

EDITORIAL

Lean Mass in Childhood Obesity: A Key Determinant of Ventricular Mass?

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Thirty years ago, the Framingham Heart study demonstrated that death from cardiovascular disease associates with echocardiographic left ventricular mass independent of standard risk factors.¹ The idea that clinical assessment of cardiac morphology could carry prognostic significance has spurred decades of investigation attempting to refine the causes and implications of increased cardiac mass. International trends in obesity have focused many investigators on morphologic cardiac sequelae; however, current paradigms are largely based on adult studies. In fact, some of the earliest ventures examining increased body mass and cardiac hypertrophy were performed in the pediatric population.² While evidence mounts that childhood obesity carries tremendous consequences for adult cardiovascular health,³ large-scale studies leveraging current imaging techniques have been lacking.

variety of outcomes were collected, including metrics of behavior and cognition, immunity, body composition, and heart and vascular development. The study design included dual-energy x-ray absorptiometry and magnetic resonance imaging (MRI) to accurately assess both body composition and cardiac morphology.

Toemen et al⁴ obtained quality cardiac MRI studies in >2800 children between the ages of 9 and 11 years with no known heart disease and confirmed that being overweight or obese was associated with greater lean mass, fat mass, and visceral adipose tissue. Cardiac size was also globally increased in the setting of obesity with higher end-diastolic chamber volumes, masses, mass-to-volume ratios, and stroke volumes for each ventricle. Interestingly, the right ventricular ejection fraction was lower in overweight or obese children while left ventricular systolic function was preserved. Notably, the blood pressure in obese children was elevated compared with normal-weight children; however, the increased cardiac output in this population made calculated systemic vascular resistance lowest in the obese cohort. When body fat distribution was accounted for independent of body mass index, the largest ventricles by both mass and volume were found in subjects with the highest fat-free or lean mass, as compared with relatively smaller hearts found in those with greater visceral adipose tissue. Higher lean mass was also associated with lower systemic vascular resistance (again because of increased cardiac output), whereas children with more fat mass and visceral adipose demonstrated higher systemic vascular resistance.

See Article by Toemen et al.

In this issue of the *Journal of the American Heart Association (JAHA)*, Toemen and colleagues⁴ provide a unique population-based perspective on the cardiac effects of pediatric obesity. The Generation R study offers robust observational data of a Dutch cohort followed from fetal life through childhood and into young adulthood.⁵ The study enrolled nearly 10 000 pregnant mothers between 2002 and 2006 with an impressive follow-up rate of 80% at 10 years. Data relevant to a

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HEMODYNAMIC EFFECTS AND MORPHOLOGIC ADAPTATION TO OBESITY

Theories for the hemodynamic implications of being overweight or obese predate the era of noninvasive imaging, but our understanding has evolved. At one time, it was thought that obesity directly opposed the effects of essential hypertension and that concentric myocardial hypertrophy in obesity was only possible with concurrent hypertension.⁶ In fact, an increased circulating blood volume is required to perfuse greater body mass, thereby increasing preload and stroke volume. With a larger vascular bed and increased cardiac output also comes lower systemic vascular resistance. However, initial conclusions that these effects would result in purely eccentric hypertrophy with predominant ventricular dilation have been modified.

The use of cardiac MRI to provide accurate and reproducible cardiac volumetric and functional assessment has significantly advanced the study of morphologic adaptations to obesity. Without the limitations of echocardiography in obese patients, even small-scale use of cardiac MRI demonstrated significant elevations in both left and right ventricular mass, end-diastolic volume, and cardiac output.⁷ The MESA (Multi-Ethnic Study of Atherosclerosis) applied cardiac MRI on a large scale to >5000 adult subjects and found that the morphology of left ventricular hypertrophy was independently associated with incident outcomes.⁸ Specifically, concentric hypertrophy with a greater left ventricular mass to volume ratio was associated with coronary heart disease and stroke. Further evaluation of the obese cohort in the MESA study found a positive association between left ventricular mass to volume ratio and all measures of obesity.⁹ Interestingly, though left ventricular systolic function was preserved, the MESA study demonstrated decreased right ventricular ejection fraction in overweight and obese patients.¹⁰ This finding was confirmed by Toemen et al⁴ and raises interesting questions regarding the unique susceptibility of the ill-prepared right ventricle to the hemodynamic challenges of obesity.

IMPLICATIONS OF BODY FAT DISTRIBUTION

As cardiac imaging has advanced, so too has the ability to study body habitus and specific adipose distribution patterns. It has become clear that the metabolic activity of fat is dependent on its anatomic location and that visceral adipose tissue surrounding both the heart and abdominal organs requires

increased cardiac output as compared with subcutaneous fat.¹¹ The Dallas Heart Study supported this theory using cardiac MRI assessment in >2700 adult subjects, nearly half of whom were obese.¹² They found visceral or “central” adiposity independently associated with concentric remodeling, whereas patients with predominantly lower body subcutaneous fat or “hip fat” had an associated eccentric remodeling pattern. These findings have been confirmed by subsequent studies and now serve as an accepted model (Figure).

This paradigm, however, requires further modification when considering the effects of childhood obesity. When accounting for increased cardiac demands, we must also recognize the relative increase in lean or “fat-free” mass that comes with being overweight. Daniels et al¹³ used echocardiography in 200 children and adolescents to demonstrate a strong association of both lean body mass and fat mass with left ventricular mass. Most notably, they found that lean body mass accounted for 75% of the variance in left ventricular mass. This finding is validated in the robust study at hand by Toemen et al⁴ and stands to inspire further work in the field. Clearly the effects of childhood obesity and the hormonal milieu during somatic growth are unique and will require ongoing investigation.

FUTURE DIRECTIONS

As Toemen et al⁴ allude, the preservation of left ventricular systolic function likely overlooks occult myocardial changes that are under way in both obese children and adults. Modern noninvasive techniques for more subtle myocardial pathology may help to further risk-stratify the cardiac sequelae of pediatric obesity. Two-dimensional speckle-tracking echocardiography has previously demonstrated impaired left ventricular longitudinal and circumferential strain in obese children with normal ejection fraction.¹⁴ Myocardial strain analyses using cardiac MRI have also demonstrated a significant association between obesity and impaired strain, most notably linked with epicardial adiposity and a pattern of concentric hypertrophy.¹⁵ Parametric mapping by cardiac MRI may also provide further insight into this field. Though the myocardial changes are presumably diffuse, global changes in T1 values could signify subtle collagen deposition and fibrosis in response to the hemodynamics of obesity.

Meanwhile, advances in cardiac MRI motion-compensation are allowing more pediatric studies to be performed free-breathing and at a younger age without anesthesia or sedation. This technology is beginning to fill in knowledge gaps that had

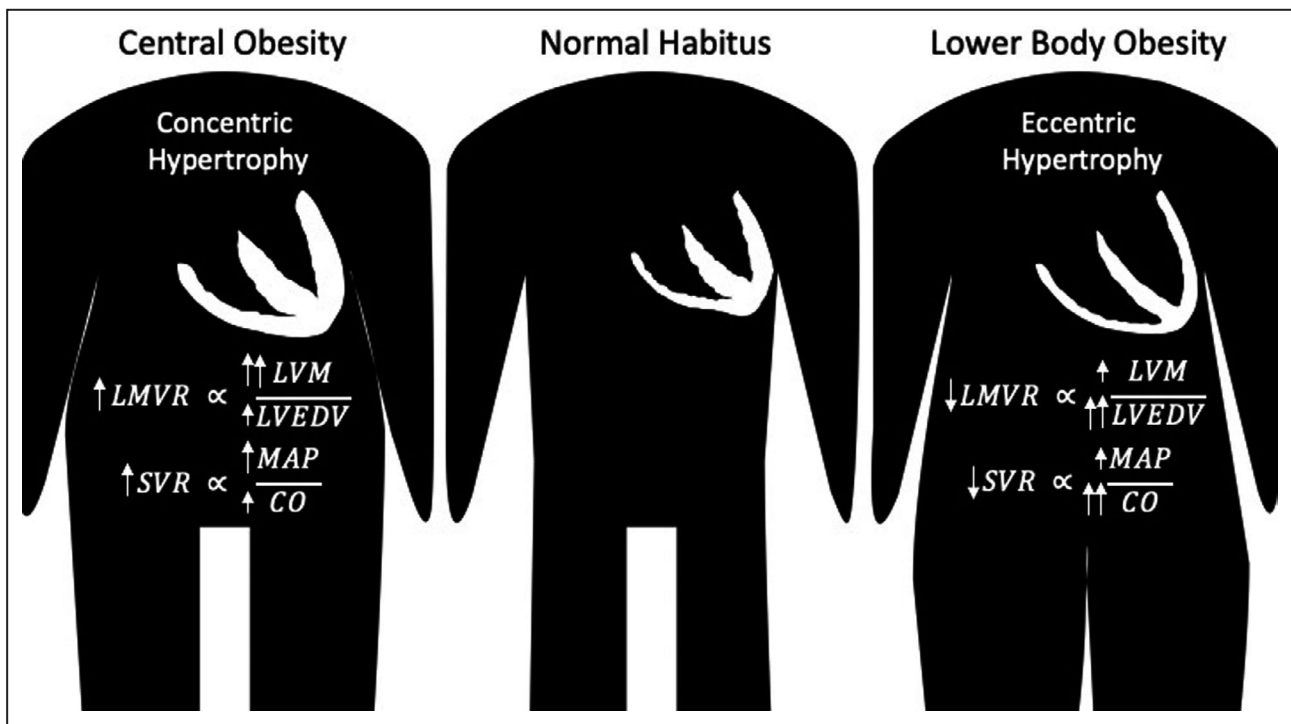


Figure. A model for ventricular morphology as a function of body fat distribution.

CO indicates cardiac output; LMVR, left ventricular mass to volume ratio; LVEDV, left ventricular end-diastolic volume; LVM, left ventricular mass; MAP, mean arterial pressure; and SVR, systemic vascular resistance.

previously been extrapolated, redefining normal pediatric cardiac measurements¹⁶ and expanding the feasible age range for cardiac MRI research in children. Future studies like that of Toemen et al⁴ may therefore be able to gather more data at younger ages and better understand the progression of the cardiac adaptations to obesity.

Pushing the boundary even earlier into fetal and neonatal cardiac morphology is also providing clues into cardiac development and maturation in the face of adversity. Though children have not developed obesity at this age, they are affected both genetically by obese parents, and by the altered cytokines and sympathetic agonism to which they are exposed throughout gestation. In fact, the R study that informs the article by Toemen et al⁴ has also associated higher fetoplacental vascular resistance (which may be related to maternal obesity and cardiovascular disease) with higher left ventricular mass and systemic blood pressure in childhood.¹⁷ A recent article featured in *JAHA* also demonstrated significant changes in cardiac development for infants born to hypertensive mothers, including decreased right ventricular volume and increased indexed right ventricular mass that persisted at 3 months of age.¹⁸ Though these findings will require additional study to determine persistence and impact on childhood and adult cardiac function, they highlight the numerous genetic and environmental factors at play.

Toemen et al⁴ have advanced our understanding not only of the cardiac sequelae of childhood obesity, but specifically of the impact of body fat distribution in this population. Their findings confirm previous morphologic changes suggested by pediatric echocardiographic and adult cardiac MRI studies, and present the first large-scale pediatric MRI-based study of overweight children. The study clearly presents nuances of pediatric cardiac adaptation in its association with lean body mass and paves the way for future investigation. Global health trends in obesity certainly warrant ongoing study to guide effective lifelong cardiac care.

ARTICLE INFORMATION

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Disclosures

None.

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