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Association of resting heart rate and cardiovascular disease mortality in hypertensive and normotensive rural Chinese

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ABSTRACT

Background: Studies have demonstrated an increased risk of cardiovascular disease (CVD)-associated death (CVD death) with increased resting heart rate (RHR); however, whether the association is consistent in rural Chinese with hypertension and normotension is unknown. We examined the association of RHR and CVD death by hypertension and normotension status in rural Chinese people.
Methods: Baseline data for 20,069 participants ≥18 years old were collected during July to August of 2007 and July to August of 2008; 17,151 (85.5%) participants were followed up in July to August of 2013 and July to October of 2014. The association of RHR and CVD death was determined by Cox proportional hazards regression.
Results: During a mean of 5.88 years (100,889 person-years) of follow-up, we recorded 479 CVD deaths (309 in hypertensive participants). CVD death increased significantly with increasing RHR, beginning from 80 beats per minute (bpm), for hypertensive and normotensive participants. After adjusting for pulse pressure and other covariates, for hypertensive participants, risk of CVD death was increased with RHR 80–89 and ≥90 bpm. However, for normotensive participants, risk of CVD death was increased with only RHR ≥ 90 bpm.
Conclusions: Risk of CVD death was associated with elevated RHR for both hypertensive and normotensive rural Chinese, and for hypertensive participants, even slightly elevated RHR was associated with CVD death.

Introduction

Cardiovascular disease (CVD) is the leading cause of death in China, accounting for 44.8% of deaths in urban areas and 41.9% in rural areas [1]. CVD deaths have a great impact on the lifespan of people in China, so identifying and managing risk factors associated with CVD deaths is crucial. Substantial prospective studies indicated that elevated resting heart rate (RHR) was an independent risk factor for CVD death [2–13] and hypertension [14–19]. Some studies demonstrated that the relative risk for CVD death is greater for people with hypertension than normotension [20–22]. However, few studies have evaluated the association between RHR and CVD mortality by blood pressure (BP). Two western cohort studies explored the relationship in hypertensive but not normotensive participants [23,24]. A French prospective study assessed CVD mortality in various RHR groups by hypertension and normotension status but did not estimate CVD mortality risk [25].

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Thus, we examined the relationship of RHR and CVD death by hypertension and normotension status in a rural adult Chinese population with a 6-year follow-up.

Methods

Study design and participants

We used a cluster randomized method to select residents ≥18 years old from rural areas of Xin'an County, Henan Province in China; participants had no severe psychological disorders, physical disabilities, Alzheimer's disease, dementia, tuberculosis, acquired immune deficiency syndrome, or other infectious diseases. We excluded 135 participants without BP or RHR measurements. Ultimately, a cohort of 20,069 adult participants was established during July to August of 2007 and July to August of 2008, and 17,151 (85.5%) were followed up in July to August of 2013 and July to October of 2014.

Baseline examination

A designed questionnaire was used to collect data on sociodemographic characteristics (gender, age, education level, and income), behavioral variables (smoking and drinking), and medical history by interviewing all participants face to face. A cigarette smoker was defined as having smoked 100 or more cigarettes during the lifetime. An alcohol drinker was defined as having consumed 12 or more times in the past year. Participants were defined as having stroke, myocardial infarction, or heart failure if they had received a diagnosis of the corresponding diseases by a physician. The details of variables and questionnaire were described previously [26]. Waist circumstance was analyzed as the mean of two measurements to the nearest 0.1 cm by using a metric measurement tape at the 1-cm surface level above the navel. An electronic sphygmomanometer (HEM-770AFuzzy, Omron, Kyoto, Japan) was used to record BP and pulse rate three times with the right arm of participants who were in a seated position after a 5-min rest and at 30-s intervals. Hypertension was determined as the mean of three measurements ≥140 mmHg for systolic BP (SBP) or ≥90 mmHg for diastolic BP (DBP) or if participants were taking antihypertensive drugs [27]; otherwise, normotensive was defined. Pulse pressure was calculated as the difference between the mean SBP and DBP. Average RHR was calculated from three repeated measurements and classified as <60, 60–69, 70–79, 80–89, and ≥90 beats per minute (bpm).

An overnight fasting venous blood sample was collected from each participant. Levels of lipids [total cholesterol (TC), triglycerides (TG), and high-density lipoprotein cholesterol (HDL-C)] and glucose were measured by using the HITACHI 7060 automatic biochemical analyzer (Tokyo, Japan). Low-density lipoprotein cholesterol (LDL-C) level was calculated by the Friedewald formula (LDL-C = TC − HDL-C − TG/2.2) [28,29]. Dyslipidemia was defined by use of lipid-lowering medications, TC ≥ 6.22 mmol/L, TG ≥ 2.26 mmol/L, HDL-C < 1.04 mmol/L, and LDL-C ≥ 2.26 mmol/L according to the China Adult Dyslipidemia Prevention Guide criteria (2007 Edition) [30]. Diabetes mellitus was diagnosed if the participant had a history of diabetes mellitus, was currently using antidiabetic agents, or had a fasting glucose level ≥7.0 mmol/L [31].

Follow-up data collection

CVD death was defined by the International Classification of Diseases, 10th Revision (ICD-10) including I00–I99 (stroke: I60-69; myocardial infarction: I63-I64; heart failure: I50). For deaths related to CVD, death time and other corresponding information were collected by face-to-face interview with relatives, local village physicians, or other health care providers with use of a designed questionnaire. We also checked the death information with vital registration data from the local Center for Disease Control and Prevention.

All interviews and examinations were performed by trained and dedicated study staff. The study was approved by the Medical Ethics Committee of Shenzhen University, and all study participants provided written informed consent.

Statistical analysis

For non-normally distributed continuous variables, data are presented as median (interquartile range). Spearman correlation was used to evaluate correlation with increased RHR and Wilcoxon rank sum test to assess the difference between responders and non-responders. For categorical variables, data are presented as number (%), and trend data were determined by the Cochran–Mantel–Haenszel test. Differences between responders and non-responders were examined by chi-square test. Person-years of follow-up were computed as date of death or follow-up interview minus date of baseline examination for each participant. Differences in CVD mortality for inter-groups of RHR and BP were assessed by Cochran–Mantel–Haenszel and chi-square tests, respectively. Cox proportional hazard regression analysis was used to evaluate the association of RHR and CVD death for hypertensive and normotensive participants by RHR group, with calculation of hazard ratios (HRs) and 95% confidence intervals (95% CIs). For the adjusted Cox model, we adjusted for gender, age, education, mean individual monthly income, tobacco and alcohol consumption, waist circumference, pulse pressure and levels of TC, TG, HDL-C, LDL-C, and fasting glucose and history of disease (dyslipidemia, diabetes mellitus, myocardial infarction, heart failure, and stroke) and medication use (antihypertensive, lipid-lowering, and antidiabetic drugs). A cumulative survival curve was established by the Kaplan–Meier method, and differences in CVD mortality among RHR groups were determined by the log rank test. All analyses involved use of SAS 9.1 (SAS Inst., Cary, NC, USA).

Results

Responders (17,151) and non-responders (2918) significantly differed in age, education, and income level (Table 1). Data for 17,151 participants (5540 hypertensive and 11,611 normotensive) were analyzed. Baseline characteristics of hypertensive and normotensive participants by RHR group are in Tables 2 and 3. For hypertensive participants, increased RHR was significantly associated with female gender; young age; reduced cigarette smoking and alcohol consumption, antihypertensive drug use, SBP, and pulse pressure; a high rate of diabetes mellitus and antidiabetic drug use; and increased waist circumference and DBP and levels of TC, TG, HDL-C, and fasting glucose ($p < 0.05$). Similar associations were observed in normotensive participants. RHR was associated with education, LDL-C level, and lipid-lowering drug use ($p < 0.05$) but not TC level ($p = 0.165$). We identified 479 deaths related to CVD during follow-up: stroke, $n = 302$; myocardial infarction, $n = 85$; heart failure, $n = 8$, and other, $n = 84$; 35 were among participants with RHR <60 bpm (25 for hypertension), 109 with RHR 60–69 bpm (71 for hypertension), 152 with RHR 70–79 bpm (98 for hypertension), 116 with RHR 80–89 bpm (70 for hypertension), and 67 with RHR ≥ 90 bpm (45 for hypertension).

CVD mortality was significantly higher for hypertensive than normotensive participants for all RHR groups ($p < 0.05$). For hypertensive and normotensive participants, CVD mortality showed a significant upward trend with increased RHR beginning from 80 bpm (1045 and 289, and 1310 and 396/100,000 person-years for

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