Clinical efficacy of various resuscitation fluids in the management of sepsis in postoperative surgical and trauma patients: a systematic review and meta-analysis

Yongjie Wang[1*], Kewu Chen[2*], Xiaolu Li[3], Jianing Guan[4]

1 Department of Critical Care Medicine, Jilin Provincial People's Hospital, Changchun, Jilin, China
2 Department of Emergency, Dazu Hospital of Chongqing Medical University, Chongqing, China
3 Intensive Care Unit, Chifeng Municipal Hospital of Inner Mongolia, Chifeng, China
4 Department of Emergency, Taizhou Central Hospital, Affiliated Hospital of Taizhou University, Taizhou Zhejiang, China

KEY WORDS

critical hypotension, resuscitation fluids, sepsis, surgery, traumatic injury

ABSTRACT

INTRODUCTION Fluid resuscitation is the primary sepsis management strategy aimed at reducing mortality and achieving better treatment outcomes in critically hypotensive patients. Still, there are significant ambiguities regarding the most suitable fluid type that would ensure optimization of patient outcomes.
AIM The aim of this systematic review and meta-analysis was to assess the clinical effectiveness of different resuscitation fluids for sepsis management in critically hypotensive patients.
MATERIALS AND METHODS A systematic search of 4 electronic databases (PubMed, EMBASE, Scopus, and Cochrane Library) was conducted to identify relevant papers published in peer-reviewed journals since database inception until June 30, 2024. Odds ratios (ORs) with 95% CIs were calculated to evaluate the impact of individual resuscitation fluids on improvements in hemodynamic parameters and all-cause mortality. Heterogeneity was assessed using the Cochran Q, I^2 statistic, and the appropriate *P* value.
RESULTS Our meta-analysis included 18 randomized controlled trials comparing the efficacy of different resuscitation fluids for sepsis management in 14 469 critically hypotensive patients. We found that Ringer's lactate solution was more effective than saline in reducing mortality (OR, 0.53; 95% CI, 0.41–0.7; $\chi^2 = 3.47$; degree of freedom [df] = 6; Z = 4.6; $I^2 = 0\%$; $P < 0.001$) and improving hemodynamic parameters (OR, 2.64; 95% CI, 2.45–2.86; $\chi^2 = 48.36$; df = 6; Z = 24.84; $I^2 = 18\%$; $P < 0.001$). However, saline was superior to albumin and hydroxyethyl starch in reaching these end points.
CONCLUSION We showed that in critically hypotensive septic patients, Ringer's lactate solution reduces all-cause mortality and improves hemodynamic parameters more effectively than saline, hydroxyethyl starch, and albumin solutions.

Correspondence to:
Jianing Guan, MB,
Department of Emergency, Taizhou Central Hospital, Affiliated Hospital of Taizhou University,
999 Donghai Boulevard,
Taizhou, Zhejiang 31000, China,
email: guanjn9249@sina.com
Received: August 2, 2024.
Revision accepted: September 5, 2024.
Published online: September 20, 2024.
Wideochir Inne Tech Maloinwazyjne. 2024; 19 (3): 275-288
doi:10.20452/wiitm.2024.17900

* YJW and KWC contributed equally to this work.

INTRODUCTION Fluid resuscitation is the primary management strategy for critically hypotensive patients, and it has played a significant role in reducing mortality over the years.[1,2] Research indicates that early fluid resuscitation effectively prevents and restricts sepsis, inhibits prevalent multiorgan failure, improves microcirculation, and reduces the systemic inflammatory response.[3,4] Fluids are a fundamental component of resuscitation of critically hypotensive patients; however, fluid management strategies are subject to significant practice variations.[5,6] Clinical research has demonstrated that colloids and crystalloids have a distinct impact on a variety of critical physiological parameters. Fluid categories for the purpose of fluid resuscitation include blood products, colloids (eg, albumin, gelatin solutions, and hydroxyethyl starch [HES]), and crystalloids, including normal saline (NS) and Ringer's lactate.[7-9] Studies examining clinical outcomes of fluid resuscitation have reported reduced length of hospital stay, decreased mortality, improved tissue perfusion, and a reduced rate of systemic inflammatory response syndrome.[10-12] Although fluid resuscitation has demonstrated exceptional treatment outcomes, there are still significant ambiguities regarding the most suitable fluid type and volumetric rates that would optimize patient outcomes. As the most frequently employed crystalloid, NS (0.9% sodium chloride, pH 7, and chloride content of 154 mmol/l) is believed to trigger hyperchloremic metabolic acidosis, which may have a direct impact on organ function and even survival.[13] Similarly, colloid solutions are considered more effective than crystalloids in achieving an equivalent hemodynamic effect; however, they are also believed to induce changes in the immune response to critical illness.[14] Furthermore, even though colloids (such as HES, gelatin, and albumin) have a prolonged half-life in plasma, they have been reported to impair glomerular filtration, and are associated with a higher risk of acute renal failure, anaphylactic shock, and death.[15] Ringer's lactate, a generally balanced crystalloid, has been recommended for aggressive fluid replacement therapy in critically hypotensive patients.[16,17]

To address the evidence gap regarding the most suitable fluid type and volumetric rates that would optimize patient outcomes, the present study systematically compiled and evaluated evidence from 18 randomized controlled trials (RCTs)[18-35] to determine the efficacy of various fluid types used for resuscitation purposes. We focused on studies analyzing critically hypotensive patients with sepsis and examining various fluid types (including colloids and crystalloids) to identify the most effective infusion for sepsis management. This systematic review and meta-analysis provides a comprehensive evaluation of existing evidence, making it a valuable contribution to the field. The findings may contribute to development of clinical practice guidelines and help improve patient outcomes in sepsis management, thus filling a significant knowledge gap in the field of fluid resuscitation.

AIM The aim of this systematic review and meta-analysis was to assess the clinical effectiveness of different resuscitation fluids for sepsis management in critically hypotensive patients.

MATERIALS AND METHODS **Search strategy and selection criteria** This meta-analysis and systematic review complies with the Assessing the Methodological Quality of Systematic Reviews (AMSTAR[36]) and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[37] The efficacy of various resuscitation fluids in septic, surgical, and trauma patients was compared through a systematic review of relevant RCTs that were selected in accordance with predefined inclusion and exclusion criteria. A comprehensive search of the scientific literature databases (EMBASE, PubMed, Scopus, and Cochrane Library) for articles published since database inception until June 30, 2024 was conducted to identify the pertinent RCTs. The search terms used were: *resuscitation fluid* OR *fluid therapy* OR *volume replacement* OR *sepsis* OR *critically hypotensive patients* OR *septic disease* OR *injury* OR *surgical patients* OR *trauma patients* OR *hydroxyethyl starch* OR *HES* OR *gelatin* OR *saline* OR *albumin* OR *Ringer's lactate* OR *crystalloids* OR *all-cause mortality* OR *organ dysfunction* OR *organ replacement therapy* OR *mortality* OR *bleeding* OR *death* OR *transfusion* OR *colloid substance* OR *hemodynamic parameters* OR *hemodialysis* OR *hemofiltration* OR *randomized controlled trial* OR *RCT* OR *systematic review* OR *meta-analysis*. Key words for agreement in both Medline and EMBASE databases were identified and evaluated using the Patient, Intervention, Comparison, Outcome (PICO) criteria.[38] The specified key words were inserted into the title / abstract / key word field during the Scopus search. In the Cochrane database, the search terms *sepsis*, *critically hypotensive patients*, and *resuscitation fluid* were used. The PICO framework was employed to establish precise selection criteria. The letter "P" indicated patients who suffered from trauma or sepsis, or underwent surgery. The letter "I" represented the intervention group, while "C", the control group. The improvement in hemodynamic parameters and all-cause mortality were the primary clinical outcomes, denoted by the letter "O". Our meta-analysis only included RCTs. Additional potentially relevant papers were identified by conducting backward and forward citation monitoring of previously published meta-analyses and included studies. **TABLE 1** illustrates the comprehensive database search strategy. The titles, abstracts, and full texts of potentially eligible articles were independently assessed by 2 reviewers (YJW and KWC). If required, a senior researcher was consulted, and any discrepancies between the 2 reviewers were resolved through discussion.

Study selection and data extraction The study included RCTs that provided comparative data on clinical effectiveness of different resuscitation fluids in critically hypotensive patients. There were no limitations with respect to the year or language of publication. The specific inclusion criteria were as follows: 1) RCT design; 2) analysis of critically hypotensive patients with sepsis; 3) participants aged at least 18 years; 4) focus on improved patient hemodynamic parameters and all-cause mortality; and 5) full-text papers with sufficient data for generating a 2 × 2 table.

Non-RCTs (case series, case-control studies, and cohort studies), narrative or expert evaluations, animal studies or trials, trials involving children, and studies that did not analyze critically hypotensive patients were excluded from analysis, as were outdated, anecdotal, or entirely expert-based bibliographic references. Patient demographic profiles and event data from the included studies were independently collected by

TABLE 1 Database search strategy

Database	Search strategy
Scopus	1 *Resuscitation fluid* OR *fluid therapy* OR *volume replacement* OR *sepsis* OR *critically hypotensive patients* OR *septic disease* OR *injury* OR *surgical patients* OR *trauma patients* OR *hydroxyethyl starch* OR *HES* OR *gelatin* OR *saline* OR *albumin* OR *Ringer's lactate* OR *crystalloids*
	2 *All-cause mortality* OR *organ dysfunction* OR *organ replacement therapy* OR *mortality* OR *bleeding* OR *death* OR *transfusion* OR *colloid substance* OR *hemodynamic parameters* OR *hemodialysis* OR *hemofiltration* OR *randomized controlled trial* OR *RCT* OR *systematic review* OR *meta-analysis*
	3 #1 and #2
PubMed	1 *Resuscitation fluid* OR *fluid therapy* (MeSH terms) OR *volume replacement* (all fields) OR *sepsis* (MeSH terms) OR *critically hypotensive patients* (all fields) OR *septic disease* (all fields) OR *injury* (all fields) OR *surgical patients* (all fields) OR *trauma patients* (all fields) OR *hydroxyethyl starch* (all fields) OR *HES* (all fields) OR *gelatin* (all fields) OR *saline* (all fields) OR *albumin* (all fields) OR *Ringer's lactate* (all fields) OR *crystalloids* (all fields)
	2 *All-cause mortality* (MeSH terms) OR *organ dysfunction* (all fields) OR *organ replacement therapy* (all fields) OR *mortality* (all fields) OR *bleeding* (all fields) OR *death* (all fields) OR *transfusion* (all fields) OR *colloid substance* (all fields) OR *hemodynamic parameters* (all fields) OR *hemodialysis* (all fields) OR *hemofiltration* (all fields) OR *randomized controlled trial* (all fields) OR *RCT* (all fields) OR *systematic review* (all fields) OR *meta-analysis* (all fields)
	3 #1 and #2
EMBASE	1 *Resuscitation fluid*/exp OR *fluid therapy*/exp OR *volume replacement*/exp OR *sepsis*/exp OR *critically hypotensive patients*/exp OR *septic disease*/exp OR *injury*/exp OR *surgical patients*/exp OR *trauma patients*/exp OR *hydroxyethyl starch*/exp OR *HES*/exp OR *gelatin*/exp OR *saline*/exp OR *albumin*/exp OR *Ringer's lactate*/exp OR *crystalloid*
	2 *All-cause mortality*/exp OR *organ dysfunction*/exp OR *organ replacement therapy*/exp OR *mortality*/exp OR *bleeding*/exp OR *death*/exp OR *transfusion*/exp OR *colloid substance*/exp OR *hemodynamic parameters*/exp OR *hemodialysis*/exp OR *hemofiltration*/exp OR *randomized controlled trial*/exp OR *RCT*/exp OR *systematic review*/exp OR *meta-analysis*/exp
	3 #1 and #2
Cochrane library	1 (*Resuscitation fluid*): ti, ab, kw OR (*fluid therapy*): ti, ab, kw OR (*volume replacement*): ti, ab, kw OR (*sepsis*): ti, ab, kw OR (*critically hypotensive patients*): ti, ab, kw OR (*septic disease*): ti, ab, kw OR (*injury*): ti, ab, kw OR (*surgical patients*): ti, ab, kw OR (*trauma patients*): ti, ab, kw OR (*hydroxyethyl starch*): ti, ab, kw OR (*HES*): ti, ab, kw OR (*gelatin*): ti, ab, kw OR (*saline*): ti, ab, kw OR (*albumin*): ti, ab, kw OR (*Ringer's lactate*): ti, ab, kw OR (*crystalloid*): ti, ab, kw (word variations have been searched)
	2 (*All-cause mortality*): ti, ab, kw OR (*organ dysfunction*): ti, ab, kw OR (*organ replacement therapy*): ti, ab, kw OR (*mortality*): ti, ab, kw OR (*bleeding*): ti, ab, kw OR (*death*): ti, ab, kw OR (*transfusion*): ti, ab, kw OR (*colloid substance*): ti, ab, kw OR (*hemodynamic parameters*): ti, ab, kw OR (*hemodialysis*): ti, ab, kw OR (*hemofiltration*): ti, ab, kw OR (*randomized controlled trials*): ti, ab, kw OR (*RCT*): ti, ab, kw OR (*systematic review*): ti, ab, kw OR (*meta-analysis*): ti, ab, kw (word variations have been searched)
	3 #1 and #2

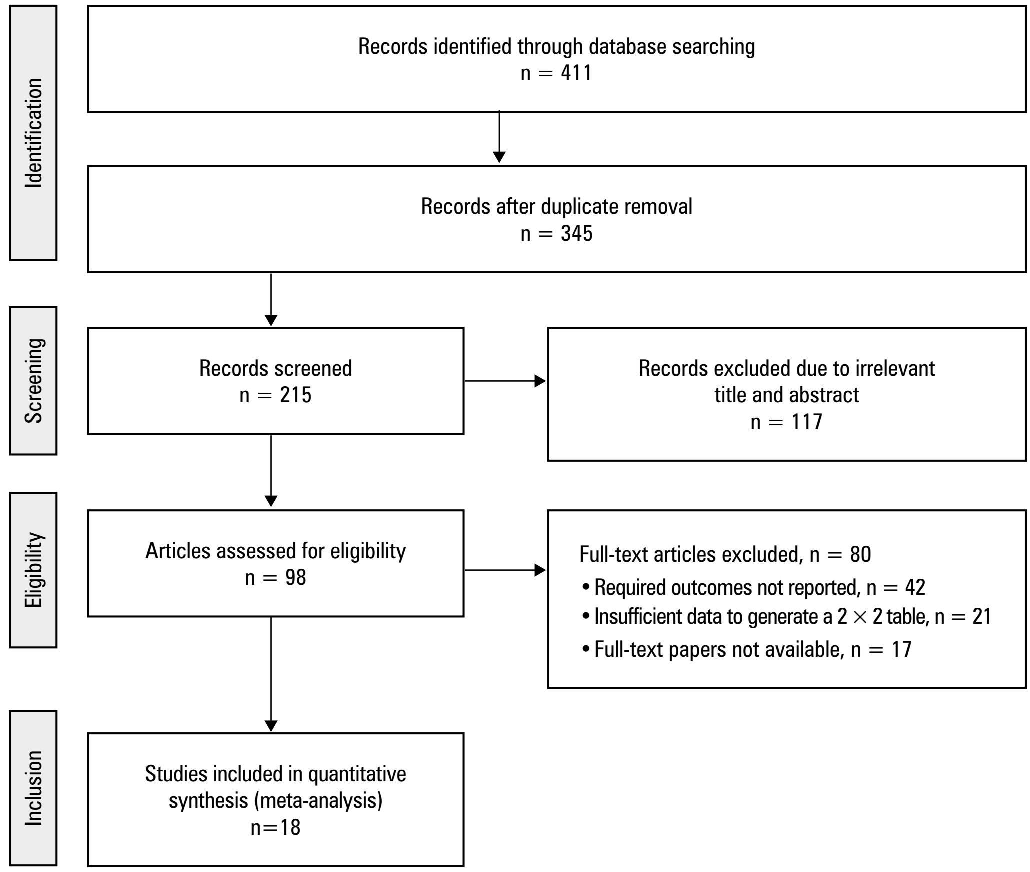
Abbreviations: exp, explosion in Emtree—searching of selected subject terms and related subjects; MeSH, medical subject headings; ti, ab, kw, title or abstract or keyword field

2 researchers using a predetermined form. The extracted information included author names and year of publication, country of study, number of included centers, total number of patients, age of participants, number of septic patients, types of resuscitation fluids used in the control and intervention arms, inclusion-exclusion criteria of the RCTs, and primary outcomes. The authors were contacted to provide supplementary information when their data were deemed insufficient or ambiguous.

Risk of bias assessment We employed a standardized questionnaire to evaluate the included studies for possible bias. Separate risk of bias assessments were carried out by 2 researchers (YJW and KWC) using the Cochrane risk-of-bias tool, version 2.[39] The tool comprises 5 components: randomization-induced bias, bias resulting from variations from intended interventions, bias due to missing outcome information, bias during outcome evaluation, and bias in selecting reported results. A third reviewer (XL) assumed the role of an arbiter to settle any arising disputes. Any potential bias was evaluated and classified as either "uncertain risk," "high risk," or "low risk." Small-study effects and publication bias were evaluated using a comparison-adjusted funnel plot.[40] The significance of bias was evaluated with the Egger regression test[41] using MedCalc software.[42]

Statistical analysis Statistical analysis was performed using Review Manager (RevMan) software, version 5.4.[43] For each study, odds ratios (ORs) and 95% CIs[44] were computed to assess binary outcomes. The DerSimonian–Laird method[45] was employed to calculate the ORs using a 2 × 2 table[46] illustrating event data. During quantitative evaluation, we excluded studies that did not report the use of any resuscitation fluid or the presence of septic patients in either group. We designed forest plots[47] to evaluate the influence of different outcome determinants using the Mantel–Haenszel fixed-effects model, since there was no interstudy heterogeneity. Statistical parameters, such as the I^2 value,[48] χ^2 value,[49] Z value,[50] and *P* value[51] were used to assess heterogeneity. The *P* value below 0.05 was deemed significant. We conducted a subgroup analysis to evaluate the efficacy of various resuscitation fluids, including Ringer's lactate vs saline, Ringer's lactate vs HES, saline vs albumin, and saline vs HES, in terms of the change in primary outcomes, such as improvement in hemodynamic parameters

FIGURE 1 Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) study flow diagram



and all-cause mortality. A hierarchical summary receiver-operating characteristic curve (HSROC) plot[52] was designed to check the test accuracy of the included RCTs.

Ethics An ethics statement is not applicable as this study is based exclusively on published literature.

RESULTS

Study selection outcomes This study was conducted through an exhaustive electronic search of 4 databases. Consequently, 411 studies were identified as meeting the inclusion criteria specified in the PICO framework. A total of 345 articles were selected for review, while 66 were excluded due to duplicate content. A subsequent assessment of eligibility was conducted for 215 papers following additional screening. Of those, 117 were excluded due to irrelevant titles and abstracts, and the remaining 98 were subjected to a further assessment. However, after applying the inclusion–exclusion criteria, 80 studies were found ineligible and were excluded. This was primarily due to a lack of required outcomes, insufficient data to generate 2 × 2 tables, or unavailability of full-text papers. Finally, 18 RCTs that met the predetermined inclusion–exclusion criteria were included in this meta-analysis, as illustrated in the study flow diagram based on the PRISMA guidelines (**FIGURE 1**). Overall, they presented data of 14 469 patients aged 18 years or older. The efficacy of Ringer's lactate solution vs saline was compared in 7 of the 18 included studies.[19,23,24,28,30,32,35] Additionally, 4 studies compared saline with albumin,[21,22,26,27] 4 compared saline with HES,[25,29,31,34] and the remaining 3 studies compared Ringer's lactate with HES.[18,20,33] A comprehensive overview of patient demographic characteristics is provided in **TABLE 2**. All the included studies provided event data for the generation of 2 × 2 tables to facilitate this meta-analysis.

Risk of bias assessment We conducted a risk of bias evaluation to determine the study's overall quality score. **TABLE 3** displays the results of the risk of bias assessment for each of the 18 included RCTs. The meta-analysis showed a low risk of bias, as indicated by the traffic light plot for bias assessment shown in **FIGURE 2** and the summary plot shown in **FIGURE 3**. Out of the 18 RCTs, 13 had a low risk of bias. The risk of bias for 3 RCTs was moderate due to issues related to deviations from the intended intervention or bias in the measurement of the outcome. The remaining 2 RCTs showed a high risk of bias, specifically in the measurement of the outcome and the selection of reported results, respectively.

Subgroup analysis assessing the effect of different resuscitation fluids on all-cause mortality To determine the effect of different resuscitation fluids on all-cause mortality, we used the event data extracted from the included trials to calculate the ORs. **FIGURE 4A** presents a comparison

TABLE 2 Characteristics of the included randomized controlled trials (continued on the next page)

Author	Country of study	Included centers, n	Patients, n	Patient age, y	Sepsis patients, n	Control arm	Intervention arm	Inclusion criteria	Exclusion criteria	Primary outcomes
Angsubhakorn et al[18]	Thailand	1	34	46	34	HES	RL	Sepsis, multiple traumas, or other causes of hypovolemic shock	Age <18 y, pregnancy, admission to the ICU following transplantation surgery, previous fluid resuscitation during the current admission	Hemodynamic parameters and 90-day mortality
Annane et al (CRISTAL)[19]	Worldwide	57	2857	63	1553	Saline	RL	Sepsis, multiple traumas, or other causes of hypovolemic shock	Chronic organ failure requiring replacement therapies, or patients with diabetes mellitus or known aortic aneurysm	Hemodynamic parameters and 90-day mortality
Brunkhorst et al (VISEP)[20]	Germany	18	537	65	537	HES	RL	Severe sepsis or septic shock	Patients with hemodynamic instability requiring aggressive resuscitation during the first 100 minutes	Hemodynamic parameters and 90-day mortality
Caironi et al (ALBIOS)[21]	Italy	100	1818	69	1818	Saline	Albumin	Severe sepsis or septic shock	Age <18 y, pregnancy, admission to the ICU following transplantation surgery, previous fluid resuscitation during the current admission	Hemodynamic parameters and 90-day mortality
Charpentier et al (EARSS)[22]	France	29	798	66	798	Saline	Albumin	Suspected hypovolemia, septic shock and severe respiratory failure	Chronic organ failure requiring replacement therapies, or patients with diabetes mellitus or known aortic aneurysm	Hemodynamic parameters and 28-day mortality
Cuellar et al[23]	Mexico	1	88	50	88	Saline	RL	Suspected hypovolemia, septic shock, and severe respiratory failure	Chronic organ failure requiring replacement therapies, or patients with diabetes mellitus or known aortic aneurysm	Hemodynamic parameters and 30-day mortality
De-Madaria et al[24]	Spain	18	744	60	249	Saline	RL	Suspected hypovolemia, septic shock, and severe respiratory failure	Chronic organ failure requiring replacement therapies, or patients with diabetes mellitus or known aortic aneurysm	Hemodynamic parameters and 90-day mortality
Dubin et al[25]	Argentina	2	20	65	20	HES	Saline	Severe sepsis or septic shock	Chronic organ failure requiring replacement therapies, or patients with diabetes mellitus or known aortic aneurysm	Hemodynamic parameters and 31-day mortality
Finfer et al (SAFE)[26]	Australia and New Zealand	16	1218	58	1218	Saline	Albumin	Septic shock and severe respiratory failure	Age <18 y, pregnancy, admission to the ICU following transplantation surgery, previous fluid resuscitation during the current admission	Hemodynamic parameters and 28-day mortality
Friedman et al[27]	Belgium	1	34	66	34	Saline	Albumin	Suspected hypovolemia, septic shock, and severe respiratory failure	Hemodynamic instability requiring aggressive resuscitation during the first 100 minutes	Hemodynamic parameters and in--hospital mortality

TABLE 2 Characteristics of the included randomized controlled trials (continued from the previous page)

Author	Country of study	Included centers, n	Patients, n	Patient age, y	Sepsis patients, n	Control arm	Intervention arm	Inclusion criteria	Exclusion criteria	Primary outcomes
Li et al[28]	China	1	912	50	912	Saline	RL	Suspected hypovolemia, septic shock, and severe respiratory failure	Age <18 y, admission to the ICU following cardiac surgery, body burn, liver transplantation surgery, previous fluid resuscitation during the current admission	Hemodynamic parameters and 90-day mortality
Li et al[29]	China	1	60	45	60	HES	Saline	Septic shock and severe respiratory failure	Age <18 y, pregnancy, admission to the ICU following transplantation surgery, previous fluid resuscitation during the current admission	Hemodynamic parameters and 28-day mortality
Semler et al (SMART)[30]	United States	1	2336	58	2336	Saline	RL	Severe sepsis or septic shock	Chronic organ failure requiring replacement therapies, or patients with diabetes mellitus or known aortic aneurysm	Hemodynamic parameters and 30-day mortality
McIntyre et al (FINESS)[31]	Canada and New Zealand	4	40	64	40	HES	Saline	Sepsis, multiple traumas, or other causes of hypovolemic shock	Age <18 y, other forms of shock, chronic renal failure requiring dialysis, pregnancy, previous admission to the ICU with septic shock during the current hospitalization	Hemodynamic parameters and 28-day mortality
Messallam et al[32]	United States	1	310	47	208	Saline	RL	Sepsis, multiple traumas, or other cause of hypovolemic shock	Age <18 y, pregnacyt, admission to the ICU following transplantation surgery, previous fluid resuscitation during the current admission	Hemodynamic parameters and 30-days mortality
Molnar et al[33]	United Kingdom	1	30	56	30	HES	RL	Septic shock and severe respiratory failure	Chronic organ failure requiring replacement therapies, or patients with diabetes mellitus or with known aortic aneurysm	Hemodynamic parameters and in--hospital mortality
Myburgh et al (CHEST)[34]	Australia and New Zealand	32	1937	63	1937	HES	Saline	Sepsis, multiple traumas, or other causes of hypovolemic shock	Age <18 y, pregnancy, admission to the ICU following transplantation surgery, previous fluid resuscitation during the current admission	Hemodynamic parameters and 90-day mortality
Perner et al (6S)[35]	Scandinavia	26	804	67	798	Saline	RL	Severe sepsis or septic shock	Age <18 y, pregnancy, admission to the ICU following transplantation surgery, previous fluid resuscitation during the current admission	Hemodynamic parameters and 90-day mortality

Abbreviations: HES, hydroxyethyl starch; ICU, intensive care unit; RL, Ringer's lactate

TABLE 3 Risk assessment of the included studies using the Cochrane risk-of-bias tool

Signaling question	Angsubhakorn et al[18]	Annane et al[19]	Brunkhorst et al[20]	Caironi et al[21]	Charpentier et al[22]	Cuellar et al[23]	De--Madaria et al[24]	Dubin et al[25]	Finfer et al[26]	Friedman et al[27]	Li et al[28]	Li et al[29]	Semler et al[30]	McIntyre et al[31]	Messallam et al[32]	Molnar et al[33]	Myburgh et al[34]	Perner et al[35]
Was a consecutive or random sample of patients enrolled?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Did the study avoid inappropriate exclusions?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Did all patients receive the same reference standard?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were all patients included in the analysis?	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Was the sample frame appropriate to address the target population?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were the study participants sampled in an appropriate way?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were the study participants and the setting described in detail?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were valid methods used for identification of the condition?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Was the condition measured in a standard, reliable way for all participants?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y

Abbreviations: Y, yes; N, no

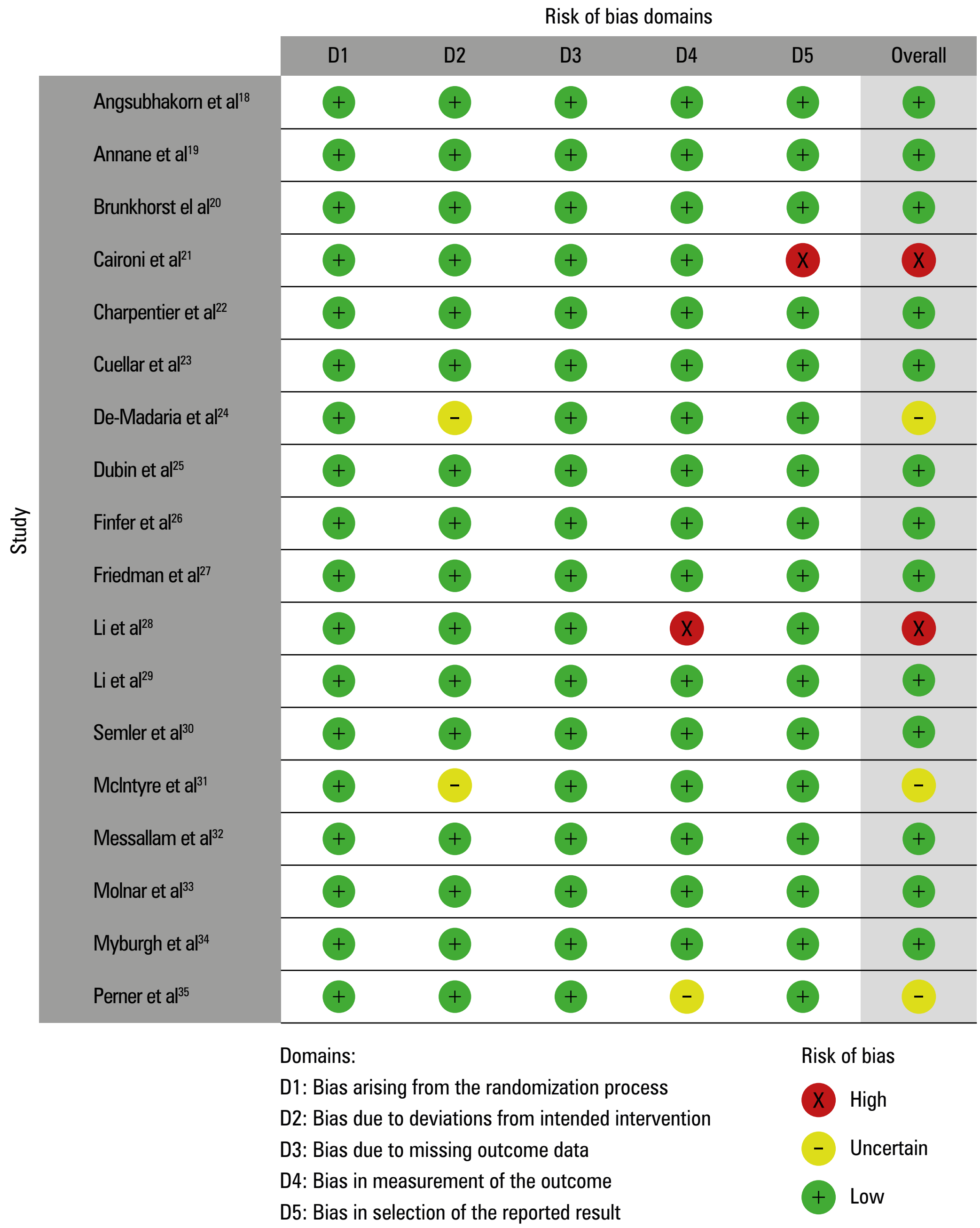


FIGURE 2 Traffic light plot for risk of bias assessment

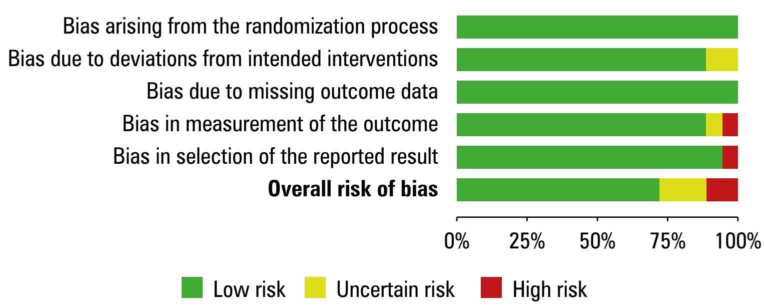


FIGURE 3 Risk of bias summary plot

of the effect of Ringer's lactate solution and HES, demonstrating that the odds of all-cause mortality were lower for the group treated with the Ringer's lactate solution (OR, 0.48; 95% CI, 0.26–0.89; $\chi^2 = 0$; df = 2; Z = 2.33; $I^2 = 0\%$; $P = 0.02$). Moreover, the symmetrical funnel plot and insignificant results of the Egger test ($P = 0.23$) indicated a low likelihood of publication bias. A comparison between Ringer's lactate solution and saline illustrated in **FIGURE 4B**

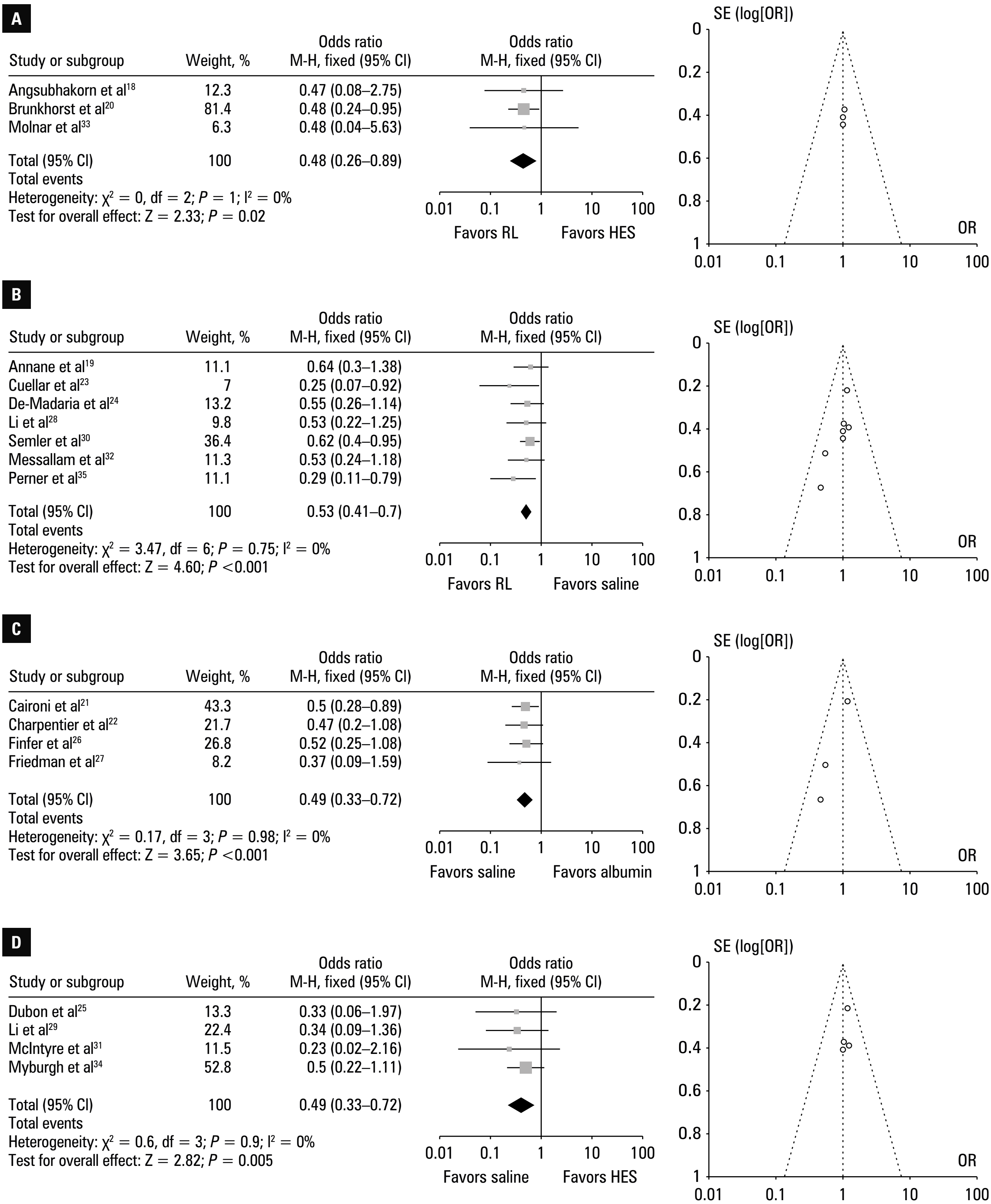


FIGURE 4 Subgroup analysis illustrating forest plots and funnel plots for all-cause mortality; **A** – Ringer's lactate (RL) vs hydroxyethyl starch (HES); **B** – RL vs saline; **C** – saline vs albumin; **D** – saline vs HES
Abbreviations: df, degrees of freedom; M-H, Mantel–Haenszel fixed-effects model

shows that the likelihood of mortality was lower for Ringer's lactate, with the OR value of 0.53 (95% CI, 0.41–0.7; χ^2 = 3.47; df = 6; Z = 4.6; I^2 = 0%; *P* <0.001). Additionally, the symmetrical shape of the funnel plot and *P* value of 0.26 indicated a low risk of publication bias. The compared effects of saline solution and albumin depicted in **FIGURE 4C** indicate a lower rate of all-cause mortality in the saline-treated group than in the albumin-treated patients, with the OR value of 0.49 (95% CI, 0.33–0.72; χ^2 = 0.17; df = 3; Z = 3.65; I^2 = 0%; *P* <0.001), and a low risk of publication bias, with a symmetrical funnel plot and *P* = 0.3 for the Egger

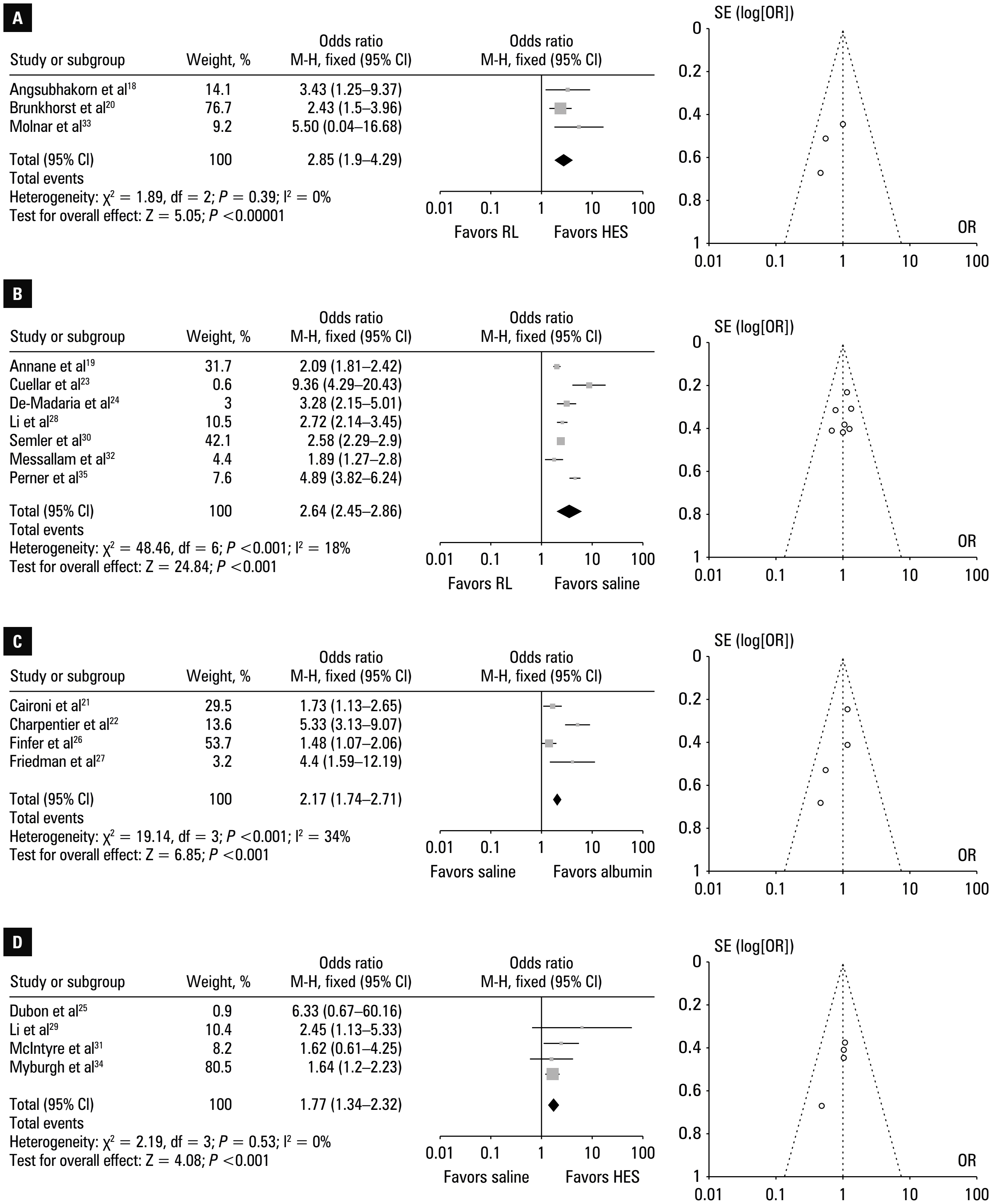


FIGURE 5 Subgroup analysis illustrating forest plots and funnel plots for improvement in hemodynamic parameters; **A** – Ringer's lactate (RL) vs hydroxyethyl starch (HES); **B** – RL vs saline; **C** – saline vs albumin; **D** – saline vs HES
Abbreviations: see FIGURE 4

test. A comparison between the saline solution and HES presented in FIGURE 4D demonstrated that the likelihood of mortality was lower in the saline-treated group, with the OR value of 0.41 (95% CI, 0.22–0.76; χ^2 = 0.6; df = 3; Z = 2.82; I^2 = 0%; P = 0.005) and low publication bias, as reflected by a symmetrical funnel plot and P = 0.34 for the Egger test.

Subgroup analysis assessing the effect of different resuscitation fluids on hemodynamic parameters To ascertain the impact of various resuscitation fluids on hemodynamic parameters, we computed the ORs in the intervention and control groups using the event data from the included RCTs. FIGURE 5A illustrates a comparison of the effect of Ringer's lactate solution and HES. The odds of improvement in hemodynamic parameters were higher in the Ringer's lactate solution–treated group (OR, 2.85; 95% CI, 1.9–4.29; χ^2 = 1.89; df = 2; Z = 5.05; I^2 = 0%; P <0.001). In addition, a symmetrical funnel plot and insignificant P value for the Egger test (P = 0.18) suggested a low probability of publication bias. A comparison of Ringer's lactate solution with saline is depicted in **FIGURE 5B**. The likelihood of improvement in hemodynamic parameters was higher for Ringer's lactate than for saline, with the OR value of 2.64 (95% CI, 2.45–2.86; χ^2 = 48.36; df = 6; Z = 24.84; I^2 = 18%; P <0.001). Furthermore, a symmetrical shape of the funnel plot and a P value of 0.33 suggested a low risk of publication bias. The comparative effects of saline solution and albumin are depicted in **FIGURE 5C**, which shows a more notable improvement in hemodynamic parameters among the saline-treated patients than in those treated with albumin (OR, 2.17; 95% CI, 1.74–2.71; χ^2 = 19.14; df = 3; Z = 6.85, I^2 = 34%; P <0.001). The risk of publication bias was low, with a symmetrical funnel plot and P = 0.397 for the Egger test. **FIGURE 5D** illustrates a comparison of saline solution with HES, demonstrating that the likelihood of improvement in hemodynamic parameters was higher in the saline-treated group, with the OR value of 1.77 (95% CI, 1.34–2.32; χ^2 = 2.19; df = 3; Z = 4.08; I^2 = 0%; P <0.001) and low publication bias, , as reflected by a symmetrical funnel plot and P = 0.22 for the Egger test.

Hierarchical summary receiver operating characteristic curve plot for test accuracy of included studies

A HSROC diagram used to assess the test accuracy of each study is presented in **FIGURE 6**. The test accuracy of all the included studies was high, as indicated by the clustering of all data points in the upper left corner, whereas the sensitivity values were nearly 1 and the specificity values were almost 0. The area under the curve of the HSROC was 0.9 (95% CI, 0.7–0.95), which reflects inherent reliability of the diagnostic tests.

DISCUSSION

Sepsis is a severe condition in which the body's immune defense mechanisms fail to adequately respond to an infection. The body attacks its own tissues, which often results in organ dysfunction.[53,54] Toxins produced by bacteria can impair the heart's capacity to pump blood to organs, which is conducive to blood pressure lowering, if left untreated. Sepsis may lead to septic shock[55] and critical hypotension that can potentially harm the liver, kidneys, lungs, and other organs.[56] Fluid management in critically hypotensive septic patients has been the subject of close attention in recent years.[57,58] Fluid resuscitation involves administration of a variety of drug types and formulations, as well as selection of adequate infusion schedules and doses. Patient outcomes are directly affected by these parameters.[59,60] Consequently, a comprehensive understanding of the therapeutic benefits and adverse effects of these fluids is critical to determine the most suitable form of their administration. Resuscitation fluids play a crucial role in sepsis treatment, as they replenish intravascular volume, restore blood pressure, and maintain tissue perfusion. Crystalloids, such as NS and Ringer's lactate, help increase intravascular volume and sodium content, raising blood pressure and improving cardiac output. Colloids, such as albumin and HES, induce oncotic pressure, whereby the fluid moves fluid into the intravascular space and blood volume is maintained. Additionally, some colloids may modulate the immune response and reduce inflammation. Blood products, including fresh frozen plasma and packed red blood cells, help restore blood's oxygen-carrying capacity and coagulation factors. These fluids also contribute to mitigating the systemic inflammatory response syndrome and multiorgan dysfunction associated with sepsis. By replenishing fluids and electrolytes, as well as enhancing oxygen-carrying capacity of blood, resuscitation fluids help stabilize patient hemodynamic status, thereby reducing the risk of organ failure and mortality.[61-64] The choice of fluid depends on specific patient needs, and a balanced approach often involves a combination of crystalloids, colloids, and blood products to achieve optimal resuscitation.

It has been reported that NS is the most frequently used crystalloid worldwide for the management of sepsis in critically hypotensive patients. However, it is known to cause hyperchloremic acidosis that can impair renal function and increase the risk of infections.[65,66] We found that Ringer's lactate solution was more effective than saline in reducing mortality (OR, 0.53; 95% CI, 0.41–0.7) and improving hemodynamic parameters (OR, 2.64; 95% CI, 2.45–2.86). However, saline was shown to outperform albumin and HES in this respect. Ringer's lactate solution is a balanced or buffered solution used for fluid replacement. It is a type of isotonic, crystalloid fluid that is composed of sodium, chloride, potassium, calcium, and lactate in the form of sodium lactate. It has an osmolarity of 273 mOsm/l and a pH of approximately 6.5. In contrast, the osmolarity of NS is approximately 286 mOsm/l. Ringer's lactate is primarily used in aggressive volume resuscitation of patients with blood loss or burn injuries, and in clinical scenarios such as acute pancreatitis and sepsis.[67-69] Ringer's lactate solution helps achieve volume resuscitation by increasing perfusion and expanding intravascular volume. It also provides the body with sodium lactate, a bioenergetic fuel that the human body is designed to metabolize under ischemic conditions, which reduces cellular mortality.[70]

Our findings concur with previous meta-analyses and sepsis guidelines[71,72] that recommend crystalloids as the preferred resuscitation fluids. In their systematic review and sequential network meta-analyses of resuscitation fluid types in sepsis, surgical, and trauma patients,

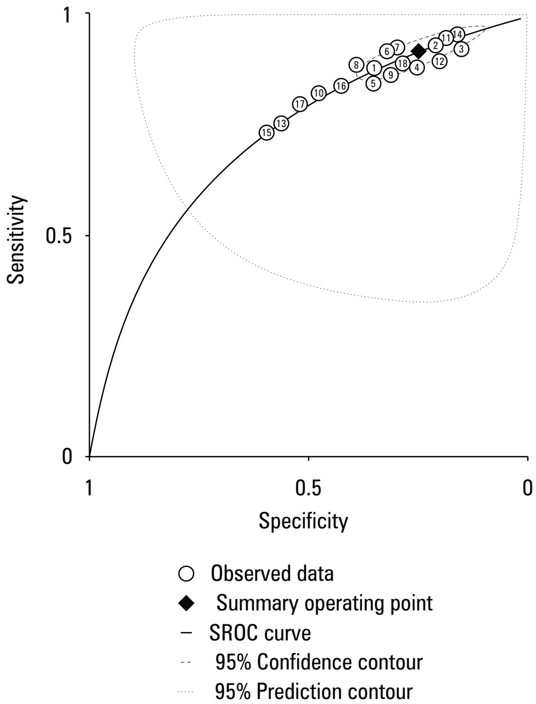


FIGURE 6 Hierarchical summary receiver operating characteristic (SROC) plot. Each examined study is represented by a circle, with the point estimate corresponding to cumulative sensitivity. Specificity is represented by a square, whereas the dashed line indicates the related 95% CI. The curve is represented as a linear line. The curve that summarizes the overall diagnostic accuracy is depicted by the regression line.

Tseng et al[73] concluded that balanced crystalloids and albumin reduced mortality more effectively than laevorotatory HES (L-HES) and saline in septic patients. However, in traumatic brain injury patients, saline or L-HES performed better than albumin or balanced crystalloids. In a similar vein, Liu et al[74] reported that balanced crystalloids were probably the best option for a majority of critically ill patients who required fluid resuscitation. Nevertheless, utilization of HES was linked to an elevated risk of renal replacement therapy and an elevated incidence of acute kidney injury. These findings confirmed that for septic and surgical patients, balanced crystalloids, specifically Ringer's lactate, were the most effective resuscitation fluids. They have been demonstrated to result in lower mortality rates, improved hemodynamic parameters, reduced risks of acute kidney injury, and lower blood transfusion volumes, as compared with saline and L-HES. However, Meyhoff et al[75] found very little low-quality evidence supporting the decision on high vs low volumes of intravenous fluid therapy in adults with sepsis. Similarly, Meyhoff et al[76] concluded that among adult patients with septic shock treated in an intensive care unit, intravenous fluid restriction did not result in fewer deaths at 90 days than standard intravenous fluid therapy. Furthermore, Zhang et al[77] documented the possible advantages and effectiveness of the goal-directed fluid therapy approach, led by the Vigileo-FloTrac system, on the intestinal mucosal barrier for fluid infusion in elderly patients diagnosed with colorectal cancer.

Limitations Certain limitations of our study need to be acknowledged. It is of vital importance to recognize the potential selection bias of our research, as a substantial number of studies were excluded. Secondly, our meta-analysis comprised only 18 studies of considerable heterogeneity related to varying fluid infusion quantities, fluid resuscitation procedures, and fluid intervention durations. Thirdly, the combined trials included distinct critically hypotensive septic patient populations that required immediate volume resuscitation. This factor had a potentially significant impact on the variation observed between the trials. Furthermore, variability in fluid administration protocols and variation of septic and critically hypotensive patients across the included studies also might have affected the results. Lastly, this study comprised a restricted number of RCTs and a small sample size for precise comparisons. Therefore, it is crucial to conduct further research on a larger sample and a larger number of RCTs in order to ascertain the optimal resuscitation fluid for sepsis management in critically hypotensive patients.

CONCLUSIONS The findings of our systematic review and meta-analysis indicate that Ringer's lactate solution is more effective than saline, HES, and albumin solutions in reducing all-cause mortality and improving hemodynamic parameters in critically hypotensive septic patients. Even though saline outperformed albumin and HES, due to the limitations of the included studies, further rigorous quality research is required for extensive comparison of different resuscitation fluid therapies and validation of these findings. Moreover, research into sepsis pathophysiology and innovative delivery methods would also enhance fluid resuscitation strategies, improving patient outcomes and quality of life.

ARTICLE INFORMATION

ACKNOWLEDGMENTS None.

FUNDING None.

CONTRIBUTION STATEMENT YW conceived the concept of and designed the study; KC analyzed the data; XL, collected the data and participated in data analysis; JG was responsible for drafting and editing the manuscript. All authors read and approved the final version of the manuscript.

CONFLICT OF INTEREST None declared.

HOW TO CITE Wang Y, Chen K, Li X, Guan J. Clinical efficacy of various resuscitation fluids in the management of sepsis in postoperative surgical and trauma patients: a systematic review and meta-analysis. Wideochir Inne Tech Maloinwazyjne. 2024; 19: 275-288. doi:10.20452/wiitm.2024.17900

REFERENCES

1 Casey JD, Brown RM, Semler MW. Resuscitation fluids. Curr Opin Crit Care. 2018; 24: 512-518.

2 Frazee E, Kashani K. Fluid management for critically ill patients: a review of the current state of fluid therapy in the intensive care unit. Kidney Dis (Basel). 2016; 2: 64-71.

3 Zhou Y, Wang Y, Li Q, et al. The effects of early restrictive fluid resuscitation on the clinical outcomes in sepsis patients. Am J Transl Res. 2021; 13: 11482-11490.

4 Moschopoulos CD, Dimopoulou D, Dimopoulou A, et al. New insights into the fluid management in patients with septic shock. Medicina (Kaunas). 2023; 59: 1047-1066.

5 Malbrain MLNG, Langer T, Annane D, et al. Intravenous fluid therapy in the perioperative and critical care setting: executive summary of the International Fluid Academy (IFA). Ann Intensive Care. 2020; 10: 64-83.

6 Messina A, Bakker J, Chew M, et al. Pathophysiology of fluid administration in critically ill patients. Intensive Care Med Exp. 2022; 10: 46-60.

7 Bunn F, Trivedi D. Colloid solutions for fluid resuscitation. Cochrane Database Syst Rev. 2012; 2012: CD001319.

8 Martin GS, Bassett P. Crystalloids vs. colloids for fluid resuscitation in the intensive care unit: a systematic review and meta-analysis. J Crit Care. 2019; 50: 144-154.

9 Boer C, Bossers SM, Koning NJ. Choice of fluid type: physiological concepts and perioperative indications. Br J Anaesth. 2018; 120: 384-396.

10 Shahnoor H, Divi R, Addi Palle LR, et al. The effects of restrictive fluid resuscitation on the clinical outcomes in patients with sepsis or septic shock: a meta-analysis of randomized-controlled trials. Cureus. 2023; 15: e45620.

11 Iskander KN, Osuchowski MF, Stearns-Kurosawa DJ, et al. Sepsis: multiple abnormalities, heterogeneous responses, and evolving understanding. Physiol Rev. 2013; 93: 1247-1288.

12 Munroe ES, Hyzy RC, Semler MW, et al. Evolving management practices for early sepsis-induced hypoperfusion: a narrative review. Am J Respir Crit Care Med. 2023; 207: 1283-1299.

13 Semler MW, Rice TW. Saline is not the first choice for crystalloid resuscitation fluids. Crit Care Med. 2016; 44: 1541-1544.

14 Lewis SR, Pritchard MW, Evans DJ, et al. Colloids versus crystalloids for fluid resuscitation in critically ill people. Cochrane Database Syst Rev. 2018; 8: CD000567.

15 Mitra S, Khandelwal P. Are all colloids same? How to select the right colloid? Indian J Anaesth. 2009; 53: 592-607.

16 Ramesh GH, Uma JC, Farhath S. Fluid resuscitation in trauma: what are the best strategies and fluids? Int J Emerg Med. 2019; 12: 38-43.

17 Wiedermann, Christian J. Phases of fluid management and the roles of human albumin solution in perioperative and critically ill patients. Curr Med Res Opin. 2020; 36: 1961-1973.

18 Angsubhakorn A, Tipchaichatta K, Chirapongsathorn S. Comparison of aggressive versus standard intravenous hydration for clinical improvement among patients with mild acute pancreatitis: a randomized controlled trial. Pancreatology. 2021; 21: 1224-1230.

19 Annane D, Siami S, Jaber S, et al; CRISTAL Investigators. Effects of fluid resuscitation with colloids vs crystalloids on mortality in critically ill patients presenting with hypovolemic shock: the CRISTAL randomized trial. JAMA. 2013; 310: 1809-1817.

20 Brunkhorst FM, Engel C, Bloos F, et al; German Competence Network Sepsis (SepNet). Intensive insulin therapy and pentastarch resuscitation in severe sepsis. N Engl J Med. 2008; 358: 125-1239.

21 Caironi P, Tognoni G, Masson S, et al; ALBIOS Study Investigators. Albumin replacement in patients with severe sepsis or septic shock. N Engl J Med. 2014; 370: 1412-1421.

22 Charpentier J, Mira JP. Efficacy and tolerance of hyperoncotic albumin administration in septic shock patients: the EARSS study. Intensive Care Med. 2011; 37: S115-S0438.

23 Cuéllar-Monterrubio JE, Monreal-Robles R, González-Moreno EI, et al. Nonaggressive versus aggressive intravenous fluid therapy in acute pancreatitis with more than 24 hours from disease onset: a randomized controlled trial. Pancreas. 2020; 49: 579-583.

24 de-Madaria E, Herrera-Marante I, González-Camacho V, et al. Fluid resuscitation with lactated Ringer's solution vs normal saline in acute pancreatitis: a triple-blind, randomized, controlled trial. United European Gastroenterol J. 2018; 6: 63-72.

25 Dubin A, Pozo MO, Casabella CA, et al. Comparison of 6% hydroxyethyl starch 130/0.4 and saline solution for resuscitation of the microcirculation during the early goal-directed therapy of septic patients. J Crit Care. 2010; 25: 659.e1-659.e6598.

26 Finfer S, Bellomo R, Boyce N, et al; SAFE Study Investigators. A comparison of albumin and saline for fluid resuscitation in the intensive care unit. N Engl J Med. 2004; 350: 2247-2256.

27 Friedman G, Jankowski S, Shahla M, et al. Hemodynamic effects of 6% and 10% hydroxyethyl starch solutions versus 4% albumin solution in septic patients. J Clin Anesth. 2008; 20: 528-533.

28 Li L, Jin T, Wen S, et al. Early rapid fluid therapy is associated with increased rate of noninvasive positive-pressure ventilation in hemoconcentrated patients with severe acute pancreatitis. Dig Dis Sci. 2020; 65: 2700-2711.

29 Li F, Sun H, Han XD. The effect of different fluids on early fluid resuscitation in septic shock [in Chinese]. Zhongguo Wei Zhong Bing Ji Jiu Yi Xue. 2008; 20: 472-475.

30 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.

31 McIntyre LA, Fergusson D, Cook DJ, et al; Canadian Critical Care Trials Group. Fluid resuscitation in the management of early septic shock (FINESS): a randomized controlled feasibility trial. Can J Anaesth. 2008; 55: 819-826.

32 Messallam AA, Body CB, Berger S, et al. Impact of early aggressive fluid resuscitation in acute pancreatitis. Pancreatology. 2021; 21: 69-73.

33 Molnár Z, Mikor A, Leiner T, Szakmány T. Fluid resuscitation with colloids of different molecular weight in septic shock. Intensive Care Med. 2004; 30: 1356-1360.

34 Myburgh JA, Finfer S, Bellomo R, et al; CHEST Investigators; Australian and New Zealand Intensive Care Society Clinical Trials Group. Hydroxyethyl starch or saline for fluid resuscitation in intensive care. N Engl J Med. 2012; 367: 1901-1911.

35 Perner A, Haase N, Guttormsen AB, et al; 6S Trial Group; Scandinavian Critical Care Trials Group. Hydroxyethyl starch 130/0.42 versus Ringer's acetate in severe sepsis. N Engl J Med. 2012; 367: 124-134.

36 Shea BJ, Reeves BC, Wells G, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ. 2017; 358: j4008.

37 Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Syst Rev. 2021; 10: 89.

38 Brown D. A Review of the PubMed PICO Tool: using evidence-based practice in health education. Health Promot Pract. 2020; 21: 496-498.

39 Higgins JP, Altman DG, Gøtzsche PC, et al; Cochrane Bias Methods Group; Cochrane Statistical Methods Group. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ. 2011; 343: d5928.

40 Sterne JA, Egger M. Funnel plots for detecting bias in meta-analysis: guidelines on choice of axis. J Clin Epidemiol. 2001; 54: 1046-1055.

41 Shi L, Chu H, Lin L. A Bayesian approach to assessing small-study effects in meta-analysis of a binary outcome with controlled false positive rate. Res Synth Methods. 2020; 11: 535-552.

42 Elovic A, Pourmand A. MDCalc medical calculator app review. J Digit Imaging. 2019; 32: 682-684.

43 Schmidt L, Shokraneh F, Steinhausen K, Adams CE. Introducing RAPTOR: RevMan parsing tool for reviewers. Syst Rev. 2019; 8: 151-154.

44 Szumilas M. Explaining odds ratios. J Can Acad Child Adolesc Psychiatry. 2010; 19: 227-229.

45 George BJ, Aban IB. An application of meta-analysis based on DerSimonian and Laird method. J Nucl Cardiol. 2016; 23: 690-692.

46 Parikh R, Mathai A, Parikh S, et al. Understanding and using sensitivity, specificity and predictive values. Indian J Ophthalmol. 2008; 56: 45-50.

47 Dettori JR, Norvell DC, Chapman JR. Seeing the forest by looking at the trees: how to interpret a meta-analysis forest plot. Global Spine J. 2021; 11: 614-616.

48 Huedo-Medina TB, Sánchez-Meca J, Marín-Martínez F, Botella J. Assessing heterogeneity in meta-analysis: Q statistic or I^2 index? Psychol Methods. 2006; 11: 193-206.

49 Ugoni A, Walker BF. The Chi square test: an introduction. COMSIG Rev. 1995; 4: 61-64.

50 Lan KK, Soo Y, Siu C, Wang M. The use of weighted Z-tests in medical research. J Biopharm Stat. 2005; 15: 625-639.

51 Andrade C. The *P* value and statistical significance: misunderstandings, explanations, challenges, and alternatives. Indian J Psychol Med. 2019; 41: 210-215.

52 Toft N, Nielsen SS. Summary receiver operating characteristics (SROC) and hierarchical SROC models for analysis of diagnostic test evaluations of antibody ELISAs for paratuberculosis. Prev Vet Med. 2009; 92: 249-255.

53 Gauer R, Forbes D, Boyer N. Sepsis: diagnosis and management. Am Fam Physician. 2020; 101: 409-418.

54 Gyawali B, Ramakrishna K, Dhamoon AS. Sepsis: the evolution in definition, pathophysiology, and management. SAGE Open Med. 2019; 7: 2050312119835043.

55 Hotchkiss RS, Moldawer LL, Opal SM, et al. Sepsis and septic shock. Nat Rev Dis Primers. 2016; 2: 16045.

56 Caraballo C, Jaimes F. Organ dysfunction in sepsis: an ominous trajectory from infection to death. Yale J Biol Med. 2019; 92: 629-640.

57 Zampieri FG, Bagshaw SM, Semler MW. Fluid therapy for critically ill adults with sepsis: a review. JAMA. 2023; 329: 1967-1980.

58 Seitz KP, Qian ET, Semler MW. Intravenous fluid therapy in sepsis. Nutr Clin Pract. 2022; 37: 990-1003.

59 Lutz J, Levenbrown Y, Hossain MJ, et al. Impact of intravenous fluid administration on cardiac output and oxygenation during cardiopulmonary resuscitation. Intensive Care Med Exp. 2023; 11: 13-24.

60 Lira A, Pinsky MR. Choices in fluid type and volume during resuscitation: impact on patient outcomes. Ann Intensive Care. 2014; 4: 38-50.

61 Rochwerg B, Alhazzani W, Sindi A, et al; Fluids in Sepsis and Septic Shock Group. Fluid resuscitation in sepsis: a systematic review and network meta-analysis. Ann Intern Med. 2014; 161: 347-355.

62 Kuttab HI, Evans CG, Lykins JD, et al. The effect of fluid resuscitation timing in early sepsis resuscitation. J Intensive Care Med. 2023; 38: 1051-1059.

63 Winters ME, Sherwin R, Vilke GM, Wardi G. What is the preferred resuscitation fluid for patients with severe sepsis and septic shock? J Emerg Med. 2017; 53: 928-939.

64 Semler MW, Rice TW. Sepsis resuscitation: fluid choice and dose. Clin Chest Med. 2016; 37: 241-250.

65 Filis C, Vasileiadis I, Koutsoukou A. Hyperchloraemia in sepsis. Ann Intensive Care. 2018; 8: 43-50.

66 Sagar N, Lohiya S. A comprehensive review of chloride management in critically ill patients. Cureus. 2024; 16: e55625.

67 Young P, Bailey M, Beasley R, et al; SPLIT Investigators; ANZICS CTG. Effect of a buffered crystalloid solution vs saline on acute kidney injury among patients in the intensive care unit: the SPLIT randomized clinical trial. JAMA. 2015; 314: 1701-1710.

68 Joosten A, Delaporte A, Ickx B, et al. Crystalloid versus colloid for intraoperative goal-directed fluid therapy using a closed-loop system: a randomized, double-blinded, controlled trial in major abdominal surgery. Anesthesiology. 2018; 128: 55-66.

69 Obradovic M, Luf F, Reiterer C, et al. The effect of goal-directed crystalloid versus colloid administration on postoperative spirometry parameters: a substudy of a randomized controlled clinical trial. Perioper Med (Lond). 2024; 13: 28-39.

70 Khatua B, Yaron JR, El-Kurdi B, et al. Ringer's lactate prevents early organ failure by providing extracellular calcium. J Clin Med. 2020; 9: 263-280.

71 Oczkowski S, Alshamsi F, Belley-Cote E, et al. Surviving Sepsis Campaign Guidelines 2021: highlights for the practicing clinician. Pol Arch Intern Med. 2022; 132: 16290.

72 Evans L, Rhodes A, Alhazzani W, et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2021. Crit Care Med. 2021; 49: e1063-e1143.

73 Tseng CH, Chen TT, Wu MY, et al. Resuscitation fluid types in sepsis, surgical, and trauma patients: a systematic review and sequential network meta-analyses. Crit Care. 2020; 24: 693-704.

74 Liu C, Mao Z, Hu P, et al. Fluid resuscitation in critically ill patients: a systematic review and network meta-analysis. Ther Clin Risk Manag. 2018; 14: 1701-1709.

75 Meyhoff TS, Møller MH, Hjortrup PB, et al. Lower vs higher fluid volumes during initial management of sepsis: a systematic review with meta--analysis and trial sequential analysis. Chest. 2020; 157: 1478-1496.

76 Meyhoff TS, Hjortrup PB, Wetterslev J, et al; CLASSIC Trial Group. Restriction of intravenous fluid in ICU patients with septic shock. N Engl J Med. 2022; 386: 2459-2470.

77 Zhang Y, Zhan L, Li D, et al. Influence of goal-directed fluid therapy guided by the Vigileo-FloTrac™ system on intestinal mucosal barrier function in elderly patients with colorectal cancer. Wideochir Inne Tech Maloinwazyjne. 2023; 18: 460-466.