

Postoperative Fluid Therapy in Adult Cardiac Surgical Patients and Acute Kidney Injury: A Prospective Observational Study

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Abstract

Background Normal saline (0.9% NS) is a common intravenous fluid used worldwide. Recent studies have shown that NS use is associated with increased incidence of acute kidney injury (AKI) and a need for renal replacement therapy (RRT). The practice is changing toward using balanced solutions to prevent AKI. Postcardiac surgery patients are more prone to develop AKI after cardiopulmonary bypass (CPB). We aim to study the type of fluid administered, incidence of AKI, need for RRT, and overall outcome of these patients.

Methods This prospective observational study was conducted in the cardiothoracic intensive care unit (cardiothoracic and vascular surgery intensive care unit) in a cohort of 197 adult patients who underwent on pump cardiac surgery in our hospital from July 2021 to October 2021 as a pilot study. Data was analyzed using SPSS 20.0 (IBM, Chicago, Illinois, United States). A p -value < 0.05 was considered significant.

Results In our study, 58 (29.34%) patients developed AKI in the first three postoperative days and 16 (8.12%) patients required RRT. Incidence of AKI was found to be higher in patients who received NS only, as fluid of choice was 34.48% compared with other intravenous fluids. Patients with AKI had higher positive fluid balance ($p < 0.001$), longer CPB ($p < 0.001$), and aortic cross clamp ($p = 0.006$) times. Intensive care unit and hospital stay and mortality rates were higher in AKI patients than those without AKI ($p < 0.001$).

Conclusion Our study demonstrated that NS was the commonly used crystalloid in our patients and was associated with increased incidence of AKI and RRT when compared with other balanced salts solutions.

Keywords

- ▶ acute kidney injury
- ▶ cardiac surgery
- ▶ cardiopulmonary bypass
- ▶ intravenous fluid therapy

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Introduction

Intravenous fluid administration is the most common intervention in intensive care units (ICU) to improve hemodynamic status and organ perfusion and acute kidney injury (AKI) is a common problem.¹ Normal saline (0.9%NS) remains the standard resuscitation fluid.² Recent studies have shown that use of NS compared with chloride-restrictive fluids is associated with increased incidence of AKI and need for renal replacement therapy (RRT).^{3–5} High chloride concentrations in NS may be associated with hyperchloremic metabolic acidosis. Extracellular chloride influences the tone of the afferent glomerular arteriole, thereby affecting the glomerular filtration rate.^{6–9} The practice is changing toward using balanced salt solutions (composition approximately similar to plasma) to prevent these complications. The existing literature suggested that using a balanced solution is associated with a reduced incidence of AKI and of death compared with NS,¹⁰ although the recent Balanced Crystalloids versus Saline in Critically Ill Adult study (SMART trail) could not find any such difference.¹¹

Literature demonstrated that use of colloids increases the risk of kidney injury in critically ill patients. Hydroxyethyl starch is less expensive among colloids, but it has adverse effects on coagulation and a twofold increased risk of AKI compared with crystalloids.¹² The Saline versus Albumin Fluid Evaluation (SAFE) study confirmed that albumin was safe, but there was no difference in 28-day survival between saline and albumin administration in critically ill patients.¹³

Postcardiac surgery patients are a different subset of patients. They usually have multiple comorbidities and are more prone to AKI after cardiopulmonary bypass (CPB).^{14,15} The type and/or amount of intravenous fluid in an immediate postoperative patient may affect the renal outcome. The practice of fluid administration in cardiac surgical ICUs differs from institute to institute, and no defined guidelines exist. We aim to study the type of fluid administered, the incidence of AKI, need for RRT, and overall outcome of these patients.

Materials and Methods

This prospective observational study was conducted in the cardiothoracic intensive care unit (cardiothoracic and vascular surgery intensive care unit) in a cohort of 197 consecutive adult patients who underwent elective cardiac surgery with CPB from July 2021 to October 2021. Patients were excluded if they were under 18 years of age, chronic kidney disease, or received preoperative RRT.

The intravenous fluids were administered as per patient profile and according to our ICU protocol. Institute Ethics Committee approved this study. Written and informed consent was obtained from patients or close relatives before enrolling them for the study. In our study, postoperative AKI staging was defined by kidney disease improving global outcome (KDIGO) criteria.

Intravenous fluid of choice depended on the individual patient profile, their volume requirement at different stages

in the postoperative period to maintain optimal preloading conditions with primary aim of generating optimal cardiac output with ideal body organ perfusion. This choice of crystalloid or colloids or combinations was used in patients depending on their hemodynamic need and in accordance with the ICU protocol and with intensivist's guidance. Various combinations of intravenous fluids used in this study were as follows: only 0.9%NS, only Ringer lactate (RL), combinations of NS + 5% albumin (5%A), or NS + RL + 5% albumin.

Detailed data regarding different intravenous fluid administered as maintenance as well as bolus in first 3 days, urine output, cumulative fluid balance were noted.

We also collected the baseline characteristics such as age, gender, weight, comorbidities, comprehensive cardiac diagnosis, sequential organ failure assessment (SOFA) score, and serum creatinine at ICU admission. Hematology and biochemical laboratory parameters, arterial blood gases, and daily SOFA scores were documented in three consecutive postoperative days. Data pertaining to the diagnosis of sepsis as per SEPSIS-3 definition were also collected. Finally, incidence of AKI, AKI stages as per KDIGO criteria, indications for RRT if it was required, ICU and hospital length of stay, and 30-day survival status of the patient were documented.

Objectives

Primary objective was to identify any possible relationship between the incidence of new-onset AKI with the type of intravenous fluid administered. Secondary objectives are to compare NS with balanced crystalloid on renal outcomes and mortality.

Statistical analysis was conducted with SPSS 20.0 (IBM, Chicago, Illinois, United States). Continuous variables were expressed as mean + standard deviation and categorical variables were expressed as frequency and/or percentage. Differences between AKI or non-AKI tested with students *t*-test and Mann-Whitney U test for continuous variable. A *p*-value < 0.05 was considered significant.

Results

Over the 3-month study period, a total of 315 patients were admitted to the surgical ICU. After applying exclusion criteria, 197 patients were included in our study, and data were analyzed and results obtained. All patients received different fluids as isolated NS or RL, or combination with 5% albumin in cardiac surgical ICU postoperatively. Postoperative AKI defined by consensus KDIGO criteria.

As delineated in ► **Table 1**, average age was 47.59 ± 12.33 years versus 45.58 ± 14.49 years in AKI and non-AKI group, respectively. Weight was higher in the AKI group than the non-AKI group 61.56 ± 15.23 and 56.70 ± 13.48 kg, respectively. As seen from ► **Table 2**, 37 patients received only NS as maintenance intravenous (stand-alone) fluid (37/197). Sixteen of one-hundred ninety seven patients received only RL in the whole cohort. Thirty of one-hundred ninety seven patients received both NS and RL. One-hundred six of one-hundred ninety seven patients received 5% albumin in

Table 1 Patient, demographics, associated comorbidities, and perioperative findings

Demographic data	AKI group (n = 58)	Non-AKI group (n = 139)	p-Value
Age in years	47.59 ± 12.33	45.58 ± 14.49	0.357
Weight in kilograms	61.56 ± 15.23	56.70 ± 13.48	0.027
Gender, male	33(16.75)	88 (44.67)	–
Serum creatinine	1.06 ± 0.38	0.91 ± 0.29	0.002
SOFA score at admission	3.50 ± 2.08	4.5 ± 2.65	0.011
Associated comorbidities			
Diabetes mellites	21 (10.65)	37(18.78)	–
Hypertension	23(11.67)	47(23.85)	–
LVEF <40%	16(8.12)	27(13.71)	–
COPD	20(10.15)	9(4.56)	–
Hypothyroidism on thyroxine	12(6.09)	16(8.12)	–
Perioperative findings			
Emergency surgery	3(1.52)	7 (3.55)	–
CABG	22(11.28)	49(25.12)	–
Mitral valve	16(8.12)	34(17.43)	–
Aortic valve	11(5.58)	24(12.31)	–
Double valve	8(3.04)	15(6.09)	–
Aortic surgeries	4(2.03)	14(7.69)	–
CPB time, min	166.45 ± 63.68	137.9 ± 54.7	<0.001
ACC time, min	109.62 ± 34.64	90 ± 47.36	0.006

Abbreviations: AKI, acute kidney injury; ACC, aortic cross clamp time; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; CPB, cardiopulmonary bypass; LVEF, left ventricular ejection fraction; SOFA, sequential organ failure assessment.

combination with either NS or RL. Eighty-nine (NS mixed with other fluids) plus 37 only received NS, and 126 patients received NS as an intravenous fluid. Fifty-eight of one-hundred ninety seven patients in our cohort developed AKI. Among them, 51 patients had been administered NS either alone or in combination with other fluids. Rest 139 patients did not have renal impairment and 102/139 non-AKI patients received NS either as a single fluid or mixed with others. Twenty patients out of 58 (29.31%) in the AKI group and 17 out of 139 (14.39%) in the non-AKI group received NS, which was statistically significant ($p = 0.014$). We documented that RL was given to 4 out of 58 (6.9%) patients and 12 out of 139 (8.63%) in AKI and non-AKI groups, respectively ($p = 0.466$). Fifteen of fifty-eight (25.86%) in the AKI group and 51/139 (36.69%) patients in the non-AKI group had received NS plus 5% albumin, but this was not statistically significant. Cumulative fluid balance was signifi-

Table 2 Relationship of different IV fluids used in ICU after cardiac surgery with AKI

Type of fluid received	AKI group n = 58(%)	Non-AKI group n = 139(%)	p-Value
NS	20 (34.48)	17 (14.39)	0.014
RL	4 (6.9)	12 (8.63)	0.466
NS plus RL	3 (5.17)	27 (19.42)	0.007
NS plus 5% albumin	15 (25.86)	51 (36.69)	0.095
RL plus 5% albumin	0 (0)	15 (10.79)	0.009
NS plus RL plus 5% albumin	18(31.03)	7 (5.04)	<0.001
Blood transfusion,	42(72.41)	100 (71.94)	0.946
Total urine output	4.30 ± 2.51	5.98 ± 1.502	<0.001
Positive CFB	1.48 ± 1.33	0.86 ± 1.16	<0.001
Negative CFB	0.265 ± 0.82	0.31 ± 0.69	0.023

Abbreviations: AKI, acute kidney injury; CFB, cumulative fluid balance; ICU, intensive care unit; IV, intravenous; NS, normal saline; RL, Ringer lactate.

Table 3 Incidence of renal impairment as per KDIGO criteria

KDIGO stages	POD1	POD2	POD3
Stage 1	32(16.41%)	15(7.69%)	13(6.66%)
Stage 2	13(6.66%)	21(10.76%)	15(7.69%)
Stage 3	7(3.58%)	22(11.28%)	17(8.72%)

Abbreviations: KDIGO, kidney disease improving global outcome; POD1, postoperative day 1.

icantly more positive in AKI patients than non-AKI patients (►Table 2).

As documented in ►Table 3, more stage 3 KDIGO patients were found in postoperative days 2 and 3, whereas stage 1 KDIGO has more patients on day 1. ►Table 4 describes the various laboratory parameters in both AKI and non-AKI groups of patients. Hemoglobin in gm/dL was comparable in both AKI and non-AKI patients (10.73 ± 1.17 vs. 10.37 ± 1.25 ; $p = 0.059$). Blood urea (62.34 ± 28.72 vs. 39.29 ± 20.40 ; $p < 0.001$) and serum creatinine (2.12 ± 1.240 vs. 0.9447 ± 0.365 ; $p < 0.001$) were elevated in the AKI patients than those without AKI, which were statistically significant. pH, base deficit, and HCO_3^- showed a statistically significant difference between the groups. Serum Na^+ , serum K^+ , and serum Cl^- in mEq/L in both the groups (AKI vs. non-AKI) were (143.36 ± 4.89 vs. 141.4 ± 5.27 ; $p = 0.018$), (4.7 ± 0.67 vs. 4.1 ± 0.24 , $p < 0.001$), and (105.86 ± 4.31 vs. 104.65 ± 4.66 ; $p = 0.088$), respectively. Similarly, statistically elevated SOFA score found in AKI group than non-AKI group (9.78 ± 3.34 vs. 7.47 ± 3.15 , $p < 0.001$). As found in ►Table 5, 16 out of 58 AKI patients received RRT, which was statistically significant ($p = 0.001$) in comparison to non-AKI group. Also, it was observed that ICU (9.17 ± 4.18 vs. 6.47 ± 2.42 ; $p < 0.001$) and

Table 4 Laboratory parameters between AKI versus non-AKI group

Laboratory parameters	AKI group (n = 58)	Non-AKI group (n = 139)	p-Value
Hemoglobin, gm/dL	10.73 ± 1.17	10.37 ± 1.25	0.059
Blood urea, mg/dL	62.34 ± 28.72	39.29 ± 20.40	0.001
Serum creatinine, mg/dL	2.12 ± 1.240	.9447 ± 0.365	0.001
pH	7.37 ± 0.030	7.401 ± .027	0.001
PaCO ₂ , mm Hg	35.47 ± 4.11	35.16 ± 3.78	0.852
PaO ₂ , mm Hg	138.94 ± 24.77	150.49 ± 28.77	0.018
Base excess	0.33 ± 0.60	0.295 ± .54	0.988
Base deficit	4.29 ± 2.98	2.64 ± 1.85	0.001
HCO ₃ , mmol/L	20.78 ± 2.79	22.25 ± 2.00	0.001
Serum lactate, mmol/L	1.97 ± 1.26	2.047 ± 1.07	0.324
Serum Na ⁺ , mmol/L	143.36 ± 4.89	141.4 ± 5.27	0.018
Serum K ⁺ , mmol/L	4.7 ± 0.46	4.1 ± 0.24	0.001
Serum Cl ⁻ , mmol/L	105.86 ± 4.31	104.65 ± 4.66	0.088
SOFA score	9.78 ± 3.34	7.47 ± 3.15	0.001

Abbreviations: AKI, acute kidney injury; PaCO₂, partial pressure of carbon dioxide; PaO₂, partial pressure of oxygen; SOFA score, sequential organ failure assessment score.

Table 5 Outcomes of our study

Outcome	AKI group n, (%)	Non-AKI group n, (%)	p-Value
RRT	16(8.21%)	0	0.001
ICU stay, in days	9.17 ± 4.18	6.47 ± 2.42	0.001
Hospital stay, in days	17.77 ± 7.59	12.89 ± 5.58	0.001
ICU deaths	5 (2.56%)	3 (1.53%)	0.036
In hospital deaths @30days	3(1.54%)	1 (0.51%)	0.07

Abbreviations: AKI, acute kidney injury; ICU, intensive care unit; RRT, renal replacement therapy.

hospital (17.77 ± 7.59 vs. 12.89 ± 5.58; $p < 0.001$) stays in days were longer in AKI patients than those without AKI. Similarly, ICU and hospital deaths were (8.62 vs. 2.16%; $p = 0.036$) and (5.56 vs. 0.74%; $p = 0.07$) higher in AKI group of patients, respectively.

Discussion

A total of 315 patients were admitted to the surgical ICU during the 3 months study period. After applying exclusion criteria, 118 patients were excluded, and the remaining 197 patients were included in this prospective observational study. All patients received different intravenous fluids as isolated NS, RL, and/or a combination of both NS, RL with or without 5% albumin, as noted in **Table 2**. Maintaining adequate renal perfusion is also essential because the kidneys receive 25% of the cardiac output and produce 180 L

filtrate per day.¹⁶ There are two important aspects of fluid management in the postoperative cardiac surgical patients— one is the maintenance of euolemia/optimal preloading conditions for better perfusion of vital organs, including kidneys, and second is the type of intravenous fluid to be kept the kidneys safe.

In our study, out of 197 patients, 58 (29.34%) developed different stages of AKI in the first three postoperative days after adult cardiac surgery and 16 (8.12%) patients required RRT. Another study recorded an AKI incidence rate of 48% in 267 patients following aortic arch surgery.¹⁷ However, Eng- lberger et al recently showed a relatively low incidence rate of AKI (17.7%) and RRT (2.1%) among 851 patients who underwent elective thoracic aortic surgery.¹⁸

Incidence of different stages of AKI was found to be higher in those who received NS as the only fluid of choice at 34.48%, followed by various other fluid combinations such as NS plus RL plus 5% albumin, NS plus 5% albumin, RL, and NS plus RL were 31.03, 25.86, 6.9, and 5.17%, respectively (**Table 2**). A recent study by Bhaskaran et al found that perioperative use of chloride-restricted intravenous fluids is associated with statistically significant lower incidence of AKI stage I, while chloride-liberal intravenous fluids are associated with hyperchloremic acidosis and increased incidence of AKI stage I post-coronary artery bypass grafting patients.¹⁹ Similar results were described by Krajewski et al who showed that postoperative fluid resuscitation with balanced crystalloids reduced the incidence of AKI when compared with NS.¹⁰ However, Young et al showed that balanced crystalloid solutions produce no difference in the risk of AKI compared with NS.²⁰ Martin and Bassett discussed the difference between the use of crystalloids and colloids for resuscitation in critically ill patients. They found that colloids are a more

effective fluid to achieve resuscitation endpoint than crystalloids but did not study their effects on kidney function.²¹

AKI patients had statistically significant low cumulative urine output than those without AKI with or without diuretics therapy ($p < 0.001$). Patients with AKI had higher positive cumulative fluid balance ($p < 0.001$) and lower negative cumulative fluid balance ($p = 0.023$) than those without AKI. The similar results were found in Haase-Fielitz A et al study, which showed that postoperative positive fluid balance management is strongly associated with a higher AKI rate in postcardiac surgery. However, there is no association between the volume of negative fluid balance and AKI incidence.²²

In our study, longer duration of CPB ($p < 0.001$) and aortic cross clamp time (ACC) ($p = 0.006$) was found to be statistically significant in AKI patients than without AKI. Patients with prolonged CPB could result in significant inflammation and oxidative stress effect on mitochondrial oxidative phosphorylation, causing hinderance in energy metabolism and ATP production, which contributes to multiorgan dysfunction, including renal dysfunction. Xu et al found that CPB time was an independent predictor of postoperative AKI. Every 10 minutes increase in CPB time was associated with a 17.1% higher risk of postoperative AKI.¹⁴ However, Mancini et al found that the association between the time on CPB and AKI requiring dialysis lost its statistical significance after adjusting for confounders.²³

Appropriate fluid management after cardiac surgery is extremely complex, especially post-CPB patients had significant volume shifts and fluid can be “sequestered” in the extravascular, interstitial space. This situation leads to a confusing clinical picture of a fluid overload but an intravascularly volume-depleted patient. Using diuretics in these patients leads to further intravascular volume contraction, which in turn causes poor organ perfusion and, AKI.^{24,25}

In our study, blood urea and serum creatinine in AKI patients were significantly elevated than those without AKI ($p < 0.001$) as per the KDIGO criteria. Similarly, Lower pH, lower serum HCO_3^- , and higher base deficit were statistically significant in patients with AKI than in those without AKI ($p < 0.001$). The mortality was higher in those patients with oliguria, and positive fluid balance requiring RRT. Schrier showed high SOFA scores in sepsis and associated AKI in ICU patients.²⁶ Though none of our patients had culture-positive sepsis, they had higher SOFA scores in AKI patients compared with non-AKI patients; this could be explained by either inflammatory response and culture negative sepsis due to prophylactic broad-spectrum antibiotic coverage.

In this study, 16 (8.21%) required RRT, which was indicated in 9 out of 16 patients for hyperkalemia and 7 out of 16 for oliguria with volume overload in AKI patients. None of the patients received RRT in non-AKI patients. ICU and hospital stay were higher in AKI patients than in those without AKI ($p < 0.001$) in this study. We also found statistically significant higher ICU and hospital mortality rates in AKI than in non-AKI patients. A large meta-analysis also reported a significantly longer CICU stay for AKI patients compared with non-AKI patients (5.4 vs. 2.2 days).²⁷ Though few early

postoperative follow-up studies suggested that most patients recovered from their AKI episodes, longer-term follow-up studies reported that 20% of patients with AKI after cardiac surgery may require long-term renal follow-up.^{28,29}

This study has some limitations: This is a pilot study only comprising of very small number of patients. Numbers were less because of less elective cardiac surgical cases amid of coronavirus disease 2019 pandemic causing resource relocation and interventions of cardiac surgical programs. Being a single-center study results may not be generalized. We have not studied the other confounding variables, such as hemodynamics and vasopressors, which are potential risks for causing renal injury in cardiac surgical patients.

Conclusion

AKI is one of the common complications and multifactorial in nature in postoperative cardiac surgical patients. The incidence of AKI was 29.4%, in which 8.21% patients required RRT and the 30-day hospital mortality was 2.54% in AKI patients receiving RRT. Our study demonstrated that NS as the commonly used crystalloid in our patients and was associated with increased incidence of AKI and RRT when compared with other balanced salts solutions.

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None.

Conflict of Interest
None declared.

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