Is Obesity a Risk Factor for Mortality in Coronary Artery Bypass Surgery?

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Background—The published articles examining obesity and CABG surgery contain conflicting results about the role of body mass index (BMI) as a risk factor for in-hospital mortality.

Methods and Results—We studied 16,218 patients who underwent isolated CABG in the Providence Health System Cardiovascular Study Group database from 1997 to 2003. The effect of BMI on in-hospital mortality was assessed by logistic regression, with BMI group (underweight, normal, overweight, and 3 subgroups of obesity) as a categorical variable or transformations, including fractional polynomials, of BMI as a continuous variable. BMI was not a statistically significant risk factor for mortality in any of these assessments. However, using cumulative sum techniques, we found that the lowest risk-adjusted CABG in-hospital mortality was in the high-normal and that overweight BMI subgroup patients with lower or higher BMI had slightly increased mortality.

Conclusions—Body size is not a significant risk factor for CABG mortality, but the lowest mortality is found in the high-normal and overweight subgroups compared with obese and underweight. (Circulation. 2005;111:3359-3365.)

Key Words: coronary disease ■ mortality ■ obesity ■ risk factors ■ surgery

In the United States, obesity has risen at an epidemic rate during the past 20 years. Results from the 1999 to 2000 National Health and Nutrition Examination Survey indicate that an estimated 64% of US adults are either overweight or obese, defined as having a body mass index (BMI) ≥25 kg/m².1 Obesity is also a major contributor to the risk of cardiovascular disease.2 These facts have resulted in an increase in the prevalence of obesity in the CABG surgery population in our country.

The literature dealing with obesity as a risk factor for in-hospital mortality after CABG contains conflicting results. Of 17 studies3-19 that dealt specifically with BMI as a risk factor, only the study with the largest sample size3 found obesity to be significant. Another study with a medium-sized sample4 found high BMI to be protective, and 3 studies found obesity to be significant. Another study with a medium-sized sample5-7 found “underweight” (very low BMI) to be a risk factor. The remaining 12 studies did not find any effect of BMI.8-19

Motivated by these apparently contradictory findings, we used the Providence Health System Cardiovascular Study Group (PHS) database to investigate the role of BMI in CABG operative (in-hospital) mortality.

Methods

Clinical Material

From January 1997 through December 2003, 16,232 patients underwent isolated CABG in 9 Providence Health System hospitals. All those hospitals with cardiac surgery programs participate in the PHS, which requires prospectively collecting data according to standard definitions and transmitting them to an independent coordinating center for merging into a common database. The 14 patients with incomplete data on height and/or weight were excluded, leaving 16,218 patients for study.

Statistical Methods

BMI, weight in kilograms divided by the square of height in meters (kg/m²), is the widely accepted way to estimate body fat and overall health risk from obesity or undernutrition. According to the National Institutes of Health (NIH),20 the normal BMI range is 18.5 to 24.9 kg/m², 25 to 29.9 kg/m² is overweight, and ≥30 kg/m² is obese. Obesity is further subdivided into mild (30.0 to 34.9 kg/m²), moderate (35.0 to 39.9 kg/m²), and extreme (40.0 kg/m²). A BMI <18.5 kg/m² is considered underweight.

Demographic, historical, and perioperative variables known to affect mortality were selected for analysis. Comparisons of these variables between normal and other BMI subgroups were done through the use of ANOVA with Scheffé’s post hoc correction for continuous variables and through logistic regression with BMI subgroup as the only risk factor for dichotomous variables.

A previously developed PHS logistic regression model21 that was validated on recent patients was used for all patients to investigate the possible effect of body size on mortality. To assess the properties of the logistic regression models, the c statistic (area under the receiver-operating characteristic curve)22 was used to measure discrimination, and the Hosmer-Lemeshow χ² test statistic23 was used to measure calibration. As an additional verification of the PHS model, we performed the link test.24 The link test is a simple method to assess the overall model specification by computing a new regression model using as predictor variables the risk score from the original model plus its square (quadratic term). If the additional...
quadratic term is significant, there is evidence of model misspecification, indicating that there may be additional variables missing from the model. (However, this test does not guarantee that there are no missing terms; even if this term is not significant, there are still probably unknown risk factors missing that could be added to the model.)

The logistic regression model assumes that the logit (logarithm of the odds) of death is a linear function of the risk factor—in this case, BMI. However, it is often the case in biomedical models that a mathematical transformation (like the square or square root) of the risk factor provides a better fit. Thus, BMI was tested both as a continuous variable, including BMI itself and several transformations (BMI$^{-1}$, BMI$^{1/2}$, BMI, BMI, In(BMI), BMI$^{2}$, and as a categorical variable (BMI group). The components of BMI, height, and weight were tested, along with body surface area (BSA). As the ultimate extension of this exercise, the method of fractional polynomials (FPs) was used. This method considers, in an organized way, the logit plus several powers ($-2, -1, -0.5, 0.5, 1, 2, 3$) of the continuous variable (BMI), either singly or 2 at a time, as possible additions to the predictor variables already in the model. Then, the likelihood ratios from the resulting models are compared to select optimal transformation(s) of BMI. When the dependent (outcome) variable is dichotomous (death), it is difficult to appreciate its relationship to a continuous risk factor graphically. A cumulative sum (cusum) technique was used to overcome this difficulty and to examine the role of BMI at the individual patient level.

For other adverse outcomes, cerebrovascular accident, myocardial infarction, deep sternal infection, renal failure requiring dialysis, blood transfusion usage, postoperative length of stay $>$14 days, mechanical ventilation in an intensive care unit $>$24 hours, reoperation for cardiac reason, and postoperative coronary angiograph intervention were selected for analysis. We dichotomized the outcome variables and used logistic regression to determine the effect of BMI.

Statistical analyses were performed with SPSS version 11.0, SPSS Inc (logistic regression, ANOVA); Stata version 8.2, Stata Corp (fractional polynomials, link test, cusum); and S-PLUS version 6.1, Insightful Corp (graphics). A value of $P<0.05$ was considered significant.

### Results

#### Patient Characteristics and Mortality

Patient characteristics and raw (unadjusted) mortality are tabulated by BMI group in Table 1. The mean values are shown for each subgroup and are given in bold if the value is significantly different ($P<0.05$) from that of the normal BMI subgroup. The distribution of height and weight is shown in Figure 1, with the iso-lines of BMI superimposed. The distribution of BMI in this CABG series is skewed to the right (toward obesity). Altogether, 37% of patients were obese; this increased from 32% to 40% over the duration of the study.

Obese patients were younger and more often female. Obese patients also had more diabetes, systemic hypertension, and pulmonary hypertension. Underweight patients were older, were more often female, and had more peripheral vascular disease, chronic obstructive pulmonary disease, congestive heart failure, myocardial infarction, ventricular arrhythmia, mitral insufficiency, left main disease, and New York Heart Association functional class III and IV.

Obese patients had less mortality; underweight patients had higher (unadjusted) mortality. Examination of the causes of death showed no obvious differences between BMI groups.

#### Risk-Adjusted Mortality

A previous CABG risk model developed using PHS patients operated on from January 1997 to June 2002 included 12 risk factors (identified in Table 1) but no variables related to body size. Before using this model, we performed a validation step by computing predictions for the new patients added since it was developed (July 2002 to December 2003). The old model fit the new patient data well; the c statistic was 0.811, and the Hosmer-Lemeshow statistic was 10.07 ($P=0.26$).

Thus, all 16 218 cases from January 1997 to December 2003 were combined for the present investigation. Of these, 219 patients (1.4%) did not have all of the risk factors required for the risk model; the remaining 15 999 were used to see whether the increased sample size (since the original model was developed) might help to identify a body size effect. The risk model fit the entire data set well; the c statistic was 0.806, and Hosmer-Lemeshow statistic was 3.77 ($P=0.88$). When the link test was used on the combined data set, the quadratic term was not significant ($P=0.55$), providing no evidence of incorrect model specification.

Predicted mortality decreased with increasing BMI (Figure 2). This means that in general the underweight patients are in worse condition considering all risk factors in the model and that obese patients are in relatively better condition. Observed mortality (Figure 2) follows that predicted by the model (without body size variables) fairly well, except for a somewhat lower risk from the mid-normal through the overweight group. Thus, after adjustment for other risk factors, there appears to be some unexplained risk of mortality in the underweight and obese subgroups compared with the middle BMI subgroup.

The linear combination of the 12 risk factors from this model produced a mortality risk score (the linear combination of risk factors) for each patient. Multivariable logistic regression was then used to see whether various quantifications of body size might significantly contribute to this risk. We tried to improve this model by adding single variables and combinations and transformations of variables reflecting body size or obesity, as shown in Table 2. None of the individual measures or their transformations entered the model either singly (group A in Table 2) or in combination (group B). Treating BMI as a 6-level categorical variable (group C) also did not add significantly to the model. The method of FPs was then used as a unified search for optimal transformation of BMI. This produced 2 more regression models, neither of which made a significant contribution to the risk. A first-degree FP selected a single transformation of BMI, its cube ($P=0.52$). A second-degree FP selected 2 transformations of BMI, the inverse and the inverse times the logarithm ($P=0.27$). Higher-degree FPs were not tried.

Finally, a cusum technique was used to visualize the relationship of BMI to risk-adjusted mortality. The cumulative sum over BMI of observed death ($1=$yes, $0=$no) minus predicted death from the risk model ($0< P<1$) was plotted (Figure 3). The curve goes up when observed deaths are more than expected and down when the observed deaths are less than expected. The highest and lowest points occur at BMIs of $\approx23$ and $30 \text{kg/m}^2$; in that range, the patients have lower mortality than elsewhere. This collaborates the observation from Figure 2. However, the total drop in this range, from a maximum of $\approx10$ more deaths than expected to a minimum...
of ∼15 fewer deaths than expected, amounts to a mortality reduction in this BMI range of <0.2%.

**Morbidity**

The raw (unadjusted) mortality and morbidity are shown in Table 3. The underweight patients had a higher percentage of postoperative cerebrovascular accident, blood transfusion, reoperation, ventilation in an intensive care unit >24 hours, and length of stay >14 days. The obese patients had more deep sternal infection.

The results of the multivariate analysis for postoperative morbidity are shown in Table 4. The odds ratio (OR) and probability value of BMI adjusted with other risk factors are listed. BMI is a risk factor for deep sternal infection and renal failure and is a protective factor for blood transfusion, coronary angiograph intervention, and reoperation.

**Discussion**

BMI was associated with many patient characteristics, especially age and gender. Women had higher BMIs than men in the same age group. Younger patients had higher BMIs than elders. More women are in the underweight and obesity subgroups. Because age and gender are important risk factors for mortality, we must determine the relationship between BMI and mortality after adjusting for the effects of age, gender, and other risk factors.
Previous Studies
Of 13 general risk models for mortality after CABG from a recent literature search, only the 2 largest studies, from the Society of Thoracic Surgeons (STS) National Cardiac Surgery Database and from New York State, included obesity. None of them included underweight as a risk factor. Two of them, STS and Northern New England Cardiovascular Disease Study Group, included BSA. The number of risk factors varied greatly in these studies and correlated strongly with the number of patients studied ($r=0.96$).

Because the STS database has the most CABG patients, we further examined all their previous risk models. The STS has published CABG risk models for 9 different years, included in 5 articles. The number of risk factors increased with the number of cases available for analysis; only when the model had $\geq 30$ factors did obesity enter the model. Interestingly, the models of 1995 and 1996 included both BSA and obesity, and the 1999 model has BSA only.

Apropos to the present investigation, we found 17 further studies that dealt specifically with obesity as a risk factor for mortality and morbidity. Only one study, the largest study using the STS database, found obesity to be significant for death, with ORs of 1.21 for BMI of 35 to 40 kg/m$^2$ and 1.58 for BMI $\geq 40$ kg/m$^2$. One other study found it to be protective.

Thus, most CABG risk models and special investigations of obesity do not find obesity to be significant; only studies with a huge number of patients and dozens of other risk factors do. This is consistent with obesity having a small clinical effect; in general, the smaller the clinical size of an effect, the larger the number of patients needed to confirm it statistically.

We found that BMI is a risk factor for deep sternal infection, which is coincident with many other studies.

**TABLE 2. Multivariable Logistic Regression Analysis for Mortality**

<table>
<thead>
<tr>
<th>Type*/Factors With RS Entered Into the Model</th>
<th>$P$</th>
<th>OR† (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI$^{-1}$ ($\times 10$)</td>
<td>0.90</td>
<td>0.90 (0.17–4.85)</td>
</tr>
<tr>
<td>BMI$^{1/2}$</td>
<td>0.51</td>
<td>1.08 (0.86–1.36)</td>
</tr>
<tr>
<td>BMI</td>
<td>0.44</td>
<td>1.01 (0.99–1.03)</td>
</tr>
<tr>
<td>BMI$^2$</td>
<td>0.34</td>
<td>1.00 (1.00–1.00)</td>
</tr>
<tr>
<td>BMI$^3$</td>
<td>0.32</td>
<td>1.00 (1.00–1.00)</td>
</tr>
<tr>
<td>ln(BMI)</td>
<td>0.59</td>
<td>1.02 (0.64–2.18)</td>
</tr>
<tr>
<td>BSA</td>
<td>0.78</td>
<td>0.93 (0.57–1.53)</td>
</tr>
<tr>
<td>Height</td>
<td>0.34</td>
<td>0.99 (0.98–1.01)</td>
</tr>
<tr>
<td>Weight</td>
<td>0.82</td>
<td>1.00 (0.99–1.01)</td>
</tr>
<tr>
<td>B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>0.33</td>
<td>0.94 (0.84–1.06)</td>
</tr>
<tr>
<td>BMI$^2$</td>
<td>0.25</td>
<td>1.00 (1.00–1.00)</td>
</tr>
<tr>
<td>BMI</td>
<td>0.24</td>
<td>1.02 (0.99–1.04)</td>
</tr>
<tr>
<td>BSA</td>
<td>0.36</td>
<td>0.75 (0.41–1.39)</td>
</tr>
<tr>
<td>Weight</td>
<td>0.43</td>
<td>1.00 (1.00–1.01)</td>
</tr>
<tr>
<td>Height</td>
<td>0.23</td>
<td>0.99 (0.98–1.01)</td>
</tr>
<tr>
<td>C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI group</td>
<td>0.28</td>
<td></td>
</tr>
<tr>
<td>Underweight</td>
<td>1.87</td>
<td>(0.79–4.42)</td>
</tr>
<tr>
<td>Normal Baseline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overweight</td>
<td>0.92</td>
<td>(0.73–1.28)</td>
</tr>
<tr>
<td>Mild obesity</td>
<td>1.25</td>
<td>(0.90–1.72)</td>
</tr>
<tr>
<td>Moderate obesity</td>
<td>1.14</td>
<td>(0.73–1.87)</td>
</tr>
<tr>
<td>Extreme obesity</td>
<td>1.23</td>
<td>(0.69–2.55)</td>
</tr>
</tbody>
</table>

*Variable type. A, B, and C indicate different variable grouping strategies—(see text).
†OR for various measures of body size after adjustment for risk score (RS) from the PHS CABG risk model. Components of RS are indicated in Table 1.
We also have the same findings as other studies\textsuperscript{4–6,11–13} that obese patients have less postoperative bleeding and fewer blood transfusions.

**BMI Grouping**

The direct comparison of results among these previous studies of BMI and CABG outcomes is problematic because of different definitions and groupings of BMI values. Many studies use the NIH BMI subgroups for analysis. However, NIH determined the overweight and obesity subgroups on the basis of the risks of natural morbidity (hypertension; dyslipidemia; type 2 diabetes; coronary heart disease; stroke; gallbladder disease; osteoarthritis; sleep apnea and respiratory problems; and endometrial, breast, prostate, and colon cancers). In addition, NIH determined the underweight category on the basis of the risks of undernutrition, infertility, and impaired immunocompetence.\textsuperscript{20} Thus, using this categorization to analyze the operative risk of CABG may not be suitable. We tried to keep the BMI variable continuous and found, using the method of FP and cusum, that the lowest mortality was in the high-normal and overweight subgroups, with BMI in the range 23 to 30 kg/m\textsuperscript{2} (Figure 3). Our study of mortality risk model for valve surgery also found that a BMI of 20 to 32 kg/m\textsuperscript{2} is a protective factor for death.\textsuperscript{35} Thus, when undergoing the physical insult of surgery, a little extra fat may be a protective factor. However, one must consider that in general, and especially after a CABG procedure, there is a negative effect on overall health, particularly coronary health, associated with being over one’s ideal body weight.

**Study Limitations**

Our study and most of the others used BMI to determine obesity. However, BMI has its limitations. BMI may not accurately reflect body fatness in people who are very short (<5 ft) and in older people who tend to lose muscle mass as they age, people of Indian or Asian descent whose frame size is smaller, and athletes who have large amounts of muscle mass. A recent study found that in the same patient groups, the prevalence of obesity, defined by BMI, waist circumference, and waist-to-hip ratio, could vary 3-fold. It concluded that waist circumference is an easy method that reflects central obesity more accurately.\textsuperscript{36} Albumin level is also considered an index for obesity. Our database did not contain the variables needed to test these other methods of defining obesity.

This analysis depends in part on baseline mortality. Our results are similar to the STS national database, which reported on 559,000 patients operated on during 1997 to 2000,\textsuperscript{3} with an overall mortality of 2.6% compared with 2.2% in this study and a mortality of 2.6% in patients with BMI >35 kg/m\textsuperscript{2} compared with 2.3% in this study.

There were only 90 underweight patients (0.6%) in our study cohort and 7 deaths among them. This small number limits the power and precision for the study of this group. On the other hand, our risk model did not contain every conceivable risk factor, but only those supported by our data. The difference in mortality that we did see with underweight patients may have been due to other risk factors not in our model rather than the intrinsic small size itself.

**Conclusions**

Body size is not a significant risk factor for CABG mortality, but the lowest mortality is found in the high-normal and}

### Table 3. Postoperative Morbidity by BMI Groups

<table>
<thead>
<tr>
<th>BMI Category</th>
<th>Underweight</th>
<th>Normal</th>
<th>Overweight</th>
<th>Mild Obesity</th>
<th>Moderate Obesity</th>
<th>Extreme Obesity</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deep sternal infection</td>
<td>0</td>
<td>0.3</td>
<td>0.3</td>
<td>0.6</td>
<td>1.1</td>
<td>1.4</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Renal failure</td>
<td>0</td>
<td>2.3</td>
<td>1.7</td>
<td>1.3</td>
<td>2.1</td>
<td>1.9</td>
<td>0.02</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>67.0</td>
<td>47.8</td>
<td>34.8</td>
<td>28.9</td>
<td>27.6</td>
<td>26.9</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Reoperation</td>
<td>6.7</td>
<td>3.8</td>
<td>2.8</td>
<td>1.9</td>
<td>1.8</td>
<td>1.7</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Coronary angiograph intervention</td>
<td>1.3</td>
<td>0.6</td>
<td>0.5</td>
<td>0.3</td>
<td>0.2</td>
<td>0.2</td>
<td>0.14</td>
</tr>
<tr>
<td>Cerebrovascular accident</td>
<td>3.3</td>
<td>2.6</td>
<td>2.0</td>
<td>1.5</td>
<td>1.5</td>
<td>1.7</td>
<td>0.01</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>2.2</td>
<td>1.6</td>
<td>1.4</td>
<td>1.2</td>
<td>1.1</td>
<td>1.1</td>
<td>0.67</td>
</tr>
<tr>
<td>ICU ventilation &gt;24 h</td>
<td>10.1</td>
<td>7.5</td>
<td>5.2</td>
<td>4.9</td>
<td>7.5</td>
<td>7.4</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Length of stay &gt;14 d</td>
<td>8.8</td>
<td>3.8</td>
<td>2.8</td>
<td>2.5</td>
<td>3.5</td>
<td>5.6</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

ICU indicates intensive care unit.
overweight subgroups (compared with obese and underweight).

**Acknowledgments**

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**References**


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