Resting Heart Rate Trajectory Pattern Predicts Arterial Stiffness in a Community-Based Chinese Cohort

Shuohua Chen,* Weijuan Li,* Cheng Jin, Anand Vaidya, Jingli Gao, Hui Yang, Shouling Wu, Xiang Gao

Objective—To examine whether the long-term resting heart rate (RHR) pattern can predict the risk of having arterial stiffness in a large ongoing cohort.

Approach and Results—This community-based cohort included 12554 participants in the Kailun study, who were free of myocardial infarction, stroke, arrhythmia, and cancer. We used latent mixture modeling to identify RHR trajectories in 2006, 2008, and 2010. We used multivariate linear regression model to examine the association between RHR trajectory patterns and the risk of having arterial stiffness, which was assessed by brachial–ankle pulse wave velocity in 2010 to 2016. We adjusted for possible confounding factors, including socioeconomic status, lifestyle factors, use of medications, comorbidities, and serum concentrations of lipids, glucose, and high-sensitivity C-reactive proteins. We identified 5 distinct RHR trajectory patterns based on their 2006 status and on the pattern of change during 2006 to 2010 (low–stable, moderate–stable, moderate–increasing, elevated–decreasing, and elevated–stable). We found that individuals with elevated–stable RHR trajectory pattern had the highest brachial–ankle pulse wave velocity value and individuals with the low–stable RHR trajectory pattern had the lowest value (adjusted mean difference=157 cm/s; P<0.001). Adjusted odds ratio for risk of having arterial stiffness (brachial–ankle pulse wave velocity $\geq$1400 cm/s) was 4.14 (95% confidence interval, 2.61–6.57) relative to these 2 extreme categories. Consistently, a higher average RHR, a higher annual RHR increase rate, and a higher RHR variability were all associated with a higher risk of having arterial stiffness.


Key Words: ankle | atherosclerosis | cohort study | coronary artery disease

Resting heart rate (RHR) is a simple and useful indicator of autonomic balance and metabolic rate. Emerging evidence has demonstrated an association between an elevated RHR and a higher risk of adverse cardiovascular events and mortality. However, the underlying mechanisms are not well understood. It has been suggested that RHR may impact future cardiovascular disease risk via its association with arterial stiffness, one of the earliest detectable manifestations of adverse structural and functional changes within the vessel wall. An elevated RHR was associated with arterial stiffness in 2 large cross-sectional studies. In a small Japanese cohort, Tomiyama et al reported a synergistic role of high baseline RHR and increase in heart rate during a 5- to 6-year follow-up period in accelerating age-associated increases in arterial stiffness. However, to the best of our knowledge, whether RHR pattern for a longer period can predict the arterial stiffness has not been studied in any large population.

Pulse wave velocity (PWV) is the most validated method to quantify arterial stiffness noninvasively. PWV is considered the golden-standard index of arterial stiffness and a maker of atherosclerosis. PWV has a strong predictive value of future cardiovascular events in general population or in patients with hypertension, diabetes mellitus, or end-stage renal diseases. Recently, brachial–ankle PWV (baPWV) measurement, which is easy and convenient to be performed and can be widely used in large-scale populations, has become available in clinical settings. baPWV values have been associated with cardiovascular events, including coronary artery disease, peripheral artery disease, and stroke.

Therefore, we examined the association between RHR trajectory pattern during a 4-year follow-up period and the risk of having arterial stiffness, which was measured by baPWV, in a large ongoing Chinese cohort.


Nonstandard Abbreviations and Acronyms

- baPWV: brachial–ankle pulse wave velocity
- PWV: pulse wave velocity
- RHR: resting heart rate

Materials and Methods

Materials and Methods are available in the online-only Data Supplement.

Results

Five distinct RHR trajectories during a 4-year follow-up period were identified (Figure 1). During 2006 to 2010, 18.2% participants (n=2282) had an RHR consistently <70 bpm (referred to as low–stable pattern); 69.8% participants (n=8768) had an RHR between 70 and 80 bpm (referred to as moderate–stable pattern); 6% participants (n=758) had an RHR of ≥80 bpm at baseline in 2006, which increased to ≥90 bpm during follow-up (referred to as moderate–increasing pattern), 1.1% participants (n=135) had an RHR consistently >100 bpm (referred to as elevated–stable pattern); and 4.9% participants (n=611) had an RHR between 90 and 100 bpm at baseline in 2006, which decreased to ≥80 bpm during follow-up (referred to as elevated–decreasing pattern). The basic characteristics of the 12,554 participants are presented in Table 1.

Then, we examined whether the RHR trajectory pattern between 2006 and 2010 could predict the future risk of having arterial stiffness, which was assessed by baPWV between 2006 and 2010. Relative to individuals with low–stable RHR trajectory, individuals in the other 4 patterns had significantly higher baPWV levels (Table 2; Figure II in the online-only Data Supplement). Of note, although individuals with moderate–stable and moderate–increasing RHR patterns had similar baseline RHR (70–80 bpm), individuals with moderate–increasing RHR pattern had a significantly higher baPWV (1528±13 versus 1486±9 cm/s), indicating that RHR changes had an impact on the risk of arterial stiffness. Exclusion of participants who had hypertension (Table 2) generated similar results. After further adjustment for RHR in 2006 or in 2010, the trend remained the same and significant (data not shown). Although further adjustment for RHR at the time of baPWV assessment led to great attenuation of the association between RHR trajectories during 2006 to 2010 and baPWV in 2010 to 2016, the difference between the elevated–stable and low–stable patterns remained significant (adjusted difference=33.8; 95% confidence interval, 8.61–59.0). However, these results should be interpreted with caution because of concerns of overadjustment. We observed a significant interaction between age and RHR trajectories (P_interaction<0.001) but not for sex (P_interaction=0.26). The association between heart rate and baPWV was stronger among individuals ≥60 years of age, relative to younger adults (Table 2).

The RHR trajectory pattern was a strong predictor of having arterial stiffness (baPWV ≥1400 cm/s)—adjusted odds ratio was 4.14 (95% confidence interval, 2.61–6.57) for the elevated–stable versus low–stable RHR patterns (Figure 2).

We further found that a higher average RHR, a higher annual RHR increase rate, and a higher RHR variability between 2006 and 2010 were all associated with a significantly higher baPWV, a marker of arterial stiffness (Table 3).

Discussion

In this study, we observed heterogeneous RHR trajectory patterns in a large cohort of 12,554 participants during a 4-year follow-up. We identified 5 unique RHR trajectory patterns. Individuals with elevated–stable RHR trajectory pattern (RHR 90–100 bpm) had the highest risk of having arterial stiffness, which was assessed by baPWV, and individuals with low–stable RHR trajectory pattern (RHR 60–70 bpm) had the lowest risk after adjustment for potential confounding factors, including socioeconomic status, lifestyle factors, use of medications, comorbidities, and serum concentrations of lipids, glucose, and high-sensitivity C-reactive proteins. When baseline RHR was further adjusted, RHR trajectories were still independently associated with the risk of having arterial stiffness.

A large body of epidemiological evidences has shown that RHR is associated with cardiovascular morbidity and mortality.2–4,19,20 As a consequence, increased RHR has emerged as an independent risk factor both in primary prevention and in patients with hypertension, coronary artery disease, and myocardial infarction.21 It was estimated that for each 15 bpm increase in RHR, the risk of cardiovascular disease can be increased by 24% in men and 32% in women.19 Despite the compelling evidences from epidemiological studies, it is challengeable to determine the actual role of RHR in cardiovascular events because of the complex interaction among the various risk factors.22 There have been several potential mechanisms proposed, including increased sympathetic tones, increased vascular sheer stress and endothelial damage by increased heart rate, and accelerated atherosclerosis. In animal studies, accelerated heart rate is associated with cellular signaling events leading to vascular oxidative stress, endothelial...
dysfunction, and acceleration of atherogenesis. Mangoni et al. provided experimental evidence that progressive increases in heart rate caused by atrial pacing in rats led to marked reductions in carotid artery compliance. In a 6-year follow-up of patients who were treated for hypertension, high RHR was associated with an accelerated progression of arterial stiffness, as estimated by carotid/femoral PWV. Our results also support that not only a single RHR measurement or an average RHR value but also the trend of RHR change over time are important predictors of arterial stiffness.

### Table 1. Basic Characteristics in 2006 According to the Resting Heart Rate Trajectory Patterns, Among 12,554 Kailuan Participants

<table>
<thead>
<tr>
<th></th>
<th>Low–Stable</th>
<th>Moderate–Stable</th>
<th>Moderate–Increasing</th>
<th>Elevated–Decreasing</th>
<th>Elevated–Stable</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td>2282 (18.2)</td>
<td>8768 (69.8)</td>
<td>758 (6.0)</td>
<td>611 (4.9)</td>
<td>135 (1.1)</td>
</tr>
<tr>
<td>Age*, y</td>
<td>46.8±11.8</td>
<td>44.4±11.0</td>
<td>44±11.1</td>
<td>43.9±10.5</td>
<td>45.1±11.4</td>
</tr>
<tr>
<td>Men, %</td>
<td>63.5</td>
<td>58.9</td>
<td>69.7</td>
<td>67.5</td>
<td>62.7</td>
</tr>
<tr>
<td>BMI*†, kg/m²</td>
<td>24.6±3.0</td>
<td>24.7±3.2</td>
<td>24.9±3.2</td>
<td>24.7±3.4</td>
<td>24.1±3.3</td>
</tr>
<tr>
<td>Smoking status, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>30.4</td>
<td>29.5</td>
<td>53.4</td>
<td>38.7</td>
<td>28.4</td>
</tr>
<tr>
<td>Past</td>
<td>5.3</td>
<td>3.7</td>
<td>3.3</td>
<td>3</td>
<td>6.7</td>
</tr>
<tr>
<td>Never</td>
<td>64.3</td>
<td>66.8</td>
<td>43.3</td>
<td>58.4</td>
<td>64.9</td>
</tr>
<tr>
<td>Alcohol intake status, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>41.1</td>
<td>37.4</td>
<td>47.3</td>
<td>42.1</td>
<td>34.3</td>
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<td>Past</td>
<td>2.3</td>
<td>2</td>
<td>2.3</td>
<td>1</td>
<td>3.7</td>
</tr>
<tr>
<td>Never</td>
<td>56.6</td>
<td>65.6</td>
<td>50.5</td>
<td>56.9</td>
<td>61.9</td>
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<tr>
<td>Physical activity status, %</td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Never</td>
<td>8.4</td>
<td>10.8</td>
<td>17.3</td>
<td>10.3</td>
<td>12.1</td>
</tr>
<tr>
<td>1–2 times/wk</td>
<td>74.9</td>
<td>78</td>
<td>72.3</td>
<td>81</td>
<td>80.3</td>
</tr>
<tr>
<td>≥3 times/wk</td>
<td>16.7</td>
<td>11.2</td>
<td>10.4</td>
<td>8.7</td>
<td>7.6</td>
</tr>
<tr>
<td>Education status, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Illiteracy or elementary school</td>
<td>5.2</td>
<td>4.7</td>
<td>8.5</td>
<td>4.7</td>
<td>8.4</td>
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<tr>
<td>Middle school</td>
<td>78</td>
<td>82.1</td>
<td>81.4</td>
<td>83.6</td>
<td>87</td>
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<tr>
<td>College/university</td>
<td>16.8</td>
<td>13.2</td>
<td>10</td>
<td>11.8</td>
<td>14.8</td>
</tr>
<tr>
<td>Average income, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;500 ¥/mo</td>
<td>23.8</td>
<td>26.6</td>
<td>36.1</td>
<td>27.2</td>
<td>35.1</td>
</tr>
<tr>
<td>500 to 2999 ¥/mo</td>
<td>62.2</td>
<td>64.1</td>
<td>56</td>
<td>62.7</td>
<td>58</td>
</tr>
<tr>
<td>≥3000 ¥/mo</td>
<td>14.1</td>
<td>9.3</td>
<td>7.9</td>
<td>10.1</td>
<td>6.9</td>
</tr>
<tr>
<td>Diabetes mellitus status, %</td>
<td>5.2</td>
<td>8.1</td>
<td>13.6</td>
<td>12.9</td>
<td>17</td>
</tr>
<tr>
<td>Hypertension status, %</td>
<td>31.4</td>
<td>37.1</td>
<td>54.2</td>
<td>49.1</td>
<td>51.1</td>
</tr>
<tr>
<td>Use of antihypertensive agent, %</td>
<td>9.6</td>
<td>9.6</td>
<td>13.5</td>
<td>14</td>
<td>11.1</td>
</tr>
<tr>
<td>TG*†, mmol/L</td>
<td>1.21 (0.91–1.91)</td>
<td>1.28 (0.91–1.91)</td>
<td>1.44 (1.01–2.27)</td>
<td>1.48 (1.06–2.29)</td>
<td>1.33 (0.95–1.95)</td>
</tr>
<tr>
<td>TC*†, mmol/L</td>
<td>4.87±0.87</td>
<td>4.9±0.88</td>
<td>5.09±0.92</td>
<td>5.14±0.97</td>
<td>5.06±0.98</td>
</tr>
<tr>
<td>LDL-C*†, mmol/L</td>
<td>2.42±0.67</td>
<td>2.47±0.65</td>
<td>2.67±0.68</td>
<td>2.5±0.61</td>
<td>2.5±0.67</td>
</tr>
<tr>
<td>HDL-C*†, mmol/L</td>
<td>1.56±0.34</td>
<td>1.53±0.33</td>
<td>1.57±0.30</td>
<td>1.63±0.32</td>
<td>1.62±0.36</td>
</tr>
<tr>
<td>FGB*†, mmol/L</td>
<td>5.18±0.89</td>
<td>5.4±1.17</td>
<td>5.79±1.58</td>
<td>5.8±1.70</td>
<td>6.12±1.64</td>
</tr>
<tr>
<td>hsCRP*†, mmol/L</td>
<td>1.0 (0.5–2.0)</td>
<td>1.18 (0.61–2.3)</td>
<td>1.27 (0.71–2.40)</td>
<td>1.25 (0.67–2.35)</td>
<td>1.47 (0.69–2.92)</td>
</tr>
</tbody>
</table>

BMI indicates body mass index; FBG, fasting blood glucose; HDL-C, high-density lipoprotein cholesterol; hsCRP, high-sensitivity C-reactive protein; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; and TG, triglycerides.

*Values are given in means±SD.
‡Values are given in median and interquartile range.
that can affect RHR and PWV, and physical activities that can affect RHR and PWV, and physical activities that can modify RHR and comorbidities, and RHR and its change over time remain independent risk factors for accelerated arterial stiffness. It remains to be seen whether this association translates to a higher incidence of cardiovascular events and longer follow-up will be needed for these events to occur.

It is important to note that whether heart rate patterns represent a cause or consequence of arterial stiffness is a worthy question to be considered and one that our cross-sectional methodology cannot definitely disentangle. On one hand, our results suggested that higher RHR and increasing heart rate trajectories over time were associated with higher arterial stiffness measured via baPWV. On the other hand, previous studies have shown that the assessment of arterial stiffness itself can be positively confounded by higher heart rate, thereby suggesting that the real-time measurement of baPWV may be influenced by the heart rate at the time of assessment or that greater arterial stiffness in itself induces higher heart rates. The idea that greater arterial stiffness causes higher heart rate makes physiological sense; therefore, the directionality or bidirectionality of our predictor and outcomes may be much more complex than our analyses suggest. Our study methodologies may be limited in that they cannot discern these potential interpretations; however, regardless of the direction or type of the interpretation, the observation that higher heart rate and increasing heart rate over time are associated with greater arterial stiffness is robust in our current study and in many smaller studies conducted before ours.

Although RHR trajectories were significantly associated with altered baPWV levels in age-stratified analyses, the association seemed to be more pronounced in elderly participants, relative to those with younger age. Previous studies regarding whether age modified the association between RHR and cardiovascular events or risk factors generated inconsistent results. For example, 2 previous studies reported that the associations between faster RHR and risk of hypertension and diabetes mellitus were stronger in participants with younger age. In contrast, in another study regarding total and cardiovascular disease mortality, the interaction between age and (13% to 17%) protects endothelium-dependent vasorelaxation, although no human studies have been performed to investigate whether there is any benefit of slowing RHR as a primary prevention strategy of cardiovascular disease. Our analysis adjusted for the potential confounding factors, including medications that can affect RHR and PWV, and physical activities that can...
RHR was not significant. In this context, further studies are warranted to examine whether the observed significant interaction between age and RHR trajectories in relation to arterial stiffness reflected true biological effects or was because of chance.

The advantages of our study are the large number of participants and repeated RHR measurements for a long period. Our study has a few limitations. Our study population only included individuals from the Kailun cohort, Tangshan community. More studies in the general population with different ethnic, education, and cultural background may be needed to make the study results more generalizable. Our study should be considered as a cross-sectional analysis because we did not assess baPWV repeatedly. The direction of the observed association, thus, cannot be inferred. Furthermore, because the baPWV assessments were completed in all participants in 2016, it remains to be seen whether the RHR pattern and its potential effect on baPWV can predict future risks of cardiovascular events. Longer follow-up is needed.

In conclusion, in this large community-based cohort, we found that RHR trajectory pattern is an independent risk factor for accelerated arteriosclerosis. Further longitudinal studies are warranted to examine whether RHR is associated with subsequent changes in arteriosclerosis status.

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Disclosures
None.

Table 3. Mean Difference and 95% Confidence Intervals in baPWV According to the Resting Heart Rate in Cumulative Average, Increase Rate, and Variability of Heart Rate From 2006 to 2010

<table>
<thead>
<tr>
<th>Range, bpm</th>
<th>&lt;60</th>
<th>61 to 70</th>
<th>71 to 80</th>
<th>81 to 90</th>
<th>&gt;90</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean difference</td>
<td>0 (reference)</td>
<td>47.8 (18.1 to 77.5)</td>
<td>91.8 (61 to 123)</td>
<td>139 (103 to 174)</td>
<td>217 (171 to 264)</td>
</tr>
<tr>
<td>P trend</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| Range, bpm per year | <−2.24 | −2.25 to 0.49 | −0.5 to 0.74 | 0.5 to 2.5 | >2.5 |
| Mean difference | 0 (reference) | 32.1 (16.7 to 47.6) | 48.9 (32.9 to 64.9) | 64.3 (48.1 to 80.5) | 111 (94.4 to 128) |
| P trend | <0.001 |

| Range, bpm | <2.30 | 2.31 to 4.23 | 4.24 to 6.10 | 6.11 to 9.18 | >9.19 |
| Mean difference of baPWV | 0 (reference) | 14 (−1.08 to 29.2) | 6.32 (−8.82 to 21.5) | 9.27 (−6.06 to 24.6) | 30.5 (15.1 to 45.8) |
| P trend | <0.001 |

dbaPWV indicates brachial–ankle pulse wave velocity. The values are adjusted for age, sex, smoking status (current, past, or never), alcohol intake status (current, past, or never), education status (illiteracy or elementary school, middle school, or college/university), physical activity status (never, sometimes, or active), average monthly income of each family member (<500, 500 to 3000, or ≥3000 Y), body mass index, use of antihypertensive agents (yes/no), hypertension status (yes/no), diabetes mellitus status (yes/no), and average serum concentrations of triglycerides, high-density lipoprotein cholesterol, total cholesterol, and high-sensitivity C-reactive protein during 2006 to 2010.

References


**Highlights**

- In this large community-based cohort including 12,554 Chinese participants who were free of cardiovascular diseases and cancer, we identified 5 distinct resting heart rate (RHR) trajectory patterns based on their 2006 status and on the pattern of change during 2006 to 2010.
- We found that individuals with elevated–stable RHR trajectory pattern were ≈3 times more likely to have arterial stiffness in 2010 to 2016, as assessed by brachial–ankle pulse wave velocity ≥1400 cm/s, relative to individuals with the low–stable RHR trajectory pattern.
- We also observed that a higher average RHR, a higher annual RHR increase rate, and a higher RHR variability were all associated with a higher risk of having arterial stiffness.
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Correction to: Resting Heart Rate Trajectory Pattern Predicts Arterial Stiffness in a Community-Based Chinese Cohort

In the article by Chen et al, “Resting Heart Rate Trajectory Pattern Predicts Arterial Stiffness in a Community-Based Chinese Cohort,” which published in the February issue of the journal (*Arterioscler Thromb Vasc Biol*. 2017;37:359–364. DOI: 10.1161/ATVBAHA.116.308674), a correction was needed.

The first author’s name was spelled incorrectly. The correct name is Shuohua Chen.

The authors apologize for the error.

This correction has been made to the current online version of the article, which is available at http://atvb.ahajournals.org/content/37/2/359.

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*Arterioscler Thromb Vasc Biol* is available at http://atvb.ahajournals.org DOI: 10.1161/ATV.000000000000047
Materials and Methods

**Study Design and Participants**

The Kailuan study is an ongoing cohort study, based on the Kailuan community in the city of Tangshan, China, aiming to investigate risk factors associated with common chronic diseases, such as myocardial infarction, stroke and cancers. Detailed information regarding study design and procedures was published previously. In brief, between 2006 and 2007, a total of 101,510 adult participants, including 81,110 men and 20,400 women, were recruited from 11 hospitals in the Kailuan community. All participants underwent questionnaire assessment, clinical examinations and laboratory tests upon enrollment and were followed up every two years.

Study samples of the current analysis included 17,156 Kailuan participants with PWV assessment between 2010 and 2016 that were initially designed to address various chronic diseases/conditions and their indicators, including asymptomatic polyvascular abnormalities, peripheral arterial disease, aging, and maternal health. Relative to those without PWV data (n=84,354), participants with PWV data were younger (46.5 vs 53.0 y), had a larger proportion of women (36.5% vs 16.7%), but had similar RHR (73.5 vs 73.9 bpm). In the current analysis, we excluded 3,195 participants without HR measurement in 2006 or 2008 or 2010. We further excluded 734 participants with self-reported arrhythmia or arrhythmia documented by a 12-lead electrocardiogram, 105 participants who were taking beta blockade agents, and 568 participants who had a diagnosis of myocardial infarction, stroke or cancer in or prior to 2010. A total of 12,554 participants were included in our analysis of the association between RHR trajectory pattern and baPWV (flowchart of the participants exclusion was shown in Figure 1). Information
on demographic characteristics, medical co-morbidities, home medications (e.g. beta-blockers), lifestyle factors (e.g. smoking, alcohol consumption, and physical activities) was collected via questionnaires. Physical examinations (e.g. RHR assessment) were conducted by trained field workers during each visit. Laboratory tests, including total cholesterol, triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, glucose, high sensitive C-reactive protein, were performed by auto-analyzer (Hitachi 747; Hitachi, Tokyo, Japan) at the central laboratory of Kailuan hospital. The study protocol was approved by the Ethics Committee of the Kailuan Hospital, in compliance with the guidelines of the World Association Declaration of Helsinki. All participants provided written informed consent.

Assessment of RHR

In 2006, 2008 and 2010, trained field workers (nurses and physicians) conducted face-to-face surveys and performed the physical examinations. After being seated for at least 5 minutes, HR was recorded based on the results of a 10-second 12-lead electrocardiogram performed with participant in a supine position. The number of R-R intervals (number of QRS complexes -1) was divided by the time difference between the first and last heartbeat, and the results were converted to beats per minute (bpm).

Assessment of baPWV

baPWV was assessed by BP-203 RPE III networked arteriosclerosis detection device [Omron health medical (China) Co., LTD] following the manufacturer’s recommendations, which was performed by specially trained physicians and nurses. Measurements were taken between 7AM
and 9AM on the examination day. Smoking and drinking of caffeinated drinks or alcohol were prohibited for at least 3 hours, and exercise was prohibited for at least 30 minutes before baPWV measurements. After being seated for at least 5 minutes in a room with temperature controlled between 22°C and 25°C, participants were asked to lay down on the examine table in a supine position and keep quite during the measurement. Cuffs were wrapped on both arms and ankles. The lower edge of the arm cuff was positioned 2-3 cm above the transverse striation of cubital fossa, while the lower edge of the ankle cuff was positioned 1-2 cm above the superior aspect of medial malleolus. The electrocardiogram electrodes were placed on both wrists, and a microphone for detecting heart sounds was placed on the left edge of the sternum.

**Statistical Analysis**

All analyses were conducted using SAS, version 9.3 (SAS Institute, Inc., Cary, North Carolina, USA). Latent mixture modeling (PROC TRAJ) was used to identify subgroups that share similar underlying HR trajectories. Model fit was assessed using the Bayesian Information Criterion (BIC). We initiated a model with five trajectory patterns, which was identified best fit, and then compared the BIC to that with 4, 3, 2, and 1, respectively. We used multivariate regression models to estimate the association between five HR trajectories and baPWV levels, after adjustment for potential cofounders including age, sex, smoking status (current, past or never), alcohol intake (current, past, or never), education (illiteracy or elementary school, middle school, or college/university), physical activity (never, sometimes or active), average monthly income of each family member (<500, 500-3000, or ≥ 3000 ¥), body mass index, use of antihypertensive agents (yes/no), hypertension status (yes/no), diabetes mellitus status (yes/no), and average serum concentrations of triglycerides, high-density lipoprotein cholesterol, total cholesterol, and
log-transformed high sensitive C-reactive protein during 2006-2010. We explored potential interactions between the RHR trajectories and age (y) and sex, in relation to baPWV levels, after adjusting for aforementioned covariates.

As secondary exposures, we also calculated cumulative average RHR (average of all available RHR values during the 4-year period), annual RHR increasing rate (the slope of the simple linear regression model in which a RHR value was the response variable and follow-up duration was the independent variable) and RHR variability (as assessed by standard division) during 2006-2010, and examined their associations with bpPWV levels.

We also used logistical regression model to calculate odds ratios (ORs) and their 95% confidence intervals (95%CIs) for having arterial stiffness (bpPWV>1400 cm/s), across the RHR categories, after adjustment for aforementioned covariates. Previous studies suggested that a cutoff value of 1400 cm/s for baPWV could be used for screening participants with high cardiovascular risks, and was recommended in the guideline for cardiovascular disease presentation in China.


In this community-based study including 12,554 Chinese adults, we observed that resting heart rate trajectory patterns over 4 years were associated with their future risk of having arterial stiffness, as suggested by brachial-ankle pulse wave velocity $\geq 1400$ cm/s.