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Independent and combined effects of resting heart rate and pulse pressure with metabolic syndrome in Chinese rural population: The Henan Rural Cohort study

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ABSTRACT

Background: We examined the independent and cumulative associations of resting heart rate and pulse pressure with metabolic syndrome in Chinese rural population based on epidemiological research.
Methods: A total of 38,708 participants were derived from the Henan Rural Cohort study. Restricted cubic splines and logistic regression model were used to estimate the odds ratios and 95% confidence intervals of metabolic syndrome risk in relation to resting heart rate and pulse pressure.
Results: After adjusting for potential confounders, the odds ratio (95% confidence intervals) of resting heart rate and pulse pressure in the highest quartile with the risk of metabolic syndrome were 1.59 (1.48–1.70) and1.81 (1.67–1.95), respectively. Simultaneously, the cumulative effect analysis indicated that the adjusted the odd ratio of resting heart rate and pulse pressure in the highest quartile was 2.89 (2.40–3.47). Furthermore, there was a significantly additive interaction between resting heart rate and pulse pressure on the risk of metabolic syndrome.
Conclusion: Increased resting heart rate and pulse pressure are associated with the higher risk of metabolic syndrome as well as the influences of resting heart rate with pulse pressure might cumulatively increase the risk of metabolic syndrome. However, the potential clinical application remains to be determined.

1. Introduction

Metabolic syndrome (MetS) is a complex of interrelated risk factors for cardiovascular disease (CVD) [1]. Meta-analysis showed that the risks for incidence and mortality of cardiovascular disease were 1.93 and 2.91 for the individuals with the MetS [2]. Moreover, the prevalence of MetS is rapidly increasing worldwide. According to data from the National Health and Nutrition Examination Survey (NHANES) 2003–2012, the prevalence of MetS increased from 32.9% to 34.7% in America [3]. This increasing trend also has been observed in Asian countries [4], which is presenting a major challenge for public health as well as becoming a socio-economic problem in the near future. Rural populations are especially vulnerable receiving fewer preventive health screenings than the urban counterparts. Due to condition limitation, it seems not easy to conduct the metabolic syndrome test in large rural population in resource limited settings. Therefore, developing an inexpensive and reliable tool to identify individual at an increased risk is urgent and essential in epidemiological and clinical settings.

Resting heart rate (RHR) is an important parameter in assessing the prevalence of MetS [5]. Pulse pressure (PP) is also a risk factor, probably as a marker of central artery stiffness, and it has been suggested that lowering pulse pressure may be a useful predictor of the effectiveness of antihypertensive drug therapy [6, 7]. Several studies have illustrated that high RHR [8–11] and high PP [12] are both independent risk factors for CVD. Some epidemiologic studies in Japan [13–16] and South Korea [17] as well as meta-analysis [18] have demonstrated that the increase of RHR is independently associated with higher risk of MetS. Although similar association has also been reported

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in China [19–21], previous studies were mainly involved in urban population [19], occupational population [20] or the eldly [21], and data from rural population are limited. On the other hand, some studies conducted in Greece, Italian and Korean [22–24], and Taiwan [25] also investigated the association between PP and MetS, while the results were inconsistent in different populations. Simultaneously, in recent years, interest has been aroused by an awareness that the RHR–CVD association may be explained by the association between heart rate and blood pressure [26, 27]. Several reports have revealed the association of MetS with increased heart rate and PP [28, 29].However, whether RHR and PP have cumulative effect on the risk of MetS has not been fully elucidated.

2. Materials and methods

2.1. Study subjects

The study population was derived from the Henan Rural Cohort study, which was performed in the rural areas in Henan province and registered before the onset of patient enrollment in Chinese Clinical Trial Register. A total of 39,259 participants aged 18–79 y were screened during 2015–2017. Subjects were excluded if they did not have RHR data ($n = 49$), lacked laboratory results necessary for a complete MetS evaluation ($n = 71$), had history of cancer ($n = 331$) or kidney failure ($n = 18$) or heart failure ($n = 82$). Finally, 38,708 eligible subjects were included for the present analysis. The protocol of this study was approved by the Zhengzhou University Life Science Ethics Committee. Informed consent was obtained from all respondents.

2.2. Assessment of resting heart rate and pulse pressure

According to the America Heart Association's standardized protocol [30], systolic blood pressure (SBP) and diastolic blood pressure (DBP) was measured 3 times for each subject who was required to sit at least 5 min by using electronic sphygmomanometer (Omron HEM-7071A). PP was calculated by SBP subtracting DBP. During 2015–2017, RHR was evaluated by the pulse rate that taken at the time of blood pressure measuring. Average of the 3 readings was taken for the analysis. If a difference > 5 mmHg or 5 beats per min was observed, the closest 2 values were used to calculate the mean value. At the same time, RHR of some 16,513 participants was measured and calculated from electrocardiogram (Nihon Kohden ECG-9130P) recordings after subjects acclimating setting at least 30 min and in supine position at least 5 min in 2017.

2.3. Assessment of potential covariates

Collected data included basic information such as social and demographic characteristic, details in health and lifestyle as described previously [31]. Briefly, anthropometric parameters were measured twice and the average readings were taken for statistical analysis. Weight and height (with light clothes and shoes off) were measured using standard measuring equipment to the nearest 0.1 kg and 0.1 cm, respectively. Waist circumference (WC) was measured at the mid-point between the lowest rib and the iliac crest to the nearest 0.1 cm. The medication history in the last 2 weeks including antihypertensive agents and the medication of treatment for coronary heart disease and stroke and family history of diseases (hypertension, diabetes mellitus, coronary heart disease, hyperlipidemia, etc) were collected. Family history was defined as the parents or siblings of participants with a history of disease.

After overnight fasting (at least 8 h), venous blood were drawn by clinical physicians. Blood samples were centrifuged for 10 min at 3000 rpm, and the serum was stored at −80 °C for future analyses. Fasting plasma glucose (FPG), triglycerides (TC) and Triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) were measured by ROCHE Cobas C501 analyzer.

2.4. Defined of MetS

MetS was defined according to the criteria set by the International Diabetes Federation (IDF) [32]. In brief, participants were diagnosed as MetS if they were centrally obese (WC ≥ 90 cm for men and WC ≥ 80 cm for women) and had at least 2 of the following: (1) raised triglycerides (TC) (≥1.7 mmol/l); (2) reduced high density lipoprotein (HDL-C) (< 1.04 mmol/l in men and < 1.30 mmol/l in women); (3) raised blood pressure (systolic blood pressure ≥130 mmHg and/or diastolic blood pressure ≥85 mmHg) or use of anti-hypertensive medicine; and (4) raised fasting plasma glucose (≥5.6 mmol/l) or previously diagnosed type 2 diabetes mellitus.

2.5. Statistical analysis

RHR and PP were stratified into 4 levels according to quartiles. Characteristics of the participants were described as mean ± SD for continuous variables and numbers (percentages) for categorical variables. *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. Besides, prevalence of MetS by quartiles of RHR and PP was calculated and tested by trend χ^2 test. The age standardized prevalence of MetS was calculated according to the sixth census data in China.

To evaluate the clustered metabolic risk, a MetS risk score varied from 0 to 5 was constructed by the abnormal numbers of WC, TC, HDL-C, blood pressure and fasting blood glucose. Specifically, if it is not metabolic syndrome, the score is 0; if the component of metabolic syndrome is one, the score is 1; when the components of metabolic syndrome are 2, the score is 2; when the components of metabolic syndrome are 3, the score is 3; when the components of metabolic syndrome are 4, the score is 4; and when the components of metabolic syndrome are 5, the score is 5. A lower score therefore indicates lower risk. Logistic regression models were used to evaluate the odds ratio (*ORs*) and 95% confidence interval (*CIs*) of the RHR quartiles, per SD increment of RHR with risk of MetS after adjusting for age, education level, marital status, smoking, drinking, high fat diet, physical activity, the medication history in the last 2 weeks including antihypertensive agents and the medication of treatment for coronary heart disease and stroke and the family history of hypertension, diabetes mellitus, coronary heart disease and hyperlipidemia. Additionally, the dose-response relationship between RHR, PP levels and risk of MetS were tested by restricted cubic splines using 5 knots at the 5th, 25th, 50th, 75th and 95th percentiles of RHR and PP levels respectively, for RHR with 61 beats per min (bpm) and for PP with 30 mmHg (approximate the first knot) as the reference group. Finally, a cumulative effect analysis was conducted by combining RHR with PP, taking RHR < 68 bpm and PP < 39 mmHg as the reference. We further examined the interaction between these 2 variables by including an additive interaction term in the regression model. The statistical analyses were performed through SAS 9.1 software package. $P < .05$ was considered as statistically significant.

3. Results

3.1. Demographic characteristics of the participants

The general characteristics of the population were shown in Table 1 according to RHR and PP quartiles, respectively. Among the 38,708 participants (15,319 men and 23,389 women), the mean age was 55.53 years old. Overall, 11,903 participants were MetS patients, and the crude and age-standardized prevalence of MetS were 30.75% and 23.83%, respectively. The prevalence of MetS was 25.10%, 29.71%,