Childhood Obesity Predicts Adult Metabolic Syndrome: The Fels Longitudinal Study

Shumei S. Sun, PhD, Ruohong Liang, MS, Terry T-K Huang, PhD, MPH, Stephen R. Daniels, MD, PhD, Silva Arslanian, MD, Kiang Liu, PhD, Gilman D. Grave, MD, and Roger M. Siervogel, PhD

Objectives   To determine the age of significant divergence in body mass index (BMI) and waist circumference in adults with and without the metabolic syndrome, and to provide age- and sex-specific childhood values that predict adult metabolic syndrome.

Study design   Part 1 of this study is a retrospective cohort study of 92 men and 59 women (mean age, 51 years) who had metabolic syndrome and 154 randomly selected adults matched for age and sex who did not have the syndrome. Part 2 is a study of predictive accuracy in a validation sample of 743 participants.

Results   The first appearance of differences between adults with and without metabolic syndrome occurred at ages 8 and 13 for BMI and 6 and 13 for waist circumference in boys and girls, respectively. Odds ratios (ORs) for the metabolic syndrome at 30 years and older ranged from 1.4 to 1.9 across age groups in boys and from 0.8 to 2.8 across age groups in girls if BMI exceeded criterion values in childhood. The corresponding ORs for waist circumference ranged from 2.5 to 31.4 in boys and 1.7 to 2.5 in girls. These ORs increased with the number of examinations.

Conclusions   Children with BMI and waist circumference values exceeding the established criterion values are at increased risk for the adult metabolic syndrome. *(J Pediatr 2008;152:191-200)*

The availability of long-term serial data from the Fels Longitudinal Study presents opportunities to directly link obesity, centralized fat pattern, and the metabolic syndrome in adulthood to body mass index (BMI) and waist circumference measured decades earlier in the same individuals as children and to establish criterion values for BMI and waist circumference that predict obesity, centralized fat patterns, and the metabolic syndrome later in life. Recently, we derived age- and sex-specific childhood blood pressures that predict hypertension and the metabolic syndrome in adulthood using a random-effects model in a discovery sample and validated these criterion values in a larger sample using logistic regression.[1] In the present study, we apply a similar approach to ascertaining age- and sex-specific values in childhood for BMI and waist circumference that predict the metabolic syndrome later in life.

The National Cholesterol Education Program's (NCEP) Adult Treatment Panel (ATP) III guidelines define the metabolic syndrome in adults as a cluster of 3, 4, or 5 risk factors that exceed criterion values: waist circumference >102 cm for men and >88 cm for women, systolic blood pressure ≥130 mm Hg and/or diastolic blood pressure ≥85 mm Hg, fasting plasma triglycerides ≥150 mg/dL, fasting plasma high-density lipoprotein (HDL) cholesterol <40 mg/dL for men and <50 mg/dL for women, and fasting plasma glucose ≥110 mg/dL.[2] In 2003, the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus recommended lowering the criterion for impaired fasting plasma glucose to 100 mg/dL.[3]

ATP	Adult Treatment Panel	NCEP	National Cholesterol Education Program
BMI	Body mass index	NHANES	National Health and Nutrition Examination Survey
CDC	Centers for Disease Control and Prevention		
EBMI	Elevated body mass index	OR	Odds ratio
EWC	Elevated waist circumference	ROC	Receiver operating characteristics
HDL	High-density lipoprotein		

Currently, there is no agreement on the definition of the metabolic syndrome in children or adolescents. In recent reports, investigators have used arbitrary thresholds for levels of fasting plasma triglycerides, fasting plasma HDL cholesterol, and fasting plasma glucose, coupled with age- and sex-specific ≥90th percentiles for waist circumference and blood pressure from the National Health and Nutrition Examination Survey (NHANES) III to assess the prevalence of the metabolic syndrome in children and adolescents.[4-6] In this study, we take a different approach to ascertaining the onset of the metabolic syndrome in children by linking the adult metabolic syndrome directly to childhood risk factors measured in the same individuals decades earlier. This direct linkage permits us to establish criterion values for risk factors in childhood that predict the metabolic syndrome later in life. Equally important is the fact that measured values for these risk factors that fall below the childhood criterion values may be used to predict metabolic health in adulthood.

In the present study, we analyzed serial data for BMI and waist circumference from the Fels Longitudinal Study in the same subjects over many decades. We identified the earliest age of divergence of values for BMI and waist circumference in childhood among adults with the metabolic syndrome and age- and sex-matched adults without the metabolic syndrome. We also established age- and sex-specific criterion values of childhood BMI and waist circumference for predicting the metabolic syndrome later in life in a discovery sample of 305 subjects in the Fels Longitudinal Study and validated the predictive accuracy of these childhood criterion values in a sample of 743 subjects in the Fels Longitudinal Study.

METHODS

Study Sample

The 743 study participants (360 men and 383 women) were drawn from the Fels Longitudinal Study; they were 20 years and older at the time of analysis and had been followed since birth.[7] Childhood measurements include weight, height, waist circumference, annual hand-wrist bone age, and blood pressure. These parameters were measured at birth; at 1, 3, 6, 9, and 12 months; every 6 months to age 18 years; and every 2 years thereafter. When these participants reached age 8 years, additional measurements were added to the examination, including levels of fasting plasma lipids and lipoproteins, fasting plasma glucose, and fasting plasma insulin. Approximately 8% of the Fels study participants have been lost to follow-up, but their anthropometric, metabolic and cardiovascular data at last visit do not differ from those of the 92% remaining in the study.

The present study comprises 2 parts. Part 1 is a retrospective cohort study in a discovery sample of 151 subjects (92 men and 59 women; mean age, 51 years) from the Fels Longitudinal Study population. These subjects met the ATP III criteria for the metabolic syndrome. They were matched by age and sex to 154 randomly selected men and women within the Fels study population who did not meet the ATP III criteria. Each of these 305 subjects had been examined an average of 37 times and had no missing values for the 5 risk factors for the metabolic syndrome during their years of participation in the Fels study. Data from these 305 subjects were used to identify the age in childhood when BMI and waist circumference diverge between adults with and without the metabolic syndrome and to establish age- and sex-specific criterion values for these parameters in childhood that predict the metabolic syndrome later in life.

In Part 2 of the study, we validated the accuracy of the age- and sex-specific criterion values for BMI and waist circumference in childhood that we established in Part 1 to predict obesity, waist circumference exceeding ATP III criteria, and the metabolic syndrome later in life. The 743 subjects in Part 2 included the 305 subjects in Part 1. The total of 743 subjects comprised 144 men and 138 women with at least 3 risk factor measurements that exceeded the ATP III threshold values for the metabolic syndrome and 216 men and 245 women with at least 3 risk factor measurements that did not exceed those thresholds. We reviewed the childhood BMI and waist circumference data of the 743 subjects in the validation sample to determine whether their BMI and waist circumference exceeded the age- and sex-specific criterion values that we established in Part 1 at any time during their childhood.

Measurement Protocols

Anthropometric measurements were obtained according to procedures outlined in the *Anthropometric Standardization Reference Manual*.[8] Waist circumference was measured at the suprailiac crest, which is comparable to the method used in the NHANES. Weight was measured to 0.1 kg using a SECA scale, and height was measured to 0.1 cm using a Holtain stadiometer. Waist circumferences were measured twice, and the average values were used for statistical analyses.

We obtained birth weights from hospital records and assessed bone age from hand-wrist radiographs taken at each annual visit.[9] We used relative bone age (bone age minus chronological age) to assess the state of biological maturity. A positive relative bone age indicates accelerated maturity, which may hasten the appearance of risk factors in childhood for the metabolic syndrome later in life. All procedures were approved by the Institutional Review Board of Wright State University, and all participants provided written consent to join the Fels Longitudinal Study.

Statistical Analysis

PART 1: DISCOVERY SAMPLE ANALYSIS. We used a random-effects model[10] to analyze the complete set of serial data simultaneously. This model is expressed as

$$y_{ijk} = \mu + \alpha_i + \beta_j + \gamma_{ik} + \delta_{ij}x_{ijk} + \varepsilon_{ijk},$$

where y_{ijk} is the dependent variable (ie, serial childhood BMI or waist circumference), i denotes the group variable (adults with the metabolic syndrome versus adults without the metabolic syndrome), j denotes the subject, k denotes the within-