Obesity and heart failure: epidemiology, pathophysiology, clinical manifestations, and management

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Obesity is a risk factor for heart failure (HF) in both men and women. The mortality risk of overweight and class I and II obese adults with HF is lower than that of normal weight or underweight adults with HF of comparable severity, a phenomenon referred to as the obesity paradox. Severe obesity produces hemodynamic alterations that predispose to changes in cardiac morphology and ventricular function, which may lead to the development of HF. The presence of systemic hypertension, sleep apnea, and hypoventilation, comorbidities that occur commonly with severe obesity, may contribute to HF in such patients. The resultant syndrome is known as obesity cardiomyopathy. Substantial weight loss in severely obese persons is capable of reversing most obesity-related abnormalities of cardiac performance and morphology and improving the clinical manifestations of obesity cardiomyopathy. (Translational Research 2014;164:345–356)

Abbreviations: BMI = body mass index; CAD = coronary artery disease; CBV = central blood volume; CO = cardiac output; CV = cardiovascular; HF = heart failure; HTN = hypertension; LV = left ventricular or left ventricle; LVEDP = left ventricular end-diastolic pressure; LVEF = left ventricular ejection fraction; LVH = left ventricular hypertrophy; RAAS = renin angiotensin-aldosterone system; RV = right ventricular or right ventricle; SV = stroke volume; SVR = systemic vascular resistance; QTc = corrected QT interval; WHO = World Health Organization

INTRODUCTION

Obesity is both a risk factor for and a direct cause of heart failure (HF) and is associated with a variety of adverse hemodynamic changes that predispose to cardiac remodeling and ventricular dysfunction.[1-3] These alterations are most pronounced in severely obese persons and may predispose to the development of HF, even in the absence of comorbidities such as coronary artery disease (CAD), valvular heart disease, pericardial disease, and congenital heart disease.[1,2] Recently, a variety of neurohormonal and metabolic abnormalities associated with obesity have been identified that may contribute to cardiac remodeling, ventricular dysfunction, and subsequent HF.[1,3] In this review, we describe the epidemiology, pathophysiology, and clinical manifestations of HF as they relate to obesity in adults. We also discuss the management of HF attributable to severe obesity with special emphasis on the role of purposeful weight loss.

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DEFINITIONS

The World Health Organization (WHO) classifies obesity in terms of body mass index (BMI).[4] The WHO classification is as follows: underweight (BMI $<$ 18.5 kg/m^2), normal weight (BMI: 18.5–24.9 kg/m^2), overweight (BMI: 25.0–29.9 kg/m^2), class I obesity (BMI: 30.0–34.9 kg/m^2), class II obesity (BMI: 35.0–39.9 kg/m^2), and class III obesity (BMI $\geq$ 40 kg/m^2).[4] In recent years the term "superobesity" has been used to characterize those whose BMI is $\geq$50 kg/m^2.[5,6] For the purpose of this review, the term "severe obesity" will apply to persons with class III obesity including those with superobesity. Central obesity has most commonly been defined as a waist circumference $>$102 cm in males and $>$88 cm in females.[7] Peripheral obesity is traditionally defined as waist circumferences at or below these thresholds.[7] Central obesity has also been defined as a waist-to-hip ratio of $>$0.9 in males and $>$0.85 in females.[7]

The American College of Cardiology and American Heart Association define HF as "a complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the heart to fill with or eject blood."[8] However, most of the studies concerning HF and obesity predate this definition. Many of these studies used the Framingham criteria described by Mckee et al[9] to define HF.

EPIDEMIOLOGY

HF afflicts 23 million persons worldwide and 5.8 million persons in the United States.[8,10,11] Reportedly, 40%–71% (mean: 56%) of those with HF have a normal or near normal left ventricular or left ventricle (LV) ejection fraction (LVEF).[9,10] In a study of 6076 patients hospitalized and discharged with a diagnosis of HF reported by Owan et al,[12] the incidence of obesity was 41.4% in subjects with a preserved LVEF and 35.5% in those with a reduced LVEF. It has been estimated that obesity is present in up to 86% of all patients with HF and a preserved LVEF, many of them elderly.[13]

It is well established that class III obesity is a risk factor for HF, even in the absence of comorbidities including systemic hypertension (HTN) and CAD.[14-17] In a study of 74 normotensive class III obese subjects, nearly one-third had clinical evidence of HF.[14] The probability of HF increased markedly when the duration of obesity exceeded 10 years with prevalence rates of 70% at 20 years and 90% at 30 years. Obesity also appears to be a risk factor for HF in overweight patients and those with class I and II obesity. In a study of 5881 participants in the Framingham Heart Study (mean age: 55 years; 54% women), 496 (8.4%) developed HF over a mean follow-up period of 14 years.[15] After adjustment for traditional risk factors there was an increased risk of HF of 5% in men and 7% in women for every unit increase in BMI. The risk of HF was significantly greater in overweight than in normal weight subjects and significantly greater in obese than in overweight patients in both men and woman. Baena-Diez et al[16] found obesity to be and independent risk factor for HF in a low risk Mediterranean population. These studies did not consider the distribution of fat, but limited evidence suggests that abdominal obesity may be independently associated with a high risk for the development of HF, particularly in the elderly.[17]

Epidemiologic studies have demonstrated unequivocally that in the general population, HF confers disproportionately high mortality risk over time.[8-11] However, analysis of mortality risk in HF populations strongly suggests that the risk of death is lower in overweight and class I and II obese patients than in normal weight or underweight subjects based on BMI classification.[1,2,18-22] In 2008, Oreopoulos et al[18] reported the results of a meta-analysis involving 28,209 patients with HF. They compared all-cause and cardiovascular (CV) mortality in patients with a normal BMI with those who were overweight and with subjects who were obese based on WHO criteria. Compared with patients with a normal BMI all-cause mortality decreased by 16% and 33%, respectively, in overweight and obese subjects. CV mortality decreased by 19% and 40%, respectively, in the overweight and obese subgroups compared with the normal BMI subgroups. This "obesity paradox" appears to be consistent in diverse HF populations including both genders, those with peripheral and central obesity, persons with chronic and acute decompensated HF, patients with preserved and reduced LVEFs, and in the elderly.[1,2,19-22] It has become increasingly clear that underweight patients with HF (BMI $<$ 18.5 kg/m^2) have the worst prognosis followed by normal weight subjects (BMI: 18.5–24.9 kg/m^2).[1,2,19-22] Overweight and class I obese patients have the best prognosis[1,2,19-22] Class II obese patients have a better prognosis than underweight and normal weight persons, but exhibit a trend toward a worse prognosis compared with overweight and class I obese patients.[1,2,19-22] When included, class III obese patients have a worse prognosis than overweight, class I and II obese patients, and a similar prognosis as underweight subjects.[1,2] Lavie et al[1,2] have provided the following explanations as potential mechanisms for the obesity paradox in patients with HF: (1) nonpurposeful weight loss because of catabolic diseases; (2) younger age at presentation; (3) lower prevalence of cigarette smoking; (4) greater metabolic reserves; (5) less frailty and cachexia; (6) lower natriuretic peptide levels; (7) higher prevalence of dyspnea resulting in earlier evaluation, diagnosis, and therapy; (8) higher blood pressure facilitating the use of CV medications; (9) attenuated response to the renin angiotensin-aldosterone