

Review

Obesity and the Obesity Paradox in Heart Failure

Pritha P. Gupta, MD, Gregg C. Fonarow, MD, and Tamara B. Horwich, MD, MS

Department of Medicine, David Geffen School of Medicine, University of California, Los Angeles, and Ahmanson-UCLA Cardiomyopathy Center, Ronald Reagan-UCLA Medical Center, Los Angeles, California, USA

ABSTRACT

Obesity has reached epidemic proportions in the general population and is associated with an increased risk for the development of new-onset heart failure (HF). However, in acute and chronic HF, overweight and mild to moderate obesity is associated with substantially improved survival compared with normal weight. This phenomenon has been termed the “obesity paradox” in HF. The majority of data pertaining to the obesity paradox identifies obesity with body mass index; however, the reliability of this method has been questioned. Newer studies have explored the use of other measures of body fat and body composition, including waist circumference, waist-to-hip ratio, skinfold thickness, and bioelectrical impedance analysis of body composition. The relationship between the obesity paradox and cardiorespiratory fitness in HF is also discussed in this review, and we explore the various potential explanations for the obesity paradox and summarize the current evidence and guidelines for intentional weight loss treatments for HF in the obese population.

RÉSUMÉ

L'obésité a atteint des proportions épidémiques dans la population générale et est associée à une augmentation du risque de développement de nouveaux cas d'insuffisance cardiaque (IC). Cependant, dans l'IC aiguë et chronique, la surcharge pondérale et l'obésité légère à modérée sont associées à une amélioration substantielle de la survie comparativement au poids normal. Ce phénomène a été appelé le « paradoxe de l'obésité » dans l'IC. La majorité des données concernant le paradoxe de l'obésité définissent l'obésité par l'indice de masse corporelle. Cependant, la fiabilité de cette méthode a été remise en question. De plus récentes études ont exploré l'utilisation d'autres mesures des réserves lipidiques de l'organisme et de la composition corporelle telles que le tour de taille, le rapport taille-hanches, l'épaisseur des plis cutanés et la mesure de la composition corporelle grâce à une analyse dite d'impédance bio-électrique. Dans cette revue, nous traitons également du lien entre le paradoxe de l'obésité et la capacité cardiorespiratoire dans l'IC, explorons les diverses explications de ce paradoxe, et résumons les données et les lignes directrices actuelles sur les traitements basés sur la perte de poids intentionnelle lors d'IC dans la population obèse.

Prevalence of Obesity in the General Population

Obesity has increased in prevalence in recent years in the United States and worldwide. Between 2009 and 2010, the percentage of obese patients identified by body mass index (BMI) ≥ 30 kg/m² in the US National Health and Nutrition Examination Survey nearly tripled, from 13.4% to 36.1%. Morbidly obese or super obese individuals with BMI ≥ 40 kg/m² increased by a multiple of 6, from 0.9% to 6.6%. According to the US National Health and Nutrition Examination Survey, more than one third of the US population is obese, and the distribution of BMI in the United States has drastically shifted toward higher values. Considering the adverse effects of obesity on left ventricular (LV) structure,

diastolic and systolic function, and other risk factors for heart failure (HF), including hypertension and coronary artery disease, it is not surprising that HF incidence and prevalence is increased in obese patients.

Obesity as a Risk Factor for HF

One of the first mentions of a causal relationship between obesity and HF was in 1956 in a case report entitled “Heart Failure Due to Extreme Obesity.” Cardiopulmonary failure developed in an obese woman because of the physical mass of adipose tissue weighing on her chest wall, leading to respiratory failure and subsequently cor pulmonale and death.¹ A similar case was reported in the *New England Journal of Medicine* in 1957.² Although the early literature highlighted the purely physical effects of obesity on HF, we now understand that the role of obesity in HF is complex and that it has adverse effects on LV structure, LV function, and other risk factors for HF, including hypertension and coronary artery disease. Salient studies thus far in this field are listed [Table 1](#). In 1992, Kasper et al.³ first described “the cardiomyopathy of obesity” based on hemodynamic and endomyocardial biopsy

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Corresponding author: Dr Tamara B. Horwich, Division of Cardiology, David Geffen School of Medicine at UCLA, 10833 Le Conte Ave CHS A2-237, Los Angeles, California 90095-1679, USA. Tel.: +1-310-794-4757; fax: +1-310-206-91433.

E-mail: thorwich@mednet.ucla.edu

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Table 1. Select studies of obesity and outcome in patients with heart failure

Study, year	Population	NYHA class	Sample size	Mean age/% female	BMI categories reported (kg/m ²)	Ottawa-Newcastle Quality Assessment Score (maximum total 9)	Mean follow-up yr
Bozkurt et al. ⁴ 2005 (USA)	Post hoc analysis of the DIG database	I-IV	7788	63/24	24% normal, 18.5-24.9; overweight, 25.0-29.9; obese, ≥ 30	8	3
Butler et al. ⁵ 2005 (USA)	Post hoc analysis of 2 FDA-approved clinical trials for LVAD placement	IV	222	51/13	13% underweight/low-normal, < 23.0; normal, 23.0-26.3; overweight, 26.4-29.4; obese, ≥ 29.4	8	1
Cicoira et al. ⁶ 2007 (Italy)	Post hoc analysis of the Val-HeFT study	II-IV	4463	63/18	18% underweight/low-normal < 22.0; normal, 22.0-24.9; overweight, 25.0-29.9; obese ≥ 30	9	1
Davos et al. ⁷ 2003 (UK)	Retrospective single-centre cohort	I-IV	525	61/17	17% nonelevated BMI < 25.0; overweight, 25.0-29.0; obese, ≥ 29-34.0; moderately/severely obese, ≥ 34.0	9	3
Gustafsson et al. ⁸ 2005 (Denmark)	Post hoc analysis of the DIAMOND-CHF study	III-IV	4504	72/39	39% underweight < 18.5; normal, 18.5-24.9; overweight, 25.0-29.9; obese, ≥ 30	9	6
Kenchaiah et al. ⁹ 2007 (USA)	Post hoc analysis of the CHARM study	II-IV	7599	66/32	32% underweight/low-normal < 22.5; normal, 22.5-24.9; overweight, 25.0-29.9; obese, 30.0-34.9; moderately/severely obese, ≥ 35.0	9	3
Hall et al. ¹⁰ 2005 (USA)	Retrospective 20-hospital integrated health care system	NYHA class not given	2707	Age and sex not reported	Nonelevated BMI < 24.3; overweight, 24.4-28.5; obese, 28.6-34.1; moderately/severely obese, ≥ 34.2	8	3
Kristorp et al. ¹¹ 2005 (Denmark)	Prospective single centre	I-III (1 patient was IV)	195	69/28	28% nonelevated BMI < 25; overweight, 25-29.9; obese, ≥ 30	9	2.5
Lavie et al. ¹² 2013 (USA)	Retrospective single-centre cohort	I-III	206	54/19	19% normal, 18.5-24.9; overweight, 25.0-29.9; obese ≥ 30	8	1.5
Padwal et al. ¹³ 2014 (Canada)	Subanalysis of the MAGGIC meta-analysis	II-III	967	66.8/32	Nonelevated BMI < 22.5-24.9; overweight, 25-29.9; obese, 30-34.9; moderately/severely obese, ≥ 35	8	3

BMI, body mass index; CHARM, Candesartan in Heart Failure: Assessment of Reduction in Mortality and Morbidity; DIG, Digitalis Investigation Group; FDA, Food and Drug Administration; LVAD, left ventricular assist device; DIAMOND-CHF, Danish Investigations of Arrhythmia and Mortality—Congestive Heart Failure; MAGGIC, Meta-Analysis Global Group in Chronic Heart Failure; NYHA, New York Heart Association; Val-HeFT, Valsartan Heart Failure Trial.

abnormalities associated with marked obesity when compared with lean controls. Analysis of 519 patients showed that BMI was positively correlated with right heart pressures and cardiac output, pulmonary vascular resistance index, and systolic blood pressure. A significantly higher percentage of obese patients were found to have idiopathic dilated cardiomyopathy compared with lean patients. A specific cause for dilated cardiomyopathy was found in 64.5% of the lean patients compared with only 23.3% of the obese patients. The most common finding on endomyocardial biopsy samples in the obese group was mild myocyte hypertrophy (67%).

In 2002, Kenchaiah et al.¹⁴ published the first large study demonstrating the association of increased BMI and an increased risk of HF in 5881 participants of the Framingham Heart Study. BMI was found to correlate with HF risk in a dose-dependent fashion: HF risk increased by 5% in men and 7% in women for each single-unit increase in BMI, even after adjustment for demographics and other known risk factors such as diabetes, hypertension, and cholesterol levels. This positive correlation between BMI and HF risk for the obese, as well as for overweight individuals, was confirmed in the larger Physicians' Health Study of 21,094 men without known coronary artery disease.¹⁵ Overweight participants had a 49% increase in HF risk compared with lean participants, and obese participants had a 180% increase (95% confidence interval [CI], 124-250).

Similar trends have been demonstrated in non-US populations. A study of 59,178 Finnish participants demonstrated the graded link between BMI and HF risk, with multivariate adjusted hazard ratios (HRs) of HF for normal, overweight, and obese BMI of 1.00, 1.25, and 1.99 for men and 1.00, 1.33, and 2.06 for women, respectively. Levitan et al.¹⁶ analyzed 2 population-based prospective cohorts of 80,630 Swedish men and women; not only higher BMI but also higher waist circumference (WC), waist-to-hip ratio, and waist-to-height ratio were associated with higher risk of hospitalization for HF and mortality.

In a recently published study in 2014, young adulthood obesity surfaced as an important risk factor for ischemic heart disease and HF in individuals without pre-existing ischemic heart disease.¹⁷ A population-based cohort study of 12,850 Danish male patients was conducted with a 36-year follow-up starting at age 22 years. The 36-year risk was 7.3% for ischemic heart disease and 0.8% for HF without pre-existing ischemic heart disease among men of normal weight and 11.1% and 4.0% among obese men, respectively. Comparing obese men with men of normal weight, the adjusted HR was 6.68 (95% CI, 2.85-15.66) for HF without pre-existing ischemic heart disease.¹⁷

There are several plausible mechanisms for the association of obesity and increased risk for HF.¹⁸ An indirect but well known and documented mechanism is the effect of obesity on HF through other risk factors (Fig. 1). Increased BMI is a risk factor for hypertension, diabetes mellitus, and dyslipidemia, all of which augment the risk of myocardial infarction, an important antecedent of HF. In addition, hypertension and diabetes mellitus independently increase the risk of HF. Elevated BMI has also been shown to be associated with altered LV remodeling, possibly owing to increased hemodynamic load, neurohormonal activation, and increased oxidative stress.¹⁹ Studies have suggested that obesity may have a

direct effect on the myocardium by demonstrating loss of cardiac function through cardiac steatosis and lipopoptosis. In 2013, a study by Granér et al.²⁰ found that cardiac steatosis is associated with visceral obesity in nondiabetic obese men and suggested that visceral obesity is the best predictor of epicardial and pericardial fat in abdominally obese individuals.

Notably, obesity is associated with obstructive sleep apnea (OSA), which is associated with incident HF. In a substantial proportion of patients with HF, OSA may play a role in the pathogenesis and progression of cardiac failure through mechanical, adrenergic, and vascular mechanisms.²¹ However, more research is required to determine basic mechanisms by which OSA exerts its adverse effects on the cardiovascular system. Further research is also needed to clarify to what extent OSA mediates the relationship between obesity and the risk of HF.

Structural and Functional Changes in the Heart in Obesity

There is evidence that obesity is associated with structural and functional changes in the heart in both humans and animal models. These changes include but are not limited to LV hypertrophy and subclinical impairment of LV systolic and diastolic function, and they are thought to be precursors to more overt forms of cardiac dysfunction and HF.²²

Studies have concluded that obesity is independently associated with LV hypertrophy and that both LV cavity size and wall thickness are increased in obese persons compared with age-matched controls.^{23,24} Wall thickness is commonly increased to a greater extent than cavity size; thus, there appears to be a slight predominance of concentric cardiac hypertrophy compared with an eccentric pattern of hypertrophy.²² A few studies suggest that LV mass may be increased in obesity but that the increase is appropriate for body size if obesity is without common comorbid conditions such as hypertension, diabetes, and coronary artery disease.^{25,26}

Many studies have evaluated LV systolic function in obesity, and the findings of these studies are variable. More recently, several studies have found that LV ejection fraction is normal or even supranormal in the majority of obese individuals, even those with severe obesity.^{23,26} However, even if the ejection fraction is normal, myocardial function is often reduced when it is measured with more sensitive echocardiographic assessments of LV function, such as midwall LV fractional shortening, systolic velocity measured with tissue Doppler, or systolic strain rate.^{25,27}

Prevalence of Obesity in the Population With HF

The incidence and prevalence of HF and its associated mortality is increasing at alarming rates. Despite the progress made in the development of several new therapies in HF management, the overall 5-year mortality rate for HF remains extremely high at nearly 50%.²⁸ Studies have determined that up to 32%-49% of patients with HF are obese and 31% to 40% are overweight (BMI, 25.0-29.9 kg/m²).^{9,29} A very small proportion of patients with HF are classified as underweight. Patient who are overweight and obese commonly present with

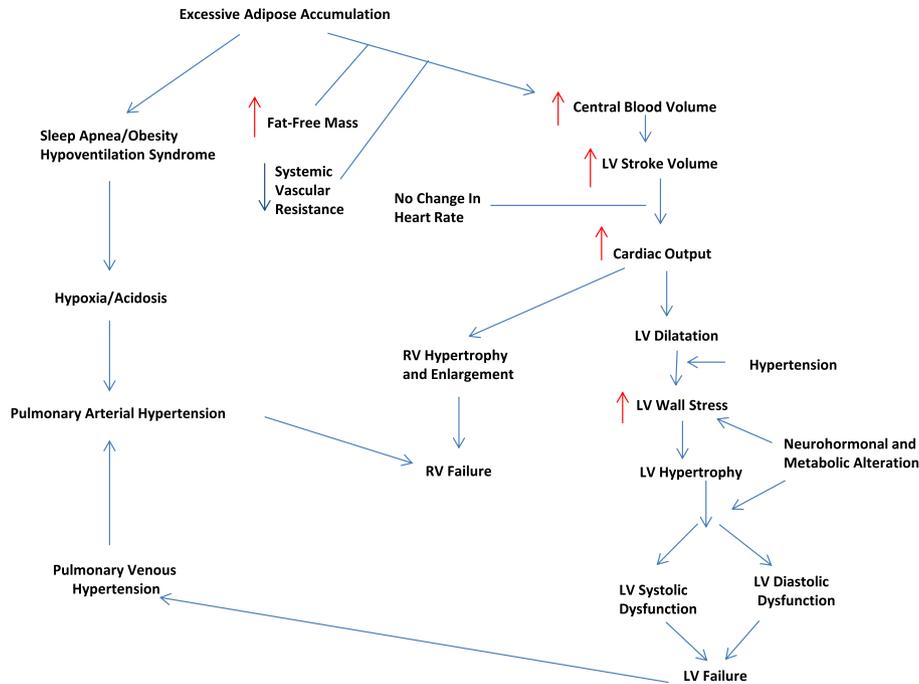


Figure 1. Proposed pathophysiological processes of cardiomyopathy in obesity. The central hemodynamic alterations that result from excessive adipose accumulation in severely obese patients, as well as their subsequent effects on cardiac morphologic features and ventricular function, are shown. Left ventricular (LV) hypertrophy in severe obesity may be eccentric or concentric. Factors influencing LV remodelling and geometry include severity and duration of obesity, duration and severity of adverse LV loading conditions (particularly hypertension), and possibly neurohormonal and metabolic abnormalities such as increased sympathetic nervous resistance with hyperleptinemia, adiponectin deficiency, lipotoxicity, and lipopoptosis. These alterations may contribute to the development of LV failure, which, facilitated by pulmonary arterial hypertension from sleep apnea/obesity hypoventilation, may subsequently lead to right ventricular failure. Adapted from Alpert et al.¹⁸ with permission from Elsevier.

signs and symptoms of HF 10 years earlier than their leaner counterparts. Of note, obesity is significantly more prevalent in patients with HF with preserved ejection fraction compared with those with reduced ejection fraction.³⁰

Obesity and Brain Natriuretic Peptide

The role of natriuretic peptides in the clinical expression of chronic HF has been established.³¹ Studies have shown that natriuretic peptide levels are reduced in the obese state, partly related to altered clearance receptors and peptide degradation.^{32,33} Mehra et al.³⁴ compared brain natriuretic peptide (BNP) levels in obese and nonobese patients with respect to New York Heart Association functional class and lean body weight-adjusted peak aerobic oxygen consumption. Plasma levels of tumor necrosis factor- α , interleukin-6, and soluble intercellular adhesion molecule-1 were measured in a subset of patients. Levels of BNP were significantly lower in obese than in nonobese patients (205 ± 22 pg/mL and 335 ± 39 pg/mL, respectively) despite a similar severity of HF and cytokine levels. Multivariate regression analysis identified BMI as an independent negative correlate of BNP level, demonstrating that obesity is an important and independent determinant of peripheral BNP expression in patients with HF. These findings not only speak to the usefulness of BNP as a diagnostic test in obese patients with HF but also provide insight into certain potential underlying pathophysiological mechanisms that relate to the development of HF in obese patients. Reduced levels of circulating BNP may lead to early

loss of natriuretic-mediated vasodilation, lesser antagonism of the renin-angiotensin system, or loss of natriuretic ability in obese patients.

Obesity and Survival in Heart Failure: The Obesity Paradox

Although elevated BMI is well established as a risk factor for HF, a surprising relationship between BMI and outcomes in those with established HF has been observed. This unexpected relationship between BMI and survival in HF was first described by Horwich et al.³⁵ in 2001. Survival data for a cohort of 1203 patients with advanced systolic HF at a single university transplantation centre was analyzed and revealed that patients with higher BMI (> 27.8 kg/m²) were found to have significantly improved risk-adjusted transplant-free survival. The worst outcomes were seen in the underweight group, followed closely by normal-weight patients. Although elevated BMI is well established as a risk factor for HF, this study revealed that elevated BMI was not a risk factor for increased mortality but rather was associated with a trend toward improved survival (Fig. 2). This counterintuitive epidemiologic association between survival outcomes and traditional risk factors is termed “reverse epidemiology” or “obesity paradox” and has now been well documented in numerous studies and in the HF literature. In 2005, a subsequent analysis of 7767 stable outpatients with chronic HF enrolled in the Digitalis Intervention Group also revealed lower risk-adjusted mortality rates in overweight and obese

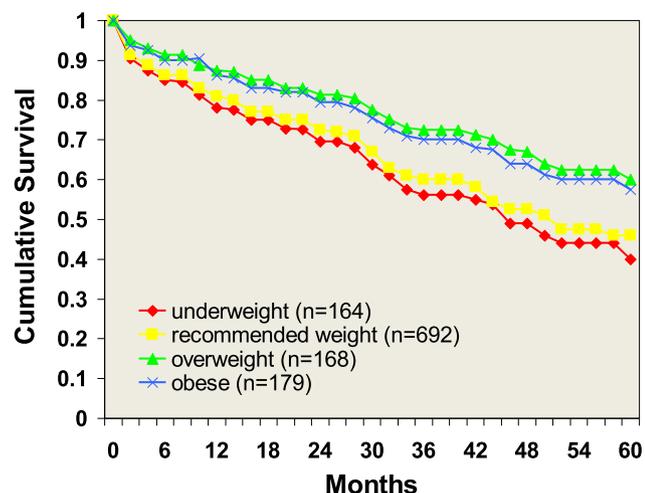


Figure 2. Risk-adjusted survival curves for the 4 body mass index (BMI) categories at 5 years. The variables entered into the equation were age, sex, hypertension, diabetes mellitus, left ventricular ejection fraction, hemodynamic variables, peak VO_2 , mitral regurgitation, tricuspid regurgitation, medications, and serum sodium, creatinine, and lipid levels. Survival was significantly better for the overweight and obese BMI categories. Adapted from Horwich et al.³⁵ with permission from Elsevier.

compared with normal-weight patients, with HRs of 0.88 (0.80-0.96) and 0.81 (0.72-0.92), respectively.⁴ Another subanalysis of a large randomized controlled trial of 7599 patients with symptomatic HF with either reduced or preserved systolic function showed that patients in lower BMI categories (underweight and normal weight) had a graded increase in the risk of death; the group with the highest BMI ($> 35 \text{ kg/m}^2$) had a risk similar to those with a BMI of 30.0-34.9 kg/m^2 .⁹ A meta-analysis of 9 observational HF studies ($n = 28,209$) by Oreopoulos et al.³⁶ also found that overweight and obese individuals, respectively, had reduced cardiovascular (-19% and -40%, respectively) and all-cause (-16% and -33%, respectively) mortality during 2.7 years of follow-up compared with those without an elevated BMI. Another analysis of BMI and its relationship to in-hospital mortality for 108,927 patients with decompensated HF identified a 10% reduction in mortality for every 5-unit increase in BMI.³⁷

The Obesity Paradox in Different HF Subgroups

The obesity paradox may not be uniform across all populations. Given the heterogeneity of those affected by HF,

recent studies have made efforts to better characterize the obesity paradox in specific subgroups. A recent study of 6142 patients across 4 continents used Cox proportional hazard models and a net reclassification index to describe associations of BMI with all-cause mortality and found that the protective association of BMI with mortality was confined to persons older than 75 of age (HR, 0.82), decreased cardiac function (ejection fraction $< 50\%$; HR, 0.85), no diabetes (HR, 0.86), and de novo HF (HR, 0.89).³⁸ Another study by Zamora et al.³⁹ found that when comparing mortality in obese and nonobese patients with different causes of HF, the obesity paradox was observed only in patients with nonischemic HF.

Recently, the role of sex in HF outcomes was investigated in a prospective study following 2718 patients with HF at a single university centre. BMI and WC were measured at baseline, and multivariate analysis revealed that normal BMI and normal WC were associated with higher relative risk for the primary outcome of death, urgent heart transplantation, or ventricular assist device placement in men (BMI, 1.34; WC, 2.02) and in women (BMI, 1.38; WC, 2.99). High BMI and WC were associated with improved outcomes in both sexes.⁴⁰

Proposed Mechanisms for the Obesity Paradox in HF

The exact mechanisms underlying the obesity paradox have not been clearly defined. Several theories exist (Table 2). A common explanation for the increased survival seen in obese patients with HF is that the additional adipose tissue provides greater reserves against the catabolic changes associated with the disease process that can lead to cardiac cachexia, which is a syndrome involving progressive weight loss and alterations in body composition and carries a devastating prognosis in HF as well as in other disease states. In 1 HF population, 50% of those with cachexia (defined as a nonintentional documented weight loss of at least 7.5% of previous normal weight over 6 months) had died at 18-month follow-up (HR, 3.73; 95% CI, 1.93-7.23 compared with those without cachexia).⁴¹ This highlights the possible protective role of adipose tissue in HF as an energy reserve in the setting of chronic illness. One study from the Cleveland Clinic demonstrated that patients with morbid obesity experienced the highest all-cause mortality/transplantation (HR 2.46; 95% CI, 1.4-4.30), which was far greater than that of the nonobese group (HR, 1.44; 95% CI, 1.09-1.91), when both groups were compared with obese study participants.⁴² Another explanation for the obesity paradox is that obese patients may experience greater functional impairment and therefore may present earlier in their disease course.³⁵

Table 2. Different methods of identifying obesity in the HF population

Method	Strengths	Weaknesses
Body mass index	Widely used and studied	Reliability has been questioned
WC	Increased WC is associated with improved outcomes in advanced HF	Reliability has been questioned
Waist-hip ratio	Easy to obtain	Not widely studied in HF
Skinfold estimates of percent BF	Increased BF is associated with improved outcomes in HF	Not widely studied in HF
Bioelectrical impedance analysis of body composition	Potential to be used at bedside or in clinics	Not readily available
Dual-energy x-ray absorptiometry	Fairly accurate for assessing body composition	Expensive, requires technical expertise
Computed tomography and magnetic resonance imaging	Gold standards for assessing body composition	Expensive, radiation exposure

BF, body fat; HF, heart failure; WC, waist circumference.

Table 3. Major research needed to further evaluate obesity and the obesity paradox in HF

Head-to-head comparison of the various methods to evaluate body composition in patients with HF and their associations with outcomes
Using methods of body composition analysis, identify whether increased fat mass or lean muscle mass, or both, are independently associated with improved survival in HF
Measure visceral or ectopic fats, including pericardial fat, in patients with HF using CT or MRI and correlate with HF characteristics and outcomes
Further evaluate with the causal association between obstructive sleep apnea, obesity, and incident HF
Explore potential mechanisms that may account for the obesity paradox in patients with HF and other chronic disease states
Evaluate in prospective randomized clinical trials if intentional weight loss results in improved quality of life and clinical outcomes in overweight and obese patients with HF
Determine to what degree therapeutic goals in HF should be based on weight, body composition, metabolic indices, biomarkers, measures of cardiorespiratory fitness, other parameters, or a combination
Ascertain optimal exercise and dietary recommendations for overweight and obese patients with HF overall and in specific patient populations based on age, sex, race/ethnicity, ejection fraction group, and comorbid conditions

HF, heart failure.

Finally, 1 potential explanation for the paradoxical link between obesity and HF is the way that most studies have chosen to identify obesity. For reasons of widespread acceptance and ease of use, BMI has been used to estimate body composition and identify overweight, obese, and morbidly obese patients. However, the reliability of BMI as a true representation of adiposity has been questioned. Some experts maintain that fat mass distribution, along with cardiorespiratory fitness and total fitness, are more accurate determinants of mortality in HF.^{4,5}

Identifying Obesity: Looking Beyond BMI to Measure Adiposity

There are numerous alternative techniques that may prove to be more accurate to define obesity when compared with BMI (Table 2). These techniques include WC, waist-to-hip ratio, skinfold estimates of percent body fat (BF), dual x-ray absorptiometry (DEXA), and bioelectrical impedance analysis (BIA) of body composition.

WC is an established predictor of cardiovascular risk in the general population,^{43,44} and it is also a simple and inexpensive way to assess for abdominal obesity. In 344 patients with HF and systolic dysfunction, Clark et al.⁴⁵ analyzed the prognostic value of BMI and WC and found lower total mortality in those patients with higher values of both parameters. In a recent study of 2254 patients in the Spanish Red Nacional de Investigación en Insuficiencia Cardíaca (REDINSCOR) Registry, BMI and WC were found to be independent predictors of lower total mortality in obese and overweight patients with chronic HF. Interestingly, however, the protective effect of BMI was lost in patients with a WC > 120 cm. In future studies, WC should be measured together with BMI to better predict the prognosis of chronic HF.

BIA is another noninvasive albeit slightly more costly and less readily available technique to evaluate changes in body composition. In a community-based study in the United Kingdom, 1025 patients with chronic HF underwent BIA; percent BF, fat mass, and fat-free mass were associated with

increased risk, and percent BF was a significant predictor of mortality in a multivariable model.⁴⁶ A recent study found BIA to be safe for use with pacemakers and defibrillators, broadening its potential use in populations with advanced HF.⁴⁷ Preliminary data from a study by Thomas et al.⁴⁸ that used BIA to assess body composition in 354 patients with HF compared the relative contributions of lean body mass (LBM) and body fat mass (BFM) to the obesity paradox. They found that higher fat mass is protective in HF and higher lean mass may be protective in HF but not significantly. The data also suggest that a body composition of low LBM and low BFM is the least protective in HF, whereas high LBM and high BFM is most protective.

One additional consideration is that DEXA and traditional BIA analysis both assume a constant fluid hydration status, which is likely not the case in the patient with HF. Vectorial analysis of BIA (BIVA) is a promising method to evaluate body composition in patients with HF. BIVA is a pattern analysis of impedance measurements (resistance and reactance) plotted as a vector in a coordinate system and, most importantly, it is independent of hydration status.^{49,50} For a more complete understanding of the obesity paradox in HF, further investigations of body composition and outcomes in HF are warranted, keeping hydration status in mind.

Cardiorespiratory Fitness and Prognosis in Obese Patients With HF

Cardiorespiratory fitness (CRF), measured as peak oxygen uptake (V_{O_2}) or minute ventilation (V_E)/carbon dioxide production (V_{CO_2}), has been identified as an important predictor of survival in HF. Chase et al.⁵¹ studied a cohort of 744 patients with HF and found that although obese patients had significantly lower V_E/V_{CO_2} slopes than in normal and overweight patients, V_E/V_{CO_2} was a strong independent predictor of improved survival irrespective of BMI. A more recent study demonstrated that CRF level may actually mitigate or even negate the impact of the obesity paradox in HF. In a study of 2066 patients with systolic HF, Lavie et al.¹² found that BMI was a significant predictor of age- and sex-adjusted survival in the group with low peak V_{O_2} (< 14 mL/ O_2 /kg), but not in the high-CRF group. These findings suggest that exercise training to improve CRF is reasonable.

In the largest multicentre randomized controlled study of exercise training in patients with HF, the Heart Failure: A Controlled Trial Investigating Outcomes of Exercise Training HF (ACTION) trial randomized 2331 patients with HF into groups of standard care or standard care plus regular aerobic exercise training. The study demonstrated that after adjustment for highly prognostic predictors of all-cause mortality, exercise was associated with at least modest improvements in all-cause mortality, hospitalization, and cardiovascular mortality.⁵² Therefore, exercise appears to be safe and beneficial regarding improved quality of life for patients with HF.

Clinical Implications for Weight Management in Patients With HF

Despite the potential benefits of weight loss in the prevention of HF, weight loss recommendations for other populations may not be appropriate for patients with established

HF. There are no large-scale studies of the safety or efficacy of weight loss with diet, exercise, or bariatric surgery in obese patients with HF. Despite this gap in evidence, the major HF societies have variable recommendations regarding intentional weight loss interventions in HF. The American Heart Association does not have any specific recommendation for weight loss at any level of BMI.⁵³ The Heart Failure Society of America recommends intentional weight loss for BMI > 30 kg/m²,⁵⁴ and the European Society of Cardiology defers to other guidelines for management of obesity in HF.⁵⁵ None of the major societies recommends weight loss for overweight patients with HF. The reasons for these variations are likely related to a lack of data regarding intentional weight reduction and long-term prognosis in HF. Further studies are needed to determine the impact of intentional weight loss in patients with HF, including the safety and efficacy of bariatric surgery, which appears to be safe and effective in some small studies.⁵⁶

Conclusions

Obesity is a risk factor for the development of incident HF, and population-wide HF prevention efforts should include efforts to prevent and treat obesity. However, the association of obesity and improved survival in acute and chronic HF is also well established across multiple measures of adiposity. Further investigation is required for a more complete understanding of this substantial associated survival benefit in HF and the underlying pathophysiological processes involved (Table 3). A better understanding of the role of CRF in the relationship between obesity and outcomes may lead to better risk assessment. Furthermore, although intentional weight loss is known to improve hemodynamic function and cardiac structure in patients without HF, additional research is needed to generate evidence-based guidelines for weight management in established HF in the overweight and obese population.

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The authors have no conflicts of interest to disclose.

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