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Birth Weight and Carotid Artery Intima-Media Thickness

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Abstract

Objectives—To determine the association between birth weight and carotid artery intima-media thickness (CIMT), a measure of atherogenesis, in a population of 11-year-old children.

Study design—CIMT measured by high-resolution ultrasound, and birth registry data were available for 670 children of the Southern California Children's Health Study. Multivariate regression analyses were performed to investigate the association between birth weight and CIMT, with adjustment for child's health status and lifestyle, pregnancy information, and parental health.

Results—Mean CIMT was 0.57 mm (SD 0.04). We found a nonlinear association between birth weight and CIMT, with an increase in CIMT of 0.014 mm in the fifth (*P* value .01) compared with the third birth weight quintile. These associations were robust in subsample analyses in children considered normal-weight by gestational age or in term-born children. No significant association with CIMT was found for the lowest quintile.

Conclusions—Greater birth weight was significantly associated with increased CIMT at age 11 years. No evidence for an impact of lower birth weight was found. The predictive value of childhood CIMT on future cardiovascular outcomes is largely unknown, but strong associations between childhood cardiovascular disease risk factors and adult vascular disease suggest that increased CIMT in childhood may be clinically important.

The hypothesis of the developmental origins of cardiovascular disease (CVD) was first raised by Barker and Osmond[1] in the year 1986. Since then, evidence in support of the hypothesis and the importance of intrauterine exposures and birth outcomes has grown. In various studies authors have shown early changes of the vasculature in childhood and the long-term clinical importance of early cardiovascular risk factors in children,[2,3] as well as

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the adverse impact of specific intrauterine exposures such as maternal smoking[4] or maternal hypercholesterolemia.[5] However, the question as to whether birth weight, as a proxy for the intrauterine environment and development, is associated with CVD remains unclear.

In general, studies on birth weight and vascular properties yield stronger associations with small for gestational age (SGA) and intrauterine growth restriction (IUGR) than with low birth weight.[6–9] Studies in newborns raise the question of the observations being a transient phenomenon.[9,10] This objection is partly refuted by studies in adult populations showing an association of birth weight and intima-media thickness (IMT); however, studies in adults remain inconsistent.[7,11,12] Interestingly, the greater birth weight range or children large for gestational age (LGA) remains understudied, although obesity in childhood has been associated with vascular health[13–15] and fetal overnutrition is associated with childhood obesity and metabolic dysfunction,[16] both main determinants of cardiovascular health. On the basis of these uncertainties, we investigated the hypothesis that both lower and greater birth weight is associated with carotid artery intima-media thickness (CIMT) in a population-based study of schoolchildren.

Methods

This study was nested in the ongoing Southern California Children's Health Study.[17] From the 5341 kindergarten and first graders who were first enrolled in 2002, we sampled 738 children in 2007 to participate in a study of atherosclerosis. The children were recruited from public schools in 8 communities. Information was collected on personal, parental, and sociodemographic characteristics through questionnaire assessment; systolic/diastolic blood pressure, heart rate, height, and weight were measured; and B-mode carotid artery ultrasound was performed for assessment of CIMT. Heart rate, CIMT, and blood pressure were assessed by a single imaging specialist from the USC Atherosclerosis Research Unit, Core Imaging and Reading Center. The birth record for each participant was obtained from the state of California following necessary approvals.

Of the 738 eligible participants, 47 were excluded because they were born outside the State of California, inability to match to birth record, or indeterminate birth weight, leaving 691 participants in the study population. We excluded an additional 18 children born as part of a multiple pregnancy and 3 children with missing data on covariates, leaving 670 children for analyses.

The study protocol was approved by the institutional review board for human studies at the University of Southern California. Written informed consent was provided by a parent of the study subject, and verbal assent was provided by the participant.

High-resolution B-mode ultrasound images of the right common carotid artery were obtained with a portable Bio-sound MyLab 25 ultrasound system (Esaote North America, Inc, Indianapolis, Indiana) attached to a 10-MHz linear array transducer and read by a single operator. The imaging protocol, as described previously,[18,19] standardizes the timing, location, and distance over which CIMT is measured, ensuring comparability across participants (patents 2005, 2006, 2011). The jugular vein and carotid artery were imaged

transversely and then longitudinally with the jugular vein stacked above the carotid artery. All images contained internal anatomical landmarks for reproducing probe angulation, and a 3-lead electrocardiogram was recorded simultaneously with the B-mode image to ensure that CIMT was measured at the R-wave in the cardiac cycle. Common carotid artery far-wall IMT was determined as the average of 70 to 100 measurements between the intima-lumen and media-adventitia interfaces along a 1-cm length defined by an electronic ruler proximal to the carotid artery bulb by automated computerized edge detection with an in-house developed software package (Prowin, patents 2005, 2006, 2011).[18,19]

Immediately after the IMT scan, blood pressure and heart rate were measured by standard techniques after the subject was recumbent for at least 10 minutes. Blood pressure was measured 3 times in 1-minute intervals with the use of an OMRON blood pressure monitor (OMRON, Tokyo, Japan) with automatic cuff inflation and deflation. Heart rate was measured with a 3-lead electrocardiogram as part of the Bio-sound MyLab 25 ultrasound system. The subject's standing height with the subject in stocking feet was measured to the nearest centimeter by the use of a metal measuring tape placed perpendicularly to the floor through the use of a construction-type bubble level and a measurement block to properly align head orientation. Weight was measured to the nearest pound with a medical-grade scale calibrated before each day's testing with the use of predetermined calibration weights.

Birth weight, gestational age, mode of delivery, and other reproductive data were obtained from California birth records. Birth certificate information for California-born children who participated in the Children's Health Study (CHS) was obtained by computerized linkage of participants with the California Department of Public Health, Birth Statistical Master Files, and Birth Cohort Files. Data obtained from California birth certificates included birth weight, gestational age, maternal age at birth, maternal residence postal code at birth, parity, pregnancy complications, and marital status. The estimated date of conception was assigned by the use of the birth date and gestational age, corrected for the average 2-week difference between the last menstrual period and conception. Gestational age was recorded for 640 children. Missing data were imputed by the use of weeks of prematurity if reported by the mother on the baseline questionnaire (n = 6) and otherwise a normal duration of pregnancy of 280 days was assumed (n = 73). Appropriate weight for gestational age (AGA) was defined as a birth weight between the 10th and 90th percentile on the basis of the sex-specific intrauterine growth curves by Olsen et al.[20] SGA was defined as <10th percentile for gestational age and sex and LGA correspondingly >90th percentile.

The study questionnaire included questions on medical history of the biological mothers and fathers, such as stroke, heart failure, heart attack, or angina. In addition, parents were asked whether they had ever had high blood pressure, high cholesterol, or diabetes. Further covariates on health, sociodemographic, and lifestyle characteristics were taken from the yearly surveys since first enrollment in 2002. Parental health information and pregnancy characteristics were reported in the first survey. Children's health and lifestyle data were collected at each survey.

Statistical Analyses

Basic descriptive analyses and univariate associations between CIMT and birth characteristics, sociodemographic, and lifestyle factors were investigated for the analytic sample and compared with the total study population. Second, multivariate regression analyses were performed in the full analytic sample and in the following subsamples: (1) singleton births who were AGA as determined by the intrauterine weight curves of Olsen et al[20] (n = 562); and (2) singletons born at term (n = 531). Term born was defined as birth between gestational weeks 37–41. The final model was adjusted for child's sex, age, body mass index (BMI), systolic blood pressure measurement, and asthma status at time of CIMT measurement; maternal cardiovascular and metabolic pregnancy complications; delivery mode; annual household income; and race/ethnicity and study community. Additional covariates evaluated but not included in the final regression model because of a lack of confounding (<10% change in risk estimates) were physical activity, secondhand tobacco smoke exposure, parental history of CVD (stroke, myocardial infarction, hypertension) and metabolic disease history (diabetes, hypercholesterolemia), height and height squared of the child at CIMT measurement, and parental education.

Nonlinearity of the association was tested in the entire sample by introducing polynomials, tertiles, and quintiles of the exposure. To account for the nonlinear association, birth weight was expressed as quintiles. The third quintile, centered on the average birth weight, was considered the reference value. Nonlinearity of the association was confirmed by spline and generalized additive model analyses. Interaction terms for sex, BMI, and race/ethnicity were investigated by including interaction terms.

Potential misclassification and -interpretation of birth weight by sex and gestational weeks was addressed in different ways: one, the final model was run with and without these covariates; second, birth weight was regressed on sex and gestational weeks and the residuals then used as an independent variable in the model; and third, the definition of normal weight by Olsen et al[20] are based on sex and gestational weeks. In a sensitivity analysis, normal birth weight additionally was defined on the basis of the widely known World Health Organization growth charts,[21] which do not take gestational age into account but are based on sex-specific weight distributions of healthy newborns. Further sensitivity analyses were conducted in restricted data sets, first, excluding potential outliers (subjects with residuals >2 or <−2) and, second, excluding children missing birth record data on gestational age. In addition, stratified analyses by parental history of cardiovascular risk were performed and the strata of SGA (n = 48) and LGA (n = 60) children investigated. All analyses were performed with STATA 11 (Stata Corp, College Station, Texas), with significance level assumed at 0.05 for testing two-sided hypotheses.

Results

The analytic sample consisting of 670 children did not differ in main characteristics when we compared it with the entire study population with CIMT data, which included children without birth weight data (n = 738; Table I; available at www.jpeds.com). Most children were AGA (84%, as determined by Olsen et al[20]). Nine percent had a birth weight in the <10th percentile (SGA) and 7% was > 90th percentile (LGA). The birth statistics

documented gestational diabetes in 12 mothers and pre-eclampsia or pregnancy-induced hypertension in 13 mothers. Forty-four percent of the parents had reported a CVD or a cardiovascular risk factor, such as hypertension (mothers, n = 64, fathers, n = 99), myocardial infarction (mothers, n = 1; fathers, n = 9), stroke (mothers, n = 2; fathers, n = 5), hypercholesterolemia (mothers, n = 82; fathers, n = 144), or diabetes (mothers n = 27, fathers n = 27). Further characteristics of the study population are listed in Table II.

The mean CIMT in the study population was 0.57 mm. In unadjusted regression analysis the greatest birth quintile was significantly and positively associated with CIMT. Next to known determinants of CIMT (ie, sex, race/ethnicity, height, and BMI) we found CIMT to be positively associated with cesarean delivery (P = .006), preterm birth (P = .075), and asthma status (P = .101; Table III).

The continuous birth weight variable and the birth weight residual proved significantly associated with an increase of CIMT (Table IV). However, evidence emerged of a nonlinear association between birth weight and CIMT, supported by the introduction of quadratic (P = .125) and cubic birth weight (P = .05) terms. In the final adjusted model with birth weight categorized as quintiles, CIMT in the 5th birth weight quintile was 0.014 mm (P = .01) thicker compared with CIMT in the 3rd quintile (Table IV). CIMT in children of lower birth weights, quintile 1 and 2, did not show a significant difference compared with the reference category. However, in the strata of children with positive parental history of cardiovascular risk, in subsample B as well as in the sensitivity analysis based on the World Health Organization growth charts (Table V; available at www.jpeds.com), a weak indication of a U-shaped association was present. Both SGA and LGA children were at risk of thicker CIMT; however, because of small numbers, the multivariate results were nonsignificant (Table VI; available at www.jpeds.com). The model using quintiles of birth weight residuals adjusted for gestational age showed significantly greater CIMT in children whose birth weight was markedly higher than that expected given their gestational age and sex (Table IV). However, there was no evidence of nonlinearity for the residuals of birth weight. We observed no evidence for interaction by sex, BMI, or race/ethnicity.

We examined the association between CIMT and birth weight in 2 subsamples: populations restricted to AGA children and to children born at term. The observed significant increase in CIMT in the greatest birth weight quintile compared with the reference quintile was consistent across all analyses (Table VII).

In further sensitivity analyses, we excluded children with imputed gestational age and observed associations consistent with the results in the full sample (Table VI). In addition, when we excluded potential outliers from the full sample, analyses yielded stronger results with a greater increase in CIMT in the 4th (difference in CIMT 0.010 mm, P value .05) and the 5th birth weight quintile (5^{th} quintile difference in CIMT 0.016, P value .001; Table VI) compared with the reference quintile.

Discussion

Birth weight as well as cardiovascular risk may be genetically determined. Although we did not have data on parental birth weight, adjustment for reported parental history of CVD or risk did not alter the observed association. Residual confounding by family predisposition to CVD can nevertheless not be completely excluded because parents might not have known their own CVD risk or disease status at the time of birth, and disease status in grandparents was not collected in the study. Some confounding could also remain because of the lack of blood markers, data on nutrition, and pubertal status. One of the strengths of the study is the linkage of the cohort data with birth certificates, ensuring timely and valid recording of birth weight. The data on gestational age obtained from birth certificates are more prone to error than birth weight data because gestational age is calculated by the last date of menstruation, which may be difficult to recollect. However, we would expect any potential bias introduced from such misclassification to be nondifferential with respect to birth outcome and the CIMT measure.

In this children's cohort, high birth weight was an independent factor for increased CIMT. This finding stands in contrast to studies on SGA, IUGR, or low birth weight and vascular properties[7] but is in line with a recent publication on high birth weight and atrial fibrillation[22] and with studies on birth weight and obesity,[23] a major risk factor for adult CVD. Birth weight often is believed to reflect both the degree of maturation because birth weight naturally increases with gestational age and the intrauterine environment, which conditions "physiologically healthy" or "unhealthy" development. The observed association between high birth weight and CIMT could be related to a long-term impact of the maturity at birth, even though our models accounting for gestational age as a proxy for maturity and the model using the residual birth adjusted for gestational age weight term yielded similar results. A more probable mechanism for the association is a hyper-metabolic state in utero causing increased growth and weight gain of the fetus and an increased postnatal cardiovascular risk profile. This speculation is supported by studies on adult obesity and diabetes mellitus, having shown associations with high birth weight and hyperglycemic intrauterine environments.[14,24] Also, maternal hyperglycemia, found more frequently in obese mothers, leads to fetal hyperglycemia, resulting in fetal hyperinsulinemia, increased insulin growth factor and leptin levels, as well as increased fetal body size.[25,26] Exposure to maternal diabetes in utero accelerates BMI growth in late childhood, thus increasing long-term obesity and CVD risk.[27] Children of diabetic mothers as well as macrosomic children (children greater than the 90th birth weight percentile) of healthy mothers have greater CIMT than normal birth weight children of healthy mothers.[25] Oren et al[28] found a positive relationship between birth weight and arterial stiffness in young adults, which was driven by impaired glucose tolerance. Thus far, little research on macrosomic children of nondiabetic mothers has been conducted, although there is increasing evidence that BMI in children is associated positively with an increase in CIMT.[29–31]

Another mechanism may lie in a potential disequilibrium of the antioxidant and oxidant system in children deviating from the expected intrauterine growth pattern. Increased pre- and postpartum oxidative stress has been found not only in children with IUGR but also in LGA infants.[32] Oxidative stress may be increased in utero as the result of maternal

complications in pregnancy, such as pre-eclampsia, gestational diabetes or maternal cardiovascular risk factors, hypertension, or hypercholesterolemia but also has been found in SGA newborns of healthy mothers.[33] Neonates with significant deficiencies in antioxidant defense might not be sufficiently adapted to a postnatal oxidative rich environment.[34,35] The suggested mechanisms of increased risk in an overnourished infant may in part also hold true for normal birth weights and potentially explain the differences that we observe across the normal birth weight range in our cohort.

We are limited in our ability to investigate these potential pathways further. Several key questions remain, including whether CIMT in school-aged children is predictive of cardiovascular health in adulthood or whether the observed differences are transient phenomena. The well-documented association between cardiovascular risk factors in childhood and adult CIMT[2,3] supports the hypothesis that CIMT correlates with the general cardiovascular risk in childhood and likely with CVD risk in adulthood.[31] The effects we observe in the CHS are small compared with effects attributed to adult risk factors. However, in view of the increasing prevalence of maternal obesity in pregnancy[36] and the metabolic consequences for the offspring, the impact of high birth weight on CIMT is likely to be of relevance.

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Glossary

AGA	Appropriate weight for gestational age
BMI	Body mass index
CHS	Children’s Health Study
CIMT	Carotid artery intima-media thickness
CVD	Cardiovascular disease
IMT	Intima-media thickness
IUGR	Intrauterine growth restriction
LGA	Large for gestational age
SGA	Small for gestational age

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Table I

Selected sociodemographic, lifestyle, and health-related characteristics of CHS CIMT study participants with and without birth weight data

	Full study sample		Analytic sample	
	N = 738	%	N = 670	%
Sex				
Girls	380	51	347	52
Boys	358	49	323	48
Term born				
Term	589	80	531	79
Preterm	44	6	35	5
Postterm	105	14	104	16
Mode of delivery				
Vaginal	549	74	537	80
Cesarean	143	19	133	20
Missing	46	6	0	0
Ethnicity				
Asian	35	5	28	4
Hispanic white	410	56	374	56
Non-Hispanic white	236	32	221	33
Other	57	8	47	7
Pregnancy complications*				
Yes	34	5	31	5
Parental history of CVD risk†				
Yes	323	44	298	44

	n	Mean	SD	n	Mean	SD
Age at CIMT scan, years	697	11.3	0.6	670	11.3	0.6
Gestational age, weeks	738	39.8	2.0	670	39.9	2.0
BMI, kg/m^2	737	20.0	4.1	670	20.0	4.1
Blood pressure, systolic, mmHg	735	104.7	8.5	670	104.8	8.4
Blood pressure, diastolic, mmHg	735	57.0	6.2	670	57.0	6.1

* Reported pregnancy complications: eclampsia, pre-eclampsia, gestational diabetes, gestational hypertension, and cardiac disease.

† Parents with self-reported diabetes, hypercholesterolemia, hypertension, myocardial infarction, heart failure, or stroke.

Table II

Main sociodemographic, lifestyle, and health-related characteristics of Southern California Health Study: CIMT study participants

	n	%
Sex		
Girls	347	51.8
Boys	323	48.2
Term born		
Term	531	79.3
Preterm	35	5.2
Postterm	104	15.5
BMI		
>85th percentile	243	37.3
>95th Percentile	115	17.2
Mode of delivery		
Vaginal	537	80.2
Cesarean	133	19.9
Pregnancy complications		
No	639	95.4
Yes	31	4.6
Asthma (lifetime prevalence)		
No	513	76.6
Yes	157	23.4
Race/ethnicity		
Non-Hispanic white	221	33
Hispanic white	374	55.8
Asian	28	4.2
Other	47	7
Income		
Low	156	23.3
High	514	76.7
Parents with history of cardiovascular risk*		
No	372	55.5
Yes	298	44.5

	n	Mean	SD
Age at IMT scan (yrs.)	670	11.3	0.63
Birth weight (g)	670	3418	522
Gestational age (wks.)	670	39.9	1.96
BMI, kg/m^2	670	20.0	4.08
BMI z-scores†	670	0.5	1.05
Blood pressure, mmHg			

	n	Mean	SD
Systolic	670	104.8	8.4
Diastolic	670	57.0	6.1

* Parents with self-reported diabetes, hypercholesterolemia, hypertension, myocardial infarction, heart failure, or stroke.

† Calculated using the Centers for Disease Control and Prevention 2000 reference values.

Table III

Mean CIMT by birth and parental health characteristics*

	n	Mean CIMT, mm (SD)	*P* value†
Sex			
Girls	347	0.561 (0.04)	Ref
Boys	323	0.573 (0.04)	.001
Birth weight quintiles, g			
1: 709–3005	141	0.565 (0.04)	.565
2: 3010–3317	137	0.562 (0.04)	.912
3: 3320–3544	137	0.562 (0.05)	Ref
4: 3545–3830	138	0.568 (0.05)	.252
5: 3840–5216	138	0.576 (0.05)	.012
Term born			
Term	531	0.553 (0.04)	Ref
Preterm	35	0.567 (0.04)	.075
Postterm	104	0.573 (0.05)	.224
Mode of delivery			
Vaginal	537	0.569 (0.04)	Ref
Cesarean	133	0.578 (0.04)	.006
Pregnancy complications			
No	639	0.566 (0.04)	Ref
Yes	31	0.578 (0.04)	.164
Asthma status			
No	513	0.565 (0.04)	Ref
Yes	157	0.572 (0.05)	.101
Parents with history of cardiovascular risk*			
No	372	0.565 (0.05)	Ref
Yes	298	0.569 (0.04)	.205

Ref, reference category; *g*, range of actual birth weight of study participants in each quintile.

*Parents with self-reported diabetes, hypercholesterolemia, hypertension, myocardial infarction, heart failure, or stroke.

†Unadjusted linear regression analyses.

Table IV

Association between birth weight quintiles and quintiles of birth weight residuals* and CIMT in the CHS CIMT study population and subsamples

	Main model† Full sample, N = 670				Main model‡ Full sample, N = 670		
	CIMTd	**95% CI**	***P* value**		**CIMTd**	**95% CI**	***P* value**
Birth weight (unit: 100 g)	0.0007	0.0001–0.0014	.026	Birth weight residuals* (unit: 100 g)	0.0019	0.0004–0.0035	.0014
Birth weight quintiles, g				Quintiles of birth weight residuals‡			
1: 709–3005	0.0054	−0.005 to 0.016	.32	Quintile residual 1	Reference		
2: 3010–3317	0.0018	−0.009 to 0.012	.74	Quintile residual 2	0.0053	−0.005 to 0.016	.322
3: 3320–3544		Reference		Quintile residual 3	0.0121	0.002–0.023	.024
4: 3545–3830	0.0057	−0.005 to 0.016	.27	Quintile residual 4	0.0094	−0.001 to 0.020	.077
5: 3840–5216	0.0135	0.0032–0.024	.01	Quintile residual 5	0.0181	0.008–0.029	.001

CIMTd, difference in carotid artery intima-media thickness (mm); *g*, range of actual birth weight of study participants in each quintile.

*Residuals of birth weight regressed on gestational age and sex.

†Adjusted for child's age at carotid artery IMT scan, sex, BMI, systolic blood pressure, asthma status, race/ethnicity, delivery mode, maternal pregnancy complications, income, and study area.

‡Main model without sex.

Table V

Association between birth weight quintiles and CIMT: sensitivity analyses

	Excluding potential outliers,[*,†] n = 637			Children with birth record data on gestational age,[†,‡] n = 637			Normal weight defined by WHO growth charts,[†,§] n = 517		
Birth weight quintiles	**CIMTd**	**95% CI**	***P* value**	**CIMTd**	**95% CI**	***P* value**	**CIMTd**	**95% CI**	***P* value**
1: 709–3005 g	0.0056	−0.0037 to 0.0150	.24	0.0057	−0.0050 to 0.0164	.29	0.0089	−0.0037 to 0.0215	.17
2: 3010–3317 g	0.0066	−0.0026 to 0.0157	.16	−0.0007	−0.0112 to 0.0097	.89	0.0015	−0.0088 to 0.0119	.77
3: 3320–3544 g	Ref.			Ref.			Ref.		
4: 3545–3830 g	0.0092	0.0001–0.0183	.05	0.0053	−0.0051 to 0.0156	.32	0.0055	−0.0047 to 0.0157	.29
5: 3840–5216 g	0.0161	0.0070–0.0253	<.01	0.0113	0.0009–0.0218	.03	0.0135	−0.0022 to 0.0291	.09

CIMTd, difference in carotid intima-media thickness; *WHO*, World Health Organization.

[*] Excluding residuals >2 or <−2.

[†] Adjusted for child's age at CIMT scan, sex, BMI, systolic blood pressure, asthma status, race/ethnicity, delivery mode, maternal pregnancy complications, income, and study area.

[‡] Sample excluding the 33 children without data on gestational age from birth records.

[§] WHO growth charts: sex-specific birth weight of healthy newborns.

Table VI

Association between birth weight and CIMT using different exposure terms

N = 670	Δ mm CIMT	95% CI	*P* value
Continuous birth weight (unit: 100 g)			
Birth weight*	0.0007	0.0001–0.0014	.026
Birth weight†	0.0008	0.0002–0.0014	.015
Birth weight‡	0.0006	−0.0001 to 0.0013	.117
Birth weight groups by gestational age*			
AGA (n = 562)	Ref.		
SGA (n = 48)	0.0024	−0.0093 to 0.0141	.689
LGA (n = 60)	0.0067	−0.0063 to 0.0197	.312

*Main model adjustment: adjusted for child's age at CIMT scan, sex, BMI, systolic blood pressure, asthma status, race/ethnicity, delivery mode, maternal pregnancy complications, income, and study area.

†Main model adjustment without sex.

‡Main model adjustment with gestational age, in addition.

Table VII

Association between birth weight quintiles and CIMT in the CHS CIMT study subsamples

	Subsample A [*]: normal weight by gestational age,[†] n = 562			Subsample B[*]: term born, [‡] n = 531		
Difference in IMT	**CIMTd**	**95% CI**	***P* value**	**CIMTd**	**95% CI**	***P* value**
Birth weight quintiles						
1: 709 – 3005 g	0.0034	−0.010 to 0.017	.62	0.0084	−0.004 to 0.021	.18
2: 3010 – 3317 g	0.0017	−0.009 to 0.013	.76	0.0047	−0.007 to 0.016	.42
3: 3320 – 3544 g	Reference			Reference		
4: 3545 – 3830 g	0.0060	−0.005 to 0.017	.27	0.0087	−0.003 to 0.020	.13
5: 3840 – 5216 g	0.0137	0.002–0.025	.02	0.0122	0.001–0.024	.04

NWA, normal weight for gestational age.

[*] Adjusted for child's age at CIMT scan, sex, BMI, systolic blood pressure, asthma status, race/ethnicity, delivery mode, maternal pregnancy complications, income, and study area.

[†] Based on intrauterine growth curves by Olsen et al.[20]

[‡] Children born between 37 and 41 gestational weeks.