JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
VOL. 64, NO. 15, 2014

ISSN 0735-1097/$36.00
PUBLISHED BY ELSEVIER INC.
http://dx.doi.org/10.1016/j.jacc.2014.07.962

EDITORIAL COMMENT

Childhood Obesity and Adulthood Cardiovascular Disease*

Quantifying the Lifetime Cumulative Burden of Cardiovascular Risk Factors

Sheldon E. Litwin, MD

There is broad awareness that obesity rates in adults have increased dramatically (~2-fold) in the past 3 decades. Although the total prevalence of obesity remains lower in children than in adults, the rate of increase in childhood obesity has been nearly double that in adults (1). We should find this particularly worrisome because obese children are much more likely than are normal-weight children to become obese adults (2–4). Even more disconcerting are the observations that obese children are more likely to develop cardiovascular disease (CVD) compared with adults, and that subsequent weight loss may not entirely eliminate that excess risk (5). As childhood obesity becomes more prevalent, we can reasonably anticipate substantial amplification of obesity-related complications in adults.

Obesity is strongly associated with several important comorbidities that often contribute to the development of CVD. Most important among these are elevated blood pressure, insulin resistance, and dyslipidemia, 3 key elements of the metabolic syndrome. All of these conditions are increasingly recognized in today's youth, prompting the growth of new specialties and clinics geared toward treating hypertension, diabetes, fatty liver, and hypercholesterolemia in children as young as grade-school age.

Fatty streaks in the aorta and coronary arteries, precursors of atherosclerosis, begin to appear in childhood, and the presence of such fatty streaks in youth is related to serum levels of total and low-density lipoprotein cholesterol (6). We know intuitively that increasingly early and prolonged exposure to pathological disturbances, such as hypertension and dyslipidemia, will contribute to premature CVD in ever-younger adult populations. Indeed, one large registry of adult patients with non-ST-segment elevation myocardial infarction revealed that the most obese patients in the registry were nearly 15 years younger than the least obese patients (7).

The long-term epidemiological study of the effects of obesity in children is difficult for various reasons. Although seemingly straightforward, defining *obesity* in children with rapidly changing body size is challenging, but age-specific *Z*-statistics have been used to deal with this issue. Loss to follow-up in today's mobile population presents another major challenge to outcomes studies—especially those with cardiovascular endpoints likely to require 40 or more years of monitoring to detect. Fortunately, a few enterprising and tenacious groups of investigators in different parts of the world have maintained long-term studies of childhood risk factors for CVD. The Bogalusa Heart Study, begun in the 1970s, is one of these efforts. This study alone has contributed >1,000 papers to published medical reports. Thanks to these investigators, we are now gaining a greater understanding of how childhood risk factors lead to the later development of clinically apparent CVD. In this issue of the *Journal*, Lai et al. (8) use a novel approach to quantifying the cumulative burden, from childhood onward, of elevated blood pressure

*Editorials published in the *Journal of the American College of Cardiology* reflect the views of the authors and do not necessarily represent the views of *JACC* or the American College of Cardiology.

From the Department of Internal Medicine, Division of Cardiology, Medical University of South Carolina, Charleston, South Carolina. Dr. Litwin has reported that he has no relationships relevant to the contents of this paper to disclose.

and adiposity to study their effects on left ventricular (LV) mass and geometry in 1,061 subjects.

SEE PAGE 1580

Understanding the evolution of the end-organ damage that occurs gradually over decades requires methods that can account for the inevitable variations in the presence and severity of individual or multiple risk factors. For example, 8-year-old child A might have mild obesity and mildly elevated blood pressure, both of which remain relatively constant in severity over the next 30 years. In contrast, child B might enjoy normal body weight and blood pressure at age 8 but becomes progressively obese and overtly hypertensive as years pass. How then does one compare the impact of these different combinations and trajectories of comorbid conditions? The Bogalusa Heart Study investigators utilize a novel statistical tool that they previously developed (9), to integrate the effects of blood pressure and body mass index (BMI) measured at least 4 times over a mean follow-up of 28 years. They assessed total area under the curve (AUC) for the cumulative overall burden of each factor, or incremental AUC, to isolate the effects of trends over time without the consideration of baseline levels of BMI or blood pressure. It is not entirely surprising that higher values of BMI and blood pressure in childhood and adulthood, as well as total and incremental AUC, all were related to higher LV mass and LV hypertrophy.

Interestingly, incorporating the AUC measurements as the independent variable in several statistical models, the Bogalusa investigators found that BMI was a stronger correlate of eccentric hypertrophy in adults than was blood pressure. These findings differ somewhat from those from other recent studies, including a few that have used cardiac magnetic resonance to assess LV mass and geometry (10,11). Conventional thinking has held that hypertension produces concentric hypertrophy, whereas obesity is predominantly associated with eccentric hypertrophy. The latter point of view was related, in theory, to the volume load on the heart of chronically elevated cardiac output. Contrary to this standard thinking, several recent large-scale, cross-sectional studies have shown that obese adults most often had concentric, not eccentric, LV geometry (10,12). The interaction of comorbidities such as increasing severity of obesity, hypertension, and nocturnal hypoxemia due to sleep-disordered breathing appeared to synergistically contribute to more severe LV hypertrophy (10). As is typically the case, differences between studies in terms of exclusion criteria, age, ethnicity, blood pressure, medications, and degree of obesity likely explain the somewhat discordant results. In particular, in the present work, patients being treated for hypertension were excluded, mean systolic blood pressures were well within the normal range (110 to 128 mm Hg), and the mean BMI was only 28 to 31 kg/m^2 at the final examination. Regardless, the methodological tactic used in this paper should prove valuable for quantifying the cumulative burden of any risk factor or combination of risk factors over time in longitudinal studies.

Investigators from 4 large-scale, longitudinal, childhood-to-adulthood studies (Bogalusa, Louisiana; Muscatine, Iowa; Finland; and Australia) are now collaborating as the International Childhood Cardiovascular Cohort (i3C) Consortium. This type of collaborative effort is highly commendable and likely to yield extraordinary new knowledge that will benefit the global health community in understanding the effects of childhood obesity. Although we eagerly await the insights that will emerge from the collaboration, we cannot forestall embarking on the monumental effort that will be required to find methods to control or, better yet, prevent the growing crisis of childhood obesity.

REPRINT REQUESTS AND CORRESPONDENCE: Dr. Sheldon E. Litwin, Department of Internal Medicine, Division of Cardiology, Medical University of South Carolina, 25 Courtenay Street, Charleston, South Carolina 29412. E-mail: litwins@musc.edu.

REFERENCES

1. Daniels SR, Jacobson MS, McCrindle BW, Eckel RH, Sanner BM. American Heart Association Childhood Obesity Research Summit: executive summary. Circulation 2009;119:2114–23.

2. Baker JL, Olsen LW, Sorensen TI. Childhood body-mass index and the risk of coronary heart disease in adulthood. N Engl J Med 2007;357:2329–37.

3. Juonala M, Magnussen CG, Berenson GS, et al. Childhood adiposity, adult adiposity, and cardiovascular risk factors. N Engl J Med 2011;365:1876–85.

4. Park MH, Falconer C, Viner RM, Kinra S. The impact of childhood obesity on morbidity and mortality in adulthood: a systematic review. Obes Rev 2012;13:985–1000.

5. Must A, Jacques PF, Dallal GE, Bajema CJ, Dietz WH. Long-term morbidity and mortality of overweight adolescents. A follow-up of the Harvard Growth Study of 1922 to 1935. N Engl J Med 1992;327:1350–5.

6. Strong JP, Malcom GT, Newman WP 3rd, Oalmann MC. Early lesions of atherosclerosis in childhood and youth: natural history and risk factors. J Am Coll Nutr 1992;11 Suppl:51S–4S.

7. Madala MC, Franklin BA, Chen AY, et al. Obesity and age of first non-ST-segment elevation myocardial infarction. J Am Coll Cardiol 2008;52:979–85.

8. Lai C-C, Sun D, Cen R, et al. Impact of long-term burden of excessive adiposity and elevated blood pressure from childhood on adulthood left ventricular remodeling patterns: the Bogalusa Heart Study. J Am Coll Cardiol 2014;64:1580–7.

9. Cook NR, Rosner BA, Chen W, Srinivasan SR, Berenson GS. Using the area under the curve to reduce measurement error in predicting young adult blood pressure from childhood measures. Stats Med 2004;23:3421–35.

10. Avelar E, Cloward TV, Walker JM, et al. Left ventricular hypertrophy in severe obesity: interactions among blood pressure, nocturnal hypoxemia, and body mass. Hypertension 2007;49:34–9.

11. Turkbey EB, Jorgensen NW, Johnson WC, et al. Physical activity and physiological cardiac remodelling in a community setting: the Multi-Ethnic Study of Atherosclerosis (MESA). Heart 2010;96:42–8.

12. Turkbey EB, McClelland RL, Kronmal RA, et al. The impact of obesity on the left ventricle: the Multi-Ethnic Study of Atherosclerosis (MESA). J Am Coll Cardiol Img 2010;3:266–74.

KEY WORDS body mass index, cardiovascular disease, childhood obesity, hypertension, risk factors