Waist Circumference, Body Mass Index, and Survival in Systolic Heart Failure: The Obesity Paradox Revisited

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ABSTRACT

Background: Higher body mass index (BMI) is associated with improved heart failure (HF) survival, but the role of waist circumference (WC) in HF outcomes has not been studied.

Methods and Results: A total of 344 patients with advanced systolic HF had WC and BMI measured at presentation. High WC was defined as ≥88 cm in women and ≥102 cm in men, and high BMI as ≥25 kg/m^2. Two-year urgent heart transplant (UT)−free survival in high vs normal WC groups was 77.9% vs 64.3% ($P = .025$) and in high vs normal BMI was 89.8% vs 58.2% ($P < .001$). After multivariable adjustment, normal WC compared with high WC was associated with higher all-cause mortality (risk ratio [RR] 2.76, 95% confidence interval [CI] 1.34−5.71) and higher risk of death/UT (RR 2.14, 95% CI 1.25−3.68). The best outcomes were seen in those with both high WC and high BMI.

Conclusions: High WC, an alternative anthropometric index of obesity more specific to abdominal adiposity, high BMI, and the combination of high WC/high BMI were each associated with improved outcomes in this advanced HF cohort, lending further support for an obesity paradox in HF. The role of body composition in HF survival should be a focus of future investigation. (*J Cardiac Fail 2011;17:374−380*)

Key Words: Cardiomyopathy, outcomes, mortality, adiposity.

Obesity, as indexed by high body mass index (BMI) or high waist circumference (WC), is associated with increased risk of new-onset cardiovascular disease as well as increased risk of new-onset heart failure (HF).[1,2] Despite this association between obesity and cardiovascular risk in the general population, multiple studies of patients with HF have demonstrated an "obesity paradox": high BMI is a strong independent predictor of improved outcomes for patients with chronic HF.[3−6] BMI (kg/m^2) is the most widely used classification of obesity and correlates with total fat mass.[7,8] However, BMI may not accurately distinguish between percentage body fat and lean mass, especially at intermediate ranges. Furthermore, the relationship between BMI and percentage body fat varies with gender, race, and age.[9,10] WC, a perimeter of the abdomen variably measured at the midpoint between the lowest rib and the iliac crest, the umbilicus, or the minimum or maximum waist perimeter, is an alternative anthropometric index more specific for abdominal and visceral fat. Although the obesity paradox for BMI in HF has been well established, whether WC is also a prognostic factor in HF has not been previously studied.

Methods

Study Subjects

A total of 581 patients were referred to a single university medical center for heart transplant evaluation between May 2006 and August 2009. All subjects were followed in a comprehensive HF management program as previously described.[4] Patients with left ventricular ejection fraction (LVEF) >40% (n = 118), those without WC data within 3 months of referral (n = 146), and those

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without height recorded (n = 3) were excluded. Furthermore, because underweight HF patients may have "cardiac cachexia," known to be associated with worse prognosis, those classified as underweight (BMI <18.5 kg/m^2; n = 7) were excluded from the analysis.[11,12] The final study group consisted of 344 subjects. Medical record review was approved by the Medical Institutional Review Board of the University of California, Los Angeles.

Baseline Data

WC and body weight were measured at time of initial referral or within 3 months. Height was recorded at the time of initial referral or at subsequent clinic visits. Patients deemed by physicians to be hypervolemic had WC and weight recorded after hemodynamic optimization to remove the confounding effects of edema on these measurements. WC was measured at the midpoint between the lowest rib and the iliac crest; patients were classified as high or normal WC based on gender-specific thresholds for increased cardiometabolic risk (high WC: in women $\geq$88 cm, men $\geq$102 cm).[13] Patients were divided into BMI categories based on World Health Organization/National Institutes of Health guidelines: underweight (BMI <18.5 kg/m^2 [excluded from study cohort]), healthy weight (BMI 18.5–24.9 kg/m^2), overweight (BMI 25–29.9 kg/m^2), and obese (BMI $\geq$30.0 kg/m^2).[12] Hemodynamic parameters and medical treatments were also recorded after invasive hemodynamic monitoring using Swan-Ganz catheterization, when necessary. Laboratory testing, echocardiography, and cardiopulmonary exercise tests all occurred within 3 months of the initial referral. Past medical history was extracted from medical record review.

End Points

This study examined 2 end points: 1) death or urgent status IA heart transplant (UT); and 2) all-cause mortality. In the first end point, we analyzed UT as deaths under the assumption that these patients would have died without a transplant.[14] For both end points, nonurgent transplants (statuses IB and II) were censored and considered as a nonfatal end of follow-up.

Statistical Analyses

For purposes of analysis, we considered 2 BMI groups: normal BMI (healthy weight, BMI 18.5–24.9 kg/m^2) and high BMI (overweight and obese, BMI $\geq$25.0 kg/m^2). Actuarial survival curves for the 2 WC groups and 2 BMI groups as well as for 4 combined WC/BMI groups were calculated by using the Kaplan-Meier estimate, and differences between curves were calculated by using the log-rank statistic. Univariate survival analyses were performed with the likelihood ratio test, using the Cox model for baseline variables of WC, BMI, and the combined variables WC/BMI. Multivariate analysis adjusting for known predictors in HF, including gender, diabetes history, LVEF, HF etiology, and New York Heart Association (NYHA) functional class, was performed by Cox proportional hazards regression analysis to estimate adjusted odds ratios and 95% confidence intervals (CIs) for potential predictors of survival. The Cox model retained all independent variables with $P < .15$. Statistics were calculated using the SPSS version 16.0 statistical package.

Results

The cohort was 72.7% male, with a mean age of 53.3 ± 13.1 years. NYHA functional class was I or II in 34.8% of patients and III or IV in 65.2%. Mean LVEF was 23.1 ± 7.4%. Etiologies of HF were classified as ischemic (38.8%) versus nonischemic (idiopathic, valvular, alcohol-induced, hypertrophic, or postpartum cardiomyopathy; 61.2%). Over one-half of the subjects (52.9%) had a high WC. The median WC was 100.0 cm (interquartile range 90.0–112.0; Fig. 1, left). Median BMI was 27.7 kg/m^2 (interquartile range 23.9–32.2; Fig. 1, right). Approximately two-thirds of the subjects (66.9%) had high BMI: 31% were overweight and 36% obese. Of the obese patients, 56 (45%) had a BMI >35 and 15 (12%) had a BMI >40.

The baseline characteristics of the cohort stratified by WC and BMI are summarized in Table 1. Both high WC and high BMI were associated with younger age, higher LVEF, diabetes, and hypertension. HF medication use was similar between the two groups. After pulmonary artery catheter–guided medical therapy, the high-WC and high-BMI groups had significantly higher systolic and diastolic blood pressures; no significant differences existed between WC and BMI groups regarding pulmonary artery pressures, pulmonary capillary wedge pressure, or cardiac index (data not shown).

Outcomes

During 2 years of follow-up, 40 deaths and 28 UTs occurred, with 26 deaths and 24 UTs occurring in the first year. Two of the UT patients had left ventricular assist devices (LVADs) placed before transplantation. A third LVAD recipient was still living at end of follow-up. Of the 40 total deaths, 6 were sudden, 15 were progressive HF deaths, 2 were due to multisystem organ failure, 1 was a myocardial infarction, and 15 were from unknown or other causes.

High-WC patients had significantly better survival free from death or UT than normal-WC patients (77.9% vs 64.3%; $P = .025$; Fig. 2A). Higher-BMI patients also had better outcomes (89.8 vs 58.2%; $P < .001$; Fig. 2B). When the patients were stratified by both WC and BMI, those with both high WC and high BMI had the best event-free survival rates (80.4%) and those with high WC/normal BMI and normal WC/normal BMI had the lowest UT-free survival (56.6% and 58.2%, respectively); intermediate UT-free survival rates were seen in normal-WC/high-BMI patients (72.9%, $P = .001$; Fig. 2C).

For the outcome of all-cause mortality, high-WC patients tended to have better survival than normal-WC patients (83.8% vs 76.6%); this difference became statistically significant ($P = .006$) after adjustment for multiple prognostic factors. High BMI compared with normal BMI was associated with lower all-cause mortality (86.2% vs 68.1%; $P < .001$). When patients were grouped by the combination of WC and BMI, high-WC/high-BMI and normal-WC/high-BMI patients had the best 2-year survival rates (87.1%