The Risk of Acute Kidney Injury With Co-Occurrence of Anemia and Hypotension During Cardiopulmonary Bypass Relative to Anemia Alone

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Background. **Postoperative acute kidney injury (AKI) is a common serious consequence of cardiac surgery. One recent study found higher AKI rates when anemia and hypotension occurred during cardiopulmonary bypass (CPB) relative to anemia alone. To revalidate this post hoc observation we analyzed detailed data from a large cardiac surgery cohort.**

Methods. **Patient, procedural, and outcome data were collected for nonemergent aortocoronary bypass and valve surgeries between July 2001 and September 2012. The occurrence of AKI (as defined by the Acute Kidney Injury Network criteria) was analyzed relative to known renal risk factors, and CPB hematocrit and blood pressure determinations in univariate and multivariable linear regression analyses.**

Results. **In our 3,963-patient cohort, we did not observe different AKI rates with the co-occurrence of anemia and hypotension relative to anemia alone (41.6% versus 44.3%; $p = 0.39$). Secondary analyses using linear definitions for AKI, CPB anemia, and hypotensive burden, and assessing for coincident timing also did not demonstrate significant association of anemia and hypotension with AKI risk relative to anemia alone.**

Conclusions. **In a large cohort of cardiac surgery patients, we did not confirm any association of cardiac surgery–related AKI risk with the co-occurrence of hypotension and anemia during CPB relative to anemia alone. More detailed analyses also failed to support an anemia-hypotension interaction. Additional studies are required to better understand the relationship among anemia, hypotension during CPB, and postoperative AKI, but existing evidence is insufficient to support changes in clinical practice.**

(Ann Thorac Surg 2014;97:865–72)

Acute kidney injury (AKI) is a common serious complication of cardiac surgery associated with postoperative morbidity, mortality, and increased cost. As many as 30% of patients undergoing nonemergent cardiac surgery procedures sustain AKI, with 1% to 2% requiring renal replacement therapy [1-3]. Even modest AKI episodes are linked to adverse outcome [4], and patients requiring new-onset postoperative dialysis have mortality rates exceeding 60% [5]. Many perioperative AKI risk factors relate to variables that may reduce oxygen delivery to tissues, such as anemia and hypoperfusion [1].

Prevention remains the primary strategy to combat AKI. Given the kidney's vulnerability to ischemia/reperfusion injury, factors amenable to treatment such as anemia and hypotension during cardiopulmonary bypass (CPB) have therefore gained attention [6, 7]. We and others have previously reported an association of low hematocrit values (eg, less than 21% to 24%) during CPB with increased AKI risk [8-10]. Notably, low blood pressure during CPB (eg, less than 50 mm Hg with preserved perfusion rates) has not been associated with changes in AKI risk in several studies [8, 11-13]. However, a recent study noted increased AKI risk when CPB anemia and hypotension occurred, compared with anemia alone [13]. The researchers highlighted the secondary post hoc nature of their observation, and the importance that it be validated in another patient population. Therefore, we tested the hypothesis that AKI risk is increased when anemia and hypotension occur during CPB relative to anemia alone.

Patients and Methods

Patient Selection

With Institutional Review Board approval, a study sample was identified from the population of consecutive adult patients undergoing on-pump nonemergent (aortocoronary bypass graft) CABG and valve surgery at a single institution between July 2001 and September 2012 (Fig 1). Excluded were patients with end-stage renal disease,

Accepted for publication Sept 16, 2013.

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Published by Elsevier Inc

0003-4975/$36.00
http://dx.doi.org/10.1016/j.athoracsur.2013.09.060

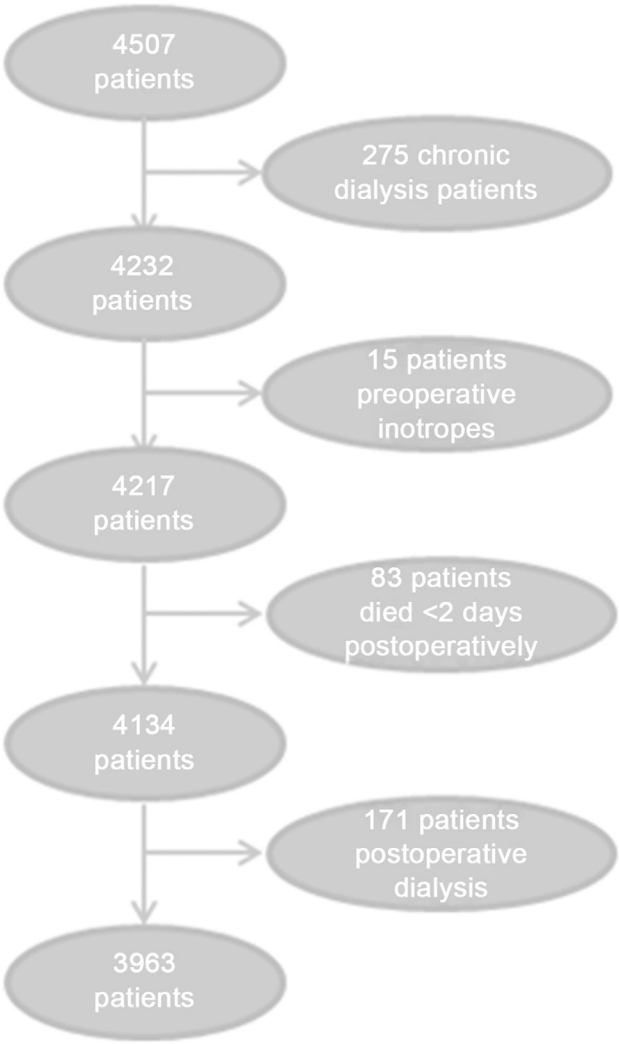

Fig 1. Flow chart identifying criteria for patient inclusion in the study sample.

preoperative need for inotropes, and redo or emergent procedures. Additional postprocedure exclusion criteria included patients requiring renal replacement therapy or death within the first 2 days, because in these circumstances serum creatinine values do not accurately reflect the degree of AKI. Patient and procedural data collected included previously known renal risk factors (Table 1) [1, 3]; these were obtained from the Duke Databank for Cardiovascular Diseases. The databank is prospectively compiled during the hospital stay from contemporaneous medical records, custom data sheets, and laboratory results; quality assurance includes subsequent random chart review for completeness. Survival data was provided by the Duke Clinical Research Institute Follow-Up Group [14]. Data pertaining to CPB were obtained from automated anesthesia records (Innovian Anesthesia; Dräger Medical, Telford, PA). Information pertaining to the postoperative course were from the prospectively gathered Duke Quality Measurement and Management Initiative database.

Renal Function Assessment

Preoperative creatinine and daily postoperative serum creatinine values were measured until hospital discharge as per institutional protocol. Serum creatinine was measured using the Jaffe technique (UniCel DxC 800; Beckman Coulter, Brea, CA) with a normal range of 31 to 76 μmol/L (0.4 to 1.0 mg/dL) for females and 46 to 99 μmol/L (0.6 to 1.3 mg/dL) for males. Preoperative serum creatinine was obtained within 1 week before surgery, and defined as the value recorded closest to but not on the day of surgery. The peak postoperative creatinine ($Cr_{max}Post$) value was the highest of the daily in-hospital postoperative creatinine values. The primary outcome of AKI was characterized using Acute Kidney Injury Network criteria [15] modified to reflect the absence of urine output data (postoperative serum creatinine rise greater than 50% or 0.3 mg/dL within a 48-hour period), as in the study by Haase and colleagues [13]. Linear characterizations of AKI were also generated, using the preoperative to peak postoperative change in serum creatinine expressed as an absolute value (ΔCr) or as a percentage of CrPre (%ΔCr).

Anemia and Hypotension

During CPB, hematocrit was assessed every 30 minutes (GEM Premier 3000 and IL 682 CO-Oximeter; Instrumentation Laboratories, Bedford, MA). Mean arterial blood pressure was recorded automatically every 30 seconds; values below 20 mm Hg or above 299 mm Hg were considered erroneous and excluded from analysis. A previously reported index of CPB hypotension, logTM50 [10] that was also employed for this purpose in the paper by Haase and colleagues, was then calculated for each patient to quantify a burden of hypotension during CPB. LogTM50 is the log of the degree-duration integral of mean CPB blood pressures below 50 mm Hg multiplied by the duration in minutes. For example, a 10-minute episode during which the blood pressure was 30 mm Hg would be reflected by a TM50 of 200 min · mm Hg, as calculated by the following: $10 \text{ min} \times (50 - 30 \text{ mm Hg}) = 200 \text{ min} \cdot \text{mm Hg}$. Likewise, a 60-minute episode at 40 mm Hg would accumulate a TM50 of 600 min · mm Hg.

Anesthesia and Surgery

Anesthesia was managed per the attending anesthesiologist's preference. Use of agents with potential renal effects (eg, intravenous dopamine, antifibrinolytic agents) was not regulated. Although availability of the various antifibrinolytic agents (eg, aprotinin) changed during the study period, administration of ε-aminocaproic acid was typical for elective nonemergent coronary artery bypass graft surgery and valve procedures such as those in the sample population throughout the study period [10].

The CPB circuit was primed with mannitol (50 g 25% solution), sodium bicarbonate (50 mEq 8.4% solution), heparin (10,000 units), albumin (50 mg 25% solution), crystalloid solution (Normosol; Hospira, Lake Forest, IL), and packed red blood cells if necessary to achieve a hematocrit no lower than 0.20 during CPB. Extracorporeal