Untangling the “Heavy” Cardiovascular Burden of Obesity and the “Obesity Paradox”

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New Orleans, La
Obesity and Cardiovascular Diseases

- Obesity increasing in epidemic proportions
- Body mass index (BMI) is primarily used
- Body fatness, waist circumference (WC), waist to hip ratio (WHR), and waist to height ratio may be superior

Lavie CJ et al. JACC 2009;53:1925-1932
Obesity and Cardiovascular Diseases

- 70% of adults in US are overweight or obese
- Morbid obesity especially increased
- Obesity is second to only tobacco abuse as the #1 cause of preventable death in US
- Due to obesity, we may soon see a reversal in the steady increase in life expectancy

Lavie CJ et al. JACC 2009;53:1925-1932
Adverse Effects of Obesity

- Increases in insulin resistance
  - Glucose intolerance
- Metabolic Syndrome
- Type 2 Diabetes Mellitus
- Hypertension
- Abnormal LV Geometry
  - Concentric Remodeling
  - LVH

Lavie CJ et al.  JACC 2009;53:1925-1932
Adverse Effects of Obesity

DYSLIPIDEMIA

- Elevated total cholesterol
- Elevated VLDL and triglycerides
- Elevated LDL and small, dense particles
- Elevated non-HDL
- Elevated apolipoprotein B
- Reduced HDL and apolipoprotein A-1

Lavie CJ et al. JACC 2009;53:1925-1932
Adverse Effects of Obesity

- Abnormal endothelial function
- Abnormal systolic and diastolic LV function
- Increased systemic inflammation (e.g., CRP)
- Increased Pro-thrombotic state
- Albuminuria
- Obstructive sleep apnea / sleep disordered breathing

Lavie CJ et al. JACC 2009;53:1925-1932
Cardiovascular Diseases Associated With Obesity

- Hypertension
- Heart Failure
- Coronary Heart Disease
- Atrial Fibrillation
- Complex Ventricular Dysrhythmias
- Stroke
- Venous Thromboembolism
- OSA / SDB

Lavie CJ et al. JACC 2009;53:1925-1932
Higher BMI $\to$ ↑ Risk of Development of Mortality in the General Population

**BMI Associated Death Risk:**

- **General Population**

Higher BMI $\Rightarrow$ ↑ Risk of Development of Mortality in the General Population

**Calle et al, N Engl J Med 341:1097-1105**
Meta-Analysis of BMI and Survival

- 97 studies, 2.88 million individuals, >270,000 deaths
- Relative to normal weight, obesity (all grades combined) and grades 2 and 3 obesity were associated with higher all-cause mortality
- Grade 1 obesity was associated with a trend for lower mortality (HR 0.95; CI 0.88-1.01), and overweight had significantly lower mortality (HR 0.94; CI 0.91-0.96)

Flegal KM et al. JAMA 2013;309(1):71-82
Although obesity has been implicated as one of the major risk factors for most CV diseases, including HTN, HF, and CHD, evidence from clinical cohorts of patients with established CV diseases indicates an “obesity paradox” because overweight and obese with these diseases tend to have a more favorable short- and long-term prognosis.

Lavie CJ et al.  JACC 2009;53:1925-1932
Obesity and Hypertension

- Obesity increases levels of BP
- Obesity increases CR and LVH, independent of BP
- Obesity increases metabolic abnormalities in HTN
- Despite the increased prevalence, obese hypertensives have a favorable prognosis

Lavie CJ et al. JACC 2009;53:1925-1932
BMI and HTN Prognosis

![Graph showing BMI and HTN prognosis with data points for different BMI categories and outcomes.](image-url)

“Obesity Paradox” and Hypertension

In aggregate, although obesity is a powerful risk factor for hypertension and LVH, obese hypertensive patients may paradoxically have a better prognosis, possibly due to low SVR and PRA.

Lavie CJ et al. JACC 2009;53:1925-1932
BMI and HF Prognosis

Cumulative Survival vs. Months

- Underweight (n=164)
- Recommended Weight (n=692)
- Overweight (n=168)
- Obese (n=179)

Horwich TB et al. J Am Coll Cardiol 2001;38;789-795
The message from >28,000 CHF patients:
Once you have heart failure, bigger = live longer
BMI and HF Hospital Mortality

• 108,927 decompensated HF patients
• Higher BMI associated with lower mortality
• For every 5-unit increase in BMI, HF mortality was 10% lower (p < 0.001)

Body Composition and HF Prognosis

Lavie et al. Am J Cardiol 2003;91:891-894
Possible Reasons for Obesity Paradox in Heart Failure

- Advanced HF is catabolic state; obese may have more metabolic reserve
- Adipose tissue produces TNF-α receptors that may neutralize TNF-α
- Obese have lower ANP and PRA
- Obese have higher BP, so may tolerate more meds
- Higher circulating lipoproteins may detoxify lipopolysaccharides that effect inflammatory cytokines

Lavie CJ et al. JACC 2009;53:1925-1932
Obesity and CHD

• Obesity adversely effects most major CV risk factors (HTN, dyslipidemia, MetS/T2DM)

• Obesity probably an independent CHD risk factor

• Obesity strongly related with 1st premature MI at young age (Mandala MC et al. JACC 2008;52:979-985)

Lavie CJ et al. JACC 2009;53:1925-1932
Obesity Paradox and CHD

- 40 cohort studies of over 250,000 CHD patients followed for 3.8 years
- Overweight and obese had lower risk of total and CV mortality compared with underweight and “normal” weight patients
- Similar in stable CHD, PCI and CABG
- In BMI ≥ 35 kg/m², there was excess risk of CV mortality without an increase on total mortality

Obesity Paradox and CHD

• 529 consecutive CHD patients post events
• Overweight and obese (n = 393) had more adverse CHD risk profiles than leaner patients (n = 136)
• During 3-year follow-up, overweight/obese had significantly lower mortality

Obesity Paradox and CHD

Obesity Paradox and CHD

Body Composition and Coronary Heart Disease Mortality—An Obesity or a Lean Paradox?

CARL J. LAVIE, MD; ALBAN DE SCHUTTER, MD; DHARMENDRAKUMAR PATEL, MD; SURYA M. ARTHAM, MD; RICHARD V. MILANI, MD

OBJECTIVE: To determine the combined effects of body mass index (BMI) and body fat (BF) on prognosis in coronary heart disease (CHD) to better understand the “obesity paradox.”

PATIENTS AND METHODS: We studied 581 patients with CHD between January 1, 2000, and July 31, 2005, who were divided into low (<25) and high BMI (≥25), as well as low (≤25% men and ≤35% women) and high BF (>25% in men and >35% in women). Four groups were analyzed by total mortality during the 3-year follow-up by National Death Index: low BF/low BMI (n=119), high BF/low BMI (n=26), low BF/high BMI (n=125), and high BF/high BMI (n=311).

RESULTS: During the 3-year follow-up, mortality was highest in the low BF/low BMI group (31%), which was significantly (P<.001) higher than that in the other 3 groups (3.9%, 3.2%, and 2.6%, respectively); using the high BF/high BMI group as a reference, the low BF/low BMI group had a 4.24-fold increase in mortality (confidence interval [CI], 1.76-10.23; P=.001). In multivariate logistic regression for mortality, when entered individually, both high BMI (odds ratio [OR], 0.75; CI, 0.59-0.90) and high BF (OR, 0.89; CI, 0.52-0.95) as continuous variables were independent predictors of better survival, whereas low BMI (OR, 3.60; CI, 1.37-9.47) and low BF (OR, 3.52; CI, 1.34-9.23) as categorical variables were independent predictors of higher mortality.

CONCLUSION: Although both low BF and low BMI are independent predictors of mortality in patients with CHD, only patients with combined low BF/low BMI appear to be at particularly high risk of mortality during follow-up. Studies are needed to determine optimal body composition in the secondary prevention of CHD.


Many large studies of cohorts with CHD have demonstrated this obesity paradox, which has also been demonstrated in a large meta-analysis by Romano-Corral et al from Mayo Clinic who analyzed 40 cohort studies totaling more than 250,000 patients with CHD grouped according to BMI.

Although BMI is the most frequently used method to assess overweightness/obesity, especially in large epidemiologic studies, this method has been criticized because BMI does not always reflect true body fatness. Some investigators have theorized that at least part of the inconsistent relationship between obesity and major CV disease events, including mortality, may be due to the inaccurate diagnosis of obesity by the BMI assessment and that defining obesity by other methods, including waist circumference, waist/hip ratio, as well as percent body fat (BF) may be more accurate. We have recently demonstrated this obesity paradox in a cohort of CHD patients using both BMI and BF determinations. To our knowledge, no prior studies have determined the independent effects of both BMI and BF on mortality in a cohort of CHD patients. Therefore, in the current evaluation, we determined the combined and independent impact of both BMI and BF on mortality in a cohort with stable CHD.

PATIENTS AND METHODS

We retrospectively reviewed the case records of 581 consecutive patients with stable CHD who were referred for potential entry into formal cardiac rehabilitation programs between January 1, 2000, and July 31, 2005, and who had baseline anthropometric, lipid, and clinical data, as we have previously described. Patients were divided into low (<25) and high (≥25) BF groups.
The "Obesity Paradox" in CHD

Survival (%)

Time to Event (Days)

*\(p<0.0001\) compared with other groups

The "Obesity Paradox" in CHD

*p<0.0001 compared to other group

<table>
<thead>
<tr>
<th>Group</th>
<th>3-year Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n=311) High BF/High BMI</td>
<td>2.6</td>
</tr>
<tr>
<td>(n=125) Low BF/High BMI</td>
<td>3.2</td>
</tr>
<tr>
<td>(n=26) High BF/Low BMI</td>
<td>3.9</td>
</tr>
<tr>
<td>(n=119) Low BF/Low BMI</td>
<td>10.9*</td>
</tr>
<tr>
<td>(n=113) Low BF/Low BMI†</td>
<td>8.9*</td>
</tr>
</tbody>
</table>

† Excludes 6 underweight (BMI < 18.5 kg/m²) who had 50% mortality

Body Composition and CHD Mortality

Survival (%)

- Underweight
- Normal
- Overweight
- Obese

* p < 0.0001 compared to other groups
† p = 0.02 compared with Overweight

Time to Event (Months)

De Schutter A, Lavie CJ et al. Am J Cardiol, online December, 2012
Body Composition and Survival in Stable Coronary Heart Disease

Impact of Lean Mass Index and Body Fat in the “Obesity Paradox”

Carl J. Lavie, MD,*† Alban De Schutter, MD, MSc,‡ Dharmendrakumar A. Patel, MD, MPH,* Abel Romero-Corral, MD, MSc,§ Surya M. Artham, MD, MPH,* Richard V. Milani, MD*

New Orleans, Louisiana; Weston, Florida; Philadelphia, Pennsylvania; and Baton Rouge, Louisiana

Objectives
Our goal was to determine the impact of lean mass index (LMI) and body fat (BF) on survival in patients with coronary heart disease (CHD).

Background
An inverse relationship between obesity and prognosis has been demonstrated (the “obesity paradox”) in CHD, which has been explained by limitations in the use of body mass index in defining body composition.

Methods
We studied 570 consecutive patients with CHD who were referred to cardiac rehabilitation, stratified as Low (≤25% in men and ≤35% in women) and High (>25% in men and >35% in women) BF and as Low (≤18.9 kg/m² in men and ≤15.4 kg/m² in women) and High LMI, and followed for 3 years for survival.

Results
Mortality is inversely related to LMI (p < 0.0001). Mortality was highest in the Low BF/Low LMI group (15%), which was significantly higher than in the other 3 groups, and lowest in the High BF/High LMI group (2.2%), which was significantly lower than in the other 3 groups. In Cox regression analysis as categoric variables, low LMI (hazard ratio [HR]: 3.1; confidence interval [CI]: 1.3 to 7.1) and low BF (HR: 2.6; CI: 1.1 to 6.4) predicted higher mortality, and as continuous variables, high BF (HR: 0.91; CI: 0.85 to 0.97) and high LMI (HR: 0.81; CI: 0.65 to 1.00) predicted lower mortality.

Conclusions
In patients with stable CHD, both LMI and BF predict mortality, with mortality particularly high in those with Low LMI/Low BF and lowest in those with High LMI/High BF. Determination of optimal body composition in primary and secondary CHD prevention is needed. (J Am Coll Cardiol 2012;60:1374–80) © 2012 by the American College of Cardiology Foundation
Lean Mass Index and CHD Mortality

- LMIGRPN1 High
- MIGRPN1 Medium
- MIGRPN1 Low

*p<.0001 vs High LMI; p=0.003 vs Medium LMI

Lavie CJ et al. JACC 2012;60: 1374-1380
Body Fat, Lean Mass Index and CHD Mortality

Lavie CJ et al. JACC 2012; 60: 1374-1380

3-Year Mortality (%)

Survival Time (Days)

* = p<0.0001 compared with other 3 groups
+ = p=0.003 vs High BF / Low LMI; p=0.03 vs Low BF / High LMI
Obesity Paradox and CHD Mechanisms

- None of the studies accounted for non-purposeful weight loss
- Lower renin and ANP in obese
- Confounders
- COPD
- Impact of Fitness
- Baseline genetic differences

Obesity Paradox and CHD
Impact of Central Obesity and Fitness

The Obesity Paradox, Cardiorespiratory Fitness, and Coronary Heart Disease

Paul A. McAuley, PhD; Enrique G. Artero, PhD; Xuemei Sui, MD; Duck-chul Lee, PhD; Timothy S. Church, MD, MPH, PhD; Carl J. Lavie, MD; Jonathan N. Myers, PhD; Vanessa España-Romero, PhD; and Steven N. Blair, PED

Abstract

Objective: To investigate associations of cardiorespiratory fitness (CRF) and different measures of adiposity with cardiovascular disease (CVD) and all-cause mortality in men with known or suspected coronary heart disease (CHD).

Patients and Methods: We analyzed data from 9563 men (mean age, 47.4 years) with documented or suspected CHD in the Aerobics Center Longitudinal Study (August 13, 1977, to December 30, 2002) using baseline body mass index (BMI) and CRF (quantified as the duration of a symptom-limited maximal treadmill exercise test). Waist circumference (WC) and percent body fat (BF) were measured using standard procedures.

Results: There were 733 deaths (348 of CVD) during a mean follow-up of 13.4 years. After adjustment for age, examination year, and multiple baseline risk factors, men with low fitness had a higher risk of all-cause mortality in the BMI categories of normal weight (hazard ratio [HR], 1.60; 95% confidence interval [CI], 1.24-2.03), obese class I (HR, 1.38; 95% CI, 1.04-1.82), and obese class II/III (HR, 2.43; 95% CI, 1.55-3.80) but not overweight (HR, 1.09; 95% CI, 0.88-1.36) compared with the normal-weight and high-fitness reference group. We observed a similar pattern for WC and percent BF tertiles and for CVD mortality. Among men with high fitness, there were no significant differences in CVD and all-cause mortality risk across BMI, WC, and percent BF categories.

Conclusion: In men with documented or suspected CHD, CRF greatly modifies the relation of adiposity to mortality. Using adiposity to assess mortality risk in patients with CHD may be misleading unless fitness is considered.

A decade ago, Gruberg and colleagues1 coined the term obesity paradox to describe Although higher levels of adiposity are associated with increased mortality risk in men in the Aer-
Impact of Fitness on All-Cause Mortality in CHD

**BMI**

<table>
<thead>
<tr>
<th></th>
<th>Normal BMI</th>
<th>Overweight I</th>
<th>II/III</th>
<th>Obese I</th>
<th>II/III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (deaths)</td>
<td>2718 (206)</td>
<td>3093 (156)</td>
<td>531 (15)</td>
<td>28 (2)</td>
<td></td>
</tr>
<tr>
<td>Patients (deaths)</td>
<td>568 (97)</td>
<td>1555 (156)</td>
<td>786 (76)</td>
<td>284 (23)</td>
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</tr>
</tbody>
</table>

**Waist Circumference**

<table>
<thead>
<tr>
<th></th>
<th>Low WC</th>
<th>Middle WC</th>
<th>Upper WC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (deaths)</td>
<td>2802 (182)</td>
<td>2198 (132)</td>
<td>1370 (65)</td>
</tr>
<tr>
<td>Patients (deaths)</td>
<td>539 (82)</td>
<td>875 (86)</td>
<td>1779 (186)</td>
</tr>
</tbody>
</table>

**% Body Fat**

<table>
<thead>
<tr>
<th></th>
<th>Low % BF</th>
<th>Middle % BF</th>
<th>Upper % BF</th>
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</thead>
<tbody>
<tr>
<td>Patients (deaths)</td>
<td>2760 (168)</td>
<td>2233 (123)</td>
<td>1377 (88)</td>
</tr>
<tr>
<td>Patients (deaths)</td>
<td>468 (72)</td>
<td>882 (99)</td>
<td>1843 (183)</td>
</tr>
</tbody>
</table>

Impact of Fitness on CVD Mortality in CHD

**BMI**

<table>
<thead>
<tr>
<th></th>
<th>Normal I/II</th>
<th>Overweight I/II</th>
<th>Obese I/II</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (deaths)</td>
<td>2718 (83)</td>
<td>3093 (70)</td>
<td>559 (5)</td>
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</table>

<table>
<thead>
<tr>
<th></th>
<th>Normal I/II</th>
<th>Overweight I/II</th>
<th>Obese I/II</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (deaths)</td>
<td>568 (48)</td>
<td>1555 (89)</td>
<td>1070 (53)</td>
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</table>

**Waist Circumference**

<table>
<thead>
<tr>
<th></th>
<th>Low WC</th>
<th>Middle WC</th>
<th>Upper WC</th>
<th>P-value</th>
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<tbody>
<tr>
<td>Patients (deaths)</td>
<td>2802 (68)</td>
<td>2198 (66)</td>
<td>1370 (24)</td>
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<table>
<thead>
<tr>
<th></th>
<th>Low WC</th>
<th>Middle WC</th>
<th>Upper WC</th>
<th>P-value</th>
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<td>Patients (deaths)</td>
<td>539 (46)</td>
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<td>1779 (105)</td>
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**% Body Fat**

<table>
<thead>
<tr>
<th></th>
<th>Low % BF</th>
<th>Middle % BF</th>
<th>Upper % BF</th>
<th>P-value</th>
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<tbody>
<tr>
<td>Patients (deaths)</td>
<td>2760 (69)</td>
<td>2233 (52)</td>
<td>1377 (37)</td>
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</table>

<table>
<thead>
<tr>
<th></th>
<th>Low % BF</th>
<th>Middle % BF</th>
<th>Upper % BF</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (deaths)</td>
<td>468 (32)</td>
<td>882 (61)</td>
<td>1843 (97)</td>
<td></td>
</tr>
</tbody>
</table>

Obesity Paradox and CVD
Impact of Cardiorespiratory Fitness

- Goel K et al. Am Heart J 2011;16(3):590-597
- Lavie CJ et al. Circulation 2012; Nov, in press
## Baseline Characteristics (n=35,607)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>60 ± 15 years</td>
</tr>
<tr>
<td>Gender</td>
<td>53% female</td>
</tr>
<tr>
<td>BMI</td>
<td>29.2 ± 6.7 kg/m²</td>
</tr>
<tr>
<td>EF</td>
<td>60 ± 5 %</td>
</tr>
<tr>
<td>LVMI</td>
<td>82 ± 32 g/m²</td>
</tr>
<tr>
<td>RWT</td>
<td>0.43 ± 0.07</td>
</tr>
</tbody>
</table>

Lavie CJ et al; Am J Cardiol 2007;100:1460-1464
LV Geometry and Obese Mortality

* p<0.0001

Lavie CJ et al; Am J Cardiol 2007;100:1460-1464
BMI and Mortality

Lavie CJ et al; Am J Cardiol 2007; 100: 1460-1464
### Multivariate Analysis
(n= 35,607)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Chi-Square</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Higher age</td>
<td>785</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Lower BMI</td>
<td>32.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Male gender</td>
<td>10.3</td>
<td>= 0.0013</td>
</tr>
<tr>
<td>Higher RWT</td>
<td>7.6</td>
<td>= 0.0006</td>
</tr>
</tbody>
</table>

Lavie CJ et al; Am J Cardiol 2007;100:1460-1464
## Multivariate Predictors of Mortality

(n=11,792)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Chi-Square</th>
<th>P-Value</th>
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</thead>
<tbody>
<tr>
<td>Higher age</td>
<td>198</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Higher RWT</td>
<td>22.0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>High BMI</td>
<td>14.4</td>
<td>=0.0001</td>
</tr>
<tr>
<td>Higher LVMI</td>
<td>13.5</td>
<td>=0.0002</td>
</tr>
<tr>
<td>Male gender</td>
<td>8.9</td>
<td>=0.03</td>
</tr>
</tbody>
</table>

Lavie CJ et al; Am J Cardiol 2007;100:1460-1464
Mortality Prevalence by BMI Categories in Females

<table>
<thead>
<tr>
<th>BMI Category</th>
<th>Mean</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;18.5</td>
<td>17.1 ± 1.550</td>
<td>17,532</td>
</tr>
<tr>
<td>18.5-25</td>
<td>27.4 ± 1.7539</td>
<td>1,7579</td>
</tr>
<tr>
<td>25-30</td>
<td>32.3 ± 1.4045</td>
<td>5,044</td>
</tr>
<tr>
<td>30-35</td>
<td>41.1 ± 6.5421</td>
<td>5,421</td>
</tr>
</tbody>
</table>

Mortality in Four LV Geometric Patterns in Females with Preserved Systolic Function

Obesity and Atrial Fibrillation

- As with obesity, AF is also epidemic, and is expected to increase by 2.5-fold by 2050.
- May be due to HTN, CHD, and HF.
- Obesity appears to be a significant AF risk factor.
- In a meta-analysis of 16 studies of 125,000 subjects, obesity increased the risk of AF by 49% (Wanahita N, Messerli FH et al. Am Heart J 2008;155: 310-315.)

## ARRIRM Study (n=4,060)

### Table 2  Final Multivariate Model for All-cause Mortality

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hazard Ratio</th>
<th>95% CI</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (continuous distribution)</td>
<td>0.95</td>
<td>0.93-0.98</td>
<td>.003</td>
</tr>
<tr>
<td>Age</td>
<td>1.05</td>
<td>1.03-1.06</td>
<td>.02</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>2.16</td>
<td>1.71-2.72</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>1.81</td>
<td>1.44-2.28</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.96</td>
<td>1.53-2.51</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Smoking</td>
<td>1.72</td>
<td>1.26-2.37</td>
<td>.007</td>
</tr>
<tr>
<td>Rhythm control arm</td>
<td>1.30</td>
<td>1.04-1.61</td>
<td>.02</td>
</tr>
</tbody>
</table>

BMI = body mass index; CI = confidence interval.

Male sex (P = .73), beta-blocker therapy (P = .08), and hypertension (P = .12) were removed on running stepwise selection.
Obesity Paradox in Atrial Fibrillation

ARRIRM Study (n=4,060)

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Combined Endpoint</strong></td>
<td></td>
</tr>
<tr>
<td>Overweight vs Normal</td>
<td>0.73 (0.59-0.92, 0.007)</td>
</tr>
<tr>
<td>Obese vs Normal</td>
<td>0.63 (0.49-0.82, 0.0004)</td>
</tr>
<tr>
<td><strong>Cardiovascular Mortality</strong></td>
<td></td>
</tr>
<tr>
<td>Overweight vs Normal</td>
<td>0.38 (0.25-0.58, &lt;0.0001)</td>
</tr>
<tr>
<td>Obese vs Normal</td>
<td>0.65 (0.51-0.83, 0.0005)</td>
</tr>
<tr>
<td><strong>All cause Mortality</strong></td>
<td></td>
</tr>
<tr>
<td>Overweight vs Normal</td>
<td>0.66 (0.48-0.92, 0.01)</td>
</tr>
<tr>
<td>Obese vs Normal</td>
<td>0.58 (0.42-0.80, 0.0009)</td>
</tr>
</tbody>
</table>

Weight Loss in CV Diseases

- Obesity increases most CV risk factors and CV diseases
- However, an “obesity paradox” is present
- Weight loss improves risk factors
- Impact of weight loss on CV events remains controversial

Potential Adverse Effects of Weight Loss

- Obesity Paradox
- Prolonged QTc and increased ventricular dysrhythmias (starvation, very low calorie, liquid protein diets, and obesity surgeries)
- Pharmacologic agents have limited efficacy and considerable toxicity

Weight Loss and Lifestyle Modifications

• Calorie restriction and exercise training is safe and is associated with 60% reduction in development of T2DM
  – Knowler WL et al. NEJM 2002;346:393-403

• CRET reduces MS by 37%
  – Milani RV, Lavie CJ. AJC 2003;92:50-54

• In 1,500 CHD patients, 6 month weight loss programs associated with lower CHD events in 4 years

• In 377 patients at Mayo Clinic, weight loss, even in those with BMI < 25 kg/m², was associated with reduced mortality/CV events
Weight Loss in CV Diseases

• In HTN, weight loss reduces BP and LVH
• In HF, weight loss improves LVM, systolic and diastolic LV function, and functional class
• Obesity surgery improves CHD risk factors, T2DM, and short- and long-term mortality
• Obesity surgery in small studies is safe in CHD and HF

Obesity, HF and Weight Loss
Guideline Statements

- American Heart Association: 40 kg/m²
- Heart Failure Society of America: 35 kg/m²
- European Society of Cardiology: 30 kg/m²
- Canadian Cardiovascular Society: 30 kg/m²
- Vastly different cut-points due to minimal data by which to base these exact recommendations
- Clearly further research is needed to determine ideal BMI and body composition in CVD, including systolic and diastolic HF
Obesity and CV Diseases

Summary and Conclusions

• Overwhelming evidence supports the importance of obesity in the pathogenesis and progression of most CV diseases
• An Obesity Paradox exists
• At present, evidence supports purposeful weight reduction
• If the current obesity epidemic continues, we may soon witness an unfortunate end to the steady increase in life expectancy

Untangling the “Heavy” Cardiovascular Burden of Obesity and the “Obesity Paradox”

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