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ORIGINAL INVESTIGATION

Effects of Plasma-Lyte® and 0.9% saline in renal function after deceased-donor kidney transplant: a randomized controlled trial

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Anesthesia;
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Acid-base equilibrium

Abstract
Background: The influence of different crystalloid solutions infused during deceased-donor kidney transplant on the incidence of delayed graft function remains unclear. We investigated the influence of Plasma-Lyte® vs. 0.9% saline on the incidence of delayed graft function in deceased-donor kidney transplant recipients.
Methods: We conducted a single-blind randomized controlled trial of 104 patients aged 18 to 65 years who underwent deceased-donor kidney transplant under general anesthesia. Patients were randomly assigned to receive either Plasma-Lyte® (n = 52) or 0.9% saline (n = 52), at the same infusion volume, for intraoperative fluid replacement. The primary outcome was the occurrence of delayed graft function. Secondary outcomes included metabolic and electrolytic changes at the end of surgery.
Results: Two patients in the Plasma-Lyte® group and one in the 0.9% saline group died postoperatively and were not included for analysis. The incidence of delayed graft function in Plasma-Lyte® and 0.9% saline groups were 60.0% (95% Confidence Interval [95% CI 46.2–72.4]) and 74.5% (95% CI 61.1–84.4), respectively (p = 0.140). Mean (standard deviation) values of immediate postoperative pH and serum chloride levels in Plasma-Lyte® and 0.9% saline groups were 7.306 (0.071) and 7.273 (0.061) (p = 0.013), and 99.6 (4.2) mEq.L^{-1} and 103.3 (5.6) mEq.L^{-1}, respectively (p < 0.001). All other postoperative metabolic and electrolyte variables were not statistically different at the immediate postoperative period (p > 0.05).

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Conclusion: In deceased-donor kidney transplant recipients, the incidence of delayed graft function is not influenced by Plasma-Lyte® or 0.9% saline used for intraoperative fluid replacement.

Introduction

Kidney transplant provides an important treatment option for patients with end-stage renal disease, with an increase in 5-year survival compared to those who remain on dialysis.[1,2] In addition, transplant recipients have an important improvement in quality of life in terms of physical, psychosocial, and overall well-being perceptions.[3]

In the United States, in 2018, approximately 60% of patients waiting for an organ transplant were in the kidney waiting list, and most of the performed transplants were from deceased donors.[4] In Brazil, kidney transplant was the most common solid organ transplant performed in 2019 and approximately 80% of these organs were from deceased donors.[5]

Deceased-donor kidney transplant is still associated with some challenges in postoperative management, especially the occurrence of delayed graft function. This is a form of acute kidney injury that occurs immediately after the transplant, affecting up to 80% of deceased-donor graft recipients.[6–8] Morbidity and mortality increase with this condition, which alone represents a risk factor for acute rejection and long-term graft survival.[9]

Intraoperative fluid replacement has important hemodynamic implications and impact on postoperative morbidity. In kidney transplant, fluid replacement solutions must be used with caution, avoiding fluid overload and providing good renal perfusion and good kidney function to allow early diuresis, which is an important prognostic factor associated with early and 1-year graft function.[10,11] Isotonic saline solutions can cause hyperchloremic acidosis accompanied by hyperkalemia if compared to the same volume of lactated Ringer's solution.[12] Plasma-Lyte® is a crystalloid solution similar to plasma in electrolyte concentration, osmolarity, and pH. This solution has been shown to better maintain the acid-base balance in major abdominal surgery and even in kidney transplant.[13,14]

Current knowledge of the results of the use of different fluid replacement solutions in kidney transplant is limited to metabolic and acid-base changes. Few studies have evaluated the impact of using different crystalloid solutions on post-transplant complications, and none have evaluated their impact on the incidence of delayed graft function and its duration.

This study aimed to compare the influence of two crystalloid solutions used for intraoperative fluid replacement, Plasma-Lyte® vs. 0.9% saline, on the incidence of delayed graft function in deceased-donor kidney transplant recipients. We also evaluated the influence of these solutions on immediate postoperative acid-base and electrolyte balance.

Methods

Participants and eligibility criteria

After approval by the Research Ethics Committee of our institution, we conducted a single-blind, randomized, controlled trial of adult patients undergoing deceased-donor kidney transplant. The trial was designed and reported according to the Consolidated Standards of Reporting Trials (CONSORT) statement and is registered at the Brazilian Clinical Trials Registry platform (ReBEC, number RBR-9t7r5p, https://ensaiosclinicos.gov.br/rg/RBR-9t7r5p). We prospectively included patients in the study from July 2017 to July 2019.

Eligible participants were all patients aged 18 to 65 years, of both sexes, with American Society of Anesthesiologists (ASA) physical status III and IV, and on regular hemodialysis for treating end-stage renal disease. Patients with hemoglobin < 8 $g.dL^{-1}$ at the time of admission for transplant were excluded. During preanesthetic evaluation, patients were informed of the study purpose and procedures, and those interested in participating provided written informed consent for enrollment in the study.

Interventions

In the operating room, patients were monitored with a cardioscope, pulse oximeter, automated noninvasive blood pressure monitor, and capnograph with a gas analyzer after tracheal intubation. A peripheral venous line was obtained with a 16G or 18G catheter. After the induction of anesthesia and after the performance of the Allen's test, invasive blood pressure was monitored with the insertion of a 20G catheter in one of the radial arteries. The use of a central intravenous line was obtained according to clinical judgment of the anesthesiologists.

Patients in both groups underwent balanced general inhalational anesthesia. Induction of anesthesia was standardized for all patients, who received midazolam (3 to 5 mg, intravenously [IV]), fentanyl (5 $\mu g.kg^{-1}$ IV), etomidate (0.3 $mg.kg^{-1}$ IV), and cisatracurium (0.15 $mg.kg^{-1}$IV). Anesthesia was maintained with remifentanil (0.1 to 0.3 $\mu g.kg^{-1}.min^{-1}$ IV) and isoflurane at an alveolar concentration of 1.2 to 1.6%, fresh gas flow of 1.6 $L.min^{-1}$, and fraction of inspired oxygen of 40%. Additional doses of cisatracurium were administered according to clinical judgment. Ventilation was controlled with a tidal volume of 8 $mL.kg^{-1}$, calculated according to ideal body weight, with the respiratory rate necessary to maintain the fraction of expired carbon dioxide between 30 and 40 mmHg.

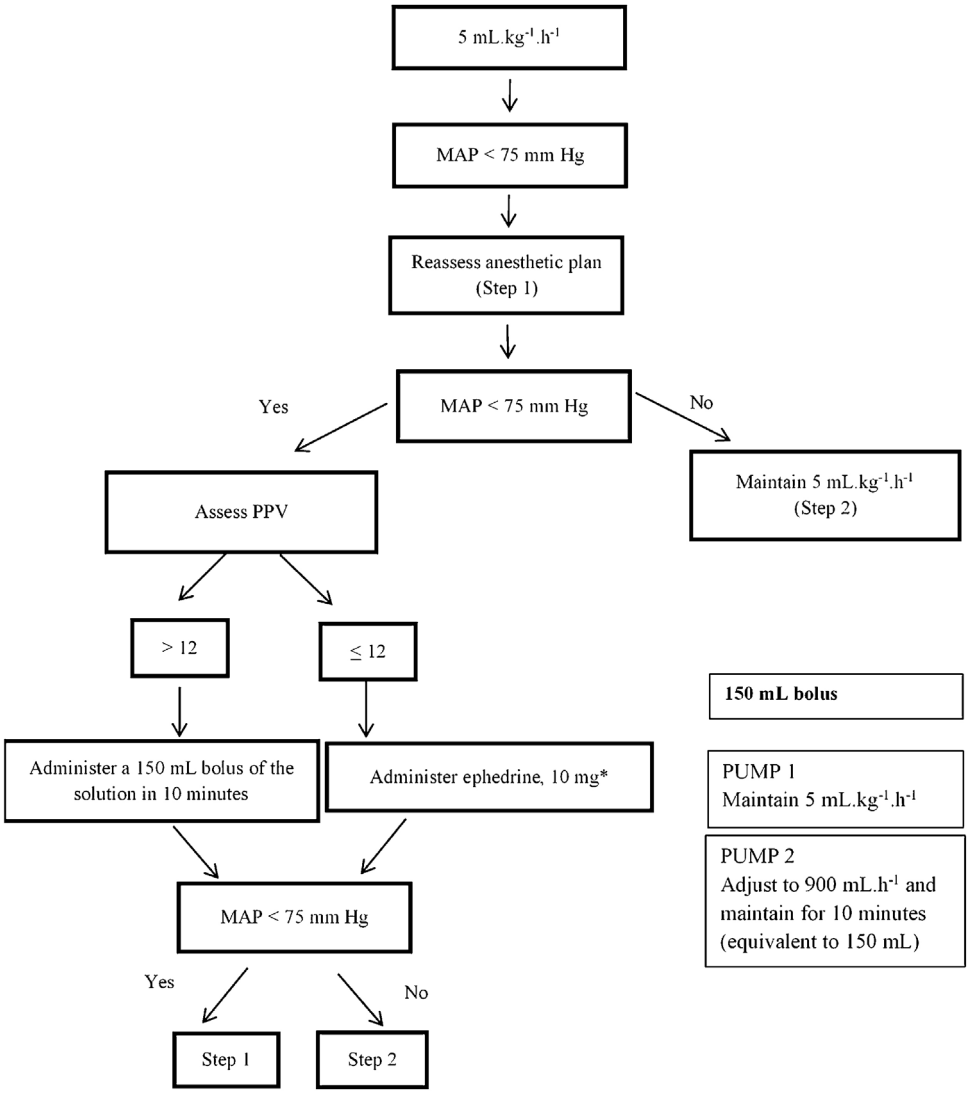

Figure 1 Flow diagram for controlling the administration of crystalloids according to invasive Mean Arterial Pressure (MAP) and Pulse Pressure Variation (PPV). Administer 5 mL.kg^{-1}.h^{-1} of the drawn solution. *If the patient is permanently with MAP < 75 mmHg (after 5 boluses of 150 mL and/or 50 mg of ephedrine), initiate norepinephrine and do not administer additional boluses (unless indicated by the analysis of other clinical criteria: heart rate; peripheral perfusion; mucous membranes; central venous pressure, if any).

In the operating room, the solution to be administered was randomly drawn for each patient using previously sealed opaque envelopes containing the name of the crystalloid to be used. The anesthesiologist was not blinded to the solution to be used. The volume of crystalloid infused in each patient was 5 mL.kg^{-1}.h^{-1}, and the necessary adjustments were guided by mean arterial pressure and pulse pressure variation, according to the protocol established for this study (Fig. 1). Thus, the patients differed only in the type of crystalloid solution, either Plasma-Lyte® (n = 52) (balanced crystalloid solution containing 140 mEq.L^{-1} sodium, 5 mEq.L^{-1} potassium, 3 mEq.L^{-1} magnesium, 98 mEq.L^{-1} chloride, 27 mEq.L^{-1} acetate, and 23 mEq.L^{-1} gluconate; osmolarity = 294 mOsmol.L^{-1} and pH = 7.4) or 0.9% saline (n = 52) (crystalloid solution with 154 mEq.L^{-1} sodium and 154 mEq.L^{-1} chloride; osmolarity = 308 mOsmol.L^{-1} and pH∼5.5). The use of packed red blood cells was indicated when the hemoglobin concentration was below 8 mg.dL^{-1} during surgery or according to clinical judgment. The use of other blood components as well as the correction of low serum calcium values were done at the discretion of the anesthesiologist.

All patients received 40 mg of intravenous furosemide and 0.5 g.kg^{-1} of 20% mannitol solution 5 to 10 minutes before completion of the arterial anastomosis. Immunosuppression followed the institution's protocol.

For postoperative analgesia, patients received tramadol (100 mg IV), metamizole (2 g IV) and morphine (0.05 mg.kg^{-1} IV) as a rescue treatment. The prophylaxis for postoperative nausea and vomiting was provided with ondansetron (8 mg IV) and metoclopramide (10 mg IV) administered at the end of the surgical procedure. We did not plan to reverse neuromuscular block, but it could be done according to clinical judgment. With return of adequate ventilatory function

and after awakening, patients were extubated and taken to the postanesthesia care unit, where they stayed for at least 90 minutes. Patients were discharged to the ward after achieving a score of 9 or 10 on the Aldrete-Kroulik scale.

After surgery, patients with diuresis received 0.45% saline in a volume corresponding to 80% of the volume of diuresis observed in the preceding hour. This fluid replacement strategy was applied every hour for 12 hours following transplant. Patients who remained without diuresis received no parenteral solution. Twelve hours after transplant, all patients were started on a light diet as tolerated.

Outcomes

The primary outcome was the occurrence of delayed graft function, defined as the need for postoperative dialysis within 7 days of transplant, assessed in a dichotomous manner (i.e., yes/no). Secondary outcomes included the duration of delayed graft function (in days, assessed as the time elapsed from transplant to the last postoperative dialysis session before hospital discharge), the number of dialysis sessions after transplant, and acid-base and electrolyte changes determined by the solutions at the end of the surgical procedure (immediate postoperative period). To this end, arterial and venous blood samples were collected 1 hour before surgery (preoperative period) and at the end of the surgical procedure. Blood pH, sodium bicarbonate, and excess base values were considered in this analysis. We also analyzed sodium, potassium, chloride, and calcium levels.

Evaluators blinded to group allocation assessed all the outcomes. The variables used to control sample homogeneity were the time of the last dialysis session performed before transplant, operative time, graft cold ischemia time, and venous and arterial anastomosis time.

Statistical analysis

To detect a reduction of 50% in the incidence of delayed graft function with the use of Plasma-Lyte® compared with 0.9% saline, considering that 60% of deceased-donor kidney transplant recipients develop this condition, with a power of 80% and significance level of 5%, a sample size of at least 49 patients per group was necessary to test the hypothesis. Thus, the total number of patients was divided into two groups with a 1:1 allocation ratio by electronic randomization using 13 blocks of eight patients, with an equal distribution of groups in each block (52 patients per group). The allocation sequence was concealed by placing the results in opaque and sealed envelopes that were opened only in the operating room. The envelopes were sequentially numbered from 1 to 104, and the study followed the numerical order of the envelopes.

Qualitative variables were compared by the Chi-Square test for proportions. The Shapiro-Wilk test was assessed for normality. Quantitative variables were compared by independent or paired Student's *t*-test, as appropriated. Non-normally distributed values were compared by Mann-Whitney test for independent variables. A p-value < 0.05 was considered statistically significant (GraphPad Prism 7.0, San Diego, CA, USA).

Results

Of all 104 randomized patients, three patients (two in the Plasma-Lyte® group and one in the 0.9% saline group) died of surgical complications in the immediate postoperative period and were not included in the statistical analysis. In both groups, some blood analyses were not done due to clotted or inappropriate blood samples. Patient recruitment and the randomization flow diagram are summarized in Figure 2.

The groups did not differ in demographic characteristics (Table 1) or intraoperative variables (Table 2).

There was no statistically significant difference in the incidence of delayed graft function between the two groups. The number of postoperative dialysis sessions up to patient discharge was not different between groups, neither was the number of elapsed days until the last postoperative dialysis session, before hospital discharge (Table 3). The immediate postoperative pH values were significantly different between groups, with higher values in the Plasma-Lyte® group. The analysis of serum chloride levels showed a statistically significant difference in both, preoperative and immediate postoperative values between groups. Although not statistically significant, as compared to their own preoperative values, postoperative serum chloride levels were reduced in the Plasma-Lyte® group, while they increased in the 0.9% saline group. No other significant differences were seen in immediate postoperative electrolytes or acid-base balance between groups (Table 4).

Discussion

Changes in the acid-base and electrolyte balance are frequently observed during the perioperative period, regardless of the type of surgery. Multiple factors can affect fluid homeostasis and renal function, including preoperative fasting time, insensible losses, underlying disease, surgical site, the magnitude of the surgical procedure, and intravenous fluid type and volume.[15] Administration of intravenous solutions is one of the factors that can be controlled by the anesthesiologist, particularly the use of crystalloid solutions.

The use of solutions with supraphysiological concentrations of chloride, such as 0.9% saline, increases the filtered load of sodium chloride, which leads to an increased detection of chloride in the dense macula at the end of the nephron. This situation is followed by the release of signaling substances (such as adenosine) by the macula densa. These mediators increase the tone of the afferent arteriole (vasoconstriction) and, consequently, decrease the glomerular blood flow and glomerular filtration rate. The importance of this pathophysiological mechanism was discussed in a review conducted by Mårtensson and Bellomo.[16] In this review, some studies comparing chloride-rich solutions with restrictive chloride administration showed a decrease in acute kidney injury incidence when less chloride was administered. These studies involved patients in intensive care unit or undergoing major surgery, and for this reason, a direct comparison with our results cannot be done. Similarly, to our results, a systematic review of randomized controlled trials examining the effect of lower-chloride solutions versus normal saline on delayed graft function, hyperkalemia, and

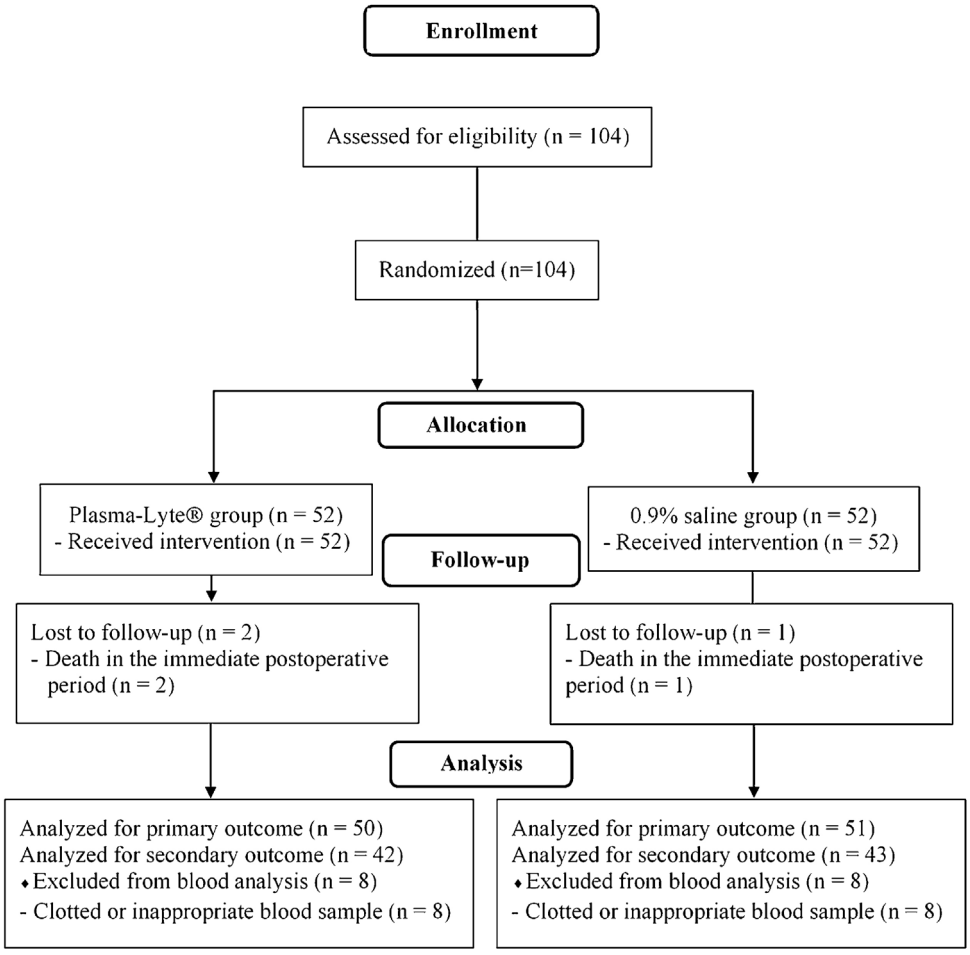

Figure 2 CONSORT flow diagram.

Table 1 Patients' characteristics.

Characteristic	Plasma-Lyte® group (n = 50)	0.9% saline group (n = 51)	*p*-value
Sex (female)	20 (40.0)	19 (37.3)	0.839
Age (years)	45.9 (10.7)	47.2 (10.5)	0.533
Height (cm)	167.6 (8.0)	167.1 (8.8)	0.799
Dry weight (kg)	71.0 (12.8)	74.6 (13.5)	0.171
Current weight (kg)	71.5 (13.0)	75.9 (13.7)	0.108
Graft cold ischemia time (h)	23 (4)	23 (7)	0.826
Time since last dialysis (h)	15 (4–48)	13 (2–32)	0.634
Main associated clinical conditions			
Hypertension	40 (80.0)	40 (78.4)	1.000
Diabetes mellitus	13 (26.0)	11 (21.6)	0.645
Smoker	5 (10.0)	12 (23.5)	0.109

Values are presented as absolute number (percentage), mean (Standard Deviation [SD]), or median (1^{st}–3^{rd} quartiles).

acid-base status in kidney transplant recipients showed no difference on the incidence of delayed graft function.[17] Nonetheless, this systematic review included three small studies not designed to evaluate delayed graft function and also performing living-donor transplantation. Overall, the incidence of delayed graft function reported in this systematic review was very low, usually that seen with living-donor kidney transplants. So far, no randomized prospective studies have yet been designed to analyze the incidence of delayed graft function comparing solutions with different chloride concentrations.

The fact that the administration of solutions with a higher chloride concentration in the perioperative period leads to worsening renal function in the postoperative period of major surgery has been a matter of debate. The results have been conflicting even in patients at higher risk for postopera-

Table 2 Intraoperative variables.

Variable	Plasma-Lyte® group (n = 50)	0.9% saline group (n = 51)	*p*-value
Operative time (min)	212 (39)	208 (42)	0.578
Anesthesia time (min)	282 (55)	269 (41)	0.167
Venous anastomosis time (min)	26 (11)	26 (10)	0.953
Arterial anastomosis time (min)	25 (9)	26 (11)	0.664
Total volume of crystalloid administered intraoperatively (mL)	1.628 (595)	1.627 (532)	0.996
Administration of packed red blood cells (n)	2 (4.0)	1 (1.9)	0.617
Use of vasopressors (n)	33 (66.0)	36 (70.6)	0.672
Correction of calcium (n)	6 (12.0)	10 (19.6)	0.414

Values are presented as absolute number (percentage) or mean (SD). n, number of patients.

Table 3 Perioperative variables.

Variable	Plasma-Lyte® group (n = 50)	0.9% saline group (n = 51)	*p*-value
Delayed graft function (n)	30 (60.0 [46.2–72.4])	38 (74.5 [61.1–84.4])	0.140
Weight gain on postoperative day 1 (kg)	1.6 (1.9)	2.2 (2.3)	0.136
First dialysis session after surgery (days)[a]	3 (2–4)	2 (2–3)	0.292
Postoperative dialysis (n)[a]	3 (2–4)	3 (2–4)	0.719
Last postoperative dialysis session before hospital discharge (d)[a]	6 (5–11)	7 (5–11)	0.433
Length of hospital stay (days)	13 (9–17)	17 (11–21)	0.061

Values are presented as number (percentage [95% Confidence Interval]), mean (SD), or median (1^{st}–3^{rd}quartiles). n, number of patients; d, days after surgery.
[a] Refer to 30 and 38 patients with delayed graft function in the Plasma-Lyte® and 0.9% saline groups, respectively.

tive renal dysfunction.[18] However, in experimental models, the use of high volumes of solutions with a high chloride concentration was unable to show worsening of hemodynamics and renal function compared to balanced solutions with a lower chloride concentration.[19,20]

The use of balanced solutions with a pH equal or close to 7.0 has been associated with fewer changes in ions and acid-base balance, especially in kidney transplant.[21,22] In our study, higher postoperative pH values and lower serum chloride values were observed for the Plasma-Lyte® group. The difference in the serum chloride values between the groups was already noted in the preoperative analysis. Nonetheless, it was enhanced in the immediate postoperative period as there was a decrease in the serum chloride values in the Plasma-Lyte® group and an increase in its values in the 0.9% saline group. These interpretations have to be done considering the losses in blood sample tests and a smaller number of subjects analyzed than those for the primary outcome. We considered these changes to be mild, as no immediate clinical intervention was judged necessary to correct them.

The present trial showed a mean reduction of approximately 15% in the incidence of delayed graft function in deceased-donor kidney transplant recipients who received Plasma-Lyte® as fluid replacement therapy compared with those who received 0.9% saline. Even considering this difference, this outcome did not have statistical significance and, for this reason, the Plasma-Lyte® solution cannot be considered superior to the 0.9% saline solution on the reduction of the incidence of delayed graft function.

We also showed a mean reduction of approximately 24% in length of hospital stay but this difference was not statistically significant, either. Length of hospital stay is associated with increased susceptibility to surgical site infections and consequently increased patient mortality and morbidity,[23,24] which is particularly concerning in patients receiving immunosuppressive therapy, such as kidney transplant recipients. Nonetheless, similarly to the findings for delayed graft function, according to the statistical analysis, the Plasma-Lyte® solution does not reduce the length of hospital stay when compared to the 0.9% saline solution.

Administering intravenous fluids to patients undergoing kidney transplant is a complex process that goes beyond the crystalloid type and infusion regimen. We based our fluid infusion on hemodynamic goals, but there is not a consensus on this issue. Goal-directed fluid therapy has shown a reduction in postoperative complications, length of hospital stays, mortality, and hospital costs in high-risk surgical patients.[25] Even though the infusion of crystalloids guided by central venous pressure resulted in better short-term renal function in kidney transplants from living donors,[26] recent studies have provided more questions than answers.[27]

The comparative analysis of electrolyte and acid-base changes between the Plasma-Lyte® and 0.9% saline groups showed that our regimen of crystalloid infusion, as a goal-directed therapy, ended up in a total amount of fluid infused unable to promote major changes in the acid-base and electrolyte balance. The occurrence of minimal changes, according to the range of variation, especially in serum chloride and pH values, may justify, at least in part, the absence of statistical differences in the primary outcome.

Table 4 Variables related to intraoperative acid-base and electrolyte balance.

Variable	Plasma-Lyte® group (n = 42)	0.9% saline group (n = 43)	Between-group difference	*p*-value
pH				
Preoperative	7.363 (0.070)	7.340 (0.070)	0.023 (-0.005 to 0.051)	0.109
Postoperative	7.306 (0.071)	7.273 (0.061)	0.033 (0.007 to 0.059)	0.013
Intragroup variation	0.057 (0.029 to 0.085)	0.067 (0.042 to 0.093)		0.339
p-value	< 0.001	< 0.001		
Base excess ($mEq.L^{-1}$)				
Preoperative	-1.9 (4.4)	-3.3 (4.1)	1.4 (-0.28 to 3.08)	0.117
Postoperative	-4.6 (4.3)	-6.0 (4.5)	1.4 (-0.34 to 3.14)	0.115
Intragroup variation	2.7 (0.94 to 4.37)	2.7 (1.03 to 4.41)		0.642
p-value	0.002	0.002		
Sodium bicarbonate ($mEq.L^{-1}$)				
Preoperative	22.9 (3.5)	21.3 (4.1)	1.6 (0.09 to 3.11)	0.039
Postoperative	20.7 (3.3)	19.6 (3.0)	1.1 (-0.15 to 2.35)	0.087
Intragroup variation	2.2 (0.86 to 3.58)	1.7 (0.28 to 3.10)		0.439
p-value	0.001	0.018		
Sodium ($mEq.L^{-1}$)				
Preoperative	138.7 (4.0)	140.9 (4.0)	-2.2 (-3.78 to -0.62)	0.008
Postoperative	134.8 (3.6)	135.7 (4.6)	-0.9 (-2.53 to 0.73)	0.275
Intragroup variation	3.93 (2.39 to 5.46)	5.13 (3.41 to 6.86)		0.067
p-value	< 0.001	< 0.001		
Potassium ($mEq.L^{-1}$)				
Preoperative	4.9 (0.8)	5.0 (0.8)	-0.1 (-0.42 to 0.22)	0.598
Postoperative	5.1 (0.9)	5.1 (0.8)	0 (-0.34 to 0.34)	0.934
Intragroup variation	-0.18 (-0.52 to 0.16)	-0.11 (-0.42 to 0.20)		0.811
p-value	0.299	0.494		
Chloride ($mEq.L^{-1}$)				
Preoperative	100.8 (4.1)	102.9 (5.5)	-2.1 (-4.02 to -0.18)	0.033
Postoperative	99.6 (4.2)	103.3 (5.6)	-3.7 (-5.66 to -1.74)	< 0.001
Intragroup variation	1.2 (-0.50 to 2.91)	-0.4 (-2.65 to 1.87)		0.084
p-value	0.164	0.733		
Calcium ($mg.dL^{-1}$)				
Preoperative	9.5 (1.2)	9.5 (1.6)	0 (-0.56 to 0.56)	0.996
Postoperative	8.2 (1.6)	8.0 (2.2)	0.2 (-0.56 to 0.96)	0.644
Intragroup variation	1.2 (0.65 to 1.82)	1.4 (0.66 to 2.17)		0.618
p-value	< 0.001	< 0.001		

Values are presented as mean (SD) or number (95% Confidence Interval). Intragroup variation is preoperative minus postoperative values, and between group difference is Plasma-Lyte® group minus 0.9% saline group.

The extent of ischemia-reperfusion injury causing delayed graft function is a multifactorial process in which the contribution of the individual components has not been fully elucidated because many factors are interrelated. Cold ischemia time (time interval between organ cold storage and warming by restoration of blood flow) is considered one of the most important factors contributing to the occurrence of delayed graft function after kidney transplant. Prospective complement-dependent cytotoxicity crossmatching accounts for most of the time consumed.[28] In our study, the long cold ischemia time seen in both groups may have contributed to the high incidence of delayed graft function. Delayed graft function remains a cause of great concern due to its implications for the patient and the health care system. Given the wide variety of agents involved, Irish et al.[29] developed a model to predict the risk of delayed graft function using donor and recipient data at the time of transplant. They found that the main risk factors are cold ischemia time, donor serum creatinine, recipient body mass index, deceased donor, and donor age greater than 16 years.

The type of intravenous fluid used intraoperatively adds a new element to be investigated in the list of causes of delayed kidney graft function. With the same purpose of our study, i.e., elucidating whether a simple measure such as changing the fluid to be used during a renal transplant could influence the incidence of delayed graft function, Collins et al.,[30] in a multi-center ongoing trial, are comparing a balanced low-chloride fluid (Plasma-Lyte®) with the traditional 0.9% saline in deceased-donor kidney transplant. Their trial will allow to overcome some limitations of the present study, such as the limited sample size and the fact that it was conducted in a single center and allow the generalization of the results to the population of patients undergoing kidney transplant. Other limitation of our study, involving our secondary outcomes, was the inability to analyze some blood samples due to clotting or insufficient blood.

Conclusions

In deceased-donor kidney transplant recipients, the incidence of delayed graft function is not influenced by the solution used for intraoperative fluid replacement, Plasma-Lyte® or 0.9% saline. A small reduction in immediate postoperative serum chloride values together with higher pH values are also observed in patients receiving Plasma-Lyte®.

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The study was approved by the Research Ethics Committee of Botucatu School of Medicine, Universidade Estadual Paulista, Brazil (UNESP, protocol number 1.874.338 and *Plataforma Brasil* CAAE number 62033816.0.0000.5411).

The trial was designed and reported according to the Consolidated Standards of Reporting Trials (CONSORT) statement and is registered at the Brazilian Clinical Trials Registry platform (ReBEC, number RBR-9t7r5p, https://ensaiosclinicos.gov.br/rg/RBR-9t7r5p).

Authors contributions

Conception and design: PNJ, LED, LGMA, NSPM

Analysis and interpretation: PNJ, LGMA, LGB, NSPM

Data collection: PNJ, LED, CMUO

Writing the article: PNJ, LED

Critical revision of the article: PNJ, LED, CMUO, LGMA, LGB, NSPM

Final approval of the article: PNJ, LED, CMUO, LGMA, LGB, NSPM

Statistical analysis: PNJ

Overall responsibility: PNJ

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Conflicts of interest

The authors declare no conflicts of interest.

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