included in the registry. The FIT Project was approved by the Henry Ford Hospital Institutional Review Board.

Study Cohort
We initially excluded all patients who did not have known CAD at the time of stress testing (n=59,695), thereby creating a subgroup of patients from The FIT Project with known CAD at baseline (n=10,190) (Figure 1). Known CAD was defined as previous MI, PCI, CABG surgery, or documented CAD on a previous angiogram. Patients with missing covariates of interest were further excluded (n=338), leaving a total of 9852 patients with known CAD for analysis. We subsequently categorized the remaining cohort into 3 subgroups according to their baseline revascularization status: nonrevascularized (n=4543), previous PCI (n=2719), and previous CABG surgery (n=2590). For this study, patients with both previous PCI and CABG surgery (n=375) were categorized into the CABG surgery group.

Exercise Testing
All of the patients underwent routine, clinically referred, symptom-limited treadmill stress testing using the standard Bruce protocol.³¹ In accordance with clinical guidelines,³² treadmill testing was terminated at the discretion of the supervising clinician for reasons that included substantial arrhythmias; abnormal hemodynamic responses; diagnostic ST-segment changes; exercise-limiting symptoms, such as chest pain or shortness of breath; or if the patient was unwilling or unable to continue.

Resting heart rate and blood pressure were measured before stress testing by clinical personnel. Exercise capacity, expressed in estimated metabolic equivalents (METs), was calculated using a treadmill controller system (Q-Stress; Quinton Instruments) and was categorized into 4 groups based on distribution of data: less than 6, 6 to 9.9, 10 to 11.9, or greater than or equal to 12 METs.

Medical History and Medication Use
A medical history, including age, sex, race, indication for stress testing, risk factor burden, active medication use, and history of medical conditions, was obtained by nurses or exercise physiologists immediately before the stress test. Medication use and medical history were supplemented and verified by an electronic
query of the EMR, administrative databases, and pharmacy claims files from enrollees in the integrated health plan. Race was defined exclusively by self-report and was categorized by administrators into common identifications (white, black, or other). Obesity was defined by self-report or assessment by the clinician historian. Current smoking was defined as self-reported active smoking at the time of testing. Indication for stress testing was extracted from the stress test requisition provided by the referring physician and was subsequently categorized by administrators into common indications (eg, ischemia evaluation/risk stratification, chest pain, shortness of breath, and preoperative evaluation).

A database-verified diagnosis was considered present when the appropriate International Classification of Diseases, Ninth Revision code was present on 3 or more separate encounters in the health system. Diabetes mellitus, dyslipidemia, and hypertension were defined by self-report, previous diagnosis, database-verified diagnosis, or use of medications for the respective medical conditions. β-Adrenergic blocking agents and angiotensin-converting enzyme inhibitors were considered antihypertensive medications for this analysis. Previous atrial fibrillation and congestive heart failure were defined as previous clinical diagnosis of paroxysmal or persistent atrial fibrillation and systolic or diastolic heart failure, respectively.

Follow-up and Ascertainment of Outcomes
Patients were followed for a mean ± SD of 11.6±5, 6.3±5, and 6.1±5 years for the occurrence of all-cause mortality, MI, and downstream revascularizations, respectively.

Mortality was ascertained in April 2013, after federal law changes in 2011 limited reporting of protected state death records.33 An algorithmic search of the Social Security Death Index Death Master File was completed using social security number, first name, last name, and date of birth data.

Myocardial infarction and downstream revascularizations were ascertained in May 2010 through linkage with administrative claims files from services delivered by the affiliated group practice or reimbursed by the health plan. Linkage was performed using appropriate International Classification of Diseases,
Ninth Revision and Current Procedural Terminology codes for MI, PCI, and CABG surgery. For nonmortality outcomes, patients were censored at their last contact with the Henry Ford Health System when ongoing coverage with the health plan could no longer be confirmed to minimize bias from loss to follow-up.

Statistical Analyses
Groups were compared using \( \chi^2 \) testing or analysis of variance techniques as appropriate. The crude cumulative incidences for mortality, MI, and downstream revascularizations were derived from Kaplan-Meier estimates at median follow-up times of 11.5, 5.6, and 5.3 years, respectively. We used Cox regression models to calculate hazard ratios (HRs) for mortality, MI, and downstream revascularizations, with adjustment for age; sex; race; obesity; resting heart rate and systolic and diastolic blood pressures; history of hypertension, dyslipidemia, smoking, diabetes mellitus, atrial fibrillation, or heart failure; indication for stress testing; medications used to treat chronic obstructive pulmonary disease, hypertension, or hyperlipidemia; aspirin; clopidogrel; and \( \beta \)-adrenergic blocking agents, lipid-lowering medication, and clopidogrel (\( P < .001 \)). The CABG surgery group was significantly older, was less likely to be obese or to smoke, and had a higher proportion of men and white patients (\( P < .001 \)).

The total cohort achieved a mean \( \pm \) SD exercise capacity of 7.0\( \pm \)3 METs. The PCI group had the highest mean \( \pm \) SD exercise capacity of 7.6\( \pm \)3 METs, and the CABG surgery group had the lowest mean \( \pm \) SD exercise capacity of 6.6\( \pm \)3 METs.

Unadjusted Survival
During follow-up, 3824 deaths (39%), 1880 MIs (19%), and 1930 downstream revascularizations (20%) were observed. Table 2 shows the crude cumulative incidences for mortality, MI, and downstream revascularizations at their respective median follow-up times. The highest MET category generally had the lowest cumulative incidence of mortality, MI, and downstream revascularizations in each revascularization group (\( P < .001 \)) (Supplemental Table 1; available online at http://www.mayoclinicproceedings.org). Of the patients who died, those with the highest exercise capacity lived more than 3 years longer after their stress test than patients with the lowest exercise capacity (10.6 vs 7.5 years; \( P < .001 \)). In each MET category, the PCI and CABG surgery groups had lower incidences of MI and downstream revascularizations than the nonrevascularized group (\( P < .001 \)).

Adjusted Survival
Figure 2 shows the association between exercise capacity and the adjusted risk of mortality, MI, and downstream revascularizations in each revascularization group (see also Supplemental Table 2; available online at http://www.mayoclinicproceedings.org). A graded decrease in mortality risk was observed with increasing METs in all patients, regardless of their baseline revascularization status (\( P < .001 \)). In contrast, a significant association between a higher exercise capacity and a lower risk of MI was generally observed only in the revascularized groups (\( P < .001 \)). The risk of downstream revascularizations was generally lower with increasing MET categories, but significance was not always observed until the higher MET categories, particularly in the CABG surgery group.
In the adjusted models with exercise capacity analyzed as a continuous variable, similar results as in Figure 2 were observed for all 3 outcomes regardless of which method was used for analysis (Supplemental Table 3; available online at http://www.mayoclinicproceedings.org). Each 1-MET increment in exercise capacity was associated with a 13% reduction in mortality risk in the total cohort (HR, 0.87; 95% CI, 0.86-0.88), with similar per-MET reductions seen in the nonrevascularized (HR, 0.87; 95% CI, 0.85-0.89), PCI (HR, 0.87; 95% CI, 0.85-0.90), and CABG surgery (HR, 0.86; 95% CI, 0.84-0.89) groups.

Similarly, each 1-MET increment in exercise capacity was not associated with lower risk for MI in the nonrevascularized (HR, 0.98; 95% CI, 0.96-1.01) group, but was in
the PCI (HR, 0.88; 95% CI, 0.84-0.92) and CAGB surgery (HR, 0.93; 95% CI, 0.90-0.97) groups. Per-MET reductions in revascularization risk for the nonrevascularized, PCI, and CAGB surgery groups were 6% (HR, 0.94; 95% CI, 0.92-0.96), 9% (HR, 0.91; 95% CI, 0.88-0.95), and 4% (HR, 0.96; 95% CI, 0.92-0.99), respectively.

In univariate models, low exercise capacity was comparable with age as a predictor of mortality ($z=33.0$ for both) and was a more significant predictor than established cardiac risk factors, such as diabetes ($z=16.1$), hypertension ($z=8.1$), dyslipidemia ($z=7.3$), obesity ($z=5.4$), sex ($z=1.5$), and smoking status ($z=1.4$). Low exercise capacity was also a significant predictor of MI and downstream revascularizations (Supplemental Table 4; available online at http://www.mayoclinicproceedings.org).

**Interaction Between Exercise Capacity and Baseline Revascularization Status**

Table 3 shows the adjusted effect of baseline revascularization status on risks of mortality, MI, and downstream revascularizations in each MET category. Risk of mortality did not significantly differ between revascularization groups in each strata of exercise capacity (Supplemental Figure; available online at http://www.mayoclinicproceedings.org). In contrast, the risk of MI and downstream revascularizations were lower in the PCI and CAGB surgery groups relative to the nonrevascularized group ($P=.003$). When the effect of exercise capacity and baseline revascularization status on the risk of the 3 end points were jointly examined (Figure 3 and Supplemental Table 5; available online at http://www.mayoclinicproceedings.org), exercise capacity remained inversely associated with mortality, MI, and revascularization risk in all the revascularization groups except risk of MI in the nonrevascularized group.

**Sensitivity Analyses**

We performed sensitivity analyses (1) excluding those who died within 1 year of their stress test ($n=227$), (2) excluding those who underwent stress testing for preoperative cardiac evaluations ($n=279$), (3) excluding patients with heart failure ($n=670$), (4) excluding those without body mass index data ($n=6278$), and (5) with further adjustment for the decade in which each stress test took place to account for improvements in the management of CAD over time. There were no significant changes compared with the main results (Figure 2 and Table 3). We also examined patients with a known left ventricular ejection fraction ($n=5319$), who may represent a less healthy subset in the cohort owing to the clinical suspicion of heart failure or structural cardiac abnormalities. In this subgroup, only the association between exercise capacity and the risk of MI and downstream revascularizations in the

### Table 2. Crude Cumulative Incidences at Median Follow-up

<table>
<thead>
<tr>
<th>Outcome and revascularization status</th>
<th>&lt;6 METs</th>
<th>6-9.9 METs</th>
<th>10-11.9 METs</th>
<th>≥12 METs</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause mortality (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No PCI, no CAGB surgery ($n=4543$)</td>
<td>47 (45-50)</td>
<td>25 (23-28)</td>
<td>15 (13-17)</td>
<td>6 (4-9)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Previous PCI ($n=2719$)</td>
<td>40 (37-44)</td>
<td>20 (18-23)</td>
<td>16 (13-19)</td>
<td>7 (5-11)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Previous CAGB surgery ($n=2590$)</td>
<td>49 (46-52)</td>
<td>29 (26-33)</td>
<td>19 (15-23)</td>
<td>9 (5-14)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Myocardial infarction (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No PCI, no CAGB surgery ($n=4486$)</td>
<td>22 (20-24)</td>
<td>18 (16-20)</td>
<td>16 (13-18)</td>
<td>18 (14-23)</td>
<td>.007</td>
</tr>
<tr>
<td>Previous PCI ($n=2717$)</td>
<td>16 (13-19)</td>
<td>10 (8-12)</td>
<td>6 (4-9)</td>
<td>3 (1-6)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Previous CAGB surgery ($n=2587$)</td>
<td>15 (12-17)</td>
<td>8 (6-10)</td>
<td>10 (7-14)</td>
<td>3 (1-8)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Downstream revascularizations (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No PCI, no CAGB surgery ($n=4538$)</td>
<td>24 (22-26)</td>
<td>20 (18-22)</td>
<td>15 (13-18)</td>
<td>11 (8-15)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Previous PCI ($n=2719$)</td>
<td>18 (15-21)</td>
<td>18 (15-21)</td>
<td>11 (9-14)</td>
<td>10 (7-15)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Previous CAGB surgery ($n=2590$)</td>
<td>13 (11-16)</td>
<td>12 (10-14)</td>
<td>13 (10-17)</td>
<td>5 (2-10)</td>
<td>.01</td>
</tr>
</tbody>
</table>

* CAGB = coronary artery bypass graft; MET = metabolic equivalent; PCI = percutaneous coronary intervention.

*Unadjusted Kaplan-Meier estimates for crude cumulative incidence of all-cause mortality, myocardial infarction, and downstream revascularizations at median follow-up times of 11.5, 5.6, and 5.3 years, respectively, are stratified by MET categories and revascularization groups. Data are given as mean percentages (95% CI). There were 62 and 5 patients excluded from the myocardial infarction— and revascularization-free survival estimates, respectively, as the event occurred on the same day as the stress test and the relative timing of events could not be ascertained with certainty.
nonrevascularized group was attenuated (Supplemental Table 6; available online at http://www.mayoclinicproceedings.org).

Results of the exercise stress test may have influenced the decision to revascularize or may have led to further invasive testing, both potentially altering disease progression. Therefore, an additional sensitivity analysis excluding those who underwent a revascularization procedure within 180 days of their stress test (n=999) was performed, with significant attenuation of revascularization risk only in the PCI group (Supplemental Table 7; available online at http://www.mayoclinicproceedings.org).

DISCUSSION

In this diverse cohort of patients with CAD seen in clinical practice, a higher exercise capacity was associated with a lower risk of all-cause mortality and downstream revascularizations in all patients with CAD and a lower risk of MI in patients with previous PCI or CABG surgery. Furthermore, nonrevascularized and revascularized patients who achieved similar baseline exercise capacities had an equivalent risk of all-cause mortality. These findings reinforce the prognostic importance of exercise capacity in all patients with CAD.

Exercise Capacity and Mortality Risk

We found that each 1-MET increment in exercise capacity was associated with an approximate 13% reduction in risk of all-cause mortality irrespective of revascularization status in this cohort of patients seen in noncardiac rehabilitation settings. This finding is slightly higher than the 9% per-MET mortality risk reduction that was reported in men with cardiovascular disease referred for exercise testing and is markedly lower than the estimated per-MET mortality risk reductions of 31% to 45% reported in cardiac rehabilitation cohorts. As patients are usually referred to cardiac rehabilitation only after major cardiovascular events, the discrepancy in reported values between these distinct cohorts likely reflects different stages of recovery and severity of CAD, although different medical therapies, medication adherences, and methods of determining exercise capacity may also have contributed. Because of intrinsic differences between these populations, a direct comparison between studies is limited.

Nevertheless, these findings suggest that the protective effect of higher exercise capacity previously observed in cardiac rehabilitation cohorts can be generalized to all patients with CAD seen in everyday practice. Furthermore, the reductions in risk of mortality seen in this cohort were comparable with the per-MET mortality risk reduction.
risk reductions of 10% to 17% reported in healthy individuals,1,3 suggesting that the importance of exercise capacity is not diminished in patients with CAD, a finding with important public health implications.

Exercise Capacity and Risk of MI and Revascularization

To our knowledge, data on the association between exercise capacity and risk of MI and downstream revascularizations is lacking in patients with CAD. A higher baseline exercise capacity was, in general, incrementally associated with a lower risk of MI and downstream revascularizations, potentially owing to an increase in cardiac reserve or coronary collateralization, the latter of which may lead to reduced angina symptoms and clinically manifest MI.37 In contrast, there was no meaningful decrease in risk of MI with higher exercise capacity in patients with nonrevascularized CAD. This latter observation was similar to reports in which (1) exercise capacity was not associated with reductions in risk of MI in healthy women, and with only small reductions in risk in men,38 and (2) cardiac rehabilitation, which increases exercise capacity, was not associated with lower incidence of MI.39

Nonrevascularized patients in the present cohort all had a history of MI—a risk factor for future MIs—that may have potentially obscured any association between exercise capacity and risk of MI. However, we also cannot exclude whether these findings had another underlying pathophysiologic explanation. Nevertheless, higher exercise capacity continued to be associated with lower risk of MI in previously revascularized patients and lower risk of downstream revascularizations in all patients with CAD.

Determinants of Overall Survival

The interactive effect between exercise capacity and revascularization status on outcomes has not been previously described. In The FIT Project, there were no differences in overall survival between nonrevascularized and revascularized patients once exercise capacity was accounted for. The 5-year overall survival rate in this cohort (88%) was comparable with that in the BARI 2D (Bypass Angioplasty Revascularization Investigation 2 Diabetes) and COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) trials (88% and 92%, respectively),26-28 which concluded that elective revascularization procedures did not improve overall survival beyond OMT alone for managing stable CAD. The disparity in risk of MI between nonrevascularized and revascularized patients widened with greater exercise capacity despite equal risk of mortality, potentially supporting hypotheses that higher exercise capacity may protect against fatal MI events.40

The present findings suggest that exercise capacity is a more central determinant of overall survival compared with revascularization status. Furthermore, it is consistent with the prevailing notion that OMT, which includes improving and maintaining exercise capacity, should be maximized in patients with stable CAD before performing costly and invasive procedures.

Implications of Low Exercise Capacity

Exercise capacity was a more significant predictor of mortality in this cohort than were most established cardiac risk factors, such as diabetes, sex, dyslipidemia, hypertension, and smoking. Patients with the lowest exercise capacity in this cohort had the highest risk of mortality, MI, and downstream revascularizations, and of the patients who died, those with lower exercise capacity tended to live shorter. However, the largest incremental decreases in risk of mortality were also observed between the lowest and second-lowest strata of exercise capacity in every

### TABLE 3. Effect of Revascularization Status on Outcomes in MET Categoriesa,b

<table>
<thead>
<tr>
<th>Outcome and MET category</th>
<th>No PCI, no CABG surgery</th>
<th>PCI</th>
<th>CABG surgery</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mortality</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;6 METs</td>
<td>1 [Reference]</td>
<td>0.90 (0.79-1.02)</td>
<td>1.03 (0.93-1.14)</td>
<td>&gt;.05</td>
</tr>
<tr>
<td>6-9.9 METs</td>
<td>1 [Reference]</td>
<td>0.87 (0.73-1.03)</td>
<td>1.07 (0.93-1.24)</td>
<td>&gt;.05</td>
</tr>
<tr>
<td>10-11.9 METs</td>
<td>1 [Reference]</td>
<td>1.12 (0.88-1.43)</td>
<td>1.10 (0.86-1.40)</td>
<td>&gt;.05</td>
</tr>
<tr>
<td>≥12 METs</td>
<td>1 [Reference]</td>
<td>0.88 (0.49-1.59)</td>
<td>1.67 (0.97-2.88)</td>
<td>&gt;.05</td>
</tr>
<tr>
<td><strong>Myocardial infarction</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;6 METs</td>
<td>1 [Reference]</td>
<td>0.71 (0.58-0.87)</td>
<td>0.75 (0.63-0.89)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>6-9.9 METs</td>
<td>1 [Reference]</td>
<td>0.52 (0.41-0.66)</td>
<td>0.61 (0.49-0.75)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>10-11.9 METs</td>
<td>1 [Reference]</td>
<td>0.44 (0.32-0.60)</td>
<td>0.65 (0.49-0.87)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>≥12 METs</td>
<td>1 [Reference]</td>
<td>0.13 (0.07-0.27)</td>
<td>0.28 (0.14-0.53)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><strong>Revascularizations</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;6 METs</td>
<td>1 [Reference]</td>
<td>0.60 (0.49-0.73)</td>
<td>0.51 (0.42-0.61)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>6-9.9 METs</td>
<td>1 [Reference]</td>
<td>0.67 (0.55-0.83)</td>
<td>0.51 (0.41-0.63)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>10-11.9 METs</td>
<td>1 [Reference]</td>
<td>0.47 (0.35-0.62)</td>
<td>0.59 (0.45-0.78)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>≥12 METs</td>
<td>1 [Reference]</td>
<td>0.49 (0.31-0.78)</td>
<td>0.36 (0.20-0.65)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

aCABG = coronary artery bypass graft; MET = metabolic equivalent; PCI = percutaneous coronary intervention.

bData are given as adjusted hazard ratios (95% CIs).
This finding is consistent with previous studies in apparently healthy individuals, elderly, hypertensive, and diabetic patients; and some CAD cohorts, which concluded that the least physically fit patients may potentially benefit the most from increasing their exercise capacity. Overall, these results suggest that even modest increments in exercise capacity may potentially provide substantial benefits, independent of revascularization status. Gains in exercise capacity of 11% to 35% are safely achieved through exercise training in patients with CAD, with greater benefit observed among those with lower exercise capacity, further emphasizing the importance for physicians to consider these programs as part of their treatment regimen.

**Limitations**

The main study limitations include the lack of data regarding cardiovascular-specific mortality, the baseline severity of CAD, and the date and anatomy of previous revascularizations. Key factors influencing adverse outcomes and baseline revascularization status, such as frailty, depression, poor renal function, exercise-induced ischemia, and other comorbidities, may also not have been fully accounted for. Medical history was derived partly through self-report and presumed indications for medications, which may have been prescribed for other conditions. Furthermore, treadmill test results were available to physicians and may have influenced the decision to revascularize in the follow-up period. Sensitivity analyses were conducted to control for potential confounders from misidentifications in medical history and from stress test results influencing revascularization decisions.

Similar to all cohort studies, a causal relationship between exercise capacity and the end points cannot be concluded despite the supportive results. The present study may also include geographic, selection, or survivorship biases due to the inclusion and exclusion criteria. Furthermore, exercise capacity is partly determined by genetics, which may affect individual responses to exercise training.

Exercise capacity was estimated from the achieved speed and elevation after the Bruce protocol, which may overestimate true exercise capacity. Last, HRs were calculated using results from an initial stress test that may not reflect the patients’ true exercise capacities owing to symptomatic concerns; however, this is representative of what is seen in clinical practice and, as such, is of clinical relevance.

**CONCLUSION**

Exercise capacity was a strong predictor of survival in this cohort. Furthermore, there were no observed differences in risk of mortality between nonrevascularized and revascularized
patients who had similar baseline exercise capacities. These results reinforce the prognostic value of exercise capacity.

**SUPPLEMENTAL ONLINE MATERIAL**

Supplemental material can be found online at http://www.mayoclinicproceedings.org.

**Abbreviations and Acronyms:** CABG = coronary artery bypass graft; CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease; EMR = electronic medical record; FIT = Henry Ford Exercise Testing; HR = hazard ratio; Hx = history; MET = metabolic equivalent; MI = myocardial infarction; OMT = optimal medical therapy; PCI = percutaneous coronary intervention

**Data Previously Presented:** These data were presented in part at the 2013 American Heart Association Scientific Sessions in Dallas, TX.

**Correspondence:** Address to Michael J. Blaha, MD, MPH, Johns Hopkins Ciccarone Center for the Prevention of Heart Disease, 600 N Wolfe St, Carnegie 565A, Baltimore, MD 21287 (mblaha1@jhmi.edu).

**REFERENCES**


