Renal injury is associated with operative mortality after cardiac surgery for women and men

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Objectives: The purpose of this study was to determine whether acute renal injury develops more frequently in women than in men after cardiac surgery and whether this complication is associated with operative mortality in women.

Methods: Prospectively collected data were evaluated from 9461 patients undergoing coronary artery bypass graft surgery, cardiac valve surgery, or both (3080 women) and not receiving preoperative dialysis. The glomerular filtration rate was estimated by using the Modification of Diet in Renal Disease equations with the last plasma creatinine level before surgical intervention (baseline) and the highest level of the first postoperative week. The primary renal injury outcome was the composite end point of renal injury according to RIFLE criteria (estimated glomerular filtration rate decrease >50% from baseline value) or failure.

Results: Thirty-day operative mortality and renal injury were more common in women than in men (5.9% vs 2.8%, $P = .01$; 5.1% vs 3.6%, $P < .001$, respectively). Nonetheless, patient sex was not independently associated with risk for renal injury when the baseline estimated glomerular filtration rate was included in multivariate modeling. Perioperative complications, intensive care unit length of stay, and mortality were more frequent for patients with than without renal injury (women, 20.6% vs 3.2%, $P < .0001$; men, 18.3% vs 2.2%, $P < .001$). Renal injury was independently associated with 30-day mortality for women (odds ratio, 3.96; 95% confidence interval, 1.86–8.44; $P < .0001$) and men (odds ratio, 4.05; 95% confidence interval, 2.19–7.48; $P < .0001$).

Conclusions: Postoperative renal injury is independently associated with 30-day mortality regardless of patient sex. Higher rates of renal injury in women compared with men might be explained in part by a higher prevalence of low estimated glomerular filtration rate before surgical intervention. (J Thorac Cardiovasc Surg 2010;140:1367-73)

Women are at higher risk for mortality after cardiac surgery than are men, but an explanation for this higher risk is not completely clear.[1] Understanding the sex-specific causes of operative mortality is fundamental for developing preventative strategies. Acute renal failure develops in 5% to 30% of patients after cardiac surgery when cardiopulmonary bypass (CPB) is used, predisposing affected patients to in-hospital and long-term mortality.[2-6] Even small increases in serum creatinine levels (0.5 mg/dL) after surgical intervention are associated with high mortality, longer length of hospitalization, and higher hospital costs.[4,6] Female sex has been identified as an independent risk factor for postoperative renal failure, although it has not been a consistent finding.[2,5-7] Notably, investigators who have evaluated the role of postoperative renal dysfunction in patient outcomes have not separately considered the effect of female sex.[2-6] This omission is important because women represented a minority (<30%) of patients in these studies, and the small number might limit extrapolation of data derived predominately from men. Furthermore, compared with men, women usually have less muscle mass and are typically older at the time of surgical intervention; both of these factors could affect the levels of serum creatinine.[1,8] Thus the purpose of this study was to evaluate whether acute renal injury that develops after cardiac surgery is more common in women than in men and whether it is associated with operative mortality in women.

MATERIALS AND METHODS

Study Design and Patient Population

All study procedures were approved by the institutional review board of the Johns Hopkins Medical Institutions, and each patient provided written informed consent for data collection and analysis before surgical intervention. Data were prospectively collected by trained abstractors from an electronic medical records system at the Johns Hopkins Hospital as part of data collection for the Society of Thoracic Surgeons (STS) National Cardiac Surgery Database.[9] Data collected included inpatient medical records, review of outpatient records, letter mailings, and telephone interviews. Patients receiving preoperative dialysis were excluded from the study. We identified 9461 consecutive patients (≥30 years old) who had undergone coronary

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Abbreviations and Acronyms

CABG = coronary artery bypass grafting
CPB = cardiopulmonary bypass
eGFR = estimated glomerular filtration rate
RIFLE = Risk, Injury, Failure, Loss, and End-Stage Kidney Disease
STS = Society of Thoracic Surgeons

artery bypass grafting (CABG) surgery, cardiac valve surgery, or both between January 1, 1995, and December 31, 2006. Patients' serum creatinine levels were obtained from a system-wide electronic patient record database.

Study End Points

Serum creatinine levels were measured as part of clinical care before and after surgical intervention. The testing was carried out at the Clinical Chemistry Laboratory of the Johns Hopkins Hospital with commercial kits (Roche Diagnostics, Indianapolis, Ind) that had a sensitivity of 0.2 mg/dL (1995 to February 2003) or 0.1 mg/dL (February 2003 onward). The last measurement before the day of surgical intervention was considered the baseline value when more than 1 preoperative serum creatinine result was available. In determining the change from baseline values, we considered the maximum serum creatinine level as the highest level obtained during the first 7 days after surgical intervention. The estimated glomerular filtration rate (eGFR) was estimated by using the Modification of Diet in Renal Disease equations: $eGFR = 175 \times (Scr)^{-1.154} \times (Age)^{-0.203}$ in milliliters per minute per 1.73 m^2 of body surface area (the product was multiplied by 0.742 if the subject was female or by 1.212 if the subject was African American).[10,11]

There is no universally accepted definition of renal injury after cardiac surgery. We based our definition of renal injury on the Risk, Injury, Failure, Loss, and End-Stage Kidney Disease (RIFLE) criteria: (1) *risk* when eGFR decreases greater than 25% from baseline value; (2) *injury* when eGFR decreases greater than 50% from baseline value; and (3) *failure* when the plasma creatinine level is 350 μmol/L or greater or when there is an acute increase of 44 μmol/L or greater from the baseline value.[12] We also included new dialysis as an indicator of renal failure. The primary renal outcome of this study was the composite end point of renal injury or failure.

Statistical Analyses

Relevant clinical, demographic, and outcome variables from files in our STS databases were extracted and merged into a STATA 10.0 data set, which was used for all statistical analyses (StataCorp, College Station, Tex). In initial confirmatory analyses we considered univariate tests of associations between operative mortality and renal injury on sex, clinical measures, and complications from surgical intervention. These analyses consisted of the χ^2 test for categorical variables and the Student's t test or, when appropriate, the nonparametric Kruskal–Wallis test for continuous measures. Demographic and operative outcome variables with a P value of less than .1 in univariate analyses or those that were deemed to be clinically significant were considered in the multivariable logistic regression model predicting renal injury and operative mortality. Here operative mortality was defined as death from any cause that occurred during hospitalization or after discharge but within 30 days after surgical intervention. We considered spline parameters to account for possible nonlinear associations for continuous variables on renal injury or operative mortality. Definitions for clinical variables were those used by the STS database found at http://www.sts.org/sections/stsnationaldatabase/datamanagers/adultcardiacdb/datacollection/index.html.

RESULTS

Patient characteristics for the 9150 survivors and the 311 patients who experienced operative mortality are listed in Table 1 according to patient sex. Operative mortality was higher for women than for men (4.2% vs 3.0%, $P = .001$). Compared with survivors, women and men who died were older and were more likely than surviving patients of the same sex to have low eGFRs before surgical intervention. Other differences between survivors and nonsurvivors for each sex are noted in Table 1. Comparisons of the frequency of variables that differed between nonsurviving women and men are listed in Table 1. For the most part, variables associated with mortality were similar between women and men, with a few exceptions. Compared with nonsurviving men, women who experienced operative mortality had a higher frequency of diabetes, left ventricular ejection fraction of less than 50%, hypercholesterolemia, hypertension, prior myocardial infarction, and current smoking. Nonsurviving women had a lower frequency of triple-vessel coronary artery disease than did nonsurviving men. Differences in the type of operation between female and male nonsurvivors were noted.

Baseline eGFR, the frequency of different levels of reduced eGFR, and the distribution of RIFLE criteria for renal injury by patient sex are listed in Table 2. Women had a lower eGFR before surgical intervention than did men, and higher frequencies of women had eGFRs of less than 30 mL/min per 1.73 m^2 of body surface area and eGFRs of 30 to 60 mL/min per 1.73 m^2 of body surface area. Forty-four women and 33 men were reported to have new dialysis after surgical intervention but were not listed as having renal injury or failure based on the RIFLE criteria (because of dialysis correction of serum creatinine levels); these patients were included in the renal injury outcome. The primary renal injury outcome occurred in 5.1% of women and 3.6% of men ($P < .001$). The χ^2 value for each category is provided in Table 2 and shows that most of the weighting for the combined P value was from the RIFLE categories of ''risk'' or ''injury,'' suggesting that these 2 categories drive the statistical association between sex and RIFLE criteria.

Characteristics for surviving and nonsurviving patients with and without renal injury for each sex are listed in Table 3. Although many univariate predictors of mortality for patients with renal injury were similar for women and men, differences were noted. As in Table 1, the frequency of variables that differed between survivors and nonsurvivors for each sex are listed, and comparisons between nonsurviving women and men are provided for these variables. In contrast to nonsurviving men, women with renal injury who died had a higher frequency of left ventricular ejection fraction of less than 30%, hypercholesterolemia, hypertension, triple-vessel coronary artery disease, and significant left main coronary stenosis. Nonsurviving women with renal injury had

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