Resting heart rate is associated with the risk of metabolic syndrome and its components among Dong adults in southwest China: The China Multi-Ethnic Cohort (CMEC) Study

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Abstract

Background

High resting heart rate (RHR), one abnormal manifestation of autonomic nervous system, was associated with metabolic disorders. However, the association between RHR and metabolic syndrome (MetS) and its components remains controversial. This study aimed to explore the link between RHR and MetS and its components.

Methods

The study included 6,589 Dong adults (1,434 patients) from the China Multi-Ethnic Cohort (CMEC) Study. Logistic regression model was used to calculate odds ratios (ORs) and 95% confidence intervals (CIs) and assess the association between RHR and MetS, clustered metabolic risk, and MetS components. Restricted cubic splines model was used to evaluate the dose–response relationship between RHR and MetS and its components.

Results

A positive association existed between RHR and MetS, and people in the highest RHR quartile had a higher MetS risk (OR 1.75 [95% CI 1.42–2.15]) than those in the lowest quartile. The clustered metabolic risk associated with RHR ($P < 0.05$). Furthermore, RHR was related to elevated blood pressure (BP), elevated triglycerides (TG), and elevated fasting plasma glucose (FPG), the ORs (95% CIs) for the highest versus lowest RHR quartile were 2.06 (1.75–2.43), 1.37 (1.17–1.62), and 2.53 (2.04–3.14), respectively. Similar results were found in sensitivity and subgroup analyses. Also, non-linear dose-response relationship existed between RHR and MetS and elevated levels of BP, TG, and FPG ($P < 0.001$).

Conclusions

RHR was related to the risk of MetS and three MetS components (elevated BP, elevated TG, and elevated FPG). RHR may be a useful indicator for MetS.

Background

Metabolic syndrome (MetS), a complex group of metabolic disorders and clustering of cardiovascular risk factors[1], include central obesity, elevated triglycerides (TG), elevated blood pressure (BP), elevated fasting plasma glucose (FPG), and decreased high-density lipoprotein-cholesterol (HDL-C) through some of its definition criteria[2, 3]. MetS and its components are related to a series of adverse outcomes, including cardiovascular disease (CVD)[4, 5], diabetes[5, 6], kidney disease[7], and even some specific

cancers[8, 9]. Nearly 25% of the world population has MetS, and the prevalence of MetS is rising[1]. Thus, MetS is worthy of our attention due to its adverse outcomes and current prevalence.

Resting heart rate (RHR), a simple and easy to measure index, is considered one part of the autonomic nervous system, and is related to chronic heart failure, stroke, other CVD, cancer, chronic kidney disease, and mortality[10–13]. Also, autonomic nervous system is considered to be an essential component of the endogenous system for maintaining energy homeostasis that related to metabolism[14, 15]. Thus, RHR may be a potential therapeutic target for metabolic disorders.

Many studies have evaluated the relationship between RHR and the risk of MetS and its components based on epidemiological surveys[16–20]. However, the conclusions are inconsistent. Some studies found a positive correlation between RHR and MetS[16, 17], while a few studies found negative association in obesity person or male[18, 20]. In the study of RHR and MetS components, one study showed that RHR was positively associated with the risks of high BP, high TG, and high FPG[17], while another study in male population showed that RHR was not related to all MetS components, although a positive relationship between RHR and MetS was reported[18]. And little attention was paid on the clustered metabolic risk of MetS components. The relationship between RHR and MetS and its components needs to be further explored.

China is a multi-ethnic country, and Dong is one of the ethnic groups with distinctively national characteristics. However, whether RHR is positively associated with the risk of MetS and its components and the clustered metabolic risk of MetS components among Dong adults remains unknown. Therefore, we made two hypotheses to test: first, a positive correlation exists between RHR and MetS; second, RHR relates to the components of MetS.

Methods

Study Design and Participants

Participants aged 30–79 years were enrolled in the population-based cross-sectional study from The China Multi-Ethnic Cohort (CMEC) Study between July 2018 and April 2019, using a multistage, stratified cluster sampling method, in Guizhou Province, China. We recruited initially 7,239 individuals and all people completed a questionnaire, had physical measurements taken, and provided biological samples. After excluding individuals who missed data about diagnosis of MetS (n=644) or missed data of RHR (n=6), 6,589 participants remained in our study sample for observational analyses of the RHR–MetS and its components relationship ultimately.

The study protocol was approved by the Sichuan University Medical Ethical Review Board (K2016038) and the Research Ethics Committee of The Affiliated Hospital of Guizhou Medical University (2018[094]). Written informed consent from all study participants were obtained before taking part in the study.

Data Collection and Measurements

The sociodemographic characteristics, health-related behaviors, and medical history, including sex, age, marital status, residency, educational level, smoking status, alcohol drinking, tea intake, beverage intake, physical activity, taking antiarrhythmic or antihypertensive drugs, and family history of hypertension or diabetes, were collected by face-to-face interviews. Details about the investigation were previously published[21, 22].

Smokers were defined as people who had smoked 100 or more cigarettes during their lifetime[23]. Alcohol drinkers were defined as having consumed alcohol once or more times per week in the past half year[24]. Tea drinkers were defined as people who had consumed tea per week, which lasting more than six months. Beverage drinkers were defined as having consumed beverage weekly and sustained for six months or more. The level of physical activity for each individual was calculated by summing the metabolic equivalent tasks (METs)-hours/day for activities related to occupation, transportation, housework, and leisure-time activities[25]. Taking antiarrhythmic or antihypertensive drugs were defined as the use of antiarrhythmic or antihypertensive drugs in the past two weeks at the time of investigation. Family history of hypertension or diabetes was defined as having at least one first-degree family member with hypertension or diabetes.

Height, weight, and waist circumference (WC) were measured in duplicate using

standard methods. BP level, including systolic blood pressure (SBP) and diastolic blood pressure (DBP), and RHR level were measured in triplicate by using an electronic BP monitor (HEM-770AFuzzy, Omron, Japan) with participants in a seated position after at least a 5-min rest and at 30-sec intervals[26], and the mean was used for this analysis. Body mass index (BMI) was calculated as weight (kg) divided by height (m) squared.

An overnight fasting blood sample was taken for the measurement of FPG, total cholesterol (TC), TG, HDL-C, and low-density lipoprotein-cholesterol (LDL-C) levels.

Outcomes and Definitions

The Guideline for Prevention and Treatment of Type 2 Diabetes in Chinese (2013 edition)[3] were applied in the diagnosis of MetS and its components, and MetS requires the presence of at least three out of five factors: 1) central obesity (WC ≥ 90 cm for males and ≥ 85 cm for females); 2) elevated BP (SBP ≥ 130 mmHg or DBP ≥ 85 mmHg or drug treatment for hypertension); 3) elevated TG (TG ≥ 1.70 mmol/L); 4) elevated FPG (FPG ≥ 6.1 mmol/L or drug treatment for elevated glucose); 5) decreased HDL-C (HDL-C < 1.04 mmol/L). The information of medication was collected on the basis of a selfreported history.

Statistical Analyses

Participants were grouped into four categories based on RHR level in quartiles (Q1-Q4). All continuous variables were non normal distribution and presented as median (interquartile range), and categorical variables were expressed as number (percentage). Participants characteristics of each group were compared by Kruskal-Wallis *H* or Chi-square tests. Also, the test for trend was performed with a

polynomial linear contrast test in ANOVA test and logistic regression for continuous and categorical variables, respectively.

Logistic regression model was used to calculate adjusted odds ratios (ORs) and 95% confidence intervals (95% CIs). Primarily, RHR level was assessed in quartiles and lowest quartile as the reference group, the test for trend was performed by logistic regression model after the RHR of each group was converted into a continuous variable replaced by the median value of each group[16]. Also, we treated RHR as a continuous variable and calculated the ORs and 95% CIs per 5 *beats/min* increment in RHR. Model 1 was initially sex- and age-adjusted; Model 2 was further adjusted for marital status, residency, educational level, smoking status, alcohol drinking, tea intake, beverage intake, and physical activity; Model 3 was additionally adjusted for BMI, TC, and LDL-C based on Model 2. In addition, the association between RHR and the clustered metabolic risk based on the abnormal metabolic numbers of MetS components was investigated, participants with 0 abnormal metabolic numbers was considered the reference group. MetS components include central obesity, elevated BP, elevated TG, decreased HDL-C, and elevated FPG. Sensitivity analyses was conducted to test the robustness of the results by excluding participants who took antiarrhythmic or antihypertensive drugs in Model 4 and further excluding participants with family history of hypertension or diabetes in Model 5. Participants were then sub-grouped by sex, age (30–59 and 60–79 years), educational level (middle school or below, and high school or above), smoking status, alcohol drinking, physical activity (tertile, T1-T3), and BMI categories (< 24, 24–27.9, and ≥ 28 kg/m^2). To describe the RHR–MetS dose-response relationship, restricted cubic splines model was incorporated in multivariable logistic regression model with adjusted for Model 3.

Analyses involved the use of SPSS 22.0 (SPSS Inc., Chicago, IL, USA) and Stata 12.0 (Stata Corp, College Station, Texas). All reported *P* values were two-sided, with $P < 0.05$ considered statistically significant.

Results

Participants characteristics

The characteristics of participants by quartile of RHR in present study are showed in Table 1. A total of 6,589 individuals (21.76% patients) were included, the distribution of male, age, rural residence, high school or higher education, smoking, physical activity, WC, SBP, DBP, TC, TG, HDL-C, FPG, BMI, central obesity, elevated BP, elevated TG, decreased HDL-C, and elevated FPG were significantly different among the quartile of RHR ($P < 0.05$, $P_{trend} < 0.05$). Also, the prevalence of MetS increased substantially with increasing RHR quartile (16.18%, 19.52%, 23.68%, and 27.78% for Q1, Q2, Q3, and Q4, respectively, $P_{trend} < 0.001$, Figure 1). Similar significant upward trends were observed in MetS components.

Association between RHR and the risk of MetS

Table 2 showed the association between RHR and the risk of MetS. In total participants, the risk of MetS was altered with changes in RHR. After adjusting for potential confounding variables (Model 3), the adjusted ORs (95% CIs) for MetS with quartiles 2, 3, and 4 of RHR were 1.06 (0.86-1.31), 1.38 (1.13-1.70),

and 1.75 (1.42-2.15), respectively, as compared to the lowest quartile (P_{trend} < 0.001). The risk of MetS was increased with per 5 *beats/min* increase in RHR (OR 1.11, 95% CI 1.08-1.15; Model 3). The positive association between RHR and the risk of MetS persisted on further excluding participants who took antiarrhythmic drugs or antihypertensive drugs, or with family history of hypertension or diabetes (Model 4 and Model 5). Similar results in subgroup analyses were observed (Table 2).

Association between RHR and the clustered metabolic risk

To further evaluate the association between RHR and the risk of MetS, the clustered metabolic risk of MetS components by RHR was explored. The multi-adjusted ORs and 95% CIs for the cumulative risk of the metabolic abnormalities according to RHR level were shown in Table 3. With RHR quartile 1 as the reference, the ORs (95% CIs) of 1, 2, 3, 4, and 5 metabolic abnormalities in participants with quartile 4 were 1.32 (1.07-1.62), 2.14 (1.69-2.72), 2.53 (1.90-3.36), 4.16 (2.84-6.08), and 2.95 (1.36-6.40), respectively. The significantly increased risk of the metabolic abnormalities associated with per 5 *beats/min* increase in RHR was observed for people with 1 (OR 1.07, 95% CI 1.03-1.11), 2 (1.16, 1.11-1.21), 3 (1.21, 1.15-1.26), 4 (1.31, 1.24-1.39), and 5 (1.20, 1.06-1.36) abnormal metabolic numbers of MetS components (all P < 0.05; Model 3). However, when further consideration was given to taking antiarrhythmic or antihypertensive drugs and family history of hypertension or diabetes, the association of RHR with the risk of 5 metabolic abnormalities became meaningless (P > 0.05; Model 4 and Model 5).

Association between RHR and the risk of MetS components

After adjusting for potential confounding factors (Model 3), a positive correlation was found between RHR and elevated BP, elevated TG, and elevated FPG. The multivariate-adjusted ORs (95% CIs) with quartiles 2, 3, and 4 of RHR were 0.95 (0.81-1.11), 1.10 (0.94-1.29), and 1.53 (1.31-1.80), respectively, for elevated BP, and 1.06 (0.91-1.25), 1.34 (1.14-1.57), and 1.37 (1.17-1.62), respectively, for elevated TG, and 1.28 (1.01-1.61), 1.50 (1.20-1.89), and 2.53 (2.04-3.14), respectively, for elevated FPG, as compared to the lowest quartile (P_{trend} < 0.001). The risk of elevated BP, elevated TG, and elevated FPG were increased with per 5 *beats/min* increase in RHR, the adjusted ORs (95% CIs) were 1.09 (1.06-1.12), 1.06 (1.03-1.09), and 1.19 (1.16-1.23), respectively (Table 3). Similar results in sensitivity analyses (Model 4 and Model 5) and subgroup analyses (Supplementary Tables 1-5) were observed.

Dose-response association between RHR and MetS and MetS components

To further explore the relationship between RHR and MetS components, the dose-response analyses were conducted. Restricted cubic splines model indicated non-linear dose-response association of RHR with the risk of MetS and elevated BP, elevated TG, and elevated FPG (Figure 2, Supplementary Figure 1, P < 0.001).

Discussion

In the present cross-sectional study, a positive association between high RHR and increased risk of MetS was observed among Dong adults in southwest China. Also, the clustered metabolic risk was associated with increased RHR level. After further exploration, RHR was related to elevated BP, elevated TG, and elevated FPG, it is further proved that RHR was not associated with all 5 MetS components but some MetS components. In addition, non-linear dose-response relationships between RHR and MetS, elevated BP, elevated TG, and elevated FPG were observed.

A biological mechanism may help us understand this relationship. The homeostasis of systemic metabolism, an important process coordinated and regulated throughout the body, may be involved in the development of metabolic disorders when disturbances exist[14]. The autonomic nervous system is an important part of this process, and one of its abnormal manifestations is high RHR[17]. Speculatively, high RHR may break the balance of the homeostasis of systemic metabolism and lead to the abnormal expression of some hormone signals that related to lipid metabolism and blood pressure, such as insulin, adiponectin and leptin[14], and cause a series of metabolic disorders. The specific mechanism is still unclear and needs to be further explored.

Some epidemiological studies have reported the positive relationship between RHR and MetS[16–20, 27, 28], but the conclusions are controversial. A study involved coal miners showed that RHR was an independent risk factor for existing MetS and could be a powerful predictor for future incidence of MetS[16]. Another recent publication reported that RHR was associated with a higher prevalence of MetS, whether RHR could be an indicator for MetS among individuals requires further investigation, and negative association was found in the subgroup of diabetes, hypertension, dyslipidemia, and insulin resistance[17]. It is speculated that the possible reason is that these subgroups are all components of MetS. In addition, sex differences were reported[18, 20, 28]. Two studies insisted that high RHR was only associated with the risk of MetS in male[28] or non-obese male[18] but not in female, while another study came to the opposite conclusion that RHR was correlated with the development of MS in female rather than in male[20]. Also, a study including 30,519 older participants (≥ 50 years) in China showed that RHR was independently associated with MetS[27]. Importantly, to our best knowledge, most of the above-mentioned observational studies mainly explored the association between high RHR and the risk of MetS without consideration of medication and family history, rare subgroup analyses, or discussion on dose-response relationship. Compared with published articles, present study proved that RHR was associated with the increased risk of MetS. And this association didn't change when participants who took antiarrhythmic drugs or antihypertensive drugs, or with family history of hypertension or diabetes were further excluded. And several subgroup analyses were conducted in this study, the results didn't markedly change compared with primary analyses and present findings except for the subgroup older than 60 years old which is not consistent with previous study[27], the relationship between RHR and MetS may be affected by age due to the special physiological conditions of the elderly. Also, we observed the RHR-MetS dose-response relationship.

Some recent studies reported that higher RHR was associated with a greater risk of hypertension[29, 30], elevated TG[31], and diabetes[30, 32, 33]. However, the clustered metabolic risk has not been fully

explored. Additionally, as far as we know, the clustered metabolic risk, which indicated the severity of MetS based on the abnormal metabolic numbers of MetS component, associated with RHR was not investigated in previous studies. We found that compared with the absence of MetS, RHR was related to the severity of MetS except for 5 simultaneous abnormal components. Also, we found RHR was related to elevated BP, elevated TG, and elevated FPG on further exploration and similar reports in previous studies[16, 17] and non-linear dose-response association of RHR with elevated levels of BP, TG, and FPG were explored. This indicated that reduce the level of RHR or keep it at a normal level is critical for those at high risk with MetS and those at high-clustered risk with several abnormal metabolic components, and RHR may play a role in the control of BP, TG, and FPG.

In addition, as one inexpensive and noninvasive indicator, RHR can be obtained by some electronic devices, primary care setting, or pay-per-view routine physical examination. However, it has not attracted wide attention. People may pay attention to their heart rate at special times (such as exercise, dating, or the important moments that affect mental state) which is not named RHR. Even in hospitals, this indicator is only measured when patients need to diagnose heart related diseases or with the exception of emergency and critical care. In fact, RHR may play an important role in the prevention and control of MetS, elevated BP, elevated TG, and elevated FPG through present and previous studies. In the area where our research object is located, the economy is underdeveloped, the medical conditions are poor, and the disease burden of chronic diseases is heavy[34, 35]. If our hypothesis is established and the possible mechanism is solved, RHR will play an immeasurable role in the prevention and control of MetS in similar regions. In addition, RHR should be considered when establishing MetS prediction model or carrying out MetS screening or prognosis evaluation in the future.

Our study has some strengths. Primarily, we did dose-response relationship in present study. Also, the clustered metabolic risk based on MetS components was evaluated and more analyses of each component. In addition, this study involved a more comprehensive approach and consideration of medication and family history and more comprehensive subgroup analyses were explored. However, our study has several limitations. First, the participants were Dong adults, the applicability of observed association for other ethnic groups remains to be discussed. Second, given the observational nature of the study, causal inference may be difficult to make. Final, although several potential confounders were adjusted in present study and the results did not change materially, other unmeasured or unknown factors may affect the association between RHR and the risk of MetS and its components.

Conclusions

In conclusion, the present findings provided evidence that the risk of MetS increased with increase of RHR, and this association may be produced by affecting BP, TG, and FPG. The specific mechanism needs to be further explored. In addition, RHR may be a potential therapeutic target for metabolic disorders such as MetS, hypertension, hyperlipidemia, and diabetes, or one simple and inexpensive indicator for management and control of similar chronic diseases.

Abbreviations

BMI, Body mass index; BP, Blood pressure; CVD, Cardiovascular disease; CI, Confidence interval; DBP, Diastolic blood pressure; FPG, Fasting plasma glucose; HDL-C, High-density lipoprotein-cholesterol; LDL-C, Low-density lipoprotein-cholesterol; MetS, Metabolic syndrome; METs, Metabolic equivalent tasks; OR, Odds ratio; Q, Quartile; RHR, Resting heart rate; SBP, Systolic blood pressure; T, Tertile; TC, Total cholesterol; TG, Triglycerides; WC, Waist circumference.

Declarations

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Authors' Contributions

XZ, FH, JPZ, and PL designed and conducted the research; XZ and FH analyzed the data, wrote the paper, and contributed equally to this study; ZXQ, LLL, JY, XJT, XL, JPZ, PL revising it critically for important intellectual content; and XZ and FH had primary responsibility for the final content. All authors were involved in the collection of data and approval the final version of the manuscript.

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Availability of data and materials

The datasets used and/or analyzed in the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The study protocol was approved by the Sichuan University Medical Ethical Review Board (K2016038) and the Research Ethics Committee of The Affiliated Hospital of Guizhou Medical University (2018[094]). Written informed consent from all study participants were obtained before taking part in the study.

Consent for publication

Not applicable.

Conflict of interest

The authors declare that they have no competing interests.

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Tables

Table 1. Characteristics of study participants by quartile of resting heart rate

Characteristics	RHR quartile				*P value*	P_{trend}
	Q1 (n=1,619)	Q2 (n=1,691)	Q3 (n=1,681)	Q4 (n=1,598)		
Range (*beats/min*)	<67	67-74	75-81	>81		
Male (%)	653 (40.33)	578 (34.18)	541 (32.18)	551 (34.8)	<0.001	<0.001
Age (years)	58.07 (49.17-67.33)	52.38 (44.59-60.92)	51.18 (44.50-58.63)	50.11 (44.66-55.78)	<0.001	<0.001
Rural (%)	1,344 (83.01)	1,324 (78.30)	1,251 (74.42)	1,228 (76.85)	<0.001	<0.001
Married or cohabitating (%)	1,424 (87.96)	1,492 (88.23)	1,503 (89.41)	1,411 (88.30)	0.568	0.524
High school or higher (%)	254 (15.69)	316 (18.69)	355 (21.12)	343 (21.46)	<0.001	<0.001
Smoking (%)	320 (19.77)	284 (16.79)	271 (16.12)	248 (15.52)	0.007	0.001
Alcohol drinking (%)	263 (16.24)	259 (15.32)	253 (15.05)	209 (13.08)	0.082	0.015
Tea intake (%)	232 (14.33)	220 (13.01)	217 (12.91)	229 (14.33)	0.449	0.979
Beverage intake (%)	53 (3.27)	45 (2.66)	39 (2.32)	46 (2.88)	0.404	0.399
Taking antiarrhythmic drug (%)	20 (1.24)	20 (1.18)	18 (1.07)	281 (1.75)	0.328	0.258
Taking antihypertensive drug (%)	164 (10.13)	164 (9.70)	169 (10.05)	191 (11.95)	0.147	0.087
Family history of hypertension (%)	395 (24.40)	434 (25.67)	436 (25.94)	375 (23.47)	0.325	0.608
Family history of diabetes (%)	86 (5.31)	106 (6.27)	110 (6.54)	97 (6.07)	0.491	0.334
Physical activity (METs-h/d)	8.20 (5.30-11.10)	18.70 (16.04-21.63)	30.08 (27.30-33.30)	45.75 (40.50-54.90)	<0.001	<0.001
WC (cm)	84.40 (77.00-91.30)	83.90 (75.60-90.00)	82.30 (75.20-89.50)	81.60 (74.60-88.60)	<0.001	0.001
SBP (mmHg)	125.00	123.00	121.00	120.00	0.001	0.609

	(112.00-140.00)	(110.00-137.00)	(110.00-136.00)	(110.00-133.00)		
DBP (mmHg)	80.00 (73.00-88.00)	79.00 (72.00-88.00)	79.00 (72.00-87.00)	79.00 (72.00-86.00)	<0.001	<0.001
TC (mmol/L)	4.99 (4.38-5.63)	4.86 (4.28-5.50)	4.83 (4.25-5.47)	4.78 (4.22-5.42)	<0.001	<0.001
TG (mmol/L)	1.54 (1.11-2.33)	1.53 (1.09-2.19)	1.52 (1.08-2.24)	1.43 (1.05-2.14)	<0.001	<0.001
HDL-C (mmol/L)	1.44 (1.20-1.70)	1.45 (1.21-1.71)	1.46 (1.22-1.71)	1.47 (1.23-1.76)	<0.001	0.001
LDL-C (mmol/L)	3.06 (2.44-3.64)	2.91 (2.35-3.49)	2.89 (2.35-3.47)	2.86 (2.34-3.39)	0.675	0.228
FPG (mmol/L)	5.34 (5.00-5.77)	5.28 (4.95-5.69)	5.23 (4.93-5.64)	5.26 (4.93-5.61)	<0.001	<0.001
BMI (kg/m^2)	23.88 (21.50-26.17)	23.88 (21.60-26.26)	23.62 (21.34-26.08)	23.48 (21.14-25.79)	<0.001	<0.001

Data are number (%) or median (interquartile range).
RHR, resting heart rate; Q, quartile; METs-h/d, metabolic equivalent tasks-hours/day; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol; FPG, fasting plasma glucose; BMI, body mass index; MetS, metabolic syndrome; BP, blood pressure.

P value was obtained by Kruskal-Wallis *H* or Chi-square tests. P_{trend} was obtained by a polynomial linear contrast test in ANOVA test or logistic regression.

Table 2. Association between resting heart rate and the risk of metabolic syndrome

	RHR quartile				*P*trend	Per 5 beats/min increase
	Q1	Q2	Q3	Q4		
Total						
Model 1	ref	1.34 (1.11-1.60)	1.79 (1.50-2.13)	2.15 (1.81-2.56)	<0.001	1.13 (1.10-1.16)
Model 2	ref	1.30 (1.08-1.58)	1.71 (1.43-2.04)	2.05 (1.72-2.45)	<0.001	1.13 (1.10-1.16)
Model 3	ref	1.06 (0.86-1.31)	1.38 (1.13-1.70)	1.75 (1.42-2.15)	<0.001	1.11 (1.08-1.15)
Model 4	ref	1.02 (0.81-1.29)	1.32 (1.05-1.66)	1.68 (1.34-2.11)	<0.001	1.11 (1.07-1.16)
Model 5	ref	0.97 (0.74-1.27)	1.18 (0.90-1.55)	1.56 (1.19-2.04)	<0.001	1.10 (1.06-1.15)
Sex						
Male	ref	1.23 (0.88-1.72)	1.71 (1.23-2.39)	2.12 (1.53-2.94)	<0.001	1.13 (1.07-1.19)
Female	ref	0.90 (0.69-1.18)	1.13 (0.87-1.47)	1.46 (1.12-1.90)	0.001	1.09 (1.05-1.14)
Age group (years)						
30-59	ref	1.10 (0.85-1.43)	1.73 (1.34-2.23)	2.23 (1.72-2.88)	<0.001	1.17 (1.12-1.22)
60-79	ref	1.09 (0.77-1.55)	0.88 (0.66-1.26)	1.19 (0.83-1.69)	0.509	1.03 (0.97-1.09)
Education level						
Middle school or below	ref	1.05 (0.84-1.32)	1.32 (1.05-1.66)	1.65 (1.31-2.07)	<0.001	1.10 (1.06-1.14)
High school or above	ref	1.07 (0.64-1.77)	1.68 (1.03-2.73)	2.24 (1.38-3.64)	<0.001	1.16 (1.06-1.25)
Smoking status						
Non or former	ref	1.02 (0.81-1.28)	1.26 (1.00-1.58)	1.73 (1.38-2.17)	<0.001	1.12 (1.08-1.16)
Current	ref	1.23 (0.75-2.03)	2.00 (1.22-3.31)	1.81 (1.09-3.00)	0.008	1.08 (1.00-1.17)
Alcohol drinking						
Yes	ref	1.38 (0.82-	2.24 (1.32-	2.15 (1.24-	0.002	1.11 (1.02-1.22)

		2.35)	3.80)	3.74)		
No	ref	1.01 (0.80-1.26)	1.25 (1.00-1.56)	1.68 (1.34-2.10)	<0.001	1.11 (1.07-1.15)
Physical activity (METs-h/d)						
T1	ref	1.13 (0.79-1.61)	1.39 (0.98-1.96)	2.06 (1.46-2.91)	<0.001	1.13 (1.07-1.19)
T2	ref	1.00 (0.69-1.43)	1.64 (1.15-2.34)	1.45 (1.01-2.09)	0.007	1.10 (1.04-1.17)
T3	ref	1.07 (0.74-1.55)	1.19 (0.82-1.75)	1.78 (1.23-2.59)	0.002	1.10 (1.04-1.18)
BMI categories (kg/m2)						
< 24	ref	1.11 (0.72-1.73)	1.36 (0.89-2.09)	1.81 (1.20-2.74)	0.003	1.12 (1.05-1.20)
24-27.9	ref	0.92 (0.70-1.21)	1.18 (0.90-1.55)	1.57 (1.19-2.08)	<0.001	1.11 (1.05-1.16)
≥ 28	ref	1.51 (0.92-2.48)	2.14 (1.31-3.49)	2.86 (1.74-4.70)	<0.001	1.18 (1.09-1.28)

Data are odds ratios (ORs) and 95% confidence intervals (CIs).
RHR, resting heart rate; BMI, body mass index; Q, quartile; METs-h/d, metabolic equivalent tasks-hours/day; T, tertile; ref, reference.
Model 1: Adjusted for sex and age.
Model 2: Adjusted for Model 1 as well as marital status, residency, educational level, smoking status, alcohol drinking, tea intake, beverage intake, and physical activity.
Model 3: Adjusted for Model 2 and further adjusted body mass index, total cholesterol, and low-density lipoprotein-cholesterol.
Model 4: Adjusted for Model 3 and further excluded participants who took antiarrhythmic drugs or antihypertensive drugs.
Model 5: Adjusted for Model 3 and further excluded participants who took antiarrhythmic drugs or antihypertensive drugs, or with family history of hypertension or diabetes.
Subgroup analyses were adjusted for all variables in Model 3 except for stratification variables.

Table 3. Association between resting heart rate and the clustered metabolic risk of metabolic syndrome components

Adjusted Model	Number of MetS components	RHR quartile				P_{trend}	Per 5 beats/min increase
		Q1	Q2	Q3	Q4		
Model 1							
	0	ref	ref	ref	ref	ref	ref
	1	ref	1.15 (0.96-1.38)	1.35 (1.13-1.63)	1.20 (0.99-1.45)	0.023	1.05 (1.02-1.09)
	2	ref	1.40 (1.14-1.69)	1.71 (1.40-2.09)	1.81 (1.48-2.22)	<0.001	1.12 (1.08-1.15)
	3	ref	1.53 (1.21-1.93)	2.24 (1.78-2.83)	2.33 (1.84-2.95)	<0.001	1.17 (1.12-1.21)
	4	ref	1.58 (1.10-2.27)	2.74 (1.94-3.86)	4.19 (3.02-5.83)	<0.001	1.27 (1.21-1.34)
	5	ref	1.82 (0.86-3.86)	2.35 (1.10-5.01)	2.87 (1.38-5.98)	0.003	1.17 (1.05-1.30)
Model 2							
	0	ref	ref	ref	ref	ref	ref
	1	ref	1.12 (0.93-1.34)	1.29 (1.07-1.55)	1.15 (0.95-1.39)	0.078	1.04 (1.03-1.05)
	2	ref	1.37 (1.12-1.67)	1.66 (1.35-2.03)	1.76 (1.43-2.16)	<0.001	1.11 (1.07-1.15)
	3	ref	1.47 (1.16-1.86)	2.10 (1.66-2.66)	2.19 (1.73-2.78)	<0.001	1.16 (1.11-1.20)
	4	ref	1.48 (1.03-2.13)	2.48 (1.75-3.52)	3.80 (2.70-5.30)	<0.001	1.26 (1.20-1.32)
	5	ref	1.74 (0.81-3.69)	2.16 (1.01-4.63)	2.65 (1.27-5.53)	0.007	1.15 (1.03-1.29)
Model 3							
	0	ref	ref	ref	ref	ref	ref

	1	ref	1.06 (0.88-1.29)	1.26 (1.04-1.54)	1.32 (1.07-1.62)	0.003	1.07 (1.03-1.11)
	2	ref	1.21 (0.96-1.51)	1.53 (1.22-1.93)	2.14 (1.69-2.72)	<0.001	1.16 (1.11-1.21)
	3	ref	1.20 (0.91-1.58)	1.81 (1.37-2.39)	2.53 (1.90-3.36)	<0.001	1.21 (1.15-1.26)
	4	ref	1.17 (0.78-1.75)	2.04 (1.38-3.01)	4.16 (2.84-6.08)	<0.001	1.31 (1.24-1.39)
	5	ref	1.26 (0.57-2.81)	1.76 (0.79-3.89)	2.95 (1.36-6.40)	0.003	1.20 (1.06-1.36)
Model 4							
	0	ref	ref	ref	ref	ref	ref
	1	ref	1.09 (0.89-1.32)	1.31 (1.07-1.60)	1.30 (1.05-1.61)	0.005	1.07 (1.03-1.11)
	2	ref	1.28 (1.01-1.63)	1.64 (1.29-2.10)	2.67 (1.77-2.91)	<0.001	1.17 (1.12-1.22)
	3	ref	1.19 (0.89-1.61)	1.82 (1.35-2.46)	2.52 (1.86-3.42)	<0.001	1.22 (1.16-1.28)
	4	ref	1.15 (0.73-1.82)	1.85 (1.19-2.89)	3.84 (2.51-5.89)	<0.001	1.31 (1.22-1.40)
	5	ref	1.15 (0.42-3.11)	2.03 (0.79-5.27)	2.41 (0.90-6.45)	0.041	1.16 (0.98-1.36)
Model 5							
	0	ref	ref	ref	ref	ref	ref
	1	ref	1.02 (0.82-1.28)	1.17 (0.93-1.48)	1.28 (1.00-1.63)	0.029	1.07 (1.03-1.11)
	2	ref	1.31 (0.99-1.72)	1.66 (1.26-2.02)	2.44 (1.83-3.25)	<0.001	1.18 (1.12-1.23)
	3	ref	1.10 (0.78-1.56)	1.58 (1.11-2.25)	2.55 (1.79-3.64)	<0.001	1.22 (1.15-1.30)

4		ref	1.09 (0.64-1.87)	1.60 (0.94-2.73)	3.23 (1.94-5.39)	<0.001	1.27 (1.17-1.38)
5		ref	0.91 (0.30-1.78)	1.10 (0.35-3.46)	1.15 (0.33-3.96)	0.760	1.03 (0.84-1.26)

Data are odds ratios (ORs) and 95% confidence intervals (CIs).
RHR, resting heart rate; Q, quartile; ref, reference; MetS, metabolic syndrome.
Model 1: Adjusted for sex and age.
Model 2: Adjusted for Model 1 as well as marital status, residency, educational level, smoking status, alcohol drinking, tea intake, beverage intake, and physical activity.
Model 3: Adjusted for Model 2 and further adjusted body mass index, total cholesterol, and low-density lipoprotein-cholesterol.
Model 4: Adjusted for Model 3 and further excluded participants who took antiarrhythmic drugs or antihypertensive drugs.
Model 5: Adjusted for Model 3 and further excluded participants who took antiarrhythmic drugs or antihypertensive drugs, or with family history of hypertension or diabetes.

Table 4. Association between resting heart rate and the risk of metabolic syndrome components

	RHR quartile				P_{trend}	Per 5 *beats/min* increase
	Q1	Q2	Q3	Q4		
Central obesity	ref	1.12 (0.90-1.39)	1.09 (0.88-1.36)	1.18 (0.95-1.47)	0.185	1.03 (1.00-1.07)
Elevated BP	ref	0.95 (0.81-1.11)	1.10 (0.94-1.29)	1.53 (1.31-1.80)	<0.001	1.09 (1.06-1.12)
Elevated TG	ref	1.06 (0.91-1.25)	1.34 (1.14-1.57)	1.37 (1.17-1.62)	<0.001	1.06 (1.03-1.09)
Decreased HDL-C	ref	1.10 (0.86-1.41)	1.26 (0.99-1.61)	1.11 (0.87-1.43)	0.334	0.99 (0.95-1.03)
Elevated FPG	ref	1.28 (1.01-1.61)	1.50 (1.20-1.89)	2.53 (2.04-3.14)	<0.001	1.19 (1.16-1.23)

Data are odds ratios (ORs) and 95% confidence intervals (CIs).
RHR, resting heart rate; Q, quartile; BP, blood pressure; TG, triglycerides; HDL-C, high-density lipoprotein-cholesterol; FPG, fasting plasma glucose; ref, reference.
Adjusted for sex, age, marital status, residency, educational level, smoking status, alcohol drinking, tea intake, beverage intake, physical activity, body mass index, total cholesterol, and low-density lipoprotein-cholesterol.

Figures

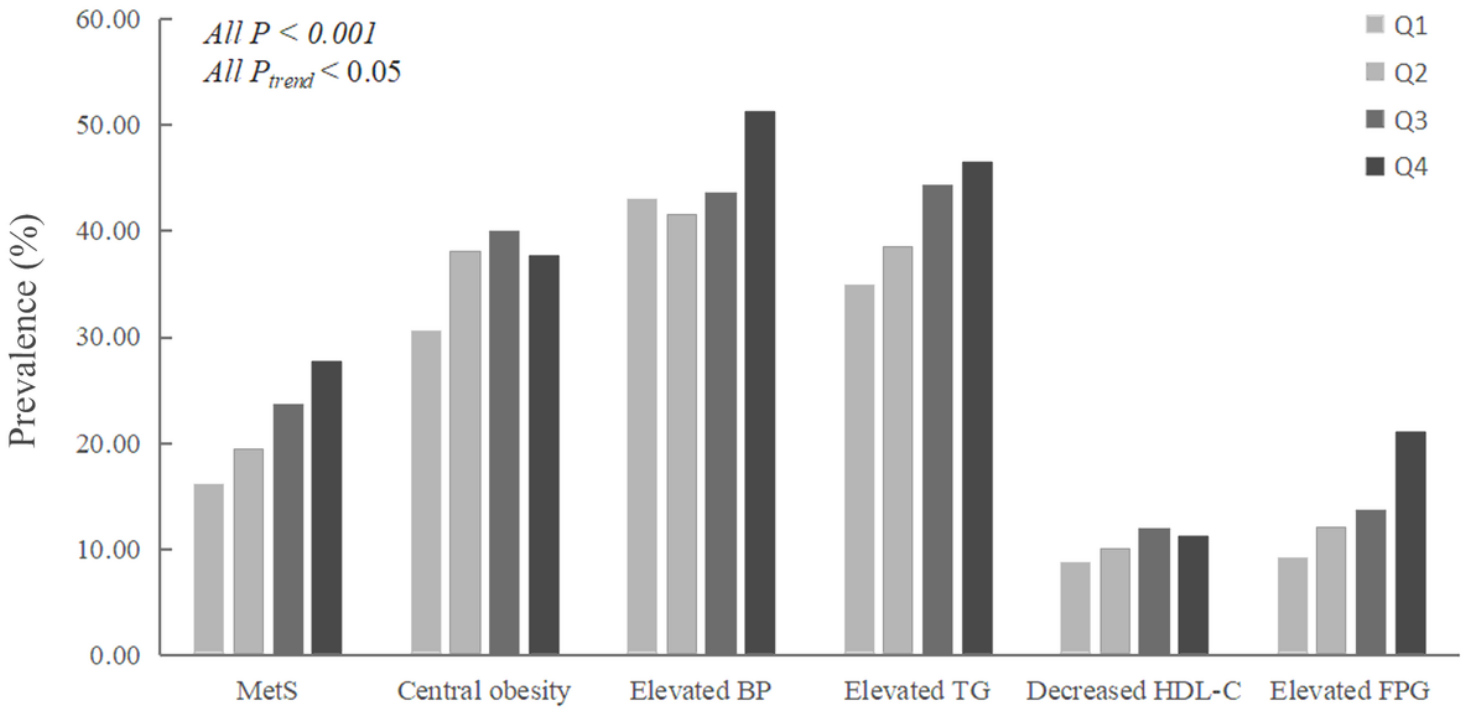

Figure 1

Prevalence of metabolic syndrome and its components by quartiles of resting heart rate. RHR, resting heart rate; Q, quartile; MetS, metabolic syndrome; BP, blood pressure; TG, triglycerides; HDL-C, high-density lipoprotein-cholesterol; FPG, fasting plasma glucose.

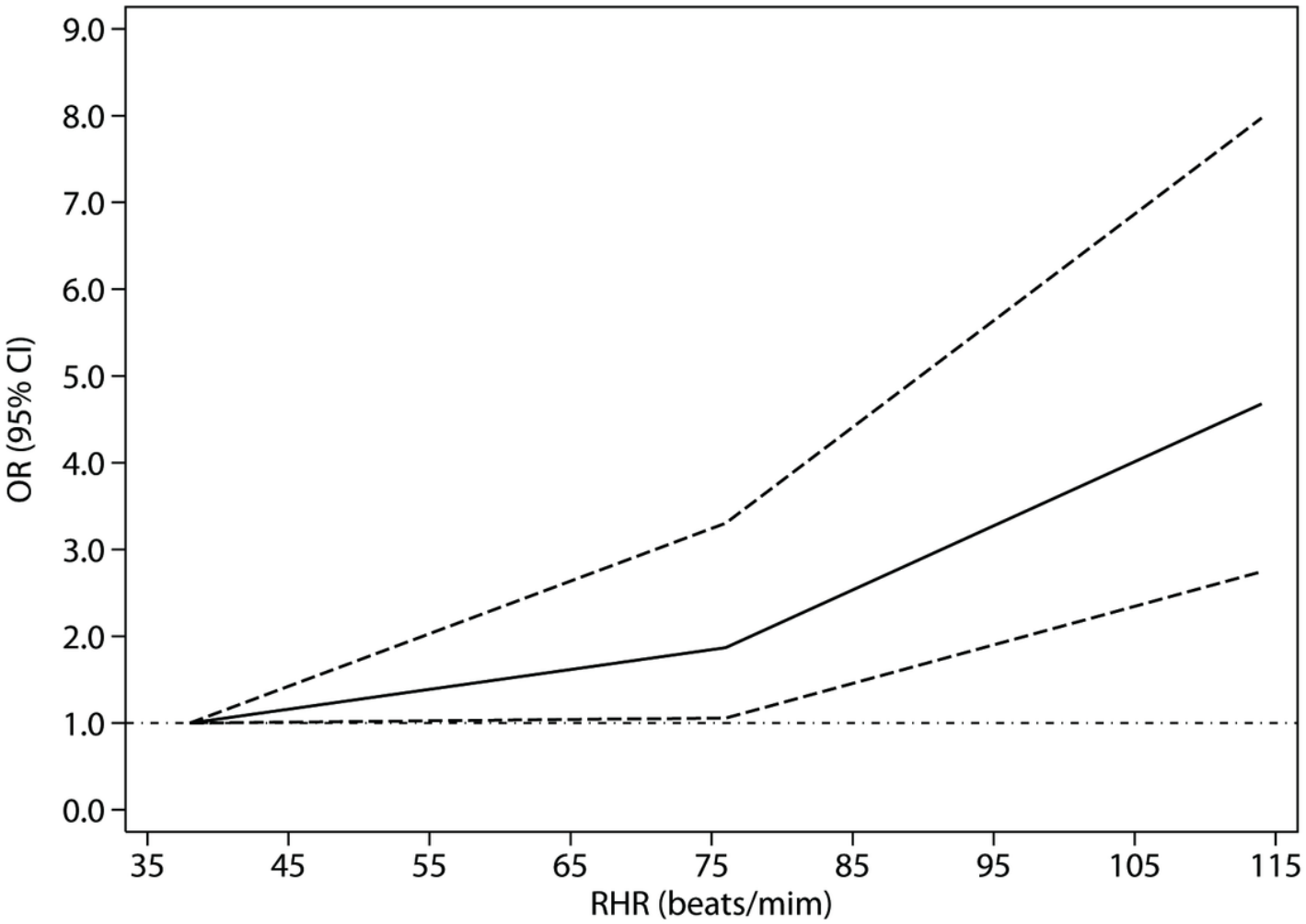

Figure 2

Dose-response association between resting heart rate and metabolic syndrome modeled using restricted cubic splines model. The fitted values of odds ratios are showed by solid lines, and the corresponding 95% confidence intervals are indicated by the dashed lines. OR, odds ratio; 95% CI, 95% confidence interval; RHR, resting heart rate.

Supplementary Files

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- SupplementaryMaterial.docx