## Acute Renal Failure After Cardiac Surgery for Carcinoid Heart Disease: Incidence, Risk Factors, and Prognosis

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• Background: Cardiac surgery for carcinoid heart disease may be associated with acute renal failure (ARF) and multiorgan dysfunction postoperatively. This study was performed to determine the incidence, risk factors, and prognosis of ARF after cardiac surgery for carcinoid heart disease. Methods: This is a case-control study of 86 consecutive patients who underwent cardiac surgery for carcinoid heart disease. ARF is defined as hemodialysis requirement or serum creatinine level 50% greater than baseline, resulting in an estimated creatinine clearance less than 40 mL/min (0.67 mL/s). Preoperative, operative, and postoperative characteristics were examined and compared between groups to determine risk factors and prognosis of ARF. Results: ARF occurred in 22% of cases (19 of 86 patients). Preoperative characteristics and type of procedure did not differ between groups. Operative variables associated with ARF by means of univariate analysis included longer surgical and bypass times, intra-aortic balloon pump use, and perioperative epinephrine requirement. Postoperatively, ARF was associated with epinephrine use, prolonged mechanical ventilation, prolonged intensive care unit admission, and higher Acute Physiology and Chronic Health Evaluation II scores. Perioperative mortality in the ARF group was 47% versus 4.5% in the control group (odds ratio, 36.1; 95% confidence interval, 8.0 to 261.8). Conclusion: ARF developed in a relatively high proportion of this cohort, but traditional preoperative risks failed to predict post-cardiac surgery ARF. Variables closely related to perioperative hemodynamic compromise were associated with ARF. ARF portends a particularly poor prognosis in this cohort that is explained largely by multiorgan failure syndrome. Am J Kidney Dis 45:826-832.

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INDEX WORDS: Acute renal failure (ARF); carcinoid heart disease; thoracic surgery; risk factor.

► ARCINOID SYNDROME is characterized by cutaneous flushing, diarrhea, and wheezing caused by the release of vasoactive products from metastatic carcinoid tumors.<sup>1-3</sup> Carcinoid heart disease occurs in more than 50% of patients with carcinoid syndrome and carries a poor prognosis.<sup>1,2</sup> Manifestations of carcinoid heart disease include primarily right-sided valvular disease, including the combination of tricuspid valve regurgitation and mixed pulmonary valve regurgitation and stenosis. Subsequent right-sided heart failure results in substantial morbidity and mortality.<sup>3,4</sup> Cardiac surgery to replace affected valves has improved symptoms in surgical survivors and possibly promoted regression of carcinoid metastases, but has been

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associated with significant perioperative morbidity in select patients.<sup>4-6</sup>

Acute renal failure (ARF) complicating cardiac surgery is a well-known independent risk factor for postoperative death.<sup>7</sup> Depending on the definition, ARF occurs in 3% to 28% of patients after cardiac surgery.8-12 Post-cardiac surgery ARF requiring dialysis occurs less frequently, with an incidence of 1% to 15%.7,12,13 Previously reported risk factors for ARF after cardiac surgery include older age, baseline renal insufficiency, diabetes mellitus, prior cardiac surgery, left ventricular dysfunction, heart failure, and perioperative variables associated with hemodynamic compromise (intra-aortic balloon pump [IABP] use, prolonged bypass, and reoperation for bleeding).<sup>9,12,14-16</sup> Cardiac valve surgery, with or without simultaneous coronary artery bypass grafting (CABG), has been associated with a greater incidence of postoperative renal dysfunction than CABG alone.9,14,17

A number of studies have reported outcomes of cardiac surgery for patients with carcinoid heart disease.<sup>4,5,18,19</sup> In a study by Robiolio et al,<sup>18</sup> 5 of 8 patients died within the first 30 days postoperatively, and 1 of the 5 deaths was attributed to renal failure. In another study of surgical outcomes of 26 patients with carcinoid heart disease, 2 of 9 early postoperative deaths were

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secondary to multisystem failure.<sup>4</sup> Although these studies showed that renal failure and multisystem dysfunction can complicate the surgical management of patients with carcinoid heart disease, no study specifically examined the incidence and outcome of ARF in this setting.

The purpose of the present study is to determine the incidence and prognosis of ARF after cardiac surgery for carcinoid heart disease. Additionally, we sought to identify risk factors for postoperative ARF and determine whether previously reported risk factors for post-cardiac surgery ARF were applicable to this unique population.

## METHODS

Our institutional review board reviewed and approved this study protocol. We retrospectively reviewed medical records of 86 patients with carcinoid heart disease who underwent 90 consecutive cardiac surgeries at our institution between July 7, 1985, and October 31, 2001. Four patients underwent 2 operations, but only data related to the first surgery were included in this study. Minnesota Statute 144.335 (Patient Consent to Release of Records) was observed with respect to patient confidentiality. This law states that patients have the right to deny access to their medical records for the purpose of research.

Preoperative clinical characteristics, including patient demographics, New York Heart Association class, left ventricular ejection fraction, urinary 5-hydroxyindoleacetic acid (5-HIAA) level, serum blood urea nitrogen level, serum creatinine level, estimated creatinine clearance, preexisting hypertension or diabetes mellitus, and preoperative use of angiotensin-converting enzyme inhibitors or nonsteroidal anti-inflammatory drugs, were abstracted.

Surgical variables that were examined included type of surgical procedure, volume and rate of urine output, surgical time, cardiopulmonary bypass (CPB) and aortic cross-clamp time, nadir surgical mean arterial pressure, use of epinephrine, IABP use, need for reinitiation of CPB, and need for surgical reexploration for hemorrhage.

Surgical and anesthetic management in a subset of this cohort has been described previously.<sup>5</sup> Specifically, octreotide was administered as necessary to ameliorate signs and symptoms of carcinoid crisis.

Postoperative variables that were assessed included peak serum blood urea nitrogen and creatinine levels, type of antibiotic used, occurrence of sepsis as defined by attending clinicians, type and duration of vasopressor support, duration of mechanical ventilation, Acute Physiology and Chronic Health Evaluation II (APACHE II) scores, intensive care unit (ICU) days, and total hospital days. APACHE II scores were calculated for all patients for the first 24 hours postoperatively and for the day of dialysis therapy initiation in patients requiring hemodialysis.<sup>20</sup> Perioperative death is defined as any death occurring within 30 days of surgery. Date and cause of death were obtained from death certificates. In patients meeting criteria for ARF, onset of oliguria, need for dialytic support, and type and duration of dialytic support were recorded. Oliguria is defined as urine output less than 400 mL/d.

ARF was defined a priori as the need for hemodialysis or an increase in serum creatinine level greater than 50% above baseline, resulting in an estimated creatinine clearance of less than 40 mL/min (0.67 mL/s), calculated using the equation of Cockcroft and Gault.<sup>21</sup> We believed the creatinine clearance cutoff value would approximate the level of renal dysfunction that, in clinical practice, would result in alterations in patient management (for example, antibiotic dosing). Nineteen patients met criteria for postoperative ARF. The 67 patients without ARF served as a control group.

Statistical analyses used Fisher exact test for comparison of categorical variables and Wilcoxon rank-sum test for comparison of continuous values. Statistical significance was assumed at *P* less than 0.05. The number of outcome events did not permit multivariable analysis; therefore, we identified risk factors by means of univariate analysis. With respect to ARF, logistic regression was used to determine odds ratios for perioperative death, both with and without adjustment for severity of illness (APACHE II scores). Statistical analyses were performed using a statistical software package for personal computers (JMP, version 5.0; SAS Institute Inc, Cary, NC). Continuous data are expressed as mean  $\pm$  SD.

## RESULTS

Postoperative ARF occurred in 22% of patients (19 of 86 patients) in this study. Compared with patients without ARF, there were no statistically significant demographic or baseline clinical differences (Table 1). Variables associated with the extent of carcinoid heart disease, including New York Heart Association class, left ventricular ejection fraction, and urinary 5-HIAA level, did not differ between groups (Table 1).

Type of procedure and complexity of surgery, based on the number of valves simultaneously replaced or repaired, did not differ between groups (Table 2). Intraoperative variables are listed in Table 2. CABG was performed at the time of valve surgery in 18% of patients (12 of 67 patients) in the no-ARF group and 5% of patients (1 of 19 patients) in the ARF group (P =0.28). By means of univariate analysis, patients with postoperative ARF were more likely to have prolonged surgical time (P = 0.0024) and CPB time (P = 0.035). Patients with ARF were more likely to require epinephrine intraoperatively (P = 0.0006) or an IABP for perioperative hemodynamic support (P = 0.0003). Intraoperative use of somatostatin analogue and total dose

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