Obesity and Post-Cardiopulmonary Bypass-Associated Acute Kidney Injury: A Single-Center Retrospective Analysis

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Objective: The authors specifically explored the association of obesity (based on body mass index [BMI]) and the risk of developing acute kidney injury after cardiopulmonary bypass (AKI_{CPB}).

Design: Single-center retrospective study.

Setting: Academic medical center.

Participants and Interventions: After IRB approval, 376 eligible adults who underwent cardiac surgery with cardiopulmonary bypass between 2006-2010 were included in the final retrospective analysis. Patients undergoing "off-pump" procedures, cardiac transplants, repair of congenital heart disease, and patients with preoperative circulatory assist devices were excluded.

Results: The overall incidence of developing AKI_{CPB} in this population based on the Acute Kidney Injury Network serum creatinine criteria was 39% (147 of 376). Among the BMI classes, the morbidly obese cohort (ie, BMI >40 kg/m^2) had a significantly greater risk of developing AKI_{CPB} than those in lower BMI classes. BMI >40 kg/m^2 was significantly associated with development of AKI_{CPB} even after accounting for covariates (ie, diabetes mellitus, hypertension, age, severity of illness, and CPB time) (overall $p = 0.018$). The odds ratio of AKI_{CPB} in the BMI >40 kg/m^2 cohort relative to BMI <25 kg/m^2 was 2.39 (95% CI: 0.98, 5.82; $p = 0.055$), with no significant difference in risk of developing AKI_{CPB} among the 4 lower BMI classes.

Conclusion: BMI >40 kg/m^2 is associated with a significantly higher risk of developing of AKI_{CPB}.

KEY WORDS: *morbid obesity, acute kidney injury, cardiopulmonary bypass, BMI*

THE PREVALENCE of obesity worldwide, and especially in developed countries, has reached epidemic proportions. Up to 30% of all patients admitted to adult intensive care units in the United States are obese and about 7% are morbidly obese.[1] Obesity is associated with a cluster of risk factors for cardiovascular disease, known as the metabolic syndrome (MeS), which includes hypertension, dyslipidemia, insulin resistance, and diabetes mellitus (DM).[2] Obese patients in general are at an increased risk for developing acute kidney injury (AKI) due to their disproportionately higher burden of comorbidities and due to underlying structural changes that occur in the kidneys of obese patients in spite of normal serum chemistries.[3,4] Several studies previously have established the association between a high body mass index (BMI) and an increased prevalence of chronic kidney disease.[5] Studies examining the association between obesity and postoperative AKI in patients undergoing noncardiac and nonbariatric surgery have yielded disparate results.[6–8] There have been relatively few studies examining obesity (based on BMI) as an independent predictor of postoperative AKI in patients undergoing cardiac surgery with cardiopulmonary bypass (AKI_{CPB}).[9,10] In this retrospective analysis, the authors explored the association of obesity (based on BMI) and the risk of developing AKI_{CPB}.

MATERIALS AND METHODS

The local institutional review board approved the study, waiving the requirement for informed consent. This was a retrospective analysis of patients who underwent cardiac surgery with CPB between 2006-2010 at a single academic medical center. A total of 376 eligible adult patients were included in the final analysis. The study excluded patients undergoing "off-pump" procedures, mini-CABG, cardiac transplants, repair of congenital heart disease, patients with preoperative circulatory assist devices, surgical procedures exclusively on the aorta (such as aneurysm, and dissection repairs procedures) and patients already on renal replacement therapy (RRT).

Preoperative data points included age, gender, height, weight, current smoking status, diabetes mellitus, hypertension, preoperative kidney function (defined as the latest available serum creatinine prior to admission), perioperative cardiac function including preoperative ejection fraction by echocardiography, and history of congestive heart failure (NYHA >2). Also included were history of previous cardiac surgery and elective versus emergent status of the current surgery.

Intraoperative variables included cardiac output data from a pulmonary artery catheter or echocardiography, duration of CPB in minutes, aortic cross-clamp times, type of cardiac surgery, transfusion support and types of transfusion products, and the use of diuretics intraoperatively. No aprotinin was used in any of the cases included in the final cohort.

Postoperative variables included duration of mechanical ventilation, need for reintubation within 72 hours, low-cardiac-output state (defined by the use of vasopressor and/or inotrope to maintain a prespecified cardiac index (eg, CI $>$ 2.2 L/min/m²) in the therapeutic range prescribed by the surgeon or attending intensivist), and transfusion support (including use of packed red blood cells, fresh frozen plasma, cryoprecipitate, and recombinant factor VII) in the first 24 hours of the post-surgical period.

Cardiopulmonary bypass was maintained intraoperatively using centrifugal pumps with circuits primed with an institutional standardized solution containing Plasmalyte A, albumin, 25 g, mannitol, 25 g, furosemide, 20 mg, bicarbonate, 25 mEq and heparin, 10,000 units). The pump flow rates were approximately 2.4 L/min/m^2 with a mean arterial pressure goal of $\geq$60 mmHg.

The primary outcome was development of AKI based on the acute kidney injury network (AKIN) serum creatinine (sCr) criteria. The AKIN criteria have been utilized and validated in prospective studies in patients with AKI after cardiac surgery.[11] Stage 1 in the AKIN classification includes patients with an increase in sCr of at least 0.3 mg/dL over baseline, because there is accumulating evidence that even minor increments in serum creatinine are associated with adverse outcomes.

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1053-0770/2605-0031$36.00/0
http://dx.doi.org/10.1053/j.jvca.2013.05.037

Stage 2 is defined as an increase of 200% to 299% over the baseline sCr. Any patient treated with RRT, irrespective of urine output or sCr, or with a threefold or greater rise in sCr, is categorized as stage 3 in the AKIN system. The AKIN classification uses a 48-hour time window for assessment of renal function based on the evidence that adverse outcomes were reported when the creatinine elevation occurred within 24 to 48 hours of hospitalization.[12] The authors chose to use the creatinine-based definition of AKI, with the most recent serum creatinine including up to day of surgery being considered the baseline value. The first postoperative creatinine values were assessed after 12 hours post-bypass to account for some of the fluid shifts and normalization of volume of distribution of serum Cr. Preoperative renal insufficiency was defined as a baseline serum Cr ≥1.2 mg/dL. The decision to initiate renal replacement therapy was at the discretion of the attending consultant nephrologist.

Because BMI remains the most widely used and validated measure of obesity, it was used as a measure of obesity in this study. The body mass index was calculated as BMI = [weight (lbs)/height (inches)^2] × 703 or BMI = weight (kg)/height (m^2). Patients were classified based on the NIH definition for overweight and obesity according to BMI, with normal (BMI < 25 kg/m^2), overweight (BMI 25 to < 30 kg/m^2), obesity class I (BMI 30 to <35 kg/m^2), obesity class II (BMI 35 to < 40 kg/m^2), and obesity class III (BMI ≥ 40 kg/m^2).

The authors used the numeric Euroscore (European System for Cardiac Operative Risk Evaluation) as a measure of the severity of illness in this study and not necessarily to predict outcome. The numeric Euroscore is a composite of variables, including age, gender, COPD, extracardiac atherosclerosis, threshold serum creatinine, active endocarditis, type of cardiac surgery, recent MI, and emergent status of surgery, that has been studied widely and validated in multiple countries and ethnic populations.[13,14]

Incidence of AKI_{CPB} was compared among the BMI classes using Pearson χ^2 test. Demographic, preoperative, intraoperative, and postoperative variables were compared among the BMI groups using one-way ANOVA or Kruskal-Wallis test for the continuous variables and Pearson χ^2 test for the categoric variables. The association of the demographic, preoperative, intraoperative, and postoperative variables with AKI_{CPB} was tested using two-sample *t* test or Wilcoxon rank-sum test for the continuous variables and Pearson χ^2 test for the categoric variables. The variables that differed among the BMI groups and those that showed a significant association with AKI_{CPB} then were used as covariates in a multivariable logistic regression model to assess the effect of BMI on AKI_{CPB} while controlling for covariates.

All statistical analyses were performed using SAS (version 9.3). Values are expressed as means ± SD, or median (interquartile range [IQR]) for continuous variables, and as frequency counts (%) for the categoric variables. The results of the logistic regression are reported as odds ratios (OR) with 95% confidence intervals (CI).

RESULTS

This study included 376 patients who underwent cardiac surgery with cardiopulmonary bypass. The overall incidence of developing AKI_{CPB} in this population based on the AKIN serum creatinine criteria was 39% (147 of 376). In the cohort of patients who developed AKI_{CPB}, 19.94% (75 of 376) of patients had a normal baseline serum Cr, and 19.14% (72 of 376) had preexisting kidney dysfunction.

The distribution of patients by BMI class was as follows: 90 (24%) BMI < 25 kg/m^2; 112 (30%) 25 to ≤ 30 kg/m^2; 86 (23%) 30 to ≤ 35 kg/m^2; 46 (12%) 35 to ≤ 40 kg/m^2; and 42 (11%) BMI ≥ 40 kg/m^2.

The incidence of AKI_{CPB} (with 95% confidence intervals) by BMI class is presented in Figure 1. Comparison of the incidence of AKI_{CPB} showed a significant difference among the 5 BMI classes (Pearson χ^2 test, p = 0.014). This difference was due primarily to BMI ≥ 40 kg/m^2 having a higher incidence of AKI_{CPB} (60%; 95% CI: 43%, 74%) compared with the lower BMI classes. The incidence of AKI_{CPB} was similar among BMI classes <25, 25 to 30, 30 to 35, and 35 ≤ 40.

A comparison of the demographic and clinical variables between the cohorts who developed AKI and no AKI are outlined in Table 1. Because other confounding variables may have had an effect on the differences observed in the incidence of AKI_{CPB}, the authors compared previously published independent risk factors as variables for AKI_{CPB}, among the BMI classes. These independent risk factors included DM, packed red blood cell transfusions, age, CPB time, preexisting kidney disease, preoperative ejection fraction <40, and type of cardiac surgery.

Patients with BMI > 40 kg/m^2 included a higher proportion of patients of female gender (p < 0.0001) and a higher proportion with diabetes mellitus (p < 0.0001) and hypertension (p < 0.0001). CPB times were longer in those with BMI ≥ 40 kg/m^2 compared with the other BMI classes (p = 0.070) except for the BMI < 25 kg/m^2 cohort. There were no statistically significant differences in age (p = 0.192), peripheral vascular disease (p = 0.964), baseline serum creatinine (p = 0.225), rates of emergency surgery (p = 0.219), low EF <40% (p = 0.947), and numeric Euroscore (p = 0.197) among the BMI classes.

In addition to comparing these variables among the BMI classes, the association of these variables with AKI_{CPB} also was tested. The results of these tests are summarized in Table 2. Of the potential confounders that were tested, age (p = 0.005), diabetes mellitus (p = 0.002), hypertension (p = 0.001), preexisting kidney disease (p = 0.0003), type of cardiac surgery (p < 0.0001), length of CPB (p < 0.0002), intraoperative packed red blood cell transfusions (p = 0.003), baseline creatinine (p = 0.002), and a higher admission numeric Euroscore (p < 0.0001) were significantly associated with the development of AKI_{CPB}. Interestingly, in this patient population, the preoperative ejection fraction of <40 (p = 0.501) was not significantly associated with an increased risk of developing AKI_{CPB}.

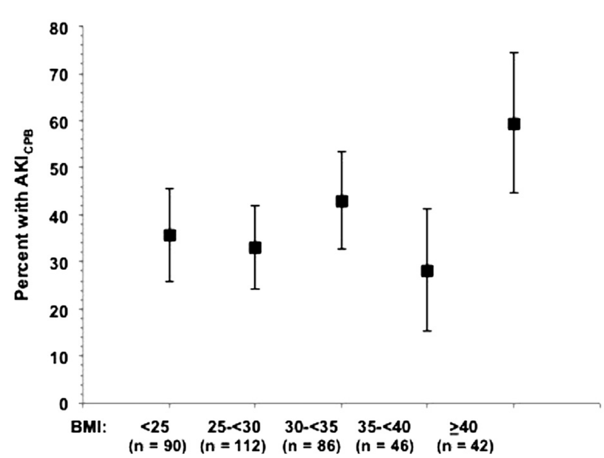

Fig 1. Incidence of acute kidney injury postcardiopulmonary bypass by BMI class (with 95% confidence intervals). Abbreviations: AKI_{CPB}, acute kidney injury after cardiopulmonary bypass; BMI, body mass index. (Color version of figure is available online.)