A Patient with AKI after Cardiac Surgery

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Abstract

Up to 30% of patients undergoing cardiac surgery develop AKI, with 1% requiring RRT. AKI is an independent risk factor for morbidity and mortality. Postoperatively, even minimal changes in serum creatinine are associated with a substantial increase in mortality. No intervention has been definitely proven effective in reducing kidney injury. The successful prevention and management of AKI involves identifying patients at risk for AKI, recognizing subtle abnormalities in a timely manner, performing basic clinical assessments, and responding appropriately to data obtained. With that in mind, in this Attending Rounds, a woman with AKI in the setting of cardiac surgery is presented to highlight the use of history, physical exam, hemodynamic monitoring, laboratory data trends, and urine indices in establishing the correct diagnosis and appropriate management.


Introduction

A 71-year-old woman was admitted for elective re-do coronary artery bypass graft (CABG). Cardiac angiography 6 days before admission revealed severe three-vessel coronary artery disease with preserved ejection fraction. Past medical history was significant for coronary artery disease with previous three-vessel CABG, hypertension, morbid obesity, hyperlipidemia, stage 3 CKD with baseline creatinine of 1.5 mg/dl, and colon cancer status post colectomy and ileorectal anastomosis. Home medications included benazepril, amlodipine, furosemide, isosorbide dinitrate, metoprolol, rosuvastatin, aspirin, and ferrous sulfate.

On admission, her vital signs were temperature=98.0°F, BP=162/83 mmHg, pulse=51/min, respiration=16/min, weight=108 kg, and O2 saturation=99% on room air. Examination revealed clear breath sounds, 2/6 systolic murmur at the sternal border, benign abdomen, and trace ankle edema bilaterally. Admission laboratory values are noted in Table 1. She was given intravenous cefazolin (1 g every 8 hours) preoperatively and underwent off-pump three-vessel re-do CABG without complications. Intraoperatively, she received 1 unit blood transfusion by cell salvage. Postoperatively, she developed atrial fibrillation that was rate-controlled with amiodarone and metoprolol. She was also given a single 500-ml bolus of hydroxyethyl starch for a central venous pressure (CVP) of 8 cm H2O. She was transferred to the floor on postoperative day 2. Cefazolin was discontinued on transfer, and her urinary catheter was removed. Benazepril and furosemide were held.

On postoperative day 3, she developed respiratory distress and was treated with intravenous furosemide (80 mg daily) for the next 4 days, with worsening BUN and creatinine concentrations (Table 1). Unfortunately, the patient’s intake and output were not consistently recorded. On postoperative day 8, cardiac surgery inserted a dialysis catheter and consulted nephrology for dialytic management of volume overload.

In the 24 hours preceding consultation, the patient was noted to have systolic BPs as low as 90 mmHg, and low-dose dopamine had been added to increase renal perfusion. At the time of consultation, the patient was confused and anxious with the following vital signs: temperature=97.0°F, BP=103/66 mmHg, pulse=98/min, respiration=26/min, weight=119 kg, and O2 saturation=93% on 4-L nasal cannula. Urine output was documented as 450 ml over the past 24 hours. She was noted to be in mild respiratory distress with no jugular venous distention. Pulmonary examination revealed a few scattered crackles on the left and decreased breath sounds at the bases. Cardiac examination was significant for an irregular rhythm. On abdominal examination, she had decreased bowel sounds and mild distention. No ascites was detected. She had increased bilateral lower extremity edema. There was no asterixis, rash, or evidence of embolic phenomena.

Chest x-ray showed a large cardiac silhouette with mild venous congestion and small bilateral effusions. Abdominal x-ray showed diffuse gaseous distention of the bowel consistent with adynamic ileus. Laboratory tests are shown in Table 1, with additional tests showing phosphorous=7.0 mg/dl, calcium=8.8 mg/dl, albumin=3.2 g/dl, total bilirubin=1.6 mg/dl, indirect bilirubin=1.0 mg/dl, alkaline phosphatase=70 IU/L, alanine transferase=319 IU/L, aspartate transaminase=357 IU/L, and international normalized ratio=2.9 (on warfarin). Her medications at time of consultation included dopamine, amiodarone, esomprazole, aspirin, metoprolol, warfarin, and pain medications.

Nephrology requested urinary catheter placement, renal ultrasound, urinalysis, and urine chemistries. A nasogastric tube was placed with moderate output. Renal ultrasound showed the right kidney to be 10.6 cm and the left kidney to be 9.9 cm, with no ascites or obstruction. Urinalysis revealed specific gravity of
1.020, pH of 5.0, 0–2 red blood cells, and 0–5 white blood cells. Urine eosinophils were negative, and urine microscopy revealed multiple hyaline casts. Urine sodium was 10 mEq/L, with fractional excretion of sodium (FENa) at 0.2% and fractional excretion of urea (FEurea) at 14%. Despite relief of abdominal distention by nasogastric suction, the patient’s respiratory status worsened with O2 saturation at 86%. Nephrology recommended transferring the patient to the cardiac care unit for closer monitoring.

Case Discussion
This patient developed AKI in the setting of cardiac surgery. Cardiac surgery–associated AKI (CSA-AKI) is associated with increased morbidity and mortality; 5% to 30% of cardiac surgery patients experience some degree of AKI, depending on the patient’s risk factors before surgery (1). The Cleveland Clinic risk score for the postoperative need of dialysis in patients undergoing cardiac surgery identified women, surgery type (valve replacement with or without CABG), preoperative cardiovascular status (such as congestive heart failure or use of an intra-aortic balloon pump), and preoperative renal function to be significant predictors of CSA-AKI (2). The Cleveland Clinic score has been validated in multiple cohorts and shown to have fairly high discrimination in tested populations (3,4).

Other risk factors specific for CSA-AKI include advanced age, diabetes mellitus, morbid obesity (defined as a body mass index >40 kg/m²), and intravenous contrast exposure (5–7) (Table 2). Studies on the association between the risk of postoperative AKI and the timing of contrast exposure before cardiac surgery have shown mixed results. Some studies have shown that the risk of AKI after CABB is inversely related to the time between cardiac angiography and CABG, including one recent meta-analysis that found that a time interval of 1 day or less between angiography and on-pump cardiac surgery was associated with increased risk of AKI (8,9). Others have reported no increased risk of AKI based on timing of contrast (10). In our case, the patient’s angiogram preceded surgery by more than 5 days. According to the Cleveland Clinic risk score, our patient’s estimated risk for dialysis after cardiac surgery was 1.8% given her risk factors: woman, CKD, redo surgery, and morbid obesity (2). No validated scoring system exists for predicting the risk of less severe AKI.

Differential Diagnosis
The pathophysiology of CSA-AKI is multifactorial and results from vascular and tubular injury, ischemia and reperfusion injury, neurohumoral activation, inflammation,
oxidative stress, metabolic abnormalities, and exogenous and endogenous toxins (11). Many cardiac surgery patients have impaired renal autoregulation caused by conditions of reduced renal perfusion or decreased renal reserve, such as CKD, and administration of drugs, such as nonsteroidal anti-inflammatory drugs, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and contrast (12). The role of perioperative angiotensin-converting enzyme inhibitors and/or angiotensin receptor blockers in CSA-AKI is controversial. Although some observational studies suggest that the use of these medications before cardiac surgery is associated with a higher risk of postoperative AKI and death, other studies have reported no increase in the risk of postoperative AKI after CABG or even a decreased incidence of AKI (12–14). The patient was also on a statin before surgery. Statins have been shown to attenuate inflammation and oxidative stress. Although some studies have shown that perioperative statin use can reduce the incidence of postoperative AKI or the need for RRT, other studies have not supported these findings (15–19).

Cardiac surgery induces a systemic inflammatory response from operative trauma, exposure to the cardiopulmonary bypass (CPB) circuit, blood transfusions, and hypothermia (20–23). CPB decreases the effective renal perfusion pressure up to 30% and contributes to ischemia and reperfusion injury (24). Renal perfusion is worsened by longer bypass times, intra-aortic balloon pump use, cardiogenic shock, vasopressor and inotrope use, and hemodilution with hematocrit <25% (25–27). Evidence also suggests that lack of pulsatile blood flow can impair kidney perfusion, despite relative preservation of mean arterial pressure (28). Macroscopic and microscopic emboli are released during aortic cannulation and aortic clamp placement and release (29). The shearing force of CPB can cause hemolysis with increased free plasma hemoglobin (30). Free plasma hemoglobin leads to organic and inorganic oxygen radical reactions, lipid peroxidation, and the formation of damaging hydroxyl radicals (31). Finally, ischemic muscle injury during surgery can result in rhabdomyolysis.

Additional etiologies of AKI include other states of renal hypoperfusion (e.g., hypovolemia, heart failure, and sepsis), major vascular occlusion, intrinsic nonischemic renal disease (e.g., GN and interstitial nephritis), medications, and obstructive uropathy. Plaque rupture with cholesterol embolization to distal small- and medium-sized arteries after cardiac angiography and/or cardiovascular surgery causes AKI and ischemic end organ damage through mechanical plugging and inflammation. In acute decompensated heart failure (ADHF), elevated renal venous pressure causes distended renal venules with increased tubular fluid pressure and backleak, leading to venous congestion and cardiorenal syndrome type 1 (CRS1) (32). The increased renal venous pressure also stimulates local sympathetic nerve activity and the renin angiotensin aldosterone system, causing intra-renal arterial vasconstriction. An elevated CVP, indicative of increased renal venous pressure, has been shown to be the strongest factor for development of AKI in the setting of CRS1 and is an independent predictor of AKI after cardiac surgery (33). Ascites and bowel and abdominal wall edema from ADHF can increase intra-abdominal pressure (IAP), leading to worsening renal perfusion and abdominal compartment syndrome (ACS) (32). Other nonsurgical risk factors for ACS include mechanical ventilation, elevation of the head of bed, obesity, ileus, sepsis, large volume resuscitation, and pancreatitis (34). Finally, normotensive ischemic AKI can occur in the absence of overt hypotension when a patient attains a lower BP than the patient’s range of renal autoregulation (35). Risk factors include vascular disease, hypertension, and CKD.

**Back to Our Patient**

Based just on her history and clinical course, our patient was initially assumed to have renal ischemia from surgery, which was exacerbated by postoperative hypotension and aggressive diuresis, leading to acute tubular necrosis (ATN). However, her physical examination findings did not support hypovolemia and seemed more consistent with volume overload, despite a normal jugular venous pressure; moreover, she was 11 kg over her preoperative weight. Her creatinine began to rise on postoperative day 3. At that time, she had already transferred from the cardiac care unit to the floor and was developing symptoms of shortness of breath. Her serum creatinine levels on postoperative days 1 and 2 were lower than her baseline creatinine, suggesting possible dilution from intravenous fluids and positive fluid balance status. Because her surgery was off pump, she did not have the risks of renal ischemia associated with CPB. A meta-analysis of 22 randomized controlled trials found that off-pump CABG was associated with 40% lower odds of postoperative AKI (P=0.002) (36). Using propensity score-adjusted analyses in a large cohort of over 742,909 patients, Chawla et al. (37) suggested that patients with CKD experienced less death or incident RRT when treated with off-pump compared with on-pump CABG. These findings are supported by a recent large randomized controlled trial of 4752 patients, which showed off-pump CABG to decrease the risk of AKI (relative risk, 0.87; 95% confidence interval, 0.80 to 0.96; P=0.01) (38). Our patient also did not have intraoperative hypotension, significant blood loss, multiple blood transfusions, or evidence of hemolysis by laboratory values.

Potential nephrotoxic medications that she received perioperatively included iodinated contrast, antibiotics, and hydroxyethyl starch. Contrast-induced nephropathy was unlikely, because she received the cardiac angiogram more than 5 days before surgery. Drug-induced acute interstitial nephritis (AIN) from cefazolin was also unlikely, because AIN is usually associated with a slowly rising serum creatinine developing after 7–10 days of drug exposure. Furthermore, the antibiotic was discontinued before the rise in serum creatinine. Cholesterol emboli after heart catheterization or surgery were unlikely, because there were no systemic findings of embolic phenomenon. Hydroxyethyl starch has been associated with increased rates of AKI and need for RRT (39). Because our patient received only a single bolus and the AKI developed much later, it was doubtful that it contributed to her AKI. Given all of the above findings, her AKI was not thought to be caused by preoperative or intraoperative events.

Other causes of AKI considered were decreased cardiac performance, sepsis, volume depletion, hemodynamic instability, and ACS. Pulmonary embolus was thought to be unlikely given her therapeutic international normalized ratio and negative lower extremity venous Dopplers. She
did not have a fever, a significantly elevated white blood cell count, or an obvious source of sepsis. Her increase in serum creatinine concentration seemed to correlate with her worsening respiratory status and clinical symptoms of volume overload. However, intravascular volume status was difficult to assess with her morbid obesity, and she did not have obvious jugular venous distention, which would be expected in CRS1. Moreover, despite diuretic therapy with negative fluid balance status, her breathing did not improve, and the serum creatinine concentration continued to worsen. With relief of her abdominal distention after nasogastric suction, ACS was thought to be unlikely, although she did not have bladder pressure measured. The possibility of normotensive ischemic AKI was entertained, because her systolic BP remained on the low side compared with her BP values before surgery. Accordingly, it was thought that her AKI was either prerenal (caused by decreased effective arterial volume from a cardiac pump problem) or had already advanced to ATN from prolonged renal hypoperfusion. Urine studies were used to help differentiate the diagnosis.

Her urinalysis had a high specific gravity, and urine microscopy showed hyaline casts with no cellular sediment, making ATN, AIN, and GN less likely. Her FENa and FEurea were both low. Despite a prerenal state, the FENa can be different from in CKD or with diuretic use. The FEurea is more sensitive and specific in the setting of diuretics (40). Conversely, an FENa<1% may be seen in patients with contrast-induced nephropathy, GN, and obstruction (41). The patient’s BUN to creatinine ratio of >20, low urine sodium, low FENa, low FEurea, and benign urine sediment suggested that she had prerenal AKI and not ATN. With her normal jugular venous pressure in the setting of worsening dyspnea and lower extremity edema, additional assessment of her volume status was needed.

Assessment of Intravascular Volume in Critically Ill Patients

The assessment of volume status in surgical and critically ill patients can be difficult. There is no single ideal technique for assessing volume status or volume responsiveness (characterized by an increase in cardiac output with a fluid challenge). Often, multiple methods have to be used. Static pressure measurements include CVP, pulmonary artery occlusion pressure, and echocardiography. Although CVP and pulmonary artery occlusion pressure have traditionally been used to guide fluid management, numerous studies have shown poor correlation of these parameters with predicting volume status, fluid responsiveness, and cardiac performance (42). Multiple factors affect the reliability of these parameters, including changes in venous tone, intrathoracic pressures (positive end expiratory pressure), left and right ventricular compliance, and IAP. Trending of the CVP over time or in response to a fluid challenge may provide more reliable information regarding intravascular volume status than a single isolated value. Transesophageal echocardiography has been used to predict fluid responsiveness by assessing the left ventricular end diastolic area. However, interpretation is limited without baseline echocardiographic measurements for comparison (42).

Dynamic pressure measurement techniques include pulse pressure variation (PPV), stroke volume variation (SVV), esophageal Doppler monitoring, respiratory variation in vena cava diameter, and straight leg raising. PPV and SVV reflect respiratory changes in arterial pressure during positive pressure ventilation and more reliably predict whether a patient will benefit from volume. The magnitude of these changes is affected by the fluid status of the patient; the greater the variation, the more likely the patient’s hemodynamics will improve with volume. PPV is a more reliable measure than SVV, because it is a direct measurement, whereas SVV is calculated from pulse contour analysis. PPV value of >13% has the highest sensitivity and specificity in predicting volume responsiveness (43). Both PPV and SVV measurements are only reliable in patients who are mechanically ventilated and without cardiac arrhythmias; accuracy can also be affected by titration of inotropic or vasopressor agents (43). Because PPV can be affected by tidal volume, the tidal volume must be at least 8 ml/kg for accurate results. Fluid responsiveness can also be predicted by the respiratory variation in aortic blood flow as assessed by esophageal Doppler or transesophageal echocardiography in patients on positive pressure ventilation.

Visualization of the inferior vena cava (IVC) with echocardiography or transabdominal ultrasound can be used to assess both volume status and volume responsiveness and has been increasingly used for intravascular volume assessment. A collapsed IVC suggests volume depletion, whereas a distended IVC reflects a high right atrial pressure. In hypovolemia, the percentage collapse of the IVC is proportionally higher than in volume overload states and can be quantified by the calculation of the collapsibility or caval index. The caval index is written as a percentage: 100% indicates almost complete collapse, whereas 0% signifies minimal collapse. In hypovolemia, the IVC diameter will be decreased, and the percentage collapse will be greater than 50%. Patients with increased intravascular volume will have a large IVC diameter and minimal collapse on inspiration. In a spontaneously breathing patient, a 50% decrease in IVC diameter with inspiration indicates volume responsiveness; in a ventilated patient, a 12% increase in IVC diameter with inspiration predicts volume responsiveness (44). The technique is difficult to perform with accuracy in obese patients and unreliable in patients with increased IAP. Passive leg raising transiently increases venous return and cardiac output in patients who are preload-responsive. While the patient’s upper body is kept horizontal, the legs are passively raised to 45°. An increase in cardiac output>10% indicates volume responsiveness (43). Passive leg raising is unreliable in patients with elevated IAP.

Subsequent Clinical Course

In our patient, hemodynamic monitoring showed a CVP of 9 cm H₂O. Her IVC was 2 cm in diameter with minimal IVC compressibility by bedside ultrasound, indicating that her volume status was not fluid-responsive. Transthoracic echocardiogram revealed a large posterior hematoma behind the right atrium compressing the right atrium and producing tamponade physiology. Thus, inadequate forward cardiac output in the setting of inflow compression was thought to explain her inability to diurese with resultant
AKI. She was bolused with 1 L normal saline and evaluated by cardiac surgery for tamponade. Because she had no pulsus paradoxus with deep inspiration, surgery felt initially that her echocardiography results were not physiologically important and did not explain her AKI, and a noncontrast chest computed tomography scan was recommended. It showed a moderate-sized loculated hematoma along the right atrium. Repeat echocardiography with bubble contrast showed striking effacement of the right atrium and distention of the IVC. Repeat laboratory tests showed worsening renal function, effacement of the right atrium and distention of the IVC. Immediately postoperatively, her urine output increased, and by the next morning, her BUN improved to 127 mg/dl, and her creatinine improved to 3.3 mg/dl. Over the next several days, her renal function continued to improve.

Management
This case highlights the importance of urine studies, urine microscopy, and intravascular volume assessment techniques in diagnosing the etiology of CSA-AKI and determining appropriate management. Our patient was initially presumed to have ATN with need for RRT. However, the patient’s clinical findings and urinary indices supported a prerenal and reversible etiology. Initiating RRT in this patient without additional evaluation would have been detrimental in the setting of tamponade. In cardiac tamponade, fluid accumulation in the pericardial cavity impedes cardiac filling and decreases cardiac output, leading to hypotension. Renal autoregulation is impaired, resulting in reduced renal perfusion. The diagnosis of regional tamponade in postcardiac surgery is challenging, because the classic findings of hypotension, tachycardia, pulsus paradoxus, and increased CVP may be absent; also, the sensitivity of echocardiography is decreased (45). In this situation, computed tomography imaging has been shown to be beneficial in making the diagnosis (46).

More commonly, CSA-AKI results in ATN and management should be supportive, with emphasis on preventing additional kidney injury and treating fluid overload and metabolic and electrolyte issues as they arise. Multiple pharmacological agents have failed to show conclusive benefits in mitigating kidney injury. These agents include fenoldopam, dopamine, theophylline, diuretics, mannitol, steroids, N-acetylcysteine, sodium bicarbonate infusion, calcium channel blockers, pentoxifylline, and atrial natriuretic peptides (16,21,47–62). Dopamine can help initiate diuresis when a loop diuretic is insufficient but does not provide any renoprotective benefit and should not be used to increase renal perfusion (63). Furthermore, dopamine can cause arrhythmias, myocardial ischemia, and intestinal ischemia, even at low doses.

The lack of success in pharmacological agents for treating CSA-AKI may be because of the difficulty in recognizing AKI in this population based on the serum creatinine concentration, thus delaying therapy. In AKI, the GFR declines significantly before a rise in serum creatinine occurs. Moreover, the use of serum creatinine to detect and assess the severity of AKI is limited, because age, sex, muscle mass, tubular secretion, fluid overload, and other comorbid conditions (cirrhosis) can decrease creatinine production or dilute it. In critically ill patients, positive fluid balance has been shown to dilute the serum creatinine and delay the recognition of AKI (64). In contrast, AKI cases, defined by an absolute increase in serum creatinine ≥0.3 mg/dl within 48 hours (Acute Kidney Injury Network [AKIN] classification) after cardiac surgery, were found to overdiagnose AKI, because the increases in creatinine postoperatively represented the return of diluted creatinine values to the preoperative baseline levels (65). In CSA-AKI, serum creatinine should be corrected for fluid balance to improve recognition of AKI based on the AKIN classification. The addition of biomarkers, like IL-18, urinary/ plasma neutrophil gelatinase-associated lipocalcin, urinary kidney injury molecule-1, urinary IL-18, and liver fatty acid-binding protein, may improve the prediction of risk of AKI in cardiac surgery.

Indications for Initiation of RRT
Fortunately, our patient did not require RRT. Nevertheless, 1% of patients require RRT after cardiac surgery. Beyond initiation of RRT for severe hyperkalemia, metabolic acidosis, volume overload, uremia, and certain intoxications, the optimal timing of RRT in AKI is controversial. Although observational studies using cutoff values of serum urea or creatinine to define early versus late suggest that early initiation of RRT in AKI is associated with improved patient survival, these studies have significant limitations (66,67). In multiple recent observational studies, fluid overload of >10% (defined by the total input minus total output divided by initial body weight and multiplied by 100) has been associated with increased mortality in critically ill patients with AKI and a decreased likelihood of renal recovery (68–70). Oliguria has also been shown to be a predictor of mortality (71). In the postoperative patient with AKI, the decision for initiating RRT should consider the overall clinical state of the patient, including fluid balance status, presence of oliguria, other organ dysfunction, catabolic state, and other conditions in which the kidneys cannot meet the metabolic and fluid demands placed on them. Given the recent data regarding fluid overload and worse outcomes, early initiation of RRT should be considered in patients with AKI and significant fluid accumulation.

RRT Modality Options
Options for RRT therapy for AKI include intermittent hemodialysis (IHD), peritoneal dialysis (PD), continuous RRT (CRRT), and hybrid therapies, such as sustained low-efficiency dialysis or prolonged intermittent RRT (PIRRT). Although CRRT has been preferred in hemodynamically unstable intensive care unit (ICU) patients, prospective randomized clinical trials have not shown a benefit of CRRT over IHD or PIRRT for survival or renal recovery (72). Moreover, PIRRT has been shown to provide hemodynamic stability and solute control comparable to CRRT (73). A recent meta-analysis of PD in AKI concluded that there was no significant difference in outcomes between PD and other forms of RRT and that PD may be a viable option in select AKI patients; however, Schneider et al. (74)
noted that most studies were done in low-resource areas. In general, selection of RRT in the ICU should be based on the patient’s needs at time of initiation, goals for solute clearance and volume control, resource availability, and expertise. Most clinicians choose IHD for stable patients and CRRT or PiRRT for those patients with unstable hemodynamics, multiorgan failure, or high catabolic states. IHD removes potassium more efficiently in acute life-threatening conditions and requires minimal anticoagulation, which reduces the risk of bleeding. CRRT is preferred in patients with acute brain injury or increased intracranial pressure, because rapid fluid and solute shifts in IHD can exacerbate cerebral edema (73). In the treatment of AKI in the ICU, IHD has been associated with progressively positive fluid balances, whereas CRRT has been shown to facilitate net fluid removal (69). CRRT as initial treatment for AKI has also been associated with higher rates of renal recovery (75).

The different modes of CRRT for solute removal include continuous venovenous hemofiltration (CVVH), continuous venovenous hemodialysis, and continuous venovenous hemodiafiltration. CVVH is used with the conviction that convective therapy removes cytokines and reduces the effects of the systemic inflammatory response syndrome. However, controlled studies have failed to show a significant or sustained reduction in cytokine plasma concentrations with CVVH or an improvement in outcome (76–81). A recent meta-analysis comparing the outcomes of hemofiltration with hemodialysis for the treatment of AKI found no benefit of CVVH in survival or clinical outcomes, such as RRT dependence, organ dysfunction, or vasopressor use, and instead, it led to shorter filter life (82). Presently, there is insufficient data to recommend one type of CRRT modality over another, and CRRT modality choice should be guided by technique expertise and resource availability.

**Dose of RRT**

The delivery of dialysis dose in AKI is another controversial issue. Quantification of the delivery of RRT in AKI has been based mostly on urea clearance, which may not be the ideal marker in AKI. Using urea kinetics, two randomized controlled studies (Randomized Evaluation of Normal Versus Augmented Level Replacement Therapy [RENAI] and Acute Renal Failure Trial Network) compared an intensive treatment strategy with more conventional renal support (83,84). Both studies showed that more intensive RRT dose did not improve patient survival, recovery of renal function, or duration of RRT. Both studies also showed that the actual delivered dose was well over 85% of the prescribed dose, which is higher than the dose commonly achieved in standard clinical practice. It is conceivable that any benefit of higher doses of RRT may be offset by increased electrolyte imbalances, such as hypokalemia and hypophosphatemia, increased nutrient loss, and increased drug clearances, with underdosing of antibiotics. Based on these studies, IHD provided three times a week is sufficient as long as the delivered Kt/V is at least 1.2. In AKI patients treated with CRRT, a minimal effluent flow rate of 20–25 ml/kg per hour is adequate as long as the target dose of therapy is actually delivered. The RRT prescription should be tailored to the individual patient. Volume balance, acid-base status, electrolyte homeostasis, and nutrition should also be considered as part of delivering an optimal RRT dose. Higher CRRT and IHD doses may be needed for hypercatabolic patients, and more frequent IHD treatments may be needed for volume management. Particular effort should be made to ensure appropriate nutrition, repletion of electrolytes, and dosing of medications.

**Questions**

**Dr. Keith Wille (University of Alabama at Birmingham [UAB]—Pulmonary and Critical Care Faculty)**

Is there any role of ultrafiltration (UF) for ADHF after cardiac surgery?

A.J.T.

UF offers the theoretical benefits of controlled volume removal, greater net loss of sodium, and less neurohormonal activation compared with diuretics. To date, two randomized clinical trials have compared the use of slow continuous UF with diuretics. The Ultrafiltration Versus Intravenous Diuretics for Patients Hospitalized for Acute Decompensated Heart Failure (UNLOAD) trial showed greater weight loss and decreased readmission rates in the UF group (85). However, the study was criticized for using suboptimal diuretic doses in the diuretic group. Given the problems with the UNLOAD study, the Cardiorenal Rescue Study in Acute Decompensated Heart Failure (CARESS-HF) trial was done with a more rigorous diuretic regimen in the diuretic group. The study failed to show benefit of UF compared with a stepwise pharmacological approach with diuretics. In addition, the UF group had more AKI and more complications, including bleeding and vascular access-related adverse effects (86). Of note, patients in the CARESS-HF study had higher all-cause mortality, higher baseline serum creatinine, and more diabetes compared with the patients in the UNLOAD study. Based on the CARESS-HF trial, UF cannot be recommended as first-line therapy for ADHF. The Study of Heart Failure Hospitalizations after Aquapheresis Therapy Compared with Intravenous Diuretic Treatment, known as the AVOID-HF trial, is an ongoing randomized controlled trial recruiting 800 patients (NCT01474200) to determine whether patients will have fewer heart failure events after receiving UF therapy compared with intravenous diuretics.

**Dr. Eric Wallace (UAB—Nephrology Faculty)**

This patient, at the time of kidney injury, was 11 kg over her admission weight; has this degree of volume resuscitation been associated with AKI?

A.J.T.

There is increasing evidence that positive fluid balances of ≥10% of body weight are associated with worsening organ dysfunction and poor outcomes in the critically ill and postoperative patients (69). Although there are no randomized trials, this amount of fluid overload can potentially increase the risk of AKI and delay renal recovery (69,87). Excessive fluid resuscitation has been shown to increase intra-abdominal pressure, which increases renal venous pressure and reduces renal blood flow, resulting
in AKI (34). Similarly, increased CVP in ADHF is an independent predictor of AKI and associated with an increased risk of intra-abdominal hypertension (33). Because our patient weighed 119 kg and was 11 kg over her preoperative weight of 108 kg, she was in excess of 10% fluid overload. Additional clinical trials are clearly needed to examine optimal fluid balance and renal outcomes. Current evidence seems to support more restrictive fluid management strategies.

Disclosures

A.J.T. is a member of the Gambro Expert Panel and has served as a consultant for Gambro.

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