Arterial stiffness in junior high school students: Longitudinal observations

Hiroshi Fujiwara,1 Hisakazu Nakajima,1 Fumio Inoue,1,4 Kitaro Kosaka,1 Hiroaki Asano3 and Kengo Yoshii2
Departments of 1Pediatrics and 2Mathematics and Statistics in Medical Sciences, Graduate School of Medical Science, and 3School of Nursing, Kyoto Prefectural University of Medicine, Hirokoji-Kawaramachi, Kamigyo, and 4Department of Education, Kyoto University of Education, Fukakusa, Fushimi, Kyoto, Japan

Abstract

Background: Early atherosclerotic change is found even in childhood, and there is an urgent need to clarify the factors causing childhood atherosclerosis and take preventive measures. Early detection of the contributing risk factors is crucial to facilitate preventive measures. Pulse wave velocity (PWV) is a widely used technique for the assessment of atherosclerosis in children.

Methods: Lifestyle questionnaire, brachio-ankle PWV (baPWV) and anthropometric data were obtained from junior high school students in an urban area of Japan between 2006 and 2008, from seventh to ninth grades.

Results: Mean baPWV increased from 867.4 ± 99.5 m/s to 944.5 ± 117.5 m/s in boys, and from 864.0 ± 99.5 m/s to 923.0 ± 101.3 m/s in girls. Obese students had higher baPWV than non-obese students in both genders across each grade. On logistic regression analysis of ninth grade student data, high baPWV was dependent on systolic blood pressure (SBP), time watching television (TV) and symptoms of depression and anxiety, whereas low baPWV was dependent on time playing video games, light exercise, sleep and indoor play, as well as good friendship and motivation.

Conclusion: Systolic blood pressure, time watching TV, and symptoms of depression and anxiety may contribute to arterial stiffness and be related to obesity in junior high school students.

Key words atherosclerosis, junior high school, lifestyle, longitudinal study, pulse wave velocity.
Cohlin, Tokyo, Japan). Following a resting period of 5 min, baPWV was measured in each arm simultaneously, and the mean baPWV was recorded. Body fat percentage (%) was measured using a bioelectrical impedance analyzer (SS-103, Sekisui Chemical, Tokyo, Japan). Percentage of overweight was calculated using the following equation:

\[
\text{Percentage of overweight(%) = \left(\frac{\text{measured weight} - \text{standard weight}}{\text{standard weight}}\right) \times 100}
\]

Standard weight was determined according to the mean age and height of each gender, in accordance with the Japanese school health report in the year 2000. Obese students were defined as those with percentage of overweight ≥20%. The lifestyle questionnaire was designed according to the Report of Surveillance of Health in School Children and Adolescents21 conducted by Japan Society of School Health, to which psychological factors and motivational status were added. Time for indoor play was defined as time reading books or listening to music in their room after school, excluding the time watching TV, and video games. Vigorous exercise was defined as exercise with lasting fatigue till the next day, and light exercise was defined as exercise without fatigue. These definitions were given in the questionnaire. Data were obtained from the same students as they progressed through school from the year 2006 (when they were in seventh grade) to 2008 (when they were in ninth grade). None of the students moved or dropped out during the 3 years of the study.

**Statistical analysis**

Statistical analysis was performed using SPSS 22.0 (IBM, Chicago, IL, USA). The impact of gender differences on baPWV was addressed by assessing the measured variables separately for each gender type. Means were compared using either t-test or analysis of variance (ANOVA) and Bonferroni post-hoc test. Difference in means in each grade was tested with repeated-measures ANOVA. Significance was defined as \( P < 0.05 \). Logistic regression analysis was used to assess the relationship between baPWV and the parameters measured in this study. The variable reduction method was applied to all of the variables measured.

**Results**

Table 1 lists the subject characteristics. There were significant gender differences in height, weight, waist size, waist/height ratio, percentage of overweight, body fat %, SBP, heart rate and sleep time (duration) across each grade. Gender differences in body mass index (BMI), DBP, and baPWV, however, were found only in ninth grade students. There were differences in height, weight, waist circumference, percentage of overweight, body fat %, BMI, heart rate, baPWV, ankle–brachial index (ABI) and time for sleep between genders across each grade. For both genders, decreased sleep time, time spent on vigorous exercise, time for games, and increase in the time studying were noted from the eighth grade to the ninth grade. Significant correlations were found in time studying versus time for video games and time watching TV in the ninth grade (time studying vs time for video games: boys, \( r = -0.139, P < 0.01 \); girls, \( r = -0.155, P < 0.01 \); time studying vs time watching TV: boys, \( r = -0.091, P < 0.01 \); girls, \( r = -0.117, P < 0.01 \)). Increase in the time studying was inversely related to the increase in time for video games (boys, \( r = -0.168, P < 0.01 \); girls, \( r = -0.128, P < 0.01 \)).

Brachio-ankle PWV was higher in obese students than in non-obese students in each gender and grade (Table 2). baPWV data were grouped by percentile and categorized into the following: G1, baPWV <25th percentile (low); G2, baPWV 25th–75th percentiles (normal); and G3, baPWV >75th percentile (high). In boys, high baPWV was associated with increases in weight, percentage of overweight, body fat %, blood pressure, and heart rate (Table 3). In girls, high baPWV was associated with increases in body fat %, blood pressure and heart rate (Table 3).

Depending on the change in baPWV in the 3 year period, students were divided into four groups: group A, normal to normal; group B, normal to high; group C, high to normal; and group D, high to high, whereby normal was defined as baPWV <75th percentile, and high as baPWV >75th percentile. SBP, DBP, and heart rate were significantly higher in group D than in group A for each gender and grade (Table 4). In boys, time watching TV was significantly higher in group D than in group A.

On logistic regression analysis, (i) baPWV was inversely associated with baPWV increment from the seventh grade to the ninth grade (Table 5); and (ii) baPWV in the seventh and eighth grade was predictive of baPWV in the ninth grade. On logistic regression analysis of baPWV data from students across all grades, OR was highest for baPWV in seventh grade students in both genders (boys: inverse OR, 3.24; girls: inverse OR, 3.51; Table 5). In boys, this was followed by weight (OR, 1.85), body fat% (inverse OR, 1.76), and BMI (OR, 1.68) in eighth grade students; and TV viewing duration (OR, 1.54), orthostatic dysfunction (OR, 1.52), and general fatigue (OR, 1.50) in seventh grade students. In girls, this was followed by study duration in seventh grade students (OR, 1.45), degree of concentration (OR, 1.42), motivation (inverse OR, 1.41), and weight (OR, 1.31) in eighth grade students, and having a pale face (inverse OR, 1.35) and time spent on vigorous exercise (OR, 1.33) in seventh grade students (Table 5).

Logistic regression analysis was used to identify indicators of high baPWV in the seventh grade (Table 6). In both boys and girls, high OR was noted for baPWV in the eighth grade (boys: OR, 3.90; girls: OR, 3.98) and baPWV in the seventh grade (boys: OR, 2.64; girls: OR, 3.71). In boys, eighth and seventh grade baPWV were followed by feeling sick at bathing in the eighth grade (OR, 1.80), time for video games in the eighth grade (inverse OR, 1.78), time for light exercise in the seventh grade (inverse OR, 1.62), SBP in the seventh and eighth grade (OR, 1.62, 1.60, respectively), sleep time in the seventh grade (inverse OR, 1.58), headache (OR, 1.56),
Table 1  Subject characteristics

| Gender   | Seventh grade | Eighth grade | Ninth grade | Among all grade |
|----------|---------------|--------------|-------------|----------------|
|          | n  | Mean  | SD  | P-value | Mean  | SD  | P-value | Mean  | SD  | P-value |
|          | Boys|    |     | vs girls† |        |     |         |        |     |         |
|          | Girls|  |    |          | Boys vs girls† |        |         |        |     |         |
|          |         | Boys|    |         | Girls |    |         |        |     |         |
|          |         |    |    |         |        |     |         |        |     |         |
| Age (years) | Boys  | 930 | 12.5 | 0.5 | n.s. | 13.5 | 0.5 | n.s. | 14.5 | 0.5 | n.s. |
|           | Girls  | 799 | 12.6 | 0.5 | n.s. | 13.6 | 0.5 | n.s. | 14.6 | 0.5 | n.s. |
| Height (cm) | Boys  | 930 | 154.9 | 8.2 | ** | 161.9 | 7.4 | ** | 166.3 | 6.3 | ** |
|           | Girls  | 799 | 152.9 | 5.7 | ** | 155.5 | 5.3 | ** | 156.6 | 5.3 | ** |
| Weight (kg) | Boys  | 930 | 45.5 | 10.4 | ** | 51.3 | 9.1 | ** | 56.4 | 11.4 | ** |
|           | Girls  | 799 | 43.6 | 7.5 | ** | 47.1 | 7.4 | ** | 49.2 | 7.4 | ** |
| WC (cm) | Boys  | 928 | 66.8 | 8.8 | ** | 69.1 | 9.1 | ** | 71.5 | 9.1 | ** |
|           | Girls  | 798 | 65.0 | 6.8 | ** | 67.9 | 7.0 | ** | 68.6 | 6.8 | ** |
| Waist/height ratio | Boys  | 928 | 0.431 | 0.051 | ** | 0.427 | 0.051 | ** | 0.430 | 0.051 | ** |
|           | Girls  | 798 | 0.425 | 0.041 | ** | 0.437 | 0.043 | ** | 0.438 | 0.042 | ** |
| Percentage of overweight (%) | Boys  | 930 | -1.9 | 15.8 | ** | 1.3 | 16.7 | ** | 3.2 | 17.4 | ** |
|           | Girls  | 799 | -3.8 | 13.6 | ** | -1.2 | 13.6 | ** | -1.1 | 13.1 | ** |
| Body fat (%) | Boys  | 928 | 15.9 | 5.8 | ** | 15.1 | 6.0 | ** | 15.3 | 6.3 | ** |
|           | Girls  | 797 | 20.8 | 4.9 | ** | 21.6 | 4.3 | ** | 22.1 | 4.8 | ** |
| BMI | Boys  | 930 | 18.8 | 3.2 | n.s. | 19.5 | 3.4 | n.s. | 20.3 | 3.5 | * |
|           | Girls  | 799 | 18.2 | 2.6 | ** | 19.4 | 2.7 | ** | 20.0 | 2.7 | ** |
| SBP (mmHg) | Boys  | 930 | 110.3 | 10.8 | ** | 112.0 | 10.6 | ** | 117.5 | 10.9 | ** |
|           | Girls  | 799 | 107.4 | 9.4 | ** | 107.6 | 9.5 | ** | 109.6 | 9.4 | n.s. (0.051) |
| DBP (mmHg) | Boys  | 930 | 58.1 | 6.5 | n.s. | 58.6 | 6.2 | n.s. | 62.4 | 7.0 | ** |
|           | Girls  | 799 | 58.3 | 6.4 | n.s. | 58.4 | 6.3 | n.s. | 60.4 | 6.3 | n.s. |
| Heart rate (beats/min) | Boys  | 930 | 71.9 | 10.7 | ** | 69.4 | 11.1 | ** | 72.2 | 11.6 | ** |
|           | Girls  | 799 | 74.8 | 10.8 | ** | 72.9 | 11.2 | ** | 73.9 | 11.2 | n.s. (0.060) |
| baPWV (cm/s) | Boys  | 930 | 867.4 | 96.8 | n.s. | 879.2 | 111.9 | n.s. | 944.5 | 117.7 | ** |
|           | Girls  | 799 | 864.2 | 99.5 | n.s. | 876.2 | 101.3 | n.s. | 923.0 | 101.3 | ** |
| ABI | Boys  | 930 | 1.023 | 0.085 | ** | 1.024 | 0.086 | ** | 1.011 | 0.083 | n.s. |
|           | Girls  | 799 | 0.991 | 0.080 | ** | 1.004 | 0.082 | ** | 1.005 | 0.077 | ** |
| Sleeping time (min) | Boys  | 917 | 459.1 | 66.3 | ** | 459.4 | 66.1 | ** | 442.4 | 70.4 | ** |
|           | Girls  | 792 | 442.5 | 67.0 | ** | 451.2 | 61.8 | ** | 432.2 | 66.6 | ** |
| Time spent on vigorous exercise (min) | Boys  | 930 | 70.4 | 84.2 | ** | 74.4 | 81.2 | ** | 39.7 | 60.7 | ** |
|           | Girls  | 799 | 59.9 | 72.8 | ** | 52.0 | 72.9 | ** | 19.0 | 39.9 | ** |
| Light exercise (min) | Boys  | 930 | 17.4 | 34.3 | n.s. | 19.8 | 37.2 | * | 19.9 | 35.3 | * |
|           | Girls  | 799 | 15.3 | 32.3 | n.s. | 16.6 | 29.7 | n.s. | 16.7 | 30.1 | n.s. |
| Time for indoor play (min) | Boys  | 930 | 57.8 | 74.4 | n.s. | 58.2 | 70.0 | n.s. | 58.3 | 69.7 | n.s. |
|           | Girls  | 799 | 60.1 | 73.9 | n.s. | 64.5 | 78.2 | n.s. | 58.2 | 73.6 | n.s. |
| Time for video games (min) | Boys  | 930 | 58.9 | 74.4 | ** | 68.8 | 75.7 | ** | 61.7 | 77.2 | ** |
|           | Girls  | 799 | 40.1 | 73.9 | ** | 46.2 | 71.8 | ** | 39.9 | 69.4 | n.s. |
| Time watching TV (min) | Boys  | 930 | 100.5 | 85.1 | ** | 102.6 | 81.2 | ** | 92.2 | 81.7 | ** |
|           | Girls  | 799 | 120.7 | 97.9 | ** | 111.1 | 90.7 | ** | 100.3 | 83.0 | ** |
| Time studying (min) | Boys  | 930 | 60.3 | 64.9 | n.s. | 53.2 | 54.5 | ** | 77.0 | 69.1 | ** |
|           | Girls  | 799 | 64.5 | 57.5 | ** | 61.4 | 57.2 | ** | 92.0 | 74.2 | ** |

*P < 0.05, **P < 0.01. †-test; ‡repeated-measures ANOVA; §Bonferroni post-hoc test. ABI, ankle–brachial index; baPWV, brachio-ankle pulse wave velocity; BMI, body mass index; DBP, diastolic blood pressure; SBP, systolic blood pressure; WC, waist circumference.
time watching TV (OR, 1.51) in the seventh grade, dizziness (inverse OR, 1.46), general fatigue (OR, 1.44), time for indoor play (inverse OR, 1.40), stagefright in the eighth grade (OR, 1.40), and good friendship in the seventh grade (inverse OR, 1.39). In girls, eighth and seventh grade baPWV were followed by SBP in the eighth grade (OR, 1.96), having breakfast in the seventh grade (OR, 1.89), lack of sleep in the eighth grade (OR, 1.89), emotional ups and downs in the seventh grade (OR, 1.71), ABI in the seventh grade (OR, 1.60), concentration in the eighth grade (inverse OR, 1.54), feeling sick in the morning (OR, 1.52), stagefright (OR, 1.44), and time for video games in the seventh grade (inverse OR, 1.39).

Discussion

In this study, statistical analysis was conducted according to gender because there is much difference in physical growth, blood pressure, and baPWV between boys and girls.10,22 No significant differences in baPWV were seen between genders in the seventh and eighth grade. Ninth grade data, however, showed significant gender differences in baPWV, and blood pressure, suggesting the effect of sex hormones on vascular elasticity. Estrogen may inhibit atherosclerosis by increasing nitric oxide production and suppressing pathological proliferation of vascular smooth muscle.23 The mean age of menarche is 12.2 years in Japan,24 but the pubertal stage including the age of menarche was not checked in this study. Therefore we could not estimate the effect of estrogen on PWV in this study.

The increase in baPWV between the eighth and ninth grade was larger than that between the seventh and eighth grade. This may be explained by increased stress and anxiety from the high school entrance test, and decreased sleep time and time spent on vigorous exercise resulting from the increased study time (Table 1).

In the seventh grade, baPWV was inversely associated with baPWV increment in both genders. In the eighth grade, weight was positively associated with baPWV increment in both genders. This suggests that weight gain from the seventh grade to the eighth grade may be associated with baPWV increment. In boys, time watching TV had an OR of 1.54 for baPWV increment. Increased time watching TV may result in reduced sleep and exercise, and an increase in sedentary time. In girls, time studying, concentration and time spent on vigorous exercise were all positively associated with baPWV increment. These activities require mental strain, which may result in increased sympathetic activity and consequentially result in baPWV increment. There is a possibility that many of the students who spent a lot of time on vigorous exercise in the seventh grade continued their sports activity into ninth grade. Being successful at both study and club activities might require reduction in time for video games, indoor play, and sleep.

Hypertension and dyslipidemia are key atherosclerosis risk factors in children.25,26 These risk factors tend to be present in obese children. In this study, obese students had higher
Arterial stiffness: Junior high students

Table 3 Parameters vs baPWV tertile in ninth grade students

|         | baPWV | P-value | Among all groups
|---------|-------|---------|------------------|
|         | Group 1 (low) | Group 2 (normal) | Group 3 (high) | G1 vs G2 | G1 vs G3 | G2 vs G3 |
| Boys n  | 232   | 466     | 232   | ** | ** | ** | ** |
| baPWV (cm/s) | 806.3 ± 43.9 | 934.7 ± 45.0 | 1,102.5 ± 72.4 | ** | ** | ** | ** |
| Height (cm) | 165.8 ± 6.2 | 166.5 ± 6.4 | 166.5 ± 6.2 | n.s. |   |   |   |
| Weight (kg) | 55.1 ± 12.9 | 56.4 ± 10.7 | 58.1 ± 11.2 | * | * |   |   |
| WC (cm)    | 70.7 ± 10.0 | 71.5 ± 8.5 | 72.5 ± 9.2 | n.s. |   |   |   |
| Waist/height | 0.426 ± 0.055 | 0.429 ± 0.048 | 0.435 ± 0.052 | n.s. |   |   |   |
| Percentage of overweight (%) | 1.2 ± 19.5 | 2.7 ± 5.8 | 5.8 ± 17.2 | * | * |   |   |
| Body fat % | 14.6 ± 15.2 | 15.2 ± 6.0 | 16.2 ± 6.4 | * | * |   |   |
| BMI       | 19.9 ± 4.0 | 20.2 ± 3.2 | 20.9 ± 3.5 | ** | ** |   |   |
| SBP (mmHg) | 110.6 ± 8.8 | 117.2 ± 10.1 | 125.1 ± 9.4 | ** | ** | ** | ** |
| DBP (mmHg) | 57.9 ± 5.6 | 62.2 ± 6.3 | 67.3 ± 6.6 | ** | ** | ** | ** |
| Heart rate (beats/min) | 68.6 ± 9.9 | 72.0 ± 11.4 | 76.3 ± 12.3 | ** | ** | ** | ** |
| ABI       | 1.024 ± 0.09 | 1.009 ± 0.079 | 1.002 ± 0.088 | * |   |   |   |
| Sleep time (min) | 442.5 ± 66.6 | 441.9 ± 71.3 | 440.6 ± 72.1 | n.s. |   |   |   |
| Vigorous exercise (min) | 42.8 ± 64.0 | 39.6 ± 58.3 | 36.8 ± 62.3 | n.s. |   |   |   |
| Light exercise (min) | 20.0 ± 35.7 | 21.5 ± 38.5 | 16.6 ± 27.0 | n.s. |   |   |   |
| Time for indoor play (min) | 52.6 ± 61.0 | 59.3 ± 72.5 | 62.0 ± 71.9 | n.s. |   |   |   |
| Time for video games (min) | 63.7 ± 80.7 | 62.1 ± 76.5 | 58.8 ± 75.2 | n.s. |   |   |   |
| Time watching TV (min) | 82.2 ± 71.6 | 93.4 ± 84.3 | 99.7 ± 85.1 | n.s. |   |   |   |
| Time studying (min) | 79.6 ± 69.2 | 76.3 ± 66.7 | 76.0 ± 73.8 | n.s. |   |   |   |
| Girls n  | 199   | 400     | 200   |   |   |   |   |
| baPWV (cm/s) | 802.1 ± 40.1 | 916.2 ± 39.2 | 1,056.7 ± 61.5 | ** | ** | ** | ** |
| Height (cm) | 156.5 ± 5.4 | 156.9 ± 5.2 | 156.9 ± 5.6 | n.s. |   |   |   |
| Weight (kg) | 48.4 ± 7.0 | 49.3 ± 6.9 | 49.7 ± 8.6 | n.s. |   |   |   |
| WC (cm)    | 67.8 ± 6.7 | 68.6 ± 6.4 | 69.4 ± 7.6 | n.s. |   |   |   |
| Waist/height | 0.433 ± 0.420 | 0.438 ± 0.040 | 0.443 ± 0.046 | n.s. |   |   |   |
| Percentage of overweight (%) | −2.6 ± 12.1 | −1.2 ± 12.5 | −0.3 ± 14.9 | n.s. |   |   |   |
| Body fat % | 21.4 ± 4.4 | 22.2 ± 5.0 | 22.7 ± 4.8 | * | * |   |   |
| BMI       | 19.7 ± 2.4 | 20.0 ± 2.5 | 20.2 ± 3.0 | * | * |   |   |
| SBP (mmHg) | 104.0 ± 7.3 | 108.8 ± 8.1 | 116.7 ± 9.5 | ** | ** | ** | ** |
| DBP (mmHg) | 56.5 ± 4.7 | 60.0 ± 5.6 | 65.2 ± 6.3 | ** | ** | ** | ** |
| Heart rate (beats/min) | 70.5 ± 9.3 | 72.8 ± 10.3 | 79.4 ± 12.7 | ** | ** |   |   |
| ABI       | 1.009 ± 0.081 | 1.007 ± 0.074 | 0.995 ± 0.077 | n.s. |   |   |   |
| Sleep time (min) | 420.0 ± 67.7 | 434.3 ± 66.9 | 438.7 ± 64.2 | * | * |   |   |
| Vigorous exercise (min) | 18.4 ± 40.9 | 18.5 ± 39.6 | 20.6 ± 39.8 | n.s. |   |   |   |
| Light exercise (min) | 17.9 ± 26.9 | 16.8 ± 33.2 | 15.2 ± 26.3 | n.s. |   |   |   |
| Time for indoor play (min) | 57.2 ± 77.3 | 56.9 ± 74.0 | 61.9 ± 68.9 | n.s. |   |   |   |
| Time for video games (min) | 41.5 ± 74.6 | 39.3 ± 69.4 | 39.3 ± 64.3 | n.s. |   |   |   |
| Time watching TV (min) | 96.7 ± 88.2 | 101.9 ± 85.8 | 101.0 ± 71.5 | n.s. |   |   |   |
| Time studying (min) | 94.7 ± 77.9 | 91.5 ± 75.8 | 90.3 ± 67.3 | n.s. |   |   |   |

*P < 0.05, **P < 0.01, †One-way ANOVA; ‡Bonferroni post-hoc test. ABI, ankle-brachial index; baPWV, brachio-ankle pulse wave velocity; BMI, body mass index; DBP, diastolic blood pressure; SBP, systolic blood pressure; WC, waist circumference.

 baPWV than non-obese students, suggesting that obesity may play an important role in the development of atherosclerosis in children. The present results were consistent with studies by Hudson et al. and Cote et al., who similarly concluded that obese children had higher PWV compared with non-obese children.12,13

In the present study there was also a positive association between baPWV in the seventh and eighth grade and baPWV in the ninth grade; Therefore, students with high baPWV in the ninth grade were likely to have had high baPWV in the seventh and eighth grade (and vice versa). SBP was also associated with baPWV, particularly in boys; SBP in the seventh and eighth grade was predictive of baPWV in the ninth grade. Interestingly, although the obese students had higher baPWV than non-obese students, obesity itself was not a significant contributor toward baPWV on logistic regression analysis. Taken together, these results suggest that perhaps it is not obesity itself, but rather the factors associated with obesity, such as hypertension, reduced time for exercise, increased time watching TV, and symptoms of depression, that have an impact on baPWV.

Hypertension is an important risk factor for high baPWV in both boys and girls.27–29 Continued hypertension may result in pathophysiological changes such as thickening of the intima and media, which can result in functional changes and PWV elevation.26 It is important to note that although measurement of PWV is widely accepted in the assessment of arterial stiffness, its accuracy is influenced by changes in blood pressure. As a result, the use of cardio-ankle vascular index (CAVI),
### Table 4 Parameters vs pattern of change in baPWV

| Boys | n  | A  | B  | C  | D  | Among all groups<sup>1</sup> | P-value |
|------|----|----|----|----|----|-----------------------------|--------|
|      |    | A  | B  | C  | D  | A vs B<sup>2</sup> | A vs C<sup>2</sup> | A vs D<sup>2</sup> | B vs C<sup>2</sup> | B vs D<sup>2</sup> | C vs D<sup>2</sup> |
| Seventh grade baPWV (cm/s) | 591 | 819.4 ± 65.1 | 851.4 ± 53.5 | 987.9 ± 51.3 | 1,002 ± 53.9 | ** ** ** ** ** ** | ** ** ** ** ** ** |
| SBP (mmHg) | 105 | 104.5 ± 8.9 | 114.1 ± 10.2 | 113.7 ± 12.4 | 117.8 ± 10.0 | ** ** ** ** ** ** | ** ** ** ** ** ** |
| DBP (mmHg) | 107 | 56.2 ± 5.4 | 59.3 ± 5.5 | 61.5 ± 7.7 | 63.2 ± 6.4 | ** ** ** ** ** ** | ** ** ** ** ** ** |
| Heart rate (beats/min) | 127 | 70.4 ± 10.0 | 72.7 ± 10.6 | 75.8 ± 11.7 | 75.2 ± 11.4 | ** ** ** ** ** ** | ** ** ** ** ** ** |
| Sleeping time (min) | 459.0 ± 66.0 | 456.9 ± 70.1 | 459.6 ± 66.9 | 457.0 ± 64.7 | n.s. | ** ** ** ** ** ** | ** ** ** ** ** ** |
| Vigorous exercise (min) | 719.9 ± 81.0 | 71.3 ± 91.6 | 57.6 ± 73.5 | 73.5 ± 94.5 | n.s. | ** ** ** ** ** ** | ** ** ** ** ** ** |
| Light exercise (min) | 17.4 ± 32.8 | 12.1 ± 19.3 | 21.4 ± 45.0 | 18.4 ± 43.0 | n.s. | ** ** ** ** ** ** | ** ** ** ** ** ** |
| Time for video games (min) | 59.5 ± 78.6 | 58.6 ± 75.7 | 53.0 ± 72.0 | 61.3 ± 75.0 | n.s. | ** ** ** ** ** ** | ** ** ** ** ** ** |
| Time watching | 97.7 ± 85.4 | 104.5 ± 79.7 | 88.4 ± 89.4 | 120.1 ± 82.1 | * | * | * | * | * | * |
| Eighth grade baPWV (cm/s) | 837.7 ± 58.2 | 903.2 ± 90.8 | 920.6 ± 94.4 | 1,017.5 ± 119.6 | ** ** ** ** ** ** | ** ** ** ** ** ** | ** ** ** ** ** ** |
| SBP (mmHg) | 109.7 ± 9.4 | 114.8 ± 9.1 | 112.8 ± 12.7 | 120.1 ± 10.8 | ** ** ** ** ** ** | ** ** ** ** ** ** | ** ** ** ** ** ** |
| DBP (mmHg) | 57.3 ± 5.6 | 59.4 ± 6.4 | 59.4 ± 6.6 | 63.3 ± 6.2 | ** ** ** ** ** ** | ** ** ** ** ** ** | ** ** ** ** ** ** |
| Heart rate (beats/min) | 68.2 ± 10.2 | 69.8 ± 11.0 | 71.4 ± 11.3 | 73.4 ± 13.0 | ** ** ** ** ** ** | ** ** ** ** ** ** | ** ** ** ** ** ** |
| Sleeping time (min) | 459.2 ± 63.7 | 453.8 ± 70.7 | 460.1 ± 73.7 | 458.9 ± 71.1 | n.s. | ** ** ** ** ** ** | ** ** ** ** ** ** | ** ** ** ** ** ** |
| Vigorous exercise (min) | 75.9 ± 81.4 | 65.7 ± 77.8 | 67.1 ± 74.7 | 80.7 ± 88.0 | n.s. | ** ** ** ** ** ** | ** ** ** ** ** ** | ** ** ** ** ** ** |
| Light exercise (min) | 220.0 ± 41.7 | 16.0 ± 29.1 | 13.3 ± 20.1 | 18.1 ± 30.6 | n.s. | ** ** ** ** ** ** | ** ** ** ** ** ** | ** ** ** ** ** ** |
| Time for video games (min) | 69.5 ± 77.4 | 65.0 ± 68.4 | 71.7 ± 72.6 | 66.7 ± 76.6 | n.s. | ** ** ** ** ** ** | ** ** ** ** ** ** | ** ** ** ** ** ** |
| Time watching | 94.4 ± 78.3 | 111.7 ± 76.3 | 117.0 ± 87.2 | 121.1 ± 87.8 | * | * | * | * | * | * |
| TV (min) | 117.2 ± 97.5 | 118.8 ± 95.1 | 117.5 ± 84.9 | 141.7 ± 109.0 | n.s. | ** ** ** ** ** ** | ** ** ** ** ** ** | ** ** ** ** ** ** |
| Fifth grade baPWV (cm/s) | 841.6 ± 85.5 | 910.1 ± 95.8 | 907.5 ± 70.8 | 983.4 ± 105.8 | ** ** ** ** ** ** | ** ** ** ** ** ** | ** ** ** ** ** ** |
| SBP (mmHg) | 105.7 ± 8.7 | 109.9 ± 8.9 | 108.3 ± 9.0 | 113.8 ± 11.0 | ** ** ** ** ** ** | ** ** ** ** ** ** | ** ** ** ** ** ** |
| DBP (mmHg) | 57.2 ± 5.9 | 59.3 ± 6.2 | 58.8 ± 6.1 | 62.7 ± 6.9 | ** ** ** ** ** ** | ** ** ** ** ** ** | ** ** ** ** ** ** |
| Heart rate (beats/min) | 71.5 ± 10.3 | 72.6 ± 12.1 | 73.6 ± 10.7 | 79.0 ± 11.6 | ** ** ** ** ** ** | ** ** ** ** ** ** | ** ** ** ** ** ** |
| Sleeping time (min) | 446.0 ± 81.1 | 451.9 ± 59.4 | 460.7 ± 59.4 | 456.2 ± 69.2 | n.s. | ** ** ** ** ** ** | ** ** ** ** ** ** | ** ** ** ** ** ** |
| Vigorous exercise (min) | 53.9 ± 72.9 | 66.1 ± 51.5 | 70.5 ± 30.4 | 30.4 ± 52.1 | n.s. | ** ** ** ** ** ** | ** ** ** ** ** ** | ** ** ** ** ** ** |
| Light exercise (min) | 16.2 ± 30.7 | 17.0 ± 25.2 | 18.4 ± 24.9 | 16.4 ± 32.8 | n.s. | ** ** ** ** ** ** | ** ** ** ** ** ** | ** ** ** ** ** ** |
| Time for video games (min) | 460.0 ± 713.4 | 43.8 ± 74.5 | 54.5 ± 76.7 | 41.6 ± 67.3 | n.s. | ** ** ** ** ** ** | ** ** ** ** ** ** | ** ** ** ** ** ** |
| Time watching | 106.8 ± 927.9 | 115.0 ± 82.8 | 116.2 ± 87.1 | 123.5 ± 90.7 | n.s. | ** ** ** ** ** ** | ** ** ** ** ** ** | ** ** ** ** ** ** |

*P < 0.05, **P < 0.01. Group A, normal to normal; group B, normal to high; group C, high to normal; group D, high to high. †One-way ANOVA; ‡Bonferroni post-hoc test.

baPWV, brachio-ankle pulse wave velocity; DBP, diastolic blood pressure; SPB, systolic blood pressure.
which is based on the stiffness parameter and is theoretically independent of blood pressure, has been favored by some investigators.\(^3\)\(^0\),\(^3\)\(^1\) Some studies, however, have reported lower CAVI in obese children compared with non-obese children, suggesting that vascular adaptation to obesity had occurred.\(^3\)\(^0\)

Obesity and hypertension are independent risk factors of atherosclerosis.\(^2\)\(^6\),\(^2\)\(^7\) Importantly, childhood hypertension has been associated with atherosclerosis in adulthood.\(^2\)\(^5\),\(^2\)\(^8\) Similarly, the relationship between PWV and obesity in children has been well studied.\(^1\)\(^0\),\(^1\)\(^1\),\(^1\)\(^5\) In the present study, we assessed the contribution of various parameters to the increased baPWV observed in junior high school students. We found that high baPWV was associated with reduced time for light exercise and increased time watching TV. These factors are consistent

| Table 5 | Significant indicators of baPWV increase from seventh to ninth grade |
|---------|---------------------------------------------------------------------|
| Variables | OR | 95%CI | Remark |
| **Boys** | | | |
| baPWV 7th grade | 3.24 | 2.48 | 4.24 | † |
| Weight 7th grade | 1.85 | 1.27 | 2.68 | |
| Body fat % 8th grade | 1.76 | 1.33 | 2.34 | † |
| BMI 8th grade | 1.68 | 1.14 | 2.48 | |
| Time watching TV 7th grade | 1.54 | 1.18 | 2.02 | |
| Orthostatic dysfunction 7th grade | 1.52 | 1.13 | 2.03 | |
| General fatigue 7th grade | 1.50 | 1.14 | 1.98 | |
| **Girls** | | | |
| baPWV 7th grade | 3.51 | 2.65 | 4.63 | † |
| Time studying 7th grade | 1.45 | 1.09 | 1.92 | |
| Concentration 8th grade | 1.42 | 1.04 | 1.95 | |
| Having motivation 8th grade | 1.41 | 1.06 | 1.87 | † |
| Weight 8th grade | 1.39 | 1.05 | 1.83 | † |
| Pale face 7th grade | 1.35 | 1.00 | 1.83 | † |
| Time spent on vigorous exercise 7th grade | 1.33 | 1.00 | 1.76 | |

\(†\)Inverse OR used for OR <1. baPWV, brachio-ankle pulse wave velocity; BMI, body mass index.

| Table 6 | Significant indicators of high baPWV in ninth grade |
|---------|---------------------------------------------------------------------|
| Variables | OR | 95%CI | Remark |
| **Boys** | | | |
| baPWV 8th grade | 3.90 | 2.82 | 5.41 | |
| baPWV 7th grade | 2.64 | 1.91 | 3.65 | |
| Feeling sick at bathing 8th grade | 1.80 | 1.19 | 2.71 | |
| Time for video games 8th grade | 1.78 | 1.31 | 2.40 | † |
| Time spent on light exercise 7th grade | 1.62 | 1.20 | 2.18 | † |
| SBP 7th grade | 1.62 | 1.16 | 2.26 | |
| SBP 8th grade | 1.60 | 1.15 | 2.23 | |
| Sleeping time 7th grade | 1.58 | 1.18 | 2.12 | † |
| Headache 7th grade | 1.56 | 1.16 | 2.10 | |
| Time watching TV 7th grade | 1.51 | 1.10 | 2.08 | |
| Dizziness 8th grade | 1.46 | 1.05 | 2.02 | † |
| General fatigue 8th grade | 1.44 | 1.03 | 2.00 | |
| Time for indoor play 8th grade | 1.40 | 1.03 | 1.91 | † |
| Anxiety about acting 8th grade | 1.40 | 1.03 | 1.89 | |
| Good friendship 7th grade | 1.39 | 1.03 | 1.89 | † |
| **Girls** | | | |
| baPWV 8th grade | 3.98 | 2.78 | 5.71 | |
| baPWV 7th grade | 3.71 | 2.61 | 5.27 | |
| SBP 8th grade | 1.86 | 1.39 | 2.77 | |
| Having breakfast 7th grade | 1.89 | 1.25 | 2.87 | |
| Lack of sleep 8th grade | 1.84 | 1.33 | 2.55 | |
| Emotional ups and downs 7th grade | 1.71 | 1.21 | 2.42 | |
| ABI 7th grade | 1.66 | 1.21 | 2.29 | |
| Concentration 8th grade | 1.60 | 1.11 | 2.32 | |
| Having motivation 8th grade | 1.54 | 1.10 | 2.15 | † |
| Feeling sick during morning 7th grade | 1.52 | 1.09 | 2.11 | |
| Anxiety about acting 7th grade | 1.44 | 1.02 | 2.02 | |
| Time for video games 7th grade | 1.39 | 1.01 | 1.93 | † |

\(†\)Inverse OR used for OR <1. ABI, ankle–brachial index; baPWV, brachio-ankle pulse wave velocity; SBP, systolic blood pressure.
with reduced activity, and promote obesity and arterial stiffness.\textsuperscript{32,33} Additionally, reduced time for sleep, and also anger and symptoms of anxiety may contribute to sympathetic excitation, resulting in elevation of blood pressure and heart rate, promoting arterial stiffness. In children, reduced time for sleep has been associated with obesity and atherosclerosis.\textsuperscript{34,35} In this study, many psychological symptoms such as feeling sick during bath time, headaches, general fatigue, anxiety, and emotional ups and downs were associated with increased baPWV. Psychological stresses have been previously reported to induce transient endothelial dysfunction.\textsuperscript{36} Symptoms of depression and anxiety have also been reported to mediate subclinical atherosclerosis.\textsuperscript{37,38} In young girls, anger has been shown to raise blood pressure and have an impact on cardio-toxic autonomic and hemodynamic profiles.\textsuperscript{39} May et al. reported that trait forgiveness was associated with a more cardioprotective profile, and proposed that decreasing anger while increasing forgiveness may have clinical relevance;\textsuperscript{39} this suggests that stress-coping education and the implementation of interventional programs aimed at suppressing anger may be useful in the prevention of atherosclerosis in children.

In the present study, increased game and indoor play time was associated with low baPWV. This is in contrast to previous reports in which time watching TV was associated with high baPWV.\textsuperscript{40} TV watching, much like games and indoor play, is considered a sedentary activity.\textsuperscript{41} In the present study, however, time watching TV was twice the length of time for games or indoor play, compromising time for sleep and exercise. In contrast, there are many elements of game and indoor play that may have a positive influence on mood,\textsuperscript{42} and be considered not only an effective relaxation tool, but also a useful means for establishing good friendship.

Taken together, increased sympathetic stress through elevation of blood pressure, increase in heart rate, symptoms of nervousness, anxiety, and anger, may contribute to high baPWV. Activities that promote parasympathetic activity such as adequate time for sleep, light exercise, and game and indoor play with friends may lower baPWV and, consequently, reduce the risk of atherosclerosis. We therefore propose that implementation of preventive measures such as regular measurement of blood pressure, adequate sleep,\textsuperscript{43,44} lifestyle changes, and the introduction of stress-coping educational and interventional programs, may reduce the risk of early development of atherosclerosis in children.

Acknowledgment

This research was supported by a Grants-In-Aid Scientific Research of Japan Society for the Promotion of Science (grant no. 26350832; research title “Development of preventive program for lifestyle-related disease by using the result of school health check”).

Disclosure

The authors declare no conflict of interest.

Author contributions

H.F. contributed to the conception and design of this study; H.A. and K.Y. performed the statistical analysis. F.I. drafted the manuscript. H.N. and K.K. critically reviewed the manuscript and supervised the whole study process. All authors read and approved the final manuscript.

References

1 Lobstein T, Baur L, Uauy R. IASO International Obesity TaskForce. Obesity in children and young people: a crisis in public health. Obes. Rev. 2004; 5 (Suppl 1): 4–104.
2 Lobstein T, Jackson-Leach R. Planning for the worst: estimates of obesity and comorbidities in school-age children in 2025. Pediatr. Obes. 2016; 11: 321–5.
3 Skinner AC, Perrin EM, Moss LA, Skelton JA. Cardiometabolic risks and severity of obesity in children and young adults. N. Engl. J. Med. 2015; 373: 1307–17.
4 Le J, Zhang D, Menees S, Chen J, Raghuviree G. “Vascular age” is advanced in children with atherosclerosis-promoting risk factors. Circ. Cardiovasc. Imaging 2010; 3: 8–14.
5 Hayman LL, Meininger JC, Daniels SR et al. Primary prevention of cardiovascular disease in nursing practice: focus on children and youth. A scientific statement from the American Heart Association Committee on atherosclerosis, hypertension, and obesity in youth of the Council on Cardiovascular Disease in the Young, Council on Cardiovascular Nursing, Council on Epidemiology and Prevention, and Council on Nutrition, Physical Activity, and Metabolism. Circulation 2007; 116: 344–57.
6 Urbina EM, Williams RV, Alpert BS et al. Noninvasive assessment of subclinical atherosclerosis in children and adolescents. Recommendations for standard assessment for clinical research. A scientific statement from the American Heart Association. Hypertension 2009; 54: 919–50.
7 Park MH, Skow Á, De Matteis S et al. Adiposity and carotid-intima media thickness in children and adolescents: a systematic review. BMC Pediatr. 2015; 15: 161.
8 Weberruss H, Pirzer R, Bohm B, Pozza RD, Hetz N, Oberhoffer R. Intima-media thickness and arterial function in obese and non-obese children. BMC Obes. 2016; 3: 2.
9 Ryder JR, Dengel DR, Jacobs DR, Sinaiko AR, Kelly AS, Steinberger J. Relations among adiposity and insulin resistance with flow-mediated dilation, carotid intima-media thickness, and arterial stiffness in children. J. Pediatr. 2016; 168: 205–11.
10 Niboshi A, Hamaoka K, Sakata K, Inoue F. Characteristics of brachial-ankle pulse wave velocity in Japanese children. Eur. J. Pediatr. 2006; 165: 625–9.
11 Miyai N, Utsumi M, Gowa Y et al. Age-specific nomogram of brachial-ankle pulse wave velocity in Japanese adolescents. Clin. Exp. Hypertens. 2013; 35: 95–101.
12 Hudson LD, Rapala A, Khan T, Williams B, Viner RM. Evidence for contemporary arterial stiffening in obese children and adolescents using pulse wave velocity: a systematic review and meta-analysis. Atherosclerosis 2015; 241: 376–86.
13 Cote AT, Phillips AA, Harris KC, Sandor GG, Panagiotopoulos C, Devlin AM. Obesity and arterial stiffness in children: systematic review and meta-analysis. Arterioscler. Thromb. Vasc. Biol. 2015; 35: 1038–44.
14 Cote AT, Harris KC, Panagiotopoulos C, Sandor GG, Devlin AM. Childhood obesity and cardiovascular dysfunction. J. Am. Coll. Cardiol. 2013; 62: 1309–19.
15 Thurn D, Doyon A, Sözeri B et al. Aortic pulse wave velocity in healthy children and adolescents: reference values for the vicorder device and modifying factors. Am. J. Hypertens. 2015; 28: 1480–8.
16 Curcio S, García-Espinoza V, Arana M et al. Growing-related changes in arterial properties of healthy children, adolescents, and young adults nonexposed to cardiovascular risk factors: analysis of gender-related differences. Int. J. Hypertens. 2016; 2016: 4982676.
17 Dangardt F, Chen Y, Berggren K, Osika W, Friberg P. Increased rate of arterial stiffening with obesity in adolescents: a five-year follow-up study. PLoS ONE 2013; 8: e57454.
18 Chu C, Dai Y, Mu J et al. Associations of risk factors in childhood with arterial stiffness 26 years later: the Hanzhong adolescent hypertension cohort. J. Hypertens. 2017; 35 (Suppl 1): 810–815.
19 Chen Y, Dangardt F, Osika W, Berggren K, Gronowitz E, Friberg P. Age- and sex-related differences in vascular function and vascular response to mental stress. Longitudinal and cross-sectional studies in a cohort of healthy children and adolescents. Atherosclerosis 2012; 220: 269–74.
20 Sugiru R, Murata M. Problems with body mass index as an index to evaluate physical status of children in puberty. Pediatr. Int. 2011; 53: 634–42.
21 Committee for Surveillance of Health in School Children and Adolescents. [2002 Surveillance of Health in School Children and Adolescents Project Report.] Japan Society of School Health, Tokyo, 2004 (in Japanese).
22 Ahimastos AA, Formosa M, Dart AM, Kingwell BA. Gender differences in large artery stiffness pre- and post puberty. J. Clin. Endocrinol. Metab. 2003; 88: 5375–80.
23 Mendelsohn ME, Karas RH. The protective effects of estrogen on the cardiovascular system. N. Engl. J. Med. 1999; 340: 1801–11.
24 Hosokawa M, Imazeki S, Mizunuma H, Kubota T, Hayashi K. Secular trends in age at menarche and time to establish regular menstrual cycling in Japanese women born between 1930 and 1985. BMC Womens Health 2012; 12: 19.
25 Berenson GS, Srinivasan SR, Bao W, Newman WP 3rd, Tracy RE, Wattigney WA. Association between multiple cardiovascular risk factors and atherosclerosis in children and young adults. The Bogalusa Heart Study. N. Engl. J. Med. 1998; 338: 1650–6.
26 Litwin M, Feber J, Ruzicka M. Vascular aging: lessons from pediatric hypertension. Can. J. Cardiol. 2016; 32: 642–9.
27 Lurbe E, Torro I, Garcia-Vicent C, Alvarez J, Fernandez-Fornoso JA, Redon J. Blood pressure and obesity exert independent influences on pulse wave velocity in youth. Hypertension 2012; 60: 550–5.
28 Curcio S, García-Espinoza V, Castro JM et al. High blood pressure states in children, adolescents, and young adults associate accelerated vascular aging, with a higher impact in females’ arterial properties. Pediatr. Cardiol. 2017; 38: 840–52.
29 Kulsum-Meccini N, Goss C, Kozel BA, Garbutt JM, Schechtman KB, Dharmidharka VR. Effects of obesity and hypertension on pulse wave velocity in children. J. Clin. Hypertens. (Greenwich) 2017; 19: 221–6.
30 Philip R, Alpert BS, Schwingshackl A et al. Inverse relationship between cardio-ankle vascular index and body mass index in healthy children. J. Pediatr. 2015; 167: 361–5.
31 Morita N, Kambayashi I, Okuda T et al. Inverse relationship between sleep duration and cardio-ankle vascular index in children. J. Atheroscler. Thromb. 2017; 24: 819–26.
32 Pahkala K, Laitinen TT, Heinonen OF et al. Association of fitness with vascular intima-media thickness and elasticity in adolescence. Pediatrics 2013; 132: e77.
33 Rodrigues AN, Perez AJ, Carletti L, Bissoli NS, Abreu GR. The association between cardiorespiratory fitness and cardiovascular risk in adolescents. J. Pediatr. (Rio J.) 2007; 83: 429–35.
34 Li L, Zhang S, Huang Y, Chen K. Sleep duration and obesity in children: a systematic review and meta-analysis of prospective cohort studies. J. Paediatr. Child Health 2017; 53: 378–85.
35 Li L, Fu J, Yu XT et al. Sleep duration and cardiometabolic risk among Chinese school-aged children: do adipokines play a mediating role? Sleep 2017; 40: zsx042. https://doi.org/10.1093/sleep/zsx042
36 Ghidioni L, Donald AE, Cropley M et al. Mental stress induces transient endothelial dysfunction in humans. Circulation 2000; 102: 2473–8.
37 Bomhof-Roordink H, Seldenrijk A, van Hout HP, van Marwijk HW, Diamant M, Penninx BW. Associations between life stress and subclinical cardiovascular disease are partly mediated by depressive and anxiety symptoms. J. Psychosom. Res. 2015; 78: 332–9.
38 Hernandez R, Allen NB, Liu K et al. Association of depressive symptoms, trait anxiety, and perceived stress with subclinical atherosclerosis: results from the Chicago Healthy Aging Study (CHAS). Prev. Med. 2014; 61: 54–60.
39 May RW, Sanchez-Gonzalez MA, Hawkins KA, Batchelor WB, Fincham FD. Effect of anger and trait forgiveness on cardiovascular risk in young adult females. Am. J. Cardiol. 2014; 114: 47–52.
40 van de Laar RJ, Stehouwer CD, Prins MH, van Mechelen W, Twisk JW, Ferreira I. Self-reported time spent watching television is associated with arterial stiffness in young adults: the Amsterdam Growth and Health Longitudinal Study. Br. J. Sports Med. 2014; 48: 256–64.
41 Carson V, Hunter S, Kuzik N et al. Systematic review of sedentary behavior and health indicators in school-aged children and youth: an update. Appl. Physiol. Nutr. Metab. 2016; 41: S240–65.
42 Jones CM, Scholes L, Johnson D, Katsikitis M, Carras MC. Gaming well: links between videogames and flourishing mental health. Front. Psychol. 2014; 5: 260.
43 Hart CN, Hawley NL, Wing RR. Development of a behavioral sleep intervention as a novel approach for pediatric obesity in school-aged children. Sleep Med. Clin. 2016; 11: 515–23.
44 Bonuck KA, Blank A, True-Felt B, Chervin R. Promoting sleep health among families of young children in head start: protocol for a social-ecological approach. Prev. Chronic Dis. 2016; 13: E121.