Association between systolic blood pressure trajectories and hypertension risk at late adolescence: results from 10-year longitudinal follow-up in Chinese boys

Xijie Wang, Bin Dong, Sizhe Huang, Zhaogeng Yang, Jun Ma, Jie Hu

ABSTRACT

Objective To identify various systolic blood pressure (SBP) trajectories in Chinese boys between 7 and 18 years of age, and to explore their high blood pressure (HBP) risk in their late adolescence years.

Design and settings A population-based cohort study in Guangdong, China.

Participants 4541 normal tensive boys who started primary school in 2005 in Zhongshan, Guangdong were included.

Outcomes Blood pressure and relevant measurements were obtained by annual physical examinations between 2005 and 2016. HBP was defined by SBP or diastolic blood pressure ≥95th percentile for children under 13, and BP ≥130/80 mm Hg for children ≥13 years old. Logistic regression for panel data and log-binomial regression model was used to estimate the risk of HBP among SBP trajectory groups.

Results Four distinct SBP trajectory groups via group-based trajectory modelling: low stable (13.0%), low rising (42.4%), rising (37.4%) and high rising (7.3%). The overall incidence rates of HBP during the follow-up ranged from 40.24 (95% CI 36.68 to 44.19)/1000 person-years in the low stable group to 97.08 (95% CI 94.93 to 99.27)/1000 person-years in the high rising group. Compared with children with low stable SBP, those of other SBP trajectories suffered 3.05 (95% CI 2.64 to 3.46) to 4.64 (95% CI 4.18 to 5.09) times of higher risk of HBP in their late adolescence, regardless of their age, body mass index and BP level at baseline.

Conclusions Subgroups of SBP trajectories existed in Chinese boys, and are related to hypertension risk at late adolescence. Regular physical examinations could help identify those with higher risks at the beginning of pubertal growth.

INTRODUCTION

Hypertension is a leading cause of mortality worldwide, and accounts for half of the cardiovascular disease (CVD) events in adults. Although the majority of paediatric population would not be diagnosed as hypertension, high-risk population could be asymptomatic, with their blood pressure (BP) gradually progressed to hypertension. Elevated BP has negative impact on children's cardiovascular system, and the damage could last through lifetime.

In this context, it is suggested that approaches that identifying those at greatest risk of developing hypertension in early life to be adopted to promote effective risk reduction, and to implement age-appropriate prevention and intervention strategies in paediatric population. Adolescents are at a critical transition from children to adults, whose BP levels could be affected by many developmental factors including intra-uterine, postnatal, familial, psychosocial and individual influences, making it difficult to recognise high-risk population before they have hypertensive symptoms. BP trajectory, however, provides a rather intuitive view on BP change, and may help to identify children with elevated hypertension risk.
Recent studies have shown that BP trajectory, especially systolic BP (SBP) trajectory, is one of the most important predictors of future cardiovascular morbidity and mortality. Patterns of BP trajectories in white and black children have been reported with several representative cohorts like the Dunedin Multidisciplinary Health and Development Study from New Zealand, Birth to Twenty from South Africa or the Georgia Stress and Heart (GSH) study from the United States. However, this information is limited on Asian children. As the Asian society is experiencing rapid growth in hypertension prevalence due to growing ageing populations and the subsequent incidence of hypertension-related haemorrhagic stroke is high, BP trajectories for Asian children may provide important information for developing region-specific strategies on disease prevention.

In this study, using physical examination data from primary and middle schools of Zhongshan city in Guangzhou province between 2005 and 2016, we aimed to identify latent groups of boys sharing SBP developmental trajectories from 7 to 18 years, and to describe the association between SBP trajectory groups and hypertension risk in their late adolescence.

MATERIALS AND METHODS
Data source
Datasets collected from the Zhongshan school physical examinations between 2005 and 2016 were used in this study. All students from municipal primary and secondary schools in Zhongshan, Guangdong, were required to have an annual physical examination. All assessments were conducted by qualified medical physicians from medical establishments, and the results of each examination were recorded immediately into computer system by school nurses after the examination. Students who started grade one between 2005 and 2006 were included in this study, and were assessed annually to their 16–18 years old. Details of the study recruitment was illustrated in online supplemental figure 1. The use of the present dataset has been approved by Zhongshan Health Care Centers for Primary and Secondary School. All personal information which could lead to identify the specific child was removed from the data before use.

Patient and public involvement
No patient was involved in the present study.

Measurements
Height was measured using the portable stadiometer (model TZG, China) to the nearest 0.1 cm, with students standing straight barefoot. Weight was measured with lever type weight scale (model RGT-140, China) to the nearest 0.1 kg with students wearing undergarments. Body mass index (BMI) was calculated as weight (kg)/height^2 (m^2).

BP was measured by auscultatory method with mercury sphygmomanometers (model XJ11D, China), and appropriate cuffs. Participants were asked to sit quietly for at least 5 min prior to the first reading. SBP was determined by onset of the first Korotkoff sound and diastolic BP (DBP) was determined by the fifth Korotkoff sound. BP was measured twice with 5 min gap between the two measurements from the right arm, and the average of SBP and DBP values were recorded. This process was repeated if the difference between the two measurements was ≥10 mm Hg (either for SBP or DBP).

High BP (HBP) during the follow-up was defined if the single-occasion measurement of BP ≥95th percentile for children under 13, and BP ≥130/80 mm Hg for children ≥13 years old. HBP at endpoint was defined with the BP outcomes of the last two measurements for each participant (when both measurements were defined as HBP).

Statistical analysis
The present study included a total of 38,518 measurements from 4,541 boys who were normal tensive at first measurement (baseline). Group-based trajectory modeling was performed to identify different trajectory groups of SBP. A censored normal model for continuous variables was conducted by sex with the following steps. First, a one-trajectory model was conducted to determine whether shapes of SBP trajectories were linear, quadratic or cubic according to the Bayesian information criteria (BIC). Second, the number of trajectory groups in the model was increased by one and these two steps were repeated until the best fit model was found. Model selection was mainly based on the absolute value of BIC. However, it was modified by (1) BIC decreased at least 20, (2) high mean posterior probability (>0.7) and (3) the odds of correct classification based on the posterior probabilities of group membership >5 for each group. Since the best model for boys and girls were different, only data of boys were analysed in the present study, and the best-fit model was cubic trajectories of four groups. The model fitting outcomes were displayed in online supplemental table 1.

Incidence rate and 95% CIs of HBP during the follow-up were calculated for each age. Logit regression for panel data was used to estimate HBP risk among four trajectory groups during the follow-up, while log-binomial regression model was used to evaluate the hypertension risk of the four groups at endpoint. Tendency for differences across trajectory groups was conducted with a linear trend test. Children’s age, living area (urban or rural), SBP, DBP, height and weight at baseline, as well as the difference between endpoint and baseline BMI z score (ΔBMI z score) were adjusted.

All analyses were performed using Stata V.14.0, and associations were considered significant when p<0.05.

RESULTS
According to the model fitting outcomes, a four-trajectory model with cubic specifications for all groups was
identified for boys. The means and 95% CIs of SBP were displayed in figure 1, and the trajectories were labelled as low stable (13.0% of participants), low rising (42.4%), rising (37.4%) and high rising (7.3%). Beginning at 7 years old, the four trajectories differed significantly from each other at all ages.

The characteristics at baseline as well as those during follow-up were displayed in tables 1 and 2. Children’s baseline height, weight, BMI z score, SBP and DBP were all significantly higher in those from higher SBP trajectory groups (all p values for trend <0.05). The average follow-up time was 8.3 (SD: 1.1) years, and the incidence rate of HBP ranged from 40.24 (95% CI 36.68 to 44.19)/1000 person-years in low stable group to 97.08 (95% CI 94.93 to 99.27)/1000 person-years in high rising group. The difference of BMI z score remained approximately the same from baseline to the endpoint survey.

Incidence rates and 95% CIs of HBP for each age were calculated and displayed in figure 2 by SBP trajectory group. A peak age of HBP incidence rate was discovered for each trajectory group, and that of lower SBP trajectory groups came earlier than those of higher trajectory groups. The incidence rate of HBP was constantly higher in the groups of higher SBP trajectory among all age groups, and enlarged divergence was observed with the increase of age.

The HBP risk during the follow-up, as well as HBP at endpoint, was also estimated among the four trajectory groups. Compared with low stable group, the HBP risk during the follow-up increased for 0.85 (95% CI 0.75 to 0.96) to 2.98 (95% CI 2.86 to 3.11) in crude model and for 0.85 (95% CI 0.74 to 0.95) to 2.95 (95% CI: 2.80 to 3.06) in adjusted model. The trend that children of higher SBP trajectory had higher risk of HBP during the follow-up was significant in both crude and adjusted models. No participants from low stable group were defined as hypertension at endpoint. Compared with low rising group, where 1.3% of the participants were hypertensive at endpoint, participants from rising group and high rising group faced 3.05 (95% CI 2.64 to 3.46) and 4.64 (95% CI 4.18 to 5.09) times higher risk of hypertension in their late adolescence, respectively. The results did not change with adjustment of baseline age, SBP, DBP, weight, height and Δ BMI z score (table 3).

**DISCUSSION**

Using the longitudinal data from annual physical examinations with an average follow-up of 8.3 years, we identified four distinct SBP trajectories in Chinese boys aged 7–18 years. According to the results, boys of the higher SBP trajectories had greater risk of hypertension during their childhood, and had 3–4 times higher risk of becoming hypertension in their late adolescence. To our knowledge, this is one of the first studies mapping SBP trajectory groups in Asian children, and estimating the long-term risk of hypertension in late adolescence by different SBP trajectory groups.

In 2015, researchers from New Zealand identified four distinct BP trajectories for SBP in a longitudinal birth...
cohort study, and the participants were tracked to 38 years old. The SBP trajectories between 7 and 18 years
of age were confirmed to exist in Chinese boys, and children in higher trajectory groups had significant higher risk of hypertension throughout their adolescence. Children's health status would have direct influence on their adulthood well-being.22 23 A large cohort of 2.3 million adolescents in Israel found that established hypertension at age 16–19 was independently associated with elevated stroke mortality in midlife.24 Hypertension at this age period was also found to be positively related to other cardiovascular and cerebrovascular events,22 25 and end-stage renal disease.26 By exploring the associations between SBP trajectories and end-stage renal disease,26 we found that subgroups with different SBP trajectories could be detected from their BP outcome in late adolescence. More importantly, we found that subgroups with different SBP trajectories could also predict their BP outcome in late adolescence.26

Table 2 Characteristics of participants during follow-up, by systolic blood pressure trajectory groups

<table>
<thead>
<tr>
<th>Variables</th>
<th>Overall</th>
<th>Low stable</th>
<th>Low rising</th>
<th>Rising</th>
<th>High rising</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean follow-up year, year (SD)</td>
<td>8.3 (1.1)</td>
<td>8.3 (1.2)</td>
<td>8.3 (1.1)</td>
<td>8.3 (1.1)</td>
<td>8.5 (1.1)</td>
<td>0.010</td>
</tr>
<tr>
<td>Incident HBP per 1000 person-years (95% CI)</td>
<td>71.17 (69.93 to 72.44)</td>
<td>40.24 (36.68 to 44.19)</td>
<td>66.41 (64.48 to 68.40)</td>
<td>85.20 (83.96 to 86.40)</td>
<td>97.08 (94.93 to 99.27)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HBP at endpoint, n (%)</td>
<td>584 (12.9)</td>
<td>0</td>
<td>25 (1.3)</td>
<td>369 (21.8)</td>
<td>190 (57.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Height, at end point, cm, mean (SD)</td>
<td>172.0 (5.9)</td>
<td>170.3 (5.7)</td>
<td>171.6 (5.9)</td>
<td>172.7 (5.7)</td>
<td>173.8 (5.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Weight at end point, kg, mean (SD)</td>
<td>60.9 (10.5)</td>
<td>53.9 (6.9)</td>
<td>58.5 (8.4)</td>
<td>63.7 (10.0)</td>
<td>72.4 (14.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI z score at end point, mean (SD)</td>
<td>−0.46 (1.15)</td>
<td>−1.20 (0.97)</td>
<td>−0.7 (1.02)</td>
<td>−0.13 (1.07)</td>
<td>0.64 (1.20)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ΔBMI z score*, mean (SD)</td>
<td>−0.13 (0.89)</td>
<td>−0.23 (0.84)</td>
<td>−0.15 (0.85)</td>
<td>−0.06 (0.92)</td>
<td>−0.16 (1.03)</td>
<td>0.002</td>
</tr>
<tr>
<td>SBP at end point, mm Hg, mean (SD)</td>
<td>120.8 (10.2)</td>
<td>108.7 (7.3)</td>
<td>117.5 (8.0)</td>
<td>126.7 (7.2)</td>
<td>132.0 (7.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DBP at end point, mm Hg, mean (SD)</td>
<td>67.6 (6.8)</td>
<td>63.9 (4.8)</td>
<td>66.4 (5.8)</td>
<td>69.3 (7.1)</td>
<td>72.0 (7.9)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

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were deemed as HBP if participants’ last two measurements were within the reference range of datasets from annual school health examinations. Risk factors of HBP development, such as lifestyle information, were unavailable. Future studies with adjusting for relevant risk behaviour information may provide further insights.

CONCLUSIONS
To conclude, the present study mapped four groups of SBP trajectories in Chinese boys aged 7–18 years old and estimated the risk of hypertension for different groups. These findings suggest that regular BP measurement could be used to identify children with elevated risk of hypertension in early age, namely at the start of puberty growth. Intervention strategies for high-risk children at or before this period could help to reduce the risk of hypertension in adolescence, as well as CVD risk in their adulthood.

Table 3 Hypertensive risks of Chinese boys aged 7–18 years from different systolic blood pressure trajectory groups (coefficients and 95% CIs)

<table>
<thead>
<tr>
<th>Trajectory group</th>
<th>High blood pressure during follow-up</th>
<th>High blood pressure at endpoint</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Crude model</td>
<td>Adjusted model</td>
</tr>
<tr>
<td>Low stable</td>
<td>0 (Reference)</td>
<td>0 (Reference)</td>
</tr>
<tr>
<td>Low rising</td>
<td>0.85 (0.75 to 0.96)</td>
<td>0.85 (0.74 to 0.95)</td>
</tr>
<tr>
<td>Rising</td>
<td>1.83 (1.73 to 1.93)</td>
<td>1.82 (1.71 to 1.92)</td>
</tr>
<tr>
<td>High rising</td>
<td>2.98 (2.86 to 3.11)</td>
<td>2.93 (2.80 to 3.06)</td>
</tr>
<tr>
<td>P for trend</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Baseline age, living area, baseline systolic and diastolic blood pressure, baseline weight and height, ΔBMI z score were covariates in the adjusted model.

*There were no hypertensive participants in the group of low stable trajectory at endpoint.

BMI, body mass index; NA, not available.
REFERENCES