(CVD) risk factors, CV structure and function, and increases the prevalence of most CVD, including coronary heart disease (CHD) and heart failure (HF) \((2,3)\). Nevertheless, we reported an obesity paradox in 6 studies of 22,807 patients with HF \((4)\); a meta-analysis of 89 studies in 1.3 million patients with established CHD which confirmed a strong obesity paradox \((5)\); and a meta-analysis by Flegal et al. \((6)\) of 97 studies in 2.9 million people which showed that overweight subjects had a significant 6% lower mortality than subjects with normal body mass index, and that class I obesity had a strong trend of 5% lower mortality. Therefore, denying the obesity paradox in 2015 is foolish in our opinion and represents a “head-in-the-sand” position, although certainly confounding factors may be involved.

Additionally, we believe that despite the obesity paradox, intentional weight loss, especially in more severe obesity, would be advantageous. There is some suggestion that intentional weight loss may reduce major clinical endpoints in CHD and in the general population \((2)\). Weight loss also improves hemodynamics, CV structure and function, and functional classification in HF, but we are not aware of any data to prove that weight reduction reduces major clinical end-points.

Nevertheless, in a perfect world, maintaining high fitness and prevention of weight gain in children, adolescents, and adults would go a long way in the prevention and treatment of most CVD, including HF \((2,3)\).

*Carl J. Lavie, MD
Hector O. Ventura, MD
*Department of Cardiovascular Diseases
John Ochsner Heart & Vascular Institute
Ochsner Clinical School - The University of Queensland
School of Medicine
Section of Cardiology
1514 Jefferson Highway
New Orleans, Louisiana 70121
E-mail: clavier@ochsner.org
http://dx.doi.org/10.1016/j.jchf.2015.11.006

Please note: Dr. Lavie is the author of the book “The Obesity Paradox”; and has served as a consultant and speaker for the Coca-Cola Company (on fitness and not any of their products). Dr. Ventura has reported that he has no relationships relevant to the contents of this paper to disclose.

REFERENCES

3. Lavie CJ. There truly is an obesity paradox. Heart 2015; Available online. Posted Aug 12.

Concerning the Role of Gender Difference in Obesity Paradox in Patients With Heart Failure

Several studies demonstrate the presence of an “obesity paradox” among patients with several chronic diseases, and this obesity paradox shows that lower (rather than higher) body mass index is a risk factor for increased mortality. In particular, the presence of a significant degree of obesity (i.e., at least up to a body mass index of 30 to 35 kg/m²) is associated with lower mortality \((1-3)\). However, when Vest and colleagues. \((4)\) analyzed their data by gender, they surprisingly found that well-established obesity paradox is valid for women but not for men. Most studies with a considerable amount of patients could not show such a gender-specific difference in obesity paradox \((1,2)\).

Although Vest et al. \((4)\) have adjusted their data for a variety of potential cofounders, they did not adjust for coronary artery disease (CAD). It should be considered that CAD was more frequent in men than women \((4)\). This may have had a significant impact on the survival rate in the male study cohort.

In this regard, implementation of other established survival markers in heart failure, such as N-terminal pro-B-type natriuretic peptide, as von Haehling et al. \((5)\) discussed in their article, would be of help to shed more light on the conflicting results in this study.

The study protocol by Vest et al. \((4)\) allowed cardiopulmonary exercise testing using either treadmill for most patients and bicycle exercise in a minority of patients. However, it is well-known that the results differ significantly depending on exercise method, and we question the validity of this mix of test methods. Did the authors adjust for this effect? Because values gained from bicycle and treadmill are not directly comparable, how did the authors overcome these differences?
Letters to the Editor

J A C C : H E A R T F A I L U R E V O L . 4 , N O . 3 , 2 0 1 6
M A R C H 2 0 1 6 : 2 3 2 – 6

Amir Emami, MD
Marcelo R. Dos Santos, PhD
Stefan D. Anker, MD, PhD
Stephan von Haehling, MD, PhD
*Anja Sandek, MD, PhD
*Department of Cardiology and Pulmonology
University Medical Center Göttingen
Heart Center Göttingen
Robert Koch Strasse 40
37075 Göttingen
Germany
E-mail: anja.sandek@med.uni-goettingen.de
http://dx.doi.org/10.1016/j.jchf.2015.11.012

Please note: The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

REFERENCES


REPLY: Concerning the Role of Gender Difference in Obesity Paradox in Patients With Heart Failure

We thank Dr. Emami and colleagues for their interest in our paper on a differential effect of excess adiposity in female and male subjects. We agree that selecting model covariates to adjust sufficiently for baseline differences between the sexes, without overfitting the model, was one of the most challenging aspects of this analysis. We opted to adjust for ischemic cardiomyopathy etiology (present for 26% of female and 54% of male subjects), which is a strong predictor of heart failure outcomes (1). We did not additionally adjust for coronary artery disease (CAD), present in 30% of female and 57% of male subjects, because ischemic etiology and CAD were highly correlated; only 3% of the cohort had a nonischemic etiology with superimposed CAD. Both the nonischemic (Figure 2A in the original article) and ischemic (Figure 2B in the original article) subgroups had the same relationship between body mass index (BMI) and mortality, stratified by sex (2).

We had sparse data on brain (B-type) natriuretic peptide (BNP) or N-terminal pro-BNP (NT-proBNP) in this 1995 to 2011 cohort. However, BNP or NT-proBNP can be problematic when risk adjusting for the impact of BMI on mortality; higher BNP is an independent predictor of mortality in heart failure (3), but higher BMI is associated with lower BNP levels (4). We agree that prognostic biomarkers that are less likely to be affected by adiposity, perhaps such as soluble Toll-like receptor-2 (ST2) (5), may add additional risk adjustment.

Very few subjects underwent a bicycle exercise stress test (n = 46; 1.2%), as opposed to a treadmill exercise stress test (n = 3,765; 98.8%). As expected, the median peak oxygen consumption attained by bicycle-tested subjects was lower than that in treadmill-tested subjects (median 11.6 vs. 15.9 ml/kg/min). However, we did not adjust for the method of stress as a model covariate because in 1.2% of the cohort, the bicycle stress method fell well below the usual frequency threshold (10%) that merits model entry.

To our knowledge, no similar analyses have used a restricted cubic spline model, which can discern nonlinear relationships between BMI and mortality that differ among subgroups. We would encourage other investigators to use this analytic technique to determine whether a sex-specific relationship between BMI and mortality exists in other large cohorts with systolic heart failure.

Amanda R. Vest, MBBS
Yuping Wu, PhD
Rory Hachamovitch, MD, MSc
James B. Young, MD
*Leslie S. Cho, MD
*Section of Preventative Cardiology and Rehabilitation
Cleveland Clinic
9500 Euclid Avenue
Mail code JB-1
Cleveland, Ohio 44195
E-mail: chol@ccf.org
http://dx.doi.org/10.1016/j.jchf.2015.11.014

Please note: The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

REFERENCES