MAYO CLINIC

REVIEW

Obesity and Heart Failure: Focus on the Obesity Paradox

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Abstract

The escalating prevalence of obesity has been linked to substantial increases in both metabolic and cardiovascular disease. Nevertheless, the direct effects of obesity on cardiovascular health and function require further exploration. In particular, the relationship between obesity and cardiac function has received intense scrutiny. Although obesity increases the risk for development of heart failure (HF), it appears to exert a protective effect in patients in whom HF has already been diagnosed (the "obesity paradox"). The protective effects of obesity in patients with previously diagnosed HF are the focus of particularly intense research. Several explanations have been proposed, but most studies are limited by the use of body mass index to classify obesity. Because body mass index does not distinguish between fat mass, fat-free mass, and lean mass, individuals with similar body mass indices may have vastly different body composition. This article discusses the roles of body composition, diet, cardiorespiratory fitness, and weight loss in the development of cardiac dysfunction and HF and the potential protective role that body composition compartments might play in improving HF prognosis. Based on an intensive literature search (Pubmed, Google Scholar) and critical review of the literature, we also discuss how a multidisciplinary approach including a nutritional intervention targeted to reduce systemic inflammation and lean mass–targeted exercise training could potentially exert beneficial effects for patients with HF.

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Obesity (ie, body mass index [BMI; calculated as weight in kilograms divided by height in meters squared], ≥30 kg/m^2) has increased to epidemic proportions since 1980.[1] In 2014, nearly 1.9 billion adults worldwide were overweight, and more than 600 million were obese.[1,2] Obesity is an independent risk factor for several chronic noncommunicable diseases (NCDs) including diabetes, cancer, and cardiovascular disease (CVD), the lattermost which includes heart failure (HF). This cluster of NCDs collectively represents the major causes of death worldwide.[1-6] In this context, there clearly appears to be a cause and effect relationship between obesity and the increased risk for development of one or more NCDs.

The interplay between obesity and HF is complex. Paradoxically, although obesity increases the risk of HF, once a diagnosis is confirmed, patients with HF who are also obese have a better prognosis compared with their leaner counterparts. This phenomenon has been termed *the obesity paradox*.[6-9]

In this review, we describe the role of obesity in the development of HF and the possible mechanism(s) through which obesity may exert protective effects in HF. We also discuss the role of diet and systemic inflammation and their involvement in cardiac dysfunction as well as potential body composition–, diet-, and systemic inflammation–targeted therapeutic strategies.

MATERIAL AND METHODS

For this critical review, we identified articles by searching original studies, review articles, and editorials published in peer-reviewed journals indexed in PubMed and Google Scholar between January 1, 1960, and March 30, 2016. The comprehensive electronic literature search included the use of key words and their combination: *obesity*, *heart failure*, *heart failure with reduced ejection fraction*, *heart failure with preserved ejection fraction*, *obesity and heart failure*, *obesity paradox*, *obesity paradox in heart failure*, *body composition*, *body composition and heart failure*, *lean mass*, *weight loss and heart failure*,

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ARTICLE HIGHLIGHTS

- Obesity is an independent risk factor for the development of heart failure.
- Heart failure affects about 38 million people worldwide, almost 6 million in the United States alone.
- Although obesity increases the risk of heart failure, overweight or obesity exert protective effects in patients with a confirmed heart failure diagnosis, describing an obesity paradox.
- Body mass index does not distinguish between fat mass, fat-free mass, and lean mass.
- The obesity paradox may not be present in sarcopenic obese patients.
- Body composition assessment should be performed in patients with heart failure for better risk stratification.
- Interventions aimed at increasing lean mass and reducing systemic inflammation may be protective in heart failure.

diet and heart failure, *diet and cardiac function*, *inflammation and heart failure*, *sarcopenia*, *sarcopenia and heart failure*, *sarcopenic obesity*, *sarcopenic obesity and heart failure*, and *inflammation and heart failure*. Of more than 1000 articles found, 139 were considered to be relevant to the scope of this critical review. The search was restricted to articles published in English. The reference lists of the chosen studies were also reviewed to identify potential additional pertinent articles.

OBESITY AND HF: DEFINITIONS AND EPIDEMIOLOGY

The World Health Organization defines obesity and overweight as "an abnormal or excessive fat accumulation…to the extent that health may be impaired."[1] However, universal cutoffs of body fat to diagnose overweight and obesity have not been established. Therefore, overweight and obesity are usually diagnosed in individuals with a BMI of 25 kg/m^2 or higher and a BMI of 30 kg/m^2 or higher, respectively. Visceral obesity, often considered a better tool than BMI to determine a more complete cardiometabolic risk,[10,11] is defined as a waist circumference of more than 102 cm in males and more than 88 cm in females, although race-related cutoffs have been proposed.[12]

Heart failure is "a complex clinical syndrome that results from any structural or functional impairment of ventricular filling and/or ejection of blood."[13] Heart failure affects about 38 million people worldwide, almost 6 million in the United States alone with nearly 915,000 new cases every year.[14] Moreover, it is the most common reason for hospital admissions in patients aged 65 years or older.[14,15] Although the survival rate in patients with HF has improved in recent history, the death rate remains very high: more than 30% of patients die within 5 years of an HF diagnosis.[14,15]

Approximately half of the patients with HF have a reduced left ventricular (LV) ejection fraction (LVEF) or systolic dysfunction (ie, HF with reduced ejection fraction [HFrEF]), while the remaining half present with preserved LVEF (ie, HF with preserved ejection fraction [HFpEF]),[13,16] usually characterized by the presence of diastolic dysfunction, also known as diastolic HF. These 2 forms of HF have very different pathophysiologic mechanisms, which are highlighted by the fact that beneficial therapeutic strategies in HFrEF have failed to improve outcomes in HFpEF.[13-18] For instance, in HFrEF, the renin-angiotensin-aldosterone system represents a target for several drugs proven to reduce mortality and complications.[13,19] However, similar pharmacological approaches targeting the renin-angiotensin-aldosterone system failed to produce beneficial effects in patients with HFpEF.

Despite sharing very similar signs and symptoms, such as fluid retention, shortness of breath, and exercise intolerance, HFpEF and HFrEF differ not only on the differences in LVEF but also in epidemiology and clinical characteristics.[13,15-18] Heart failure with preserved ejection fraction is more prevalent in women and it more characteristically associates with obesity; up to 85% of patients with HFpEF are in fact obese,[6,20] while in HFrEF, obesity prevalence is usually lower than 50%.[21,22]

As mentioned previously, obesity increases the risk of HF[4,5,23] (Figure 1). Overall, approximately 38% of patients with HF are obese.[20] The mechanism(s) behind the association of obesity with HF, particularly with HFpEF, are not well known, although several plausible

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