Editorial

Normal Weight Obesity
Is Bigger Really Badder?

Sheldon E. Litwin, MD

Increasing attention is being focused on the role(s) that obesity may play in the development of cardiovascular disease, particularly congestive heart failure (CHF). Several indirect or associated effects are potential culprits. For example, obesity is strongly associated with many atherosclerotic risk factors, including arterial hypertension, insulin resistance, diabetes, and dyslipidemia. Therefore, it is not surprising that obese people tend to have premature and accelerated coronary artery disease, a common precursor of CHF. In addition to promoting coronary heart disease, obesity has been associated with atrial fibrillation, another condition that can contribute to CHF. Lastly, obesity often adversely impacts right heart function via the ill effects of sleep disordered breathing or restrictive lung disease. The aforementioned factors may individually or collectively produce a clinical syndrome of CHF in patients who are obese.

Many investigators believe that obesity may directly contribute to the development of CHF, independent of hypertension, ischemic heart disease, or arrhythmias. Hemodynamic sequelae of obesity that have been invoked as explanations for heart failure include expanded central blood volume and chronically high cardiac output. Adverse metabolic and energetic changes in the myocardium of obese subjects are also candidates for causal mechanisms along the road to CHF. Finally, deposition of fat within myocardium or myocytes has been proposed to cause mechanical disadvantages or toxic effects in the heart.

The high cardiac output in obesity, when obesity is defined by body mass index, results from an increase in absolute body size rather than an effect of fat tissue per se. Conversely, the systemic metabolic effects of obesity are thought to result mainly from biochemical signals emanating from visceral fat. These latter effects do not necessarily require an increase in total body size to be present. Gaining a clearer understanding of how obesity and/or adiposity impacts cardiac structure and function would help to better target therapies geared toward prevention and treatment of obesity-related heart disease.

In this issue of Circulation: Cardiovascular Imaging, Kosmala et al provide provocative new data that may affect our thinking about this problem. They report echocardiographic measures of left ventricular (LV) geometry and function in a subgroup of 168 adult subjects (38±7 years) enrolled in a community health screening program. All of the subjects were normal weight as assessed by body mass index <25 kg/m²; however, 43% of the subjects in this group had an increased percent of body fat measured by dual energy x-ray absorptiometry based on age and gender-specific cutoffs. The authors term the presence of normal body mass index with increased percent of body fat as “normal weight obesity.”

Compared with the normal weight subjects with normal percent of body fat, those with normal weight obesity had higher waist circumference and waist/hip ratio, higher serum low-density lipoprotein and triglycerides, lower high-density lipoprotein, reduced insulin sensitivity (measured as homeostasis model assessment of insulin resistance) and higher C-reactive protein levels. By echocardiography, LV size, wall thickness, and mass were not different between the 2 groups. LV ejection fraction and conventional measures of diastolic function (mitral ratio of peak early to late diastolic filling velocity and the deceleration time of early mitral inflow) also did not differ between the groups; however, the patients with normal weight obesity had larger left atrial dimension, lower mitral annular tissue Doppler velocities in both systole and diastole, lower longitudinal strain rate in both systole and diastole, and slightly higher ratio of early mitral inflow velocity (E) to early mitral annular diastolic velocity (e’). Using stepwise regression models, several different factors were independently associated with various individual echo Doppler abnormalities, although age was the only parameter associated with all of the abnormal echo findings. The other factors with associations to the echo abnormalities included abdominal fat mass, serum procollagen type I carboxy-terminal propeptide levels (a putative measure of collagen turnover), myocardial integrated backscatter intensity, homeostasis model assessment of insulin resistance, interleukin-18, and C-reactive protein levels.

The authors propose that the inflammatory and metabolic milieu in patients with normal weight obesity is a direct result of excess abdominal fat and that the preclinical abnormalities of cardiac function may be related to these systemic changes. Further, they suggest that the reductions in myocardial function could progress and become irreversible over time. I concur with the authors that patients with normal weight obesity may falsely assume that they have a low cardiovascular risk because of their normal body mass index; however, the mechanisms of the myocardial dysfunction and the
significance of these changes remain uncertain from my perspective. The differences in individual echo parameters between the groups were small. For example, E/e', a widely accepted (albeit debated) index of LV filling pressure, was 7.2 in the nonobese versus 8.8 in the normal weight obese group. Both groups are within the normal or low end of the equivocal range for diagnosing increased LV filling pressures (<8, considered normal; 9 to 13, equivocal; and >13, abnormal). Likewise, other tissue Doppler, strain, and strain rate measurements were very modestly different between the groups and also in or near the normal range. Do such abnormalities contribute to the development of heart failure? One may make an argument that these mild changes are not necessarily progressive and might not culminate in clinical CHF. In fact, subclinical changes in myocardial mechanics of similar magnitude to those in this study have been reported in mildly to severely obese subjects and in a wide range of age groups from pediatric to adolescent to young adult to mature adult. Moreover, there are improvements in myocardial function with weight loss, even in patients with very severe longstanding obesity. No longitudinal studies of obese subjects have demonstrated progressive worsening of LV function over time. Thus, the clinical significance of these changes remains to be demonstrated.

Despite the uncertainty as to the long-term ramifications of the mildly impaired myocardial mechanics in the normal weight obese subjects, the data from this study strongly suggest that high cardiac output, hypertension, or cardiac hypertrophy are not mandatory precursors to mechanical dysfunction in obesity. Rather, these results favor the argument that metabolic or hormonal effects in obese subjects are likely to be important.

When pondering the mechanisms that might account for the results of this interesting paper, it is important to recognize that the normal weight obese population must have reduced lean body (muscle) mass. Although we tend to focus a great deal on the adverse metabolic, neurohormonal, and cytokine-mediated effects of adipose tissue, somewhat less attention has been paid to the potentially favorable and opposing functions of skeletal muscle. Along these lines, it has been shown that increasing skeletal muscle mass via inhibition of myostatin leads to reduction in body fat and expression of fatty acid transport protein 1 in the heart causes lipotoxic cardiomyopathy. When considering the clinical significance of these results, it is important to recognize that metabolic or hormonal effects in obese subjects are likely to be important.

In view of the above findings, we should at least consider the possibility that some of the metabolic and cardiac findings described by Kosmala and colleagues may be responses to dietary intake, reduced lean muscle mass, or lack of exercise, rather than a direct effect of abdominal fat. These changes could be quickly reversible with changes in diet or physical activity and, hence, may not represent a precursor to heart failure. Despite these questions, the new paper should stimulate us to continue expanding our thinking about the definition of obesity, as well as the interplay among diet, physical activity, body composition, and cardiac function. The term normal weight obesity is likely to become a part of the lexicon of all who study or practice preventive cardiology.

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References


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