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STATE-OF-THE-ART PAPERS

Obesity and Cardiovascular Diseases

Implications Regarding Fitness, Fatness, and Severity in the Obesity Paradox

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Obesity has been increasing in epidemic proportions, with a disproportionately higher increase in morbid or class III obesity, and obesity adversely affects cardiovascular (CV) hemodynamics, structure, and function, as well as increases the prevalence of most CV diseases. Progressive declines in physical activity over 5 decades have occurred and have primarily caused the obesity epidemic. Despite the potential adverse impact of overweight and obesity, recent epidemiological data have demonstrated an association of mild obesity and, particularly, overweight on improved survival. We review in detail the obesity paradox in CV diseases where overweight and at least mildly obese patients with most CV diseases seem to have a better prognosis than do their leaner counterparts. The implications of cardiorespiratory fitness with prognosis are discussed, along with the joint impact of fitness and adiposity on the obesity paradox. Finally, in light of the obesity paradox, the potential value of purposeful weight loss and increased physical activity to affect levels of fitness is reviewed. (J Am Coll Cardiol 2014;63:1345–54)

Obesity has been increasing in epidemic proportions in both adults and children over many decades, and recently, the proportion of the population with more severe, or morbid, obesity has increased to a greater extent than has overweight and mild obesity (1–3). Currently, nearly 70% of adults are classified as either overweight or obese as compared with fewer than 40% just 40 years ago (3). One can argue about the impact of overweight and mild obesity on overall prognosis particularly without accounting for levels of cardiorespiratory fitness (fitness). Nevertheless, very recent high-profile data have suggested obesity may account for nearly 20% of overall mortality (4).

There are numerous adverse effects of overweight and obesity on general and cardiovascular (CV) health (3). Clearly, obesity worsens most of the major CV risk factors, including plasma lipids, blood pressure, glucose, inflammation, and places a "heavy" burden on the heart, negatively affecting ventricular structure and systolic and diastolic ventricular function (3,5,6). Not surprisingly, obesity is associated with the prevalence of most CV diseases, including hypertension, coronary heart disease (CHD), heart failure (HF), and atrial fibrillation (AF) (3,5). Nevertheless, substantial data, mostly published during the last decade, have demonstrated an "obesity paradox," where obese patients generally have a better short- and long-term prognosis than do their leaner counterparts with the same CV diseases (3,5).

This state-of-the-art paper briefly reviews the pathophysiology/hemodynamics of obesity, discusses possible causes of the obesity epidemic, and reviews the changing landscape of obesity on survival in the general population and in those with CV diseases, including hypertension, CHD, HF, and AF. Additionally, we discuss the impact of severe or morbid obesity on prognosis, especially in light of the obesity paradox noted at least in overweight and mildly obese patients with CV diseases. We also discuss the role of cardiorespiratory fitness (fitness) compared with fatness, and implications of fitness in the obesity paradox. Finally, we briefly review the impact of purposeful weight reduction on prognosis, especially considering the obesity paradox.

CV Pathophysiology/Hemodynamics

Overweight and obesity have many adverse effects on hemodynamics and CV structure and function (Fig. 1, Table 1) (5), which have been reviewed in detail elsewhere

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Abbreviations and Acronyms

AF = atrial fibrillation
BF = body fat
BMI = body mass index
CHD = coronary heart disease
CV = cardiovascular
HF = heart failure
LV = left ventricle/ventricular
MET = metabolic equivalent

(3,5). Obesity certainly increases total blood volume, stroke volume, and cardiac output, so typically, systemic vascular resistance in obesity is reduced for any given level of blood pressure. Although most of the increases in cardiac output in obesity are due to high stroke volume (because heart rate is typically not increased), occasionally, heart rate may be slightly increased as a result of increased activation of the sympathetic nervous system. The Frank-Starling curve in obesity is often shifted to the left as a result of increases in filling pressure and volume, which increases CV work, also leading to left ventricular (LV) changes with dilation and LV hypertrophy. Additionally, obesity can lead to enlargement of the left atrium, not only from the increased circulating blood volume, but also from alterations in LV diastolic filling (5,7). From multiple mechanisms, obesity has adverse effects on both systolic and, especially, diastolic ventricular function (8).

Etiologies of Obesity and Energy Balance

During recent years, the origins of the obesity epidemic have been in considerable dispute (9,10). Regardless of this debate, it is widely accepted that increments in body weight and overall adiposity, at the most fundamental level, are the result of chronic positive energy balance (i.e., energy expenditure < energy intake) (11,12). There has been a number of studies suggesting that energy or food intake is largely, if not completely, responsible for the obesity epidemic, essentially blaming much of the obesity epidemic in the Westernized world on poor dietary choices (13–15). One of the arguments to support this theory is that time spent in leisure-time physical activity has remained essentially unchanged in recent decades, thus leading to the conclusion that obesity is solely due to excessive energy or caloric intake (11). However, leisure-time physical activity represents a relatively small portion of total time per week, which is much more affected by occupation-related activity and household management energy expenditure.

Recently, we have demonstrated very marked declines in occupation-related physical activity during the last 5 decades (Fig. 2) (11), with similar declines in household management energy expenditure in women during this same time (Fig. 3) (12,16). In fact, the typical woman now has an energy expenditure that is more than 1,800 calories/week less than that of 5 decades ago (12). Considering the fact that generally 100 calories are burned for every mile traveled by foot, the typical woman would have to walk or run over 18 miles/week to make up for this loss of household management energy expenditure. This suggests that reductions in occupation-related activity and energy expenditure, similar to household management energy expenditure in women, largely explain the marked increased prevalence in obesity noted during recent decades (Fig. 4) (11).

Importantly, because voluntary physical activity (e.g., housework, exercise) is the only major modifiable component of total daily energy expenditure, these significant reductions are independent of the relatively nonmodifiable components of total daily energy expenditure such as resting metabolic rate (17), thermic effect of food (18), and non-exercise activity thermogenesis (19,20).

Table 1 Effects of Obesity on Cardiac Performance

Hemodynamics
Increased blood volume
Increased stroke volume
Increased arterial pressure
Increased LV wall stress
Pulmonary artery hypertension
Cardiac structure
LV concentric remodeling
LV hypertrophy (eccentric and concentric)
Left atrial enlargement
RV hypertrophy
Cardiac function
LV diastolic dysfunction
LV systolic dysfunction
RV failure
Inflammation
Increased C-reactive protein
Overexpression of tumor necrosis factor
Neurohumoral
Insulin resistance and hyperinsulinemia
Leptin insensitivity and hyperleptinemia
Reduced adiponectin
Sympathetic nervous system activation
Activation of renin-angiotensin-aldosterone system
Overexpression of peroxisome proliferator-activator receptor
Cellular
Hypertrophy
Apoptosis
Fibrosis

Adapted with permission from Lavie et al. (5).
LV = left ventricular; RV = right ventricular.

The Changing Landscape of Obesity

Recently, scientists have debated the impact of overweight and obesity on overall chronic disease, including all-cause mortality (21). In fact, it has been recently argued that obesity is accounting for almost 1 in 5 deaths worldwide. (4) On the other hand, Flegal and colleagues (21) have performed a large meta-analysis of 97 studies in nearly 2.9 million people. They demonstrated that obesity, defined by standard body mass index (BMI) criteria ($\geq$30 kg/m^2), when considering all grades, was associated with a significantly increased risk of mortality compared with normal BMI (18.5 to 25 kg/m^2). However, the optimal survival occurred at the