Increased Carotid Intima-Media Thickness and Stiffness in Obese Children

ARCANGELO IANNUZZI, MD[1]
MARIA ROSARIA LICENZIATI, MD[2]
CIRO ACAMPORA, MD[3]
VITTORIO SALVATORE, MD[1]
LUCIA AURIEMMA[2]
MARIA LUIGIA ROMANO, MD[3]
SALVATORE PANICO, MD[4]
PAOLO RUBBA, MD[4]
MAURIZIO TREVISAN, MD[5]

Obesity in childhood increases the risk of atherosclerotic disease and death in adulthood (1). A dramatic increase in overweight among children and adolescents during the past 2 decades has been documented (2). Moreover, overweight children and adolescents have an increased risk of adult obesity (3). A clustering of factors typical of the insulin resistance syndrome has been identified in 5- to 10-year-old overweight/obese African-American children (4) and in preadolescent obese children (5). The pediatric obesity epidemic accounts for most new diagnoses of type 2 diabetes, a disease once virtually confined to adulthood, in adolescence (6).

High-resolution B-mode ultrasound measurements of carotid intima-media thickness (IMT) and stiffness are markers of early, preclinical atherosclerosis. Previous observations show significantly increased IMT in familial hypercholesterolemic children (7,8) and in children with type 1 diabetes (9) and hypertension (10). Recent evidence suggests an increased arterial stiffness in familial hypercholesterolemic children (11) and in children with severe obesity (12).

However, in the study by Tounian et al. (12) there was no evidence of statistically significant differences in carotid IMT between severely obese children and control subjects; moreover, there was no subgroup analyses for boys versus girls. The present study aimed to verify whether obesity in childhood may cause premature vascular alterations in both sexes.

RESEARCH DESIGN AND METHODS

We studied 100 children with obesity consecutively recruited from the outpatient clinic of the Department of Pediatrics, A. Cardarelli Hospital, Naples, Italy, among patients evaluated for overweight or obesity and 47 healthy age-matched control subjects. The inclusion criteria for both obese children and control subjects were age 6–14 years; no personal history of diabetes or impaired fasting glucose, hypercholesterolemia, or hypertension; absence of any pharmacological therapy; and absence of cardiovascular disease in their parents. Obesity was defined as BMI >95th percentile of the reference values stated in the Centers for Disease Control and Prevention growth chart (13).

All of the children had measurements of fasting serum total cholesterol, triglycerides, apolipoproteins A and B, HDL cholesterol, plasma glucose and insulin, C-reactive protein, and glycated HbA_{1c}. An oral glucose tolerance test was performed in the obese children. The estimate of insulin resistance was calculated by a homeostasis model assessment (HOMA) score, as described by Matthews et al. (14). Quantitative B-mode ultrasound measurements of common carotid IMT and stiffness were calculated for all children following a standardized protocol. Carotid stiffness was calculated using the following formula: β = (natural logarithm systolic blood pressure − natural logarithm diastolic blood pressure)/(systolic diameter − diastolic diameter)/diastolic diameter.

Statistical analysis

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS 11). Univariate, unadjusted analyses between obese and control subjects were performed with the independent samples *t* test. Stiffness measures were not normally distributed, and a Kruskal-Wallis test was used. ANCOVA was used to evaluate the presence of confounding variables in the relationship between obesity status and vascular parameters. Models were adjusted for several confounding variables, including age, sex, systolic blood pressure, total cholesterol, HDL cholesterol, and triglycerides. Adjusted means and CIs were estimated with the use of the Bonferroni method. The coefficient of variation for each pair of IMT and diameter measurements was 3.9% for IMT measurements, 1.8% for lumen systolic diameters, and 2.5% for lumen diastolic diameters.

RESULTS

Table 1 shows anthropometrical, biochemical, and ultrasonic parameters of the arterial carotid wall in obese and nonobese children. Obese children had significantly higher blood pressure and plasma concentrations of triglycerides, cholesterol, glucose, insulin, HOMA, and C-reactive protein than control subjects. Carotid thickness and stiffness were significantly different between obese and nonobese children and in both boys and girls.

For carotid IMT, when we added traditional cardiovascular risk factors (except for blood pressure and HOMA) in

From the [1]Department of Medicine, Cava de' Tirreni Hospital, Salerno, Italy; the [2]Department of Pediatrics, A. Cardarelli Hospital, Naples, Italy; the [3]Department of Radiology, A. Cardarelli Hospital, Naples, Italy; the [4]Department of Clinical and Experimental Medicine, School of Medicine, Federico II University, Naples, Italy; and the [5]Department of Social and Preventive Medicine, School of Public Health and Health Professions, State University of New York, Buffalo, New York.

Address correspondence and reprint requests to Dr. Arcangelo Iannuzzi, MD, Cava de' Tirreni Hospital, Department of Medicine, Via de Marinis, SS18, 84013 Cava de' Tirreni, Salerno, Italy. E-mail: lelliann@libero.it.

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Abbreviations: HOMA, homeostasis model assessment; IMT, intima-media thickness.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

Table 1—*Physical characteristics and biochemical and ultrasonographic parameters*

	Entire group			Boys			Girls		
	Obese	Control subjects	*P*	Obese	Control subjects	*P*	Obese	Control subjects	*P*
n	100	47	—	61	26	—	39	21	—
Age (years)	10.0 ± 2.7	10.0 ± 2.5	0.82	10.3 ± 2.8	11.1 ± 1.9	0.13	9.6 ± 2.4	8.8 ± 2.6	0.22
Weight (kg)	58.6 ± 21.4	34.8 ± 10.0	—	62.4 ± 24.7	38.5 ± 9.3	—	52.7 ± 13.2	30.2 ± 9.1	—
Height (cm)	143.2 ± 14.9	138.7 ± 16.2	0.097	145.5 ± 16.2	146.1 ± 11.8	0.86	139.6 ± 11.9	129.4 ± 16.4	0.02
BMI (k/mg^2)	27.8 ± 5.3	17.8 ± 2.6	—	28.5 ± 5.9	17.9 ± 2.8	—	26.6 ± 3.9	17.6 ± 2.3	—
Systolic blood pressure (mmHg)	120.6 ± 15.8	98.8 ± 13.8	0.001	122.4 ± 16.9	103.4 ± 10.6	0.001	117.9 ± 13.6	93.0 ± 15.4	0.001
Diastolic blood pressure (mmHg)	76.4 ± 8.0	65.4 ± 8.3	0.001	77.1 ± 8.8	69.4 ± 6.2	0.001	75.4 ± 6.6	60.5 ± 8.0	0.001
Fasting cholesterol (mmol/l)	4.25 ± 0.74	3.96 ± 0.52	0.008	4.14 ± 0.78	3.99 ± 0.61	0.38	4.42 ± 0.65	3.93 ± 0.39	0.001
Fasting triglycerides (mmol/l)	0.91 ± 0.41	0.67 ± 0.22	0.001	0.93 ± 0.46	0.73 ± 0.24	0.008	0.87 ± 0.30	0.61 ± 0.18	0.001
Plasma fasting glucose (mmol/l)	4.55 ± 0.51	4.37 ± 0.45	0.036	4.62 ± 0.46	4.37 ± 0.52	0.030	4.45 ± 0.56	4.36 ± 0.38	0.50
Insulin (μU/ml)	16.1 ± 11.4	7.1 ± 2.1	0.001	16.4 ± 13.3	7.5 ± 2.3	0.001	15.6 ± 7.6	6.7 ± 1.8	0.001
HOMA	3.2 ± 2.1	1.4 ± 0.5	0.001	3.3 ± 2.3	1.5 ± 0.5	0.003	3.1 ± 1.6	1.3 ± 0.4	0.001
C-reactive protein	1.45 ± 0.78	1.26 ± 0.08	0.001	1.49 ± 0.45	1.26 ± 0.09	0.001	1.39 ± 0.06	1.26 ± 0.06	0.004
IMT (mm)	0.55 ± 0.08	0.49 ± 0.09	0.001	0.56 ± 0.08	0.48 ± 0.10	0.001	0.53 ± 0.09	0.49 ± 0.07	0.045
Stiffness	3.48 ± 1.26	2.38 ± 0.61	0.001	3.65 ± 1.3	2.43 ± 0.64	0.001	3.19 ± 1.17	2.32 ± 0.59	0.004

Data are means ± SD.

addition to age and sex as covariates, we still found evidence of statistically significant differences between obese children and control subjects. IMT in obese children was 0.55 mm (95% CI 0.54–0.57) and in healthy control subjects was 0.48 mm (0.46–0.51, $P = 0.001$). The further addition of C-reactive protein did not materially modify the outcome of our analyses. Adding systolic blood pressure as a covariate reduced the *P* value, but the statistical significance was retained. However, when glucose level was substituted by HOMA, the statistical significance was further reduced to a level that did not reach the formal level of statistical significance. IMT in obese children was 0.54 mm (0.52–0.56), and IMT in healthy control subjects was 0.51 mm (0.48–0.54, $P = 0.099$).

CONCLUSIONS — Obese children have significantly increased carotid IMT and stiffness compared with healthy control children. A previous study demonstrated an increased stiffness of the carotid artery in obese children (12) (a finding confirmed in the present study) but concluded that no significant difference was present in IMT between obese and nonobese children. The apparent discrepancy with the present observation could be due to the limited statistical power available for the study by Tounian et al. (12), which focuses on much smaller sample sizes (48 obese children and 27 control subjects). Increased carotid IMT and stiffness in obese boys and girls could reflect structural changes of large arteries that occur very early in atherosclerosis. The increased vascular IMT and stiffness in obese children compared with healthy control subjects suggests that obesity in children represents a powerful determinant of early manifestations of atherosclerosis and affects structural and mechanical properties of major vessels. The effect on structural changes appears to be mediated, at least in part, by the risk factors considered, especially systolic blood pressure and, most importantly, insulin resistance. Based on these findings, children affected by the insulin resistance syndrome are at particularly higher risk of developing premature cardiovascular complications. Our observation confirms that obesity and its associated comorbidities, particularly hypertension and insulin resistance, even in this young age should be regarded as a disease with vascular implications. We emphasize that weight reduction and risk-factor control in obese children for the long-term prevention of atherosclerosis and its sequelae should begin in childhood.

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