CLINICAL RESEARCH STUDY

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Exercise Heart Rate Reserve and Recovery as Predictors of Incident Type 2 Diabetes

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ABSTRACT

BACKGROUND: We tested the hypothesis that selected exercise heart rate responses, specifically those providing indices of autonomic dysfunction, may be associated with incident type 2 diabetes in 2231 apparently healthy men with normal baseline fasting glucose levels.

METHODS: Heart rate reserve was calculated as the difference between the maximal attained heart rate and the supine resting heart rate, whereas heart rate recovery was defined as the maximal heart rate minus the heart rate measured at 2 minutes of recovery after peak or symptom-limited cardiopulmonary exercise testing. Type 2 diabetes was defined as glycated hemoglobin >6.5% or fasting plasma glucose >126 mg/dL at the follow-up examination.

RESULTS: During a median follow-up interval of 5 years, 90 of the 2231 men (4.0%) developed type 2 diabetes. The relative risks of incident type 2 diabetes in men within the lowest quartiles of heart rate reserve and heart rate recovery versus men comprising the highest quartiles of heart rate reserve and heart rate recovery were 2.71 (95% confidence interval, 1.20-6.11) and 2.81 (95% confidence interval, 1.36-5.78) after adjusting for potential confounding variables. Each unit increment (1 beat/min) in heart rate reserve and heart rate recovery was associated with a 2% to 3% decreased incidence of type 2 diabetes.

CONCLUSIONS: Exercise heart rate reserve and recovery predicted incidence of type 2 diabetes in healthy men, suggesting that autonomic dysfunction may be associated with an increased likelihood for the development of this cardiometabolic risk factor.

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KEYWORDS: Exercise; Heart rate recovery; Heart rate reserve; Type 2 diabetes

A blunted heart rate response to exercise testing, an attenuated heart rate recovery immediately postexercise, or both are associated with an increased risk of cardiovascular morbidity and mortality in populations with and without documented chronic disease,[1] including patients with type 2 diabetes.[2,3] Although exercise heart rate parameters largely are influenced by cardiorespiratory fitness, which provides a biomarker of cardiopulmonary and musculoskeletal integrity,[4] the autonomic nervous system activity may serve as an important modulator of exercise heart rate responses.[5] Because the autonomic nervous system may, in part, stimulate insulin secretion in response to circulating glucose levels and be associated with insulin resistance,[6-9] derangements in autonomic function may herald the development of type 2 diabetes. However, it remains unclear whether autonomic dysfunction, as signified by impaired heart rate reserve, or attenuated heart rate recovery after peak or symptom-limited exercise testing may be a

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harbinger of type 2 diabetes. We tested the hypothesis that these autonomic indices may predict the incidence of type 2 diabetes in healthy men.

MATERIALS AND METHODS

We recruited 5616 men who participated in 2 general health examinations during 1998-2009 at Samsung Medical Center, Seoul, South Korea. Of these subjects, 3620 healthy men without hypertension, cardiovascular disease, and type 2 diabetes at baseline examination were included. Men (n = 1389) whose blood markers, maximal heart rate, and heart rate 2 minutes after the cessation of exercise testing were not measured at baseline were excluded. After these exclusions, 2231 participants (mean age, 47 years; range, 20-76 years) free of hypertension, cardiovascular disease, and type 2 diabetes who underwent peak or symptom-limited cardiopulmonary exercise testing and whose blood markers were measured at baseline were included in the analysis. Participants were followed from 1 to 12 years after the baseline examination. Type 2 diabetes was determined by glycated hemoglobin >6.5% or fasting plasma glucose >126 mg/dL, or physician diagnosis at the second examination. Written informed consent was obtained from all participants before undergoing the health screening program, and the study was approved by the medical center institutional review board.

CLINICAL SIGNIFICANCE

- Because the autonomic nervous system may, in part, stimulate insulin secretion and serve as a modulator of insulin resistance, derangements in autonomic function may herald incident type 2 diabetes.
- Exercise heart rate reserve and recovery after symptom-limited exercise testing, which are commonly used markers of autonomic nervous system dysfunction, appear to be associated with an increased risk for the development of type 2 diabetes.

Blood samples were collected in the morning after a 12-hour overnight fast and analyzed by the hospital clinical laboratory. Detailed methods of blood analysis have been described.[10] We measured insulin concentrations in a subset of participants (n = 740) at the baseline examination. Fasting glucose and glycated hemoglobin were determined using the Hexokinase, ultraviolet method (Hitachi-7600, Tokyo, Japan) and high-performance liquid chromatography method. Insulin was measured with an immunoradiometric assay using an automatic pipetting system, Gamma Counter. Fasting plasma glucose and insulin levels were used to estimate insulin resistance and pancreatic β-cell function using the following formulas[11]: fasting glucose [mg/dL] × fasting insulin [μU/L]/405 for insulin resistance (homeostatic model assessment for insulin resistance [HOMA-IR]) and (360 × insulin)/(fasting glucose − 63) % for β-cell function (HOMA-β).

Resting heart rate was measured in the supine position using a 12-lead electrocardiogram (Hewlett-Packard ECG M1700A, Palo Alto, Calif) after ≥5 minutes of quiet rest. Blood pressure was measured during seated rest using an automated blood pressure monitor (Dinamap PRO 100, Milwaukee, Wis). Participants underwent peak or symptom-limited treadmill exercise testing using the conventional Bruce protocol. End points for exercise testing included a rating of perceived exertion (6 to 20 scale) >17 (very hard) or a peak respiratory exchange ratio >1.15; if the participant achieved >90% of age-predicted maximal heart rate; patient request due to volitional fatigue; attainment of a systolic blood pressure >250 mm Hg; increasing exertional chest discomfort; threatening arrhythmias; or >1 mm of horizontal or downsloping ST-segment depression. Peak oxygen consumption (Jaeger Oxycon Delta, Eric Jaeger, Hoechberg, Germany) was defined as the highest value of somatic oxygen uptake achieved during exercise testing, expressed as mL/kg/min. Heart rate was measured during each submaximal stage, at maximal exercise, and during recovery. The maximal heart rate determined by 12-lead electrocardiograms (Quinton Q-4500, Bothell, Wash) was defined as the highest value achieved during the progressive exercise test. The recovery protocol included 1 minute of slow walking (1.2 mph, 0% grade) after maximal exercise testing followed by seated rest for 3 minutes. Heart rate reserve was calculated as the difference between the maximal heart rate and the supine resting heart rate. Heart rate recovery was defined as the maximal heart rate minus the heart rate measured at 2 minutes of recovery after exercise testing.

Statistical Analysis

Data are presented as mean ± standard deviation and proportion for continuous and categoric variables, respectively. For group comparisons by quartiles of heart rate reserve and heart rate recovery, we performed analysis of variance for continuous variables and the chi-square test for categoric ones. The associations between heart rate and homeostatic model assessment variables were estimated as Pearson's correlation coefficients after adjusting for age and body mass index. Cox proportional hazards regression was used to determine the relation of the exercise heart rate response to the incidence of type 2 diabetes using an unadjusted model and multivariable models that included age, smoking, resting heart rate, fasting glucose, and glycated hemoglobin (model 1), as well as body mass index, systolic blood pressure, total cholesterol, triglycerides/high-density lipoprotein cholesterol ratio, alcohol consumption, white blood cell count, fibrinogen, uric acid, and peak oxygen consumption (model 2). Potential confounders were selected on the basis of their previously established role as predictive factors. Statistical significance was set at $P < .05$, and

analyses were conducted using the SPSS 22.0 (SPSS, Armonk, NY).

RESULTS

Baseline characteristics of the study population are shown in Table 1. Men in the lowest quartiles of heart rate reserve or heart rate recovery were older; had higher resting heart rate, glycated hemoglobin, insulin, HOMA-IR, and white blood cell count; and were more likely to be smokers and consume alcohol than men in the highest quartiles of heart rate reserve or heart rate recovery. In addition, directly measured peak oxygen consumption was lower in men within the lowest quartiles of heart rate reserve or heart rate recovery than their counterparts in the highest quartiles.

Heart rate reserve was inversely correlated with HOMA-IR ($r = -0.11$, $P = .002$), insulin ($r = -0.11$, $P = .002$), and triglyceride/high-density lipoprotein cholesterol ratio ($r = -0.12$, $P < .001$), but not HOMA-β ($r = -0.06$, $P = .083$), whereas heart rate recovery also was negatively correlated with HOMA-IR ($r = -0.18$, $P < .001$), insulin ($r = -0.19$, $P < .001$), and triglyceride/high-density lipoprotein cholesterol ratio ($r = -0.13$, $P = .001$) and HOMA-β ($r = -0.17$, $P < .001$), after adjusting for age and body mass index.

During a median follow-up of 5 years, 90 of the 2231 men (4.0%) developed type 2 diabetes. In Table 2, the hazard ratio of incident type 2 diabetes in men within the lowest quartile of heart rate reserve versus men within the highest quartile of heart rate reserve was 2.71 (95% confidence interval, 1.20-6.11) after adjustment for age, body mass index, resting heart rate, systolic blood pressure, total cholesterol, triglyceride/high-density lipoprotein cholesterol ratio, glucose, glycated hemoglobin, fibrinogen, white blood cell count, uric acid, peak oxygen consumption, smoking, and alcohol intake. Compared with men in the highest quartile of heart rate recovery, the risk of incident type 2 diabetes was significantly higher for men in the lowest quartile of heart rate recovery (hazard ratio, 2.81; 95% confidence interval, 1.36-5.78) after adjusting for the aforementioned confounders. As a continuous variable, each increment (1 beat/min) in heart rate reserve and heart rate recovery was associated with a 2% to 3% decrease in incident type 2 diabetes after adjusting for risk factors (Table 2). In contrast, the risk of incident type 2 diabetes was not significantly higher for men in the highest quartile of resting heart rate (>68 beats/min) compared with the lowest quartile of resting heart rate (<57 beats/min) after adjusting for confounding variables (Table 3).

DISCUSSION

The novel findings of the present study were that both reduced heart rate reserve and slow heart rate recovery after maximal cardiopulmonary exercise testing, but not resting heart rate, predict incident type 2 diabetes in healthy men, independently of conventional risk factors. These associations persisted even after adjusting for fasting blood glucose, glycated hemoglobin, markers of insulin resistance (triglyceride/high-density lipoprotein cholesterol ratio), age, body mass index, and cardiorespiratory fitness, which are strongly associated with incident type 2 diabetes, highlighting the prognostic value of these commonly used heart rate indices of autonomic dysfunction. Furthermore, decreased heart rate reserve and delayed heart rate recovery were associated with a decreased insulin resistance and increased insulin concentration even after adjusting for age and body mass index at baseline. The present study adds to previous findings in 2 important ways. First, both impaired heart rate reserve and delayed heart rate recovery, widely used markers of autonomic nervous system dysfunction, predicted new-onset type 2 diabetes in healthy Asian men. Second, these associations may be mediated, at least in part, by the relation between decreased autonomic function and increased insulin resistance.

Several studies have shown that exercise heart rate parameters are associated with cardiovascular outcomes in healthy and unhealthy populations, including patients with type 2 diabetes. However, to date, few studies have examined whether these variables may be used to predict incident type 2 diabetes. Our study uniquely demonstrates that a reduced exercise heart rate reserve or slow heart rate recovery predicts the incidence of type 2 diabetes, independently of risk factors, in healthy men. Therefore, beyond conventional risk factors, the exercise heart rate response may be used as an adjunctive parameter for predicting the risk of type 2 diabetes.

The mechanisms by which an impaired heart rate response to exercise or slow heart rate recovery are associated with incident type 2 diabetes are unclear. Reduced heart rate reserve (ie, chronotropic impairment), a blunted heart rate increase in response to exercise, may signify abnormalities in autonomic balance, whereas delayed heart rate recovery, a slow heart rate recovery after exercise, may reflect lessened parasympathetic reactivation.[5] Therefore, both reduced exercise heart rate reserve and delayed heart rate recovery after exercise may signify indices of autonomic nervous system dysfunction that may contribute to the development of type 2 diabetes.[12,13] In the present study, both reduced heart rate reserve and slow heart rate recovery as indices of impaired autonomic function were associated with insulin resistance and insulin secretion, which are consistent with previous studies suggesting that autonomic dysfunction may be a forerunner of increased fasting glucose or insulin resistance.[8,14,15] The present findings also suggest causality via biological plausibility on the association between autonomic dysfunction and incident type 2 diabetes, because the reduced heart rate reserve and slow heart rate recovery were significantly related to HOMA-IR, an index of insulin resistance. Because autonomic function is associated with the release of insulin in response to circulating glucose concentrations and insulin resistance, it is possible that autonomic nervous system derangements

Table 1 Baseline Characteristics of Participants According to Heart Rate Reserve and Heart Rate Recovery Quartiles (n = 2231)

	Heart Rate Reserve					Heart Rate Recovery				
Variables	Quartile 1 (<91) (n = 681)	Quartile 2 (92-99) (n = 578)	Quartile 3 (100-107) (n = 553)	Quartile 4 (≥108) (419)	*P* Value	Quartile 1 (<44) (610)	Quartile 2 (45-51) (557)	Quartile 3 (52-59) (548)	Quartile 4 (≥60) (518)	*P* Value
Age (y)	50 (6)	48 (5)	47 (5)	44 (6)	<.001	49 (6)	48 (6)	47 (6)	46 (5)	<.001
BMI (kg/m^2)	24.5 (2.4)	24.4 (2.2)	24.3 (2.2)	24.2 (2.3)	.075	24.5 (2.5)	24.3 (2.3)	24.5 (2.2)	24.3 (2.3)	.251
Current smokers (%)	18.9	18.3	17.2	13.8	.023	19.8	19.6	18.6	10.8	<.001
Alcohol intake (%, 3 d/wk)	5.0	5.0	3.1	4.3	.017	5.1	4.5	5.3	2.5	.046
Resting HR (beats/min)	66 (9.4)	62 (7.3)	60 (6.4)	58 (6.2)	<.001	65 (9)	63 (8)	61 (7)	59 (7)	<.001
SBP (mm Hg)	117 (12)	116 (13)	117 (12)	117 (11)	.276	117 (12)	117 (12)	116 (12)	117 (11)	.870
DBP (mm Hg)	75 (9)	75 (9)	74 (9)	75 (8)	.420	74 (9)	74 (8)	75 (9)	75 (8)	.644
TC (mg/dL)	201 (33)	199 (32)	201 (34)	204 (32)	.174	203 (34)	200 (32)	200 (34)	202 (30)	.494
HDL-C (mg/dL)	49 (11)	49 (11)	50 (12)	50 (12)	.079	48 (11)	48 (11)	49 (11)	50 (12)	.077
LDL-C (mg/dL)	129 (30)	128 (29)	129 (30)	128 (29)	.924	131 (31)	129 (29)	128 (30)	126 (29)	.068
TG (mg/dL)	145 (79)	141 (76)	141 (79)	149 (77)	.334	149 (82)	143 (77)	141 (75)	142 (74)	.292
Glucose (mg/dL)	96 (10)	95 (10)	94 (9)	93 (9.3)	<.001	95 (10)	94 (10)	94 (9)	94 (9)	.206
HbA1c (%)	5.3 (0.4)	5.3 (0.4)	5.2 (0.4)	5.2 (0.4)	<.001	5.3 (0.4)	5.3 (0.4)	5.2 (0.3)	5.3 (0.4)	.013
Insulin (μU/L)*	9.1 (4.5)	8.5 (3.4)	8.5 (3.4)	8.1 (3.4)	.107	9.5 (4.2)	8.4 (3.6)	7.9 (3.3)	8.1 (3.4)	<.001
HOMA-IR*	2.17 (1.2)	1.99 (0.8)	1.98 (0.8)	1.87 (0.8)	.029	2.25 (1.1)	1.97 (0.94)	1.86 (0.82)	1.88 (0.83)	<.001
HOMA-β*	104.5 (53.4)	107.2 (55.5)	107.5 (51.7)	106.2 (62.7)	.943	116.2 (58.0)	103.3 (59.5)	98.6 (49.4)	100.3 (45.8)	.003
Uric acid (mg/dL)	5.8 (1.2)	5.9 (1.1)	5.9 (1.1)	5.9 (1.1)	.442	6.0 (1.2)	5.8 (1.1)	5.8 (1.1)	5.8 (11)	.003
WBC (×109 cells/L)	6.2 (1.7)	5.9 (1.4)	5.8 (1.5)	5.7 (1.4)	<.001	6.2 (1.7)	5.9 (1.5)	5.7 (1.5)	5.9 (1.5)	<.001
Fibrinogen (mg/dL)	287 (61)	282 (53)	280 (54)	281 (50)	.137	285 (55)	279 (56)	279 (56)	289 (64)	.007
VO_{2peak} (mL/kg/min)	33.9 (4.8)	35.6 (4.6)	36.4 (4.5)	37.4 (4.7)	<.001	34.1 (4.6)	35.4 (4.9)	36.5 (4.8)	36.7 (4.5)	<.001
HRmax (beats/min)	148 (13)	158 (7)	163 (6)	171 (7)	<.001	153 (14)	158 (11)	160 (11)	163 (11)	<.001
HR reserve (beats/min)	82 (9.5)	96 (2.3)	103 (2.2)	113 (5.5)	<.001	88 (14)	95 (11)	99 (10)	104 (10)	<.001
HR recovery (beats/min)	45 (10)	51 (10)	54 (10)	59 (12)	<.001	38 (6)	48 (2)	55 (2)	67 (7)	<.001

Values are expressed as mean (standard deviation or %).

BMI = body mass index; DBP = diastolic blood pressure; HbA1c = glycated hemoglobin; HDL-C = high-density lipoprotein cholesterol; HOMA-β = homeostatic model assessment for β-cell function; HOMA-IR= homeostatic model assessment for insulin resistance; HR = heart rate; LDL-C = low-density lipoprotein cholesterol; SBP = systolic blood pressure; TC = total cholesterol; TG = triglycerides; VO_{2peak} = peak oxygen consumption; WBC = white blood cell count.

*(n = 740).

Table 2 Relative Risks and 95% Confidence Interval of Incidence of Type 2 Diabetes by Quartiles of Heart Rate Reserve and Heart Rate Recovery (n = 2231)

Variables (Beats/min)	N	No. of Incident Cases n, (%)	Unadjusted Hazard Ratio (95% CI)	Model 1 Hazard Ratio (95% CI)	Model 2 Hazard Ratio (95% CI)
Heart rate reserve					
Quartile 1 (<91)	681	38 (5.6)	4.03 (2.01-8.05)	2.35 (1.09-5.06)	2.71 (1.20-6.11)
Quartile 2 (92-99)	578	25 (4.3)	2.49 (1.22-5.11)	1.99 (0.93-4.26)	2.17 (0.98-4.80)
Quartile 3 (100-107)	553	16 (2.9)	1.46 (0.68-3.17)	1.77 (0.81-3.88)	1.97 (0.88-4.42)
Quartile 4 (≥108)	419	11 (2.6)	1 (ref)	1 (ref)	1 (ref)
Per 1 beat/min increment			0.98 (0.96-0.98)	0.97 (0.97-1.00)	0.98 (0.96-1.00)
Heart rate recovery					
Quartile 1 (<44)	610	33 (5.4)	3.63 (1.95-6.74)	3.23 (1.63-6.38)	2.81 (1.36-5.78)
Quartile 2 (45-51)	557	21 (3.8)	1.85 (0.96-3.53)	1.63 (0.83-3.21)	1.92 (0.94-3.89)
Quartile 3 (52-59)	548	16 (2.9)	1.21 (0.61-2.39)	1.47 (0.72-2.98)	1.51 (0.74-3.10)
Quartile 4 (≥60)	518	20 (3.9)	1 (ref)	1 (ref)	1 (ref)
Per 1 beat/min increment			0.96 (0.94-0.97)	0.96 (0.95-0.99)	0.97 (0.95-0.99)

Model 1: Adjusted for age, smoking, resting heart rate, fasting glucose, and glycated hemoglobin. Model 2: Adjusted for model 1 plus body mass index, systolic blood pressure, total cholesterol, triglycerides/high-density lipoprotein cholesterol ratio, alcohol consumption, white blood cell count, fibrinogen, uric acid, and peak oxygen consumption.

CI = confidence interval.

may be an underlying factor that precede the development of type 2 diabetes.[16]

To our knowledge, 2 similar studies have investigated the prospective relationship between heart rate recovery and incident type 2 diabetes.[16,17] The risk of incident type 2 diabetes was significantly elevated in individuals with abnormal 2-minute heart rate recovery (<42 beats/min) and those within the lowest quartile of 1-minute heart rate recovery (<20 beats/min), but these risks were nullified after adjusting for baseline insulin or glucose concentrations. In the present study, slow heart rate recovery with continuous and categoric variables remained significantly associated with the incidence of type 2 diabetes, even after adjusting for fasting glucose, markers of insulin resistance, cardio-respiratory fitness, and other conventional risk factors. Accordingly, our intriguing findings suggest that autonomic dysfunction independently predicts the incidence of type 2 diabetes. It is interesting to note that resting heart rate was higher in the lowest quartiles of heart rate reserve and heart rate recovery compared with the highest quartiles. Therefore, increased resting heart rate, reflecting heightened sympathetic activity, also may suggest the development of diabetes. However, in the present study, increased resting heart rate did not predict the risk of incident diabetes. This finding is in contrast to a previous hypothesis linking a higher resting heart rate, an indicator of increased sympathetic activation, with incident diabetes.[18,19] Although some previous studies showed that an elevated resting heart rate is associated with an increased risk for the development of diabetes, these are not universal findings.[20] The resting heart rate of our cohort may be lower than the values reported in previous studies. There is also evidence that the association between resting heart rate and risk of developing diabetes is stronger among younger participants,[18] whereas our study population included apparently healthy middle-aged men who were initially free of hypertension, cardiovascular disease, and type 2 diabetes.

Currently, there is increasing interest in using the changes in heart rate response to physical or psychologic stress to predict health outcomes.[21] During these stressors,

Table 3 Relative Risks and 95% Confidence Interval of Incidence of Type 2 Diabetes by Quartiles of Resting Heart Rate (n = 2231)

Variables (Beats/min)	N	No. of Incident Cases n, (%)	Unadjusted Hazard Ratio (95% CI)	Model 1 Hazard Ratio (95% CI)	Model 2 Hazard Ratio (95% CI)
Quartile 1 (<57)	668	26 (3.9)	1 (ref)	1 (ref)	1 (ref)
Quartile 2 (58-61)	499	16 (3.2)	0.81 (0.43-1.51)	0.80 (0.43-1.50)	0.79 (0.41-1.53)
Quartile 3 (62-67)	579	27 (4.7)	1.15 (0.67-1.97)	1.06 (0.61-1.86)	1.06 (0.60-1.88)
Quartile 4 (≥68)	485	21 (4.3)	1.03 (0.58-1.83)	1.14 (0.63-2.05)	1.05 (0.57-1.93)

Model 1: Adjusted for age, smoking, fasting glucose, and glycated hemoglobin. Model 2: Adjusted for model 1 plus body mass index, systolic blood pressure, total cholesterol, triglycerides/high-density lipoprotein cholesterol ratio, alcohol consumption, white blood cell count, fibrinogen, uric acid, and peak oxygen consumption.

CI = confidence interval.

the heart rate response may be largely due to increasing sympathetic nervous system activity.[22] Our results showed that reduced heart rate reserve and delayed heart rate recovery to exercise stress are independently associated with incident diabetes after adjusting for resting heart rate and other potential confounding variables, but that resting heart rate was unrelated to incident diabetes. These findings further suggest that incident diabetes is associated with impaired parasympathetic reactivation and increased sympathetic activity.

Although previous studies used different indices of autonomic dysfunction, including QT interval[23] and heart rate variability,[24] to suggest that sympathetic/parasympathetic imbalance may predict type 2 diabetes, other investigations have failed to confirm this relation. A recent prospective study reported that decreased heart rate variability was not associated with incident type 2 diabetes in a high-risk Caucasian population. Because this prospective study was plagued by a small sample size and insufficient power,[25] these results should be interpreted with caution. Clearly, additional studies are needed to confirm the relation between autonomic nervous system dysfunction and development of type 2 diabetes, after adjusting for potential confounding variables and population disparities.

Study Limitations

The present study has several limitations. Our study population included only men, limiting the generalizability of our findings to women. Moreover, we did not control for dietary practices and family history of diabetes, which may confound the relationship between exercise heart rate response and incidence of type 2 diabetes. In addition, we did not assess the reproducibility of exercise heart rate responses in this population. Although we adjusted for the triglyceride/high-density lipoprotein cholesterol ratio as a marker of insulin resistance,[26] we did not adjust for HOMA-IR because of the limited sample size. Nevertheless, we adjusted for baseline glucose and resting heart rate and assessed cardiorespiratory fitness using directly measured peak oxygen consumption, both of which are strong confounding variables regarding the relation between exercise heart rate responses and incident type 2 diabetes. Despite these limitations, additional methodologic strengths of this prospective study are that we examined heart rate reserve and heart rate recovery as continuous and categoric variables instead of dichotomies, the statistical approach used previously.

CONCLUSIONS

Exercise heart rate reserve and recovery predicted incident type 2 diabetes, suggesting that autonomic dysfunction may be associated with an increased likelihood for the development of this cardiometabolic risk factor.

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