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Invited Commentary | Pediatrics

Visceral Adiposity—A Novel Early-Life Risk Factor for Preclinical Atherosclerosis in Adolescence

Rachel J. Shustak, MD, MSCE; Joseph W. Rossano, MD, MS

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Cardiovascular disease (CVD) is the leading cause of death worldwide.[1] Globally, approximately 20 million adults die each year from CVD—equating to nearly 1 in 3 deaths.[1] The development of CVD is not merely an adult phenomenon.[2] Arterial fatty streaks, the first (grossly visible) stage in the development of atherosclerosis, can be found in children as early as the first decade of life.[3] While fatty streaks can be reversible, childhood obesity and obesity-related comorbidities such as hypertension, hyperlipidemia, and hyperglycemia are associated with accelerated progression of atherosclerosis and development of premature CVD,[2] which is an alarming association given the climbing global rates of childhood obesity. In adults, body fat distribution has emerged as important factor associated with increased cardiovascular risk, with visceral adiposity associated with increased atherogenesis.[4]

In this context, van der Linden et al[5] present findings of a prospective birth cohort study evaluating early-life determinants of preclinical atherosclerosis, including visceral and subcutaneous adiposity. Of the 3005 healthy newborns included in the Dutch birth cohort study, Wheezing Illness Study in Leidsche Rijn (WHISTLER), van der Linden et al[5] enrolled 232 adolescents at a median (IQR) age of 14.9 (13.7-15.8) years. Follow-up occurred at 3 developmental stages: birth to 6 months, early childhood (5 years), and adolescence (12-16 years). Abdominal visceral and subcutaneous adipose tissue were measured by ultrasonography at the early-childhood and adolescent visit. Preclinical atherosclerosis was assessed by carotid intima-media thickness and carotid distensibility in adolescence.

Several noteworthy findings emerge from the analysis by van der Linden and colleagues.[5] Greater postnatal weight gain between birth and 6 months, higher early-childhood systolic blood pressure, increased early-childhood visceral adipose tissue, and a greater change in visceral adipose tissue between early life and adolescence were associated with greater carotid intima-media thickness. Likewise, higher early-childhood body mass index (BMI), a greater change in BMI between early childhood and adolescence, increased early-childhood visceral adipose tissue, and a lesser change in subcutaneous adipose tissue between early childhood and adolescence were associated with a lower distensibility coefficient, indicating higher vascular stiffness. Together, these results highlight the atherogenic role of abdominal visceral adipose tissue independent of BMI.

These conclusions must be taken in the proper context, and the authors[5] do acknowledge some of the limitations of their analysis, including its limited generalizability. The study population was recruited from a predominantly wealthy, White, and highly educated district in the Netherlands. The mean BMI of the study population in early life and adolescence was normal. Consequently, these results may not be generalizable to populations with lower income, more diversity, less education, and more obesity. Two additional limitations were the rate of loss to follow-up and missing data, both risks for selection bias. To address these concerns, the authors[5] compared the population with adolescent follow-up with those without adolescent follow-up and found that there was no difference with respect to sex, gestational age, birth weight, parental BMI, maternal smoking during pregnancy, and socioeconomic status. Those with follow-up were more likely to have White mothers. To address missingness, the authors employed multiple imputation. Finally, this study[5] did not assess the role of hyperlipidemia and hyperglycemia, 2 known factors associated with increased risk for

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premature CVD, as early-life risk factors or potential confounders of the association of adiposity with preclinical atherosclerosis.

Despite these limitations, we applaud van der Linden et al[5] for this important and novel contribution to the field of pediatric preventive cardiology. The findings suggest that assessment of adipose tissue during childhood may be a useful adjunct to standard BMI measurement for the identification of children with an adverse cardiovascular risk profile. Recently, the use of BMI as a measure of body fat has come under substantial criticism. While easy to measure and inexpensive to perform, BMI does not account for differences in body shape and composition across racial and ethnic groups, sexes, and age span.[6] While BMI has been shown to correctly identify excess adiposity in youths with severe obesity, a high degree of discordance exists between adiposity and BMI status in youth with class 1 obesity and overweight.[7] Thus, BMI must be used in conjunction with other valid measures of atherogenic risk such as adiposity.[6,7] Visceral and subcutaneous adiposity as highlighted by van der Linden et al[5] represent one such measure. However, the feasibility of performing these measurements on a large scale and their superiority over waist circumference, a less expensive and easier to perform measure, warrants further evaluation.

Ultimately, identifying early-life risk factors for subclinical atherosclerosis is essential to inform prevention and management strategies. While intensive behavior and lifestyle treatment has long been the mainstay of obesity management, it can be challenging for families to access and for clinicians to devote the time necessary. As childhood obesity rates continue to rise, alternative strategies must be considered to prevent a future crisis of premature CVD. In 2023, the American Academy of Pediatrics[8] endorsed weight loss pharmacotherapy and metabolic bariatric surgery as evidence-based treatment for children with obesity aged 12 years and older for the first-time. While controversial, these strategies have been associated with a significant decrease in visceral adipose tissue in adults.[9]

Although it is not the first study to associate early-life risk factors with preclinical atherosclerosis, this study[5] is novel in its longitudinal design and detailed evaluation of the role of adipose tissue in early-childhood. Van der Linden et al[5] highlight that exposure to early-life factors, particularly increased abdominal visceral adipose tissue, can induce lasting atherogenic changes. For clinicians, recognizing the role of body composition is essential and continued efforts must be made to break the obesity-atherosclerosis cycle.

ARTICLE INFORMATION

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Corresponding Author: Joseph W. Rossano, MD, MS, Division of Cardiology, Department of Pediatrics, The Children's Hospital of Philadelphia, Philadelphia and University of Pennsylvania Perelman School of Medicine, 34th Street & Civic Center Boulevard, Philadelphia, PA 19104 (rossanoj@email.chop.edu).

Author Affiliations: Division of Cardiology, Department of Pediatrics, Children's Hospital of Philadelphia, Philadelphia and University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania.

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