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Original Article

Evaluation of Carotid Arterial Intima-Media Thickness (IMT) and Its Relation to Clinical Parameters in Japanese Children

Hiroko Tamura[a], Takeshi Suzue[a]*, Fumihiko Jitsunari[b], and Tomohiro Hirao[a]

[a]*Department of Public Health, Faculty of Medicine, Kagawa University, Miki, Kagawa 761-0793, Japan, and*
[b]*Sanyo Gakuen University, Okayama 703-8501, Japan*

The aim of this study was to evaluate the carotid arterial intima-media thickness (IMT) and its relation to clinical parameters in Japanese children. Fifty-two healthy children (39 boys and 13 girls), aged 6-14 years, were enrolled in this cross-sectional investigation study. IMT of the common carotid artery was determined using ultrasonography. We also investigated anthropometric parameters, blood pressure (BP), lifestyles and blood examinations. The mean value of IMT was 0.4 ± 0.1 mm, which was lower than the normal value (1.0 mm) in adults. IMT was positively correlated with age (r = 0.340) and height (r = 0.346) in boys, while it was positively correlated with body mass index (BMI) (r = 0.584) and diastolic BP (DBP) (r = 0.563) in girls. In addition, IMT was associated with sleeping hours and hours of watching television (TV) by using stepwise regression analysis. In conclusion, IMT increased with aging, and it was linked to some clinical parameters of atherosclerosis and lifestyles in children. Therefore, this reference data will be helpful for future assessment of age-related change in Japanese children in clinical practice, and IMT might be a good predictor of atherosclerosis in Japanese children.

Key words: intima-media thickness (IMT), lifestyle, Japanese children, atherosclerosis

Preventing atherosclerosis is one of the public health challenges in Japan [1]. The definition of metabolic syndrome, that is, the combination of factors indicating the risk for heart attack, stroke and diabetes, one of which is atherosclerosis, has been established, and 30.7% of men and 3.6% of women have been diagnosed as having metabolic syndrome using the new criterion in Japan [2]. Atherosclerosis is closely associated with an increased risk of cardiovascular disease [3], elevation of hepatic enzymes [4] and proteinuria [5]. To provide proper management and control of atherosclerosis, the precise assessments of atherosclerosis as well as the development of effective treatments are necessary.

Intima-media thickness (IMT) is commonly used for assessing atherosclerosis [6], and it holds great promise for the non-invasive determination of the presence of atherosclerosis. The relation between IMT and the parameters of atherosclerosis has been evaluated in adults [7, 8], and Stary showed that atherosclerotic lesions in coronary arteries were observed in 531 children and young adults [9]. However, the changes in IMT in Japanese children and the relation of IMT to clinical parameters remain to be investigated. Therefore, in this study, we evaluated the relationship between IMT and clinical

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*Corresponding author. Phone: +81-87-891-2133; Fax: +81-87-891-2134
E-mail: suzue@med.kagawa-u.ac.jp (T. Suzue)

parameters such as anthropometric parameters, blood pressure (BP), lifestyle and blood examinations in a group of Japanese children.

Subjects and Methods

Subjects. Fifty-two healthy children (39 boys and 13 girls), aged 6-14 years, were enrolled in this cross-sectional investigation study. All subjects met the following criteria: (1) they had received a health check-up between 2005 and 2008 at Kagawa Children's Hospital, Kagawa, Japan; (2) their IMT, anthropometric measurements and blood examinations had been taken as part of their health check-ups; and (3) they or their parents provided written informed consent for study participation (Table 1).

The study was approved by the Ethics Committee of Kagawa Children's Hospital (H21-2).

IMT measurements. IMT of the common carotid artery was determined as previously described [10] using duplex ultrasonography with an 8-MHz linear transducer (TOSHIBA, Tokyo, Japan) by a well-trained member of the medical staff. We measured the distance from the leading edge of the first echogenic line to the leading edge of the second echogenic line on a sonographic image, and carotid IMT was defined as the mean of these maximal IMT measurements.

Anthropometric parameters. The anthropometric parameters were evaluated by using the respective parameters such as height and body weight. Body mass index (BMI) was calculated by weight/[height]^2 (kg/m^2).

BP measurements. Each participant's BP was measured after subjects rested at least 15 min in the sitting position.

Blood sampling and assays. The levels of total cholesterol, triglyceride, High-density lipoprotein (HDL)-cholesterol and HbA1c were measured at Kagawa Children's Hospital. High-sensitivity C-reactive protein (hs-CRP), adiponectine and homocystine were measured at SRL Co., Ltd. (Tokyo, Japan).

Evaluation of lifestyle. The draft scale for lifestyle-related lifestyle behavior consisted of 8 items. These items were chosen from the specific perceived barriers associated with lifestyle change in the target population [11-13]. Ratings were made on a 3 or 6 point Likert-type scale (Table 2).

Statistical analysis. Data are expressed as mean ± standard deviation (SD) values. A comparison of parameters between the 2 groups was made using the unpaired *t*-test. Simple correlation analysis was performed as well to test for the significance of the linear relationship among continuous variables. Stepwise multiple regression analysis was also used:

Table 1 Clinical profiles of enrolled subjects

	All (n=52)	Boys (n=39)	Girls (n=13)	*p*
	Mean ± SD	Mean ± SD	Mean ± SD	
Age	9.5 ± 2.7	9.3 ± 2.6	10.2 ± 2.9	n.s.
Height (cm)	136.6 ± 16.8	135.8 ± 17.2	138.9 ± 15.7	n.s.
Weight (kg)	38.8 ± 17.4	38.2 ± 17.7	40.9 ± 16.9	n.s.
Body mass index (kg/m^2)	19.8 ± 4.9	19.6 ± 4.7	20.4 ± 5.6	n.s.
Systolic blood pressure (mmHg)	112.8 ± 12.3	112.9 ± 12.2	112.3 ± 12.9	n.s.
Diastolic blood pressure (mmHg)	55.5 ± 7.9	55.7 ± 7.7	56.6 ± 8.4	n.s.
Total cholesterol (mg/dl)	167.1 ± 26.0	169.1 ± 23.5	160.9 ± 32.6	n.s.
Triglyceride (mg/dl)	93.1 ± 61.2	92.5 ± 65.6	94.6 ± 47.5	n.s.
HDL cholesterol (mg/dl)	56.9 ± 12.2	58.3 ± 13.3	52.7 ± 7.4	n.s.
HbA1c (%)	5.6 ± 4.9	4.9 ± 0.4	5.0 ± 0.4	n.s.
Hs-CRP (ng/ml)	603.2 ± 982.9	646.1 ± 1,086.8	474.5 ± 584.6	n.s.
Homocystine (nmol/mi)	5.5 ± 1.3	5.3 ± 1.3	5.8 ± 1.2	n.s.
Adiponectine (μg/ml)	13.1 ± 6.1	13.4 ± 6.1	12.2 ± 6.2	n.s.
IMT (mm)	0.4 ± 0.1	0.4 ± 0.1	0.4 ± 0.1	n.s.

p value by unpaired *t*-test, n.s.=not significant
Hs-CRP, High-sensitivity C-reactive protein; HDL cholesterol, high density lipoprotein cholesterol; IMT, intima-media thickness.

Table 2 Number of subjects in questionnaires about lifestyle

	Every day	2–4 times	No			
Eating breakfast per week	48	1	3			
Eating snacks between meals per week	36	13	3			
Eating bedtime snacks per week	7	10	35			
Eating fast food per week (*i.e.* MecDonald's)	0	7	45			
Exercise habits per week	22	23	7			
	No	Less than 30 min	30–60 min	1–2 h	2–3 h	3 h or more
Watching television per day	0	1	9	23	13	1
Playing computer games per day	9	13	18	8	3	1
	Less than 5 h	5–6 h	6–7 h	7–8 h	8–9 h	9 h or more
Sleeping hours per day	0	1	5	12	26	3

$p < 0.05$ was considered statistically significant. Statistical analysis was performed with the statistical package SPSS 11.0J for Windows (SPSS Japan, Inc., Japan).

Results

Clinical profiles are summarized in Table 1. The mean of IMT was 0.4 ± 0.1 mm (minimum 0.2 mm, maximum 0.6 mm) in either sex, and the distribution of IMT is evaluated in Fig. 1. There were no differences of clinical parameters, *i.e.*, anthropometric parameters, BP and blood examinations, between boys and girls.

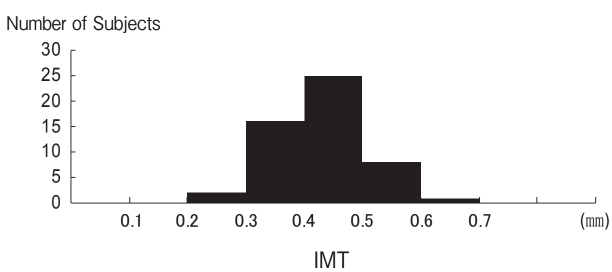

Fig. 1 Distribution of IMT in enrolled subjects. IMT: intima-media thickness.

We also investigated the relationship between IMT and age, anthropometric parameters, BP and blood examinations (Table 3). IMT was increased with age in boys ($r = 0.340$, $p = 0.034$). However, in girls, a significant relationship was not noted between IMT and age ($r = 0.376$, $p = 0.206$) (Fig. 2). In boys, IMT was positively correlated with height ($r = 0.346$, $p = 0.031$) (Table 3). In girls, IMT was positively correlated with BMI ($r = 0.584$, $p = 0.036$) and diastolic BP (DBP) ($r = 0.563$, $p = 0.045$) (Table 3). We also used stepwise multiple regression analysis to evaluate the effect of clinical parameters, *i.e.*, age, anthropometric parameters, BP and blood examinations, on IMT and found that only age was significant in all subjects. (All: IMT $= 0.287 + 0.011$ (age), $r^2 = 0.110$, $p = 0.009$, Boys: IMT $= 0.283 + 0.011$ (age), $r^2 = 0.092$, $p = 0.034$, Girls: IMT $= 0.245 + 0.008$ (BMI), $r^2 = 0.281$, $p = 0.036$).

The lifestyle of enrolled subjects as assessed by questionnaires is summarized in Table 2. We used multiple regression analysis to evaluate the effect of lifestyle parameters on IMT, and we also found that hours of watching television (TV) and hours of sleeping were significant (IMT $= 0.413 + 0.029$ (hours of

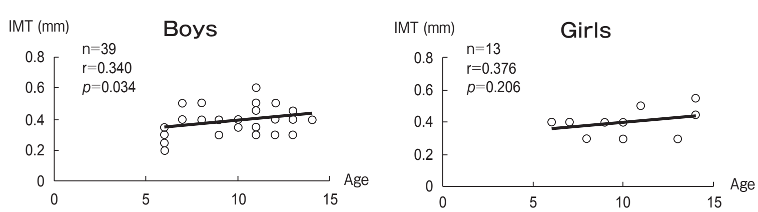

Fig. 2 Simple correlation analysis between IMT and age. IMT: intima-media thickness.

Table 3 Relationship between IMT and clinical parameters

	All (n=52)		Boys (n=39)		Girls (n=13)	
	r	*p*	r	*p*	r	*p*
Age	0.357	**0.009**	0.340	**0.034**	0.376	0.206
Height (cm)	0.307	**0.027**	0.346	**0.031**	0.130	0.673
Weight (kg)	0.340	**0.014**	0.299	0.065	0.472	0.104
Body mass index (kg/m^2)	0.352	**0.010**	0.271	0.095	0.584	**0.036**
Systolic blood pressure (mmHg)	0.247	0.077	0.177	0.281	0.500	0.082
Diastolic blood pressure (mmHg)	0.071	0.617	−0.088	0.594	0.563	**0.045**
Total cholesterol (mg/dl)	0.102	0.471	0.160	0.330	0.019	0.951
Triglyceride (mg/dl)	0.262	0.061	0.293	0.071	0.117	0.702
HDL cholesterol (mg/dl)	0.001	0.997	0.089	0.589	−0.404	0.171
HbA1c (%)	−0.136	0.336	−0.098	0.554	−0.279	0.355
Hs-CRP (ng/ml)	−0.073	0.609	−0.099	0.548	0.151	0.621
Homocystine (nmol/ml)	0.158	0.264	0.160	0.330	0.079	0.796
Adiponectine (μg/ml)	−0.137	0.334	−0.112	0.496	−0.188	0.539

watching TV) − 0.031 (sleeping hours), $r^2 = 0.130$, $p = 0.012$).

Finally, to evaluate the effect of all clinical parameters, *i.e.*, anthropometric parameters and lifestyle, we used multiple regression analysis. (All: IMT = 0.278 + 0.011 (age), $r^2 = 0.110$, $p = 0.009$, Boys: IMT = 0.283 + 0.011 (age), $r^2 = 0.092$, $p = 0.034$, Girls: IMT = 0.245 + 0.008 (sleeping hours), $r^2 = 0.281$, $p = 0.036$).

Discussion

The main findings of this study, in which we evaluated the changes in IMT and its relation to clinical parameters in 52 healthy (39 boys and 13 girls) Japanese children, were that IMT was positively correlated with age and height in boys and with BMI and DBP in girls. In addition, IMT was associated with some lifestyle parameters.

Recently, changes in atherosclerosis in children and young adults have been reported. Shiotani *et al.* investigated the brachial-ankle pulse wave velocity (PWV) and mean BP was a powerful determination for baPWV in 353 Japanese university students [14]. Yamasaki *et al.* showed that IMT in children and young adults with insulin-dependent diabetes mellitus (IDDM) was significantly higher than that in subjects without IDDM. IMT in patients with IDDM was positively linked to the duration of diabetes as well as to age [7]. Ishizu *et al.* also reported that IMT was increased with aging and that none of the known cardio-vascular disease risk factors in adults had a significant relationship with IMT in children [15]. In this study, we measured IMT in 52 Japanese children. The mean of IMT in Japanese children was under the level of recommendation (1.0 mm) in Japanese adults [16]. IMT was positively correlated with age in boys, as previously reported [15] ($r = 0.340$, $p = 0.034$). However, it was not correlated with age in girls at a significant level ($r = 0.376$, $p = 0.206$). IMT was also correlated with height in boys and with BMI and DBP in girls by simple correlation analysis. These results indicate that the relation between IMT and clinical parameters may reflect normal change with aging, and this information gathered may serve as reference data for evaluating IMT in Japanese children.

The other finding of this study was related to the link between IMT and lifestyle parameters in Japanese children. Hirata *et al.* evaluated the relationship between baPWV and exercise habits in 103 subjects over the age of 65 and found that baPWV in subjects without exercise habits was significantly higher than that in subjects with exercise habits [17]. Buil-Cosiales *et al.* reported that olive oil consumption was inversely associated with IMT in 199 subjects with high cardiovascular risk [18]. In addition, obesity indices measured in youth are significantly linked to increased IMT in adulthood [19]. Stensland-Bugge *et al.* reported that smoking as well as age, SBP, total cholesterol and BMI were independent predictors of IMT in both sexes in adults [20]. In this study, we first found that IMT was critically related to lifestyle, *i.e.*, hours of watching TV and hours of sleeping, in 52 healthy Japanese children. It seems reasonable to suggest that simply changing lifestyle might result in preventing future atherosclerosis in Japanese children. Lifestyle modification can reduce IMT in the adult population [21, 22], and therefore, we should promote a healthy lifestyle in Japanese children, which includes not watching too much TV and getting adequate good sleep. However, our study was a cross-sectional study, and the hypothesis that atherosclerosis evaluated by IMT may be caused by inappropriate lifestyle cannot be accurately proven.

Potential limitations remain in our study. First, the cross-sectional study design as well as the small sample size, especially in the case of girls, in our study makes it difficult to infer causality between IMT and clinical parameters. We could not find a relationship between IMT and age in girls. Therefore, the results obtained from this study may not apply to Japanese children. Second, we could not accurately prove the mechanism of the link between IMT and lifestyle. Third, the scale of lifestyle in this study could not be accurately or scientifically proven in Japanese children. Further prospective studies and large-sample studies of Japanese children to examine IMT and its relation to clinical parameters are needed.

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