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Effectiveness and safety of hypotension fluid resuscitation in traumatic hemorrhagic shock: a systematic review and meta-analysis of randomized controlled trials

Running head: Hypotension fluid resuscitation in hemorrhagic shock

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Abstract

Background: Although the resuscitation of an adult trauma patient has been researched and written about for the past century, the ideal fluid strategy to infuse during the initial resuscitation period remains unresolved. This work was aimed at assessing the effect of hypotensive versus conventional resuscitation strategies in traumatic hemorrhagic shock patients on mortality, and the need for blood transfusions including adverse events.

Methods: This systematic review and meta-analysis were performed following the PRISMA guidelines. Electronic databases were searched for randomized controlled trials (RCT) comparing the effect of hypotension versus conventional fluid resuscitation for traumatic hemorrhagic shock patients. Two reviewers independently performed the screening, data

extraction, and bias assessment. The data analysis was completed using the Cochrane Collaboration's software RevMan 5.4.

Results: Data from 28 RCTs on 4503 patients were included in the final meta-analysis. Patients receiving hypotension fluid resuscitation compared with conventional fluid resuscitation experienced less mortality (12.5% vs. 21.4%; RR = 0.58; 95% CI: 0.51–0.66; p < 0.001), fewer adverse events (10.8% vs. 13.4%; RR = 0.70; 95% CI: 0.59–0.83; p < 0.001), including fever acute respiratory distress syndrome (7.8% vs. 16.8%) or multiple organ dysfunction syndrome (8.6% vs. 21.6%).

Conclusions: This meta-analysis showed that hypotensive fluid resuscitation significantly reduced the mortality of hypovolemic shock patients. Findings are low in certainty and should be interpreted with caution. Therefore, there is an urgent need for larger, multicenter, randomized trials to confirm these findings.

Key words: fluid resuscitation, restricted fluid resuscitation, hemorrhagic shock, hemorrhage, meta-analysis, systematic review

INTRODUCTION

Trauma injury remains the leading cause of death among people aged less than 35 years, with 40% of trauma deaths imputable to uncontrolled hemorrhagic shock or its consequences [1, 2].

Currently, fluid resuscitation is the first step in the hemodynamic management of traumatic hemorrhagic shock [3]. The rapid vascular access and stabilization of the cardiovascular system can protect the patient from the severe consequences of hypovolemic shock. The origins of fluid resuscitation can be traced back to the thirties of the nineteenth century, when Thomas Latta performed an attempt of intravenous fluid resuscitation for the first time [4]. In the period 1879–1881 Kroneecker and Landerer stated that in cases of blood loss the most valuable thing is to rapidly restore the vascular bed volume. For this purpose, they proposed using a normal saline solution with the addition of sugar [5, 6]. The development of fluid therapy was in the 1920s, when Alfred Blalock experimented with incremental hemorrhage to induce shock in dogs [7, 8]. In his research, Blalock used blood pressure (BP), cardiac output as well as blood oxygen content from left and right ventricles to evaluate the effect of three types of treatment: saline, transfusion and pharmacological treatment.

Applying an appropriate fluid therapy strategy may restore tissue perfusion and consequently oxygenation of the body. Fluid resuscitation can be carried out based on changes in hemodynamics, diuresis, serum lactate levels or alkaline deficit. However, excessive fluid resuscitation could contribute to the development of coagulopathy of trauma [3, 9] as well as tissue edema [10], which can lead to alterations of tissue perfusion and complications such as abdominal compartment syndrome or adult respiratory distress syndrome [11, 12]. The optimal level of BP during resuscitation of hemorrhagic shock patients is still debated.

The present work aimed to assess the effect of hypotensive versus conventional resuscitation strategies in traumatic hemorrhagic shock patients on mortality, need for blood transfusion and adverse events (specifically: acute myocardial or renal failure or acute respiratory distress syndrome).

METHODS

This systematic review and meta-analysis adhere to the reporting guidelines of the Preferred Reporting Items for Systematic reviews and Meta-analyses (PRISMA) statement (**Suppl. Table 1**).

Search strategy

Available literature databases including EMBASE, MEDLINE, Google Scholar, Cochrane Central Register of Controlled Trials (CENTRAL) were searched from the inception of the databases until 18 June 2020. Searches were conducted independently by 2 persons (K.S. and L.S.). English language restrictions were not used. The papers were restricted to those with the English language. Reference lists of eligible articles were reviewed and content experts were consulted with (K.J.F. and M.J.J.) to identify additional published reports. Incomplete data were dealt with by contacting the principal authors, when possible, to ask for missing or unclear information.

The search strategy was comprised of MESH terms and keywords such as: “shock”OR, “hemorrhagic” OR, “trauma” OR, “injury” OR, “hypotensive resuscitation” OR, “limited resuscitation” OR, “fluid resuscitation” OR, “limited fluid”. To identify in-progress or terminated studies, clinicaltrials.gov registry was also searched.

Study selection

This study included randomized controlled trials (RCTs) and quasi-randomized trials. Observational studies, case reports, studies not based on original research and studies not involving patients, conference papers as well as letters to the editor were excluded from the present study.

Data extraction

Using a standardized data extraction sheet, two authors (K.S. and L.S.) independently extracted data from each report included. Any discrepancies were resolved by consensus with the third author (J.S.). When necessary for data or article clarification, personal communication was made with select study authors. Baseline patient characteristics were extracted as well as data about each trial's intervention, inclusion and exclusion criteria, mortality and adverse events. For all clinical outcomes, the number of events that occurred in each arm of each trial were tabulated.

Quality assessment

Two reviewers (J.S. and A.S.) independently assessed the methodological quality of each eligible article using the "risk of bias" assessment tool of the Cochrane Handbook [13]. The following domains were evaluated for RCTs: 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) and other bias [12]. Each was graded "yes", "no", or "unclear", which reflected a high risk of bias, low risk of bias, and uncertain bias, respectively (**Suppl. Fig. S1**). The review authors' judgments about each risk of bias item are provided in **Supplementary Figure S2**. The overall risk of bias for the study was rated 'low' if 7 or more domains were rated low, 'moderate' if 4 to 6 domains were rated low, and 'high' if 1 to 3 domains were rated low.

Statistical analysis

Statistical analysis was done by two authors (A.S. and L.S.) independently and was cross-validated. For continuous outcomes, mean difference (MD), and for dichotomous outcomes were used, and risk ratios (RR), were calculated. All continuous data with either means with standard deviations (SD) or medians with interquartile ranges as reported in the primary study are presented. When the continuous outcome was reported in a study as median, range, and interquartile range, means and standard deviations using the formula

described by Hozo et al. [13] were estimated. For descriptive purposes, absolute and relative frequencies are reported for categoric variates.

Statistical heterogeneity and inconsistency were measured by using the Cochran Q test and I^2, respectively [14]. Odds ratios (OR) with 95% confidence intervals (CI) were calculated as summary statistics. The pooled OR was calculated with the Mantel-Haenszel method. Weighted mean differences and 95% CIs were computed for continuous variables, again using a fixed-effect method in cases of low statistical inconsistency ($I^2 \leq 50\%$) and using a random-effect method in cases of moderate or high statistical inconsistency ($I^2 > 50\%$) [15]. Results were considered statistically significant at $p < 0.05$. Statistical analyses were performed with the Review Manager (version 5.4; The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark).

RESULTS

Eligible studies and their characteristics

The flowchart of the literature search is presented in Figure 1. The initial search returned 432 records from all the databases. Two more studies were identified from the references of the relevant articles. Two hundred and ninety-six records were further screened by titles and abstracts and 138 duplicate articles were removed. Unrelated articles, comments, reviews, letters, and duplicate articles were excluded. Then 47 articles were assessed by accessing the full-text. Nineteen studies were excluded because of unavailable data, duplicates, and unrelated topics. Finally, 28 studies were included in the analysis [16–43].

Assessment of quality

The quality assessment is represented in **Supplementary Figures S1 and S2**. The method of random sequence generation was perfect in all the studies. There were high risks of attrition bias, lack of intention-to-treat analysis, and selective reporting. The detailed information about blinding and allocation concealment was insufficient in most studies. None of the trials included was at low risk of bias across all domains.

Mortality

Twenty-eight studies reported overall mortality [16–23]. Mortality with hypotension fluid resuscitation was 12.5% and was statistically significant, being smaller than with the conventional fluid resuscitation group – 21.4% (RR = 0.58; 95% CI: 0.51–0.66; $I^2 = 37\%$; $p < 0.001$; Fig. 2). In contrast, only one study by Morrison et al. [28] indicated mortality rates

during the first 24 hours. According to this study, mortality for hypotension versus conventional fluid resuscitation varied and amounted to 13.6% vs. 21.7% respectively (RR = 0.63; 95% CI: 0.25–1.58; p = 0.32).

Adverse events

The polled analysis showed that hypotension fluid resuscitation compared to conventional fluid resuscitation was associated with a lower risk of adverse events (10.8% vs. 13.4%, respectively; RR = 0.70; 95% CI: 0.59–0.83; I^2 = 52%; p < 0.001).

The use of hypotension versus conventional fluid resuscitation showed a higher incidence of anemia (74.3% vs. 68.6%), thrombocytopenia (33.6% vs. 29.4%) and acute renal failure (8.8% vs. 8.1%). In other types of adverse events the relationship was reversed, and the use of hypotension fluid resuscitation was associated with a lower risk of complications (Table 1).

Fluid balance and transfusion requirements

Additional analysis showed that patients who were treated with hypotension fluid resuscitation required smaller volumes of fluids than the conventional fluid resuscitation group (MD = –1.02; 95% CI: –1.33, –0.71; I^2 = 99%; p < 0.001; Fig. 3).

Length of stay ICU/hospital

The length of stay in the Intensive Care Unit (ICU) was reported by two studies [16, 32]. The polled analysis did not show significant differences in the length of stay in ICU between the groups (MD = 0.38; 95% CI: –1.83–2.59; I^2 = 73%; p = 0.74; **Suppl. Fig. S3**). Three studies indicated length of stay in hospital [16, 29, 32]. The difference between therapeutic groups was not statistically significant (MD = –0.82; 95% CI: –2.43–0.78; I^2 = 0%; p = 0.32; **Suppl. Fig. S4**).

DISCUSSION

The purpose of this research was to compare the effects of hypovolemic and conventional fluid resuscitation on the mortality rate among patients with traumatic hemorrhagic shock. Meta-analysis for overall mortality showed that hypovolemic fluid resuscitation offered benefit in comparison with conventional fluid resuscitation for patients with traumatic hemorrhagic shock at the final follow-up (p < 0.001).

Obtaining intravascular access in hypovolemic patients (especially trauma patients) should be done as soon as possible. In patients with hemorrhage, the most important part of the procedure is to stop the hemorrhage. In such a patient's hospital setting, transfusion of blood substitutes should be limited in favor of the transfusion of blood components. It is recommended to transfuse the red blood cell concentrate in a volume that maintains the hemoglobin concentration at 7–9 g/dL. Fresh frozen plasma (FFP) should be transfused immediately at a dose of 10–15 mL/kg b.w. and further replenishment of FFP should depend on the volume of red blood cells transfused and the coagulogram. In the case of platelets, they should be transfused in sufficient quantities to maintain a concentration of 50,000/mL. To mitigate the effects of hypovolemic shock caused by the injury, transfusion of cryoprecipitate or fibrinogen concentrate may also be considered.

Fluid therapy aims not only to maintain and restore the intravascular volume but also, by optimizing the preload, to increase cardiac output and improve tissue perfusion. Discussions are still ongoing as to whether crystalloids (i.e. 0.9% saline or Ringer's Lactate) or colloidal solutions (i.e. dextran's, gelatins, HAES) should be used in the initial phase of fluid resuscitation. De Crescenzo et al. [44] indicates no beneficial effect of hypertonic saline with or without dextran in general trauma patients. In turn, Martin et al. [45] in his meta-analysis indicated that crystalloids were less efficient than colloids at stabilizing resuscitation endpoints. The application of an appropriate fluid resuscitation strategy is, therefore, more important than the type of fluid administered. Malbrain et al. [46] showed that a positive cumulative fluid balance is associated with IAH and worse outcomes. Hypotensive fluid resuscitation as shown by numerous studies may offer a survival benefit over conventional fluid resuscitation for trauma patients. It can also further reduce blood loss and thus blood product utilization. It can, therefore, be concluded that fluid resuscitation in trauma patients should be based on a specific compromise between too small a volume leading to hypoperfusion and too much hydration in patients, which may result in increased bleeding due to increased BP. The use of too large a volume of fluid can lead to "dilutive" hemorrhagic bleeding.

As indicated by numerous randomized studies — as also confirmed by this meta-analysis — hypovolemic fluid resuscitation can bring benefits in the management of the trauma patient [28, 29, 47]. However, it should be remembered that the hypotension should not last longer than one hour [22, 28]. It should be kept in mind that the rules of fluid resuscitation in trauma patients with concomitant craniocerebral trauma are different. Thereafter, as recommended by the National Institute for Health and Clinical Excellence

(NICE), it is important to increase BP (systolic BP 110–120 mmHg) as quickly as possible to secure proper brain perfusion and prevent secondary brain changes.

In this meta-analysis, hypovolemic fluid resuscitation was associated with a higher incidence of thrombocytopenia, renal failure or anemia in comparison with conventional management. The above symptoms are closely related. Thrombocytopenia is the most frequently diagnosed hemorrhagic flaw and may lead to anemia. As many authors indicate, acute kidney injury is a common feature in patients with thrombocytopenia-associated multiple organ failure with incidences as high as 42% in disseminated intravascular coagulation, 58% in thrombocytopenic purpura and 100% in hemolytic uremic syndromes. [48–50]. On the other hand, in the case of conventional fluid resuscitation, a statistically significantly higher incidence of acute respiratory distress syndrome (ARDS) or multiple organ dysfunction syndrome (MODS) was observed. Jiang et al. [51] indicate that hypovolemic/restricted fluid resuscitation can effectively eliminate inflammatory factors, improve immune function, maintain the stability of blood components, and reduce the incidences of ARDS and MODS. In the case of hypotension fluid resuscitation, there was also a higher incidence of acute myocardial infarction, which may be caused by lower myocardial overload.

Limitations of the study

The present study has some limitations. First, only in several articles study groups are appropriate, in other articles the sample size is relatively small, which led to a wide 95% confidence interval. Second, two studies referred to MAP, the others to systolic blood pressure.

CONCLUSIONS

The present study findings show significant associations between hypotensive fluid resuscitation and a decreased risk of adverse events and cardiovascular mortality in hypovolemic shock trauma patients. There is an urgent need for a large multicenter randomized trial to confirm these findings.

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Conflict of interest: None declared

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Figure 1. Flow diagram showing stages of database searching and study selection as per PRISMA guidelines.

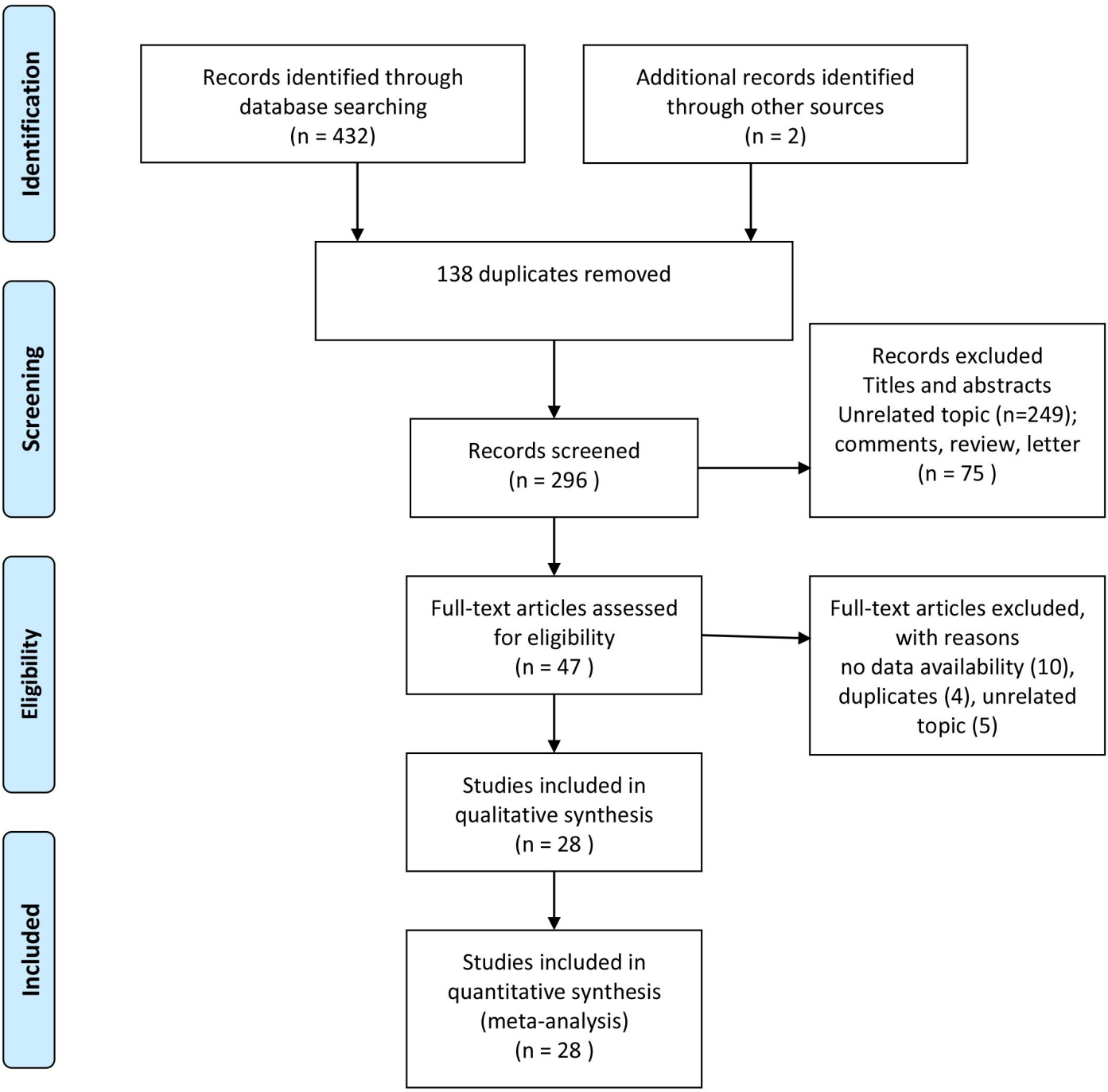
Figure 2. Forest plot of hypotension versus. conventional fluid resuscitation, relative to mortality. The center of each square represents the relative risk for individual trials, and the corresponding horizontal line stands for a 95% confidence interval. The diamonds represent pooled results.

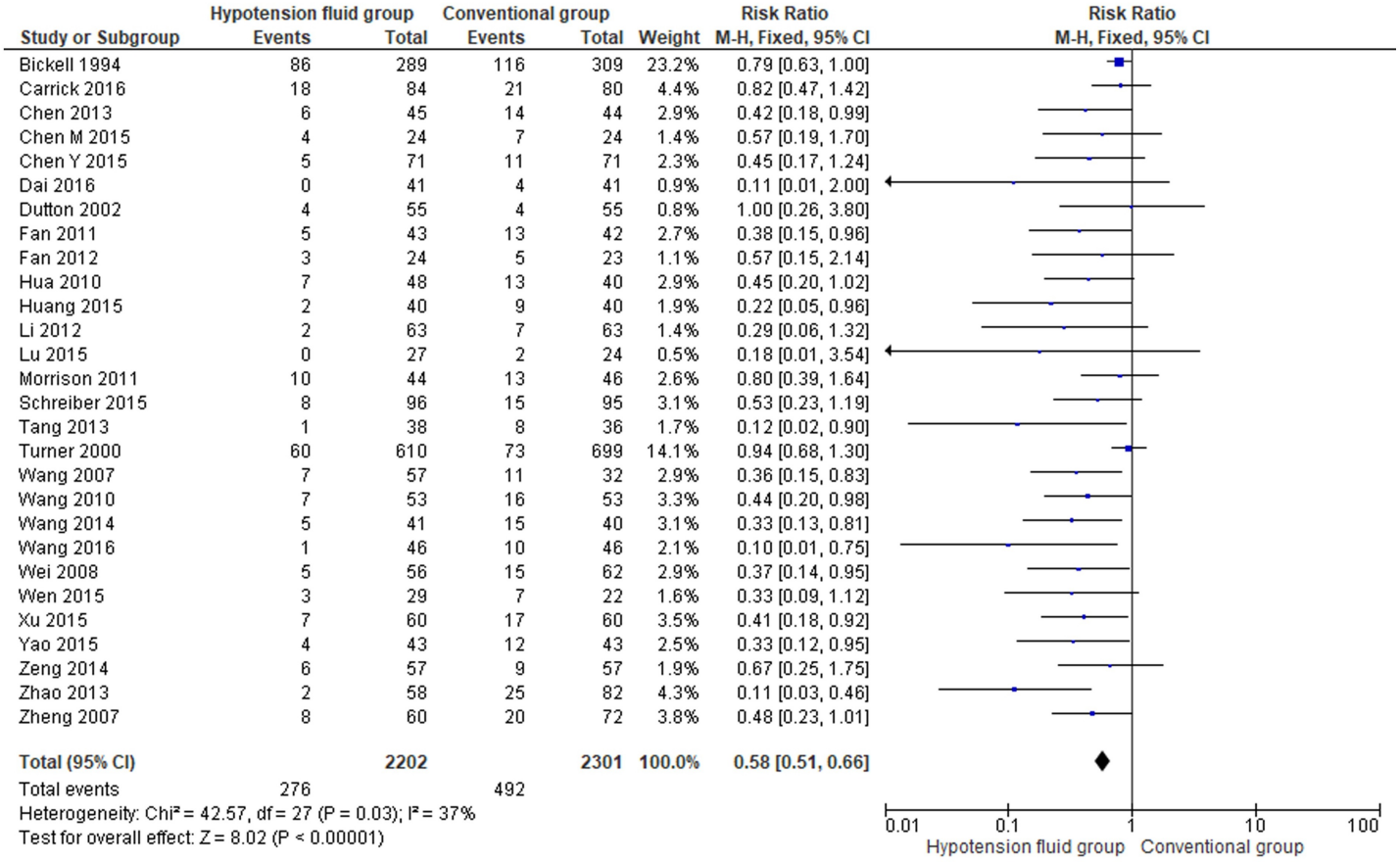
Figure 3. Forest plot of hypotension versus conventional fluid resuscitation, relative to fluid balance and transfusion requirements. The center of each square represents the mean difference for individual trials, and the corresponding horizontal line stands for 95% confidence interval. The diamonds represent pooled results.

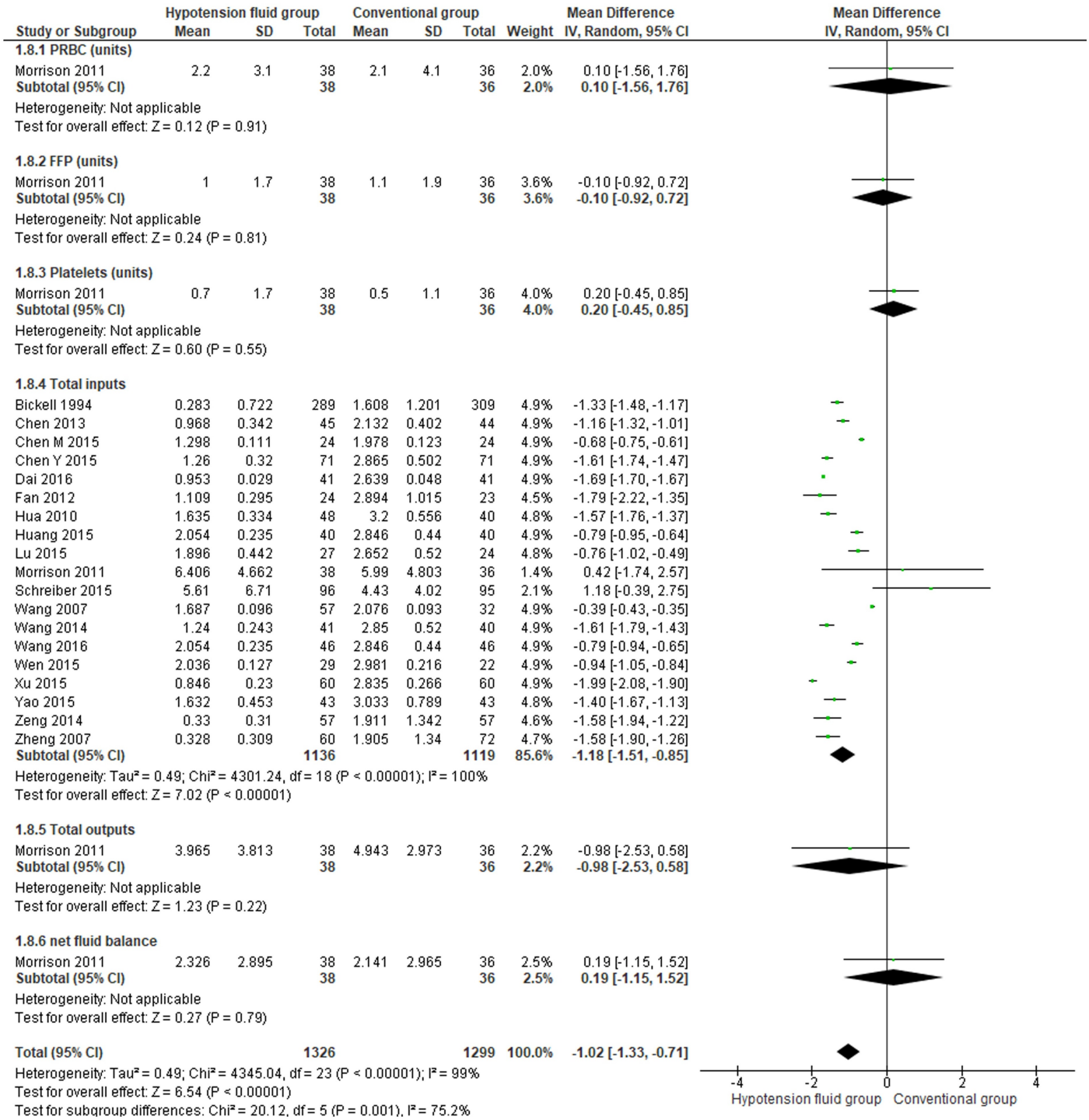
Table 1. Comparison of hypotension and conventional fluid resuscitation relative to adverse events.

	Number of trials	Hypotension fluid resuscitation	Conventional fluid resuscitation	RR or MD (95% CI)	P value	I^2 statistic, %
ARDS	13	7.8%	16.8%	0.44 [0.34–0.58]	< 0.001	0%
Acute myocardial infarction	1	1.3%	1.5%	0.88 [0.06–13.79]	0.93	–
Stroke	1	0%	3.0%	0.18 [0.01–3.61]	0.26	–
Sepsis syndrome	2	3.5%	3.9%	0.91 [0.42–1.98]	0.82	0%
MODS	10	8.6%	21.6%	0.42 [0.30–0.60]	< 0.001	0%
Any renal failure	1	14.7%	12.1%	1.21 [0.52–2.83]	0.66	–
Acute renal failure	8	8.8%	8.1%	0.99 [0.53–1.86]	0.98	61%
Anemia	2	74.3%	68.6%	1.11 [0.96–1.28]	0.16	2%
Hypotension	1	13.3%	16.7%	0.80 [0.36–1.76]	0.58	–
Coagulopathy	3	15.7%	15.8%	0.95 [0.73–1.24]	0.73	0%
Thrombocytopenia	2	33.6%	29.4%	1.21 [0.64–2.28]	0.56	54%
Pneumonia	1	7.6%	9.1%	0.84 [0.49–1.43]	0.52	–
Deterioration in T-RTS	1	7.4%	7.9%	0.93 [0.50–1.71]	0.81	–
Complications not specified	1	7.5%	8.6%	0.88 [0.61–1.27]	0.49	–

ARDS — acute respiratory distress syndrome; MORS — multiple organ dysfunction syndrome; MD — mean difference; RR — risk ratio


Identification
Screening
Eligibility
Included
Records identified through database searching (n = 432)
Additional records identified through other sources (n = 2)
138 duplicates removed
Records screened (n = 296)
Records excluded Titles and abstracts Unrelated topic (n=249); comments, review, letter (n = 75)
Full-text articles assessed for eligibility (n = 47)
Full-text articles excluded, with reasons no data availability (10), duplicates (4), unrelated topic (5)
Studies included in qualitative synthesis (n = 28)
Studies included in quantitative synthesis (meta-analysis) (n = 28)


Hypotension fluid group
Conventional group
Risk Ratio
Risk Ratio
Study or Subgroup
Events
Total
Events
Total
Weight
M-H, Fixed, 95% CI
M-H, Fixed, 95% CI
Bickell 1994 86 289 116 309 23.2% 0.79 [0.63, 1.00]
Carrick 2016 18 84 21 80 4.4% 0.82 [0.47, 1.42]
Chen 2013 6 45 14 44 2.9% 0.42 [0.18, 0.99]
Chen M 2015 4 24 7 24 1.4% 0.57 [0.19, 1.70]
Chen Y 2015 5 71 11 71 2.3% 0.45 [0.17, 1.24]
Dai 2016 0 41 4 41 0.9% 0.11 [0.01, 2.00]
Dutton 2002 4 55 4 55 0.8% 1.00 [0.26, 3.80]
Fan 2011 5 43 13 42 2.7% 0.38 [0.15, 0.96]
Fan 2012 3 24 5 23 1.1% 0.57 [0.15, 2.14]
Hua 2010 7 48 13 40 2.9% 0.45 [0.20, 1.02]
Huang 2015 2 40 9 40 1.9% 0.22 [0.05, 0.96]
Li 2012 2 63 7 63 1.4% 0.29 [0.06, 1.32]
Lu 2015 0 27 2 24 0.5% 0.18 [0.01, 3.54]
Morrison 2011 10 44 13 46 2.6% 0.80 [0.39, 1.64]
Schreiber 2015 8 96 15 95 3.1% 0.53 [0.23, 1.19]
Tang 2013 1 38 8 36 1.7% 0.12 [0.02, 0.90]
Turner 2000 60 610 73 699 14.1% 0.94 [0.68, 1.30]
Wang 2007 7 57 11 32 2.9% 0.36 [0.15, 0.83]
Wang 2010 7 53 16 53 3.3% 0.44 [0.20, 0.98]
Wang 2014 5 41 15 40 3.1% 0.33 [0.13, 0.81]
Wang 2016 1 46 10 46 2.1% 0.10 [0.01, 0.75]
Wei 2008 5 56 15 62 2.9% 0.37 [0.14, 0.95]
Wen 2015 3 29 7 22 1.6% 0.33 [0.09, 1.12]
Xu 2015 7 60 17 60 3.5% 0.41 [0.18, 0.92]
Yao 2015 4 43 12 43 2.5% 0.33 [0.12, 0.95]
Zeng 2014 6 57 9 57 1.9% 0.67 [0.25, 1.75]
Zhao 2013 2 58 25 82 4.3% 0.11 [0.03, 0.46]
Zheng 2007 8 60 20 72 3.8% 0.48 [0.23, 1.01]
Total (95% CI) 2202 2301 100.0% 0.58 [0.51, 0.66]
Total events 276 492
Heterogeneity: Chi² = 42.57, df = 27 (P = 0.03); I² = 37%
Test for overall effect: Z = 8.02 (P < 0.00001)
0.01
0.1
1
10
100
Hypotension fluid group
Conventional group


Hypotension fluid group
Conventional group
Mean Difference
Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI
IV, Random, 95% CI
1.8.1 PRBC (units)
Morrison 2011 2.2 3.1 38 2.1 4.1 36 2.0% 0.10 [-1.56, 1.76]
Subtotal (95% CI) 38 36 2.0% 0.10 [-1.56, 1.76]
Heterogeneity: Not applicable
Test for overall effect: Z = 0.12 (P = 0.91)
1.8.2 FFP (units)
Morrison 2011 1 1.7 38 1.1 1.9 36 3.6% -0.10 [-0.92, 0.72]
Subtotal (95% CI) 38 36 3.6% -0.10 [-0.92, 0.72]
Heterogeneity: Not applicable
Test for overall effect: Z = 0.24 (P = 0.81)
1.8.3 Platelets (units)
Morrison 2011 0.7 1.7 38 0.5 1.1 36 4.0% 0.20 [-0.45, 0.85]
Subtotal (95% CI) 38 36 4.0% 0.20 [-0.45, 0.85]
Heterogeneity: Not applicable
Test for overall effect: Z = 0.60 (P = 0.55)
1.8.4 Total inputs
Bickell 1994 0.283 0.722 289 1.608 1.201 309 4.9% -1.33 [-1.48, -1.17]
Chen 2013 0.968 0.342 45 2.132 0.402 44 4.9% -1.16 [-1.32, -1.01]
Chen M 2015 1.298 0.111 24 1.978 0.123 24 4.9% -0.68 [-0.75, -0.61]
Chen Y 2015 1.26 0.32 71 2.865 0.502 71 4.9% -1.61 [-1.74, -1.47]
Dai 2016 0.953 0.029 41 2.639 0.048 41 4.9% -1.69 [-1.70, -1.67]
Fan 2012 1.109 0.295 24 2.894 1.015 23 4.5% -1.79 [-2.22, -1.35]
Hua 2010 1.635 0.334 48 3.2 0.556 40 4.8% -1.57 [-1.76, -1.37]
Huang 2015 2.054 0.235 40 2.846 0.44 40 4.9% -0.79 [-0.95, -0.64]
Lu 2015 1.896 0.442 27 2.652 0.52 24 4.8% -0.76 [-1.02, -0.49]
Morrison 2011 6.406 4.662 38 5.99 4.803 36 1.4% 0.42 [-1.74, 2.57]
Schreiber 2015 5.61 6.71 96 4.43 4.02 95 2.1% 1.18 [-0.39, 2.75]
Wang 2007 1.687 0.096 57 2.076 0.093 32 4.9% -0.39 [-0.43, -0.35]
Wang 2014 1.24 0.243 41 2.85 0.52 40 4.9% -1.61 [-1.79, -1.43]
Wang 2016 2.054 0.235 46 2.846 0.44 46 4.9% -0.79 [-0.94, -0.65]
Wen 2015 2.036 0.127 29 2.981 0.216 22 4.9% -0.94 [-1.05, -0.84]
Xu 2015 0.846 0.23 60 2.835 0.266 60 4.9% -1.99 [-2.08, -1.90]
Yao 2015 1.632 0.453 43 3.033 0.789 43 4.8% -1.40 [-1.67, -1.13]
Zeng 2014 0.33 0.31 57 1.911 1.342 57 4.6% -1.58 [-1.94, -1.22]
Zheng 2007 0.328 0.309 60 1.905 1.34 72 4.7% -1.58 [-1.90, -1.26]
Subtotal (95% CI) 1136 1119 85.6% -1.18 [-1.51, -0.85]
Heterogeneity: Tau² = 0.49; Chi² = 4301.24, df = 18 (P < 0.00001); I² = 100%
Test for overall effect: Z = 7.02 (P < 0.00001)
1.8.5 Total outputs
Morrison 2011 3.965 3.813 38 4.943 2.973 36 2.2% -0.98 [-2.53, 0.58]
Subtotal (95% CI) 38 36 2.2% -0.98 [-2.53, 0.58]
Heterogeneity: Not applicable
Test for overall effect: Z = 1.23 (P = 0.22)
1.8.6 net fluid balance
Morrison 2011 2.326 2.895 38 2.141 2.965 36 2.5% 0.19 [-1.15, 1.52]
Subtotal (95% CI) 38 36 2.5% 0.19 [-1.15, 1.52]
Heterogeneity: Not applicable
Test for overall effect: Z = 0.27 (P = 0.79)
Total (95% CI) 1326 1299 100.0% -1.02 [-1.33, -0.71]
Heterogeneity: Tau² = 0.49; Chi² = 4345.04, df = 23 (P < 0.00001); I² = 99%
Test for overall effect: Z = 6.54 (P < 0.00001)
Test for subgroup differences: Chi² = 20.12, df = 5 (P = 0.001), I² = 75.2%
-4
-2
0
2
4
Hypotension fluid group
Conventional group