Original Article
Yonsei Med J 2022 Apr;63(4):380-388
https://doi.org/10.3349/ymj.2022.63.4.380
Yonsei Medical Journal
YMJ
pISSN: 0513-5796 · eISSN: 1976-2437

Effects of the Type of Intraoperative Fluid in Living Donor Kidney Transplantation: A Single-Center Retrospective Cohort Study

Seungho Jung[1], Jeongmin Kim[1], Juhan Lee[2], Su Youn Choi[1], Hye Ji Joo[1], and Bon-Nyeo Koo[1]

[1]Department of Anesthesiology and Pain Medicine, Anesthesia and Pain Research Institute, Yonsei University College of Medicine, Seoul; [2]Department of Surgery, Yonsei University College of Medicine, Seoul, Korea.

Purpose: Perioperative fluid management in kidney transplant recipients is crucial to supporting the fluid, acid-base, and electrolyte balance required for graft perfusion. However, the choice of intraoperative crystalloids in kidney transplantation remains controversial. We conducted a single-center retrospective cohort study to evaluate the impact of intraoperative fluids on acid-base and electrolyte balance and graft outcomes.

Materials and Methods: We included 282 living donor kidney transplant recipients from January 2010 to December 2017. Patients were classified into two groups based on the type of intraoperative crystalloids used (157 patients in the half saline group and 125 patients in the balanced crystalloid solutions group, Plasma-lyte).

Results: Compared with the half saline group, the Plasma-lyte group showed less metabolic acidosis and hyponatremia during surgery. Hyperkalemia incidence was not significantly different between the two groups. Changes in postoperative graft function assessed by blood urea nitrogen and creatinine were significantly different between the two groups. Patients in the Plasma-lyte group exhibited consistently higher glomerular filtration rates than those in the half saline group at 1 month and 1 year after transplantation after adjusting for demographic differences.

Conclusion: Intraoperative Plasma-lyte can lead to more favorable results in terms of acid-base balance during kidney transplantation. Patients who received Plasma-lyte showed superior postoperative graft function at 1 month and 1 year after transplantation. Further studies are needed to evaluate the superiority of intraoperative Plasma-lyte over other types of crystalloids in relation to graft outcomes.

Key Words: Kidney transplantation, fluid therapy, Plasma-lyte, acid-base balance, glomerular filtration rate

INTRODUCTION

Perioperative fluid management in patients undergoing kidney transplantation is crucial to maintain adequate intravascular volume, as well as acid-base and electrolyte balance, and may also affect graft tissue perfusion and function.[1-3] Crystalloids, such as normal saline (NS) or balanced low-chloride solutions, are the most common and widely used fluids for intraoperative management to maintain optimal intravascular volume.[4,5] Potassium-containing fluids may theoretically cause hyperkalemia in patients during kidney transplantation; therefore, NS, which lacks potassium, is typically used during the perioperative period of kidney transplantation. However, rapid administration of a large volume of NS may lead to hyperchloremic metabolic acidosis and subsequent hyperkalemia.[6-9] Hyperchloremia itself has also been reported as a risk factor associated with acute kidney injury.[10-13]

Considering the potential risk factors for acute kidney injury and adverse clinical outcomes, NS is being replaced with bal-

Received: April 6, 2021 **Revised:** November 23, 2021
Accepted: December 11, 2021
Corresponding author: Bon-Nyeo Koo, MD, PhD, Department of Anesthesiology and Pain Medicine, Anesthesia and Pain Research Institute, Yonsei University College of Medicine, 50-1 Yonsei-ro, Seodaemun-gu, Seoul 03722, Korea.
Tel: 82-2-2228-2422, Fax: 82-2-2227-7897, E-mail: KOOBN@yuhs.ac

•The authors have no potential conflicts of interest to disclose.

anced crystalloid solutions as both resuscitation and maintenance crystalloids in critical care and perioperative fluid management.[14-16] Half saline has been used as an intraoperative fluid during kidney transplantation instead of NS to prevent sodium retention and hyperchloremic metabolic acidosis in our hospital. Half saline may theoretically reduce the risk of hyperchloremic metabolic acidosis but may cause dilutional hyponatremia. Plasma-lyte, one of several balanced crystalloids, is an isotonic, buffered solution with an electrolyte composition similar to that of human plasma.[14] Plasma-lyte has a pH of 7.4 and has a lower chloride concentration than NS. In our hospital, there was a change in the intraoperative fluid from 0.45% half saline to Plasma-lyte.

Previous studies have compared clinical effects between NS and balanced crystalloids in kidney transplantation.[4,9,17-19] Balanced crystalloids showed a better metabolic profile. The effect of the type of intraoperative fluid type on postoperative graft function, however, remains uncertain. Meanwhile, tight control of intraoperative metabolic acidosis was reported to improve early kidney graft function.[20] This study aimed to compare the effects of half saline and Plasma-lyte on acid-base and electrolyte balance and postoperative kidney graft function after living donor kidney transplantation.

MATERIALS AND METHODS

Ethical considerations

This study was approved by the Institutional Review Board (IRB) of Severance Hospital (IRB No. 4-2020-0850). The requirement for informed consent was waived by the IRB due to the retrospective nature of this study.

Study design and patients

This was a single-center, retrospective cohort study. Data were obtained from electronic medical records. Patients who underwent living donor kidney transplantation between January 2010 and December 2017 were enrolled, while those who underwent multi-organ transplantation were excluded. Patients were classified into two groups based on intraoperative fluid (half saline vs. Plasma-lyte).

Demographics, perioperative fluid intake, and acid-base and electrolyte balance were compared between the two groups. Acid-base and electrolyte balance during surgery were recorded after induction of anesthesia (T0), reperfusion (T1), and during the immediate postoperative period (T2). Postoperative electrolyte concentrations were recorded on postoperative days (PODs) 1, 2, and 7. Daily urine volume and fluid balance were recorded until POD 2. Postoperative kidney graft function on PODs 1, 2, and 7 was assessed using serum blood urea nitrogen (BUN), creatinine, and estimated glomerular filtration rate (eGFR). eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation.[21] The eGFR values were calculated until 1-year post-transplantation to monitor graft outcomes. Delayed graft function was defined as the need for dialysis during the first week after transplantation. Renal biopsies were performed in cases of acute allograft dysfunction (>30% increase in serum creatinine levels, compared with the baseline value or proteinuria of >500 mg/day). Allograft biopsy samples were processed using light, immunofluorescent, and electron microscopy. All biopsy-proven acute rejections within the first 3 months post-transplantation were taken into account in the statistical analyses.

Intraoperative care

Intraoperative anesthetic management was performed according to the standard protocols of the center. General anesthesia was induced with 1.5–2.5 mg/kg propofol and 0.6 mg/kg of rocuronium and was maintained with sevoflurane or desflurane (0.85–1.2 minimum alveolar concentration). Remifentanil was continuously infused at a rate of 0.1–0.3 μg/kg/min during surgery. The radial artery was catheterized for continuous blood pressure monitoring and arterial blood gas analysis. Either 0.45% half saline or Plasma-lyte was used as an intraoperative maintenance fluid. The half saline solution included sodium (77 mEq/L) and chloride (77 mEq/L). Plasma-lyte (Plasma solution A, CJ Pharmaceutical, Seoul, Republic of Korea) contained sodium (140 mEq/L), potassium (5 mEq/L), magnesium (3 mEq/L), chloride (98 mEq/L), acetate (27 mEq/L), and gluconate (23 mEq/L). The intraoperative fluid choice was determined by our institute's protocol, which was changed from 0.45% half saline to Plasma-lyte after a discussion with surgeons and anesthesiologists. Fluid administration was guided by central venous pressure and adjusted by urine output after reperfusion of kidney graft.

Postoperative care

Postoperative care was performed according to the standard protocols of our institute. Until discharge, 0.45% half saline and 0.9% NS with sodium bicarbonate (6 mEq/L) were used alternately during the postoperative period in both groups, depending on serum sodium levels. The immunosuppressive regimens used in our hospital are presented in the Supplementary Table 1 (only online).

Statistical analyses

Continuous variables are presented as means±standard deviations or medians (interquartile ranges). Categorical variables are presented as frequencies and proportions. Intergroup comparisons were performed using an independent t-test or a Mann-Whitney U test for continuous variables and Fisher's exact test or a chi-square test for categorical variables. Linear mixed models were used adjusting the first measured values between the two groups to analyze changes in perioperative acid-base balance, electrolytes, and parameters associated with kidney graft function. The first values of each parameter were taken as co-

variates. If there were differences in baseline characteristics between the two groups, we adjusted the differences by including baseline variables as covariates in the model. Nonparametric longitudinal analyses using the nparLD package in R were conducted. Bonferroni correction was used for multiple comparisons. Univariable and multivariable linear regression analyses were conducted to evaluate factors associated with graft function at 1 month and 1 year after transplantation. Risk factors found to be associated with kidney graft function in univariable analysis or those considered to be clinically relevant factors were included in the multivariable analysis. All analyses were performed using Statistical Analysis System (SAS) statistical software (version 9.1.3. SAS Institute Inc., Cary, NC, USA) and R version 4.0.2 (R Foundation for Statistical Computing, Vienna, Austria). *P* values <0.05 were considered statistically significant.

RESULTS

Of the 282 patients included in this study, 157 received half saline and 125 received Plasma-lyte during kidney transplantation. Significant demographic differences were observed between the groups, including recipient age, donor eGFR, ABO-incompatible donors, graft kidney weight to recipient body weight ratio, and amount of fluid administration during surgery (Table 1). There were no significant differences in delayed graft function and acute rejection between the groups.

Table 1. Patient Characteristics

Characteristics	Half saline (n=157)	Plasma-lyte (n=125)	*p* value
Age (yr)	45 (33–51)	47 (37–57)	0.006
BMI (kg/m^2)	22.1 (20.1–24.2)	22.3 (20.0–24.7)	0.919
Male sex	89 (56.7)	67 (53.6)	0.604
Hypertension	126 (80.3)	103 (82.4)	0.647
Diabetes mellitus	35 (22.3)	29 (23.2)	0.857
Preemptive kidney transplant	44 (28.0)	47(37.6)	0.088
Re-transplantation	5 (3.2)	10 (8.0)	0.074
Donor age (yr)	42 (29–49)	43 (34–51)	0.083
Donor eGFR	101 (90–111)	107 (100–116)	<0.001
ABO incompatible donor	13 (8.3)	30 (24.0)	<0.001
Number of HLA mismatches	3 (2–4)	3 (2–4)	0.090
Kidney weight (g)/ body weight (kg)	2.89 (2.42–3.57)	3.18 (2.63–3.91)	0.013
Warm ischemic time (min)	35 (30–40)	35 (29–40)	0.805
Intraoperative fluid input (mL/kg/h)	9.0 (7.6–11.9)	7.0 (6.0–9.3)	<0.001
Intraoperative furosemide use (mg)	30 (20–40)	20 (20–40)	0.059
Delayed graft function	7 (4.5)	2 (1.6)	0.307
Acute rejection	14 (8.9)	11 (8.8)	>0.999

BMI, body mass index; HLA, human leukocyte antigen; eGFR, estimated glomerular filtration rate.
Values are expressed as medians (interquartile ranges) or n (%).

Perioperative acid-base balance showed significant differences between the two groups after adjusting the first measured values by the linear mixed model (Table 2). Preoperative total CO_2 levels were significantly higher in the half saline group (p=0.003). However, total CO_2 levels during surgery were significantly higher in the Plasma-lyte group. The mean serum bicarbonate concentration (reference range, 21–28 mmol/L) was significantly higher in the Plasma-lyte group than in the half saline group, even under physiologic ranges during the reperfusion (19.29±2.46 mmol/L vs. 22.93±3.48 mmol/L, p<0.001) and immediate postoperative periods (18.68±2.53 mmol/L vs. 21.85±2.84 mmol/L, p<0.001). Base excess in the extracellular fluid was also significantly higher in the Plasma-lyte group than in the half saline group during surgery. Sodium bicarbonate was administered in one patient in the half saline group and no patients in the Plasma-lyte group (data not shown).

Hyponatremia (sodium <130 mmol/L) occurred more frequently in the half saline group during the reperfusion period (p<0.001), immediate postoperative period (p<0.001) and POD 1 (p=0.032) (Table 3). Hyperchloremia (chloride >110 mmol/L) occurred more frequently in the half saline group on POD 2 and 7, although there were no significant differences between the groups (p=0.163 and 0.067, respectively). Hyperkalemia (potassium >5.5 mmol/L) at the reperfusion period occurred in five

Table 2. Perioperative Acid-Base Balance

	Half saline (n=157)	Plasma-lyte (n=125)	*p* value
pH			
T0	7.42±0.05	7.43±0.06	
T1	7.37±0.05	7.38±0.06	0.140
T2	7.38±0.05	7.39±0.04	>0.999
Bicarbonate (mmol/L)			
T0	20.22±2.66	23.60±3.61	
T1	19.29±2.46	22.93±3.48	<0.001
T2	18.68±2.53	21.85±2.84	<0.001
BE-ECF (mmol/L)			
T0	-4.45±3.30	-0.71±4.44	
T1	-6.27±3.12	-2.24±4.16	<0.001
T2	-6.72±3.02	-3.35±3.06	0.017
Lactate (mmol/L)			
T0	0.90±0.60	0.92±0.36	
T1	1.03±0.65	0.98±0.47	0.336
T2	1.14±0.79	1.14±0.64	>0.999
Total CO_2 (mmol/L)			
Preoperative period	23.03±3.58	21.07±3.07	
T0	21.17±2.64	24.64±3.70	<0.001
T1	20.32±2.50	24.02±3.27	<0.001
T2	19.57±2.92	22.72±3.16	<0.001

BE-ECF, base excess in extracellular fluid; T0, after induction of anesthesia; T1, reperfusion period; T2, immediate postoperative period.
Values are expressed as means±standard deviations. The first measured values of each parameter were taken as fixed covariates in the linear mixed model. *p* values were adjusted using Bonferroni's method.

https://doi.org/10.3349/ymj.2022.63.4.380

Table 3. Incidence of Electrolyte Abnormality

	Half saline (n=157)	Plasma-lyte (n=125)	*p* value
Hyponatremia (<130 mmol/L)			
Preoperative	19 (12.1)	11 (8.8)	>0.999
T0	34 (21.7)	32 (25.6)	>0.999
T1	68 (43.3)	19 (15.2)	<0.001
T2	69 (44.2)	4 (3.2)	<0.001
POD 1	9 (5.7)	0 (0)	0.032
POD 2	3 (1.9)	0 (0)	>0.999
POD 7	2 (1.3)	3 (2.4)	>0.999
Hyperkalemia (>5.5 mmol/L)			
T0	5 (3.2)	0 (0)	0.410
T1	5 (3.2)	1 (0.8)	>0.999
T2	0 (0.0)	1 (0.8)	>0.999
POD 1	2 (1.3)	0 (0.0)	>0.999
POD 2	2 (1.3)	2 (1.6)	>0.999
POD 7	2 (1.3)	6 (4.8)	0.867
Hyperchloremia (>110 mmol/L)			
T0	7 (4.5)	5 (4.0)	>0.999
T1	3 (1.9)	5 (4.0)	>0.999
T2	0 (0.0)	2 (1.6)	>0.999
POD 1	14 (8.9)	6 (5.0)	>0.999
POD 2	19 (12.1)	5 (4.0)	0.163
POD 7	15 (9.6)	2 (1.6)	0.067

POD, postoperative day; T0, after induction of anesthesia; T1, reperfusion period; T2, immediate postoperative period.
Values are expressed as n (%). *p* values were adjusted using Bonferroni's method.

patients in the half saline group and in one patient in the Plasma-lyte group, although the difference was not statistically significant (p>0.999).

Parameters associated with postoperative kidney graft function are shown in Table 4. We made a linear mixed model after adjusting for differences in baseline characteristics between the two groups to compare the parameters. Recipient age, donor eGFR, ABO-incompatible donors, graft kidney weight to recipient body weight ratio, amount of fluid administration during surgery, and the type of intraoperative fluid (half saline vs. Plasma-lyte) were included as fixed effects to evaluate the effect of fluid type on postoperative kidney graft function over time. BUN was lower at the immediate postoperative period (p<0.001), and creatinine was lower at the immediate postoperative period (p<0.001) and POD 1 (p=0.024). Urine volume was higher in the Plasma-lyte group at PODs 1 and 2 (p<0.001 for both). A significant difference was observed in BUN (p<0.001) and creatinine (p<0.001) change between groups over time (Fig. 1). As shown in Fig. 2, we found a significant difference between groups in eGFR change over time until 1-year after transplantation (p=0.006).

eGFR at 1 month was higher in the Plasma-lyte group (72.77±23.67 vs. 61.83±20.05, p<0.001). Graft function measured by eGFR at 1 month after transplantation was associated with sex, intraoperative Plasma-lyte use, recipient age, donor age, donor graft kidney weight to recipient body weight ratio, acute rejection, and donor eGFR in the univariable model. In the adjusted model, patients who received Plasma-lyte during the intraoperative period exhibited a 9.156 mL/min/1.73 m^2 higher eGFR at 1 month after transplantation (Table 5). eGFR at 6 months and 1 year was also higher in the Plasma-lyte group (74.04±19.27 vs. 63.92±18.64, p<0.001 and 71.83±19.65 vs. 66.20±19.80, p=0.018, respectively). Follow-up eGFR measured at 1-year post-transplantation was associated with sex, intraoperative Plasma-lyte use, donor age, donor graft kidney weight to recipient body weight ratio, acute rejection, and donor eGFR in the univariable model. Multivariable analysis revealed that intraoperative Plasma-lyte use was associated with a 4.452 mL/min/1.73 m^2 higher eGFR at 1 year after transplantation (Table 6). Male sex was not significantly associated with eGFR at 1 month and 1 year after transplantation in multivariable analysis (p=0.093 and p=0.842, respectively).

DISCUSSION

In this retrospective study, we demonstrated that Plasma-lyte administration during surgery reduces the occurrence of metabolic acidosis during the intraoperative and early postoperative periods, compared with the administration of 0.45% half saline. Postoperative kidney graft function measured using eGFR showed favorable results in the Plasma-lyte group.

Various factors may affect acid-base and electrolyte balance in patients undergoing kidney transplantation, such as the type of intravascular solution used during surgery.[8,9,19,22,23] Crystalloid fluids comprise different components based on their composition of electrolytes and the presence of buffers. Comparisons of clinical outcomes associated with different types of intravenous crystalloids used in kidney transplantation have been reported,[4,8,9,17,19,24-26] with each fluid demonstrating its own pros and cons. Recently, a balanced crystalloid solution has shown a better metabolic profile and is preferred in kidney transplantation.[27]

Metabolic acidosis after using a large volume of NS is a risk factor for subsequent hyperkalemia that is mediated by an extracellular shift of potassium ions.[19] Solutions with lower chloride content, such as balanced crystalloids, have been administered to minimize the risk of hyperchloremic metabolic acidosis.[4,28] Compared with NS, Hartman's solution contains potassium (4 mEq/L) and has a lower chloride concentration (109 mEq/L). O'Malley reported that the use of Hartman's solution reduced hyperkalemia and acidosis during kidney transplantation when compared with the use of NS.[29]

Unlike Hartman's solution, half saline does not contain potassium ions. Based on the same reasons outlined for NS, the lack of potassium ions may reduce the risk of hyperkalemia. Patients with end-stage renal disease may also have co-morbid salt-sensitive hypertension and coronary artery disease.[30] These

Table 4. Postoperative Kidney Graft Function Changes

	Half saline (n=157)	Plasma-lyte (n=125)	*p* value
BUN (mg/dL)			
Preoperative period	47.14±19.83	48.52±16.18	
Immediate postoperative period	49.86±16.78	40.98±13.34	<0.001
POD 1	35.94±15.39	31.60±12.99	0.600
POD 2	28.92±18.85	26.41±12.51	>0.999
POD 7	24.02±17.41	23.78±13.09	>0.999
Creatinine (mg/dL)			
Preoperative period	8.14±3.78	7.51±3.04	
Immediate postoperative period	6.06±2.84	4.61±2.25	<0.001
POD 1	3.64±1.93	2.91±1.84	0.024
POD 2	1.82±1.24	1.52±1.15	>0.999
POD 7	1.48±1.09	1.19±0.72	>0.999
eGFR (mL/min/1.73 m^2)			
Preoperative period	8.46±4.00	8.40±3.69	
Immediate postoperative period	12.50±7.88	15.23±7.94	0.029
POD 1	24.28±15.38	31.31±18.75	0.008
POD 2	52.40±24.56	58.75±23.72	>0.999
POD 7	65.10±25.41	69.28±21.75	>0.999
Urine volume (mL/day)			
Intraoperative period	540 (300–1000)	1045 (625–1655)	
Immediate postoperative period	7460 (5650–10110)	7900 (5250–10070)	>0.999
POD 1	6850 (5190–8740)	8185 (6500–10070)	<0.001
POD 2	5750 (4430–7260)	6750 (5565–8330)	<0.001
Fluid balance (mL)			
Immediate postoperative period	2685 (1920–3310)	1995 (1110–2610)	
POD 1	-25 (-405–300)	-150 (-510–180)	0.729
POD 2	-75 (-488–267)	-125 (-690–270)	>0.999

BUN, blood urea nitrogen; POD, postoperative day; eGFR, estimated glomerular filtration rate.
Values are expressed as means±standard deviations or medians (interquartile ranges). The first measured values of each parameter were taken as fixed covariates in the linear mixed model. *p* values were adjusted using Bonferroni's method.

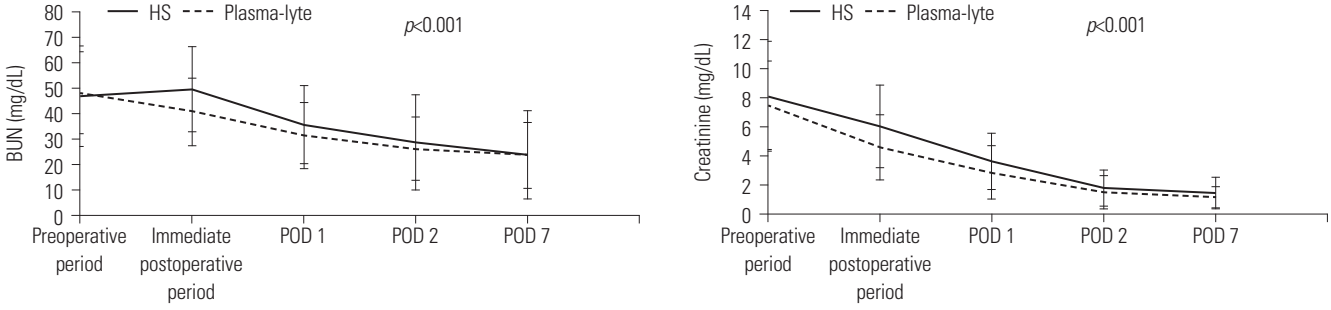

Fig. 1. Changes in BUN and creatinine during the perioperative period. Data shown as mean±standard deviation. *p* value from a linear mixed model to compare changes in BUN and creatinine over time between groups. BUN, blood urea nitrogen; POD, postoperative day; HS, half saline.

conditions may adversely affect left ventricular function.[31] Consequently, administration of a large volume of a salt solution may cause sodium retention and volume overload, which can worsen cardiac and renal function in these patients.[32-34] The lower sodium concentration in half saline may reduce the risk of such events. The risk of hyperchloremic metabolic acidosis may also be reduced with the administration of half saline compared with NS administration. This rationale supported the use of half saline during preoperative and intraoperative periods in kidney transplant patients treated at our hospital. However, the administration of a large volume of hypotonic fluid, such as half saline, may cause dilutional hyponatremia due to its lower sodium concentration. Hyponatremia may contribute to serious brain injury, and efforts to correct hyponatremia may even cause osmotic demyelinating syndrome in patients.[35] However, no experience of brain injury has been recorded over several de-

https://doi.org/10.3349/ymj.2022.63.4.380

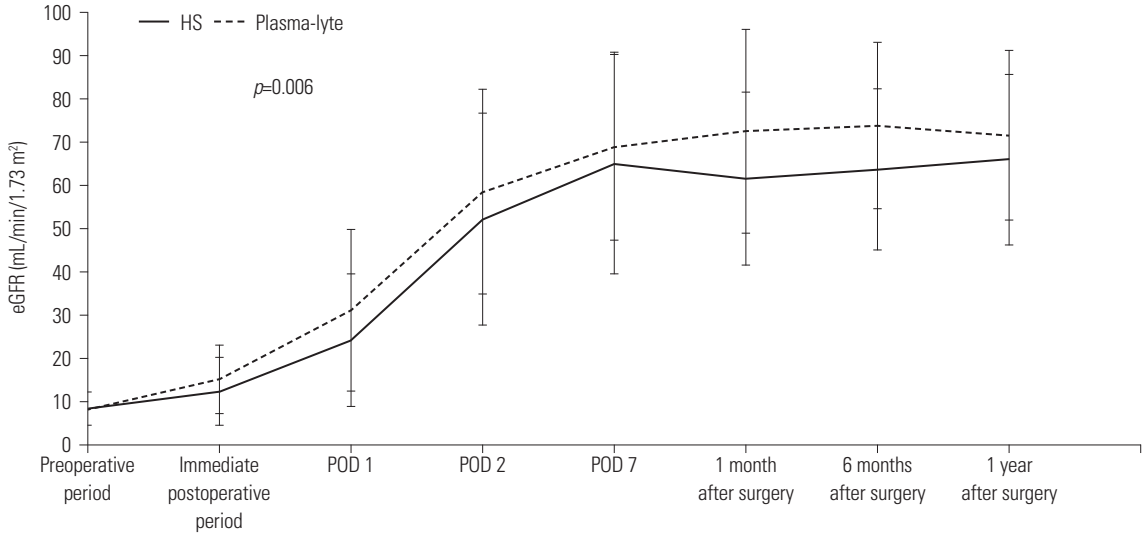

Fig. 2. Change in eGFR at 1 year after surgery. Data shown as mean±standard deviation. *p* value from a linear mixed model to compare changes in eGFR over time between groups. eGFR, estimated glomerular filtration rate; POD, postoperative day; HS, half saline.

Table 5. Factors Associated with eGFR at 1 Month after Transplantation in Univariable and Multivariable Linear Regression

	Univariable model		Multivariable model	
	β coefficient (95% CI)	*p* value	β coefficient (95% CI)	*p* value
Male sex	-6.283 (-11.514 to -1.053)	0.019	4.389 (-0.735 to 9.514)	0.093
Intraoperative Plasma-lyte use	10.941 (5.813 to 16.068)	<0.001	9.156 (4.276 to 14.036)	<0.001
Recipient age (yr)	-0.266 (-0.471 to -0.062)	0.011	-0.330 (-0.503 to -0.157)	<0.001
Donor age (yr)	-0.475 (-0.693 to -0.257)	<0.001	-0.419 (-0.677 to -0.161)	0.002
Preemptive kidney transplant	-1.504 (-7.119 to 4.110)	0.598	-1.913 (-6.481 to 2.655)	0.410
ABO incompatible donor	6.002 (-1.270 to 13.273)	0.105	4.868 (-1.321 to 11.058)	0.123
Number of HLA mismatches	-1.433 (-3.204 to 0.337)	0.112	-0.771 (-2.249 to 0.707)	0.305
Kidney weight (g)/body weight (kg)	8.680 (5.832 to 11.529)	<0.001	9.881 (6.879 to 12.883)	<0.001
Acute rejection	-18.919 (-27.886 to -9.951)	<0.001	-15.255 (-22.813 to -7.697)	<0.001
Warm ischemic time (min)	-0.126 (-0.396 to 0.145)	0.361	-0.131 (-0.350 to 0.088)	0.241
Donor eGFR	0.555 (0.376 to 0.734)	<0.001	0.322 (0.106 to 0.539)	0.004
Intraoperative vasopressor use	-1.580 (-7.403 to 4.243)	0.594	0.086 (-4.728 to 4.900)	0.972

CI, confidence interval; HLA, human leukocyte antigen; eGFR, estimated glomerular filtration rate.

Table 6. Factors Associated with eGFR at 1 Year after Transplantation in Univariable and Multivariable Linear Regression

	Univariable model		Multivariable model	
	β coefficient (95% CI)	*p* value	β coefficient (95% CI)	*p* value
Male sex	-5.913 (-10.584 to -1.241)	0.013	-0.462 (-5.008 to 4.084)	0.842
Intraoperative Plasma-lyte use	5.634 (0.954 to 10.314)	0.018	4.452 (0.150 to 8.754)	0.043
Recipient age (yr)	0.002 (-0.185 to 0.190)	0.981	-0.049 (-0.204 to 0.107)	0.538
Donor age (yr)	-0.733 (-0.915 to -0.551)	<0.001	-0.498 (-0.726 to -0.270)	<0.001
Preemptive kidney transplant	-2.028 (-7.033 to 2.977)	0.426	-0.759 (-4.791 to 3.272)	0.711
ABO incompatible donor	2.886 (-3.611 to 9.383)	0.383	2.356 (-3.092 to 7.805)	0.395
Number of HLA mismatches	-1.433 (-3.019 to 0.153)	0.076	-0.889 (-2.209 to 0.432)	0.186
Kidney weight (g)/body weight (kg)	4.277 (1.654 to 6.900)	0.001	5.134 (2.481 to 7.787)	<0.001
Acute rejection	-17.440 (-25.402 to -9.479)	<0.001	-16.458 (-23.111 to -9.806)	<0.001
Warm ischemic time (min)	-0.063 (-0.304 to 0.177)	0.603	-0.048 (-0.242 to 0.145)	0.623
Donor eGFR	0.654 (0.502 to 0.805)	<0.001	0.356 (0.165 to 0.547)	<0.001
Intraoperative vasopressor use	2.512 (-2.674 to 7.698)	0.341	3.187 (-1.062 to 7.435)	0.141

CI, confidence interval; HLA, human leukocyte antigen; eGFR, estimated glomerular filtration rate.

cades in our institute.

Several studies have reported that the use of Plasma-lyte in kidney transplantation is associated with a lower prevalence of hyperchloremic metabolic acidosis[8,17,19,25] and hyperkalemia events than NS.[9] In our study, no significant differences were observed in the incidence of hyperkalemia events between both groups during surgery. This is consistent with previous reports that have compared the use of NS-based crystalloids and balanced crystalloids containing potassium during kidney transplantation.[18,29] Metabolic acidosis was more severe in the half saline group than in the Plasma-lyte group. The buffer components in the Plasma-lyte solution may have contributed to a more favorable acid-base balance.

Early diuresis is a good marker of successful transplantation because it reflects the recovery status of kidney graft function. In this study, administration of Plasma-lyte in the intraoperative period was associated with more urine output on PODs 1 and 2 (p<0.001, both). Similarly, serum creatinine reduction over time was more rapid in the Plasma-lyte group than in the half saline group (p<0.001). Plasma-lyte use was also associated with better postoperative kidney graft function as measured by eGFR in a multivariable linear analysis at both 1 month and 1 year after transplantation (p<0.001 and p=0.043, respectively). The influence of the type of crystalloid solution used only during the intraoperative period on long-term kidney graft recovery may be limited, as reported previously.[8,19] Kidney graft function may be affected by several factors in addition to intraoperative fluid type.[36] As metabolic acidosis may negatively affect kidney function, intraoperative fluid management employing improved acid-base balance may be associated with postoperative kidney graft function.[37,38] As mentioned above, we administered half saline to prevent hyperchloremic metabolic acidosis. However, acidosis may occur without hyperchloremia. According to the Stewart method to analyze acid-base balance, the strong ion difference (SID) of half saline is zero, which is exactly the same as NS.[39] At physiologic pH, the SID is positive. Therefore, continuous administration of half saline can reduce SID and result in metabolic acidosis. In contrast, the SID of Plasma-lyte in vivo is 50, which can increase the SID of the patients and increase the tendency to develop alkalosis.

To maintain adequate intravascular volume, a larger volume of half saline is needed than that of Plasma-lyte due to the lower tonicity of half saline. This may lead to more distribution of free water to the interstitial space in the half saline group. Renal interstitial edema might impair renal function because the kidney is an encapsulated organ and could be affected by fluid congestion and elevated tubular pressure.[40,41] Identifying a direct association between the type of intraoperative fluid used and graft outcomes at 1-year post-transplantation is challenging. Furthermore, the choice of intraoperative fluid used may affect the early recovery of kidney grafts, and better early graft function may be associated with the long-term outcomes of kidney transplantations.

Our study has a few key limitations. First, as a single-center investigation, the generalizability of this study is limited. In addition, we included only patients who underwent living donor kidney transplantation and excluded deceased donor kidney transplantation. However, this made it possible to maintain homogeneity in surgical technique, intraoperative anesthetic management, postoperative management including fluid therapy, immunosuppressive regimen, and follow-up protocol. Second, although we tried to reduce indication bias and adjusted baseline demographic differences between groups due to the retrospective design of the study, the design is still unlikely to be perfect. Third, it is uncertain that the impact of Plasma-lyte on postoperative graft function is due to its favorable intraoperative acid-base balance or chloride concentration. Further study comparing Plasma-lyte with another type of fluid that is more balanced than half saline and with lower chloride content than Plasma-lyte, such as half saline mixed with 50–75 mEq of sodium bicarbonate, could help determine the intraoperative fluid choice.

In conclusion, intraoperative Plasma-lyte use was associated with more favorable results in terms of acid-base balance during kidney transplantation. Compared to the administration of half saline, Plasma-lyte administration did not lead to an increase in the occurrence of hyperkalemia. Patients receiving Plasma-lyte showed superior postoperative graft function at 1 month and 1 year after transplantation. Further studies are needed to evaluate the superiority of intraoperative Plasma-lyte over other types of crystalloids with regards to graft outcomes.

AUTHOR CONTRIBUTIONS

Conceptualization: Bon-Nyeo Koo. Data curation: Juhan Lee, Su Youn Choi, and Hye Ji Joo. Formal analysis: Seungho Jung and Su Youn Choi. Investigation: Hye Ji Joo. Methodology: Seungho Jung and Juhan Lee. Project administration: Jeongmin Kim and Bon-Nyeo Koo. Resources: Jeongmin Kim. Software: Su Youn Choi. Supervision: Bon-Nyeo Koo. Validation: Su Youn Choi. Visualization: Jeongmin Kim. Writing—original draft: Seungho Jung. Writing—review & editing: Jeongmin Kim, Juhan Lee, and Bon-Nyeo Koo. Approval of final manuscript: all authors.

ORCID iDs

Seungho Jung https://orcid.org/0000-0001-6220-6766
Jeongmin Kim https://orcid.org/0000-0002-0468-8012
Juhan Lee https://orcid.org/0000-0003-4910-2596
Su Youn Choi https://orcid.org/0000-0002-2951-5361
Hye Ji Joo https://orcid.org/0000-0003-4194-5820
Bon-Nyeo Koo https://orcid.org/0000-0002-3189-1673

REFERENCES

1. Schnuelle P, Johannes van der Woude F. Perioperative fluid management in renal transplantation: a narrative review of the literature. Transpl Int 2006;19:947-59.
2. Calixto Fernandes MH, Schricker T, Magder S, Hatzakorzian R.

https://doi.org/10.3349/ymj.2022.63.4.380

Perioperative fluid management in kidney transplantation: a black box. Crit Care 2018;22:14.
3. Othman MM, Ismael AZ, Hammouda GE. The impact of timing of maximal crystalloid hydration on early graft function during kidney transplantation. Anesth Analg 2010;110:1440-6.
4. Wan S, Roberts MA, Mount P. Normal saline versus lower-chloride solutions for kidney transplantation. Cochrane Database Syst Rev 2016;2016:CD010741.
5. Collins MG, Fahim MA, Pascoe EM, Dansie KB, Hawley CM, Clayton PA, et al. Study protocol for better evidence for selecting transplant fluids (BEST-fluids): a pragmatic, registry-based, multi-center, double-blind, randomized controlled trial evaluating the effect of intravenous fluid therapy with Plasma-Lyte 148 versus 0.9% saline on delayed graft function in deceased donor kidney transplantation. Trials 2020;21:428.
6. Prough DS, Bidani A. Hyperchloremic metabolic acidosis is a predictable consequence of intraoperative infusion of 0.9% saline. Anesthesiology 1999;90:1247-9.
7. Scheingraber S, Rehm M, Sehmisch C, Finsterer U. Rapid saline infusion produces hyperchloremic acidosis in patients undergoing gynecologic surgery. Anesthesiology 1999;90:1265-70.
8. Hadimioglu N, Saadawy I, Saglam T, Ertug Z, Dinckan A. The effect of different crystalloid solutions on acid-base balance and early kidney function after kidney transplantation. Anesth Analg 2008;107:264-9.
9. Weinberg L, Harris L, Bellomo R, Ierino FL, Story D, Eastwood G, et al. Effects of intraoperative and early postoperative normal saline or Plasma-Lyte 148® on hyperkalaemia in deceased donor renal transplantation: a double-blind randomized trial. Br J Anaesth 2017;119:606-15.
10. Yunos NM, Bellomo R, Hegarty C, Story D, Ho L, Bailey M. Association between a chloride-liberal vs chloride-restrictive intravenous fluid administration strategy and kidney injury in critically ill adults. JAMA 2012;308:1566-72.
11. Nadeem A, Salahuddin N, El Hazmi A, Joseph M, Bohlega B, Sallam H, et al. Chloride-liberal fluids are associated with acute kidney injury after liver transplantation. Crit Care 2014;18:625.
12. Oh TK, Song IA, Kim SJ, Lim SY, Do SH, Hwang JW, et al. Hyperchloremia and postoperative acute kidney injury: a retrospective analysis of data from the surgical intensive care unit. Crit Care 2018;22:277.
13. Lombardi G, Ferraro PM, Bargagli M, Naticchia A, D'Alonzo S, Gambaro G. Hyperchloremia and acute kidney injury: a retrospective observational cohort study on a general mixed medical-surgical not ICU-hospitalized population. Intern Emerg Med 2020;15:273-80.
14. Weinberg L, Collins N, Van Mourik K, Tan C, Bellomo R. Plasma-Lyte 148: a clinical review. World J Crit Care Med 2016;5:235-50.
15. Semler MW, Kellum JA. Balanced crystalloid solutions. Am J Respir Crit Care Med 2019;199:952-60.
16. Hammond DA, Lam SW, Rech MA, Smith MN, Westrick J, Trivedi AP, et al. Balanced crystalloids versus saline in critically ill adults: a systematic review and meta-analysis. Ann Pharmacother 2020;54:5-13.
17. Arslantas R, Dogu Z, Cevik BE. Normal saline versus balanced crystalloid solutions for kidney transplantation. Transplant Proc 2019;51:2262-4.
18. Potura E, Lindner G, Biesenbach P, Funk GC, Reiterer C, Kabon B, et al. An acetate-buffered balanced crystalloid versus 0.9% saline in patients with end-stage renal disease undergoing cadaveric renal transplantation: a prospective randomized controlled trial. Anesth Analg 2015;120:123-9.
19. Kim SY, Huh KH, Lee JR, Kim SH, Jeong SH, Choi YS. Comparison of the effects of normal saline versus Plasmalyte on acid-base balance during living donor kidney transplantation using the Stewart and base excess methods. Transplant Proc 2013;45:2191-6.
20. Etezadi F, Pourfakhr P, Mojtahedzade M, Najafi A, Moharari RS, Yarandi KK, et al. Effects of tight versus non tight control of metabolic acidosis on early renal function after kidney transplantation. Daru 2012;20:36.
21. Levey AS, Coresh J, Greene T, Stevens LA, Zhang YL, Hendriksen S, et al. Using standardized serum creatinine values in the modification of diet in renal disease study equation for estimating glomerular filtration rate. Ann Intern Med 2006;145:247-54.
22. Kim YS, Moon JI, Kim DK, Kim SI, Park K. Ratio of donor kidney weight to recipient bodyweight as an index of graft function. Lancet 2001;357:1180-1.
23. Redfield RR, Scalea JR, Zens TJ, Muth B, Kaufman DB, Djamali A, et al. Predictors and outcomes of delayed graft function after living-donor kidney transplantation. Transpl Int 2016;29:81-7.
24. Ghorbani A, Feli M, Ehsanpour A, Shahbazian H, Hayati F, Roozbeh J. Half-saline versus combined normal saline and 1/3–2/3 intravenous fluid therapy in kidney transplantation. Int J Organ Transplant Med 2011;2:101-4.
25. Adwaney A, Randall DW, Blunden MJ, Prowle JR, Kirwan CJ. Perioperative Plasma-Lyte use reduces the incidence of renal replacement therapy and hyperkalaemia following renal transplantation when compared with 0.9% saline: a retrospective cohort study. Clin Kidney J 2017;10:838-44.
26. González-Castro A, Ortiz-Lasa M, Rodriguez-Borregan JC, Rodrigo Calabia E, Ruiz San Millan JC, Dierssen Soto T. Influence of proportion of normal saline administered in the perioperative period of renal transplantation on kalemia levels. Transplant Proc 2018;50:569-71.
27. Wagener G, Bezinover D, Wang C, Kroepfl E, Diaz G, Giordano C, et al. Fluid management during kidney transplantation: a consensus statement of the Committee on Transplant Anesthesia of the American Society of Anesthesiologists. Transplantation 2021;105:1677-84.
28. Boer C, Bossers SM, Koning NJ. Choice of fluid type: physiological concepts and perioperative indications. Br J Anaesth 2018;120:384-96.
29. O'Malley CMN, Frumento RJ, Hardy MA, Benvenisty AI, Brentjens TE, Mercer JS, et al. A randomized, double-blind comparison of lactated Ringer's solution and 0.9% NaCl during renal transplantation. Anesth Analg 2005;100:1518-24.
30. Buckalew VM Jr, Berg RL, Wang SR, Porush JG, Rauch S, Schulman G. Prevalence of hypertension in 1,795 subjects with chronic renal disease: the modification of diet in renal disease study baseline cohort. Modification of Diet in Renal Disease Study Group. Am J Kidney Dis 1996;28:811-21.
31. Parfrey PS, Harnett JD, Griffiths SM, Gault MH, Barré PE. Congestive heart failure in dialysis patients. Arch Intern Med 1988;148:1519-25.
32. Yee J, Parasuraman R, Narins RG. Selective review of key perioperative renal-electrolyte disturbances in chronic renal failure patients. Chest 1999;115:149S-57.
33. Tuegel C, Bansal N. Heart failure in patients with kidney disease. Heart 2017;103:1848-53.
34. Khan S, Floris M, Pani A, Rosner MH. Sodium and volume disorders in advanced chronic kidney disease. Adv Chronic Kidney Dis 2016;23:240-6.
35. Giuliani C, Peri A. Effects of hyponatremia on the brain. J Clin Med 2014;3:1163-77.
36. Danovitch GM. Handbook of kidney transplantation. 6th ed. Philadelphia (PA): Lippincott Williams & Wilkins; 2017. p.218.

37. Messa PG, Alfieri C, Vettoretti S. Metabolic acidosis in renal transplantation: neglected but of potential clinical relevance. Nephrol Dial Transplant 2016;31:730-6.
38. Avila-Poletti D, De Azevedo L, Iommi C, Heldal K, Musso CG. Hyperchloremic metabolic acidosis in the kidney transplant patient. Postgrad Med 2019;131:171-5.
39. Fidkowski C, Helstrom J. Diagnosing metabolic acidosis in the critically ill: bridging the anion gap, Stewart, and base excess methods. Can J Anaesth 2009;56:247-56.
40. Prowle JR, Echeverri JE, Ligabo EV, Ronco C, Bellomo R. Fluid balance and acute kidney injury. Nat Rev Nephrol 2010;6:107-15.
41. Salahuddin N, Sammani M, Hamdan A, Joseph M, Al-Nemary Y, Alquaiz R, et al. Fluid overload is an independent risk factor for acute kidney injury in critically Ill patients: results of a cohort study. BMC Nephrol 2017;18:45.

https://doi.org/10.3349/ymj.2022.63.4.380