Heart Rate Recovery Following Maximal Exercise Testing as a Predictor of Cardiovascular Disease and All-Cause Mortality in Men With Diabetes

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OBJECTIVE — Heart rate recovery (HRR) is an independent prognostic indicator for cardiovascular disease (CVD) and all-cause mortality in healthy men. We examined the association of HRR to CVD-related and all-cause mortality in men with diabetes.

RESEARCH DESIGN AND METHODS — In this cohort study we examined 2,333 men with documented diabetes (mean age 49.4 years) that had baseline 5-min HRR measurement following maximal exercise (heart $rate_{peak}$ − heart $rate_{5\ min\ of\ recovery}$) at The Cooper Clinic, Dallas, TX. We identified HRR quartiles as quartile 1 <55, quartile 2 55–66, quartile 3 67–75, and quartile 4 >75 bpm. Hazard ratios (HRs) for cardiovascular and all-cause death were adjusted for age, cardiorespiratory fitness, resting heart rate, fasting blood glucose, BMI, smoking habit, alcohol consumption, total cholesterol, triglyceride, and history of CVD at baseline.

RESULTS — During a median of 14.9 years follow-up, there were 142 deaths that were considered CVD related and 287 total deaths. Compared with men in the highest quartile of HRR, adjusted HRs in the first, second, and third quartiles were 2.0 (95% CI 1.1–3.8), 1.5 (0.8–2.7), and 1.5 (0.9–2.8), respectively, for cardiovascular death (P for trend < 0.001). Similarly, for all-cause death, adjusted HRs in the first, second, and third quartiles were 2.0 (1.3–3.2), 1.5 (1.0–2.3), and 1.5 (1.1–2.3) (P for trend < 0.001).

CONCLUSIONS — Among men with diabetes, a decreased HRR, even measured as long as 5 min after recovery, was independently predictive of cardiovascular and all-cause death.

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Attenuated heart rate recovery (HRR) following maximal exercise test is a predictor of mortality in healthy adults and in those referred for diagnostic testing (1). These findings are independent of workload achieved during the test, presence or absence of myocardial perfusion defects, and changes in heart rate during the exercise test. Panzer et al. (2) recently reported that fasting plasma glucose is strongly and independently associated with abnormal HRR, even at nondiabetic levels. Similarly, data from the Framingham Heart Study have shown reduced heart rate variability and sympathetic-parasympathetic imbalance in adults with diabetes and impaired fasting glucose (3,4). The predictive effect of low HRR on outcome might be especially pronounced in patients with diabetes because of the known association of diabetes with autonomic dysfunction (5).

Regular exercise training may improve HRR (6) in healthy individuals and in patients with congestive heart failure or diabetes (7). Regular exercise also improves markers of glucose metabolism (3,5). We have previously described a strong, inverse association between cardiorespiratory fitness and 12-year mortality in a cohort of 1,263 men with documented type 2 diabetes (8). The purpose of the current research was to evaluate whether slow HRR after maximal exercise predicts cardiovascular disease (CVD) and all-cause mortality among these diabetic men.

RESEARCH DESIGN AND METHODS

Population

Participants were from the Aerobics Center Longitudinal Study (ACLS), a prospective epidemiological investigation of adults who received a health screening examination at The Cooper Clinic in Dallas, TX. All participants gave informed consent to participate in the clinical examination and follow-up study. The Cooper Institute Institutional Review Board reviewed and approved the study annually. There were 44,719 men who were examined at least once between 1970 and 1996. We identified 2,333 men with diabetes, defined as a fasting plasma glucose level ≥7.0 mmol/l (126 mg/dl) or self-reported physician diagnosed diabetes at the time of their clinical examination (9). Among these men, 891 had a fasting

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Abbreviations: ACLS, Aerobics Center Longitudinal Study; CVD, cardiovascular disease; ECG, electrocardiogram; HR, hazard ratio; HRR, heart rate recovery; MET, maximal metabolic equivalent.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

plasma glucose level <7.0 mmol/l (126 mg/dl) but instead self-reported a history of diabetes. To assess the validity of these self-reports, we noted that the 14-year CVD mortality was no different in these men than in those with documented hyperglycemia (6.2 vs. 6.0%, $P = 0.897$). Also, we have previously reported (10) on the reasonably high accuracy of self-reported physician diagnoses in our cohorts. For example, the sensitivity and specificity of self-reported hypertension in the ACLS is 82 and 98%, respectively. This study was confined to men because of the very small number of women with diabetes in our clinic population. All study participants were residents of the U.S. and ranged in age from 23 to 79 years at the baseline examination.

Clinical assessments

Each individual underwent a thorough preventive medical evaluation that included a personal and family health history, a physical examination, a questionnaire on demographic characteristics and health habits, anthropometric assessments, a maximal exercise test, resting and exercise electrocardiogram, blood chemistry tests, and blood pressure measurement. Trained technicians administered these evaluations following standardized procedures. Blood chemistry analyses were done in The Cooper Clinic laboratory, which participates in and meets quality control standards. Detailed descriptions of these methods are available elsewhere (10).

We assessed cardiorespiratory fitness using a maximal exercise test following a modified Balke protocol (11). HRR is the primary exposure for the analyses reported here. Since we only have complete information on heart rate at 5 min of recovery, HRR was defined as the heart rate decline during the first 5 min following the completion of the maximal exercise test ($\text{heart rate}_{\text{max}} - \text{heart rate}_{\text{5 min of recovery}}$). We identified quartiles of HRR recovery as quartile 1 (<55 bpm), quartile 2 (55–66), quartile 3 (67–75), and quartile 4 (>75). HRR (bpm) was considered as a continuous variable for trend tests. Resting heart rate was measured with the participants recumbent after a 5-min rest and was obtained from the electrocardiogram (ECG). For stratified analyses of resting heart rate as a dichotomous variable, median (64 bpm) of resting heart rate was used as a cut point.

The duration of exercise test with this protocol is highly correlated ($R = 0.92$) with measured maximal oxygen uptake (12). We estimated maximal metabolic equivalents (METs) attained as a measure of cardiorespiratory fitness using the formula (1.44 × [maximal minutes on treadmill] + 14.99)/3.5 (12). Based on previous work on the entire ACLS cohort, we assigned men to age-group–specific cardiorespiratory fitness categories (20–39, 40–49, 50–59, and ≥60 years) based on their total time on the exercise test, with the 20% least fit subjects as low fit, the next 40% of the distribution as moderately fit, and the 40% most fit as highly fit. The respective cut points for total treadmill time in the low-, moderate-, and high-fitness groups were 10.5 and 12.7 METs for participants 20–39 years of age, 9.9 and 12.1 METs for participants 40–49 years of age, 8.8 and 10.9 METs for participants 50–59 years of age, and 7.5 and 9.7 METs for participants ≥60 years, respectively.

Height and weight were measured using a standard beam balance scale and stadiometer. BMI was calculated as weight in kilograms divided by height in meters squared. We classified participants into three BMI categories: normal weight (18.5≤ BMI <25.0 kg/m^2), overweight (25.0≤ BMI <30.0), and obese (BMI ≥30.0) .

Blood pressures were measured using mercury column sphygmomanometers following the American Heart Association protocol (13). Men who reported a history of physician-diagnosed hypertension or who had blood pressures ≥140/90 mmHg at the examination were classified as having hypertension. We identified men with prevalent CVD at baseline as those with a clinical history of stroke or myocardial infarction or who had an abnormal ECG during the maximal exercise test.

Hypercholesterolemia was defined as a fasting total cholesterol level ≥6.2 mmol/l (240 mg/dl) or treatment with hypolipidemic drugs. Hypertriglyceridemia was defined as a level ≥1.7 mmol/l (150 mg/dl).

We categorized men into three smoking categories: current, former, and nonsmokers. Study participants provided self-reports of weekly alcohol consumption. Ethanol content of various beverages was estimated as 1.1 g for 1 oz beer, 2.7 g for 1 oz wine, and 15.1 g for 1 oz liquor. A drink was defined as 13.2 g ethanol (equivalent to the amount of alcohol in one 12-oz can of beer). We defined the four drinking groups as follows: none (referent level) and 0.1–3.9, 4.0–13.9, or ≥14.0 drinks/week (14).

Mortality surveillance

Mortality surveillance until 31 December 1996 was conducted primarily through the National Death Index, which has established validity and has been widely used in population-based cohort studies (15,16). Nosologists coded the death certificates for the underlying and up to four contributing causes of death using the ICD-9. We defined CVD mortality as death due to ICD codes 390–449.9.

Statistical analyses

Continuous variables are reported as means ± SD, while categorical variables are reported as percentages according to quartiles of HRR. To assess the association of HRR with mortality, we used the Cox proportional hazards model. We calculated age-adjusted survival curves from Cox proportional hazard models using the mean of covariates method (17). Negative log-log survival curves and time-dependent interaction terms were used to confirm the proportional hazards assumption for HRR and confounding variables. Interaction terms of HRR with cardiorespiratory fitness and other variables were formally tested. HRR as a predictor of mortality was assessed both categorically, using the highest quartile as the reference group, and, for testing trend, as a continuous variable. Logarithmic, inverse, and inverse quadratic transformations were tested and found not to improve model fit. Individual candidate predictor variables were assessed after age adjustment. Multivariate models relating HRR to outcome were adjusted for age; resting heart rate; cardiorespiratory fitness; fasting glucose, cholesterol, and triglyceride levels; systolic and diastolic blood pressure; BMI; smoking status; alcohol intake; and prior history of CVD. All P values are two tailed, and CIs are computed at the 95% level (SAS version 8.2; SAS, Cary, NC).

RESULTS

Baseline characteristics. Baseline characteristics according to quartiles of HRR are shown in Table 1. Overall, the mean ± SD age for men ($n = 2,333$) in this cohort

Table 1—*Baseline characteristics of 2,333 men with diabetes grouped by HRR at 5 min following a maximal exercise test, ACLS, 1970–1996*

Characteristic	HRR quartiles				
	Quartile 1 (<55)	Quartile 2 (55–66)	Quartile 3 (67–75)	Quartile 4 (>75)	Age-adjusted *P**
n	561	591	546	635	—
Age (years)	53.9 ± 9.1	50.7 ± 9.1	48.4 ± 8.6	45.0 ± 8.9	<0.001
Years of observation	8.8 ± 6.9	13.6 ± 7.5	16.1 ± 6.5	17.6 ± 5.8	<0.001
Deaths	101 (18.0)	82 (13.9)	66 (12.1)	38 (6.0)	0.001
CVD deaths	50 (8.9)	41 (6.9)	32 (5.9)	19 (3.0)	0.023
HRR (bpm)	43.4 ± 9.2	60.7 ± 3.3	71.0 ± 2.5	83.5 ± 7.5	<0.001
Peak heart rate (bpm)	154.1 ± 20.2	168.6 ± 14.4	176.6 ± 11.7	182.5 ± 11.5	<0.001
Resting heart rate (bpm)	69.8 ± 11.3	65.5 ± 9.9	63.1 ± 10.0	58.7 ± 9.0	<0.001
Exercise tolerance (METs)	8.60 ± 1.7	10.0 ± 1.8	10.9 ± 1.9	11.5 ± 1.9	<0.001
Low fit (low 20%)	319 (56.9)	207 (35.0)	126 (23.1)	116 (18.3)	<0.001
Fit (middle 40%)	199 (35.5)	249 (42.1)	243 (44.5)	267 (42.0)	
High fit (high 40%)	43 (7.7)	135 (22.8)	177 (32.4)	252 (39.7)	
Total cholesterol level (mmol/l)	5.9 ± 1.2	5.9 ± 1.1	5.9 ± 1.0	5.8 ± 1.0	<0.001
High cholesterol (≥6.2)	261 (46.5)	257 (43.5)	217 (39.7)	243 (38.3)	0.004
Triglyceride level (mmol/l)	2.6 ± 1.6	2.2 ± 1.4	2.0 ± 1.5	1.7 ± 1.1	<0.001
High triglyceride (≥1.7)	352 (62.7)	315 (53.3)	245 (44.9)	228 (35.9)	<0.001
Fasting glucose (mmol/l)	8.7 ± 2.8	7.5 ± 2.3	7.1 ± 2.1	6.7 ± 1.9	<0.001
High glucose (≥7.0)	469 (83.6)	382 (64.6)	291 (53.3)	272 (42.8)	<0.001
Systolic blood pressure (mmHg)	129.8 ± 14.6	129.0 ± 14.8	126.5 ± 13.5	122.4 ± 13.1	<0.001
Diastolic blood pressure (mmHg)	74.9 ± 5.7	74.4 ± 7.5	73.9 ± 7.0	73.9 ± 6.7	<0.001
High blood pressure	346 (61.7)	350 (59.2)	273 (50.0)	235 (37.0)	<0.001
BMI (kg/m^2)	29.7 ± 4.6	27.9 ± 4.0	26.7 ± 3.7	26.0 ± 3.2	<0.001
Normal weight (<25.0)	81 (14.4)	160 (27.1)	204 (37.4)	278 (43.8)	<0.001
Overweight (25.0–29.9)	240 (42.8)	271 (45.9)	249 (45.6)	285 (44.9)	
Obesity (≥30)	240 (42.8)	160 (27.1)	93 (17.0)	72 (11.3)	
Cigarette smoking					
Never	186 (33.2)	109 (32.2)	205 (37.6)	238 (37.5)	<0.000
Past	249 (44.4)	261 (44.2)	238 (43.6)	288 (45.4)	
Current	126 (22.5)	140 (23.7)	103 (18.9)	109 (17.2)	
Alcohol use (drinks/week)					
None	206 (36.7)	157 (26.6)	138 (25.3)	142 (22.4)	<0.001
Light (3–3.9)	85 (15.2)	68 (11.5)	62 (11.4)	73 (11.5)	
Moderate (4–13.9)	139 (24.8)	183 (31.0)	169 (31.0)	199 (31.3)	
Heavy (≥14)	131 (23.4)	183 (31.0)	177 (32.4)	221 (34.8)	
History of CVD at baseline	98 (17.5)	55 (9.3)	30 (5.5)	35 (5.5)	<0.001

Data are means ± SD or *n* (%). *Line regression for continuous variables and logistic regression for binomial or multinomial variables were used to calculate age-adjusted *P* values.

was 49.4 ± 9.5 years. Incrementally lower HRR was associated with poorer cardiovascular risk profiles.

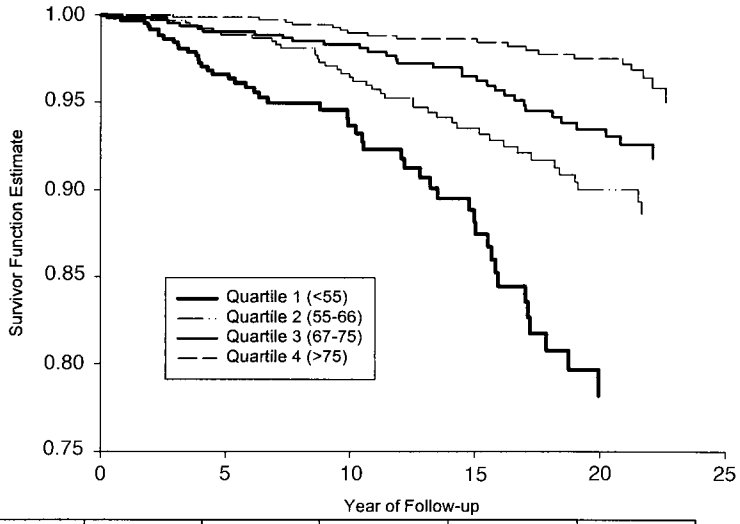
HRR and mortality. Median follow-up among survivors was 14.9 years (range 1–25). There were 142 CVD deaths and 287 deaths from all-causes. Lower HRR was associated with higher cardiovascular (Fig. 1) and all-cause mortality with similar results for the two outcomes.

Age- and multivariate-adjusted hazard ratios (HRs) for cardiovascular and all-cause deaths are presented in Table 2. In age-adjusted analyses, the strongest predictors of CVD mortality, based on likelihood ratio χ^2 values, were cardiorespiratory fitness ($\chi^2 = 35.3$) and HRR ($\chi^2 = 31.3$). Similarly, HRR was a strong predictor of all-cause mortality ($\chi^2 = 63.1$), but was weaker than cardiorespiratory fitness ($\chi^2 = 83.5$). In multivariate adjustments (Table 2), HRR remained independently predictive of CVD and all-cause death. When considered as a continuous variable, HRR was independently predictive of CVD (for 10-bpm decrease, adjusted HR 1.2, 95% CI 1.1–1.4, $P = 0.007$) and of all-cause death (1.2, 1.1–1.3, $P < 0.001$).

In supplementary analyses, we assessed the ability of HRR to predict CVD and all-cause death after adjusting for age and peak heart rate, a variable known to be closely correlated with cardiorespiratory fitness. Even after these multivariate adjustments for such highly correlated variables as cardiorespiratory fitness or peak heart rate, HRR remained predictive of CVD and all-cause death.

Stratified analyses. The results of analyses stratified by cardiovascular fitness, resting heart rate, and baseline CVD are also shown in Table 2. Decreasing HRR remained associated with increased risk of CVD and all-cause death among all subgroups, and no significant interactions were observed.

The interaction terms of HRR and car-



Population at risk:	Year 0	Year 5	Year 10	Year 15	Year 20
Quartile 1	561	455	248	165	91
Quartile 2	546	540	432	328	225
Quartile 3	591	530	478	378	280
Quartile 4	635	628	597	480	389

Figure 1—*Age-adjusted survival curves of 2,333 men with documented diabetes for CVD death by HRR quartiles, ACLS, 1970–1996. Numbers in parentheses in legend are ranges (bpm) for each quartile.*

diorespiratory fitness were tested on HRs of CVD and all-cause mortality (P = 0.877 and 0.929, respectively), while P values of the interaction terms of HRR and history of CVD at baseline for CVD and all-cause mortality were 0.805 and 0.558, respectively. P values of the interaction term of HRR and resting heart rate for CVD and all-cause mortality were 0.482 and 0.609, respectively.

CONCLUSIONS — We found that lower HRR measured even as long as 5 min following maximal exercise was independently associated with higher CVD and all-cause mortality in men with diabetes. This association persisted even after accounting for age, cardiorespiratory fitness, prior CVD, and other possible confounders. Our findings are consistent with previous research (1) that has shown strong associations between mortality and impaired HRR in adults referred for symptom-limited exercise testing and thallium scintigraphy for diagnostic purposes, but to our knowledge our results are the first to show this association in patients with diabetes. It is important to note, however, that HRR was not the strongest predictor of risk. Therefore, when assessing risk in men with diabetes, it should not be used alone but rather in conjunction with other strong predictors, such as cardiorespiratory fitness.

Epidemiological studies have consistently shown that low physical activity and low cardiorespiratory fitness are associated with high rates of cardiovascular and total mortality (18). Data also suggest that low physical activity or low cardiorespiratory fitness leads to a higher incidence of type 2 diabetes and nonfatal CVD (19). This may be due to a number of unfavorable biochemical and physiological alterations associated with inactivity (9). Low cardiorespiratory fitness is also strongly associated with increased mortality risk in men with type 2 diabetes (8).

For the current report we have expanded our cohort of men with diabetes to 2,333 individuals and have extended mortality follow-up, which led to the current total of 287 decedents. This allowed us to evaluate the interrelationships of HRR and cardiorespiratory fitness to mortality. Evidence from this study suggests that HRR is an independent predictor of CVD and all-cause mortality from cardiorespiratory fitness.

In previous studies, the association of autonomic dysfunction with diabetes has been evaluated by heart rate variability (20), where the frequency components of heart rate variability can partially distinguish parasympathetic from sympathetic influences on the heart (21). Just as exercise training has been shown to improve HRR following training, several studies (22) have shown that heart rate variability is also improved following exercise training regimens. Although we did not measure heart rate variability in this study, the strong association between faster rates of HRR and the greater percentage of fit men in the high HRR group suggest that higher levels of fitness, presumably derived from exercise training, may positively affect autonomic function in men with diabetes.

Some limitations of this study are that the participants were all men and >92% were white, well-educated, and of middle to upper socioeconomic status. However, in this population the association between conventional risk factors and CVD and diabetes is consistent with that from other studies (23). The homogeneity of our study sample on socioeconomic characteristics may be considered a strength because it reduces the likelihood of confounding by these variables. Whether our results apply to women, members of other ethnic groups, or people of low socioeconomic status remains to be determined.

This ongoing prospective study began in 1970, and the ACLS database does not contain some interesting information, such as HbA_{1c} levels, history of sulfonylurea use, and duration of diabetes. We do not have enough information for Duke treadmill exercise score calculations. During the follow-up period, the independent covariates may change, and this kind of change will reduce the association between covariates and CVD and all-cause death. We also lack information about the type of diabetes, but because this study consisted of middle-aged men, we suspect there were very few cases of type 1 diabetes. Although mortality data were primarily obtained from the National Death Index, which has established validity, there was still the possibility of misclassification of death. However, these limitations tend to bias our results toward the null. In addition, these problems of death certificate analysis are not relevant for all-cause mortality, which in our study shows results similar to CVD mortality. Since it is reasonable to assume that a large proportion of deaths in this group of men with diabetes would be expected to

Table 2—*Stratified age-adjusted and multivariate-adjusted HRs for CVD mortality and all-cause mortality in 2,333 men with diabetes, ACLS, 1970–1996*

	CVD mortality		All-cause mortality	
HRR at 5 min*	Age adjusted	Multivariate†	Age adjusted	Multivariate†
All diabetic men (n = 2,333)	142 deaths		287 deaths	
Quartile 1 (<55)	4.3 (2.5–7.4)	2.0 (1.1–3.8)	4.3 (2.9–6.4)	2.0 (1.3–3.2)
Quartile 2 (55–66)	2.3 (1.3–3.9)	1.5 (0.8–2.7)	2.2 (1.5–3.3)	1.5 (1.0–2.3)
Quartile 3 (67–75)	1.8 (1.0–3.2)	1.5 (0.9–2.8)	1.8 (1.2–2.7)	1.5 (1.1–2.3)
P value for trend‡	<0.001	0.007	<0.001	<0.001
Fit men (n = 1,565)	71 deaths		138 deaths	
Quartile 1 (<55)	3.1 (1.3–7.3)	2.0 (0.8–5.4)	4.0 (2.2–7.4)	3.0 (1.5–5.9)
Quartile 2 (55–66)	2.5 (1.2–5.1)	1.9 (0.9–4.1)	2.6 (1.5–4.4)	2.1 (1.2–3.7)
Quartile 3 (67–75)	2.3 (1.2–4.7)	2.1 (1.0–4.3)	2.4 (1.4–3.9)	2.1 (1.3–3.6)
P value for trend‡	0.016	0.283	<0.001	0.005
Unfit men (n = 768)	71 deaths		149 deaths	
Quartile 1 (<55)	2.0 (0.8–4.6)	1.7 (0.7–4.1)	1.6 (0.9–2.8)	1.3 (0.7–2.5)
Quartile 2 (55–66)	1.2 (0.5–2.8)	1.0 (0.4–2.5)	1.0 (0.6–1.9)	0.9 (0.5–1.7)
Quartile 3 (67–75)	0.7 (0.3–2.1)	0.8 (0.3–2.3)	0.9 (0.5–1.8)	0.9 (0.5–1.8)
P value for trend‡	0.001	0.008	0.001	0.009
Men with resting heart rate <64 bpm (n = 1,183)	66 deaths		123 deaths	
Quartile 1 (<55)	5.2 (2.3–11.6)	2.4 (1.0–6.1)	5.8 (3.1–10.7)	2.8 (1.4–5.7)
Quartile 2 (55–66)	3.3 (1.6–6.7)	2.3 (1.1–5.1)	3.8 (2.2–6.6)	2.6 (1.4–4.7)
Quartile 3 (67–75)	1.8 (0.9–3.9)	1.6 (0.7–3.4)	2.4 (1.4–4.2)	2.1 (1.2–3.7)
P value for trend‡	<0.001	0.011	<0.001	<0.001
Men with resting heart rate ≥64 bpm (n = 1,150)	76 deaths		164 deaths	
Quartile 1 (<55)	2.8 (1.2–6.5)	1.6 (0.7–3.9)	2.1 (1.2–3.6)	1.2 (0.7–2.2)
Quartile 2 (55–66)	1.2 (0.5–2.9)	0.9 (0.4–2.1)	0.9 (0.5–1.7)	0.7 (0.4–1.3)
Quartile 3 (67–75)	1.3 (0.6–3.3)	1.4 (0.6–3.3)	1.0 (0.6–1.8)	1.0 (0.5–1.7)
P value for trend‡	<0.001	0.087	<0.001	0.107
Men without CVD at baseline (n = 2,115)	107 deaths		232 deaths	
Quartile 1 (<55)	3.6 (1.9–6.8)	1.6 (0.8–3.4)	4.2 (2.7–6.5)	2.0 (1.2–3.3)
Quartile 2 (55–66)	2.4 (1.3–4.4)	1.5 (0.8–2.9)	2.3 (1.5–3.5)	1.5 (1.0–2.3)
Quartile 3 (67–75)	1.8 (1.0–3.4)	1.5 (0.8–2.8)	1.9 (1.2–2.9)	1.5 (1.0–2.4)
P value for trend‡	<0.001	<0.099	<0.001	0.005
Men with CVD at baseline (n = 218)	35 deaths		55 deaths	
Quartile 1 (<55)	3.6 (1.1–12.3)	2.3 (0.5–10.0)	3.1 (1.2–8.0)	1.9 (0.6–5.7)
Quartile 2 (55–66)	1.4 (0.4–5.7)	1.0 (0.2–4.4)	1.7 (0.6–4.9)	1.2 (0.4–3.7)
Quartile 3 (67–75)	1.6 (0.4–7.1)	1.5 (0.3–7.5)	1.4 (0.4–4.6)	1.1 (0.3–3.7)
P value for trend‡	0.002	0.033	<0.001	0.013

Data are HR (95% CI). *Quartile 4 (>75 bmp) as a referent for HRs. †HR of a specific variable was adjusted for all other variables, such as age, cardiorespiratory fitness, resting heart rate, fasting glucose, cholesterol, triglyceride, BMI, blood pressure, history of CVD at baseline, and cigarette and alcohol consumption. ‡Variable was treated as a continuous variable in age- and multivariate-adjusted models.

occur from CVD, mostly coronary heart disease, and since the all-cause mortality results are similar to the CVD mortality results, we do not think that this issue will cause major misinterpretation of our data.

There is evidence that heart rate at 1 or 2 min of recovery is sensitive to detection of the association of HRR and CVD events (24–26). Since we do not have complete HRR at 1 or 2 min in our database, we used HRR at 5 min. We could not determine the relative strengths of prediction of 1-, 2-, or 5-min HRR values. Another limitation is that we do not have complete data on medications, such as those for treatment of hypertension and other CVD that might affect HRR. However, we excluded individuals from the analysis if they had maximal heart rates <85% of their age-predicted maximal value (220 – age in years). In addition, many of the decedents were tested in the late 1970s and early 1980s, before β-blocking drugs were widely used. Maximal heart rate was somewhat lower in the first HRR quartile, but was still 93% of the age-predicted maximal value. Furthermore, we adjusted the HRR data for maximal exercise test tolerance and prevalent CVD, which should help reduce any potential effect modification by medications.

In conclusion, men with diabetes who had slow HRR at 5 min following a maximal exercise test had a higher risk of CVD and all-cause mortality when compared with similar men who had more rapid HRR. The high risk in men with slow HRR persisted after adjustment for cardiorespiratory fitness, baseline prevalence of CVD, and other potential confounding variables. The results of our study suggest that the exercise test, which

is simple, safe, and inexpensive, can be used as a powerful tool for clinical risk stratification in diabetic men by noting both HRR and cardiorespiratory fitness.

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