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Correlates of heart rate recovery over 20 years in a population sample

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Abstract

Introduction—Slow heart rate recovery (HRR) from a graded exercise treadmill test (GXT) is a marker of impaired parasympathetic reactivation that is associated with elevated mortality. Our objective was to test whether demographic, behavioral or coronary heart disease (CHD) risk factors during young adulthood were associated with the development of slow HRR.

Methods—Participants from the Coronary Artery Risk Development in Young Adults study underwent symptom-limited maximal GXT using a modified Balke protocol at baseline (1985–86) and 20-year follow-up (2005–06) examinations. HRR was calculated as the difference between peak heart rate (HR) and HR two-minutes following cessation of the GXT. Slow HRR was defined as 2-minute HRR < 22 beats·min⁻¹.

Results—In 2,730 participants who did not have slow HRR at baseline, mean HRR was 44 beats·min⁻¹ (SD = 11) at baseline and declined to 40 beats·min⁻¹ (SD=12) in 2005–06; slow HRR developed in 5% (n=135) of the sample by 2005–06. Female sex, black race, fewer years of education, obesity, cigarette smoking, higher depressive symptoms, higher fasting glucose, hypertension, metabolic syndrome and physical inactivity and low fitness were each associated with incident slow HRR. In a multivariable model higher BMI, larger waist, low education, fasting glucose and current smoking remained significantly associated with incident slow HRR. Increasing BMI (per SD higher) over follow-up and incident hypertension, diabetes and metabolic syndrome (in the subsets of participants who were free from those conditions at baseline), were each associated with a significantly elevated odds of incident slow HRR.

Conclusions—On average, HRR declines with aging; however, the odds of having slow HRR in early middle age is significantly associated with traditional CHD risk factors.

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Keywords

Epidemiology; Cardiovascular Disease; Exercise; Autonomic Nervous System

INTRODUCTION

Heart rate recovery (HRR) following graded exercise treadmill testing (GXT) is an established measure of autonomic nervous system function. Specifically, the rapid decline in heart rate (HR) following cessation of GXT is attributable to parasympathetic reactivation (28). Impaired parasympathetic reactivation, as indicated by a smaller difference between maximum heart rate (HR) and HR one- or two-minute post-exercise (i.e., slow HRR), is associated with elevated all-cause mortality, independent of other exercise test parameters (11, 12, 25). Most of these findings are based on symptomatic populations of middle- and older-age adults referred for exercise testing because they had symptoms of coronary heart disease (CHD). Less is known about the development of slow HRR over time in healthy young adults.

We hypothesize that the development of slow HRR in middle age is correlated with CHD risk factors (e.g., hypertension, diabetes) that have previously demonstrated an association with autonomic nervous system dysfunction. Prior population studies report that autonomic function is impaired in conjunction with lower socioeconomic status (29), negative affect (e.g., depressive symptoms), physical inactivity (8, 26) and obesity. Consequently, the goal of the present study is to investigate the association of a comprehensive set of sociodemographic characteristics, health behaviors and clinical characteristics with the development of slow HRR in healthy young adults who were followed over 20 years.

METHODS

Study Population and Design

The Coronary Artery Risk Development in Young Adults (CARDIA) study is a longitudinal cohort of the evolution of CHD risk factors in a population sample of 5,115 adults aged 18 – 30 years at baseline (1985 – 1986). Black and white men and women were recruited from Birmingham, AL, Chicago, IL, Minneapolis, MN, and Oakland, CA. Participants were re-examined 2, 5, 7, 10, 15 and 20 years after baseline; retention rates across examinations were 91%, 86%, 81%, 79%, 74%, and 72%, respectively. A detailed description of study design, sampling, and response rates is published (16). The sample for the present report was drawn from participants in the CARDIA Fitness Study, an ancillary investigation conducted in conjunction with the year 20 examination in 2005–2006 that measured fitness using a symptom limited maximal treadmill test. Our study sample is comprised of the 2730 participants who completed treadmill testing at baseline and the 20-year follow-up examination and who did not have slow HRR at baseline. Institutional review boards at each study site reviewed the protocol and procedures and approved the research. All participants provided written informed consent.

Measurements

Standardized protocols for data collection were used across study centers and examinations. Participants were asked to fast for at least 12 hours prior to examination and to avoid smoking or engaging in heavy physical activity for at least 2 hours before the examination.

Graded exercise treadmill testing—Participants who did not have a history of ischemic or congenital heart disease, were not taking cardiovascular medications other than blood pressure medications, whose blood pressure was less than 160/90 mm Hg, and who

were not currently experiencing a febrile illness were eligible to complete treadmill testing. Procedures were the same at baseline and 20 year follow up and have been previously described (30). In brief, participants underwent a symptom-limited graded exercise treadmill test using a modified Balke protocol to measure aerobic fitness. The protocol included up to nine 2-minute stages of progressively increasing difficulty, and participants were encouraged to exercise as long as possible to maximum exertion. At the end of each stage, heart rate and blood pressure were measured, and participants were asked to rate their level of exertion on the Borg scale.(4) Pre-test heart rate was the heart rate recorded as participants were standing and prior to the initiation of the treadmill. Peak heart rate was determined as the highest value recorded across all stages. HRR was calculated as the difference between peak heart rate and heart rate 2-minutes following test cessation. HRR of $<22 \text{ beats}\cdot\text{min}^{-1}$ was defined as “abnormal” (28). We chose to use HRR at 2 minutes to represent parasympathetic reactivation because our protocol involves an active walking cool-down period. By contrast, at 1-minute post exercise, the treadmill is still slowing down and lowering, which can introduce variability in the actual speed and grade depending on how long participants exercised on the treadmill (24) The speed and grade is more uniform at 2-minutes post peak exercise (28). Change in HRR over follow-up was calculated as the difference between HRR at the year 20 examination and baseline. Fitness is estimated by the duration of the treadmill test, which is directly correlated with $\text{VO}_2 \text{ max}$ (3). Age-predicted maximum heart rate was determined using the Tanaka formula ($208 - 0.7\cdot\text{age}$) (32); participants were determined to have exercised to their maximal capacity of their peak heart rate was 85% of their age predicted heart rate.

Other measures—Age, race, and sex were self-reported and medication use was determined using standard questionnaires. Height and weight were measured with a vertical ruler and a calibrated scale, respectively. Body mass index (BMI) was calculated as $\text{weight (kg)}\cdot(\text{height m}^2)^{-1}$; overweight and obesity were determined at $\text{BMI } 25 < 30 \text{ kg}\cdot(\text{m}^2)^{-1}$ and $30 \text{ kg}\cdot(\text{m}^2)^{-1}$, respectively. Waist circumference was measured laterally midway between the iliac crest and the lowest lateral portion of the rib cage and anteriorly midway between the xiphoid process of the sternum and the umbilicus. Cigarette smoking was assessed by standardized questionnaire at each examination and respondents were categorized as current, former or never smokers. For our change in smoking analysis, current smokers were defined as those who reported smoking at year 20, former smokers were those who reported current or former smoking at any examination but who reported not smoking at year 20, and never smokers reported never smoking at all seven examinations. Physical activity was assessed with the CARDIA physical activity questionnaire, an interviewer-administered self report that measures the frequency of participation in 13 different categories of recreational sports and exercise in the past 12 months. Scores were computed by multiplying the frequency of participation by estimated intensity of activity and reported as “exercise units” (EU). The reliability and validity of the instrument is comparable to other activity questionnaires (19, 20). Depressive symptoms were assessed at year 5 using the Centers for Epidemiologic Studies Depression scale (CES-D) with a score range of 0 to 60; symptom scores ≥ 16 are correlated with diagnosed depression.

After participants rested in a quiet room for five minutes, blood pressure was measured from participants in the seated position three times; the last two readings were averaged. Hypertension was determined if any of the following criteria was met: systolic blood pressure $\geq 140 \text{ mm Hg}$ or a diastolic blood pressure $\geq 90 \text{ mm Hg}$ on any visit, or reported use of antihypertensive medication. Incident hypertension was defined in participants who were free of hypertension at baseline and who met the criteria for hypertension (defined above) at any subsequent visit.

Blood samples for measurement of glucose (15) and lipids (14, 33) were collected according to standardized CARDIA procedures (16) and processed at central laboratories. Glucose was assayed at a central laboratory using the hexokinase method. Diabetes was determined when participants met any of the following criteria: measured fasting glucose levels (≥ 7.0 mmol·L⁻¹) at exam years 7, 10, 15, or 20, self-report of oral hypoglycemic medications or insulin (all exams), or a 2-hour post-load glucose (≥ 11.1 mmol·L⁻¹) at exam years 10 and 20. The incidence of diabetes over 20 years was determined among participants who did not have diabetes at baseline based on fasting glucose levels.

Metabolic syndrome was determined according to American Heart Association modification (18) of the National Cholesterol Education Program Adult Treatment Panel III definition (1) if any three of the following criteria was met: 1) fasting glucose ≥ 5.7 mmol·L⁻¹; 2) waist circumference > 88 cm (women) or > 102 cm (men); 3) SBP ≥ 130 mmHg or diastolic DBP ≥ 85 mmHg; 4) triglycerides ≥ 1.7 mmol·L⁻¹; 5) HDL-cholesterol < 1.3 mmol·L⁻¹ in women or < 1.04 mmol·L⁻¹ in men. Participants who reported using medications for diabetes or hypertension control were classified as having met the criterion for elevated glucose or blood pressure, respectively. Incident metabolic syndrome was identified in participants who did not have metabolic syndrome at baseline.

Statistical Analyses

We described baseline characteristics stratified by status of slow HRR at year 20 in 2005–2006 and compared values using t-tests for continuous variables, chi-square tests for most categorical variables and Fisher's Exact tests for categorical variables with a low prevalence (e.g., hypertension, diabetes and metabolic syndrome). Next, we generated box and whisker plots to compare distributions of the average change in HRR over 20 years by sex, race, and race-sex. Prior to calculating the odds of developing slow HRR over 20 years, we tested whether slow HRR at baseline, defined as a value below the median (among those ≥ 22 beats·min⁻¹ at baseline), modified the association of baseline risk factors with incident slow HRR. Because the association of glucose with incident slow HRR was the only factor modified by slow HRR at baseline, we present all analyses pooled by overall baseline glucose and report stratified findings for glucose in the text. For all other covariates, we present odds ratios (OR) and 95% confidence intervals (CI) of having slow HRR at year 20 per SD from the mean (i.e., standardized changes) or according to a referent (categorical variables) and adjusted for baseline HRR. Multivariable models included all independent baseline characteristics in a single model. Estimates for waist circumference and diastolic blood pressure were generated in separate multivariable models that did not include BMI and SBP, respectively. We calculated the odds of having slow HRR at follow up by changes in clinical measurements and health behaviors over 20 years, adjusted for baseline demographic characteristics and HRR. ORs and 95% CIs for changes in continuous measures were calculated per SD increase from the mean over time. Odds for incident hypertension, diabetes and metabolic syndrome were generated in the subsets of participants who did not have those conditions at baseline (n=2679, 2632 and 2681, respectively). Statistical significance was determined at $p < 0.05$. All analyses were conducted using SAS version 9 (The SAS Institute, Cary, NC).

RESULTS

From among the 2,788 participants who had valid HRR measures at baseline and the 20 year follow-up, 58 (2.1%) had slow HRR at baseline. After excluding those participants, we had 2,730 in our study sample, 56% of whom were female, 44% were black, and the mean age was 25.1 years (Table 1). The distribution of health behaviors and clinical characteristics was similar to that of the full CARDIA cohort (16). After 20 years, 135 participants (5%) had slow HRR (HRR < 22 beats·min⁻¹). Participants who had slow HRR in 2005–2006 were

significantly more likely to be female and black and a lower proportion had less than a high school education. Baseline BMI was higher, waist circumference was larger, depressive symptoms were higher, current smoking, hypertension and diabetes were each more prevalent and participants with slow HRR were less physically active and achieved a shorter duration on the treadmill among participants who went on to have slow HRR in 2005–2006 versus normal.

Between baseline and year 20, HRR declined from a mean of 44 beats·min⁻¹ (SD=11) at baseline to 40 (SD=12) beats·min⁻¹ (an average of 3.6 beats·min⁻¹) in the total sample. The absolute change was higher in men and in black participants (Figure 1). When changes were calculated relative to the baseline levels, similar patterns were apparent, though the distribution was highly skewed. The relative change in men as compared with women was -7.4% (SD=27.8) vs -3.4% (SD=31.6), respectively (p<0.05). Black participants experienced significantly (p<0.01) larger relative declines in HRR (-9.0%, SD=31.1) than white participants (-2.1%, SD=28.7) and across race-sex groups, black men (-11.7%, SD=27.2), black women (-7.2%, SD=33.4), and white men (-4.5%, SD=27.8) experienced relative declines from their baseline value, whereas white women did not change relative to baseline (0.0%, SD=29.4) (p <0.01). Findings were similar when we restricted analyses to the cohort of participants who exercised to at least 85% of their age-predicted heart rate (data not shown).

Baseline characteristics that were associated with the presence of slow HRR at year 20, taking into account baseline HRR, are reported in Table 2. Male sex, education, physical activity levels and treadmill test duration were inversely associated with the odds of having slow HRR in 2005–2006 whereas black race, waist circumference, BMI, overweight and obesity (relative to normal weight), fasting glucose, hypertension, metabolic syndrome, high depressive symptoms and current smoking were associated with a higher odds of having slow HRR. There was evidence of significant effect measure modification for the association of baseline glucose by baseline HRR. At year 20, 99 participants who had HRR below the median at baseline had developed slow HRR as compared with only 36 from among those with HRR above the median at baseline. Baseline glucose was significantly positively associated with incident slow HRR in participants whose HRR was at or above the median at baseline (OR=1.50, 95% CI: 1.15, 1.96 per 0.58 mmol·L⁻¹ [SD] higher), whereas there was no association in participants whose HRR was below the baseline median (OR=1.04, 95% CI: 0.87, 1.24 per SD). In multivariable models the baseline characteristics that remained statistically significantly associated with a higher odds of having slow HRR were BMI, baseline fasting glucose and current smoking. In a separate multivariable model that included waist circumference instead of BMI, waist circumference also remained positively associated with HRR following adjustment for other factors. Years of education remained inversely associated with the odds of having slow HRR in multivariable models.

The odds of having slow HRR at year 20 year were significantly higher per SD increase in BMI and waist circumference (OR 1.33 and 1.55, respectively) and with the incidence of diabetes, hypertension or the metabolic syndrome (OR =2.04, 2.06 and -2.78, respectively) following adjustment for age, race, sex, education and baseline HRR levels (Table 3). By contrast, the odds were lower as percent change in treadmill test duration and physical activity change increased over follow-up (OR 1.35 and 3.52, respectively). Although baseline depressive symptom scores were positively associated with slow HRR at year 20, increasing depressive symptoms over 15 years was not associated with a higher odds of having slow HRR.

DISCUSSION

Over 20 years, HRR declines in healthy young adults; however, adults who have adverse CHD risk factor profiles (e.g., higher fasting glucose, higher depressive symptoms, overweight or obesity, cigarette smoking) in young adulthood or who develop CHD risk factors over time are more likely to have slow HRR (< 22 beats·min⁻¹) by early middle age. Although a notably higher proportion of women and black participants had slow HRR at follow up, those demographic differences were eliminated once health behaviors, clinical characteristics and education were taken into account. Findings from our observational longitudinal study indicate that risk factors for slow HRR and clinical CHD are shared.

A number of parameters from a standard graded exercise treadmill test are used clinically to identify patients with functional cardiovascular abnormalities that place them at high risk for morbidity and mortality. Following cessation of the test, the heart rate falls from its maximal output to pre-test, resting levels. The rate of HRR to pre-test levels is determined in part by cardiorespiratory fitness, but primarily by the reactivation of the parasympathetic division of the autonomic nervous system. Contributions of the parasympathetic nervous system to recovery have been determined in pharmacologic blockade studies that block parasympathetic functioning and note that heart rate does not fall as fast or as far with blockade as compared with the control condition of no blockade (28). Prior research demonstrates that slow HRR, independent of other exercise test parameters, is associated with increased mortality (11, 12, 25). Most mortality studies have been carried out in convenience samples of patients referred for exercise testing based on their symptoms of heart disease or existing high risk cardiovascular profile. While cardiorespiratory fitness may be strongly associated with HRR, prior studies that adjust for treadmill duration as an estimate of fitness may be incomplete; statistical adjustment for direct measures of fitness (e.g., VO_{2max} determined by gas exchange) may be needed to fully establish the independence of parasympathetic reactivation vs fitness on HRR.

Following an intriguing report by Shishebor et al. that lower socioeconomic status was associated with slower HRR in a patient sample, we wondered whether those findings were also present in a healthy sample or whether the behaviors and clinical profiles of persons with lower socioeconomic status explained such an association. Education is a marker of socioeconomic status that is inversely associated with morbidity and mortality from cardiovascular disease (23). Adverse health risk behaviors cluster among adults with lower education and in turn, rates of obesity, hypertension and diabetes are higher (21). In CARDIA, healthy adults were sampled from three US communities and one large health maintenance organization and the distribution of participants was roughly balanced by educational attainment (16). Our findings concur with prior reports; education was inversely associated with the odds of having slow HRR over 20 years. A residual association between education and HRR remained even once health behaviors (e.g., physical activity and smoking status), other demographic (e.g., age, race, sex) characteristics and metabolic factors (e.g., BMI, waist circumference, blood pressure and fasting glucose) were taken into account. Education is a marker for multiple unmeasured parameters that are linked to socioeconomic status such as diet, financial insecurity, discrimination, stress, access to health care, and neighborhood cohesiveness that may not be captured by one simple marker at the individual level (23).

The biological plausibility of our observations arise from the considerable literature demonstrating that metabolic disorders, namely diabetes and hypertension, are associated with impaired autonomic nervous system function. Autonomic neuropathy is an established microvascular complication of diabetes. Chronic hyperglycemia may degrade the peripheral vasculature leading to neuropathy (5). Alternatively, autonomic nervous system dysfunction

may occur earlier in the course of disease than previously thought—possibly secondary to obesity and insulin resistance. Early dysfunction may interfere with hepatic glucose production, circulating glucose uptake and muscle insulin sensitivity thus prompting the development of diabetes (6, 7, 10). Our findings demonstrate that the association of fasting glucose with incident slow HRR is even stronger among participants whose HRR is already low at baseline. Similarly, the association between autonomic dysfunction and hypertension appears bi-directional. Prior reports indicate that heart rate variability, an estimate of autonomic nervous system function is impaired with increasing blood pressure—but also that lower heart rate variability is positively associated with the development of hypertension (27). By contrast, longitudinal investigations suggest that slower HRR does not precede the development of metabolic syndrome; rather, the presence of one or more components of metabolic syndrome is associated with greater declines in HRR over time (22). Consequently, our findings of a positive association of baseline fasting glucose and the incidence of diabetes, hypertension and metabolic syndrome with slow HRR over follow-up are consistent with the existing literature.

Health behaviors, namely smoking and physical inactivity were each associated with a higher likelihood of having slow HRR at follow-up. Activity is associated with a more favorable autonomic profile in other population studies that used different estimates of autonomic functioning (26). In a prior CARDIA investigation, we demonstrated that participants who were more physically active had faster HRR (8). Most prior studies report less favorable resting autonomic nervous system function and autonomic response to provocative maneuvers in smokers as compared with non-smokers (2, 9). Our longitudinal findings extend beyond prior cross-sectional reports to suggest that these adverse health behaviors precede the onset of autonomic impairment.

Unlike many prior studies of correlates of HRR that were conducted in patient referred samples, our study was conducted in a sample of young adults who participated in a longitudinal population study on cardiovascular health. Findings from our study are generalizable to the large proportion of the population without symptoms necessitating referral to exercise testing. Using repeated assessment of HRR in our longitudinal cohort study, we could determine factors associated with the development of slow HRR over follow-up. By contrast, most prior studies included a single measure of HRR.

Our findings must be interpreted in light of some limitations. HRR is not a direct measure of autonomic nervous system dysfunction, but rather is an estimate of parasympathetic responsiveness to a specific physiologic maneuver (i.e., exercise). However, prior studies that have applied pharmacologic blockade have validated the contributions of the parasympathetic nervous system to HRR (17, 31). Additionally, HRR is strongly positively correlated with components of heart rate variability thought to represent parasympathetic modulation of heart rate (13). Further studies with measures of autonomic nervous system function that represent different components of function (e.g., sympathetic input) are warranted to confirm our observations.

In summary, HRR declines in healthy adults with aging. However, whether that decline reaches levels that have been previously determined to pose a higher risk for mortality, depends on the presence and development of CHD risk factors. With the exception of educational attainment, the characteristics most strongly associated with the odds of having slow HRR in middle age are modifiable. Future intervention studies should measure changes in HRR before and after an intervention to determine whether improvements in parasympathetic reactivity are a plausible mediating pathway between the health behavior of physical activity and cardiovascular and metabolic outcomes.

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Table 1

Baseline characteristics* of all participants with baseline heart rate recovery (HRR) ≥ 22 bpm, stratified by incident slow HRR in 2005–2006

	HRR in 2005–2006				P
	Total 2730	HRR (< 22 bpm) 135 (5%)	HRR ≥ 22 bpm	HRR ≥ 22 bpm 2595 (95%)	
N					
Age	25.1 (3.6)	25.6 (3.7)	25.0 (3.6)	25.0 (3.6)	0.06
Sex (% female)	56.0	71.1	55.2	55.2	<0.01
Race (% black)	44.4	63.7	43.4	43.4	<0.01
Education (years)	14.1 (2.2)	13.0 (2.0)	14.2 (2.2)	14.2 (2.2)	<0.01
% < High School	6.3	13.3	6.0	6.0	<0.01
Waist circumference (cm)	76.9 (10.5)	83.6 (14.0)	76.5 (10.1)	76.5 (10.1)	<0.01
BMI (kg/m ²)	24.1 (4.4)	27.9 (6.9)	23.9 (4.2)	23.9 (4.2)	<0.01
Normal weight (%)	68.1	38.5	69.6	69.6	<0.01
Overweight (%)	23.1	30.4	22.8	22.8	
Obese (%)	8.8	31.1	7.7	7.7	
Systolic blood pressure (mmHg)	109.6 (10.6)	111.2 (11.9)	109.5 (10.5)	109.5 (10.5)	0.11
Diastolic blood pressure (mmHg)	68.2 (9.3)	69.5 (11.1)	68.2 (9.2)	68.2 (9.2)	0.19
Hypertension (%)	1.9	4.4	1.7	1.7	0.04
Fasting glucose (mmol/L)	4.55 (0.58)	4.70 (1.03)	4.53 (0.55)	4.53 (0.55)	0.07
Diabetes (%)	0.3	1.5	0.3	0.3	0.07
Metabolic Syndrome (%) [†]	1.8	6.7	1.5	1.5	<0.01
CES-D score [‡]	10.6 (7.9)	13.0 (8.4)	10.5 (7.9)	10.5 (7.9)	<0.01
CES-D ≥ 16 (%)	21.7	33.9	21.1	21.1	<0.01
Smoking status (%)					
Current	24.8	38.1	24.1	24.1	<0.01
Former	13.7	13.4	13.8	13.8	
Never	61.5	48.5	62.2	62.2	
Physical activity (exercise units)	427.5 (299.3)	350.5 (238.3)	431.5 (301.6)	431.5 (301.6)	<0.01
Treadmill test duration (minutes)	10.1 (2.8)	8.1 (2.7)	10.2 (2.7)	10.2 (2.7)	<0.01
Pre-test heart rate (bpm)	77.6 (14.2)	79.2 (13.2)	77.5 (14.2)	77.5 (14.2)	0.19

HRR in 2005–2006				
	Total 2730	HRR (< 22 bpm) 135 (5%)	HRR 22 bpm 2595 (95%)	P
Peak heart rate (bpm)	180.3 (14.8)	173.3 (14.3)	180.6 (14.7)	<0.01
Heart rate increase (pre test to maximum) (bpm)	102.7 (18.3)	94.2 (15.7)	103.2 (18.3)	<0.01
Age predicted maximum heart rate	161.9 (2.1)	161.6 (2.2)	161.9 (2.1)	0.06
Completed maximum exercise test (%) [‡]	90.1	83.0	90.4	<0.01

* Mean and SD unless otherwise noted

[‡] Defined in participants who had three or more of the following: fasting glucose 5.7 mmol/L; 2) waist circumference > 88 centimeters (women) or > 102 cm (men); 3) SBP 130 mmHg or diastolic DBP 85 mmHg; 4) triglycerides 1.7 mmol/L; 5) HDL-cholesterol < 1.3 mmol/L in women or < 1.04 mmol/L in men. Participants who reported using medications for diabetes or hypertension control were classified as having met the criterion for elevated glucose or blood pressure, respectively.

[‡] CES-D score from 1990–1991

[§] Maximum exercise test determined if participants exercised to at least 85% of their age-predicted maximum according to the Tanaka formula = 208 – (0.7*age)

Table 2

Baseline characteristics associated with slow HRR at year 20 examination (Odds Ratio, 95% Confidence Interval)

	Model 1*		Model 2†	
	OR	95% CI	OR	95% CI
Age (per 3.6)	1.15	(0.96, 1.38)	1.08	(0.88, 1.33)
Sex (male vs. female)	0.57	(0.39, 0.83)	0.81	(0.44, 1.51)
Race (black vs. white)	2.43	(1.69, 3.49)	1.26	(0.81, 1.96)
Education (per 2.2)	0.54	(0.44, 0.66)	0.66	(0.52, 0.84)
Waist Circumference (per 10.5)	1.66	(1.44, 1.91)	1.51	(1.24, 1.83)§
BMI (per 4.4)	1.75	(1.54, 1.99)	1.44	(1.21, 1.72)
Normal weight (Referent)	1.0	--	--	--
Overweight	2.48	(1.62, 3.79)	--	--
Obese	6.58	(4.24, 10.21)	--	--
Systolic blood pressure (per 10.6)	1.15	(0.97, 1.37)	1.10	(0.88, 1.36)
Diastolic blood pressure (per 9.3)	1.12	(0.94, 1.33)	1.14	(0.93, 1.40)¶
Hypertension (yes vs. no)	2.55	(1.05, 6.18)		
Fasting glucose (per 0.58)‡	1.18	(1.05, 1.32)	1.22	(1.03, 1.43)
Metabolic Syndrome (yes vs. no)	3.76	(1.76, 8.01)		
CES-D score (per 7.9)	1.33	(1.14, 1.55)	1.06	(0.89, 1.28)
Smoking status				
Current	2.26	(1.54, 3.32)	1.89	(1.20, 2.99)
Former	1.29	(0.75, 2.21)	1.24	(0.67, 2.32)
Never (Referent)	1.0	--		
Physical activity (per 299.3)	0.79	(0.65, 0.97)	1.09	(0.88, 1.36)
Treadmill test duration (per 2.8)	0.49	(0.40, 0.59)	0.74	(0.53, 1.04)
Pre-test heart rate (per 14.2)	0.94	(0.78, 1.13)	0.90	(0.72, 1.13)
Heart rate increase (per 18.3)	0.72	(0.61, 0.86)		

* Each covariate included independently with adjustment for baseline HRR, OR for all continuous variables calculated per SD change from the mean.

† All variables in the model displayed in addition to baseline HRR

[‡]P for interaction between baseline HRR and fasting glucose was <0.01. OR in participants whose HRR was at or above the median at baseline was 1.50, 95% CI: (1.15, 1.96) the OR for participants whose HRR was below the median at baseline was 1.04, 95% CI: (0.87, 1.24).

[§]Calculated from a separate multivariable model that does not include BMI

//Calculated from a separate multivariable model that does not include SBP.

Table 3

Adjusted association* of changes in risk factors over 20 years and HRR in 2005–2006

	Change Over 20-Years*	Cumulative incidence or proportion [†]	OR [‡]	(95% CI)
BMI change	4.9 (5.0)		1.33	(1.14, 1.54)
Waist circumference change	14.0 (10.2)		1.55	(1.31, 1.84)
Physical activity change	-77.9 (300.3)		1.35	(1.12, 1.63)
Percent change in physical activity	31.3 (311.8)		0.79	(0.57, 1.12)
Percent change in treadmill test duration	-28.7 (21.1)		3.52	(2.76, 4.46)
Depressive symptom score change	-1.6 (8.2)		0.85	(0.72, 1.02)
Incident hypertension		24.1	2.03	(1.38, 2.99)
Incident diabetes		7.6	2.06	(1.24, 3.42)
Incident metabolic syndrome		25.5	2.78	(1.92, 4.04)
Smoking status [‡]				
Never (Referent)		53.8	1.0	
Former		28.9	1.08	(0.68, 1.70)
Current		17.4	2.27	(1.46, 3.53)

Model 1: Adjusted for age, race, sex and education and baseline HRR

* Difference in the value between baseline and the 20-year follow-up visit

[†] Cumulative incidence of the risk factor among those who were free from the condition at baseline. The analysis samples for hypertension, diabetes and metabolic syndrome were 2679, 2632, and 2681, respectively.

[‡] Proportion in 2005–2006

[§] Odds ratios presented per SD change in risk factors over 20 years (continuous variables) or in participants with the incident condition as compared with those who did not develop it (referent).