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Original Article

Association of Resting Heart Rate with the Risk of Stroke in Men

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Abstract

Background: A resting heart rate may be correlated with an increased risk of stroke. Therefore, we explored the independent and joint influences of heart rate and body mass index on the incidence of stroke and its subtypes in a Chinese rural population.

Methods: Cox proportional hazard models were adopted for measuring the influence exerted by heart rate on stroke in the Tongxiang China Kadoorie Biobank prospective cohort analyses, in which 23,132 men and 32,872 women were included. Incident stroke refers to '24-hour acute focal disorder, considered to result from ischemia or intracranial hemorrhage'.

Results: Over a 6.9 year mean follow up period, 986 men and 925 women developed stroke, representing an incidence of 6.35 and 4.00 per 1,000 person-years. In contrast to men with heart rate < 69 beats/minute, men at heart rate ≥ 90 beats/minute could more probably develop stroke and ischemic stroke with representing hazard ratio [95% confidence interval (CI)] 1.29 (1.05 – 1.58), and 1.35 (1.06 – 1.71). An adjusted hazard ratio of 1.37 (95% CI = 1.06 - 1.74) and 1.46 (95% CI = 1.08 – 1.96) were respectively identified for stroke and ischemic stroke in non-overweight/obese male patients with heart rate ≥ 90 beats/minute. Joint analyses also favored the results. Unfortunately, non-significant results were found in women.

Conclusion: Higher resting heart rate acts as an independent predictor of any stroke and ischemic stroke risk in adult Chinese male but not in female. This relationship was particularly evident among non-overweight/obese male participants.

Keywords: Heart rate; Stroke; Body mass index; Prospective study

Introduction

Resting heart rate is considered a normal clinically relevant measurement process and is a possible predictor because it is closely associated with the development of many chronic diseases (1), particularly all-cause mortality (2) and the incidence of cardiovascular disease (CVD) (3). Heart rate is controlled by the autonomic nervous system and the disorder of such system balance is considered to be a factor affecting the pathogenesis of CVD. According to recent epidemiologic studies (3-9) conducted, the link between elevated heart rate and the presence of cardiovascular incidents in adults is not determined by large waist circumference, physical activity level, and systolic blood pressure (BP), revealing that heart rate acts as an independent risk element for CVD (4). Although numerous researches have studied the associations of heart rate with cardiovascular mortality (5,7,8,10,11), its association with stroke (e.g., its primary subtypes) has not been reliably studied. Existing researches have shown a paradoxical link between heart rate and stroke. For men, a higher heart rate was related to the risk of stroke in only one large Chinese cohort study (6), but not in others (7, 8); however, in women, no consistency was found in this relationship (9). Moreover, when the stroke was combined with the identified risk factors, the target heart rate remains unclear.

Under this context, we investigated the independent and joint relationship between heart rate and body mass index (BMI) with stroke for the first time in a population-based prospective study.

Methods

Study design and population

This prospective cohort study is a part of the China Kadoorie Biobank (CKB) study. CKB approaches, enrollment standards, and other details have been reported in existing studies (12-13). All of the recruiters here live in Tongxiang County, Zhejiang Province, China, and took part in the cohort study from 2004 to 2008. Recruiters were followed up annually until 1 January 2014. Participants were further excluded with the following reasons: 1) undergoing medicating process known for affecting resting heart rate (digoxin, calcium-channel blockers, antiarrhythmics, or β-blockers; n=791); 2) prevalent stroke (n=369); 3) prevalent heart failure or cancer, coronary heart disease (n=713) at the baseline examination. After these exclusions, 23,211 men and 32,872 women were included in final analyses.

The Ethics Committee of the University of Oxford (025-04), the National Center for Disease Control and Prevention in China (005/2004) approved this study. Participants were required to sign a written informed consent before volunteering.

Measurement

Sex, age, level of education, annual household income, level of physical activity, smoking and alcohol drinking status and CVD family history were all collected from the interviewer-administered electronic questionnaire at baseline. Overall exercises were changed as metabolic equivalent task hours (MET-hours/day).

Weight, waist circumference (WC) and height were detected, and body mass index (BMI) was obtained as weight in kilograms under the division by height in meters squared (kg/m^2). Heart rate was determined via pulse palpation for 30 seconds after a 10-minute rest. BP was measured after at least 5 minutes of seated rest via UA-779 digital monitor (12). Heart rate and BP were both ascertained 2 times, with the average values adopted in future studies. Hypertension was determined according to the prescription of antihypertensive drugs to a patient, or the definition of systolic BP ≥ 140mmHg, diastolic BP ≥ 90 mmHg. At baseline, self-reported diabetes was obtained. Screen-measured diabetes referred to: no self-reported diabetes but random blood glucose condition ≥ 7.0 mmol/l since the last time of eating ≥ 8 h, random blood glucose condition ≥ 11.1 mmol/l since the last time of eating < 8 h, or fasting blood glucose condition ≥ 7.0 mmol/l on further test (14).

Follow-up and outcome assessment

Information on disease diagnoses including incident stroke for participants was collected through the linkage with an established Disease Registries and the China National Health Insurance System, and matched by unique national identification number (12).

By 1 January, 2014, a total of 60 (0.1%) participants were lost to follow-up. The main outcome was the first stroke. According to the WHO, stroke is defined as '24 hours acute focal disease, believed to be caused by ischemia or intracranial hemorrhage' (15) and then classified as ischemic or hemorrhagic.

Statistical analysis

Participants were enrolled at the age when their heart rates began to be measured and dropped out at the age when they had a stroke, died, or dropped out of the study.

Descriptive statistics are expressed as percentages of categorical variables or as means ± standard deviation (SD) of continuous variables. The incidence rate per 1,000 person-years is the number of newly diagnosed stroke cases under the division, based on the total person-years of all participants.

Cox proportional hazard model was used to estimate the crude and multivariable-adjusted HRs and 95% CIs for incident stroke for rising heart rate quintiles (Q1 = reference). Covariates consisted of CVD family history (yes/no), systolic BP (continuous), physical activity (continuous), drinking (yes/no), smoking (yes/no), annual household income (category), education level (category), use of antihypertensive drugs (yes/no), BMI (continuous) and age (continuous). In joint analyzing processes, heart rate was divided as '< 90 beats/min (bpm)' and '≥ 90 bpm' in accordance with normal range of heart rate (60 - 89 bpm) in clinical practice (6). BMI was grouped according to overweight/obese status according to the Working Group on Obesity in China (WGOC) (16).

These analyses were conducted with the SAS software, version 9.2 (SAS institute, Cary, NC, USA). Each test was two-sided, and *P* value < 0.05 was considered statistical significance.

Results

Overall, 23,132 male and 32,872 female participants at baseline were finally covered. Over a mean follow-up period of 6.9 years, 986 men developed stroke (722 for ischemic stroke and 264 for hemorrhagic stroke) with an incidence of 6.35 (4.63 for ischemic stroke and 1.68 for hemorrhagic stroke) per 1,000 person-years. Stroke occurred in 925 women (708 for ischemic stroke and 210 for hemorrhagic stroke), with an incidence rate of 4.00 per 1000 person years (3.05 for ischemic stroke and 0.90 for hemorrhagic stroke). Table 1 shows that noticeable differences were identified for all characteristics except for family history of CVD. The higher heart rate, the higher systolic and diastolic BP, higher percentage of diabetes mellitus and hypertension, and lower level of physical activity were observed. Table 2 and 3 lists the basic characteristics and HRs for the females.

Table 1: Baseline characteristics of 23,132 men by resting heart rate quintile in a prospective cohort of a rural coastal population in Zhejiang province nested in the China Kadoorie Biobank (CKB) study, 2004-2013

Variables	***Heart rate (bpm)***					***P***
	Q1 <69	Q2 69-76	Q3 76-83	Q4 83-90	Q5 ≥ 90	
N	7,436	5,874	4,509	2,777	2,536	
Age (yr)	53.5 ± 9.9	52.5 ± 10.0	52.3 ± 10.1	52.7 ± 10.5	52.8 ± 10.6	<0.001
BMI (Kg/m^2)	22.6 ± 2.8	22.7 ± 2.9	22.8 ± 3.0	22.8 ± 3.2	22.7 ± 3.4	<0.001
WC (cm)	77.2± 8.8	78.0 ± 9.1	78.4 ± 9.3	78.7 ± 9.8	78.8 ± 10.2	<0.001
SBP (mmHg)	135.0 ± 20.3	135.3 ± 20.0	136.4 ± 19.8	138.5 ± 20.9	142.3 ± 21.3	<0.001
DBP (mmHg)	79.4 ± 10.3	81.1 ± 10.6	82.4 ± 10.8	83.8 ± 11.2	86.3 ± 12.0	<0.001

Current smokers, N (%)	4,888 (65.7)	3,870 (65.9)	2,974 (66.0)	1,789 (64.4)	1,588 (62.6)	0.023
Current drinkers, N (%)	2,913 (39.2)	2,277 (38.8)	1,661 (36.8)	1,114(40.1)	997 (39.3)	0.040
Total physical activity, MET-h/day	31.8 ± 15.4	31.2 ± 15.3	31.2 ± 15.5	29.5 ± 15.6	29.0 ± 16.1	<0.001
Education						<0.001
Illiteracy/primary	5,555 (74.7)	4,155 (70.7)	3,175 (70.4)	1,938 (69.8)	1,759 (69.4)	
Middle school	1,537 (20.7)	1,399 (23.8)	1,044 (23.2)	647 (23.3)	585 (23.1)	
High school or above	344 (4.6)	320 (5.4)	290 (6.4)	192 (6.9)	192 (7.6)	
Annual household income, yuan (¥)						0.001
< 10000	472 (6.3)	381 (6.5)	297 (6.6)	212 (7.6)	224 (8.8)	
10000 – 20000	972 (13.1)	719 (12.2)	599 (13.3)	386 (13.9)	354 (14.0)	
20000 – 35000	3,030 (40.7)	2,365 (40.3)	1,793 (39.8)	1,064 (38.3)	975 (38.4)	
≥35000	2,962 (39.8)	2,409 (41.0)	1,820 (40.4)	1,115 (40.2)	983 (38.8)	
Hypertension, N (%)	3,099(41.7)	2,519 (42.9)	2,055 (45.6)	1,368 (49.3)	1,525 (60.1)	<0.001
Diabetes, N (%)	101 (1.4)	83 (1.4)	83 (1.8)	68 (2.4)	72 (2.8)	<0.001
Parental history of CVD, N (%)						0.460
Mother	357 (4.8)	300 (5.1)	192 (4.3)	119 (4.3)	110 (4.3)	
Father	469 (6.3)	382 (6.5)	298 (6.6)	183 (6.6)	179 (7.1)	
Antihypertensive medication, N (%)	1000 (13.4)	767 (13.1)	613 (13.6)	425 (15.3)	432 (17.0)	<0.001

Table 2: Baseline characteristics of 32,872women by resting heart rate quintile

Variables			***Heart rate (bpm)***			***P***
	Q1<69	Q269-76	Q3 76-83	Q4 83-90	Q5 ≥ 90	
N	5,297	7,868	8,063	5,524	6,120	
Age (yr)	53.0± 9.6	52.1± 9.6	51.3 ± 9.6	50.9 ± 9.6	50.6 ± 9.8	<0.001
BMI (Kg/m²)	23.2± 3.2	23.0± 3.2	23.1± 3.2	23.1± 3.2	22.9± 3.4	<0.001
WC (cm)	76.0± 8.7	75.7± 8.7	75.7 ± 8.8	75.8 ± 8.8	75.3 ± 9.2	0.002
SBP (mmHg)	133.7± 22.5	133.0± 21.5	133.3 ± 21.3	135.0 ± 21.3	139.5 ± 21.8	<0.001
DBP (mmHg)	76.5± 9.9	78.0± 9.8	79.1 ± 10.2	80.6 ± 10.1	83.3 ± 10.6	<0.001
Current smokers, N (%)	89 (1.7)	90 (1.1)	84 (1.0)	53 (1.0)	61 (1.0)	0.002
Current drinkers, N (%)	116 (2.2)	132 (1.7)	96 (1.2)	68(1.2)	75 (1.2)	<0.001
Total physical activity, MET-h/day	30.2 ± 14.9	30.5 ± 15.1	30.2 ± 15.2	30.1 ± 15.1	29.3 ± 15.1	<0.001
Education						<0.001
Illiteracy/primary	4,698 (88.7)	6,853 (87.1)	6,866 (85.2)	4,658 (84.3)	5,226 (85.4)	

Middle school	5,10 (9.6)	8,22 (10.4)	975 (12.1)	699 (12.7)	763 (12.5)	
High school or above	89 (1.7)	193 (2.5)	222 (2.8)	167 (3.0)	131 (2.1)	
Annual household income, yuan (¥)						0.001
< 10000	407 (7.7)	505 (6.4)	529 (6.6)	315 (5.7)	376 (6.1)	
10000 – 20000	763 (14.4)	1,163 (14.8)	1,162 (14.4)	802 (14.5)	988 (16.1)	
20000 – 35000	2,224 (42.0)	3,307 (42.0)	3,386 (42.0)	2,440 (44.2)	2,680 (43.8)	
≥35000	1,903 (35.9)	2,893 (36.8)	2,986 (37.0)	1,967 (35.6)	2,076 (33.9)	
Hypertension, N (%)	2,103 (39.7)	2,972 (37.8)	3,152 (39.1)	2,294 (41.5)	3,125 (51.1)	<0.001
Diabetes, N (%)	107 (2.0)	172 (2.2)	214 (2.7)	157 (2.8)	250 (4.1)	<0.001
Parental history of CVD,N (%)						0.592
Mother	232 (4.4)	349 (4.4)	341 (4.2)	241 (4.4)	246 (4.0)	
Father	303 (5.7)	480 (6.1)	492 (6.1)	337 (6.1)	331 (5.4)	
Antihypertensive medication, N (%)	920 (17.4)	1,103 (14.0)	1,120 (13.9)	827 (15.0)	1,029 (16.8)	<0.001

Table 3: HRs and 95% CI for the incidence of stroke according to heart rate status in 32,872 women

	Stroke		***Ischemic stroke***		***Hemorrhagic stroke***	
Risk factor	Model 1	Model 2	Model 1	Model 2	Model 1	Model 2
Heart rate, bpm						
Per 1SDincrease	1.06 (0.99 - 1.14)	1.02 (0.96 - 1.09)	1.06 (0.98 - 1.14)	1.01 (0.94 - 1.09)	1.10 (0.97 - 1.26)	1.04 (0.91 - 1.19)
Quintiles						
<69	1.00	1.00	1.00	1.00	1.00	1.00
69-76	0.92 (0.74 - 1.13)	0.92 (0.75– 1.13)	0.89 (0.71 - 1.13)	0.91 (0.72 - 1.14)	1.03 (0.66 - 1.62)	1.04 (0.67 - 1.62)
76-83	1.10 (0.90 - 1.35)	1.08 (0.88– 1.32)	1.06 (0.85 - 1.33)	1.05 (0.84 - 1.32)	1.09 (0.70 - 1.70)	1.05 (0.67 - 1.65)
83-90	0.97 (0.77 - 1.22)	0.92 (0.74– 1.16)	0.86 (0.66 - 1.12)	0.83 (0.63 - 1.08)	1.52 (0.97 - 2.39)	1.41 (0.90 - 2.22)
≥ 90	1.20 (0.97 - 1.48)	1.05 (0.85 – 1.30)	1.19 (0.94 - 1.51)	1.04 (0.82 - 1.33)	1.25 (0.78 - 1.98)	1.06 (0.66 - 1.69)
P for trend	0.052	0.554	0.128	0.800	0.141	0.553

Model 1 and model 2 are shown in Table 2

Table 4 lists HRs and 95% CIs for stroke incidence regarding increased heart rate quintiles. Multivariable-adjusted HRs and 95% CIs for stroke and ischemic stroke incidence were 1.29 (1.05-1.58) and 1.35 (1.06-1.71) in men at heart rate ≥ 90 bpm compared to men with a heart rate of < 69 bpm. As a continuous variable, each SD beats/min rise in heart rate was correlated with both an 8 % increase in stroke risk (HR = 1.08, 95% CI = 1.01 – 1.14) and in ischemic stroke risk (HR = 1.08, 95% CI = 1.01 – 1.15). A positive dose-response correlation was identified between heart rate and stroke or ischemic stroke incidence (*P* for trend < 0.05).

Table 4: HRs and 95% CI for the incidence of stroke according to heart rate status in men

	Stroke		***Ischemic stroke***		***Hemorrhagic stroke***	
Risk factor	Model 1	Model 2	Model 1	Model 2	Model 1	Model 2
Heart rate, bpm						
Per 1SD increase	1.12 (1.05 –1.18)	1.08 (1.01–1.14)	1.12 (1.04 – 1.20)	1.08(1.01 – 1.15)	1.13 (1.01 – 1.27)	1.09 (0.98 - 1.22)
Quintiles						
Q1 <69	1.00	1.00	1.00	1.00	1.00	1.00
Q2 69-76	1.12 (0.94 – 1.32)	1.12 (0.95– 1.33)	1.14 (0.93 – 1.39)	1.14 (0.94 – 1.39)	1.10 (0.80 – 1.53)	1.12 (0.81 -1.55)
Q3 76-83	1.15 (0.96 – 1.38)	1.13 (0.94– 1.36)	1.20 (0.97 – 1.48)	1.17 (0.95 – 1.45)	1.05 (0.73 – 1.50)	1.04 (0.72 – 1.50)
Q4 83-90	1.12 (0.90 – 1.38)	1.07 (0.87 – 1.33)	1.07 (0.83 – 1.38)	1.03 (0.80 – 1.33)	1.28 (0.87 – 1.89)	1.22 (0.83 – 1.81)
Q5 ≥ 90	1.44 (1.18 – 1.77)	1.29 (1.05 – 1.58)	1.51 (1.20 – 1.91)	1.35 (1.06 – 1.71)	1.42 (0.96 – 2.10)	1.23 (0.82 – 1.83)
P for trend	<0.001	0.014	0.002	0.032	0.029	0.122

Model 1: Adjusted for age (years) only.
Model 2:Adjusted for age, BMI, cigarette smoking status (yes/no), alcohol drinking status (yes/no), education (illiteracy/primary, middle school, high school or above), annual household income (< 10,000, 10,000 - 20,000, 20,000 - 35,000, ≥ 35,000), physical activity, systolic BP, diabetes mellitus (yes/no), use of antihypertensive drugs and family history of CVD

Stratified analyses by BMI status in men were further conducted. Table 5 shows that the relationship between heart rate and incident stroke was particularly evident in non-overweight/obese male participants. When stratified by stroke subtype, the same was true for ischemic stroke.

Table 5: HRs and 95% CI for the incidence of stroke according to heart rate stratified by body mass index (BMI) in men

	Quintiles of heart rate (beats/min)				
Variables	Q1 < 69	Q2 69-76	Q3 76-83	Q4 83-90	Q5 ≥ 90
		BMI < 24 kg/m^2			
N	5,222 (33.6)	3,984 (25.5)	2,987 (19.1)	1,798 (11.5)	1,629 (10.3)
Multivariable HR (95% CI) ‡					
Stroke	1.00	1.21 (0.98 – 1.48)	1.26 (1.00 – 1.58)	1.12 (0.86– 1.46)	1.37 (1.06 – 1.74)
Ischemic stroke	1.00	1.22 (0.96 – 1.55)	1.26 (0.97 – 1.64)	1.09 (0.80 – 1.50)	1.46 (1.08 – 1.96)
Hemorrhagic stroke	1.00	1.40 (0.96 – 2.06)	1.28 (0.84 – 1.96)	1.10 (0.66 – 1.83)	1.34 (0.83– 2.16)
		BMI ≥ 24 kg/m^2			
N	2,214 (29.4)	1,890 (25.2)	1,522 (20.4)	979 (13.0)	907 (12.0)
Multivariable HR (95% CI) ‡					
Stroke	1.00	0.99 (0.73 – 1.34)	0.92 (0.66 – 1.27)	0.96 (0.67 – 1.39)	1.07 (0.75– 1.53)
Ischemic stroke	1.00	1.03 (0.73 – 1.46)	1.02 (0.71 – 1.48)	0.90 (0.58 – 1.38)	1.05 (0.70 – 1.59)
Hemorrhagic stroke	1.00	0.59 (0.30 – 1.15)	0.58 (0.28 –1.20)	1.37 (0.73 – 2.58)	0.83 (0.40 – 1.76)

‡: Adjusted for age, cigarette smoking status (yes/no), alcohol drinking status (yes/no), education (illiteracy/primary, middle school, high school or above), annual household income (< 10,000, 10,000 - 20,000, 20,000 - 35,000, ≥ 35,000), physical activity, systolic BP, use of antihypertensive drugs, and family history of CVD

For the subsequent exploration of the joint effect of heart rate and BMI, male participants were classified into 4 groups in terms of heart rate and the status of BMI. In contrast to non-overweight/obese at heart rate < 90 bpm, the adjusted HR (95% CI) of stroke for non-overweight/obese with heart rate ≥ 90 bpm, overweight/obese with heart rate < 90 bpm and overweight/obese with heart rate ≥ 90 bpm were 1.30 (1.04 – 1.63), 1.37 (1.18 – 1.59), and 1.62 (1.20 – 2.20), respectively. Similar results were seen in relation to ischemic stroke (Table 6). There was no significant interactive effect between heart rate and BMI on the risk of stroke or ischemic stroke.

Table 6: Joint associations of heart rate and BMI with incident stroke in men

Variables	***Heart rate (beats/min)*** <90	≥90	<90	≥90
	BMI < 24 kg/m²		BMI ≥ 24 kg/m²	
N	13,991 (89.6)	1,629 (10.4)	6,605 (87.9)	907 (12.1)
Multivariable HR (95% CI) ‡				
Stroke	1.00	1.30 (1.04 – 1.63)	1.37 (1.18 – 1.59)	1.62 (1.20 – 2.20)
Ischemic stroke	1.00	1.36 (1.05 – 1.76)	1.45 (1.22 – 1.72)	1.72 (1.21 – 2.44)
Hemorrhagic stroke	1.00	1.33 (0.88 – 2.01)	1.19 (0.89 – 1.60)	1.27 (0.66 – 2.41)

‡: Adjusted for age, cigarette smoking status (yes/no), alcohol drinking status (yes/no), education (illiteracy/primary, middle school, high school or above), annual household income (< 10,000, 10,000 - 20,000, 20,000 - 35,000, ≥ 35,000), physical activity, systolic BP, use of antihypertensive drugs, and family history of CVD.

Variables were not included in the model when used for joint analysis

Discussion

In such prospective cohort study, resting heart rate was found independently related to the risk of stroke and ischemic stroke in male individuals but not in females. This relationship was especially evident among non-overweight/obese male people.

Several studies have investigated the associations of resting heart rate with future stroke incidents. As revealed from a recent meta-analysis of prospective studies (17), per 10 bpm increase in heart rate lead to 6% increased risk for stroke, similarly with the 8% increase per 11 bpm found in our study. The REGARDS study identified a 10% increase in the risk of ischemic stroke for every 10 bpm increase in heart rate (18). The findings here supported this result that an 11% increase in heart rate was correlated with an 8% raised risk of ischemic stroke. Moreover, some of the relationships were found to be evident only in male (6, 19). Similarly, significant results were only detected in men in our study. It is unclear whether any difference is likely to result from sex hormones as studies regarding the relationships of sex hormones to resting heart rate are mixed (20).

However, most of previous studies (3,7,8,9,21) failed to investigate stroke subtypes (e.g., ischemic and hemorrhagic). High heart rate is associated with an increased risk of stroke in men, but not in women, and this association was identified only in total stroke and hemorrhagic stroke, not ischemic stroke, according to a large Chinese cohort study of adults aged 40 years or older (6). In contrast, the association in this study was observed for total stroke and ischemic stroke in men.

There are some hypotheses to explain why resting heart rate increases the risk of stroke. It is generally known that oxidative stress and dysfunction can cause atherosclerosis, while raised heart rate displays relationships to higher levels of oxidative stress and endothelial dysfunction. Reducing heart rate may enhance coronary endo-

thelial function, slow atherosclerosis and down-regulate the stroke volume (22,23).
Obesity is increasingly recognized as one of the most important modifiable risk factors for a wide range of common diseases, including type 2 diabetes, coronary heart disease, and stroke. Many studies have shown that greater obesity, as measured by BMI, is associated with a higher risk of stroke. Meta-analysis based on prospective cohort studies also found that both overweight and obesity increased the risk of stroke and ischemic stroke, but not hemorrhagic stroke (24). Our study also showed joint associations of both heart rate and BMI with incident stroke and ischemic stroke.
The present study had some advantages. It was a prospective cohort study for which the temporality of stroke and heart rate can be delineated. Most identified probable confounders, including physical activity, BP, BMI and use of antihypertensive drugs were adjusted here. Data collecting and managing processes followed strict control of quality. In addition, stroke subtypes were explored in our study.
The present study had some limitations. Heart rate or blood pressure was not measured during follow-up. As a result, we were unable to detect changes within individuals during follow-up for stroke risk. The heart rate is calculated at one point in time and may not reflect the true resting heart rate as the 24-hour dynamic heart rate monitoring process may provide more information. The baseline data was collected a long time ago and we could not avoid the temporal changes in these baseline information during the follow up. However, such limitation is inherited in most of the cohort studies and such potential misclassification should be non-differential and attenuate the associations to be null which would not materially alter the present risk estimates. We also lacked data for some covariates, such as blood lipids and information on atrial atherosclerosis.

Conclusion

In a prospective cohort study, heart rate independently predicted the incidence of global stroke and ischemic stroke in a rural Chinese male population. This association was particularly evident in non-overweight/obese men. In the future, more information will add stronger evidence on this topic.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflict of Interest

The authors declare that there is no conflict of interests.

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