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Balanced Electrolyte Solutions Versus 0.9% Saline for Kidney Transplantation: An Updated Systematic Review and Meta-analysis

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Background. Perioperative intravenous fluids are administered to kidney transplant recipients to maintain hemodynamic stability and graft perfusion; however, the ideal fluid remains uncertain. Although 0.9% saline (saline) is commonly used, its high chloride content causes hyperchloremic metabolic acidosis and may increase the risks of delayed graft function (DGF) and hyperkalemia. Balanced electrolyte solutions (BES) have a more physiological chloride concentration and may reduce these risks. Previous meta-analyses found insufficient evidence to compare BES with saline for these outcomes; however, new studies have recently been published. In this updated review, we compared the effects of BES with saline on the risk of DGF and hyperkalemia in kidney transplantation. **Methods.** MEDLINE, Embase, and CENTRAL were searched for randomized controlled trials comparing BES with saline in kidney transplantation. The primary outcomes were DGF and hyperkalemia. Eligible studies were assessed for risk of bias and data were pooled for analysis. The Grading of Recommendations Assessment, Development, and Evaluation framework was used to assess the quality of evidence. **Results.** Ten studies involving 1532 participants were included. The quality of evidence was high for deceased donor transplantation and very low for living donor transplantation. The relative risk (RR) of DGF associated with BES compared with saline was 0.83 (95% confidence interval [CI], 0.71-0.96; $P = 0.01$) in deceased donor transplantation. There was no difference in DGF in living donor transplantation (RR 0.79; 95% CI, 0.26-2.41; $P = 0.68$). There was no difference in hyperkalemia between groups (RR 0.87; 95% CI, 0.59-1.27; $P = 0.46$). **Conclusions.** Compared with saline, BES reduces the risk of DGF in deceased donor kidney transplantation without increasing hyperkalemia.

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In the setting of kidney transplantation surgery, significant volumes of intravenous crystalloid fluids are administered to transplant recipients to maintain blood pressure and ensure adequate graft perfusion, with the goal of promoting recovery of graft function. However, the ideal choice of intravenous fluid remains controversial. In many transplant centers, 0.9% sodium chloride (saline) has historically been the fluid of choice,[1] and balanced electrolyte solutions (BES) have been avoided because of their potassium content and the perceived risk of hyperkalemia in patients with kidney failure. More recently, hyperchloremic metabolic acidosis has been recognized as an adverse effect of large-volume infusions of saline, which may itself be associated with hyperkalemia and acute kidney injury (AKI).[2-4] In the early postoperative period after kidney transplantation, AKI, because of hyperchloremic metabolic acidosis, may

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exacerbate kidney ischemia-reperfusion injury and increase risks of delayed graft function (DGF).[5] DGF is defined as the requirement for dialysis within the first 7 d posttransplant and affects 30%–50% of deceased donor kidney transplants.[6] It is associated with significant short- and long-term sequelae, including an increased risk of acute rejection, decreased graft function, and shorter graft survival.[7] The pathophysiology of DGF is multifactorial and encompasses kidney insults that occur during donor death, organ retrieval surgery and preservation, ischemia-reperfusion injury with attendant activation of recipient innate and adaptive immune responses, and kidney injury related to recipient hemodynamics and the electrolyte milieu, of which intravenous fluid therapy is a key determinant.[8]

Several small single-center randomized controlled trials (RCTs) in living and deceased donor kidney transplant recipients have demonstrated that BES is associated with less hyperchloremic metabolic acidosis compared with saline[9-14]; however, whether this translates to significant improvements in transplant outcomes such as DGF and perioperative hyperkalemia has been uncertain. We previously published a Cochrane Systematic Review and meta-analysis, which concluded that there was insufficient evidence to determine the effects of BES compared with saline on these outcomes.[15] Since that publication, several additional RCTs have examined this question, including the recently published multicenter Better Evidence for Selecting Transplant Fluids (BEST-Fluids) trial.[16] In this updated systematic review and meta-analysis, we aimed to examine the role of BES compared with saline as perioperative fluids for the outcomes of DGF and hyperkalemia in kidney transplantation.

MATERIALS AND METHODS

Inclusion Criteria

We performed an updated systematic review and meta-analysis of RCTs comparing BES to saline for perioperative intravenous fluids in kidney transplantation. BES included lactated Ringer's solution (LR, also known as Hartmann's Solution or Compound Sodium Lactate), Plasmalyte (also known as Plasma-Lyte 148 or Plasma-Lyte), and Elo-Mel Isoton. There were no restrictions on the timing, rate, or duration of intravenous fluids. Participants included adult and pediatric patients who received a living or deceased donor kidney transplant. The study was exempt from institutional review board approval.

Outcomes

The primary outcomes were (1) DGF, defined as any requirement for dialysis in the first 7 d posttransplant, and (2) hyperkalemia, defined as serum potassium ≥5.5 mmol/L during study follow-up. Secondary outcomes were blood pH and serum potassium concentration at the end of surgery. Outcomes were prespecified, and the protocol for this systematic review was registered with PROSPERO (CRD42022379609), an international prospective register for systematic reviews.

Search Strategy

We used a sensitive search strategy to identify studies from MEDLINE, EMBASE, and CENTRAL databases (**Table S1, SDC,** http://links.lww.com/TXD/A684). The original review identified studies from the inception of these databases to November 26, 2015, and the current review search strategy covered citations published from November 26, 2015, to November 28, 2022, inclusive. Two independent authors (S.S.W. and M.G.C.) screened citation titles, abstracts, and full-text articles to identify studies that met the inclusion criteria. Any disagreements regarding study inclusion were resolved by discussion and referral to a third author if required.

Data Extraction

Two independent authors (S.S.W. and M.G.C.) extracted the data using standardized data extraction forms. Where there was >1 publication associated with a given study, reports were collated to provide the most complete data extraction. Data items collected included study setting and design characteristics, participant and transplantation characteristics, type and delivery of intervention and control fluids, and outcome data and safety data. Any disagreements regarding data extraction were resolved by discussion and referral to a third author if required.

Risk of Bias Assessment

The risk of bias was assessed using the Cochrane Risk-of-Bias 2 (RoB2) tool for RCTs[17] by 2 independent authors (S.S.W. and M.G.C.), with any disagreement resolved by discussion or by a third author. The RoB2 tool covers the following bias domains: (1) bias arising from the randomization process; (2) bias because of deviations from intended interventions; (3) bias because of missing outcome data; (4) bias in the measurement of the outcome; and (5) bias in the selection of the reported result. For item (2) above, the primary effect of interest was of assignment to intervention and risk of bias was assessed on an intention-to-treat basis. The RoB2 tool reports the risk of bias as "low risk," "high risk," or "some concerns" for each domain above and assesses the risk of bias individually for each outcome. The tool was therefore applied to the primary outcomes, DGF and hyperkalemia.

Data Synthesis

Primary and secondary outcome data were pooled for all studies with available data using random-effects models and presented as forest plots. For dichotomous outcomes such as DGF and hyperkalemia, the pooled effect measure was expressed as a relative risk (RR) with 95% confidence intervals (95% CIs). For continuous outcomes such as blood pH and serum potassium concentration, the pooled effect measure was expressed as a mean difference (MD) with 95% CIs.

Heterogeneity was assessed using a χ^2 test on N – 1 degrees of freedom and the I^2 test. Sources of heterogeneity were explored through prespecified subgroup analyses, including deceased compared with living donor transplantation. Sensitivity analysis was used to assess the impact of individual studies on pooled statistics and explore fixed-effects versus random-effects modeling. Meta-analyses were performed using RevMan version 5.4 (The Cochrane Collaboration 2020). Quality of evidence and pooled results were summarized using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework for the primary outcomes and presented as a GRADE evidence profile and summary of findings table.[18]

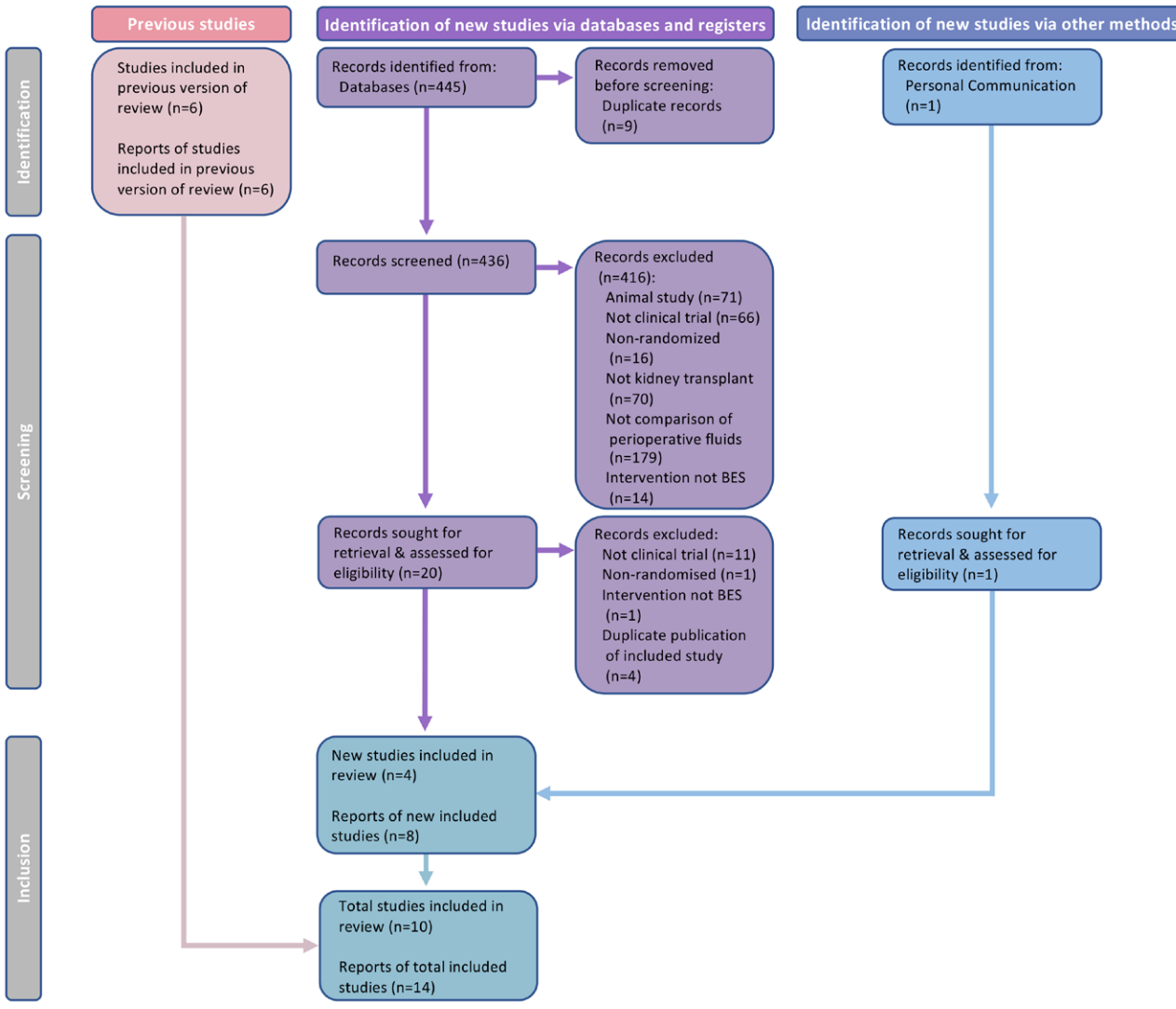


FIGURE 1. PRISMA flow diagram. BES, balanced electrolyte solution; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

RESULTS

Search Results

The search strategy identified 446 records, and 1 record was identified via personal communication.[16] After screening, 21 records were retrieved for full-text review, and 4 new studies that met the inclusion criteria were identified. Together with the 6 studies identified in the previous version of this review, there were 10 studies[9-14,16,19-21] and 1532 participants included in the current systematic review (Figure 1).

Included Studies

Characteristics of the included studies are presented in Table 1. All studies were RCTs comparing BES to saline. One multicenter RCT contributed 807 of the 1532 participants in the review.[16] The remainder of the studies were relatively small single-center studies. Five studies were conducted in deceased donor kidney transplant recipients,[14,16,19-21] 4 were conducted in living donor kidney recipients,[10-13] and 1 included both living and deceased donor kidney recipients.[9] The type of BES studied consisted of Plasmalyte in 4 studies,[13,16,19,21] LR in 3 studies,[9,11,12] both Plasmalyte and LR in 1 study,[10] Elo-Mel Isoton in 1 study,[14] and 0.45% saline with 70 mL sodium bicarbonate in 1 study.[20] Six studies[9-13,21] assigned study fluids during the intraoperative period only; 1 extended the period of study fluid assignment to immediate postanesthetic recovery,[14] and 2 studies[16,19] assigned study fluids perioperatively out to 48 h postoperatively. One study did not report the period during which study fluids were administered.[20] Seven studies reported on DGF[9,10,13,14,16,19,21] and 4 reported on hyperkalemia.[14,16,19,21] One study did not contribute data to either primary outcome.[20] Follow-up varied between 3 d and 12 mo posttransplant (Table 1).

Risk of Bias Assessment

The risk of bias assessments for each study by bias domain are shown in Figure 2 and summarized in Figure 3. For the outcome of DGF, the overall risk of bias was assessed as low risk in 14% of studies, high risk in 14% of studies, and some concerns in 72% of studies (Figure 3A). For the outcome of hyperkalemia, the overall risk of bias was assessed as low risk in 50% of studies, high risk in 25% of studies, and some concerns in 25% of studies (Figure 3B). One study that contributed to the majority of events for both primary outcomes had low risk of bias across all domains[16] (Figure 2).

TABLE 1.

Characteristics of included studies

Author	Year	Country	Design	No. of participants	Donor type	Intervention	Control	Duration of study fluid	Outcomes	Posttransplant follow-up
O'Malley[3]	2005	United States	Single-center RCT	51	Living donor (48) Deceased donor (3)	Lactated Ringer's (25)	0.9% Saline (26)	Intraoperative only	DGF Hyperkalemia Blood pH Serum K	6 mo
Hadimioglu[4]	2008	Turkey	Single-center RCT	90	Living donor	Lactated Ringer's (30) Plasmalyte (30)	0.9% Saline (30)	Intraoperative only	DGF Blood pH Serum K	7 d
Khajavi[5]	2008	Iran	Single-center RCT	52	Living donor	Lactated Ringer's (26)	0.9% Saline (26)	Intraoperative only	Blood pH Serum K	3 d
Modi[6]	2012	India	Single-center RCT	74	Living donor	Lactated Ringer's (37)	0.9% Saline (37)	Intraoperative only	Serum K	1 d
Kim[7]	2013	South Korea	Single-center RCT	60	Living donor	Plasmalyte (30)	0.9% Saline (30)	Intraoperative only	DGF Blood pH	7 d
Potura[8]	2015	Austria	Single-center RCT	148	Deceased donor DBD (145) DCD (3)	Elo-Mel Isoton (72)	0.9% Saline (76)	Intraoperative and postoperative while in recovery room	DGF Hyperkalemia Blood pH Serum K	7 d
Weinberg[9]	2017	Australia	Single-center RCT	49	Deceased donor DBD (35) DCD (14)	Plasmalyte (24)	0.9% Saline (25)	Intraoperative and 48 h postoperative	DGF Hyperkalemia Blood pH Serum K	12 mo
Pourfakhr[10]	2020	Iran	Single-center RCT	100	Deceased donor	0.45% Saline + 70 mL sodium bicarbonate	0.9% Saline	Not reported	Serum Cr to day 3 postoperative Serum Na^+, Cl^-, and base excess at 6 h postoperative	7 d
do Nascimento[11]	2022	Brazil	Single-center RCT	101	Deceased donor	Plasmalyte (50)	0.9% Saline (51)	Intraoperative only	DGF Blood pH Serum K	To hospital discharge
Collins[12]	2023	Australia and New Zealand	Multicenter Registry-linked RCT	807	Deceased donor DBD (606) DCD (201)	Plasmalyte (404)	0.9% Saline (403)	Intraoperative and 48 h postoperative	DGF Hyperkalemia Blood pH Serum K	12 mo

Cr, creatinine; DBD, donation after brain death; DCD, donation after circulatory death; DGF, delayed graft function; K, potassium; RCT, randomized controlled trial.

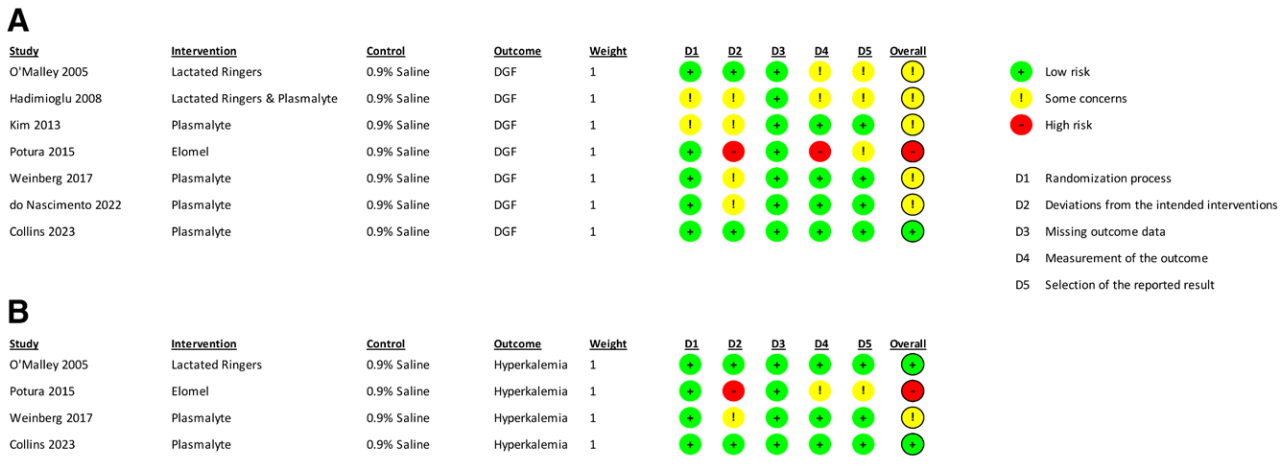


FIGURE 2. Risk of bias assessment by study and bias domains for outcomes (A) DGF and (B) hyperkalemia. DGF, delayed graft function; D1–5, domains 1–5.

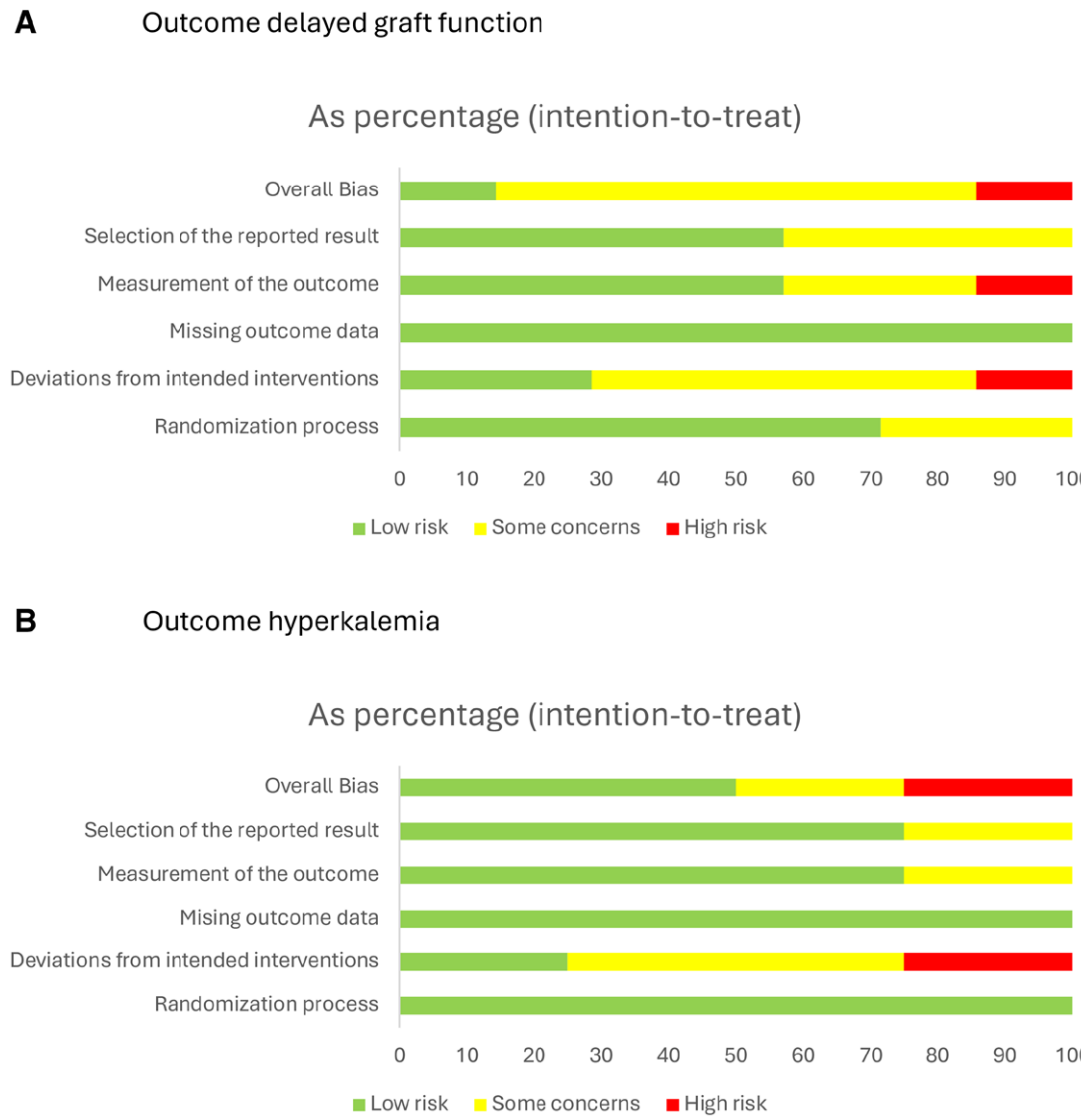


FIGURE 3. Summary of risk of bias assessment by outcomes (A) delayed graft function and (B) hyperkalemia.

TABLE 2.

Summary of pooled analyses comparing balanced electrolyte solutions with 0.9% saline by outcome and subgroup

Outcome/subgroup	Studies	Participants	Statistic	Effect	95% CI	*P*
Delayed graft function						
All kidney transplant recipients	7	1306	RR	0.82	0.71 to 0.94	0.005
Deceased donor transplant recipients	4	1105	RR	0.83	0.71 to 0.96	0.01
Living donor transplant recipients	3	201	RR	0.79	0.26 to 2.41	0.68
Hyperkalemia						
All kidney transplant recipients	4	1055	RR	0.87	0.59 to 1.27	0.46
Deceased donor transplant recipients	3	1004	RR	0.89	0.66 to 1.20	0.45
Liing donor transplant recipients	1	51	RR	0.09	0.01 to 1.62	0.10
Blood pH at end of surgery						
All kidney transplant recipients	9	1151	MD	0.05	0.03 to 0.08	<0.001
Deceased donor transplant recipients	4	898	MD	0.03	0.00 to 0.06	0.02
Living donor transplant recipients	5	253	MD	0.07	0.05 to 0.08	<0.001
Serum potassium at end of surgery						
All kidney transplant recipients	9	1350	MD	–0.15	–0.32 to 0.03	0.10
Deceased donor transplant recipients	4	1101	MD	–0.07	–0.33 to 0.18	0.58
Living donor transplant recipients	5	267	MD	–0.22	–0.46 to 0.01	0.07

CI, confidence interval; MD, mean difference; RR, relative risk.

Pooled Analysis

A summary of the pooled analyses is presented in Table 2. Seven studies contributed data for 1306 participants for the outcome of DGF. On pooled analysis, the RR of DGF associated with BES compared with saline was 0.82 (95% CI, 0.71-0.94; $P = 0.005$) with low heterogeneity ($\chi^2 = 5.06$, $df = 6$, $P = 0.54$, $I^2 = 0\%$; Figure 4A). This was driven by the 4 studies examining 1105 deceased donor kidney recipients (RR 0.83; 95% CI, 0.71-0.96; $P = 0.01$; Figure 4B), whereas there was no significant difference in risk of DGF associated with BES when data from the 3 studies that examined 201 living donor kidney recipients was pooled (RR 0.79; 95% CI, 0.26-2.41; $P = 0.68$; Figure 4C).

Four studies contributed data for 1055 participants for the outcome of hyperkalemia. Three of the studies were in deceased donor kidney recipients. There was no significant difference in risk of hyperkalemia associated with BES compared with saline (RR 0.87; 95% CI, 0.59-1.27; $P = 0.46$), although moderate heterogeneity was noted ($\chi^2 = 6.98$; $df = 3$; $P = 0.07$; $I^2 = 57\%$; Figure 5A). There was no difference in risk of hyperkalemia associated with BES compared with saline in the deceased donor subgroup (RR 0.89; 95% CI, 0.66-1.20; $P = 0.45$; Figure 5B). Only 1 study reported on hyperkalemia in living donor kidney recipients[9]; therefore, pooled analysis was not possible in this subgroup.

The pooled mean blood pH in the BES group at the end of surgery was significantly higher compared with the saline group, with a MD in pH of 0.05 (95% CI, 0.03-0.08; $P < 0.001$). There was no significant difference in mean serum potassium at the end of surgery between groups (MD in serum potassium –0.15 mmol/L; 95% CI, –0.32 to 0.03 mmol/L; $P = 0.10$; Table 2).

On sensitivity analysis examining the impact of individual studies in the deceased donor subgroup, the exclusion of the BEST-Fluids Trial[16] reduced the magnitude of effect and significance but did not alter the direction of effect for the outcomes of DGF and hyperkalemia, demonstrating the impact of this study as the largest trial in the pooled analyses. There was no change in the magnitude or direction of effect on sensitivity analysis of the remaining deceased donor trials. Sensitivity analysis using fixed-effects instead of random-effects modeling did not substantially impact results (data not shown).

The GRADE evidence profile and summary of findings are presented in Table 3. Although there was some concern for risk of bias in 3[14,19,21] of 4 studies in deceased donor kidney recipients, 73% of the data in this population came from 1 well-conducted study with low risk of bias.[16] The overall quality of evidence comparing BES to saline for the outcomes of DGF and hyperkalemia was therefore ranked as high in deceased donor transplantation studies. The overall quality of evidence was very low in living donor transplantation studies.

DISCUSSION

This systematic review and meta-analysis provides an updated synthesis of the randomized controlled data comparing BES to 0.9% saline as perioperative fluid during kidney transplantation for the outcomes of DGF and hyperkalemia. Ten studies and a total of 1532 participants were included in the review. In deceased donor transplantation, the use of BES was associated with a 17% relative reduction in the risk of DGF compared with saline with a *P* value of 0.01. No difference in DGF was detected between BES and saline groups in living donor transplantation, although only 201 participants were included in this subgroup. No difference in the risk of hyperkalemia between groups in either living or deceased donor transplantation was found. The quality of evidence was high in deceased donor transplantation and very low in living donor transplantation.

The findings of this systematic review demonstrate a benefit associated with BES compared with saline for the outcome of DGF. These results reflect the dominant role of the recently published BEST-Fluids Trial,[16] which is the largest trial comparing BES to saline in kidney transplant recipients

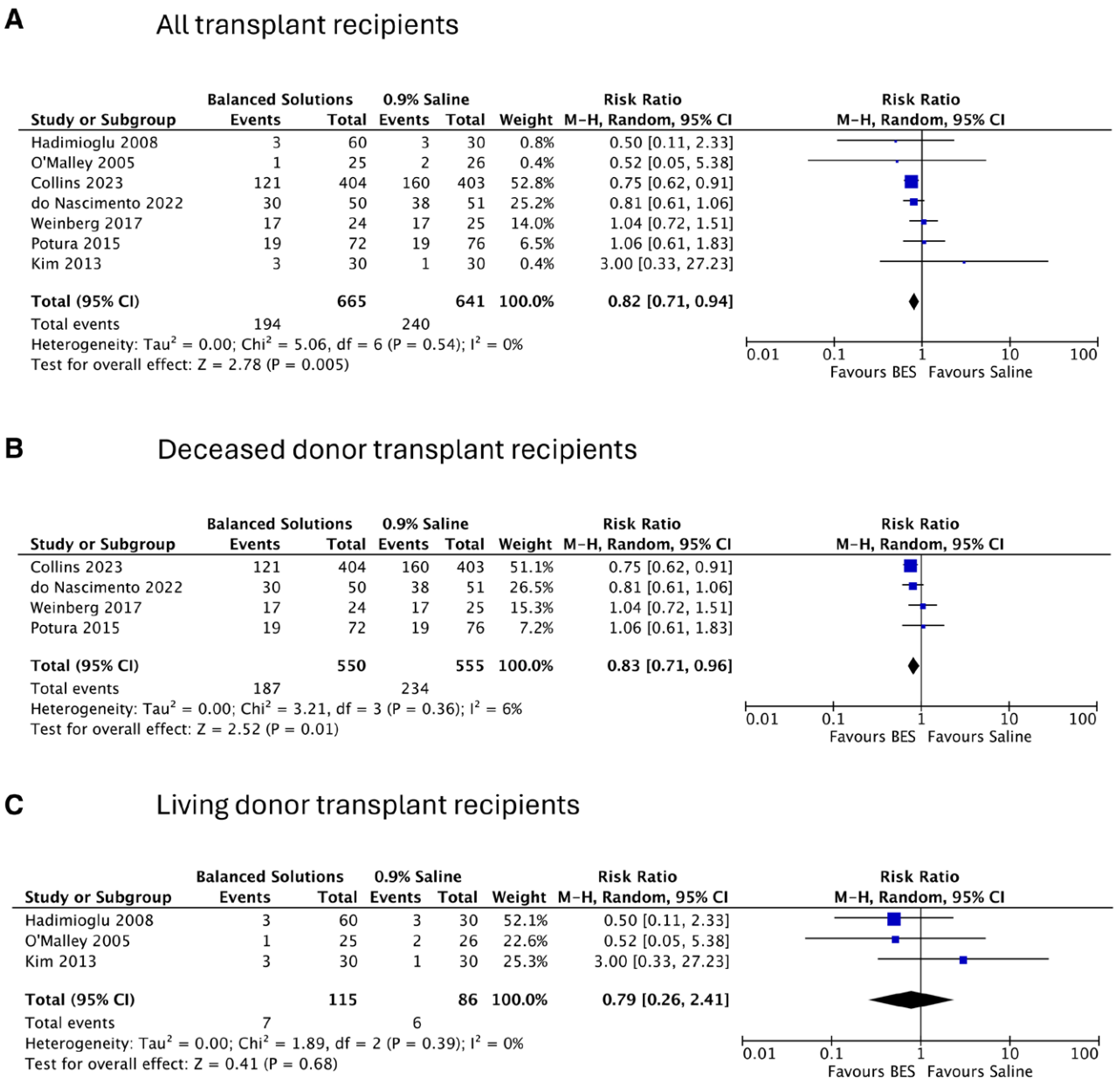
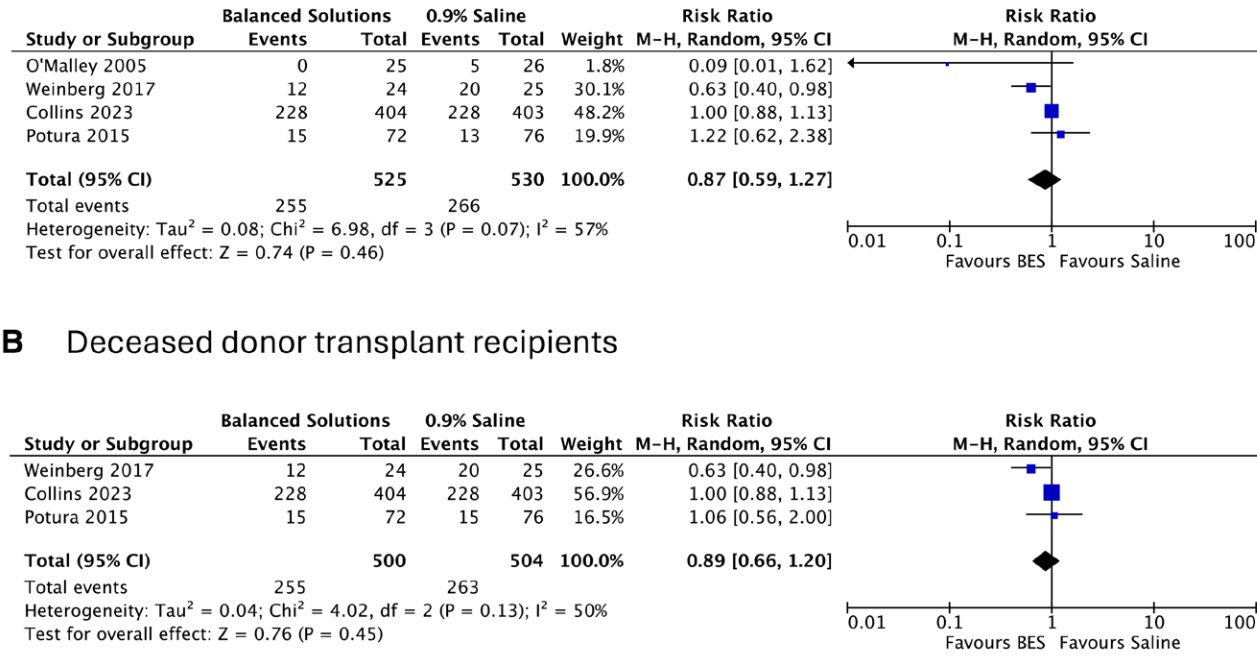


FIGURE 4. Forest plots of BES versus 0.9% saline for delayed graft function in kidney transplantation by (A) all transplant recipients, (B) deceased donor transplant recipients, and (C) living donor transplant recipients. BES, balanced electrolyte solution; CI, confidence interval; M-H, Mantel-Haenszel; saline, 0.9% saline.

to date. Indeed, >50% of participants included in this updated meta-analysis were from this trial, and sensitivity analyses confirm its impact on the magnitude of effect and statistical significance, although not on the direction of effect. Although aspects of the trial design have been questioned in subsequent correspondence,[22] the rigorous nature of the trial compared with previous studies has been widely acknowledged.[23] Previous meta-analyses on this topic, including our original Cochrane Systematic Review,[15] did not demonstrate a benefit for BES on DGF because of the small sample sizes of the included studies, and the lack of reporting on this outcome.

The reduction in risk of DGF associated with BES was limited to the deceased donor transplant subgroup and was not seen in the living donor subgroup, a result that is not unexpected. The risk of DGF is lower in living donor transplantation[24] because of the absence of predonation AKI in the donor, shorter cold ischemic times, and better donor characteristics in general, leading to less ischemia-reperfusion injury. Although this does not preclude the potential for the benefit of BES in living donor transplantation, trials in this population would need substantially larger sample sizes to be adequately powered. Only 201 participants were included in the current pooled analysis of living donor transplantation, which is underpowered to detect a potential effect.

No significant difference in the risk of hyperkalemia between interventions was identified in this analysis. This is



BES, balanced electrolyte solutions; saline, 0.9% saline; CI, confidence interval

FIGURE 5. Forest plots of BES versus 0.9% saline for hyperkalemia in kidney transplantation by (A) all transplant recipients and (B) deceased donor transplant recipients. BES, balanced electrolyte solution; CI, confidence interval; M-H, Mantel-Haenszel; saline, 0.9% saline.

consistent with data from studies in critically ill patients comparing BES to saline.[25-27] Several factors may contribute to this finding. First, although the hyperchloremic metabolic acidosis induced by saline may result in hyperkalemia, the difference in the incidence of DGF between BES and saline means that more participants who receive saline would have had dialysis treatment, which effectively and rapidly removes extracellular potassium. Second, from a physiological perspective, although the potassium in BES might affect serum potassium in the early postoperative phase, the acid-base changes associated with saline may play a more important role in driving hyperkalemia and offset any effects of administering a potassium-containing fluid, resulting in no net difference in this complication between groups. Third, from a study design perspective, there was substantial variation in the definition of hyperkalemia between studies, including in the timing of testing, the serum potassium concentration threshold used, and whether clinically apparent hyperkalemia requiring treatment was noted. This variation in definition may reduce the likelihood of detection of an effect, and it indeed may account for some of the moderate heterogeneity seen in the pooled analysis for this outcome. Other sources of heterogeneity include donor type, type of BES used, and duration of study fluid administration.

This meta-analysis has several strengths. The protocol for this review was registered with PROSPERO, an international prospective register of systematic reviews, and we adhered to current Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines on reporting of systematic reviews.[28] We used a sensitive search strategy and have included the totality of the available randomized controlled data addressing this question. Nevertheless, systematic reviews are retrospective analyses subject to the risk of bias in included studies. We addressed this by performing risk of bias assessments of individual studies and summarizing the quality of evidence using the GRADE framework. Although the quality of evidence was high for the deceased donor transplant subgroup, it remains very low in the living donor subgroup, largely because of the small number and sample size of included studies. Results of pooled analyses in this group should be interpreted with caution. The primary pooled analysis in this study was heavily influenced by the results of 1 large, well-conducted multicenter RCT performed in Australia and New Zealand.[16] Although this study has broad generalizability,[29] further studies addressing this issue in other geographical locations where patient characteristics and transplantation practices differ substantially may be warranted.

Clinical Implications and Future Directions for Research

This review provides further evidence to support the use of BES over saline as perioperative fluid for deceased donor kidney transplantation to reduce the risk of DGF. Given the significant morbidity and healthcare costs associated with DGF, this change in practice has the potential to impact patient-centered outcomes and resource management, an increasingly important consideration in the current economic climate. Cost-utility analyses may further strengthen this case.

TABLE 3.

GRADE evidence profile and summary of findings comparing balanced electrolyte solutions with 0.9% saline for kidney transplantation by donor type and outcome

Outcome	No. of studies (no. of participants)	Quality assessment					Summary of findings	
		Risk of bias[a]	Consistency	Directness	Precision	Publication bias	Relative effect (95% CI)	Quality
Deceased donor transplantation								
Delayed graft function	4 (1105)	Some concerns[b]	No important inconsistency	Direct	No important imprecision	Unlikely	RR 0.83 (0.71-0.96)	High[c]
Hyperkalemia	3 (1004)	Some concerns[d]	No important inconsistency	Direct	No important imprecision	Unlikely	RR 0.89 (0.88-1.13)	High[c]
Living donor transplantation								
Delayed graft function	3 (201)	Some concerns (–1)[e]	Unexplained heterogeneity (–1)	Direct	Imprecision (–1)	Unlikely	RR 0.79 (0.26-2.41)	Very low
Hyperkalemia	1 (51)	Low	One study only (–1)	Direct	Imprecision (–1)	Unlikely	RR 0.09 (0.01-1.62)	Very low

[a]Risk of bias assessed using the Cochrane Risk-of-Bias 2 tool for randomized controlled trials.
[b]One study unblinded[6]; 1 study single-blinded[11]; loss of intention to treat in 1 study.[9]
[c]Although some concerns for risk of bias in 3 of 4 deceased donor studies, 73% of data came from 1 well-conducted study with low risk of bias therefore quality of evidence assessed as high.
[d]One study unblinded[6]; loss of intention to treat in 1 study.[9]
[e]Randomization method not reported in 1 study[7]; no information on allocation concealment in 2 studies[3,7]; time frame for dialysis requirement posttransplant not stated in 2 studies.[3,4]
CI, confidence interval; GRADE, Grading of Recommendations Assessment, Development, and Evaluation; RR, relative risk.

CONCLUSIONS

BES reduce the risk of DGF in deceased donor transplant recipients compared with 0.9% saline without increasing the risk of hyperkalemia. There is insufficient evidence for recipients of living donor kidney transplants, and the benefit of BES in this subgroup remains uncertain.

REFERENCES

1. O'Malley CMN, Frumento RJ, Bennett-Guerrero E. Intravenous fluid therapy in renal transplant recipients: results of a US survey. *Transplant Proc*. 2002;34:3142–3145.
2. Myburgh JA, Mythen MG. Resuscitation fluids. *N Engl J Med*. 2013;369:1243–1251.
3. Rein JL, Coca SG. "I don't get no respect": the role of chloride in acute kidney injury. *Am J Physiol Renal Physiol*. 2019;316:F587–F605.
4. Chowdhury AH, Cox EF, Francis ST, et al. A randomized, controlled, double-blind crossover study on the effects of 2-L infusions of 0.9% saline and Plasma-Lyte(R) 148 on renal blood flow velocity and renal cortical tissue perfusion in healthy volunteers. *Ann Surg*. 2012;256:18–24.
5. Lobo DN, Awad S. Should chloride-rich crystalloids remain the mainstay of fluid resuscitation to prevent 'pre-renal' acute kidney injury?: con. *Kidney Int*. 2014;86:1096–1105.
6. Mannon RB. Delayed graft function: the AKI of kidney transplantation. *Nephron*. 2018;140:94–98.
7. Yarlagadda SG, Coca SG, Formica RN Jr, et al. Association between delayed graft function and allograft and patient survival: a systematic review and meta-analysis. *Nephrol Dial Transplant*. 2009;24:1039–1047.
8. Siedlecki A, Irish W, Brennan DC. Delayed graft function in the kidney transplant. *Am J Transplant*. 2011;11:2279–2296.
9. O'Malley CMN, Frumento RJ, Hardy MA, et al. A randomized, double-blind comparison of lactated Ringer's solution and 0.9% NaCl during renal transplantation. *Anesth Analg*. 2005;100:1518–1524.
10. Hadimioglu N, Saadawy I, Saglam T, et al. The effect of different crystalloid solutions on acid-base balance and early kidney function after kidney transplantation. *Anesth Analg*. 2008;107:264–269.
11. Khajavi MR, Etezadi F, Moharari RS, et al. Effects of normal saline vs. lactated Ringer's during renal transplantation. *Ren Fail*. 2008;30:535–539.
12. Modi MP, Vora KS, Parikh GP, et al. A comparative study of impact of infusion of Ringer's lactate solution versus normal saline on acid-base balance and serum electrolytes during live related renal transplantation. *Saudi J Kidney Dis Transpl*. 2012;23:135–137.
13. Kim SY, Huh KH, Lee JR, et al. 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;45:2191–2196.
14. Potura E, Lindner G, Biesenbach P, 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;120:123–129.
15. Wan S, Roberts MA, Mount P. Normal saline versus lower-chloride solutions for kidney transplantation. *Cochrane Database Syst Rev*. 2016;2016:CD010741.
16. Collins MG, Fahim MA, Pascoe EM, et al; BEST-Fluids Investigators. Balanced crystalloid solution versus saline in deceased donor kidney transplantation (BEST-Fluids): a pragmatic, double-blind, randomised, controlled trial. *Lancet*. 2023;402:105–117.
17. Sterne JAC, Savovic J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ*. 2019;366:l4898.
18. Guyatt GH, Oxman AD, Vist GE, et al. GRADE: what is "quality of evidence" and why is it important to clinicians? *BMJ*. 2008;336:995–998.
19. Weinberg L, Harris L, Bellomo R, et al. Effects of intraoperative and early postoperative normal saline or plasma-lyte 148(R) on hyperkalaemia in deceased donor renal transplantation: a double-blind randomized trial. *Br J Anaesth*. 2017;119:606–615.
20. Pourfakhr P, Shafiei M, Etezadi F, et al. Half saline-bicarbonate solution as intraoperative fluid replacement therapy leads to less acidosis and better early renal function during deceased-donor transplant. *Exp Clin Transplant*. 2020;18:34–38.
21. do Nascimento Junior P, Dohler LE, Ogawa CMU, et al. Effects of plasma-lyte and 0.9% saline in renal function after deceased-donor

kidney transplant: a randomized controlled trial. *Braz J Anesthesiol*. 2022;72:711–719.
22. Collins MG, Fahim MA, Hawley CM, et al. Questions about the BEST-Fluids trial—authors' reply. *Lancet*. 2024;403:911–912.
23. Sharif A. Choosing fluids to reduce the risk of delayed graft function after deceased donor kidney transplantation. *Lancet*. 2023;402:80–81.
24. Krishnan AR, Wong G, Chapman JR, et al. Prolonged ischemic time, delayed graft function, and graft and patient outcomes in live donor kidney transplant recipients. *Am J Transplant*. 2016;16:2714–2723.
25. Toporek AH, Semler MW, Self WH, et al; SMART Investigators and the Pragmatic Critical Care Research Group. Balanced crystalloids versus saline in critically ill adults with hyperkalemia or acute kidney injury: secondary analysis of a clinical trial. *Am J Respir Crit Care Med*. 2021;203:1322–1325.
26. Semler MW, Self WH, Wanderer JP, et al; SMART Investigators and the Pragmatic Critical Care Research Group. Balanced crystalloids versus saline in critically ill adults. *N Engl J Med*. 2018;378:829–839.
27. Finfer S, Micallef S, Hammond N, et al; PLUS Study Investigators and the Australian New Zealand Intensive Care Society Clinical Trials Group. Balanced multielectrolyte solution versus saline in critically ill adults. *N Engl J Med*. 2022;386:815–826.
28. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372:n71.
29. Collins MG, Fahim MA, Pascoe EM, et al. Baseline characteristics and representativeness of participants in the BEST-Fluids trial: a randomized trial of balanced crystalloid solution versus saline in deceased donor kidney transplantation. *Transplant Direct*. 2022;8:e1399.