The relationship between body mass index/body composition and survival in patients with heart failure

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Abstract

Purpose: The purpose of this review was to summarize the literature on the relationship between obesity and survival in persons with heart failure (HF). In particular, the article examines the ways in which studies define body size/composition (body mass index [BMI], body composition, weight, cachexia, fluid retention, or albumin) and the relationship of BMI and survival after controlling for factors such as HF severity, etiology of the HF, gender, race, age, and/or time since HF diagnosis.

Data sources: The keywords heart failure and body mass index, heart failure and obesity, and heart failure and body composition were indexed in PubMed. Articles published from 1999 to 2006 that used multivariate analyses to examine the relationship between obesity and survival in persons with HF were included in the review.

Conclusions: BMI is the standard most often used for measuring body weight in patients with HF. Yet, BMI does not address other major components of body weight (fat, lean body mass, and fluid) that may factor into the mortality of patients with HF. Four of the six studies reviewed reported a positive relationship between obesity and improved survival. However, the studies are limited by design, with the majority being cross-sectional. Furthermore, most of the data were collected through secondary data analysis from patient records in the 1990s, before contemporary HF treatment was used.

Implications for practice: Until further research solidifies a clear association between higher BMIs and improved survival in patients with HF, nurse practitioners and others should continue to counsel their patients with HF who are overweight to lose weight. Assessing BMI alone as a predictor of survival for patients with HF may be misleading and should be performed in the context of other factors. Moreover, care should be taken in managing patients with HF who are cachexic because these patients have a worrisome prognosis.

Introduction

The prevalence of heart failure (HF) in the United States is expected to increase from 5.2 million in 2004 (Rosamond et al., 2007) to 10 million by 2030 (Adams et al., 1999). This rise in HF has been attributed to the advancing age of the population; rising obesity; and the added stress of hypertension (HTN), smoking, obesity, high-fat/high-cholesterol diet, sedentary lifestyle, and diabetes mellitus (DM), all of which either cause myocardial damage or increase myocardial workload (Hall et al., 2005). Despite recent advances in the management of patients with HF, morbidity and mortality rates remain high, with an estimated 5-year mortality rate of 50% (Zevitz, 2005). In fact, HF is the only cardiovascular condition in which there has not been a substantial decline in both incidence and...
prevalence over the past 20 years (taking into account the progressive aging of the population) (Stewart, MacIntyre, Capewell, & McMurray, 2003). Thus, HF poses a great burden on the population and the healthcare system.

Nearly, a third of Americans are obese (Murphy et al., 2005). Obesity is a risk factor for HF and many other diseases, increasing the chance of developing other significant cardiovascular risk factors such as HTN, DM, and dyslipidemia. The Framingham Heart Study found that being overweight or obese was an independent predictor of HF (Kenchaiah et al., 2002). In fact, overweight women have a 50% greater risk of developing HF. Further, in patients with established HF, obesity has been found to be associated with an increased risk of mortality (Eckel, 1997) and is consistently associated with left ventricular hypertrophy and dilatation (Kenchaiah et al.). This prior evidence had led clinicians toward recommendations for weight loss for the obese in both the general population and those with HF (Adams et al., 2006). However, more recent research suggests that obesity may actually be associated with improved survival in persons already diagnosed with HF (Curtis et al., 2005; Davos et al., 2003; Gustafsson et al., 2005; Hall et al., 2005; Horwich et al., 2001; Lavie, Osman, Milani, & Mehra, 2003). This research suggests that clinicians may need to distinguish between weight management strategies for healthy individuals as opposed to those with HF (Curtis et al.).

This article reviews the current evidence regarding whether obesity is indeed protective in persons with HF. Specifically, the article examines the ways in which studies define body size/composition (by body mass index [BMI], body composition, weight, cachexia, fluid retention, or albumin) and the relationship of BMI and survival after controlling for factors such as (a) severity of HF (left ventricular ejection fraction [LVEF] and/or New York Heart Association [NYHA] functional class; Table 1), (b) etiology of HF (ischemic vs. nonischemic), (c) age, (d) gender, (e) race, and (f) time since HF diagnosis.

Method

The keywords heart failure and body mass index, heart failure and obesity, and heart failure and body composition were indexed in PubMed. All published articles from 1999 to 2006 that examined a relationship between obesity and survival in persons with HF were examined. The abstracts of original articles reporting studies of HF, obesity, and the relationship of BMI to body composition were reviewed. Articles were included in the review if the study used multivariate analyses to examine the relationship between obesity and HF survival.

Table 1 Criteria for NYHA functional classification in patients with HF

<table>
<thead>
<tr>
<th>NYHA class</th>
<th>Definition</th>
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<tr>
<td>class I</td>
<td>No limitation in physical activity. Ordinary physical activity does not cause undue fatigue, palpitations, or dyspnea.</td>
</tr>
<tr>
<td>class II</td>
<td>Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in fatigue, palpitations, or dyspnea.</td>
</tr>
<tr>
<td>class III</td>
<td>Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes fatigue, palpitations, or dyspnea.</td>
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<tr>
<td>class IV</td>
<td>Unable to carry on any physical activity without discomfort. Symptoms of cardiac insufficiency present at rest. If any physical activity is undertaken, discomfort is increased.</td>
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</table>

Note. Adapted from HFSA 2006 comprehensive heart failure practice guideline (HFSA 2006).

Review of the evidence: Link of BMI to survival

Six studies published between the years 1999 and 2006 met the criteria for the analysis (Table 2). Horwich et al. (2001) were the first to report the possible beneficial effects of obesity on the survival of patients with HF. They analyzed hospital records from 1203 patients with advanced systolic HF (NYHA classes III and IV = 93.9%) who were referred to a university medical clinic for heart transplant evaluation and were followed in a comprehensive HF management program. BMI was used as the primary index of obesity, with percent ideal body weight (PIBW) used as an alternative index of total body fat. To rule out edema as a confounder for accuracy of body size/composition, weights were measured upon conclusion of pulmonary artery catheter-guided therapy. This assured that the optimal hemodynamics and euvoolemia had been achieved (Horwich et al.). The researchers expected that obese patients with HF would have worse mortality outcomes than those with recommended weight (20.7–27.7 kg/m² for the purposes of this study). On univariate analysis, however, low LVEF, low peak VO₂ (oxygen consumption), high pulmonary capillary wedge pressure, and low use of angiotensin-converting enzyme (ACE) inhibitors were predictors of mortality at 1 year. However, higher BMI and PIBW were not predictors of mortality. Furthermore, multivariate analysis determined that a higher BMI level was not associated with improved survival at 12 months \(p = .072\). Although a higher BMI was associated with a survival benefit at 2 years \(p = .016\), the benefit was not sustained at 5 years \(p = .259\). When PIBW was used as an alternative to BMI, the same relationships held true (Horwich et al.).

Lavie et al. (2003), who retrospectively studied 209 ambulatory patients with mild-to-moderate HF (NYHA
<table>
<thead>
<tr>
<th>Study, sample size, and year of data collection</th>
<th>Overall result</th>
<th>NYHA class – n (%)</th>
<th>Severity of HF (LVEF)</th>
<th>Etiology of HF</th>
<th>Age (years)</th>
<th>Gender</th>
<th>Race</th>
</tr>
</thead>
<tbody>
<tr>
<td>Horwich et al. (2001), 1203 subjects, and between 1983 and 1999</td>
<td>BMI and PIBW were not predictors of survival at 1 year (p = .07) and 5 years (p = .259); BMI and PIBW were predictors of survival at 2 years (p = .016)</td>
<td>NYHA II = 66 (5.5); NYHA III = 401 (33.3); NYHA IV = 729 (60.6)</td>
<td>Mean LVEF = 22%; LVEF &gt; 40% were excluded</td>
<td>Ischemic = 48%</td>
<td>Average age for each category of BMI: underweight = 48.4 ± 15.4; normal weight = 53.2 ± 11.4; overweight = 52.5 ± 10.0; obese = 48.5 ± 11.5</td>
<td>Males = 76.6%</td>
<td>Not reported</td>
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<td>Lavie et al. (2003), 209 subjects, and between 1996 and 1998</td>
<td>Higher percent body fat and BMI were independent predictors of event-free survival; events included cardiovascular death (13) or urgent transplantation (15)</td>
<td>NYHA I = 21 (10.1); NYHA II = 86 (41.1); NYHA III = 102 (48.8)</td>
<td>LVEF = 19% for event group; LVEF = 24% ± 13 for event-free group</td>
<td>Ischemic = 42%</td>
<td>Major clinical events—with events: age = 53 ± 13; event-free group: age = 54 ± 12</td>
<td>Male = 81%</td>
<td>Not reported</td>
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<td>Davos et al. (2003), 525 subjects, and between 1991 and 2000</td>
<td>Improved survival in noncachectic group; in the noncachectic group, quintile 4 (mean BMI: 29.2 kg/m²) had the best 12- and 36-month survival</td>
<td>Noncachectic patients: NYHA I = 101 (19.2); NYHA II = 230 (43.8); NYHA III = 152 (28.9); NYHA IV = 42 (8)</td>
<td>Noncachectic patients: LVEF = 31.6 ± 14.8</td>
<td>Noncachectic patients: ischemic = 57%</td>
<td>Noncachectic patients: average age = 61.0 ± 12.4</td>
<td>Noncachectic patients: male = 83%</td>
<td>Not reported</td>
</tr>
<tr>
<td>Curtis et al. (2005), 7767 subjects, and between 1991 and 1993</td>
<td>Improved survival in overweight and obese group; possible plateau effect, with BMI &gt; 35 kg/m²</td>
<td>NYHA I = 1087 (14); NYHA II = 4272 (55); NYHA III/IV = 2408 (31)</td>
<td>LVEF = 31.9 ± 12.5</td>
<td>Ischemic = 68.9%</td>
<td>Age = 63.9 ± 10.9</td>
<td>Male = 75.4%</td>
<td>African American = 14.4%</td>
</tr>
<tr>
<td>Hall et al. (2005), 2707 subjects, and from 1995 to unknown</td>
<td>Improved survival with higher BMI groups</td>
<td>Not reported</td>
<td>LVEF ≤ 40%</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
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<tr>
<td>Gustafsson et al. (2005), 4700 subjects, and between 1993 and 2002</td>
<td>Improved survival with higher BMI groups—only in those with preserved LVEF and without COPD</td>
<td>NYHA III and IV only</td>
<td>LVEF ≤ 0.35</td>
<td>Ischemic = 58%</td>
<td>Age = 72.4</td>
<td>Male = 61%; more males in the overweight and obese groups</td>
<td>Not reported</td>
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classes I–III), examined the impact of obesity and various body composition parameters on clinical outcomes in patients with chronic systolic HF. Five body composition parameters were assessed: body surface area, BMI, percent body fat, total fat, and lean body weight. Using established methods, body surface area was estimated from the patient’s height and body weight and reported in square meters. Percent body fat was determined using the average of three skinfold measures to estimate total body fat (body weight in kilogram multiplied by percent body fat) and lean body weight (body weight in kilogram minus total body fat).

Patients with the lowest percentage of body surface area (2.0 m²), BMI (27.7 kg/m²), body fat (22.5%), total fat (19.7 kg), and lean body weight (65.5 kg) had the highest percentage of major clinical events (cardiovascular death and urgent transplantation). A higher percentage of body fat was the strongest independent predictor of event-free survival (p = .002). In fact, as percent body fat increased by 1%, the likelihood of clinical events decreased by more than 13%. When percent body fat was replaced by BMI and total fat, the relationships held true. Other independent predictors of event-free survival based on multivariate analysis were a nonischemic etiology and higher peak oxygen consumption. It is important to note that more than half (15) of the 28 major clinical events were urgent transplantation. Furthermore, the obese patients in this study were significantly younger than the lean patients (p < .02); yet, age, LVEF, NYHA class, and gender were not predictors of event-free survival in multivariate analysis.

Cachexia has been recognized as a risk factor for mortality, leading Davos et al. (2003) to prospectively study 589 patients with chronic HF in order to determine whether BMI had a differential effect on survival in persons with and without cardiac cachexia. Cachexia was defined as a nonedematous and unintentional weight loss of more than 7.5% over the past 6 months. The researchers hypothesized that because chronic HF appears to be an inherently catabolic state, a higher BMI might prove protective even in the absence of cachexia.

To test this hypothesis, Davos et al. (2003) compared survival rates in patients with cachexia (n = 64) to those without cachexia (n = 525). Patients with primary cachexic states (infection, malignant disorder, thyroid disorder, severe liver disease, or acquired immunodeficiency syndrome) were excluded from the study. Noncachexic patients were categorized into quintiles according to their BMI (quintile means and standard deviations were as follows—BMI at quintile 1: 22.2 kg/m² ± 1.5; at quintile 2: 24.9 kg/m² ± 0.6; at quintile 3: 26.9 kg/m² ± 0.6; at quintile 4: 29.2 kg/m² ± 0.8; and at quintile 5: 34.1 kg/m² ± 2.8).

Improved 12-month survival was found in the noncachexic group compared to the cachexic group (OR = 2.71 [95% confidence interval (CI): 1.94–3.79]; Davos et al., 2003). In other words, cachexic subjects were almost three times more likely to die than the noncachexic subjects. On average, the cachexic group was 4 years older and had a lower LVEF (by 5.3%), worse exercise capacity, and lower systolic blood pressure (by 14.9 mmHg), compared to the noncachexic group.

In the noncachexic group, subjects who were moderately obese, those with BMI values in the fourth quintile (mean ± SD BMI: 29.2 kg/m² ± 0.8), had the best survival at 1 year (p = .01) and 3 years (p < .0001). When examining survival rates, the relative risk of death compared to the improved survival for the fourth quintile was 2.3 for quintile 1 (p = .001), 1.7 for quintile 2 (p = .027), 1.8 for quintile 3 (p = .016), and 1.5 for quintile 5 (p = .14). Multivariate analysis revealed that an increased BMI, a higher LVEF, and better exercise capacity (peak oxygen consumption) were independent predictors of survival, even after correcting for age, presence of ischemic heart disease (IHD) as an etiology, NYHA class, and duration of disease. It is important to note that short-term survival rates (first 2 years) and the lowest BMI quartile of noncachexic subjects were similar to those of cachexic subjects.

Furthermore, authors considered the possibility of whether a U-shaped relationship existed between BMI and survival in HF, in which the very thin and the very obese had worse survival. However, the number of subjects in the extreme BMI categories did not permit for testing for a curvilinear relationship.

Curtis et al. (2005) also reported improved survival in patients with an increased BMI. The authors retrospectively studied the association between BMI and outcomes in 7767 stable outpatients with HF between the years 1991 and 1993 using the Digitalis Investigation Group trial database. Subjects were grouped according to BMI into four categories as defined by The United States Preventive Services Task Force (2003). More than half the participants were overweight (BMI 25.0–29.9 kg/m²) or obese (BMI ≥ 30.0 kg/m²). A smaller proportion of overweight (32.4%) and obese (28.4%) patients died during follow-up than did underweight (45%) or normal weight (37.8%) patients. Thus, patients who were overweight or obese were less likely to die, with adjusted hazard ratios of 0.88 (95% CI: 0.80–0.96) and 0.81 (95% CI: 0.72–0.92), respectively, compared to those with a normal BMI (18.5–24.9 kg/m²). Whereas, the risk of death for those underweight was greater than for those with a normal BMI, with an adjusted hazard ratio of 1.21 (95% CI: 0.95–1.53). Rates of all-cause hospitalization and hospitalization because of worsening HF were similar across BMI groups (underweight = 70.6%, normal weight = 64.7%, overweight = 65.6%, and
obese (67.2%). The relationship between BMI and HF outcomes (survival and hospitalization rates) held when subjects were stratified by LVEF, HF etiology, gender, and duration of HF. Authors, however, noted a possible plateau relationship between BMI and survival among the very obese patients (BMI > 35 kg/m²) as this subgroup had an increased risk of death.

Hall et al. (2005) examined long-term survival (6 years) of hospitalized patients with HF based on BMI, controlling for age, gender, and severity of illness. In this retrospective review of patients in a 20-hospital integrated healthcare delivery system, all 2707 patients had a primary diagnosis of HF identified by ICD-9 coding or by identification of an LVEF ≤ 40%. BMI was used as the measure of body weight and was calculated using the first measured heights/weights at hospital admission. Quartiles for this study were defined as follows—BMI at quartile 1: <24.3 kg/m², at quartile 2: 24.4–28.5 kg/m², at quartile 3: 28.6–34.1 kg/m², and at quartile 4: ≥34.2 kg/m². Three-year survival rates improved with increasing BMI quartiles (quartile 1 = 57%, quartile 2 = 61%, quartile 3 = 69%, and quartile 4 = 74%). After adjusting for age, gender, and severity of HF (not defined), survival rates were better for the three highest BMI quartiles, with adjusted hazard ratios of 0.77 (95% CI: 0.63–0.94) for quartile 1, 0.70 (95% CI: 0.56–0.86) for quartile 2, and 0.77 (95% CI: 0.59–0.99) for quartile 3, compared to those in quartile 1, with a BMI < 24.3 kg/m².

Like Hall et al. (2005), Gustafsson et al. (2005) evaluated the influence of BMI and LVEF on mortality in subjects hospitalized with HF. They examined a total of 4700 subjects with new or worsening HF from the Danish Investigations of Arrhythmia and Mortality on Dofetilide HF registry. Patients were categorized into four groups based on their BMI (underweight: <18.5 kg/m², normal weight: 18.5–24.9 kg/m², overweight: 25–30 kg/m², and obese: >30 kg/m²). These subgroups are very similar to those used by Curtis et al. (2005), as recommended by The United States Preventive Services Task Force (2003).

As in the previous studies, the risk of death decreased steadily with increasing BMI from the underweight to the obese. At the end of follow-up (ranging from 5 to 8 years), after adjusting for age and gender, the risk ratios (RRs) for death were 1.56 (95% CI: 1.33–1.84) for those underweight, 0.90 (95% CI: 0.83–0.97) for those overweight, and 0.77 (95% CI: 0.70–0.86) for the obese group. However, when a subgroup analysis was performed, the overweight or obese subjects with a decreased LVEF had an excessive risk of mortality. In fact, for those with systolic dysfunction, the obese subjects had an RR of 1.21 (95% CI: 1.01–1.45) compared to those subjects of normal weight. In other words, of the overweight and the obese, only those with preserved left ventricular function (normal or high LVEF) had improved survival. Furthermore, the authors also found that the effect of BMI on survival depended on the presence or absence of coexisting chronic obstructive pulmonary disease (COPD). Thus, this study hints that the protective effect of higher BMI status on HF survival is dependent on the presence of preserved systolic function and the absence of coexisting COPD (Gustafsson et al., 2005).

**Discussion**

Four studies included in this analysis found a significant positive association between obesity and HF survival; however, two of the four studies suggested that a nonlinear relationship may exist. Four of the six studies used body weight and height recorded during initial screening, and then categorized participants into BMI groups. Lavie et al. (2003) used body composition parameters (body surface area, percent body fat, total fat, and lean body weight) in addition to BMI. Horwich et al. (2001) used both BMI and PIBW while making sure that subjects were euvoletic prior to using those numbers for analysis. All studies divided their sample into BMI quartiles or quintiles that were roughly similar, allowing for comparison across studies. However, cross-comparison is challenging because ranges of data were not reported in all studies (only mean values).

Most of the studies used BMI measured at one point in time as the sole determinant of body composition. While BMI is a simple, commonly used measure for rating obesity level, it is misleading, given that BMI ignores the major components of body weight: fat, lean body mass, and fluid (Heyward & Wagner, 2004). Specifically, BMI does not take into account differences in the proportion of fat to lean body mass or the distribution of fat, a factor that previous research suggests is important for predicting HF survival (Heyward & Wagner). Furthermore, BMI overestimates body fat in people who are very muscular or who have edema. For example, it overestimates fat in young adult males compared to young adult females because of the lesser percent body fat in males. BMI also seems to be overestimated in Caucasians, when age- and gender-matched with other ethnic groups (Heyward & Wagner). Conversely, BMI underestimates body fat in people who have lost muscle mass, such as the elderly (Brigham and Women’s Hospital, 2003). BMI also has limitations for individuals or populations with extremes of heights or who have very long or short limb lengths in relation to trunk measurement (World Health Organization, 1995).

Davos et al. (2003) provided the best insight into the problem because the authors specifically classified subjects in terms of cachexic states. In HF, the wasting process affects not only muscle but also fat, bone, and the heart.

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**References**


HF, whereas HTN was the most common comorbid condition among white patients with HTN or combined HTN and IHD. IHD was the most etiology of HF had less favorable 6-year survival than those for systolic HF. For patients with systolic HF, mor-
stability rates are directly related to age and the presence of an ischemic etiology (Franklin & Aurigemma). However, for patients with HF older than 70 years, mortality rates for diastolic HF approach those for systolic HF. For patients with systolic HF, mortality rates are directly related to age and the presence of an ischemic etiology (Franklin & Aurigemma). In the six studies reviewed, all considered LVEF as a variable in their models for analysis.

Croft et al. (1999) found that patients with IHD as an etiology of HF had less favorable 6-year survival than those with HTN or combined HTN and IHD. IHD was the most common comorbid condition among white patients with HF, whereas HTN was the most common comorbid condition among black patients. It is possible that increased use of ACE inhibitors and blockers following myocardial infarction or as part of HTN management has reduced disease severity among HF patients with these conditions (Croft et al.).

Mortality as a result of HF has been shown to rise in parallel with age. The incidence of HF increases dramatically with age in both sexes, approximately doubling with each advancing decade (Kenchaiah et al., 2002). Comorbid conditions also influence survival. Gustafsson et al. (2005) found that the effect of BMI on mortality in HF appeared to depend on whether COPD and other diseases like renal insufficiency, stroke, and diabetes were present.

Gender and race have also been shown to be prognostic indicators for survival of patients with HF. Women with HF lived longer than men, with a median survival after the diagnosis of HF of 3.2 vs. 1.7 years (Kannel, Ho, & Thom, 1995). Black patients with HF had lower mortality than white patients during follow-up and slightly higher survival during each year of follow-up. Six-year survival was 19% among black men, 16% among white men, 25% among black women, and 23% among white women. After taking into account differences in age, white men had 10% greater mortality than black men (age-adjusted RR: 1.10 [95% CI: 1.07–1.13]; Crof et al., 1999). Yet, as shown in Table 2, the majority of the studies examined in our review did not report race and thus did not factor race into multivariate analyses. Additionally, males were over-

Conclusions

HF is the only cardiovascular condition not experiencing a substantial decline in both incidence and prevalence over the past 20 years (Stewart, MacIntyre, Capewell, & McMurray, 2003). Accordingly, continued research focusing on prevention and management of HF is needed. This review of the literature suggests an association between obesity and improved survival in patients with HF. However, until a mechanism is identified to explain this obesity paradox, causality cannot be satisfactorily explained. Given the limitations of using BMI alone, there need to be other ways to understand the relationship between weight and mortality as a result of HF. Further research is necessary to prospectively study within the context of contemporary HF treatment the prognostic implications of BMI and aspects of body composition, taking into consideration other complex factors such as natriuretic peptides, plasma norepinephrine, nutritional status, and caloric intake that relate to HF survival. With such studies, definitive weight loss recommendations for patients with HF will be forthcoming.
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References


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