Original Article

Elevated Resting Heart Rate is Associated with Dyslipidemia in Middle-aged and Elderly Chinese*

SUN Ji Chao[1,2,3], HUANG Xiao Lin[1,2], DENG Xin Ru[1,2], LV Xiao Fei[1,2], LU Jie Li[1,2], CHEN Yu Hong[1,2], BI Yu Fang[1,2], WANG Wei Qing[1,2], XU Min[1,2,#], and NING Guang[1,2,3]

1. Key Laboratory for Endocrine and Metabolic Diseases, Ministry of Health, Ruijin Hospital, Shanghai Jiaotong University School of Medicine, E-Institute of Shanghai Universities, Shanghai 200025, China; 2. Shanghai Clinical Center for Endocrine and Metabolic Diseases, Shanghai Institute of Endocrine and Metabolic Diseases, Department of Endocrine and Metabolic Diseases, Ruijin Hospital, Shanghai Jiaotong University School of Medicine, Shanghai 200025, China; 3. Laboratory of Endocrine and Metabolic Diseases, Institute of Health Sciences, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, and Shanghai Jiaotong University School of Medicine, Shanghai 200025, China

Abstract

Objective To study the relationship between resting heart rate and blood lipid level.

Methods A total of 9 415 subjects aged ≥40 years were included in the present study. Their resting heart rate was monitored and their serum levels of triglyceride (TG), total cholesterol (TC), low density lipoprotein cholesterol (LDL-C) and high density lipoprotein cholesterol (HDL-C) were measured to define dyslipidemia according to the 2007 Chinese Guidelines on Prevention and Treatment of Dyslipidemia in Adults.

Results The subjects were divided into group A with their resting heart rate <70 beats/min, group B with their resting heart rate =70-79 beats/min, group C with their resting heart rate =80-89 beats/min, and group D with their resting heart rate ≥90 beats/min. High TG, TC, and LDL-C were presented across the resting heart rate (P_{trend} <0.01). Multiple logistic regression analysis revealed that the risk of high TG and TC was higher in subjects with their resting heart rate ≥90 beats/min than in those with their resting heart rate <70 beats/min (OR=1.42; 95% CI: 1.16-1.74 and OR=1.33; 95% CI: 1.09-1.64, respectively).

Conclusion Elevated resting heart rate is associated with high TG and TC in middle-aged and elderly Chinese subjects.

Key words: Dyslipidemia; Heart rate; Triglyceride; Cholesterol

Biomed Environ Sci, 2014; 27(8): 601-605 *doi: 10.3967/bes2014.092* *ISSN: 0895-3988*

www.besjournal.com (full text) *CN: 11-2816/Q*

INTRODUCTION

It was reported that resting heart rate can accurately predict cardiovascular diseases (CVD) and sudden death[1-5]. Resting heart rate is a direct index of body sympathetic and parasympathetic balance[6]. The high risk of CVD attributable to a higher resting heart rate can be partly mediated by the dysfunction of an autonomic system, with a state of sympathetic domination and parasympathetic inhibition. It has been shown that a higher resting heart rate is related with atheroscler-

*This work is supported by grants from the Key Laboratory for Endocrine and Metabolic Diseases of Ministry of Health (1994DP131044), National Nature Science Foundation of China (81170739, 81170719, 81270877, 81222008), Shanghai New Excellent Youth Program (XYQ2011009), and the Shanghai Health Bureau Grant (2011293).

#Correspondence should be addressed to XU Min, MD, PhD; Tel: 86-21-64370045, Ext: 663340; Fax: 86-21-64749885; E-mail: della.xumin@163.com

Biographical note of first author: SUN Ji Chao, male, born in 1988, PhD candidate, majoring in Biochemistry and Molecular Biology of Type 2 Diabetes Mellitus.

osis[7], diabetes[8-9] and other metabolic disorders[10], which underlay the progress of CVD. However, few studies are available on the relationship between resting heart rate and dyslipidemia, a main cause of CVD and deaths as a result of CVD[11-12]. The association between resting heart rate and 4 major blood lipids was thus observed in this study.

SUBJECTS AND METHODS

Subjects

This study was approved by the Institutional Review Board of Ruijin Hospital. All participants gave their written informed consent.

A total of 10 375 subjects aged 40 years or older in Jiading district, Shanghai, China, were included in this study. The study was to investigate the lifestyle and environmental risk factors for diabetes and other metabolic disorders. Subjects whose heart rate or blood lipid values were missing, who had a self-reported history of strokes, myocardial infarction or CVD, who used β blockers, digoxin, non-dihydropyridine calcium channel blockers or lipid lowering drugs were excluded from the study. Finally, 9 415 were enrolled in the present study.

Data Collection, Biochemical Analysis

Demographic data, disease history, medication used, physical activity, and lifestyle factors were collected using a standard questionnaire. Physical activity was assessed according to the international physical activity questionnaire short form (IPAQ-SF) and presented as a metabolic equivalent (MET)[13]. MET-hour/week=(3.3×walking hours×walking days+ 4.0×moderate-intensity activity hours×moderate days+8.0×vigorous-intensity activity hours×vigorous days). Body weight and height were measured without shoes and heavy clothes to 0.1 Kg and 0.1 cm. Body mass index (BMI) was calculated as body weight (Kg) divided by squared body height (m^2). Blood pressure (BP) was measured 3 times at 1 min intervals after at least a 15 min rest. The average of 3 readings was used for analysis. Resting heart rate was recorded and the mean value of the 2rd and 3rd readings was averaged for analysis.

After at least 10 h of overnight fasting, a venous blood sample was collected for biochemical analysis. Fasting plasma glucose (FPG) and serum levels of TG, TC, HDL-C, and LDL-C were measured.

Definition of Dyslipidemias

According to 2007 Prevention Guidelines for Dyslipidemia in Chinese Adults[14], TG was defined as high when it was ≥2.26 mmol/L, TC was defined as high when it was ≥6.22 mmol/L, LDL-C was defined as high when it was ≥4.14 mmol/L, HDL-C was defined as low when it was <1.04 mmol/L.

Statistical Analysis

The data were analyzed using SAS version 9.3 (SAS Institute, Cary, NC) and expressed as mean±SD. The subjects were divided into group A with their resting heart rate <70 beats/min, group B with their resting heart rate =70-79 beats/min, group C with their resting heart rate =80-89 beats/min, and group D with their resting heart rate ≥90 beats/min. These cutoff points represent low, moderate and high resting heart rates[9,11]. P_{trend} across different groups was calculated using generalized linear models for continuous variables and using a Cochran-Armitage χ^2 test for categorical variables. Dyslipidemia was defined according to different cutoff levels. Odds ratio (OR) was estimated using multiple logistic regression models in groups B-D with group A as the reference. An adjusted model was controlled for sex, age, BMI, current smoking and drinking status, physical activity, systolic BP and FPG. P<0.05 was considered statistically significant.

RESULTS

General Characteristics of Subjects

The general characteristics of participants are listed in Table 1. In general, females, young subjects, non-smokers, non-drinkers and diabetics usually had a higher resting heart rate and less physical activities. No apparent trend was found in BMI among the 4 groups (P_{trend}=0.4668). The SBP, DBP, FPG, and serum levels of TG, TC, LDL-C, and HDL-C increased with resting heart rate levels (P_{trend}<0.01).

Prevalence of Dyslipidemia

The prevalence of high TG, TC, LDL-C, and low HDL-C is shown in Figure 1. The prevalence of high TG, TC, and LDL-C increased while the prevalence of low HDL-C decreased with resting heart rate (P_{trend}<0.0001, P_{trend}=0.0275).

Relation between Dyslipidemia and Resting Heart Rate

Multiple logistic regression models showed that resting heart rate was closely related with high TG, TC and LDL-C in group D *vs* A (OR=1.79, 95% CI:

1.49-2.15; OR: 1.80, 95% CI: 1.49-2.16; OR: 1.41, 95% CI: 1.15-1.73; respectively Table 2). When the age, sex, BMI, physical activity, current smoking and drinking status, SBP, DBP, and FPG into the models were used as potential covariates, the OR in group D was attenuated to 1.42 (95% CI: 1.16-1.74) for high TG, to 1.33 (95% CI: 1.09-1.64) for high TC, and to 1.10 (95% CI: 0.88-1.38) for high LDL-C.

DISCUSSION

In the present study, the resting heart rate was related to TG and TC and no apparent relation was observed between resting heart rate and LDL-C or HDL-C, after adjustment for conventional risk factors, thus providing additional evidence for the relation between resting heart rate and blood lipids.

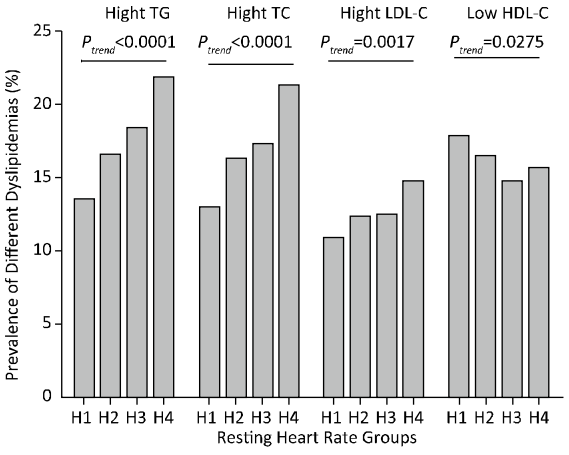

Figure 1. Prevalence of dyslipidemia in groups A-D. H1: group A; H2: group B; H3: group C; H4: group D.

Table 1. General Parameters of Subjects Included in This Study

Items	<70 (*n*=1 527)	70-79 (*n*=3 235)	80-89 (*n*=2 763)	≥90 (*n*=1 890)	P_{trend}
Age (yrs)	59.2±9.0	57.7±9.2	57.8±9.7	57.9±9.8	0.0023
Male, *n* (%)	728 (47.7)	1217 (37.6)	966 (35.0)	669 (35.4)	<0.0001
Smokers, *n* (%)	482 (32.6)	799 (25.6)	603 (22.7)	388 (21.2)	<0.0001
Drinkers, *n* (%)	392 (26.6)	648 (20.7)	543 (20.4)	356 (19.4)	<0.0001
BMI (kg/m^2)	25.02±3.12	25.01±3.09	25.15±3.31	25.03±3.48	0.4668
METs (h/w)	18.5 (0.0-37.1)	19.8 (0.0-37.9)	16.5 (0.0-34.7)	16.5 (0.0-34.7)	0.0027
SBP (mmHg)	140.3±20.1	138.4±19.9	140.4±19.5	144.2±20.1	<0.0001
DBP (mmHg)	79.5±9.6	81.1±9.8	83.6±9.9	86.9±10.6	<0.0001
TG (mmol/L)	1.26 (0.89-1.75)	1.33 (0.96-1.92)	1.40 (0.98-1.96)	1.49 (1.04-2.12)	<0.0001
TC (mmol/L)	5.22±0.97	5.30±0.97	5.37±0.99	5.47±1.13	<0.0001
LDL-C (mmol/L)	3.13±0.85	3.18±0.86	3.21±0.84	3.22±0.90	0.0022
HDL-C (mmol/L)	1.32±0.32	1.32±0.31	1.33±0.32	1.35±0.34	0.0063
FPG (mmol/L)	5.24±1.10	5.35±1.13	5.55±1.49	6.02±2.08	<0.0001
Diabetes, *n* (%)	179 (11.8)	457 (14.2)	501 (18.2)	486 (25.8)	<0.0001

Note. The data are presented as mean±SD. BMI: body mass index; METs: metabolic equivalent; SBP: systolic blood pressure; DBP: diastolic blood pressure; TG: triglyceride; TC: total cholesterol; LDL-C: low density lipoprotein cholesterol; HDL-C: high density lipoprotein cholesterol; FPG: fasting plasma glucose.

Table 2. OR and 95% CI for Dyslipidemia

Items	<70 (*n*=1 527)	70-79 (*n*=3 235)	80-89 (*n*=2 763)	≥90 (*n*=1 890)
High TG				
Crude OR	1.00	1.30 (1.10-1.55)	1.45 (1.21-1.73)	1.79 (1.49-2.15)
Adjusted OR	1.00	1.26 (1.05-1.51)	1.25 (1.03-1.51)	1.42 (1.16-1.74)
High TC				
Crude OR	1.00	1.30 (1.09-1.54)	1.38 (1.16-1.65)	1.80 (1.49-2.16)
Adjusted OR	1.00	1.22 (1.02-1.47)	1.17 (0.97-1.42)	1.33 (1.09-1.64)
High LDL-C				
Crude OR	1.00	1.16 (0.96-1.41)	1.17 (0.96-1.43)	1.41 (1.15-1.73)
Adjusted OR	1.00	1.10 (0.90-1.34)	0.99 (0.80-1.22)	1.10 (0.88-1.38)
Low HDL-C				
Crude OR	1.00	0.90 (0.77-1.06)	0.79 (0.67-0.94)	0.85 (0.71-1.02)
Adjusted OR	1.00	0.95 (0.80-1.13)	0.85 (0.71-1.02)	0.91 (0.74-1.11)

Note. TG: triglyceride; TC: total cholesterol; LDL-C: low density lipoprotein cholesterol; HDL-C: high density lipoprotein cholesterol. Adjusted OR was controlled for age, sex, BMI, physical activity, current smoking and drinking status, SBP, DBP, and FPG.

It was reported that resting heart rate can predict CVD and sudden death[1-5,15]. The predictive power of resting heart rate even overwhelms other established risk factors, such as smoking status, blood pressure and blood glucose[16-17]. Elevated resting heart rate is associated with diabetes[8-9,18-19], atherosclerosis[7,20] and other metabolic disorders[10]. However, evidence for the relationship between heart rate and dyslipidemia is scarce. To the best of our knowledge, only two studies[11-12] reported the relationship between resting heart rate and blood lipids. It was reported that non-HDL cholesterol level was 14.5% higher and TG level was 36.3% higher in males with their resting heart rate ≥90 beats/min than in those with their resting heart rate <60 beats/min (12.5% and 22.2% higher in corresponding females)[11]. Another study[12] demonstrated a significant relationship between heart rate with TC and TG level, and an inverse relationship between heart rate and HDL-C level, which are consistent with the findings in the present study. Resting heart rate is an indicator of body autonomic function. A higher resting heart rate represents a state of sympathetic stimulation and parasympathetic inhibition[21]. Such an imbalance of the autonomic system is related with hypertension[22], diabetes[23], and dyslipidemia[24]. It seems more reasonable that elevated heart rate and dyslipidemia share some common environmental and biological pathways, such as aging, obesity, hypertension and less physical activity and related body neuroendocrine changes, influencing autonomic heart rate and lipid metabolism. However, adjustment for those risk factors did not markedly alter the association observed in our study, suggesting that an independent relationship cannot be totally precluded.

It seems difficult and less worthwhile to establish an independent association between the two distinct physical phenomena. However, it is valuable when resting heart rate is considered as an indicator for risk assessment and stratification. Resting heart rate has long been neglected by physicians. The predicted value of resting heart rate was extensively tested in 2 large well-designed prospective studies[3,5]. In the 2007 European Society of Hypertension-European Society of Cardiology guidelines[25], measurement of heart rate was recommended as an important component of cardiovascular disease assessment. The measurement of heart rate was used in screening and assessment of dyslipidemia in this study.

Several limitations to our study have to be mentioned. First, the relationship between cause and effect was not established due to the nature of cross-sectional design. Second, the subjects included in this study were middle aged and elderly Chinese free from cardiovascular diseases. Third, the heart rate of subjects, measured in epidemiological investigation fields other than in the office and at home, were influenced by the 'white coat effect'[26]. The resting heart rate measured at home and the office tends to be more stable and accurate, however, the measurements in epidemiological investigation can provide an equivalent predictive value[27].

In conclusion, subjects with elevated resting heart rate are at a greater risk of dyslipidemia, especially for high TG and TC. Resting heart rate can be regarded as a powerful indicator for dyslipidemia screening and risk assessment.

ACKNOWLEDGEMENTS

The authors are highly appreciative of the subjects' participation in this study.

Received: September 23, 2013;

Accepted: December 25, 2013

REFERENCES

1. Kizilbash MA, Daviglus ML, Dyer AR, et al. Relation of heart rate with cardiovascular disease in normal-weight individuals: the Chicago Heart Association Detection Project in Industry. Prev Cardiol, 2008; 11, 141-7.
2. Cooney MT, Vartiainen E, Laatikainen T, et al. Elevated resting heart rate is an independent risk factor for cardiovascular disease in healthy men and women. Am Heart J, 2010; 159, 612-9. e613.
3. Hsia J, Larson JC, Ockene JK, et al. Resting heart rate as a low tech predictor of coronary events in women: prospective cohort study. BMJ, 2009; 338.
4. Hillis GS, Woodward M, Rodgers A, et al. Resting heart rate and the risk of death and cardiovascular complications in patients with type 2 diabetes mellitus. Diabetologia, 2012; 55, 1283-90.
5. Johansen CD, Olsen RH, Pedersen LR, et al. Resting, night-time, and 24 h heart rate as markers of cardiovascular risk in middle-aged and elderly men and women with no apparent heart disease. Eur Heart J, 2013; 34, 1732-9.
6. Opthof T. The normal range and determinants of the intrinsic heart rate in man. Cardiovasc Res, 2000; 45, 177-84.
7. Park BJ, Lee HR, Shim JY, et al. Association between resting heart rate and arterial stiffness in Korean adults. Arch Cardiovasc Dis, 2010; 103, 246-52.
8. Carnethon MR, Yan L, Greenland P, et al. Resting Heart Rate in Middle Age and Diabetes Development in Older Age. Diabetes Care, 2008; 31, 335-9.
9. Shigetoh Y, Adachi H, Yamagishi S-i, et al. Higher Heart Rate May Predispose to Obesity and Diabetes Mellitus: 20-Year

Prospective Study in a General Population. Am J Hypertens, 2008; 22, 151-5.
10. Oda E, Kawai R. Significance of heart rate in the prevalence of metabolic syndrome and its related risk factors in Japanese. Circ J, 2009; 73, 1431-6.
11. Bonaa KH, Arnesen E. Association between heart rate and atherogenic blood lipid fractions in a population. The Tromso Study. Circulation, 1992; 86, 394-405.
12. Wannamethee G, Shaper AG. The association between heart rate and blood pressure, blood lipids and other cardiovascular risk factors. J Cardiovasc Risk, 1994; 1, 223-30.
13. Lee P, Macfarlane D, Lam T, et al. Validity of the international physical activity questionnaire short form (IPAQ-SF): A systematic review. Int J Behav Nutr Phy, 2011; 8, 115.
14. Committee J. Chinese guidelines on prevention and treatment of dyslipidemia in adults. Zhonghua Xin Xue Guan Bing Za Zhi, 2007; 35, 390-419.
15. Kannel WB, Kannel C, Paffenbarger Jr RS, et al. Heart rate and cardiovascular mortality: The Framingham study. Am Heart J, 1987; 113, 1489-94.
16. Palatini P, Julius S. Heart rate and the cardiovascular risk. J Hypertens, 1997; 15, 3-17.
17. Palatini P, Benetos A, Grassi G, et al. Identification and management of the hypertensive patient with elevated heart rate: statement of a European Society of Hypertension Consensus Meeting. J Hypertens, 2006; 24, 603-10.
18. Zhang X, Shu XO, Xiang YB, et al. Resting heart rate and risk of type 2 diabetes in women. Int J Epidemiol, 2010; 39, 900-6.
19. Bemelmans RHH, Wassink AMJ, van der Graaf Y, et al. Risk of elevated resting heart rate on the development of type 2 diabetes in patients with clinically manifest vascular diseases. Eur J Endocrinol, 2012; 166, 717-25.
20. Rubin J, Blaha MJ, Budoff MJ, et al. The relationship between resting heart rate and incidence and progression of coronary artery calcification: The multi-ethnic study of atherosclerosis (MESA). Atherosclerosis, 2012; 220, 194-200.
21. ROBINSON BF, EPSTEIN SE, BEISER GD, et al. Control of Heart Rate by the Autonomic Nervous System: Studies in Man on the Interrelation Between Baroreceptor Mechanisms and Exercise. Circ Res, 1966; 19, 400-11.
22. Cleophas TJ, van Marum R. Age-Related Decline in Autonomic Control of Blood Pressure: Implications for the Pharmacological Management of Hypertension in the Elderly. Drugs Aging, 2003; 20, 313-9.
23. Yang Z, Xu B, Lu J, et al. Autonomic Test by EZSCAN in the Screening for Prediabetes and Diabetes. PLoS ONE, 2013; 8, e56480.
24. Sun K, Liu Y, Dai M, et al. Accessing Autonomic Function Can Early Screen Metabolic Syndrome. PLoS ONE, 2012; 7, e43449.
25. Mancia G, De Backer G, Dominiczak A, et al. 2007 Guidelines for the Management of Arterial Hypertension: The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). J Hypertens, 2007; 25, 1105-87.
26. Palatini P. Heart rate as predictor of outcome. Blood Press Monit, 2008; 13, 167-8.
27. Palatini P, Thijs L, Staessen JA, et al. PRedictive value of clinic and ambulatory heart rate for mortality in elderly subjects with systolic hypertension. Arch Intern Med, 2002; 162, 2313-21.