Original Article

An Overweight or Obese Status in Childhood Predicts Subclinical Atherosclerosis and Prehypertension/Hypertension in Young Adults

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***Aim*: The aim of this study, the YOung TAiwanese Cohort (YOTA) Study, was to investigate the relationship between a childhood overweight/obese status and young adult preclinical atherosclerosis, including assessments of the carotid intima-media thickness (CIMT) and prehypertension or hypertension.**

***Methods*: From among children who participated in the 1992-2000 mass urine screening program in Taiwan, we recruited 303 subjects with an elevated blood pressure (EBP) and 486 subjects with a normal BP in childhood during the period of 2006-2008. These 789 young adults received health check-ups for cardiovascular health, including examinations of blood and urine parameters, anthropometrics, BP and the CIMT, a subclinical cardiovascular risk index. Data analyses were used to evaluate the associated risks in both childhood and young adulthood.**

***Results*: The school students with a childhood overweight/obese status had a higher risk of prehypertension or hypertension, with a relative risk of 3.20 (1.40-7.33) for being overweight and 6.51 (3.36-12.63) for being obese in young adulthood at an average age of 21. A childhood overweight/obese status also predicted a higher risk of having a thicker CIMT, with a relative risk of 2.82 (1.26-6.28) and 4.17 (2.21-7.85) for being overweight and obese in adulthood, respectively, after a mean follow-up of 8.5 years. The body mass index exhibited a consistent trend from childhood to adulthood, with an adjusted R square of 0.551. The participants who were not overweight/obese in childhood also demonstrated a higher risk of prehypertension or hypertension if they became overweight or obese in adulthood.**

***Conclusions*: This study highlights the importance of preventing and treating an overweight or obese status in childhood for the primary prevention of cardiovascular disease in adulthood.**

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Key words: Childhood, Overweight, Obese, Carotid IMT, Hypertension, Adulthood

Introduction

Cardiovascular disease (CVD) is the leading cause of mortality and a major health burden worldwide, affecting many Asian populations, such as those in Taiwan, China, Japan and India[1-3]. The progression of atherosclerosis begins in early life and may modify the associated increased risk of CVD, depending on predisposing genetic and environmental factors[4-6]. With an aging population, as is the case in Taiwan, the early detection of atherosclerosis and its associated risk factors is an important step in preventing stroke and heart disease later in life.

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The worldwide increasing incidence of obesity and metabolic syndrome among children is expected to further increase the cardiovascular burden later in life[7, 8]. The Bogalusa Study[4, 9] and Pathobiological Determinants of Atherosclerosis in Youth (PDAY) Study[10] demonstrated that the process of atherosclerosis starts in early childhood. These autopsy studies showed that the presence of atherosclerotic lesions covering intimal surfaces is significantly associated with an abnormal lipid profile and cardiovascular risk factors, such as hypertension and obesity[11]. The Bogalusa Study reported that fatty streaks are a sign of early atherosclerosis, presenting in 50% of children and increasing to 85% of adults[9]. The Cardiovascular Risk in Young Finns Study also reported that measurements of the carotid intima-media thickness (CIMT) in young adults 33-39 years of age are directly related to the low-density lipoprotein cholesterol (LDL-C) level, systolic blood pressure and cigarette smoking in subjects 12-18 years of age[12]. The Bogalusa Study also indicated that childhood measurements of the LDL-C level and BMI may predict the carotid IMT in young adults[13]. Several other studies have further linked childhood adiposity and obesity to premature death from cardiovascular disease[14-17].

Therefore, studies of adolescents and young adults may provide important information for the early prevention of cardiovascular disease. However, few studies have investigated this association in Asian populations, and there is a lack of evidence tracking the correlation between an overweight/obese status and subclinical cardiovascular disease in young adults with an average age of 21 years. In order to investigate the effects of an elevated blood pressure (EBP) in childhood on cardiovascular health later in life, we conducted a follow-up study, the YOung TAiwanese Cohort (YOTA) Study, from 2006 to 2008, to examine whether a childhood and/or adolescent overweight/obese status predicts atherosclerosis and prehypertension/hypertension in young adults by measuring the CIMT and blood pressure in a cohort of young adults and adolescents.

Materials and Methods

Subjects

From 1992 to 2000, a nationwide mass urine screening for renal health was conducted among school children 6 to 18 years of age in Taiwan[8, 18-20]. The anthropometric status and blood pressure were also measured in all children diagnosed with positive proteinuria or glucosuria twice during the screening examinations (N=103,756). Among these patients, 9,227 students were found to have childhood EBP. In this study, childhood EBP (hypertension) was defined according to the criteria established in the US as a systolic BP, diastolic BP or both greater than or equal to the sex-, age- and height-percentile-specific 95th percentile BP values[21]. Students who had participated in the screening program were contacted for the present YOTA Study. **Fig. 1** shows a flow chart of the present study starting from the urinary screening program to participant recruitment[20]. We sent invitation letters to the parents of eligible students in the Taipei area. After 3-5 days, 12 trained assistants and nurses conducted telephone interviews inviting the subjects with childhood EBP to come to the hospital for a follow-up health examination. No telephone interview contact was made with normotensive students. Among the 707 subjects with childhood EBP, 303 completed the follow-up health examinations, for a response rate of 42.9%. The detailed information is available in recent reports[18, 20].

Among the 59,855 subjects with a normal BP in childhood with an address, 17,448 lived in Taipei. We randomly contacted 6,390 patients living in Taipei by mail, 5,886 of whom did not respond and 17 refused to participate. Finally, 487 subjects with a normal BP in childhood completed the follow-up health examinations, although one lacked a childhood lab examination, resulting in a response rate of 7.6% (486/6,390). The social background at that time did not favor the study, as there was great social anxiety regarding a criminal syndicate that was flourishing in most of Taiwan. Therefore, most of the methods used to contact the subjects were considered to be related to suspected criminal affairs in the period of 2006-2008. Although the response rate was very low, the basic characteristics of the subjects, such as gender and the fasting glucose and cholesterol levels in childhood exhibited no significant differences between the responders and non-responders.

With consent, 303 patients with EBP and 486 patients with a normal BP in childhood completed the follow-up study in the Taipei area. The participants provided both blood and urine specimens and underwent subclinical atherosclerotic measurements, including that of the CIMT and brachial-ankle aortic pulse wave velocity. All participants provided their informed consent at the time of recruitment, and the study protocol was approved by the institutional review committees at National Taiwan University and China Medical University.

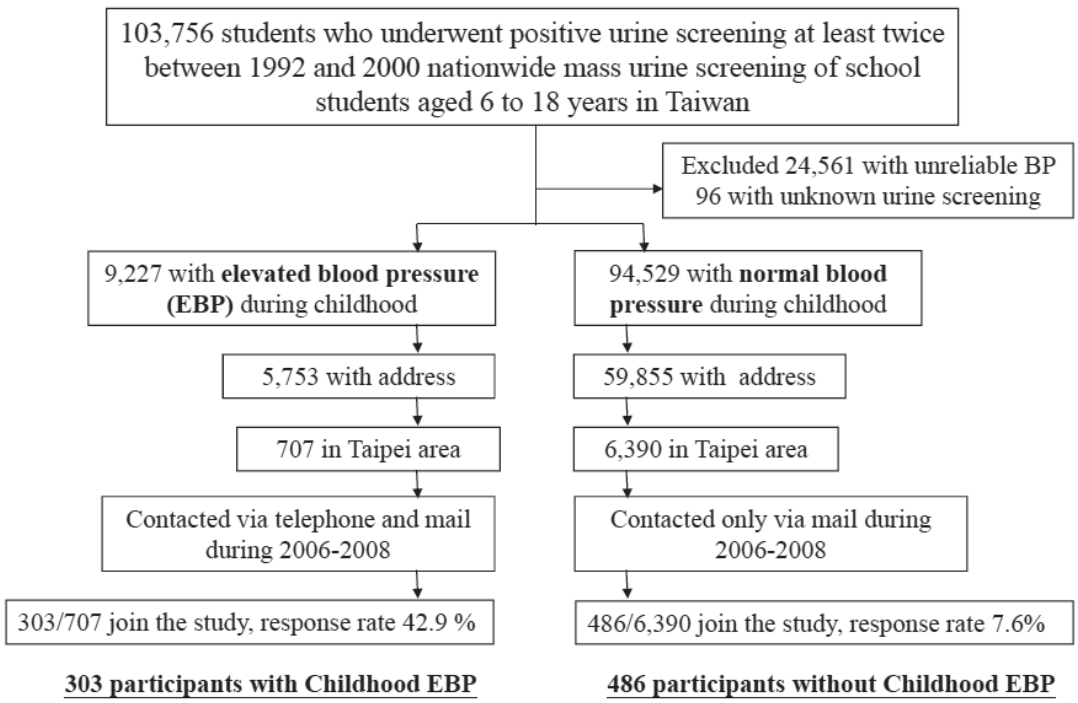

Fig. 1. Flowchart of participant recruitment based on the selection of patients with and without an elevated blood pressure (EBP) in childhood in the YOung TAiwanese Cohort (YOTA) study conducted during the period of 2006-2008.

Assessments of Vascular Risk Factors and Clinical Information

According to the criteria established by the Seventh Report of the Joint National Committee on the Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC-7), hypertension was defined as a blood pressure of 140/90 mm Hg and/or the use of anti-hypertensive agents. Prehypertension was defined as a systolic pressure of 120 to 139 mm Hg or diastolic pressure of 80 to 89 mm Hg. BP was measured using a mercury sphygmomanometer in a standardized fashion, with the cuff-size adjusted to the circumference of the arm. The mean of two measurements obtained after 5-10 minutes of rest in the seated position with the legs uncrossed in a quiet room was used as the BP measurement[8]. If the difference in the two BP measurements was greater than 10 mm Hg, a third BP measurement was obtained, and the average of the lowest two measured BP values was selected as the subject's BP.

The subjects' weight and height were also determined. The body mass index (BMI) was defined as the weight in kilograms divided by the square of the height in meters. An overweight status in childhood or adolescence was defined according to age- and gender-specific criteria for a BMI ≥ 85th percentile from 2 to 18 years of age issued by the Taiwan Department of Health (http://www.ctaso.org.tw/news5.htm)[22]. Adults (age ≥ 18 years) with a BMI of 24-26.99 kg/m^2 were defined as being overweight, while those with a BMI of 27 kg/m^2 or higher were defined as obese. Prevalent diabetes mellitus (DM) was defined as a fasting glucose level of >6.99 mmol/L and/or a history of treatment for DM. The lifestyle factors of each individual, including smoking, drinking and exercise habits, as well as a family history of CVD, hyperlipidemia, DM and hypertension, were obtained using a structured, self-administered questionnaire. In addition, dietary habits were assessed using a modified frequency scale of a simple dietary questionnaire, and a residential environment and occupational hazard exposure questionnaire was distributed.

Serum Markers

All subjects were asked to provide a 20-mL venous blood sample from an antecubital vein for extraction of serum, plasma and DNA after a fasting period of 10-14 hours. The blood glucose, serum total cholesterol, triglyceride, LDL-C and high-density lipoprotein cholesterol (HDL-C) levels were measured using an auto-analyzer (Hitachi 7250 Special; Hitachi, Tokyo, Japan) in central lab at the National Taiwan

University Hospital. For the assays, the blood samples were first centrifuged at 3,000 rpm for 15 minutes within 30 minutes of collection and then stored at -70 degree Celsius until the assessment.

Assessment of the IMT of the Carotid Arteries

The protocol for the carotid atherosclerosis measurements, including the CIMT and number of carotid atherosclerotic plaques, has been well documented[18, 20, 23, 24]. An experienced technician measured the CIMT of the extracranial carotid arteries using high-resolution B-mode ultrasonography (GE Vivid ultrasound system, Horten, Norway) equipped with a 3.5- to 10-MHz real-time B-mode scanner. A quantification package was applied to perform offline automatic calculations for vascular ultrasound. The maximum and mean values of the IMT were calculated bilaterally for the common carotid artery (CCA) proximal to the carotid bifurcation, bulb and internal carotid artery. The CCA1 and CCA2 of the distal CCA were measured at 0-1 cm and 1-2 cm, respectively, from the carotid bifurcation. The CIMT of the posterior wall of the distal CCA was measured from the leading edge of the first echogenic line (interface between the lumen and vascular intima) to the leading edge of the second line (interface between the vascular media and adventitia).

The carotid IMT measurements included the RCCA1 (right CCA, 0-1 cm), RCCA2 (right CCA, 1-2 cm), LCCA1 (left CCA, 0-1 cm), LCCA2 (left CCA, 1-2 cm), right bulb, left bulb and right and left internal carotid artery. A digitalized memory system in the DICOM format recorded all measurements. We acquired a clipped moving-image of the carotid bulb and CCA for five seconds. A computer program was used to analyze the digitized M-mode and measure the CIMT between two successive R waves. This method was employed to obtain the mean value of 150 CCA measurements on a 10-mm segment. The technician was required to conduct a reliability test by repeating the measurements in 30 subjects over two weeks. The reliability of the CIMT measurements for the bilateral CCA (mean of the right and left CCA) was excellent. The intraobserver coefficient of correlation for the CIMT measurements was 98.8% for the right CCA and 98.5% for the left CCA[20].

Statistical Analysis

The statistical analyses were performed using the SAS software program (Version 9.1.3; SAS Institute Inc., Cary, NC, USA). The data analysis first made comparisons between participants with and without childhood EBP in order to identify associations with childhood and adult risk factors measured during the follow-up period among men and women. The childhood risk factors included BMI, cholesterol, fasting glucose, systolic BP and diastolic BP, while the adult risk factors included BMI, cholesterol, fasting glucose, systolic BP, diastolic BP, HDL-C, LDL-C, DM, hypertension, smoking, drinking, an overweight status and obesity. A simple correlation analysis was used to assess the relationship between childhood BMI and adult BMI. The mean carotid IMT was calculated item by item in association with the trend in BMI for both men and women. Comparisons of the IMT and BP values between the children with and without EBP and the adult BMI rank were performed. In addition, comparisons of the IMT and BP values between the children with a BMI less or more than 85% and the adult BMI rank were made.

Continuous variables were compared between group means ± standard deviations (SD) using the Student's two-tailed *t*-test or Mann-Whitney *U*-test if not in a normal distribution. The Chi-square test was applied for categorical data. Multivariate logistic regression analyses were used to measure the strength of association between an overweight childhood BMI values and an overweight adult BMI value or obesity with respect to the risk of a thicker CIMT and/or prehypertension or hypertension in adulthood. Odds ratios (ORs) and 95% confidence intervals (CIs) for the participants with a carotid IMT ≥ 75th percentile were obtained after controlling for adult cardiovascular risk factors, including age, gender, systolic BP, fasting glucose, cholesterol, smoking and alcohol habits and household income. The corresponding ORs for the participants with prehypertension or hypertension were estimated after controlling for adult cardiovascular risk factors, including age, gender, fasting glucose, cholesterol, smoking and alcohol habits and household income.

Results

The characteristics of the participants are shown in **Table 1**. The men had higher mean BMI values and a higher prevalence of cardiovascular risk factors than the women. Meanwhile, the participants with childhood EBP had higher childhood risk factors, including BMI, cholesterol, fasting glucose, systolic BP and diastolic BP, than those without childhood EBP, with the exception of the cholesterol and fasting glucose levels in men. Compared with the participants without childhood EBP, those with childhood EBP were more likely to have metabolic syndromes, particularly an overweight or obese status (more than 2-fold

Table 1. Baseline characteristics of the subjects with and without an elevated blood pressure (EBP) in childhood in the YOung Taiwanese Cohort (YOTA) study conducted during the period of 2006-2008

Characteristics	Men			Women		
	Childhood EBP N = 132	Childhood without EBP N = 181	*p*-value	Childhood EBP N = 171	Childhood without EBP N = 305	*p*-value
Childhood risk factors						
Body mass index, kg/m^2	21.85 ± 5.03	18.20 ± 2.39	< .001	20.48 ± 4.60	18.07 ± 2.69	< .001
Cholesterol, mmol/L	4.06 ± 0.95	4.01 ± 0.85	0.659	4.51 ± 1.22	4.27 ± 0.81	0.021
Glucose AC, mmol/L	4.65 ± 0.89	4.70 ± 0.64	0.594	5.11 ± 2.02	4.66 ± 0.63	0.005
Systolic BP, mmHg	131.72 ± 13.02	102.62 ± 8.95	< .001	124.70 ± 15.05	99.99 ± 9.71	< .001
Diastolic BP, mmHg	84.61 ± 11.17	64.05 ± 7.21	< .001	86.26 ± 9.72	63.07 ± 7.72	< .001
Adulthood risk factors						
Age, years	21.49 ± 3.58	21.6 ± 3.03	0.775	20.50 ± 3.30	21.54 ± 3.30	0.001
Body mass index, kg/m^2	24.8 ± 5.50	21.78 ± 3.30	< .001	22.35 ± 4.49	20.48 ± 2.92	< .001
Cholesterol, mmol/L	4.56 ± 0.97	4.46 ± 1.02	0.352	4.54 ± 0.88	4.55 ± 0.81	0.943
Triglyceride, mmol/L	0.94 (0.68~1.41)	0.85 (0.67~1.15)	0.057	0.79 (0.56~1.04)	0.75 (0.59~0.95)	0.407
HDL-C, mmol/L	1.15 ± 0.20	1.21 ± 0.21	0.009	1.33 ± 0.28	1.41 ± 0.25	< .001
LDL-C, mmol/L	2.81 ± 0.85	2.72 ± 0.87	0.321	2.61 ± 0.80	2.51 ± 0.73	0.187
Glucose AC, mmol/L	4.92 ± 1.15	4.77 ± 0.39	0.140	5.15 ± 2.10	4.68 ± 0.45	0.005
Diabetes mellitus, %	1.52	0	0.097	3.51	0.66	0.020
Systolic BP, mm Hg	120.45 ± 16.63	111.8 ± 11.88	< .001	105.56 ± 13.89	100.8 ± 10.13	< .001
Diastolic BP, mm Hg	76.33 ± 13.13	68.17 ± 8.69	< .001	67.11 ± 11.30	62.08 ± 8.27	< .001
Hypertension, %	6.82	0.55	0.002	2.34	0.33	0.039
Smoking habit, %	18.94	26.52	0.117	4.68	7.54	0.225
Alcohol habit, %	8.33	18.78	0.009	4.68	5.57	0.674
Overweight, %	24.24	11.6	< .001	12.28	7.87	0.001
Obesity, %	24.24	7.73	< .001	12.28	3.61	< .001
Follow-up years	7.90 ± 1.95	8.54 ± 1.72	0.003	8.06 ± 2.08	9.00 ± 1.86	< .001

The data are presented as the mean ± standard deviation for continuous variables and n (%) for binary variables.
The level of triglycerides is presented as the median (Q1-Q3).

in both men and women) and hypertension (12-fold in men and 7-fold in women). The mean BP of the participants with childhood EBP among men was 131.72 ± 13.0/84.61 ± 11.17 mm Hg, which is higher than that observed in the same patients in adulthood (120.45 ± 16.63/76.33 ± 13.13 mm Hg). There was also a strong correlation between the childhood BMI measurements and the adult BMI measurements (R^2 = 0.551, $p < 0.001$) (**Fig. 2**).

All carotid IMT measurements obtained in adulthood, including the RCCA1, RCCA2, LCCA1, LCCA2, Bulb Rt, Bulb Lt, ICA Rt and ICA Lt, increased with increasing BMI in both men and women; this trend was not significant for Bulb Lt in men and women and RCCA1 in women (**Supplemental Table 1**). As shown in **Table 2**, the CIMT values were greater in the subjects with a childhood overweight/obese status than in those with a normal weight in childhood across different adult BMI ranks. As shown in **Table 3**, the CIMT values were greater in the subjects with childhood EBP than in those with a normal BP in childhood; these differences persisted across the different adult BMI ranks.

Table 4 shows the ORs of having adult carotid IMT measurements in the highest 25 percentiles in association with a childhood BMI < 85th percentile or ≥ 85th percentile. The risk of having a high CIMT was not associated with adult BMI among the subjects with a childhood BMI < 85th percentile. The adjusted OR (95% CI) increased in association with an increase in the adult BMI, to 4.17 (2.21-7.85) among those with a BMI of ≥ 27 Kg/m^2 and a childhood BMI ≥ 85th percentile. As shown in **Table 5**, the ORs of having adult prehypertension or hypertension increased in association with an increase in both adult BMI and childhood BMI. Compared to that observed in the patients with an adult BMI of < 24 Kg/m^2 and childhood BMI < 85th percentile, the adjusted OR

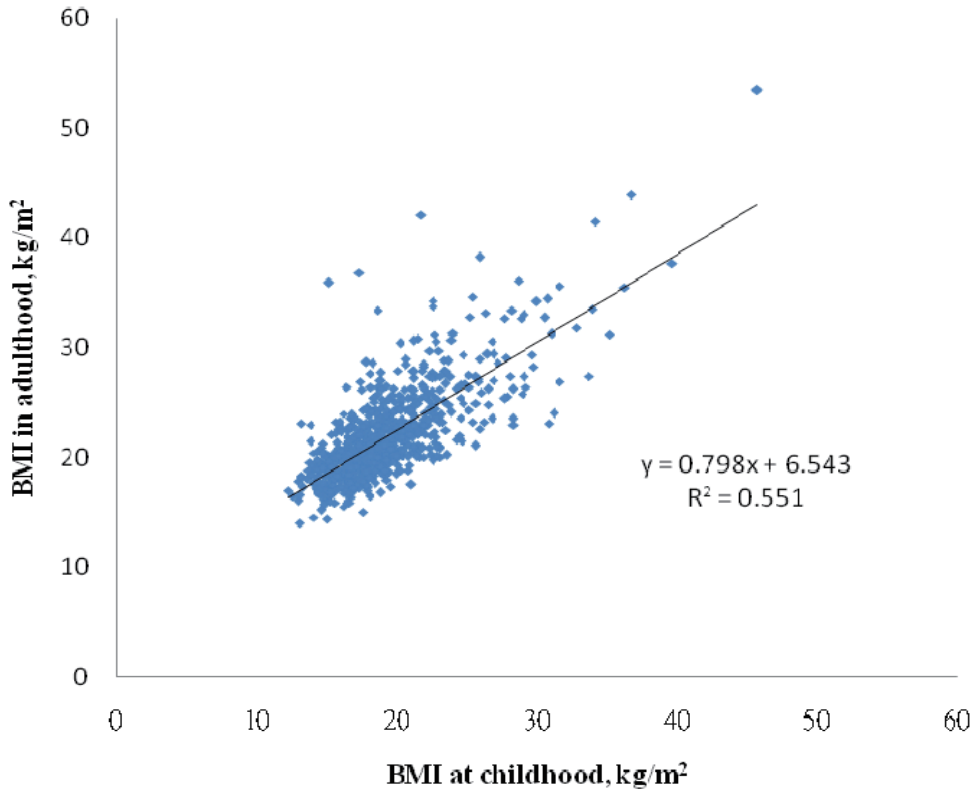

Fig. 2. Tracking of the body mass index from childhood to adulthood, with significant correlation at a p value of < 0.0001.

(95% CI) increased to 6.51 (3.36-12.63) for those with a BMI of ≥27 Kg/m^2 and a childhood BMI ≥85th percentile. However, the participants who were not overweight/obese in childhood exhibited a higher risk of prehypertension or hypertension if they became overweight or obese in adulthood.

Discussion

Early atherosclerosis and hypertension are known risk factors leading to cardiovascular disease later in life. In the present study, children with an overweight/obese status were found to be more likely to remain obese and be at a higher risk of prehypertension/hypertension and thicker CIMT values 8.5 years later as young adults, with a mean age of 21.32 years. The participants who were not overweight in childhood also exhibited a higher risk of prehypertension or hypertension if they were obese as adults. This study provides first-line evidence linking a childhood overweight/obese status and the risk of prehypertension/hypertension and subclinical atherosclerosis in adulthood in Asia.

The high level of tracking of BMI between childhood and adulthood observed in this study is similar to previous findings, including societies undergoing enormous changes in diet and activity, such as China[25]. The findings of our study are in agreement with the results of previous large cohort studies in American and European populations showing that a childhood overweight/obese status is associated with adult atherosclerosis based on the indicator, the carotid IMT[4, 5, 12, 13]. However, the follow-up time from the childhood survey to the adult survey in the present study was shorter than that used in previous studies in Western countries. In addition, the present results indicated that the pathogenesis of atherosclerosis acts via overweight/obesity-related factors, such as high BP, dyslipidemia, inflammation, insulin resistance, etc., as early as childhood or adolescence to the young adult period[7, 10, 11]. Cardiovascular risk factors in childhood may act to promote atherosclerosis if persistent across the age groups of adolescents and young adults[14, 16, 17].

The paradoxical finding that the BP values of the patients with childhood EBP were higher than the BP values in adulthood among men can be explained by the following factors. After reviewing the medication

Table 2. Carotid artery intima-media thickness (CIMT) according to the adult and childhood body mass index (BMI) categories

Childhood BMI	Adulthood BMI, kg/m^2								
	<24		*p*	24-27		*p*	≥27		*p*
	<85th percentile	≥85th percentile		<85th percentile	≥85th percentile		<85th percentile	≥85th percentile	
N	584	30		66	32		23	55	
CIMT, mm									
Rt CCA1	0.447 ± 0.06	0.483 ± 0.09	0.041	0.462 ± 0.06	0.453 ± 0.06	0.482	0.485 ± 0.08	0.488 ± 0.09	0.895
Rt CCA2	0.434 ± 0.06	0.460 ± 0.08	0.081	0.446 ± 0.05	0.455 ± 0.07	0.421	0.456 ± 0.06	0.474 ± 0.10	0.328
Lt CCA1	0.440 ± 0.06	0.461 ± 0.08	0.055	0.461 ± 0.07	0.476 ± 0.07	0.306	0.467 ± 0.07	0.498 ± 0.10	0.112
Lt CCA2	0.433 ± 0.07	0.461 ± 0.06	0.025	0.459 ± 0.08	0.471 ± 0.10	0.538	0.471 ± 0.08	0.485 ± 0.09	0.513
Rt Bulb	0.451 ± 0.10	0.463 ± 0.10	0.50	0.455 ± 0.09	0.50 ± 0.19	0.211	0.471 ± 0.10	0.531 ± 0.13	0.067
Lt Bulb	0.454 ± 0.09	0.493 ± 0.09	0.025	0.458 ± 0.07	0.497 ± 0.10	0.054	0.465 ± 0.08	0.506 ± 0.12	0.088
Rt ICA	0.408 ± 0.07	0.412 ± 0.06	0.730	0.417 ± 0.07	0.451 ± 0.09	0.048	0.402 ± 0.05	0.457 ± 0.10	0.003
Lt ICA	0.397 ± 0.06	0.429 ± 0.08	0.006	0.408 ± 0.07	0.428 ± 0.07	0.170	0.416 ± 0.07	0.441 ± 0.07	0.177
IMT, mean	0.431 ± 0.04	0.455 ± 0.05	0.004	0.442 ± 0.05	0.467 ± 0.07	0.075	0.448 ± 0.05	0.481 ± 0.08	0.064
Systolic BP, mm Hg	105.1 ± 13.4	110.5 ± 12.5	0.034	111.8 ± 13.6	114.8 ± 18.1	0.358	120.5 ± 18.4	121.1 ± 16.5	0.894
Diastolic BP, mm Hg	64.5 ± 10.1	69.3 ± 10.1	0.013	68.9 ± 10.1	71.8 ± 15.2	0.336	74.4 ± 14.6	79.7 ± 13.6	0.126

Abbreviations: CCA, common carotid artery; ICA, internal carotid artery; IMT mean = mean of IMT at eight measured sites of the carotid arteries, including Rt CCA1, Rt CCA2, Lt CCA1, Lt CCA2, Rt Bulb, Lt Bulb, Rt ICA and Lt ICA.

Table 3. Carotid artery intima-media thickness (CIMT) according to the adult body mass index (BMI) category in the patients with or without an elevated blood pressure (EBP) in childhood

Childhood EBP	Adulthood BMI, kg/m^2								
	<24		*p*	24-27		*p*	≥27		*p*
	without	with		without	with		without	with	
N	417	197		45	53		25	53	
CIMT, mm									
Rt CCA1	0.440 ± 0.05	0.468 ± 0.07	<.001	0.432 ± 0.04	0.482 ± 0.06	<.001	0.457 ± 0.06	0.501 ± 0.09	0.015
Rt CCA2	0.425 ± 0.05	0.459 ± 0.07	<.001	0.432 ± 0.04	0.464 ± 0.06	0.004	0.442 ± 0.05	0.482 ± 0.10	0.020
Lt CCA1	0.431 ± 0.05	0.461 ± 0.06	<.001	0.441 ± 0.05	0.487 ± 0.08	0.001	0.453 ± 0.08	0.507 ± 0.09	0.013
Lt CCA2	0.423 ± 0.06	0.458 ± 0.07	<.001	0.438 ± 0.06	0.484 ± 0.10	0.005	0.456 ± 0.08	0.493 ± 0.09	0.088
Rt Bulb	0.440 ± 0.10	0.473 ± 0.09	<.001	0.430 ± 0.08	0.502 ± 0.15	0.004	0.468 ± 0.09	0.534 ± 0.14	0.016
Lt Bulb	0.446 ± 0.09	0.477 ± 0.09	<.001	0.445 ± 0.07	0.491 ± 0.09	0.006	0.457 ± 0.08	0.510 ± 0.12	0.028
Rt ICA	0.399 ± 0.06	0.425 ± 0.08	<.001	0.397 ± 0.06	0.453 ± 0.09	<.001	0.407 ± 0.06	0.456 ± 0.10	0.010
Lt ICA	0.388 ± 0.05	0.420 ± 0.08	<.001	0.404 ± 0.07	0.423 ± 0.07	0.152	0.405 ± 0.07	0.446 ± 0.07	0.026
IMT, mean	0.422 ± 0.04	0.453 ± 0.05	<.001	0.426 ± 0.04	0.471 ± 0.06	<.001	0.435 ± 0.05	0.489 ± 0.07	0.002
Systolic BP, mm Hg	103.9 ± 12.2	108.6 ± 15.3	<.001	109.6 ± 13.3	115.5 ± 16.2	0.053	115.5 ± 13.8	123.5 ± 17.8	0.053
Diastolic BP, mm Hg	63.3 ± 8.9	67.9 ± 11.9	<.001	66.7 ± 10.36	72.6 ± 12.7	0.014	71.5 ± 11.5	81.2 ± 14.11	0.004

Abbreviations: CCA, common carotid artery; ICA, internal carotid artery; IMT mean = mean of IMT at eight measured sites of the carotid arteries, including Rt CCA1, Rt CCA2, Lt CCA1, Lt CCA2, Rt Bulb, Lt Bulb, Rt ICA and Lt ICA.

and dietary habits of the subjects, we found that some of the patients with childhood EBP had received antihypertensive medications, primarily men. In addition, the prevalence of a high-fat diet (poor dietary habits) among the patients with childhood EBP was slightly better than that observed in the patients with a normal BP in childhood (**Supplemental Tables 2** and **3**). We therefore propose that parents of patients diag-

Table 4. Multivariate logistic regression analysis of determinants of a thicker carotid intima-media thickness (CIMT ≥ 75th percentile)

Characteristic	OR (95% CI)	*p*-value
Childhood overweight/obesity & Adulthood obesity	4.17 (2.21-7.85)	<.001
Childhood overweight/obesity & Adulthood overweight	2.82 (1.26-6.28)	0.011
Childhood overweight/obesity & Adulthood normal weight	2.07 (0.91-4.71)	0.083
Childhood normal weight & Adulthood obesity	1.32 (0.51-3.44)	0.567
Childhood normal weight & Adulthood overweight	1.67 (0.94-2.99)	0.083
Childhood normal weight & Adulthood normal weight	1	–
Age, year	1.01 (0.95-1.06)	0.832
Male	1.37 (0.92-2.04)	0.120
Systolic BP, mm Hg	1.01 (1.00-1.03)	0.033
Fasting glucose, mmol/L	1.18 (0.99-1.40)	0.064
Cholesterol, mmol/L	1.30 (1.08-1.56)	0.006
Smoking habit, yes	0.87 (0.50-1.51)	0.618
Alcohol habit, yes	2.41 (1.33-4.36)	0.004
Household income ≥ US$1,660/month	0.75 (0.52-1.07)	0.110

The number of patients with an IMT ≥75th percentile is 196. The number of patients with a childhood BMI ≥85th percentile is 117.
The number of patients with an adult BMI of ≥27 kg/m^2 is 78, while that of patients with 24 ≤ BMI < 27 kg/m^2 is 98 and that of patients with a BMI of <24 kg/m^2 is 614.
A smoking habit is defined as a current smoker or ex-smoker.
An alcohol habit is defined as drinking alcohol at least one time per week.

Table 5. Multivariate logistic regression analysis of determinants of prehypertension and hypertension

Characteristic	OR (95% CI)	*p*-value
Childhood overweight/obesity & Adulthood obesity	6.51 (3.36-12.63)	<.001
Childhood overweight/obesity & Adulthood overweight	3.20 (1.40-7.33)	0.006
Childhood overweight/obesity & Adulthood normal weight	2.23 (0.89-5.58)	0.086
Childhood normal weight & Adulthood obesity	2.75 (1.08-6.97)	0.033
Childhood normal weight & Adulthood overweight	1.84 (1.02-3.30)	0.042
Childhood normal weight & Adulthood normal weight	1	–
Age, year	1.02 (0.96-1.08)	0.571
Male	5.67 (3.87-8.31)	<.001
Fasting glucose, mmol/L	1.21 (1.02-1.44)	0.027
Cholesterol, mmol/L	1.20 (0.98-1.46)	0.074
Smoking habit, yes	0.52 (0.29-0.92)	0.025
Alcohol habit, yes	0.96 (0.50-1.85)	0.902
Household income ≥ US$1,660/month	1.31 (0.90-1.91)	0.161

The number of patients with prehypertension or hypertension is 210. The number of patients with a childhood BMI of ≥85th percentile is 117.
The number of patients with an adult BMI of ≥27 kg/m^2 is 78, while that of patients with 24 ≤ BMI < 27 kg/m^2 is 98 and that of patients with a BMI of <24 kg/m^2 is 614.
A smoking habit is defined as a current smoker or ex-smoker.
An alcohol habit is defined as drinking alcohol at least one time per week.

nosed with EBP in childhood may have a positive impact by advising their children to adopt healthier dietary habits.

A childhood overweight/obese status is associated with a higher risk of future prehypertension or hypertension and subclinical atherosclerosis in young adulthood. However, as shown in this study, some children and adolescents who are overweight or obese become

non-obese in young adulthood and that such changes are associated with a reduction in cardiovascular risks, such as that of subclinical atherosclerosis and prehypertension/hypertension. This finding also echoes the recent results of the Bogalusa heart and cardiovascular risk in young Finns studies, in which patients with metabolic syndrome in their youth were found to have 3.4-times the risk of a high IMT in adulthood[26]. The clinical implications of this study are primarily intended for the prevention of cardiovascular disease and premature death among children who are overweight/obese. On the other hand, educational programs regarding a healthy lifestyle to normalize body weight should be initiated as early as possible in elementary and middle schools. There is an urgent need to address the worldwide "obesity epidemic in childhood" in order to prevent cardiovascular disease and premature death[27, 28].

This study was limited to recruited participants identified to be positive for proteinuria or glucosuria during the urinary screening program. Therefore, the present findings may not be generalizable to all young populations. However, all current participants were relative healthy in adulthood exhibited similar characteristics to the general population in Taiwan[29]. In addition, the incidence of hypertension and diabetes among the participants at the 8.5-year follow-up visit was low, as shown in **Table 1**, and no serious illnesses were identified. Therefore, the requirement of abnormal urine screening results in childhood does not necessarily negate the clinical relevance of this study. The strength of this study is that the study subjects were recruited from a large population of school children in Taiwan during 1992-2000 and exhibited the characteristics of a representative population for a long-term cohort study to investigate the incidence of cardiovascular and endocrine/metabolic risk factors from childhood to adulthood[14, 18, 20, 30].

In conclusion, this study documented a trend in BMI from childhood to adulthood and demonstrated that a persistent overweight or obese status contributes to the risk of preclinical atherosclerosis and a high BP in adulthood. More attention should be paid to the prevention and management of an overweight status and obesity in childhood.

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The authors have no financial relationships relevant to this article to disclose.

Conflicts of Interest

The authors have no conflicts of interest relevant to this article to disclose.

Key Messages

WHAT'S KNOWN ON THIS SUBJECT

Although childhood obesity has been linked to adulthood cardiovascular diseases, there is little evidence tracking an overweight/obese status and subclinical cardiovascular disease in young adults with an average age of 21 years.

WHAT THIS STUDY ADDS

Tracking the body mass index from childhood to young adulthood in a Taiwanese population showed a significant increase in the subclinical carotid intima-media thickness and rate of prehypertension/hypertension among the subjects with a persistent overweight/obese status.

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Supplemental Table 1. Carotid artery intima-media thickness (CIMT) according to the adult body mass index (BMI) category

	Adulthood BMI, kg/m^2					
CIMT in mm	< 21	21-24	24-27	≥ 27	*p*-value	
Locations	*n* = 395	*n* = 218	*n* = 98	*n* = 78	ANOVA	Trend
Men	*n* = 110	*n* = 104	*n* = 53	*n* = 46		
Rt CCA1	0.451 ± 0.053	0.463 ± 0.070	0.469 ± 0.053	0.506 ± 0.090	< .001	< .001
Rt CCA2	0.433 ± 0.057	0.442 ± 0.063	0.446 ± 0.049	0.473 ± 0.090	0.007	< .001
Lt CCA1	0.445 ± 0.056	0.455 ± 0.067	0.482 ± 0.070	0.500 ± 0.094	< .001	< .001
Lt CCA2	0.430 ± 0.101	0.443 ± 0.066	0.466 ± 0.070	0.489 ± 0.086	< .001	< .001
Rt Bulb	0.443 ± 0.075	0.456 ± 0.060	0.462 ± 0.091	0.517 ± 0.139	< .001	< .001
Lt Bulb	0.473 ± 0.127	0.471 ± 0.100	0.478 ± 0.079	0.507 ± 0.126	0.308	0.084
Rt ICA	0.409 ± 0.063	0.422 ± 0.070	0.438 ± 0.067	0.440 ± 0.081	0.025	0.005
Lt ICA	0.401 ± 0.065	0.424 ± 0.065	0.423 ± 0.064	0.447 ± 0.077	0.001	< .001
IMT, mean	0.436 ± 0.043	0.446 ± 0.046	0.458 ± 0.042	0.484 ± 0.076	< .001	< .001
Women	*n* = 285	*n* = 114	*n* = 45	*n* = 32		
Rt CCA1	0.443 ± 0.059	0.450 ± 0.052	0.448 ± 0.059	0.460 ± 0.070	0.407	0.165
Rt CCA2	0.435 ± 0.055	0.435 ± 0.058	0.452 ± 0.064	0.463 ± 0.082	0.023	0.003
Lt CCA1	0.434 ± 0.055	0.441 ± 0.056	0.446 ± 0.069	0.473 ± 0.084	0.005	< .001
Lt CCA2	0.429 ± 0.055	0.443 ± 0.052	0.458 ± 0.100	0.469 ± 0.091	< .001	< .001
Rt Bulb	0.450 ± 0.119	0.460 ± 0.092	0.477 ± 0.162	0.510 ± 0.109	0.041	0.006
Lt Bulb	0.449 ± 0.079	0.446 ± 0.073	0.462 ± 0.086	0.474 ± 0.086	0.251	0.057
Rt ICA	0.404 ± 0.060	0.404 ± 0.083	0.417 ± 0.092	0.441 ± 0.102	0.046	0.005
Lt ICA	0.387 ± 0.056	0.401 ± 0.070	0.405 ± 0.068	0.413 ± 0.056	0.024	0.028
IMT, mean	0.429 ± 0.041	0.435 ± 0.045	0.445 ± 0.067	0.460 ± 0.060	0.001	< .001

Abbreviations: CCA, common carotid artery; ICA, internal carotid artery; IMT mean = mean of IMT at eight measured sites of the carotid arteries, including Rt CCA1, Rt CCA2, Lt CCA1, Lt CCA2, Rt Bulb, Lt Bulb, Rt ICA and Lt ICA.

Supplemental Table 2. Basic characteristics and scores for dietary habits among the patients with an elevated blood pressure (EBP) in childhood stratified by the adult hypertension status

	Childhood with EBP			
Adulthood BP status	Hypertension	Prehypertension	Normal	*p*-value
Characteristics	N = 43	N = 80	N = 180	
Age	22.16 ± 3.65	21.56 ± 3.13	20.36 ± 3.43	0.001
Male	83.72	57.5	27.28	< .001
Body mass index, Kg/m^2	27.12 ± 7.43	24.87 ± 4.89	21.89 ± 3.69	< .001
Systolic BP, mm Hg	138.05 ± 19.42	120.53 ± 7.14	102.66 ± 9.36	< .001
Diastolic BP, mm Hg	91.74 ± 13.10	76.49 ± 6.75	63.64 ± 8.35	< .001
Anti-hypertensive med, %	23.26	0	0.56	< .001
Dietary habits score:				
Milk or Cheese	1.02 ± 1.05	1.03 ± 0.95	1.07 ± 0.94	0.911
Seafood	1.21 ± 0.72	1.23 ± 0.89	1.20 ± 0.82	0.564
Vegetable	2.50 ± 0.80	2.37 ± 0.74	2.36 ± 0.77	0.626
Fruits	1.86 ± 0.83	1.68 ± 0.95	1.75 ± 0.94	0.467
Desserts	1.48 ± 0.94	1.35 ± 0.85	1.50 ± 0.90	0.207
Coke, Soda and Soft drink	1.33 ± 1.14	1.04 ± 1.02	1.02 ± 1.02	0.979
Smoked meat	1.14 ± 0.81	1.20 ± 0.84	1.18 ± 0.89	0.935
Fatty meat	0.64 ± 0.82	0.49 ± 0.66	0.33 ± 0.60	0.01
Fast food (McDonald or KFC)	0.61 ± 0.95	0.41 ± 0.59	0.43 ± 0.56	0.200
High fat diet, %	13.95	7.5	3.89	0.044
Coffee	0.54 ± 0.84	0.62 ± 0.88	0.52 ± 0.84	0.668

Definitions of dietary habits according to the frequency score: 0 if rare or no, 1 if 1-2 times/wk, 2 if 3-4/wk, 3 if ≥ 5 times/wk
High-fat diet: fatty diet score ≥ 3, a summation score of smoked meat plus fast food plus fatty meat ≥ 3

Supplemental Table 3. Basic characteristics and scores for dietary habits among the patients with an normal blood pressure in childhood stratified by the adult hypertension status

	Childhood normal blood pressure			
Adulthood BP status	Hypertension	Prehypertension	Normal	*p*-value
Characteristics	N = 11	N = 76	N = 399	
Age	22.64 ± 2.73	21.14 ± 3.47	21.61 ± 3.15	0.269
Male	90.91	65.79	30.33	< .001
Body mass index, kg/m^2	25.99 ± 4.55	22.28 ± 3.77	20.57 ± 2.74	< .001
Systolic BP, mm Hg	138.18 ± 12.44	121.37 ± 6.14	100.99 ± 9.37	< .001
Diastolic BP, mm Hg	84.73 ± 9.48	73.21 ± 8.91	61.71 ± 7.57	< .001
Anti-hypertensive med, %	0	0	0.25	0.897
Dietary habits score:				
Milk or Cheese	1.0 ± 0.89	1.08 ± 0.86	1.07 ± 0.90	0.963
Seafood	1.27 ± 0.65	1.03 ± 0.73	1.06 ± 0.72	0.570
Vegetable	2.27 ± 0.65	2.28 ± 0.79	2.33 ± 0.78	0.828
Fruits	1.27 ± 1.01	1.66 ± 0.90	1.58 ± 0.96	0.439
Desserts	1.27 ± 0.79	1.59 ± 1.04	1.47 ± 0.96	0.500
Coke, Soda and Soft drink	1.36 ± 1.12	1.13 ± 1.10	1.03 ± 1.06	0.447
Smoked meat	1.45 ± 0.93	1.09 ± 0.79	1.12 ± 0.85	0.402
Fatty meat	1.0 ± 1.10	0.64 ± 0.90	0.45 ± 0.66	0.006
Fast food (McDonald or KFC)	0.55 ± 0.52	0.47 ± 0.62	0.51 ± 0.62	0.863
High fat diet, %	27.27	13.16	6.27	0.006
Coffee	0.45 ± 0.69	0.66 ± 0.92	0.57 ± 0.86	0.637

Definitions of dietary habits according to the frequency score: 0 if rare or no, 1 if 1-2 times/wk, 2 if 3-4/wk, 3 if ≥ 5 times/wk
High-fat diet: fatty diet score ≥ 3, a summation score of smoked meat plus fast food plus fatty meat ≥ 3