Review Article

Intravenous Fluid of Choice in Major Abdominal Surgery: A Systematic Review

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Background. Intravenous fluid therapy plays a role in maintaining the hemodynamic status for tissue perfusion and electrolyte hemostasis during surgery. Recent trials in critically ill patients reported serious side effects of some types of fluids. Since the most suitable type of fluid is debatable, a consensus in perioperative patients has not been reached.

Method. We performed a systematic review of randomized control trials (RCTs) that compared two or more types of fluids in major abdominal surgery. The outcomes were related to bleeding, hemodynamic status, length of hospital stay, and complications, such as kidney injury, electrolyte abnormality, major cardiac adverse event, nausea, vomiting, and mortality. A literature search was performed using Medline and EMBASE up to December 2019. The data were pooled to investigate the effect of fluid on macrocirculation and intravascular volume effect.

Results. Forty-three RCTs were included. Eighteen fluids were compared: nine were crystalloids and nine were colloids. The results were categorized into macrocirculation and intravascular volume effect, microcirculation, anti-inflammatory parameters, vascular permeability, renal function (colloids), renal function and electrolytes (crystalloids), coagulation and bleeding, return of bowel function, and postoperative nausea vomiting (PONV). We found that no specific type of fluid led to mortality and every type of colloid was equivalent in volume expansion and did not cause kidney injury. However, hydroxyethyl starch and dextran may lead to increased bleeding. Normal saline can cause kidney injury which can lead to renal replacement therapy, and dextrose fluid can decrease PONV. Conclusion. In our opinion, it is safe to give a balanced crystalloid as the maintenance fluid and give a colloid, such as HES130/0.4, 4% gelatin, or human albumin, as a volume expander.

1. Introduction

Many factors affect the outcome of elective surgery. Beyond the nature of the primary disease and the surgical factors, intravenous fluid therapy and inotropic drugs play a role in maintaining the hemodynamic status for tissue perfusion and electrolyte hemostasis [1, 2].

The first intravenous fluid was invented about 200 years ago and evolved progressively during world wars to replace blood plasma by adding a complex sugar, protein, and colloids. [3] While believing that 0.9% sodium chloride (NaCl) is physiologic [4] and synthetic colloids are more effective than crystalloids in restoring plasma volume [5], they are widely used for resuscitation and maintenance purposes.

During recent decades, previous knowledge has been questioned. First, it was discovered that endothelial glyco-calyx is the key structure to regulate microvascular hemodynamics, not oncotic pressure. These studies have led to a revised Starling principle and a new approach to vascular fluid dynamics [6]. Second, many large trials in critically ill patients and subsequent meta-analyses report potential clinical side effects of IV fluids, especially 0.9% NaCl which is associated with the development of metabolic acidosis that results in kidney injury and increases mortality rates [7, 8]. Synthetic colloids were also reported to cause side effects in kidney function and hemostasis [9–11]. Therefore, the use of all hydroxyethyl starches (HES) became restricted in critical illness, renal failure, or coagulopathy by the European
Our goal was to systematically review the latest evidence of perioperative intravenous fluid therapy in major abdominal surgery with a focus on the types of fluids. Volume, administration technique, and surgery beyond the abdominal field were not reviewed.

2. Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [13] guideline was used to conduct this systematic review.

2.1. Literature Search. We searched Medline (PubMed) and EMBASE (Ovid) databases on 16 December 2019. The keywords and Medical Subject Headings (MeSH) terms to search Medline were major abdominal surgery; any known intravenous fluid; and possible perioperative complication. The full search is included in Appendix S1. Search strategies were adapted for the other databases. The applied restrictions were randomized controlled trials (RCTs); English only; age more than 18 years; and human trial. The year of publication was not restricted.

2.2. Study Selection/Inclusion and Exclusion. Two levels of screening were used independently by two reviewers (SN and OA). First, the titles and abstracts of the included studies were screened and then the full text was reviewed. The included studies followed these inclusion criteria: (1) the population of patients was more than 18 years old and had undergone elective major abdominal surgery which was defined as any operation with peritoneum cavity exposure with resection and/or anastomosis; (2) intervention using two or more types or doses of intravenous fluids; and (3) the reported outcomes related to bleeding, hemodynamic status, length of hospital stay, and complications such as kidney injury, electrolyte abnormality, major cardiac adverse event, nausea, vomiting, and mortality. The excluded articles were duplicate or retracted studies, organ donor or animal studies, case reports, and case series. Any difference of opinion was resolved by discussion.

2.3. Data Extraction and Quality Assessment. Two authors (SN and OA) extracted data into a data sheet. The extracted data included type of surgery, number of patients, fluid regimen, and the primary and secondary outcomes of each paper. The quality of the studies was independently assessed with the Cochrane tool to assess the risk of bias for RCTs [14] in the following domains: randomization method; allocation concealment; blinding; data completeness; and publication bias. Any disagreement was resolved by discussion.

2.4. Data Analysis. The studies that compared the microcirculation and intravascular volume effect between colloid and crystalloid were selected for analysis. The total intraoperative volume to achieve hemodynamic parameters was used to represent the effect of crystalloid and colloid on microcirculation. The standard mean difference (SMD) was used to demonstrate the effect size of the types of fluid.

3. Results

3.1. Identification of Studies. The initial search in Medline (PubMed) and EMBASE (Ovid) identified 1,412 articles of which 421 are duplications. A further 938 were excluded because they did not fulfill the selection criteria. Fifty-six articles were then excluded for the reasons described in Figure 1. Three additional RCT studies [15–17] were added after a cross-reference review.

3.2. Study Characteristics and Patient Populations. A total of 43 RCTs were included. The total numbers of patients in the included studies varied from 21 to 259 patients. Most of the studies reported around 30 patients per intervention. The types of surgery included cystectomy, radical prostatectomy, hepatectomy, laparoscopic/open colorectal surgery, gastrectomy, open abdominal aortic aneurysm repair, laparoscopic/open cholecystectomy, kidney transplantation, and liver transplantation. The main characteristics of the studies are shown in Table 1, and the types of study fluids are shown in Table 2. Full data sheet is shown in Table S1.

3.3. Quality of the Included Studies. The results of the quality assessments of all studies are shown in Figure 2. Ten studies were considered high risk for blinding of participants due to safety issues. Two studies had a high risk of detection bias due to the open-label study. Most of the trials followed patients for a short period; therefore, missing data or lost to follow-up rates were low.

3.4. Qualitative Review

3.4.1. Macrocirculation and Intravascular Volume Effect. Table 3 shows the results of 16 trials [15–17, 21, 23, 24, 27, 30, 41, 47–51, 56, 57] that reported the volume effects of fluids. Lavo et al. [30] compared 3% NaCl to lactated Ringer’s solution (LRS) in patients who underwent pancreaticoduodenectomy using the fluid restriction technique and found lower perioperative intake in the 3% NaCl group (278 vs. 315 mL/kg, p value = 0.017) to maintain hemodynamic status. Six studies compared HES 130/0.4 (Volulyte [15–17] and Voluven [23, 27, 50]) to crystalloids. All of them reported good volume expansion according to stable hemodynamic parameters and needed both lower amounts of intraoperative fluids and inotropes to maintain hemodynamic status. Yates et al. [16] and Zhang et al. [56] who used goal-directed fluid therapy also reported colloids at crystalloid ratios of 1.6:1 and 1.67:1 to maintain the same hemodynamics in their trials. Vogt et al. [51] reported 6%
HES 200/0.5 was an economical alternative to 5% human albumin for resuscitation because they had the same volume expansion effects although a lower serum colloid osmotic pressure was reported in the HES group. Two studies [24, 48] compared HES 130/0.4 to HES 200/0.5 and found no differences in the hemodynamic parameters, but HES 200/0.5 in one study [21] had a prolonged INR (1.25 ± 0.19 vs. 1.18 ± 0.09; \( p \) value < 0.05). Ragaller et al. [41] reported HES 200 in 7.2% NaCl could restore the hemodynamics faster than HES 200 in 0.9% NaCl using pulmonary capillary wedge pressure guidance. Two studies [21, 57] compared 4% gelatin to 4.5% NaCl in 7.6% HES 40. Deng et al. [21] favored hypertonic NaCl-HES due to a more stable systemic vascular resistance index but Zhu [57] reported no significant differences in the hemodynamics.

Among the trails in which results were related to macrocirculation and intravascular volume, eight studies [16, 17, 21, 23, 27, 49, 50, 56] compared between colloid and crystalloid. Only 3 studies mentioned the mean of intraoperative fluid volume [23, 49, 56]. The SMD was −0.638 (95% CI −1.137 to −0.138, \( p = 0.012 \)). The forest plot is shown in Figure 3.

### 3.4.2. Microcirculation

Table 4 shows the results of five RCT studies [21, 34, 35, 46, 57] that examined the effects of fluid types on microcirculation via splanchnic circulation. Three studies were conducted in open abdominal aortic aneurysm [34, 35, 46]. Marik et al. [35] compared LRS to hetastarch (Hespan) and found that the HES group had higher gastric pH values which better represented microcirculation compared to crystalloids (\( p \) value < 0.001). Rittoo [46] and Mahmood et al. [34] compared HES to gelatin and found that HES 200/0.62 could maintain higher gastric pH. Deng [21] and Zhu [57] compared 4% gelatin to hypertonic NaCl-HES by the acute hypervolemic infusion technique in laparoscopic colorectal surgery. Using the gastric pH value combined with the gastric-arterial \( CO_2 \) gradient, Deng [21] reported that hypertonic NaCl-HES was better while data from Zhu [57] supported gelatin.

#### 3.4.3. Anti-Inflammatory Parameters and Vascular Permeability

Table 5 shows the results of six trials [16, 18, 33, 34, 46, 47] that studied the effects of colloids on the inflammatory process. Rittoo et al. [46, 47] and Mahmood et al. [33, 34] compared the effects of HES 200/0.62 (Elohes) and HES 130/0.4 (Voluven) to 4% gelatin (Gelofusine) in four RCTs that were performed in patients who underwent open aortic aneurysm repair. Using CRP, IL-6, and the lung injury score as biomarkers of the inflammatory process and the microalbumin/creatinine (Cr) ratio to indicate glomerular microvascular permeability, they reported that Elohes could decrease the inflammatory process by decreasing the CRP level which led to decreased microalbumin and von Willebrand factor (vWF) levels. Two studies compared medium to low molecular weight HES (HES 130/0.4 (Voluven) [16] and HES 70/0.5 (Hespander) [18]) to balanced crystalloids. They found that both solutions did not significantly decrease the inflammation parameters and did not alter vascular permeability [18].

#### 3.4.4. Renal Function (Colloid vs. Colloid/Crystalloid)

Table 6 shows the results of 10 RCTs that reported the effects of fluids on renal function. Five trials [15–18, 27] compared colloids to crystalloids and five trials [20, 26, 33, 38, 47] compared HES to other colloids or human albumin. Ando et al. [18] compared low molecular weight HES (HES 70/0.5 or Hespander) to acetate Ringer’s solution and found a significant difference in the glomerular filtration rate (GFR) and the urinary microalbumin/Cr ratio from intraoperative evaluations to discharge. Kancir et al. [27] reported no renal toxicity when HES 130/04 (Voluven) was compared to normal saline solution (NSS) using serum neutrophil gelatinase-associated lipocalin and Cr as the parameters. Three studies [15–17] compared balanced HES (Volulyte) to balanced crystalloids. The largest trial [17], which included 80 patients per group, did not show any differences in the renal function tests. In comparisons of HES to other colloids, HES 200/0.62 (Elohes) showed better renal function than 4% gelatin (Gelofusine) in two studies [33, 47] using Cr and urine albumin as the parameters. Demir et al. [20] compared HES 130/0.4 (Voluven) to 4% gelatin (Gelofusine) in patients who underwent a liver transplant and reported a nonsignificant incidence of acute kidney injury (AKI) grade I in the gelatin group (2 vs. 5). Two studies [26, 38] compared HES 130/0.4 (Voluven) to 5% human albumin and reported no differences in the renal dysfunction at neither immediate postoperation [36, 38] nor 3-month postoperation [38] using the cystatin C/Cr ratio.
Table 1: Main characteristics of the studies included in this review.

| Author, years | N | Age, range (average) | Sex (M/F) | ASA (N) | Fluid A | Fluid B | Fluid C | Operation | Primary outcome/primary endpoint |
|---------------|---|----------------------|-----------|---------|---------|---------|---------|-----------|-----------------------------------|
| Ando et al. [18], 2008 | 21 | 67 (60, 70) | 12/9 | I/II (9/12) | Acetate Ringer | HES70/0.5 (Hespan) | — | Major abdominal surgery | Urinary microalbumin/creatinine ratio |
| Chaudhary et al. [19], 2008 | 60 | 41 ± 11.06 | — | I/II | LRS 2 mL/kg | LRS 12 mL/kg | 4.5% hetastarch 12 mL/kg | Open cholecystectomy | PONV at 24 hours (VAS) |
| Demir et al. [20], 2018 | 36 | 42.72 ± 13.25 | 25/11 | I/II/III/IV (21/8/7) | 6% HES130/0.4 (Voluven) | 4% gelatin (Gelofusine) | — | Living donor liver transplant | Renal function (Cr, BUN, and GFR) |
| Deng et al. [21], 2017 | 36 | 40–80 | 20/16 | I/II | LRS | 4% gelatin (Gelofusine) | 4.5% NaCl in 7.6% HES40 | Laparoscopic colonic surgery | Mucosal blood flow (Pg-aCO2) |
| Feldheiser et al. [15], 2013 | 48 | 52.5 (45.5, 59) | — | I/II/III (4/24/20) | Jonosteril | 6% HES130/0.4 (Volulyte) | — | Cytoreductive surgery | Amount of fluid |
| Ghodraty et al. [22], 2017 | 91 | 53.2 ± 12.3 | 60/31 | I/II/III (38/53) | LRS | 6% HES130/0.4 (Voluven) | 6% HES130/0.4 (Voluven) | — | GI surgery | Presence of bowel function |
| Hung et al. [23], 2014 | 80 | 48 ± 10.7 | 48/32 | — | LRS | 0.4 (Voluven) | 0.4 (Voluven) | — | Major abdominal surgery | Thromboelastogram |
| Ickx et al. [24], 2003 | 40 | 62 (47–72) | 39/1 | II/III | 6% HES130/0.4 (Voluven) | 6% HES200/0.5 (HAES-steril) | — | Major abdominal surgery | Plasma substitution effect (CO, RVEDV) |
| Jin et al. [25], 2010 | 42 | 49 ± 10 | 15/27 | I/II | LRS | 6% HES130/0.4 (Voluven) | 6% HES130/0.4 (Voluven) | 4% gelatin (Gelofusine) | Gastrectomy | Thromboelastogram |
| Joosten et al. [17], 2018 | 160 | 62 (48–70) | 96/84 | II/III/IV (93/67/6) | Plasmalyte | 0.4 (Volulyte) | 0.4 (Volulyte) | — | Major abdominal surgery | Postoperative complication at day 2 |
| Kammerer et al. [26], 2018 | 100 | 70 (61–75) | 81/19 | I/II/III/IV (6/38/63/2) | 5% human albumin | 6% HES130/0.4 (Voluven) | — | Cystectomy | Serum cystatin C ratio (preoperative/postoperative day 90) |
| Kancir et al. [27], 2015 | 36 | 64 (4.8) | — | — | NSS | 6% HES130/0.4 (Voluven) | — | Radical cystectomy | Urine NGAL |
| Khajavi et al. [28], 2008 | 54 | 40 ± 14 | — | — | NSS | LRS | — | Living donor kidney transplant | Serum potassium and pH |
| Kim et al. [29], 2013 | 60 | 46 ± 12 | 38/22 | III/IV | NSS | Plasmalyte | — | Living donor kidney transplant | Renal function |
| Lavu et al. [30], 2014 | 259 | 68.3 (25–91) | 39%/46% | III/IV/III (167) | LRS | 3% sodium chloride | — | Pancreaticoduodenectomy | Postoperative complication |
| Liang et al. [31], 2010 | 35 | 57 ± 8 | 15/20 | I/II | 6% HES130/0.4 (Voluven) | 6% HES200/0.5 (HAES-steril) | Chloride-depleted glucose solution 5% (GSK) | Laparoscopy-assisted radical colectomy | Thromboelastogram |
| Loffel et al. [32], 2016 | 44 | 71.5 (33–82) | 30/14 | I/II/III (28/16) | Ringer maleate | — | Cystectomy | First defecation |
| Author, years | N  | Age, range (average) | Sex (M/F) | ASA (N) | Fluid A | Fluid B | Fluid C | Operation | Primary outcome/primary end point |
|--------------|----|----------------------|-----------|---------|---------|---------|---------|-----------|-------------------------------------|
| Mahmood et al. [33], 2007 | 62 | 72 (7) | 50/12 | — | 6% HES 200/0.62 (Elohes) | 6% HES130/0.4 (Voluven) | 4% gelatin (Gelofusine) | Open AAA repair | Splanchic perfusion (gastric pH) |
| Mahmood et al. [34], 2009 | 62 | 72 (7) | 50/12 | — | 6% HES 200/0.62 (Elohes) | 6% HES130/0.4 (Voluven) | 4% gelatin (Gelofusine) | Open AAA repair | Renal function (Cr, GFR) |
| Marik et al. [35], 1997 | 30 | — | — | — | LRS | 0.75 (hetastarch) | — | Open AAA repair | Maximal change of gastric pH |
| Mishra et al. [36], 2017 | 100 | 39.6 ± 11.54 | 28/72 | I/II (81/19) | NSS | 5% Dextrose | — | Laparoscopic cholecystectomy | Incidence of PONV |
| Modi et al. [37], 2012 | 72 | 18–62 | — | — | NSS | LRS | — | Living donor kidney transplant | Acidosis, potassium |
| Mukhtar et al. [38], 2009 | 40 | 51 ± 6 | 35/5 | — | 5% human albumin | 6% HES130/0.4 (Voluven) | — | Living donor liver transplant | Creatinine clearance at 24 hours |
| O’Malley et al. [39], 2005 | 51 | 44 ± 13 | 32/19 | — | NSS | LRS | — | Kidney transplant | Cr at postoperative day 3 |
| Potura et al. [40], 2015 | 148 | 56 ± 13 | 95/53 | — | NSS | Elomel-Isoton | — | Cadaveric kidney transplant | Perioperative hyperkalemia |
| Ragaller et al. [41], 2000 | 29 | 68.4 ± 8.5 | 26/3 | I/II/III | 6% HES200/0.5 + 0.9% NaCl | 6% HES200/0.5 + 7.2% NaCl | — | Open AAA repair | Amount of fluid to restore PCWP |
| Rao et al. [42], 2017 | 112 | 19–60 | — | I/II | LRS | 5% dextrose | — | Laparoscopic cholecystectomy | Incidence of PONV |
| Rasmussen et al. [43], 2014 | 33 | 64.1 (7.9) | 26/7 | I/II/III | LRS | Dextran 70 | — | Cystectomy | Thromboelastogram |
| Rasmussen et al. [44], 2015 | 37 | 68 (61.9–74.3) | 27/10 | I/II/III | LRS | 5% human albumin | — | Cystectomy | Thromboelastogram |
| Rasmussen et al. [45], 2016 | 39 | 69 (66–72) | 25/14 | I/II/III | LRS | 6% HES130/0.4 (Voluven) | — | Cystectomy | Thromboelastogram |
| Rittoo et al. [46], 2002 | 22 | 70.6 ± 2.18 | 15/7 | — | 4% gelatin (Gelofusine) | 6% HES200/0.62 (Elohes) | — | Open AAA repair | Splanchic perfusion (gastric pH) |
| Rittoo et al. [47], 2005 | 40 | 71.2 (6.7) | 30/10 | — | 4% gelatin (Gelofusine) | 6% HES200/0.62 (Elohes) | — | Open AAA repair | Inflammatory marker |
| Sander et al. [48], 2003 | 56 | 45 ± 15 | — | I/II/III (16/36/4) | 6% HES130/0.4 (Voluven) | 6% HES200/0.5 (Voluven) | — | Major gynecological surgery | Hemodynamic maintenance |
| Senagore et al. [49], 2009 | 64 | — | — | I/II/III | Standard-LR | Goal-directed LR | Goal-directed hetastarch | — | Laparoscopic colonic surgery | Length of hospital stay |
| Szturz et al. [50], 2014 | 115 | 61 (27–87) | 83/32 | I/II/III/IV | LRS | 6% HES130/0.4 (Voluven) | — | Major urological surgery | Efficiency of volume expansion |
| Vogt et al. [51], 1999 | 48 | 65 (7.1) | — | I/II/III (4/33/13) | 5% human albumin | 6% HES200/0.5 (Voluven) | — | Major urological surgery | Hemodynamic stability effect |
| Waters et al. [52], 2001 | 66 | 69.8 ± 8.7 | — | I-IV (III) | NSS | LRS | — | Open AAA repair | Change in base excess |
3.4.5. Renal Function and Electrolyte Imbalance (Balanced Solutions vs. Saline Solution). Table 7 shows the results of eight [28, 29, 37, 39, 40, 52–54] trials that studied the effects of crystalloids on renal function. Waters et al. [52] compared the effects of NS to LRS in patients who underwent open aortic repair. Six studies compared the effect of NS to balanced crystalloid solutions (LRS [28, 37, 39], Plasmalyte [29, 54], and acetate buffer crystal [40]) in kidney transplant patients. The outcomes were the same as NSS which induced hyperchloremic metabolic acidosis with hyperkalemia during the intraoperative and immediate postoperative periods. One study [54] reported that hemodialysis was needed more frequently to treat hyperkalemia in the NSS group (13 vs. 4; p value = 0.02). Weinberg et al. [53] compared Plasmalyte to Hartmann’s solution in liver resection patients. They reported no difference in renal function but Hartmann’s solution showed a higher median (interquartile range (IQR)) intraoperative bleeding of 500 mL (300,638) vs. 300 mL (200,413) (p value = 0.03) along with coagulopathy and overall complications (56% vs. 20%; p value = 0.007).

3.4.6. Coagulation Defect and Bleeding. Table 8 shows the results of eight studies that focused on bleeding tendency [16, 23, 25, 27, 31, 43–45]. With the exception of the Yates et al. [16] study, most studies were small with n < 50. The thromboelastogram (TEG) was used as the primary outcome in all of the studies. Jin et al. [25] compared 6% HES 130/0.4 (Voluven) to 4% gelatin (Gelofusine) using LRS as the control. They found that HES delayed clot formation measured by the TEG parameters (R) reaction, kinetic (K) time, and angle and impaired platelet function by decreased function of coagulation factors VIII:C and vWF. Jin et al. [25] also demonstrated that gelatin reduced clot quality at one hour after loading that was indicated by a decreased TEG maximum amplitude (MA) value. Liang et al. [31] compared HES 200/0.5 to HES 130/0.4 in laparoscopic colectomy in the preload infusion technique. They found that HES 200/0.5 resulted in an impaired TEG R time, MA value, and decreased expressions of GPIIb/IIIa and CD62P (p value < 0.05). Three studies [16, 23, 43] compared HES 130/0.4 to balanced crystalloids. Yates et al. [16] did not find a significant difference in the TEG parameters while two other reports [23, 43] found impaired TEG MA and K values (p value<0.05) in HES 130/0.4 that was associated with a greater mean (SD) blood loss (2181 (1190) vs. 1370 (603) mL; p value = 0.038) [43]. Kancir et al. [28] also reported greater mean (SD) bleeding when HES 130/0.4 (Voluven) was compared to NSS (1256 mL (669) vs. 747 mL (331); p value = 0.008). Rasmussen et al. also reported that 5% human albumin [45] and Dextran70 [44] affected TEG MA. Dextran70 was also associated with the incidence of significant bleeding (>1500 mL) in cystectomy compared to LRS (n (%):
| Fluid                      | Na⁺ (g/L) | K⁺ (g/L) | Cl⁻ (g/L) | Ca²⁺ (g/L) | Mg²⁺ (g/L) | HCO₃⁻ (g/L) | Buffer         | Glucose (g/L) | Other            | Molecular wt (kDa)/C₂:C₆ ratio | Osmolarity (mmHg) | Oncotic pressure (mmHg) | pH (in vitro) | Initial volume expansion (%) | Persistence in the body (days) | Maximal daily dose (per kg) |
|----------------------------|-----------|----------|-----------|------------|------------|-------------|----------------|---------------|----------------|-----------------------------|-------------------|---------------------------|---------------|--------------------------------|--------------------------------|-------------------------|
| Plasma                     | 140       | 5        | 100       | 4.4        | 2          | 4.4         | Lactate 1     | —             | —              | 285                          | 7.4               | —                         | —             | —                              | —                          | —                       |
| 0.9% NaCl (NSS)            | 154       | —        | 154       | —          | —          | —           | —             | —             | —              | —                           | 308               | 6                        | —             | —                              | —                          | —                       |
| 3% NaCl                    | 513       | —        | 513       | —          | —          | —           | —             | —             | —              | —                           | 1026              | 4.5                       | —             | —                              | —                          | —                       |
| 5% Dextrose                | —         | —        | —         | —          | —          | —           | —             | 50            | —              | —                           | 252               | 4.5                       | —             | —                              | —                          | —                       |
| 5% Dextrose/0.45%NaCl Lactated Ringer solution (Hartmann’s solution, LRS) | 77        | —        | 77        | —          | —          | —           | —             | 50            | —              | —                           | 406               | 4                        | —             | —                              | —                          | —                       |
| Plasmalyte                 | 140       | 5        | 98        | 3          | —          | —           | Acetate 28    | —             | —              | 273                          | 6.5               | —                         | —             | —                              | —                          | —                       |
| Jonosteril                 | 137       | 4        | 110       | 1.6        | 1.2        | —           | Acetate 27    | —             | —              | 294                          | 7.4               | —                         | —             | —                              | —                          | —                       |
| Ringer maleate (Ringerfundin) | 145       | 4        | 127       | 2.5        | 1          | —           | Acetate 23    | —             | —              | 236                          | 7.4               | —                         | —             | —                              | —                          | —                       |
| GS K solution              | 50        | 30       | 65        | 0          | 2          | —           | Lactate 18    | 50            | —              | 454                          | —                 | na                        | —             | —                              | —                          | —                       |
| 4%–5% Albumin Dextran70    | 130–160   | 130–160  | —         | —          | —          | —           | —             | 309           | 20–29                        | 309              | 5.5                       | 100            | 4–6                            | 1.5                        | —                       |
| 6% HES 670/0.75 (hetastarch) | 154       | 154      | —         | —          | —          | —           | —             | na            | 56–68                       | 670/4.5:1         | 5.5                       | 100            | 4–6                            | 1.5                        | —                       |
| 6% HES 200/0.62 (Bholos)   | 154       | 154      | —         | —          | —          | —           | —             | na            | 56–68                       | 670/4.5:1         | 5.5                       | 100            | 4–6                            | 1.5                        | —                       |
| 6% HES 200/0.5 (Hesteril)  | 154       | 154      | —         | —          | —          | —           | —             | Na            | 30–37                       | 670/4.5:1         | 5.5                       | 100            | 3–4                            | 33                         | —                       |
| 6% HES 130/0.4 NSS (Voluven) | 154       | 154      | —         | —          | —          | —           | —             | Na            | 30–37                       | 670/4.5:1         | 5.5                       | 100            | 2–3                            | 33                         | —                       |
| 6% HES 130/0.4 balanced solution (Volulyte) | 137       | 110      | 3         | —          | —          | —           | Acetate 34    | —             | 130/9:1                     | 287               | na                        | 100            | 2–3                            | 1.5                        | —                       |
| 6% HES 70/0.5 in balanced solution (Hespaider) | 137       | 4        | 110       | 3         | —          | —           | Acetate 34    | —             | 130/9:1                     | 287               | na                        | 100            | 2–3                            | 1.5                        | —                       |
| 4% succinylated gelatin (Gelofusine) | 154       | 125      | —         | —          | —          | —           | Lactate 20    | 70/3:1        | —                            | 274               | 100                       | 2–7                         | —                         | —                       |

Note. Electrolyte concentrations, osmolarity, and pH may be subject to small differences in other reports. HES = hydroxyethyl starch; kDa = kilodalton.
| Study                      | Random sequence generation (selection bias) | Allocation concealment (selection bias) | Blinding of participants and personnel (performance bias) | Blinding of outcome assessment (detection bias) | Incomplete outcome data (attrition bias) | Selective reporting (reporting bias) |
|---------------------------|---------------------------------------------|-----------------------------------------|----------------------------------------------------------|-----------------------------------------------|------------------------------------------|----------------------------------|
| Ando 2008                 | +                                           | +                                      |                                                          |                                               |                                          |                                  |
| Chaudhary 2008             | +                                           |                                          |                                                          |                                               |                                          |                                  |
| Demir 2015                | +                                           |                                          |                                                          |                                               |                                          |                                  |
| Deng 2017                 | +                                           |                                          |                                                          |                                               |                                          |                                  |
| Feldheiser 2013           | +                                           |                                          |                                                          |                                               |                                          |                                  |
| Ghodraty 2017             | +                                           |                                          |                                                          |                                               |                                          |                                  |
| Hung 2014                 | +                                           |                                          |                                                          |                                               |                                          |                                  |
| Ickx 2003                 | +                                           |                                          |                                                          |                                               |                                          |                                  |
| Jin 2010                  | +                                           |                                          |                                                          |                                               |                                          |                                  |
| Joosten 2018              | +                                           |                                          |                                                          |                                               |                                          |                                  |
| Kammerer 2018             | +                                           |                                          |                                                          |                                               |                                          |                                  |
| Kancir 2015               | +                                           |                                          |                                                          |                                               |                                          |                                  |
| Khajavi 2008               | +                                           |                                          |                                                          |                                               |                                          |                                  |
| Kim 2013                  | +                                           |                                          |                                                          |                                               |                                          |                                  |
| Lau 2014                  | +                                           |                                          |                                                          |                                               |                                          |                                  |
| Liang 2010                | +                                           |                                          |                                                          |                                               |                                          |                                  |
| Loefel 2016               | +                                           |                                          |                                                          |                                               |                                          |                                  |
| Mahmood 2007              | +                                           |                                          |                                                          |                                               |                                          |                                  |
| Mahmood 2009              | +                                           |                                          |                                                          |                                               |                                          |                                  |
| Marik 1997                | +                                           |                                          |                                                          |                                               |                                          |                                  |
| Mishra 2017               | +                                           |                                          |                                                          |                                               |                                          |                                  |
| Modi 2012                 | +                                           |                                          |                                                          |                                               |                                          |                                  |
| Mukhtar 2009              | +                                           |                                          |                                                          |                                               |                                          |                                  |
| O’Malley 2005             | +                                           |                                          |                                                          |                                               |                                          |                                  |
| Potura 2015               | +                                           |                                          |                                                          |                                               |                                          |                                  |
| Ragaller 2000             | +                                           |                                          |                                                          |                                               |                                          |                                  |
| Rao 2017                  | +                                           |                                          |                                                          |                                               |                                          |                                  |
| Rasmussen 2014            | +                                           |                                          |                                                          |                                               |                                          |                                  |
| Rasmussen 2015            | +                                           |                                          |                                                          |                                               |                                          |                                  |
| Rasmussen 2016            | +                                           |                                          |                                                          |                                               |                                          |                                  |
| Rasmussen 2017            | +                                           |                                          |                                                          |                                               |                                          |                                  |
| Rittoo 2002               | +                                           |                                          |                                                          |                                               |                                          |                                  |
| Rittoo 2005               | +                                           |                                          |                                                          |                                               |                                          |                                  |
| Sander 2003               | +                                           |                                          |                                                          |                                               |                                          |                                  |
| Szturz 2014               | +                                           |                                          |                                                          |                                               |                                          |                                  |
| Vogt 1999                 | +                                           |                                          |                                                          |                                               |                                          |                                  |
| Waters 2001               | +                                           |                                          |                                                          |                                               |                                          |                                  |
| Weinberg 2015             | +                                           |                                          |                                                          |                                               |                                          |                                  |
| Weinberg 2017             | +                                           |                                          |                                                          |                                               |                                          |                                  |
| Yates 2014                | +                                           |                                          |                                                          |                                               |                                          |                                  |
| Yuan 2008                 | +                                           |                                          |                                                          |                                               |                                          |                                  |
| Zhang 2012                | +                                           |                                          |                                                          |                                               |                                          |                                  |
| Zhu 2018                  | +                                           |                                          |                                                          |                                               |                                          |                                  |

**Figure 2:** Risk of bias of original studies.
3.4.7. Return to Bowel Function. Table 9 shows four studies that reported bowel function [16, 22, 32, 56]. Loffel et al. [32] compared chloride-depleted glucose solution 5%
to Ringer’s maleate solution and found that G5K could enhance bowel recovery time by 38 hours. Two studies that compared 6% HES 130/0.4 to balanced crystalloid reported faster bowel recovery according to the first flatus time ($86 \pm 7.2$ vs. $95 \pm 9.1; p \text{ value}<0.03$) [56] and $(73.4 \pm 20.8$ vs. $86.7 \pm 20.8; p \text{ value}=0.006$) [22]. In contrast, Yates et al. [16] conducted a large trial ($n=202$) that compared balanced crystalloid to balanced 6% HES 130/0.4 (Volulyte). The results showed no difference in the number of patients who tolerated diet at postoperative day 5 (30% vs. 32%) or in the time to first flatus.

3.4.8. Postoperative Nausea Vomiting (PONV). Table 10 shows four studies that reported the effects of fluid on PONV [19, 22, 36, 42]. Chaudary et al. [19] used preoperative intravenous volume loading by LRS and hetastarch. They found that both fluids decreased the rate of PONV and vomiting at four hours after operation compared to the IV restricted group. Two studies [36, 42] that compared LRS to 5% dextrose in laparoscopic cholecystectomy showed that 5% dextrose fluid decreased the rate of PONV by more than 50%. One study [22] showed that 6% HES 130/0.4 decreased the vomiting rate compared to LRS (11% vs. 3%; $p \text{ value}=0.266$) in gastrointestinal surgery.
3.4.9. Other. Yuan et al. [55] compared 20% human albumin to NSS in hypoalbunemia patients in major abdominal surgery during postoperative days 0–2 and found no clinical or albumin level difference to postoperative day 7. Senagore et al. [49] compared 6% hetastarch in a balanced salt solution to LRS in patients who underwent laparoscopic colorectal surgery with goal-directed therapy. They reported an increased mean number of complications per patient \((2 \pm 1.7 \text{ vs. } 4.4 \pm 4)\) and a prolonged length of hospital stay of 6 hours in the hetastarch group. Feldheiser [15] compared 6% HES 130/04 (Voluven) to balanced crystalloid and reported a higher mortality rate at 3 months after operation in patients who received HES (0 vs. 5; \(p = 0.051\)). However, 4 of the 5 had progressive diseases, and Joosten [17] reported a higher incidence of anastomosis leakage in the crystalloid (Plasmalyte) group than in the colloid (Volulyte) group (8 vs. 0; \(p = 0.946\)).

### 4. Discussion

Nowadays, the type of fluid therapy in perioperative settings is still debatable concerning the risks and benefits. The data from small single-center studies are still inconsistent. This systematic review compares each type of fluid for perioperative fluid therapy in major abdominal surgery. We found large heterogeneous outcomes due to various types of fluids compared (both colloids and crystalloids), variations in the fluid therapy protocols, types of abdominal surgery, and different parameters in outcome measurement. We attempted to group them into topics of interest.

Restoring and maintaining tissue perfusion is the primary goal of fluid therapy. In the present review using the parameters of lower fluid intake and greater hemodynamic stability, the macrocirculation or volume expansion effect showed more positive results in the colloid group compared to the crystalloid group with SMD of \(-0.638\) (95% CI \(-1.137 \text{ to } -0.138, p = 0.012\)). A lower fluid balance can decrease the incidence of complications from volume overload such as ileus, pulmonary edema, and impaired wound healing. [58] Complications from higher colloid intake were demonstrated in the Senagore trial [49] which was the first study to demonstrate goal-directed therapy using colloids compared to crystalloids. It was reported that the hetastarch group had a significantly higher volume compared to the crystalloid results that resulted in a high frequency of total postoperative complications and longer length of stay. The authors could not identify the cause of this event. When each colloid was compared, there were no differences in hemodynamic outcomes. In our opinion, each colloid has its initial volume expansion, colloid oncotic pressure, and half-life [59]. Hypertonic saline [30] (also with HES in hypertonic saline [21, 41]) demonstrates good volume expansion compared to an isotonic saline (and HES in 0.9% NaCl). Hypertonic saline draws water out of the intracellular compartment and into the intravascular space leading to restoration of the circulating volume with smaller volumes of fluid and reduced intracranial pressure in cases associated with traumatic brain injury [60]. However, a large trial in prehospital trauma patients demonstrated a nonsignificant higher mortality rate in the hypertonic saline group [61] which may also lead to coagulopathy, increased acidosis, hypothermia, kidney injury, and immunologic disorder [62]. Yates [16] and Zhang [24] studied the colloid to crystalloid ratios of 1:1.6 and 1:1.67, respectively, in perioperative settings. These ratios were higher compared to sepsis settings (1:1–1.3) [9, 10, 63] where the previously accepted ratio was 1:3 [60]. This result can be explained by endothelial dysfunction and capillary leakage in the postoperative period and sepsis [64].

Since stability of the vital signs and a decrease in the lactate level reflect macrovascular status, but not

### Table 5: Overview of randomized control trials related to anti-inflammatory parameters and vascular permeability categorized by primary outcome.

| Author, year | Fluid compared | Operation | Conclusion |
|--------------|----------------|-----------|------------|
| Rittoo [46], 2002 | 6% HES 200/0.62 (Elohes) 4% gelatin (Gelofusine) | Abdominal aortic aneurysm repair | HES 200/0.62 lowered CRP but no difference in IL-6 level |
| Rittoo [47], 2005 | 6% HES 200/0.62 (Elohes) 4% gelatin (Gelofusine) | Abdominal aortic aneurysm repair | HES 200/0.62 decreased inflammatory process and reduced endothelial activation |
| Mahmood [33], 2007 | 6% HES 200/0.62 (Elohes) | Abdominal aortic aneurysm repair | Less derangement in marker of glomerular and tubular function in HES 200/0.62 and HES130/0.4 |
| Ando [18], 2008 | HES 70/0.5 (Hespan) Acetate Ringer | Major abdominal surgery | No significant difference in inflammatory markers and vascular permeability |
| Mahmood [34], 2009 | 6% HES 200/0.62 (Elohes) 6% HES 130/0.4 (Voluven) 4% gelatin (Gelofusine) | Abdominal aortic aneurysm repair | HES 200/0.62 mostly decreased inflammatory process (CRP, but not lung injury score) |
| Yates [16], 2014 | 6% HES130/0.4 (Volulyte) Hartmann’s solution | Colorectal surgery | No significant difference in inflammatory marker |

- **Primary outcome**: inflammatory mediators (IL-6, CRP, ICAM-1, and vWF) and vascular permeability (urine albumin/Cr ratio)
- **Primary outcome was another objective but also had these outcomes**: HES200/0.62 lowered CRP but no difference in IL-6 level
- **Author, year**: Rittoo [46], 2002
- **Fluid compared**: 6% HES 200/0.62 (Elohes) 4% gelatin (Gelofusine)
- **Operation**: Abdominal aortic aneurysm repair
- **Conclusion**: HES 200/0.62 lowered CRP but no difference in IL-6 level
- **N**: 22

IL-6 = interleukin-6; CRP = C-reactive protein; ICAM-1 = intercellular adhesion molecule-1; vWF = von Willebrand factor; Cr = creatinine; HES = hydroxyethyl starch; GI = gastrointestinal; POd = postoperative day.
microcirculation [65], acceptance of these parameters may not be enough [66]. For example, abnormal splanchnic microcirculation may present in hemorrhage, sepsis, laparoscopic procedures, and in aortic cross clamp in aortic repair. Gastric mucosal hypoperfusion increases the production of mucosal CO2 (PgCO2) and decreases gastric mucosal pH (GpHi) [67]. These two parameters were used to demonstrate microcirculation in abdominal aortic aneurysm repair [34, 35, 46] during resuscitation with HES of different molecular weights, gelatin, and crystalloids. HES 130 and HES 200 were reported to have good properties to maintain microcirculation, especially HES 200. Two studies in laparoscopic colon surgery attempted to compare gelatin to 4.5% NaCl in 7.6% HES 40. One study supported gelatin [57] while the other reported no difference [21]. The reason they did not use the same variables to report the results was because Deng [21] claimed that gastric pH is disturbed by carbon dioxide pneumoperitoneum. Most of the included trials supported using colloids because they were better for microcirculation. These results were supported by Wu et al. [65] who compared NSS, 3% NaCl, 4% succinylated gelatin, and 6% HES 130/0.4 in the hemorrhagic shock rat model. This animal trial reported that all of these fluids stabilized the vital signs and renal blood flow, but only HES, gelatin, and 3% NaCl restored intestinal microcirculation that was demonstrated by laser speckle contrast imaging. Human albumin and dextran also reported effects in supporting microcirculation [66].

release of inflammatory mediators during surgery, such as C-reactive protein and tumor necrosis factor, is one of the causes of impaired endothelial barrier function due to an increase of large pores in the endothelial lining and induced glyocalyx shedding [60] which results in capillary leakage and volume maldistribution [64]. In this review, we included the in vivo anti-inflammatory effects of colloids, mostly from abdominal aneurysm repair because this

| Author, year | Fluid compared | N | Operation | Conclusion |
|-------------|----------------|---|-----------|------------|
| Mahmood [33], 2007 | 6% HES 200/0.62 (Elohes) 6% HES 130/0.4 (Voluven) 4% gelatin (Gelofusine) | 62 | Abdominal aortic aneurysm repair | Less derangement in marker of glomerular filtration and tubular function in both HES groups No difference in AKI or RRT |
| Mukhtar [38], 2009 | 5% human albumin 6% HES 130/0.4 (Voluven) 6% HES 130/0.4 (Voluven) 4% gelatin (Gelofusine) | 40 | Living donor liver transplant | No difference in serum Cr, CrCl, or cystatin C level No difference in AKI or RRT |
| Demir [20], 2015 | 6% HES 130/0.4 (Voluven) 5% human albumin 4% gelatin (Gelofusine) | 36 | Living donor liver transplant | Significantly decreased GFR in gelatin group No difference in AKI or RRT |
| Kancir [27], 2015 | 6% HES 130/0.4 (Voluven) NSS | 36 | Prostatectomy | No significant difference in renal impairment by U-NGAL, P-NGAL, and serum Cr |
| Kammerer [26], 2018 | 5% human albumin 6% HES 130/0.4 (Voluven) | 100 | Cystectomy | No significant difference in renal impairment by cystatin C ratio, P-NGAL, and GFR |

HES = hydroxyethyl starch, AKI = acute kidney injury, RRT = renal replacement therapy, CrCl = creatinine clearance, GFR = glomerular filtration rate, NSS = normal saline solution, U-NGAL = urine neutrophil gelatinase-associated lipocalin, P-NGAL = plasma neutrophil gelatinase-associated lipocalin, and Cr = creatinine.

Table 6: Overview of randomized control trials related to renal function (colloid vs. colloid/crystalloid) categorized by primary outcome.
operation can cause high endotoxin levels and inflammation from ischemic-reperfusion injury after aortic clamping [33, 34, 46, 47]. HES 200/0.62 is the best in reducing inflammation and decreasing capillary leakage followed by HES 130/0.4, but 4% gelatin did not show this effect. In abdominal surgery [16, 18], HES 70 and HES 130 did not

Table 7: Overview of randomized control trials related to renal function and electrolyte imbalance (balanced vs. saline solution/other balanced solutions) categorized by primary outcome.

| Author, year | Fluid compared | N | Operation | Conclusion |
|--------------|----------------|---|-----------|------------|
| Waters [52], 2001 | NSS, LRS | 66 | Abdominal aortic aneurysm repair | NSS had more hyperchloremic metabolic acidosis, no difference in Cr, AKI but no K report |
| O’Malley [39], 2005 | NSS, LRS | 51 | Living donor kidney transplant | NSS had more hyperchloremic metabolic acidosis, no difference in Cr, AKI, K, and incidence of dialysis to 6 months |
| Khajavi [28], 2008 | NSS, LRS | 54 | Living donor kidney transplant | NSS had higher K level postoperation, no difference in Cr level |
| Modi [37], 2012 | NSS, LRS | 72 | Living donor kidney transplant | NSS had more hyperchloremic metabolic acidosis, no difference in Cr level |
| Kim [29], 2013 | NSS, Plasmalyte | 60 | Living donor kidney transplant | NSS had more negative base excess and chloride, no difference in urine output, Cr, Cl |
| Potura [40], 2015 | Acetate-buffered crystalloid (Elomel-Isoton) | 148 | Cadaveric kidney transplant | NSS had more negative base excess, no difference in urine output, Cr, Cl, and dialysis, no difference in number of patients having K level >5.4 |
| Weinberg [53], 2015 | Hartmann solution, Plasmalyte | 60 | Major liver resection | Higher magnesium but lower calcium in Plasmalyte group, no difference in base excess and Cr |
| Weinberg [54], 2017 | NSS, Plasmalyte | 49 | Cadaveric kidney transplant | NSS had more hyperchloremic metabolic acidosis and hyperkalemia which led to dialysis or medication treatment |

NSS = normal saline solution, LRS = lactated Ringer’s solution, Cr = creatinine, AKI = acute kidney injury, and K = potassium.

Table 8: Overview of randomized control trials related to coagulation defect and bleeding categorized by primary outcome.

| Author, year | Fluid comparisons | N | Operation | Conclusion |
|--------------|-------------------|---|-----------|------------|
| Jin [25], 2010 | LRS, 6% HES 130/0.4 (Voluven), 4% gelatin (Gelofusine) | 36 | Gastrectomy | HES impaired clot initiation and impaired platelet function, gelatin reduced clot firmness, no difference in blood loss |
| Liang [31], 2010 | LRS, 6% HES 200/0.5 (HAES-steril6%), 6% HES 130/0.4 (Voluven), 6% HES 130/0.4 (Voluven) | 35 | Laparoscopy-assisted radical colectomy | HES 200/0.5 impaired clotting time, clot firmness, and impaired platelet function more than HES 130/0.4, no difference in blood loss |
| Hung [23], 2014 | LRS, 6% HES 130/0.4 (Voluven) | 80 | Major abdominal surgery | HES 130/0.4 impaired clot initiation and strength, no difference in blood loss |
| Rasmussen [43], 2014 | LRS, 6% HES 130/0.4 (Voluven) | 33 | Cystectomy | HES 130/0.4 impaired clot strength and firmness, HES 130/0.4 caused more blood loss than LRS |
| Rasmussen [44], 2015 | Dextran70, LRS | 37 | Cystectomy | Dextran70 impaired clot firmness and incidence of blood loss >1500 mL, no difference in mean blood loss |
| Rasmussen [45], 2016 | LRS, 5% human albumin | 39 | Cystectomy | 5% human albumin impaired clot firmness, no difference in blood loss |

Primary outcome was another objective but also had these outcomes:

| Author, year | Fluid comparisons | N | Operation | Conclusion |
|--------------|-------------------|---|-----------|------------|
| Yates [16], 2014 | Hartmann’s solution, 6% HES 130/0.4 (Voluven), NSS | 202 | Colorectal surgery | No significant difference in TEG or blood loss |
| Kancir [27], 2015 | LRS, 6% HES 130/0.4 (Voluven), NSS | 36 | Radical prostatectomy | Significant blood loss in HES |

HES = hydroxyethyl starch, NSS = normal saline solution, LRS = lactated Ringer’s solution, and TEG = thromboelastogram.
show significant effects in decreasing inflammation. This type of surgery may not cause as much inflammation as aortic repair. Anti-inflammatory effects of HES that were demonstrated in animal ischemic-reperfusion model [68] found that HES inhibited firm adhesion and decreased surface expression of CD11b of leukocytes. Chen et al. [69] reported that HES 130/0.4 decreased the levels of reactive oxygen species and tumor necrosis factor, while gelatin and HES 200 did not have such effects. Most of the studies in this review compared crystalloids to colloids, and most of the colloids were HES. We found that every colloid demonstrated abnormal clot firmness and platelet function, but none of them had an abnormal coagulogram. Abnormality in the TEG tended to increase in medium molecular weight HES compared to the lower molecular weight HES [31]. Only two trials [27, 43] reported that HES 130/0.4 (Voluven) increased intraoperative hemorrhage compared to a crystalloid. However, both trials were in urological surgery which has a high chance of bleeding due to the raw surface. These results were similar to the meta-analysis by Rasmussen et al. [70] which reported on human albumin and both high and medium molecular weight HES. Higher bleeding was found in the subgroup of noncardiac surgery using HES 130 but no significant decrease was found in the amount of bleeding compared to HES 200. After a multivariate analysis, two trials [44, 45] reported that TEG MA is the only factor that could reflect the amount of intraoperative bleeding. The mechanism of impaired coagulation by colloids was reported by de Jonge and Levi [71] through dilutional effect, molecular weight dependent reduction of vWF (acquired von Willebrand disease), factor VIII, and clot firmness. Gelatin and albumin had the least effect on coagulation among the colloid solutions [60].

For a comparison of crystalloids in perioperative renal function, the information available was mainly from kidney

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**Table 9: Overview of randomized control trials related to return of bowel function by primary outcome.**

| Author, year | Fluid compared | N  | Operation          | Conclusion                                                                 |
|-------------|----------------|----|--------------------|-----------------------------------------------------------------------------|
| Yates [16], 2014 | Hartmann’s solution 6% HES 130/0.4 (Voluven) | 202 | Colorectal surgery | No difference in bowel recovery time                                          |
| Loffel [32], 2016 | Chloride-depleted glucose solution 5% (G5K) Ringer maleate | 44 | Cystectomy         | G5K group could pass normal stool faster than RM (38 hours)                  |
| Ghodraty [22], 2017 | LRS 6% HES 130/0.4 (Voluven) | 91 | GI surgery         | HES 130/0.4 reduced time of postoperative ileus (13 hours)                   |

*Primary outcome was another objective but also had these outcomes

| Author, year | Fluid compared | N  | Operation          | Conclusion                                                                 |
|-------------|----------------|----|--------------------|-----------------------------------------------------------------------------|
| Zhang [56], 2012 | Restricted-LRS (20) GD-HES130/0.4 (20) | 60 | GI surgery         | Goal-directed HES 130/0.4 reduced time to pass flatus (6 hours compared to restricted group and 9 hours compared to GD-LRS) |

HES = hydroxyethyl starch, LRS = lactated Ringer’s solution, GI = gastrointestinal, and GD = goal-directed therapy.

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**Table 10: Overview of randomized control trials related to PONV by primary outcome.**

| Author, year | Fluid compared | N  | Operation          | Conclusion                                                                 |
|-------------|----------------|----|--------------------|-----------------------------------------------------------------------------|
| Chaudhary [19], 2008 | LRS 2 mL/kg LRS 12 mL/kg 4.5% hetastarch 12 mL/kg | 60 | Open cholecystectomy | Preoperative fluid supplement rate (12 mL/kg) (both colloid and crystalloid) decreases incidence of PONV, vomiting, and use of antiemetic |
| Mishra [36], 2017 | NSS 5% dextrose LRS | 100 | Laparoscopic cholecystectomy | 5% dextrose fluid reduced incidence of PONV, but not vomiting |
| Rao [42], 2017 | LRS 5% dextrose | 112 | Laparoscopic cholecystectomy | Postoperative IV loading 1000 mL of 5% dextrose fluid reduced incidence of PONV, but not vomiting |

*Primary outcome was another objective but also had these outcome

| Author, year | Fluid compared | N  | Operation          | Conclusion                                                                 |
|-------------|----------------|----|--------------------|-----------------------------------------------------------------------------|
| Ghodraty [22], 2017 | 6% HES130/0.4 (Voluven) LRS | 91 | GI surgery         | HES 130/0.4 reduced incidence of vomiting, but not PONV                     |

PONV = postoperative nausea vomiting, HES = hydroxyethyl starch, NSS = normal saline solution, LRS = lactated Ringer’s solution, and GI = gastrointestinal.
transplantation patients who have a very high risk for renal failure. Most studies compared a balanced crystalloid to NSS and reported similar results. NSS caused hyperchloremic metabolic acidosis and hyperkalemia in the intraoperative to postoperative periods. However, we did not find a significant difference in mortality rate, AKI, graft rejection, or kidney dysfunction. However, higher early postoperative renal replacement therapy (RRT) within 48 hours was needed to treat hyperkalemia in the Weinberg et al. trial [54]. A meta-analysis by Cochrane [72], which included 1,096 participants from 18 RCTs in major perioperative settings, also reported that increased serum creatinine, hyperkalemia, negative base excess, and low serum pH occurred in the postoperative period but most subsided within postoperative day 1. No significant incidence of long-term kidney dysfunction or mortality rate was reported. This was contrary to the results of the SALTED trial [73] (study in noncritical illness) and SMART trial [8] (study in critical illness). In these trials, resuscitation used NSS which significantly increased major adverse kidney event (compound outcome) within 30 days without a significant difference in mortality rates. A large volume of NSS was related to renal vasoconstriction [60]. All of the above information was compiled into a guideline that supports using balanced crystalloids for peri-interventional volume substitution [2]. However, there were some situations where NSS was indicated, such as the presence of cerebral edema and gastric outlet obstruction [60].

Following a report of osmotic nephrosis in kidney transplant recipients after administration of HES [74], renal function after the use of colloids became a concern. However, two studies found that HES administration had better tubular and glomerular function based on the RIFLE criteria and the level of serum Cr [33, 47]. Also, another study found a lower incidence of AKI grade 1 compared to gelatin [20]. Other trials showed no significant difference in AKI using HES compared to albumin [26, 38] or HES compared to crystalloids [18, 27]. The ALBIOS trial [63] reported no difference in mortality rate or RRT when albumin was compared to colloids in sepsis patients. Many large multicenter trials reported a higher incidence of RRT [9–11] and mortality rate [10] in the HES groups compared to crystalloids in sepsis patients, but they had defects in methodology [75]. In 2013, the CRISTAL trial [76] compared crystalloids (isotonic or hypertonic saline and balanced solution) to colloids (gelatin, dextran, HES, and albumin) in patients with hypovolemic shock. They reported a lower mortality rate at 30 days and lower need of vasopressor therapy in the colloid group. No differences were found in the incidence of RRT and AKI. Furthermore, the subgroups of each type of colloid still showed a lower mortality rate. A recent meta-analysis [77] which compared colloids to crystalloids reported a higher incidence of RRT and mortality rate in the pentastarch group. In a subgroup analysis of sepsis, colloids led to a higher incidence of RRT and mortality rate, but these outcomes were not significant in cardiac and general surgery. This might be explained by the mechanism of AKI in surgery where volume loss can be improved by adequate volume replacement. However, in septic AKI, microvascular dysfunction is the key mechanism [77]. Larger endothelial pores allow colloids to leak into the tissues leading to organ dysfunction, especially in the kidney [60]. Colloids with higher molecular weights, for example, pentastarch, are more harmful due to the long metabolism time.

In two trials, a solution of 5% dextrose fluid was compared to a nondextrose fluid to determine the incidence of PONV [36, 42]. The results showed that the 5% dextrose fluid decreased the incidence of PONV. However, these two trials were performed in laparoscopic cholecystectomy and the IV fluid protocol required a postoperative loading of <1000 mL. A meta-analysis which focused on PONV using dextrose fluids also included uncomplicated surgeries (laparoscopic gynecological surgery and laparoscopic cholecystectomy). The results showed a decreased incidence of PONV and the need for antiemetics by a mechanism related to hyperglycemia [78]. Colloids can decrease PONV, vomiting, and the need for antiemetics compared to crystalloids [19, 22] by increased mucosal perfusion [78].

Many factors can affect bowel function and the type of fluid is also one of them. In our review, colloids could enhance bowel function compared to crystalloids, but may not have clinical significance (7 [16], 9 [56], and 13 [22] hours). All of the indicated trials used a goal-directed protocol and found a significantly lower need for fluid in the colloid groups. Using more crystalloids to achieve the same clinical volume effect as colloids can be detrimental. Crystalloids have a propensity to filter across the capillary membrane. A greater expansion of extravascular volume leads to intestinal mucosal edema and delayed recovery in postoperative ileus [79]. However, colloids can generate oncotic pressure to maintain fluid in intravascular component [80].

4.1. Limitations. The present systematic review has some limitations that should be considered when interpreting the results. First, we had too many primary outcomes which resulted in including various types of fluids, volume administration protocols, and types of surgical procedures, which may account for the high heterogeneity of our results. Second, the trials included in this systematic review were often small and single-center studies. Third, the volume of a given fluid that may affect the outcome was not included in our review. Fourth, only major abdominal surgery was our surgical type. Therefore, the results may not apply to other types of surgery. Fifth, some types of fluid (dextran and gelatin) were restricted in Europe and America which resulted in low reliability of the data obtained. Sixth, most of the participants included were ASA class I–III. Therefore, it may be incorrect to apply this information to an emergency condition or higher ASA class. Finally, there were some flaws in our search methods which caused some important trials to be missed.

The strength of this review was we had many primary outcomes which resulted in including various types of fluids, volume administration protocols, and types of surgical procedures.
5. Conclusion

Perioperative fluid management depends on many factors such as patient status, type of operation, type of fluid, and administration technique. The colloids had an individual volume expansion effect, maintained microcirculation, and can be used interchangeably. Every colloid affected clot firmness and clot formation time, but only dextran significantly increased bleeding. NSS resulted in perioperative hyperchloremic metabolic acidosis and hyperkalemia which may lead to RRT compared to a balanced crystalloid. No specific type of fluid increased the mortality rate.

Data Availability

All data collected in this research are available for review.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

Authors’ Contributions

All authors were involved in the design, data collection, analysis, and manuscript writing.

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Supplementary Materials

The first one is “Full search term,” which consists of full search terms we used on an electronic database; it is cited as “Appendix S1” in the manuscript. The second one is “Data sheet,” which consists of full results from our systematic review; it is cited as “Table S1” in the manuscript. (Supplementary Materials)

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