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Frequency of Acute Kidney Injury in Patients Treated with Normal Saline after Off-Pump Coronary Artery Bypass Grafting

Shima Sheybani[1], Siamak Boustan[2], Shahram Amini[3*], Mona Najafnajafi[4], Mohammad Abbasi Tashnizi[5], Nahid Zirak[6]

[1] *Anesthesiologist, Department of Anesthesiology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran*
[2] *General Practitioner, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran*
[3] *Anesthesiologist, Department of Anesthesiology, Cardiac Anesthesia Research Center, Mashhad University of Medical Sciences, Mashhad, Iran*
[4] *Community Medicine, Imam Reza Clinical Research Unit, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran*
[5] *Cardiac Surgeon, Department of Cardiac Surgery, Mashhad University of Medical Sciences, Mashhad, Iran*
[6] *Anesthesiologist, Department of Anesthesiology, Cardiac Anesthesia Research Center, Mashhad University of Medical Sciences, Mashhad, Iran*

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ABSTRACT

Introduction: Acute kidney injury (AKI) is a common postoperative complication of cardiac surgery, which is associated with an increased risk of morbidity and mortality. This study investigated the frequency of postoperative AKI in low risk adult patients undergoing off-pump coronary artery bypass grafting (CABG).

Materials & Methods: All consecutive adult patients of American Society of Anesthesiologists (ASA) class II and III, who were transferred to the post-operative cardiac surgery ICU after off-pump CABG and were low risk for AKI from October 2013 to September 2014 at Emam Reza Hospital, Mashhad, Iran were enrolled in this prospective cohort study at a teaching hospital. The patients were explored for AKI development, based on risk-injury-failure-loss- end stage kidney disease (RIFLE) and acute kidney injury network (AKIN) criteria, frequency of metabolic acidosis, hypernatremia, hyperchloremia, and length of stay in ICU.

Results: According to the results of the present study, 479 patients with the mean age of 60.8±10.75 yrs were included. AKI occurred in 22 (4.4%) and23 (4.8%) patients, based on both the RIFLE and AKIN criteria, respectively with the highest rate of AKI, reported on the third and fourth post-operative days. Additionally, hyperchloremia and hypernatremia were observed in 71 (14.8%) and 76 (15.9%) patients, respectively. Only one case of mortality occurred during the study. Metabolic acidosis was reported in 112 (23.4%) patients with a high anion gap in 60 (12.5%) cases.

Conclusion: The current study demonstrated that hypernatremia and metabolic acidosis but not AKI are frequently seen in patients receiving normal saline following off pump CABG with low risk for AKI.

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Introduction

Postoperative acute kidney injury (AKI) is the second leading cause of hospital-acquired AKI (1). The incidence of AKI ranges between 3% and 30%, depending on the definition of AKI (2). Cardiac surgery-associated acute kidney injury (CSA-AKI) is associated with poor clinical outcomes including longer intensive care unit (ICU) and hospital stay, higher treatment costs,

**Corresponding author:* Shahram Amini, Cardiac Anesthesia Research Center, Department of Anesthesiology and Critical Care, Imam Reza Hospital, Mashhad, Iran. Tel: 0098 9151417235; Email: aminish@mums.ac.ir

lower quality of life, and higher long-term mortality (2, 3). Although various prevention strategies have been proposed to minimize this complication, none of them have been shown to be totally effective so far (1).

Several risk factors have been identified for CSA-AKI, including New York Heart Association (NYHA) class III/IV disease, hypertension, elevated preoperative creatinine level, peripheral vascular disease, respiratory system disorders, diabetes mellitus, cerebrovascular disease, cardiopulmonary bypass (CPB) time, aortic clamping, use of intra-aortic balloon pump, and type of surgery.

Furthermore, postoperative factors such as infection caused by re-operation, emergency surgery, and low cardiac output are other risk factors for CSA-AKI (4). Several factors have been proposed as independent risk factors for development of post cardiac surgery AKI including preoperative renal insufficiency, postoperative hypotension, CPB time more than 140 minutes, and advanced age(5).

Normal saline is an isotonic solution commonly used for intravenous fluid therapy; however, this solution may cause hyperchloremic acidosis (6). Given its high concentration, chloride (Cl) is the most important anion in balancing extracellular cations. Therefore, pronounced interstitial fluid retention and hyperchloremia are convergent effects of saline infusion, in addition to impairment in cardiac contractility and diminished inotropic response, resulting in hypotension. Despite the availability of safer and more physiologically balanced solutions, normal saline is frequently used in medical practice and is perhaps the most common resuscitative fluid (7). Nevertheless, some studies have demonstrated that high Cl-containing fluids, such as normal saline, might result in AKI (8, 9).

With this background in mind, this study investigated the effect of intravenous hydration with 0.9% saline solution on the development of postoperative AKI in adult patients undergoing off-pump CABG. The secondary objectives were assessment of AKI severity and the associated morbidities, including acid-base disorders, hypernatremia, hyperchloremia, duration of mechanical ventilation, length of stay in ICU or hospital, and ICU mortality.

Materials and Methods

This study was conducted on all consecutive patients, transferred to the cardiac surgery ICU after off-pump CABG at Imam Reza Hospital, Mashhad, Iran during October 2013-September 2014.

The exclusion criteria of the study were as follows: 1) previous history of cardiac surgery; 2) ASA class > 4; 3) history of renal diseases; 4) diabetic nephropathy; 5) serum creatinine level > 1.3 mg /dL; 6) glomerular filtration rate (GFR) < 75%; 7) ejection fraction < 40% before surgery; 8) excessive drainage during surgery; 9) need for balloon pump during and after surgery; 10) intraoperative events including excessive hemorrhage requiring more than two units of packed cells, cardiac arrest, prolonged hemodynamic instability, and cerebrovascular accident; 11) need for high-dose inotropes during surgery; and 12) lack of consent to the study protocol.

Before and during surgery, 0.9% normal saline, containing 154 mEq/L Cl, was administered according to the standard guidelines and the patient's hemodynamic and perfusion status. After the operation, the same serum was infused to 40 cc/kg within the first 24 h. All patients underwent standard anesthesia, monitoring, and fluid therapy perioperatively.

The mean arterial pressure was maintained at 70-80 mmHg and nitroglycerine infusion was applied in case of a rise in blood pressure above 140/90 mmHg during and after surgery. Following surgery and prior to ICU transfer, 5 cc arterial and venous blood samples were drawn from each patient. Na, K, ABG, and pH were measured every 4 h, while other lab tests (calcium, chlorine, magnesium, albumin, creatinine, blood urea nitrogen, lactate, PaO_2, and standard base excess [SBE]) were performed daily.

Fluid therapy was continued to maintain the urinary output at 1 cc/kg/h (minimum), lactate level was below 2 mmol/L, and mean arterial pressure (MAP) at 70-80 mmHg. In case the hemoglobin (Hb) level is below 8 g/dL, one unit of packed cell was transfused. The patients also received packed cells if Hb level ranged between 8 and 10 g/dL. In addition, vasopressor was required to keep MAP > 70 mmHg, lactate level > 2 mmol/L, and central venous oxygen saturation < 70.

In order to diagnose acid-base disorders, the traditional Henderson–Hasselbalch equation and SBE were used. AKI was diagnosed based on risk, injury, failure, loss, end-stage kidney disease (RIFLE) (which categorizes the severity of AKI according to serum creatinine and GFR level) and acute kidney injury network (AKIN) (which categorizes the severity range of AKI into three stages according to serum creatinine level and urine output) criteria (Table 1).

The patients were followed-up until hospital discharge. By considering the renal condition at a steady state, GFR was measured based on the Cockcroft-Gault equation. A medical student, blind to the study protocol, recorded all the data. The gathered information was analyzed, using independent sample t-test, Mann-Whitney test,

and Fisher's exact test through SPSS version 15.

Table 1. RIFLE and AKIN criteria

	Serum creatinine criteria	Urine output criteria
RIFLE Definition	Increase In Scr By ≥ 1 .5 times baseline within seven days	
R(Risk)	Increase in SCr by 1 .5 -< 2.0 times baseline	Less than 0.5 mL/Kg per hour for more than 6 hours
I(Injury)	Increase in SCr by 2.0 -< 3.0 times baseline	Less than 0.5 mL/Kg per hour for more than 12 hours
F(Failure)	Increase in SCr by ≥ 3.0 times baseline	Less than 0.3 mL/Kg per hour for 24 hours or anuria for 12 hours
L(Loss)	Persistent acute renal failure: complete loss Of kidney function >4 weeks	
E(ESRD)	Complete loss of kidney function >3 months	
AKIN Definition	Increase in SCr by 0.3 mg/dL or ≥ 1 .5 times baseline within 48 hours	
Stage 1	Increase in SCr by ≥0.3 mg/dL or ≥ 1 .5-<2.0 times baseline or ≥ 1 .5-<2.0 Times baseline	Less than 0.5 mL/Kg per hour for more than 6 hours
Stage 2	Increase in SCr by ≥2.0-<3.0 Times baseline	Less than 0.5 mL/Kg per hour for more than 12 hours
Stage 3	Increase in SCr by ≥3.0 Times baseline or SCr > 4 mg/dL	Less than 0.3 mL/Kg per hour for 24 hours or anuria for 12 hours

P-value less than 0.05 was considered statistically significant.

Results

The study population corresponded to a group of 479 patients, consisting of 303 (63.3%) males and 176 (36.7%) females with the mean age of 60.8±10.75 yrs. Table 2 illustrates the patients' data and demographic characteristics. Table 3 presents the surgical characteristics of the patients. The patients' mean score of European System for Cardiac Operative Risk Evaluation (EuroSCORE) was 1.46±1.01%, and the mean score of Society of Thoracic Surgeons (STS) criteria was 0.52±0.44%.

Table 2. Demographic data and comorbidities of the patients

Variablea	Mean±SD
Height (cm)	164.15±10.21
Weight (kg)	69.82±12.89
Body mass index (kg/m^2)	25.9±4.35
Age (years)	60.8±10.75
Gender (male:female)	303:176
Hypertension	249 (52)
Hyperlipidemia	170 (35.5)
Chronic bronchitis	15 (3.1)
Type II diabetes	151 (31.5)
Anemia	3 (0.63)
Smoking	71 (14.8)
Addiction	85 (17.7)
Pulmonary hypertension	6 (1.3)
Congestive heart failure	0 (0)
Cerebrovascular event	0 (0)
Peptic ulcer disease	0 (0)

Data are presented as number, number (percentage), or mean±standard deviation.

Table 3. Type of surgery performed on the patients

Type of surgery	No. (%)
Three-vessel disease	191 (39.9)
Left main artery	45 (9.9)
Others	243 (50.2)

Based on the RIFLE criteria, AKI was demonstrated to occur in 22 (4.4%) patients, with the highest rate of AKI reported on the third and fourth post-operative days. Furthermore, it was shown that 13 (2.8%), 5 (1.1%), and 4 (0.8%) patients were in the risk, injury, and failure stages, respectively. Also, according to the AKIN criteria, 23 (4.8%) patients developed AKI and were only in the first stage.

The highest mean serum creatinine level was found to be 1.16±0.86 mg/dl. Besides, the mean duration of serum creatinine rise was 1.58±1 days. The mean serum sodium concentration was 139.36±3.04 mEq/L on the first postoperative day. Also, the highest mean serum sodium and Cl levels were 142.40±6.77 and 106.52±6.13 mEq/L, respectively. In addition, hyperchloremia and hypernatremia were reported in 71 (14.8%) and 76 (15.9%) patients, respectively. Metabolic acidosis was observed in 112 (23.4%) patients with a high anion gap in 60 (12.5%) cases. The mean length of stay in ICU was 2.53±1.07 days, and only one case of ICU mortality occurred.

Discussion

Intravenous fluids are used to compensate for blood loss and insensible loss, treat electrolyte imbalances (10), and maintain hemodynamic stability and organ perfusion in critically ill patients (11).

With the emergence of new infusion fluids, clinicians have a wide range of products to select from. However, selection of a certain infusion fluid is driven more by the physician's habit rather than careful considerations (10). Therefore, accurate assessment of the intravascular volume, along with response to fluid therapy, remains one of the most challenging issues for clinicians in daily practice (11).

In previous studies, the incidence of AKI based on the RIFLE classification was reported to

be 7.9-31.9% in patients undergoing CABG with CPB (12, 13). In addition, in several studies, progression towards dialysis treatments and increased mortality were reported in 0.7-1.1% of the patients (13-16). In the current study, AKI was diagnosed in less than 5% of cases, which is lower than the rates reported in the mentioned studies; however, none of these patients in our study required dialysis. It should be noted that the sample size of the present study was much smaller than the mentioned studies and patients with predisposing factors for AKI were exclude.

Evidence suggests that the use of high Cl-containing fluids, such as normal saline, is associated with hyperchloremic metabolic acidosis, increased occurrence of kidney dysfunction, and the possibility of reduced survival rate; however, risk of mortality can be diminished when balanced salt solutions are used (7, 17). In addition, balanced crystalloid solutions, which are used to reduce the associated risks, have shown not only no harmful effects, but also benefits over normal saline (17).

In the current study, despite the 4.7-4.8% frequency of AKI, only one case of mortality occurred. This rate varies from other previous studies, which might be due to different study populations and follow-up durations (ICU mortality was measured in our study). In a study by Younos et al. in 2012 on critically ill ICU-hospitalized patients, application of chloride-limited serums led to better results (8). Additionally, in a review article published in 2012, comparison of buffer and non-buffer solutions such as normal saline showed that the use of buffer solutions resulted in a lower rate of metabolic acidosis and hyperchloremia (18).

The main limitation of the current study was lack of comparison between other crystalloid solutions and normal saline due to some restrictions during the study period in our country. Therefore we cannot contribute low incidence of AKI to normal saline and it is highly recommended to conduct further studies to compare the effects of different crystalloids on randomly selected patients with similar EuroSCORE and STS scores for AKI risk. Another limitation of the current study was that the patients were only investigated during ICU stay, which might in turn underestimate the incidence of AKI and the associated mortality and morbidity rates.

Conclusion

The present study demonstrated that AKI is not commonly seen in low risk patients undergoing off-pump CABG with very low mortality. However, hypernatremia, hyperchloremia, and metabolic acidosis are commonly seen during ICU stay in these patients.

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Conflict of Interest

The authors declare no conflict of interest.

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