Clinical Trial/Experimental Study

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Association of elevated resting pulse rate with increased risk of hypertension development in children

A prospective study in Suzhou, China

Jia Hu, MM[a,*], Hui Shen, MM[a], Guang-Ping Chu, MM[b], Han Fu, MM[c], Fei-Fei Huang, MM[a], Yan-Min Zheng, MM[a], Di Han, MM[a], Yi-Kai Zhou, MM[d], Qi Wang, MD[e], Bo Wang, MD[a], Chen-Gang Teng, MM[a], Fang Liu, MM[a], Hai-Bing Yang, MD[a,*]

Abstract

Background: Elevated resting heart rate (RHR) or resting pulse rate (RPR) is associated with increased risk of hypertension development. However, information is limited to adults. The purpose of this study is to analyze this association among Chinese children in a prospective design.

Methods: A total of 4861 children who participated in the Blood Pressure Surveillance Program (2011–2017) were selected in this research. To investigate the association between RPR and hypertension development, children were divided into 4 groups according to the quartiles of RPR at baseline. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated using logistic regression model.

Results: Over a mean follow-up of 3.0 ± 0.1 years, there were 384 cases of incident hypertension. Compared to boys and girls in the 1st quartile, those in the 4th quartile were 1.73 (95% CI 1.13, 2.65), 2.22 (95% CI 1.43, 3.45) times more likely to have hypertension, respectively. Every 10 bpm increase in RPR was associated with a 26% greater risk of hypertension development in boys (OR: 1.26; 95% CI 1.10, 1.44), while this risk was 1.28 (95% CI 1.13, 1.44) in girls. Baseline blood pressure (BP) and body mass index (BMI) did not have significant interactions with RPR on risk of hypertension development.

Conclusion: This study confirms the relationship between elevated RPR and increased risk of hypertension development in children, independent of confounders including baseline BP and BMI. An elevated RPR could be considered as a risk factor for the assessment of hypertension, no matter from a clinical setting or a public health perspective.

Abbreviations: BMI = body mass index, BP = blood pressure, CI = confidence interval, OR = odds ratio, RPR = resting pulse rate, WC = waist circumference, WGOC = Working Group of Obesity in China.

Keywords: adolescents, blood pressure, body mass index, cardiovascular risk factor, children, hypertension, resting pulse rate

1. Introduction

Childhood hypertension is a serious public health problem worldwide, especially in China.[1,2] Importantly, numbers of studies have suggested that the development of hypertension can start in childhood, children with elevated blood pressure (BP) are more likely to become hypertensive adult.[3–6] It has also been shown that children and adolescents with high BP already have evidence of early target organ disease, including left ventricular

Editor: Masanari Kuwabara.

JH and HS contributed equally and shared first coauthorship to this work.

Authorship: JH and HS were the researchers responsible for the collection, analysis, and interpretation of data, and also for drafting the manuscript. GPC, HF, QW, and FL were responsible for the analysis and interpretation of data. FFH, YMZ, DH, and BW were involved in the collection of data as well as the critical review of the paper. YKZ, CGT, HBY, and JH conceived of the study, participated in its design, coordinated the study, and reviewed the manuscript for important intellectual content.

Funding/support: This study was supported by the Youth Program of Reinvigorating the Health through Science and Education in Suzhou, China (kjxw2015035).

The authors have no conflicts of interest to disclose.

[a] Suzhou Center for Disease Prevention and Control, [b] Health Center for Women and Children of Gusu District, Suzhou, Jiangsu, [c] Xi'an Center for Disease Control and Prevention, Xi'an, Shaanxi Province, [d] MOE Key Lab of Environment and Health, Institute of Environmental Medicine, [e] Department of Epidemiology and Biostatistics, School of Public Health, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, China.

[*] Correspondence: Jia Hu, Hai-Bing Yang, Suzhou Center for Disease Prevention and Control, 72 Sanxiang Road, Suzhou, Jiangsu 215004, China (e-mail: hujia200606@163.com, yhbing111@163.com).

Medicine (2017) 96:32(e7696)

Received: 31 March 2017 / Received in final form: 10 July 2017 / Accepted: 11 July 2017

http://dx.doi.org/10.1097/MD.0000000000007696

hypertrophy and increased carotid intima-media thickness.[7,8] Target organ disease in adolescents would be associated with an increase risk of cardiovascular morbidity and mortality in adults.[9,10] Unfortunately, the prevalence of hypertension in Chinese children and adolescents has been increasing dramatically from 7.6% in 1993 to 13.8% in 2009.[11] Recognizing factors which were associated with BP and hypertension would improve our understanding of risk identification, and early targeted intervention would help to prevent and control hypertension development in high-risk children and adolescents.

Elevated resting heart rate (RHR) or resting pulse rate (RPR), which has gained attention as a potential clinical measurement, is a risk factor for cardiovascular disease.[12–14] Previous epidemiological studies have examined that elevated RHR/RPR is associated with cardiovascular events and mortality.[15,16] The relationship between RHR/RPR and hypertension has also been established among adults and children in numbers of cross-sectional studies.[17–22] Meanwhile, limited prospective studies conducted in adults have also demonstrated the association between increased RHR/RPR and high risk of hypertension development.[23,24] In Kailuan cohort study including 31,507 participants, Wang et al[23] examined the association between RHR and new-onset hypertension. With a mean follow-up period of 3.5 years, every increase of 10 beats per minute (bpm) in RHR was associated with an 8% increase in hypertension development. Compared with participants in the lowest quartile (RHR ≤ 66 bmp), those in the highest RHR quartile (RHR ≥ 78 bmp) were 1.16 times more likely to develop hypertension (hazard ratio 1.16; 95% confidence interval [CI] 1.11–1.23).

To our knowledge, despite the high prevalence of hypertension in Chinese children, the association of RHR or RPR with hypertension has not been studied in a prospective design. As we known, RHR is usually equal or close to the pulse measured at any peripheral point except in person with related cardiovascular disease. Considering the simplicity measurement and cost effectiveness of RPR, we conducted this study in a large population of Chinese children to prospectively observe potential association between RPR and hypertension development during follow-up periods, and explore whether elevated RPR was associated with increased risk of hypertension development, independent of confounders including body mass index (BMI) and BP value at baseline.

2. Materials and methods

2.1. Study areas and population

All participants in this article were selected from Blood Pressure Surveillance Program (BPSP), which aims to explore and evaluate relevant risk factors for hypertension in children. The BPSP started in 2011, the 1st follow-up was conducted in 2014 and the 2nd follow-up will be carried out in 2017. This program was conducted in 10 junior high schools from 5 districts in Suzhou of Jiangsu province, eastern of China. Students in grades 7 to 8 aged 12 to 14 years were recruited during the 2011 academic year. Detailed descriptions of the study design and study population were reported previously.[25] In this paper, we focus on the relationship of RPR to the prevalence of hypertension based on surveillance results of first 2 periods (2011 and 2014). Hypertensive subjects at baseline (n = 586) and subjects without a complete set of RPR recordings (n = 18) were excluded from the study. Finally, available data for 4861 participants were collected. Written informed consent form was obtained from children and their parents. This study was approved by the Ethics Committee of Tongji Medical College of Huazhong University of Science and Technology.

2.2. Measurements and definitions

Weight and height were measured with children in light clothing and without shoes. BMI was calculated as weight in kilograms divided by square of height in meters (kg/m^2). The age- and gender-specific BMI cutoff points recommended by the Working Group on Obesity in China, which was widely applied for Chinese children, were used to define overweight and obesity.[26] In this study, we merged overweight and obese children into abnormal BMI group.

RPR and BP were taken in a sitting position after each subject had rested for at least 15 minutes. The radial pulse was measured for 30 seconds, then multiplied by 2 and used as RPR.[27] Systolic BP (SBP) and diastolic BP (DBP) were measured using a mercury sphygmomanometer. BP was measured on the right arm with an appropriately sized cuff. SBP was recorded as the 1st Korotkoff sound and DBP as the 5th Korotkoff sound. In order to ensure accuracy of results, 3 readings of BP and RPR were carried out, which were completed within 1 month. Mean of 3 readings for RPR and BP were used in all analyses. The age- and gender-specific BP cutoffs in Chinese children and adolescents were used to define hypertension. In this definition, hypertension was defined as SBP and/or DBP at or above 95th percentile for age and gender.[28] Detailed methods were described previously.[25]

All measurements were performed by well-trained health professionals using the same type of apparatus and following the same procedures.

2.3. Statistical analysis

Continuous variables (age, weight, height, BMI, SBP, and DBP) were described as means ± standard deviation, while categorical variables (hypertension) were described as numbers and percentages. To study the association of RPR and hypertension, participants were divided into 4 groups according to RPR quartiles of boys and girls at baseline, respectively. Analysis of covariance was used to compare differences in age, anthropometric measurements, RPR, and BP among these 4 groups. The odds ratios (ORs) with 95% CIs for risk of hypertension development according to RPR groups were calculated using logistic regression model. Model 1 was the crude model. Age was adjusted in model 2. In model 3, we adjusted for age and BMI. Model 4 additionally included BP level at baseline, in addition to variables mentioned in model 3. The risk of hypertension development for every 10 bpm increase in RPR was also estimated. A further regression analysis was done to investigate the joint effects of RPR and baseline BP on the risk of hypertension development. The study children were divided into normotensive group (SBP and/or DBP <90th percentile for age and gender) and prehypertensive group (90th percentile ≤SBP and/or DBP <95th percentile for age and gender).[28] We additionally analyzed the joint effects of RPR and BMI at baseline, participants were divided into normal BMI group (NB) and abnormal BMI group (AB) according to BMI at baseline. All the interactions were analyzed by multiplicative binary logistic regression. Differences with *P*-values ≤0.05 (2-tailed) were considered to be statistically significant. All analyses were conducted using SPSS version 20 (SPSS Inc., Chicago, IL).

3. Results

A total of 4861 participants were included in the final analysis, and 2448 (50.4%) were boys. The mean age was 13.2±0.7 years, and mean RPR was 84.7±11.9 bpm at baseline. The boys' and girls' baseline characteristics stratified by RPR quartiles are shown in Tables 1 and 2, respectively. The group of participants with higher baseline RPR had higher SBP and DBP than the group with lower RPR (Table 3). There was a significant positive dose–response relationship between RPR, SBP, and DBP ($P<.05$).

Over a mean follow-up of 3.0±0.1 years (median: 3.0 years; range: 2.9–3.2 years), there were 384 cases of incident hypertension. The incidence rate of hypertension was 7.23% in boys, while 8.66% of girls have developed into hypertension. The incidence rate increased significantly with the rise in RPR

Table 1

Baseline characteristics for boys, stratified by the quartiles of resting pulse rate at baseline.

	Resting pulse rate, bpm				
	Q_1 <76	Q_2 76–83	Q_3 84–92	Q_4 >92	*P*
Number of participants, %	655 (26.76)	623 (25.45)	530 (21.65)	640 (26.14)	–
Age, y	13.36±0.67	13.24±0.69*	13.17±0.70*	13.17±0.70*	<.001
Height, cm	164.15±8.36	161.84±8.44*	161.52±8.51*	160.71±8.61*,†	<.001
Weight, kg	53.76±10.87	51.34±10.88*	52.73±12.21†	50.72±10.77*,‡	<.001
Body mass index, kg/m²	19.85±3.12	19.47±3.11*	20.06±3.59†	19.55±3.28‡	.007
Resting pulse rate, bpm	69.60±4.99	80.13±2.12*	87.58±2.32*,†	99.23±6.24*,†,‡	<.001
Systolic blood pressure, mm Hg	107.40±9.79	106.24±10.33*	107.77±10.01†	109.21±9.36*,†,‡	<.001
Diastolic blood pressure, mm Hg	64.54±7.36	65.31±7.22	67.30±7.10*,†	70.10±6.65*,†,‡	<.001

Data are presented as mean±standard deviation or percentage value.
* Significant with 1st group.
† Significant with 2nd group.
‡ Significant with 3rd group, $P<.05$.

Table 2

Baseline characteristics for girls, stratified by the quartiles of resting pulse rate at baseline.

	Resting pulse rate, bpm				
	Q_1 <78	Q_2 78–85	Q_3 86–94	Q_4 >94	*P*
Number of participants, %	666 (27.60)	643 (26.65)	508 (21.05)	596 (24.70)	–
Age, y	13.34±0.69	13.21±0.68*	13.15±0.63*	13.15±0.69*	<.001
Height, cm	158.94±6.16	158.38±5.92	157.97±6.14*	157.44±5.99*,†	<.001
Weight, kg	48.83±7.69	48.00±8.30	47.95±8.44	47.33±8.18*	.013
Body mass index, kg/m²	19.29±2.46	19.09±2.77	19.16±2.84	19.06±2.84	.435
Resting pulse rate, bpm	71.46±4.83	81.88±2.30*	90.01±2.34*,†	101.17±5.89*,†,‡	<.001
Systolic blood pressure, mm Hg	101.76±9.17	102.75±9.01*	104.40±8.90*,†	106.34±9.11*,†,‡	<.001
Diastolic blood pressure, mm Hg	65.58±6.92	67.38±6.62*	69.49±6.49*,†	71.45±6.08*,†,‡	<.001

Data are presented as mean±standard deviation or percentage value.
* Significant with 1st group.
† Significant with 2nd group.
‡ Significant with 3rd group, $P<.05$.

Table 3

Blood pressure over a 3 years follow-up, stratified by the quartiles of resting pulse rate at baseline.

	Resting pulse rate, bpm			
	Q_1	Q_2	Q_3	Q_4
Boys				
Systolic blood pressure, mm Hg*	116.98±8.82	116.44±8.95	116.83±8.31	118.10±9.85†,‡,§
Diastolic blood pressure, mm Hg*	68.83±7.93	69.99±7.63†	70.71±8.05†	72.26±7.73†,‡,§
Adjusted-systolic blood pressure, mm Hg‖	116.79±0.34	116.64±0.35	116.61±0.38	118.28±0.34*,†,‡
Adjusted-diastolic blood pressure, mm Hg‖	68.73±0.31	70.03±0.31†	70.71±0.34†	72.34±0.31†,‡,§
Girls				
Systolic blood pressure, mm Hg*	107.62±9.13	108.81±8.96†	109.05±9.66†	110.24±8.95†,‡,§
Diastolic blood pressure, mm Hg*	67.90±7.05	69.68±6.97†	70.33±7.08†	72.19±7.00†,‡,§
Adjusted-systolic blood pressure, mm Hg‖	107.50±0.35	108.86±0.35†	109.05±0.40†	110.33±0.37†,‡,§
Adjusted-diastolic blood pressure, mm Hg‖	67.84±0.27	69.70±0.28†	70.35±0.31†	72.22±0.29†,‡,§

* Data are presented as mean±standard deviation.
† Significant with 1st group.
‡ Significant with 2nd group.
§ Significant with 3rd group, $P<.05$.
‖ Data are presented as mean±standard error, adjusted for age and body mass index (BMI).

Table 4

Odds ratios (95% confidence intervals) for hypertension development, stratified by the quartiles of resting pulse rate at baseline.

RPR, bpm	Normal	Hypertension	Model 1	Model 2	Model 3	Model 4
Boys						
Q_1 <76 (N=655)	616 (94.0%)	39 (6.0%)	1.00	1.00	1.00	1.00
Q_2 76–83 (N=623)	589 (94.5%)	34 (5.5%)	0.91 (0.57, 1.46)	0.91 (0.56, 1.46)	0.96 (0.60, 1.56)	0.95 (0.58, 1.54)
Q_3 84–92 (N=530)	495 (93.4%)	35 (6.6%)	1.12 (0.70, 1.79)	1.11 (0.69, 1.78)	1.02 (0.63, 1.66)	0.95 (0.58, 1.54)
Q_4 >92 (N=640)	571 (89.2%)	69 (10.8%)	1.91 (1.27, 2.87)	1.89 (1.25, 2.85)	1.99 (1.31, 3.03)	1.73 (1.13, 2.65)
Per 10 bpm increase			1.31 (1.16, 1.49)	1.31 (1.15, 1.49)	1.33 (1.17, 1.51)	1.26 (1.10, 1.44)
Girls						
Q_1 <78 (N=666)	633 (95.0%)	33 (5.0%)	1.00	1.00	1.00	1.00
Q_2 78–85 (N=643)	590 (91.8%)	53 (8.2%)	1.72 (1.10, 2.70)	1.71 (1.09, 2.69)	1.73 (1.10, 2.72)	1.69 (1.07, 2.66)
Q_3 86–94 (N=508)	458 (90.2%)	50 (9.8%)	2.09 (1.33, 3.30)	2.08 (1.32, 3.28)	2.08 (1.31, 3.29)	1.89 (1.19, 3.01)
Q_4 >94 (N=596)	525 (88.1%)	71 (11.9%)	2.59 (1.69, 3.98)	2.58 (1.67, 3.96)	2.62 (1.70, 4.03)	2.22 (1.43, 3.45)
Per 10 bpm increase			1.34 (1.23, 1.46)	1.33 (1.22, 1.45)	1.34 (1.23, 1.46)	1.26 (1.16, 1.38)

Model 1, unadjusted. Model 2, adjusted for age. Model 3, adjusted for age and body mass index. Model 4, adjusted for age, body mass index, and blood pressure level at baseline. bpm = beats per minute, RPR = resting pulse rate.

(Table 4). The ORs and 95% CIs for risk of hypertension development according to the RPR quartiles were explored using logistic regression model in all 4 models. In model 4, compared to boys and girls in the 1st quartile, those in the 4th quartile were 1.73 (95% CI 1.13, 2.65) and 2.22 (95% CI 1.43, 3.45) times more likely to have hypertension, respectively. Every 10 bpm increase in RPR was associated with 26% (95% CI 1.10, 1.44) greater risk of hypertension development in boys; while this increased risk was 28% for girls (95% CI 1.13, 1.44).

In order to explore the baseline level of BP and BMI on the association between RPR and hypertension, the baseline BP-stratified and BMI-stratified ORs were analyzed (Figs. 1–2). There were no interactions between RPR and BP (boys: $P=.538$, girls: $P=.112$) and BMI (boys: $P=.668$, girls: $P=.594$) at baseline, respectively. Figure 1 clearly shows that those with high RPR are at higher risk of hypertension development than those with a low RPR, even within the same BMI groups. Similarly, within different BP groups, those with high RPR also have higher ORs of hypertension development than those with a low RPR (Fig. 2).

4. Discussion

In this school-based, large sample, and well-standardized prospective study, a significant association between elevated RPR and increased risk of hypertension development was observed. This association still existed after adjusting for BMI and BP at baseline. The finding suggests that elevated RPR is associated with increased risk of hypertension development, independent of potential confounders. Considering the simplicity measurement and cost effectiveness of RPR, it may be used as an indicator of increased risk for hypertension, no matter from a clinic setting or a public health perspective.

The significant association between RHR/RPR and risk of hypertension has been previously identified in a number of different studies in adults.[18,19,27] For example, 1 cohort study conducted in 21,873 adults was to examine the association of RHR with incident hypertension. After a median of 4 years follow-up, 37.4% of participants developed hypertension. Compared to participants with the lowest RHR (RHR < 70 bpm), participants in the highest group (RHR >85 bpm) had a higher hazard ratio (1.15, 95% CI 1.08, 1.23) of hypertension after adjustment for relevant confounders.[24] Wang et al also examined the association between RHR and hypertension in Kailuan cohort study including 31,507 participants. With a mean follow-up period of 3.5 years, every increase of 10 bmp in RHR was associated with an 8% increase in new on-set hypertension. Participants in the highest RHR quartile (≥78 bmp) were 1.16 (95% CI 1.11, 1.23) times more likely to develop hypertension as compared with participants in the lowest quartile (≤66 bmp).[23] The relationship of RHR with BP was also indentified in the World Health Organization-Cardiovascular Disease and Alimentary Comparison study, which included 8541 adults aged 48

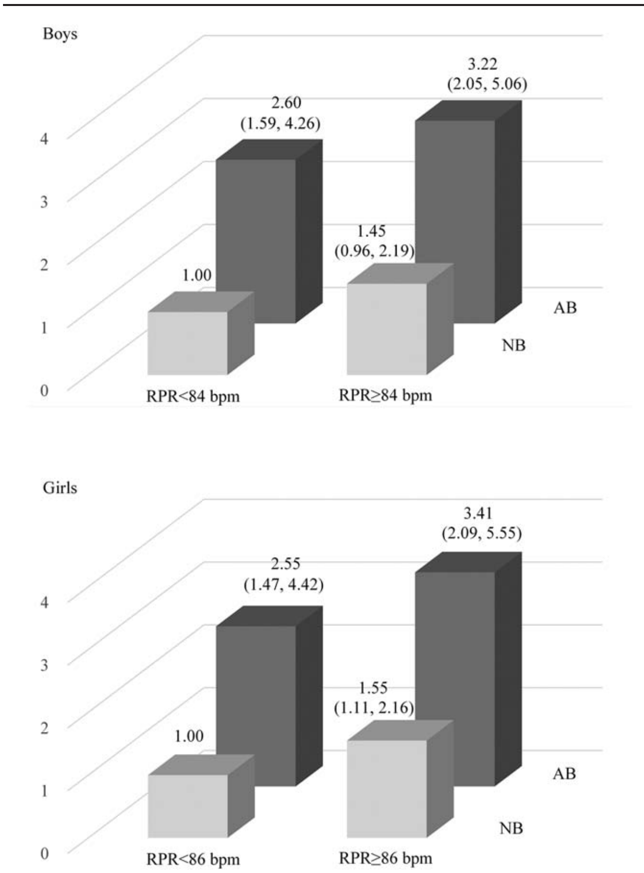

Figure 1. Odds ratios (95% confidence intervals) for the association between resting pulse rate and hypertension development, stratified by level of blood pressure at baseline. Adjusted for age, sex, and body mass index at baseline.

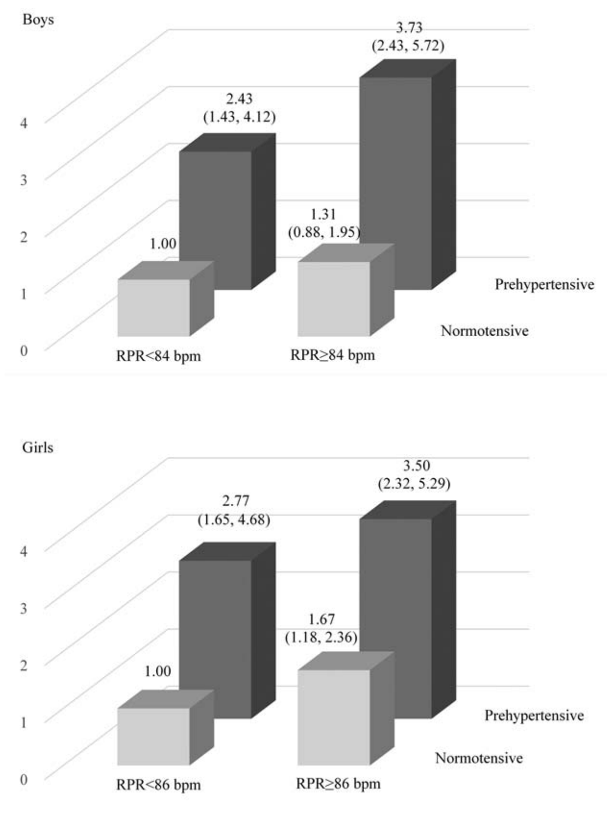

Figure 2. Odds ratios (95% confidence intervals) for the association between resting pulse rate and hypertension development, stratified by level of body mass index at baseline. Adjusted for age, sex, and body mass index at baseline.

to 56 years. Every 1 unit increase in RHR would bring a 0.27 mm Hg increase of SBP and a 0.09 mm Hg increase of DBP.[19]

The similar relationship between RHR/RPR and BP and hypertension focused on children and adolescents was also revealed in limited researches. A cross-sectional study was carried out in a sample of 356 male children and adolescents aged 8 to 18 years. Hypertensive children and adolescents presented elevated RHR (normal BP: 76.4 ± 10 bmp; elevated BP: 83.6 ± 13 bmp; $P = .001$). Children in the 4th quartile (≥86 bmp) had a higher OR (4.71, 95%CI 2.01, 11.11) than those with in the 1st quartile (RHR <70 bpm).[20] Another large study including 91,762 participants aged 9 to 18 years explored the association between BP and RPR according to waist circumference (WC), and it demonstrated that with 1 standard deviation increase in RPR, BP changed from 2.22 (95% CI 1.51, 2.93) to 3.58 mm Hg (95% CI 2.54, 4.62) in small WC group and 1.83 (95% CI 1.10, 2.56) to 4.23 mm Hg (95% CI 3.38, 5.09) in large WC group, respectively.[21] Although these authors confirmed the association between RHR/RPR and prevalence of hypertension in children and adolescents, these studies were mostly small sample size or cross-sectional design.

Our study confirms the existence of a relationship of elevated RPR to increased BP and high risk of hypertension development in a prospective children study. As we known, RHR is usually equal or close to the pulse measured at any peripheral point except in person with related cardiovascular disease. We believe our findings can fill the blank of relevant children study mentioned above. Among those relevant studies, measurements of RHR or RPR were distinct, descriptions of dose–response relationship between RHR/RPR and hypertension were different, and participants' age varied. Thus, it is difficult to compare results of the present investigation with studies mentioned above. But, we have reasons to believe that our findings together with above studies confirm the relationship between high RPR and increased risk of hypertension development in children and adolescents.

The exact mechanism has not been fully elucidated, previous studies reported different plausible explanations of biologic mechanisms for the relationship between elevated RPR and increased risk of hypertension.[14,29,30] RPR was widely used as an indicator of sympathetic activation.[31] The heightened sympathetic activity may explain why subjects with an elevated RPR tend to have an increased risk for hypertension development in later years. Several pathways have been speculated to mediate the effects of sympathetic over-activation on BP. These include arterial stiffness, adrenergic stimulation, and activation of inflammatory pathways.[30] The increased sympathetic tone also causes an increase in cardiac output, meanwhile provides sustained pulsatile stress to the blood vessels, which will lead to an increased arterial stiffening and arterial hypertension.[17,32] But these explanations were mostly applied to adults. Notwithstanding, the relationship between arterial stiffness and BP variability in children and adolescents has also been demonstrated, detailed mechanism in children needs to be explored by further research.[33,34]

The results of ORs of hypertension needed to be noticed when participants were divided into normotensive and prehypertensive groups. Positive association between RPR and risk of hypertension development persisted in children with different baseline BP groups. Within different levels of baseline BP, participants who had high RPR had higher risk of hypertension development than those with low RPR. Our findings indicate that the association between RPR and risk of hypertension development does not vary by baseline BP level. As we know, no study has been conducted to assess this association between RHR or RPR and risk of hypertension development in children with different levels of baseline BP. This finding is consistent with results of 2 limited cohort study conducted in adults.[23,24] Meanwhile, a statistically significant positive link between high RHR/RPR and high arterial stiffness has also been demonstrated, even after adjustment for BP.[35] This consistent conclusion is very important in demonstrating the relationship between RPR and risk of hypertension development, because baseline BP is also a strong determinant of future hypertension development. It highlights the role of RPR in hypertension development.

As we know, it is the first prospectively design to examine the potential associations between RPR and risk of hypertension in Chinese children and adolescents. The main strengths of our study are its prospective design, large sample size, and repeated measurements of BP and RPR, which would provide good quality control. Meanwhile, we have to admit that several limitations exist. First, this study lacked some potential confounding parameters like living environment, nutritional status, dietary pattern, and physical activity that may be associated with development of hypertension. Second, relevant information about pubertal stage of participants was not collected. Effect of sexual maturation on RPR has been demonstrated in previous researches. Third, this study lacked biological sample data such as plasma glucose and lipids level in the adjusted model. Finally, the participants in this prospective study were only from Suzhou, a city of eastern China. Considering limitation of participants, findings in this study could not be directly applied for other Chinese children with different backgrounds and lifestyles.

In conclusion, this present investigation is the first attempt to use a prospective design in a large sample size to explore the association between RPR and risk of hypertension development in China. Our findings support that elevated RPR is significantly associated with hypertension development among Chinese children. More importantly, this association was maintained after adjusting for potential confounders of baseline BP and BMI. No matter from a clinical setting or a public health perspective, an elevated RPR could be considered as a risk factor for risk assessment of hypertension among children and adolescents.

Acknowledgments

The authors thank all participating children and their parents for their collaboration. The authors also thank Youth Program of Reinvigorating the Health through Science and Education in Suzhou, China (kjxw2015035).

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