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# Obesity

## An Independent Predictor of In-Hospital Postoperative Renal Insufficiency among Patients Undergoing Cardiac Surgery?

We sought to determine, retrospectively, whether obesity was associated with adverse renal outcomes in 17,630 patients who underwent cardiac surgery from January 1995 through December 2006. Obesity was defined as a body mass index  $\geq 30 \text{ kg/m}^2$ . The primary outcome was any episode of postoperative renal insufficiency (requiring or not requiring dialysis) before hospital discharge. Outcomes were evaluated in the entire cohort and in subgroups undergoing isolated coronary artery bypass grafting (CABG), isolated valve surgery, and combined CABG and valve surgery.

The final analysis included 16,429 patients, 5,124 (31%) of whom were obese. In the entire cohort, obesity was associated both with increased risk of any postoperative renal insufficiency (odds ratio [OR], 1.37; 95% confidence interval [CI], 1.21–1.55) and with increased risk of renal insufficiency not requiring dialysis (OR, 1.41; 95% CI, 1.23–1.62). Obesity was associated with an increased risk of postoperative renal insufficiency in patients undergoing isolated CABG (OR, 1.38; 95% CI, 1.18–1.61), isolated valve surgeries (OR, 1.39; 95% CI, 1.05–1.85), and combined CABG and valve surgeries (OR, 1.35; 95% CI, 0.99–1.83; statistically nonsignificant). Development of postoperative renal insufficiency was associated with a significantly higher mortality rate ( $P < 0.0001$ ) and with a significantly longer hospital stay (23 vs 10.5 days;  $P < 0.0001$ ).

We conclude that obesity is associated with a significant increase in postoperative renal insufficiency in cardiac surgery patients, an effect that we attribute to an increase in postoperative renal failure that does not require dialysis. (*Tex Heart Inst J* 2009;36(6):540–5)

**O**besity is associated with the development of chronic kidney disease.<sup>1–6</sup> It has also been shown to be associated, in patients who have chronic kidney disease, with increased oxidative stress and inflammation,<sup>1</sup> impairment of renal endothelial function,<sup>2,3</sup> and proteinuria.<sup>4,5</sup> Inflammation appears to be an important mediator in the development of postoperative renal failure.<sup>6,7</sup> Although epidemiologic data indicate that obesity might be associated with the development of chronic kidney disease in the general population,<sup>8–10</sup> there are very few studies pertaining to obesity as an independent predictor of poor renal outcomes in patients undergoing cardiac surgeries. In most of these studies,<sup>6,7,11–15</sup> the occurrence of postoperative renal insufficiency has not been the primary outcome; moreover, the results have been inconsistent. We lack firm data on whether obesity is associated with an increase in the severity of postoperative renal failure.

The aim of this study was to determine whether obesity is an independent predictor of postoperative renal insufficiency in patients undergoing cardiac surgeries, including patients undergoing isolated coronary artery bypass grafting (CABG), isolated valve surgeries, and combined CABG and valve surgeries. We also investigated the possible association between obesity and increased severity of postoperative renal failure (that is, postoperative renal failure requiring in-hospital dialysis).

## Patients and Methods

We conducted a retrospective cohort analysis of 17,630 consecutive patients who underwent surgical procedures (CABG, valve surgery, or both) at St. Luke's Episcopal Hospital from 1 January 1995 through 31 December 2006. Of these, we excluded

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from the analysis 1,038 patients who underwent any associated procedures, including left ventricular aneurysm repair and ascending aortic repairs, and another 163 patients who experienced preoperative renal failure requiring dialysis. The study protocol was approved by the Institutional Review Board.

The remaining 16,429 patients were divided into 2 groups (obese and nonobese) on the basis of body mass index (BMI). Obesity was defined as a BMI of  $\geq 30 \text{ kg/m}^2$  (weight in kilograms divided by the square of height in meters). Patients' weights at admission to the hospital were used to calculate BMI. Patients' baseline characteristics and intraoperative variables were obtained from the Texas Heart Institute Research Database (THIRD-Base). This database had written documentation for each field coded. Data from patient charts were abstracted by 3 trained abstractors, with 95% agreement among abstractors. Monthly electronic quality-control checks were conducted to catch logical errors. When verification coding (recoding the same admission) was performed on a minimum of 10 admissions per month, it found that 95% of the data collected was correct.

The variables used for our analysis included age, sex, history of hypertension, diabetes mellitus, prior myocardial infarction, preoperative renal insufficiency, hyperlipidemia, unstable angina, peripheral vascular disease, transient ischemic attacks, cerebrovascular accident, low left ventricular ejection fraction (defined as  $<0.35$ ), need for urgent or repeat surgery, need for an intra-aortic balloon pump, New York Heart Association class at the time of surgery, and aortic cross-clamp time.

The primary outcome of interest was the occurrence of any postoperative renal insufficiency up to the time of the patient's discharge from index hospitalization for cardiac surgery. Postoperative renal insufficiency was defined as the occurrence of acute tubular necrosis, acute interstitial nephritis, postoperative anuria, or any increase in serum creatinine deemed clinically significant by the treating physician. Postoperative renal insufficiency was subdivided into renal failure requiring any dialysis session during the hospitalization and renal failure not requiring dialysis.

### Statistical Analysis

All statistical analyses were performed using SAS statistical software version 9.1 (SAS Institute, Inc.; Cary, NC). Baseline characteristics and intraoperative variables were compared in both patient groups. Differences between groups were evaluated by the  $\chi^2$  test for discrete variables and the  $t$  test for continuous variables. A  $P$  value  $<0.05$  was considered statistically significant. A multivariate logistic regression model was used to control for potential confounders and to ascertain which variables were independently associated with outcome. Variables used in the multivariate logistic regression model included all the preoperative and intraoperative variables.

Because it can be argued that obese patients on average were sicker and had a higher risk of developing postoperative renal insufficiency when compared with nonobese patients, we attempted to minimize this selection bias by performing propensity-score matching.<sup>16</sup> Propensity scores were estimated using unconditional logistic regression to determine the predicted probability of obesity for each patient. The variables used in the model after propensity-score matching are shown in Table I. Obese patients and nonobese patients were then matched 1-to-1 on the basis of these variables, resulting in successful matching of 6,866 patients (3,433 patients in each group). All predictor variables were then

**TABLE I.** Preoperative and Intraoperative Characteristics of Obese (n=3,433) versus Nonobese (n=3,433) Patients after Propensity-Score Matching

Variable	Obese Patients No. (%)	Nonobese Patients No. (%)	P Value
Age >65 yr	1,324 (38.6)	1,328 (38.7)	0.92
Women	822 (23.9)	820 (24)	0.95
Hypertension	2,744 (80)	2,750 (80.1)	0.86
Diabetes mellitus	166 (4.8)	170 (5)	0.82
Smoking	1,664 (48.5)	1,670 (48.6)	0.88
Prior myocardial infarction	1,178 (34.3)	1,239 (36.1)	0.12
Preoperative renal insufficiency (not requiring dialysis)	247 (7.2)	245 (7.1)	0.93
Hyperlipidemia	2,108 (61.4)	2,099 (61.1)	0.82
Unstable angina	1,624 (47.3)	1,547 (45.06)	0.07
Peripheral vascular disease	330 (9.6)	327 (9.5)	0.9
History of transient ischemic attack	26 (0.76)	33 (0.96)	0.36
History of cerebrovascular accident	144 (4.2)	165 (4.8)	0.22
Low LVEF ( $<0.35$ )	522 (15.2)	507 (14.77)	0.61
Preoperative intra-aortic balloon pump	84 (2.45)	91 (2.65)	0.59
NYHA functional class III/IV	2,730 (79.5)	2,747 (80)	0.6
Repeat surgery	220 (6.4)	223 (6.5)	0.88
Urgent surgery	380 (11)	380 (11)	1.0
Total bypass time $>80$ min	771 (22.5)	769 (22.4)	0.95

LVEF = left ventricular ejection fraction; NYHA = New York Heart Association

$P < 0.05$  is considered statistically significant.

entered into a multivariate stepwise logistic model to determine whether obesity was independently associated with the risk of renal insufficiency in propensity-score-matched subjects.

## Results

The final study population consisted of 16,429 patients. Of these, 11,830 (72%) patients had isolated CABG, 3,062 (19%) had isolated valve surgeries, and 1,537 (9%) had combined CABG and valve surgeries.

A total of 5,124 patients (31%) had a BMI  $\geq 30 \text{ kg/m}^2$ . In this obese cohort, 3,414 patients (63%) had a BMI between 30 and 34.99  $\text{kg/m}^2$ , 1,189 patients (23%) had a BMI between 35 and 39.99  $\text{kg/m}^2$ , and 521 patients (10%) had a BMI  $\geq 40 \text{ kg/m}^2$ .

Preoperative characteristics of obese and nonobese patients are compared in Table II. In the obese group, there were more women than men. Obese patients had

a higher prevalence of hypertension, diabetes, smoking, hyperlipidemia, and unstable angina, and had longer total bypass times. Nonobese patients were older, had a higher prevalence of peripheral vascular disease and transient ischemic attacks, and underwent more repeat operations when compared with obese patients.

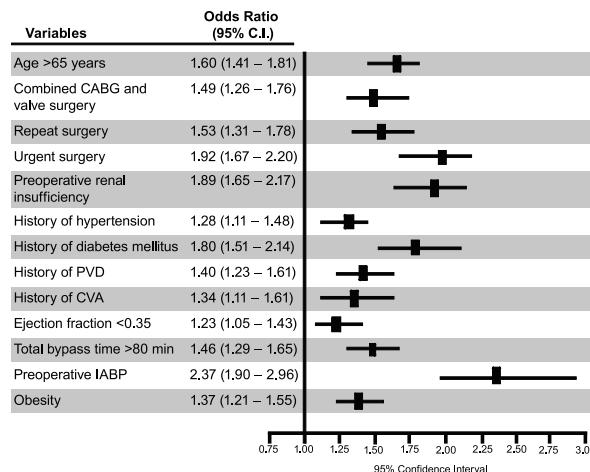
In the entire cohort, 1,437 patients (9%) had the primary outcome of postoperative renal insufficiency. Variables independently associated with the occurrence of postoperative renal insufficiency in the entire cohort are shown in Figure 1. As shown in Table III, obesity in the entire cohort was independently associated with a 37% increase in the risk of developing any postoperative renal insufficiency (odds ratio [OR], 1.37; 95% confidence interval [CI], 1.21–1.55), and this risk was mostly attributable to an increase in renal insufficiency not requiring dialysis (OR, 1.41; 95% CI, 1.23–1.62). Subgroup analysis revealed that obesity was associated with a statistically significant increased risk of renal in-

**TABLE II.** Preoperative and Intraoperative Characteristics of Obese versus Nonobese Patients Included in Retrospective Chart Review

Variable	Obese Patients n=5,124 (%)	Nonobese Patients n=11,305 (%)	P Value
Age >65 yr	2,047 (39.95)	6,112 (54.06)	<0.0001
Women	1,538 (30.02)	3,203 (28.33)	<0.02
Hypertension	4,129 (80.58)	7,582 (67.08)	<0.0001
Diabetes mellitus	593 (11.57)	686 (6.07)	<0.0001
Smoking	2,522 (49.28)	5,243 (46.4)	0.0006
Prior myocardial infarction	1,880 (36.69)	4,080 (36.1)	NS
Preoperative renal insufficiency (not requiring dialysis)	653 (12.74)	1,481 (13.1)	NS
Hyperlipidemia	3,099 (60.48)	5,890 (52.11)	<0.0001
Unstable angina	2,373 (46.31)	4,801 (42.47)	<0.0001
Peripheral vascular disease	755 (14.73)	2,200 (19.46)	<0.0001
History of transient ischemic attack	156 (3.04)	462 (4.09)	0.001
History of cerebrovascular accident	328 (6.4)	775 (6.86)	NS
Low LVEF (<0.35)	625 (12.2)	1,455 (12.87)	NS
Preoperative intra-aortic balloon pump	184 (3.59)	399 (3.53)	NS
NYHA functional class III/IV	4,105 (80.11)	9,161 (81.03)	NS
Repeat surgery	489 (9.54)	1,467 (12.98)	<0.0001
Urgent surgery	767 (14.97)	1,791 (15.84)	NS
Mean aortic cross-clamp time, min	41.59 $\pm$ 26.6	41.7 $\pm$ 26.54	NS
Mean total bypass time, min	67.88 $\pm$ 37.46	66.1 $\pm$ 36.54	0.0006

LVEF = left ventricular ejection fraction; NS = not significant; NYHA = New York Heart Association

*P* <0.05 is considered statistically significant.



**Fig. 1** Characteristics independently associated with postoperative renal insufficiency during hospitalization after cardiac surgery in our entire study population of 16,429 patients.\*

CABG = coronary artery bypass grafting; CI = confidence interval; CVA = cerebrovascular accident; IABP = intra-aortic balloon pump; PVD = peripheral vascular disease

\*Includes variables significantly associated with postoperative renal insufficiency after multivariate regression analysis.

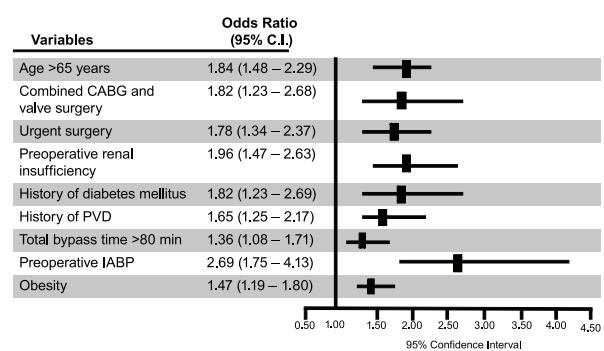
sufficiency in patients undergoing isolated CABG (OR, 1.38; 95% CI, 1.18–1.61) or isolated valve surgeries (OR, 1.39; 95% CI, 1.05–1.85) and with a statistically nonsignificant increased risk of postoperative renal insufficiency in patients undergoing combined CABG and valve surgeries (OR, 1.35; 95% CI, 0.99–1.83), as shown in Table III. Within these subgroups, the increased risk was attributable to the increase in renal insufficiency not requiring dialysis.

Patients who developed postoperative renal failure had a significantly higher 30-day mortality rate (25% vs 2.9%;  $P < 0.001$ ) and significantly prolonged length of hospital stay (mean, 23 days), when compared with

patients who did not develop any postoperative renal insufficiency (mean, 10.5 days;  $P < 0.0001$ ).

A higher risk for the development of postoperative renal insufficiency was associated with increasing severity of obesity. For the BMI categories of 30 to 34.99 kg/m<sup>2</sup>, 35 to 39.99 kg/m<sup>2</sup>, and  $\geq 40$  kg/m<sup>2</sup>, the percentages of patients who developed postoperative renal failure were 9.2%, 11.1%, and 13.1%, respectively ( $P=0.001$  for the trend).

Patient characteristics independently associated with the risk of postoperative renal insufficiency after propensity-score matching for obesity status are shown in Figure 2. Obesity was associated with a 47% increase in the likelihood of developing postoperative renal insufficiency after propensity matching (OR, 1.47; 95% CI, 1.19–1.80;  $P=0.0003$ ).



**Fig. 2** Characteristics independently associated with postoperative renal insufficiency after propensity-score matching in 6,866 patients (3,433 obese and 3,433 nonobese).\*

CABG = coronary artery bypass grafting; CI = confidence interval; IABP = intra-aortic balloon pump; PVD = peripheral vascular disease

\*Results obtained by multivariate regression analysis after propensity-score matching ( $n=6,866$  patients). Please see text in Methods section as well as Table I for list of variables matched for propensity-score analyses.

**TABLE III.** Association between Obesity and the Occurrence of Postoperative Renal Insufficiency after Multivariate Regression Analysis in the Entire Cohort of Patients and Different Surgical Subgroups

Group	Any Renal Failure OR (95% CI) n=1,437	Renal Failure Not Requiring Dialysis OR (95% CI) n=1,111	Renal Failure Requiring Dialysis OR (95% CI) n=376
Entire cohort (n=16,429)	1.37 (1.21–1.55)	1.41 (1.23–1.62)	1.04 (0.82–1.32)
Isolated CABG (n=11,830)	1.38 (1.18–1.61) n=860	1.45 (1.22–1.72) n=676	1.05 (0.78–1.44) n=208
Isolated valve surgery (n=3,062)	1.39 (1.08–1.85) n=289	1.49 (1.09–2.02) n=219	1.20 (0.73–1.99) n=81
Combined CABG and valve surgery (n=1,537)	1.35 (0.99–1.83) n=288	1.41 (1.01–1.95) n=216	1.03 (0.62–1.71) n=87

CABG = coronary artery bypass grafting; CI = confidence interval; OR = odds ratio

## Discussion

In this retrospective cohort analysis of 16,429 consecutive cases, we found that obesity was associated with a significant increase in postoperative renal insufficiency in patients undergoing cardiac surgeries. This effect—seen in the entire cohort, as well as in patients undergoing isolated CABG or isolated valve surgeries—was attributable mostly to an increase in postoperative renal failure that did not require dialysis. The risk was graded with the increasing risk that is associated with an increase in the severity of obesity. The development of postoperative renal insufficiency was associated with a significantly higher mortality rate and with a longer length of stay.

Obesity is associated with oxidative stress and endothelial dysfunction.<sup>1</sup> Obese patients are at a higher risk of developing hypertension<sup>17</sup> and diabetes,<sup>18</sup> which are also associated with elevated inflammatory response and impaired endothelial function.<sup>16,17</sup> The use of cardiopulmonary bypass for cardiac surgeries has been shown to be associated with an up-regulation of the inflammatory cascade.<sup>19,20</sup> This, together with the prevalence of risk factors associated with the development of postoperative renal insufficiency and the risk associated with obesity itself, means that obese patients may have a higher incidence of postoperative renal insufficiency.

Although epidemiologic studies have shown that obesity is independently associated with the development of chronic kidney disease,<sup>8–10,21–23</sup> studies of the association between obesity and the development of postoperative renal insufficiency have yielded disparate results.<sup>6,7,11–15,24,25</sup> Moulton and colleagues<sup>13</sup> did not find an association between obesity and postoperative renal failure, but an analysis of data from the Society of Thoracic Surgeons' database by Prabhakar and associates<sup>12</sup> showed that moderate obesity (BMI, 35–39.9 kg/m<sup>2</sup>) and severe obesity (BMI ≥40 kg/m<sup>2</sup>) were independently associated with the development of renal insufficiency in the postoperative period. The reasons for these varying results may include the small sample sizes of some studies. In addition, the development of renal insufficiency in surgical subgroups (especially isolated valve surgery and combined CABG and valve surgery) has not been well studied. Our study is one of the first to specifically evaluate the association between obesity and postoperative renal outcomes in a very large cohort of patients who underwent cardiac surgeries.

The risk estimates we obtained are comparable with those obtained in prior studies.<sup>12,25</sup> The risk estimate obtained by Prabhakar and associates<sup>12</sup> for patients with moderate obesity, defined as a BMI of 35 to 39.9 kg/m<sup>2</sup>, was 1.58 (1.50–1.67). We show that the presence of even mild forms of obesity (a BMI of 30 to 34.99 kg/m<sup>2</sup>) was independently associated with the occurrence of postoperative renal insufficiency and that patient cohorts with

higher BMIs have higher incidences of postoperative renal insufficiency—which suggests a dose–response relationship. Most of the postoperative renal failure attributable to obesity did not require dialysis, but it was associated with a significantly longer hospital stay. Our findings extend the findings from earlier studies<sup>12,25</sup> to show that obesity is associated also with an increased risk of renal insufficiency in subgroups that include patients undergoing isolated CABG or isolated valve surgeries. These subgroups have not been well studied before.

The development of postoperative renal insufficiency is an important clinical event, because it is associated with an increase in death<sup>26</sup> and with prolonged stays in the intensive care unit after cardiac surgery.<sup>27</sup> Our results support some of these earlier findings and show that patients who develop renal failure in the postoperative setting have, on average, an 8-fold higher incidence of early postoperative death and twice the length of hospital stay, when compared with patients who do not develop postoperative renal insufficiency.

## Limitations

Our study had limitations. Because we did not have postoperative serum creatinine measurements in our database, we used a clinical definition of renal failure as our outcome measure, which may have caused us to underestimate the true incidence of postoperative renal failure. However, the incidence of postoperative renal insufficiency in our cohort was comparable with those reported in prior studies of patients who had undergone cardiac surgery.<sup>11</sup> Furthermore, although we performed propensity-score matching to account for differences between the obese and nonobese groups, it is possible that some unmeasured differences between the 2 groups are responsible for observed differences in outcomes. Moreover, a BMI ≥30 kg/m<sup>2</sup> may not be the most sensitive definition of obesity, and uniform BMI cutoffs may not apply across all races and ethnic groups. Other measures, such as waist circumference and waist-to-hip ratios, might have provided a more accurate reading of the increased risk associated with obesity.<sup>28</sup> Although this was a single-institution study, the high volume of cases and the large, multiyear cohort likely enable the results to be applied, in general, to other settings; and the paucity of studies on this important topic lends interest to our findings, as well. Despite these limitations, the strengths of our study include carefully applied regression and propensity analyses.

## Conclusions

Our results have important clinical implications. If the results of our retrospective review are confirmed in the setting of a randomized clinical trial, obesity as a risk factor for the development of postoperative renal insufficiency could be viewed as modifiable. Indeed, in our

multivariate analysis, obesity was one of the few modifiable risk factors for the development of postoperative renal failure. Carefully executed randomized clinical trials are needed to confirm these preliminary findings and to determine whether preventive measures—such as preoperative weight loss in selected patients not undergoing emergent or urgent procedures and the use of perioperative statin therapy (shown to be associated with a decreased incidence of postoperative renal insufficiency<sup>29</sup>)—can ameliorate some of the detrimental renal outcomes that are associated with obesity in cardiac surgery patients.

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