Getting at the Heart of Central Obesity and the Metabolic Syndrome

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Nearly 2 billion adults and 42 million children are either obese or overweight worldwide. In the United States, a staggering 36% of all adults are obese. Obesity is a major risk factor for many cardiovascular diseases, including heart failure (HF). Obesity and weight gain are associated with increases in left ventricular (LV) mass, amplification of age-related LV stiffening, and worsening LV diastolic and systolic dysfunction — effects that are strikingly similar to what is seen in patients with the clinical syndrome of HF with preserved ejection fraction (HFpEF). 

Obesity has direct and indirect effects on the heart, including increases in myocardial load related to plasma volume expansion, worsening arterial hypertension, and increased aortic stiffness. There may be direct effects from obesity on cardiomyocytes, metabolic changes in substrate availability and cellular respiration that affect cardiac function, and altered patterns of gene expression driven by proinflammatory signaling pathways and loss of nitric oxide signaling.

To complicate matters, recent studies have shown that not all fat is the same, as central adiposity seems to carry even more harmful effects on myocardial function. However, it has been difficult to discern how much of this correlation is specific to central adiposity, common to all obesity, or is secondary to the myriad of other factors that are associated with obesity, such as insulin resistance, hypertension, renal dysfunction, and other comorbidities.

In the current issue of Circulation: Cardiovascular Imaging, Selvaraj et al present an elegant analysis revealing an independent association between central obesity and subclinical changes in LV mechanics identified using speckle-tracking strain echocardiography. The authors analyzed echo-cardiographic images from the HyperGEN study, which is a cross-sectional, population- and family-based study of 2181 participants without HF. This was a largely young (mean age, 51 years), overweight to obese population with a mean body mass index of 31 kg/m². The vast majority (80%) had central obesity, quantified by an enlarged waist:hip ratio or waist circumference. Compared to participants without central obesity, subjects with central obesity displayed more comorbidities, including hypertension, dyslipidemia, diabetes mellitus, kidney disease, higher blood pressure and body mass index, greater insulin resistance, worse kidney function, and lower baseline activity levels. Centrally obese patients also displayed more dilated ventricles, increased LV mass, left atrial dilatation, and altered systolic and diastolic LV mechanics. Notably, there was no difference in EF, reinforcing the limitations of this index of LV performance.

To determine whether the observed abnormalities in LV structure and function were specific to central obesity or merely related to confounding factors, the authors took full advantage of this detailed, prospectively obtained data set to adjust for virtually all of the key measurable parameters that might plausibly explain the correlation between central obesity and myocardial function, including age, sex, race, body mass index, self-reported activity levels, blood pressure, heart rate, glucose and lipid levels, renal function, LV mass, and medication usage. After this comprehensive adjustment, central obesity (categorically defined) and waist:hip ratio (continuous) each remained significantly associated with subclinical systolic dysfunction (decreased global longitudinal strain, lower systolic strain rate, and tissue velocities) and diastolic dysfunction (lower diastolic strain rate, tissue velocities, and higher E/e′ ratio). In contrast to central obesity, peripheral adiposity (as measured by triceps and subscapularis thickness) was only weakly correlated with e′ velocity and showed no correlation with the other systolic or diastolic strain parameters, providing further evidence that body composition (central fat) as opposed to generalized obesity is the most crucial to correlate. The authors appropriately conclude from these data that central obesity is independently associated with adverse cardiac mechanics.

This finding is enormously important because it suggests that treatments aimed at reducing central adiposity could prevent or perhaps even reverse these changes in LV mechanics that ultimately contribute to reduced exercise capacity, the clinical syndrome of HFpEF, and increased risk of death. The current data importantly extend on previous studies showing that central obesity or metabolic syndrome is associated with more severe diastolic dysfunction and decreased longitudinal strain when compared with generalized obesity. Less data are available on systolic myocardial mechanics, but the current data are in agreement with another recent study from Russo et al showing lower global longitudinal strain with increasing waist:hip ratio and waist circumference. Together with these earlier studies, the current data from Selvaraj et al establish that there is something important and specific about central adiposity that is particularly detrimental to cardiac function.

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As in all cross-sectional analyses, causation cannot be proven from this correlation, and the mechanisms explaining the relationship between central obesity and adverse LV mechanics remain unclear. Arterial pulsatile load is increased with central obesity but was not directly measured in the current analysis. However, it has previously been shown that increases in body weight are correlated with increased LV diastolic stiffness even after adjusting for arterial load. Central obesity is also associated with greater age-related increases in LV systolic stiffness in women, which is also typical of HFpEF, even as other indices of LV systolic function become impaired. This provides further support for the importance of central obesity and metabolic syndrome in contributing to the changes in myocardial structure and function that lead to HFpEF. Central fat is metabolically more active than peripheral fat, and the current data suggest that myocardial dysfunction noted in patients with central obesity (with or without HF) can be considered to be a form of metabolic heart disease that may require its own specific treatments.

What then are the next steps? The data from Selvaraj et al. in concert with previous studies raises the possibility that treating central obesity might prevent or treat early stages of LV dysfunction that lead to HFpEF. Clinical trials testing this approach are urgently needed. Perhaps, targeting the downstream metabolic and inflammatory sequelae of central fat may be effective. Alternatively, weight loss and of itself would have beneficial reductions in both central and peripheral fat depots. Kitzman et al. recently showed in an elegant trial that weight loss through caloric restriction reduces LV mass and inflammatory markers, enhances diastolic LV filling, and improves exercise capacity and quality of life in patients with HFpEF. Importantly, these salubrious effects from diet were coupled with highly significant reductions in abdominal and visceral fat. Future study is indicated to determine whether this result can be replicated using other methods to achieve weight loss, and in other patient populations. We might want to start with the billions of obese or overweight people worldwide, or better yet, the millions of adults that likely display abnormal LV mechanics and metabolic heart disease in the absence of HF symptoms, who will go on to develop symptomatic HFpEF in the coming years if we do not do something about it soon.

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References


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