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Ultrasound-guided fluid resuscitation versus usual care guided fluid resuscitation in patients with septic shock: a systematic review and meta-analysis

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Abstract

Background: Ultrasound is widely used in critical care for fluid resuscitation in critically ill patients. We conducted a systematic review to assess the relationship between ultrasound-guided fluid resuscitation strategies and usual care in septic shock.

Methods: We searched PubMed, Embase, Cochrane Library, Web of Science, and registers for randomized controlled trials to evaluate the prognosis of ultrasound-guided fluid resuscitation in patients with septic shock.

Results: Twelve randomized controlled studies with 947 participants were included. Ultrasound-guided fluid resuscitation in patients with septic shock was associated with reduced mortality (risk ratio: 0.78; 95% confidence interval [CI]: 0.65 to 0.94; P = 0.007) and 24-hour fluid volume (mean differences [MD]: –1.02; 95% CI: –1.28 to –0.75; $P < 0.001$), low heterogeneity ($I^2 = 29\%$, $I^2 = 0\%$), and increased dose of norepinephrine (MD: 0.07; 95% CI: 0.02–0.11; P = 0.002) and dobutamine dose (MD: 2.2; 95% CI: 0.35–4.04; P = 0.02), with low heterogeneity ($I^2 = 45\%$, $I^2 = 0\%$). There was no reduction in the risk of dobutamine use (risk ratio: 1.67; 95% CI: 0.52 to 5.36; P = 0.39; $I^2 = 0\%$). Inferior vena cava–related measures reduced the length of hospital stay (MD: –2.91; 95% CI: –5.2 to –0.62; P = 0.01; low heterogeneity, $I^2 = 8\%$) and length of intensive care unit stay (MD: –2.77; 95% CI: –4.51 to –1.02; P = 0.002; low heterogeneity, $I^2 = 0\%$). The use of the passive leg-raising test combined with echocardiography to assess fluid reactivity was superior. Ultrasound-guided fluid resuscitation did not significantly change the length of the free intensive care unit stay (MD: 1.5; 95% CI: –3.81 to 6.81; P = 0.58; $I^2 = 0\%$).

Conclusion: Ultrasound-guided fluid resuscitation in patients with septic shock is beneficial, especially when using inferior vena cava–related measures and the passive leg-raising test combined with echocardiography.

Keywords: Meta-analysis, Mortality, Resuscitation, Septic shock, Systematic review, Ultrasonography

Introduction

Sepsis is a dysfunctional host state caused by a dysregulated reaction to infection, and septic shock is a severe form of sepsis.[1] Septic shock has attracted extensive attention due to its high morbidity and mortality, with current estimates of 30 million episodes and 6 million deaths annually.[2] Although new therapies have been developed, effective treatment remains complex and challenging.[3] However, in-depth research on severe sepsis has provided a deeper understanding of its pathogenesis and treatment of septic shock. In 2003, research on critical care and infectious diseases developed guidelines for the management of septic shock to improve outcomes.[4]

Fluid resuscitation is one of the most common treatment options for septic shock. According to the surviving sepsis campaign guidelines (SSC) in 2004, early goal-directed therapy (EGDT) should be administered within the first 6 hours after septic shock.[4] The EGDT can improve tissue perfusion by monitoring hemodynamic parameters and responses to fluid resuscitation and vasopressor medications and is considered a usual care strategy.[5] However, there is some evidence that usual care strategies do not improve outcomes.[6,7] For example, several studies have revealed that early administration of large amounts of crystalloids does not improve prognosis due to complications, and restrictive fluid resuscitation reduces the use of vasoactive drugs and mechanical ventilation.[8–10] The 2021 SSC guidelines recommend that at least 30 mL/kg of crystalloids be administered intravenously within 3 hours in initial resuscitation. Noninvasive tools are also recommended to assess hemodynamic status, including echocardiography.[11] However, the effects of ultrasound-guided fluid resuscitation and usual care strategies remain controversial.[12]

Ultrasound has been used in critical care medicine for more than 30 years because of its simplicity and noninvasiveness, as it allows sustainable monitoring.[13] In recent years, ultrasound technology has developed rapidly and has been applied in intensive care units (ICUs) for ultrasound-guided interventional radiology, hemodynamic monitoring, and organ perfusion assessment.[14–18] Ultrasound has also been used to guide fluid resuscitation in patients with septic shock (eg, using lung ultrasound B-line scores) and fluid management in patients with extravascular pulmonary water.[19] Cardiac function and fluid responsiveness of patients can be assessed by monitoring cardiac structure size, left ventricular ejection fraction, and left ventricular

All data generated or analyzed during this study are included in this published article and its supplementary information files.

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outflow tract velocity time integral (LVOT-VTI).[15,20,21] Furthermore, fluid responsiveness can be more accurately assessed by the diameter of the inferior vena cava (IVC) and the degree of morphological variability.[22]

To date, there are no consistent conclusions regarding the use of initial ultrasound-guided fluid resuscitation in patients with septic shock because the findings of clinical studies are controversial. To obtain reliable evidence, we conducted a systematic review and meta-analysis to compare ultrasound guidance with the usual care strategy in patients with septic shock.

Materials and methods

This systematic review and meta-analysis was registered in The International Prospective Register of Systematic Reviews (PROSPERO) (CRD42022326566) and conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[23]

Data sources and searches

We searched the PubMed, Embase, Cochrane Library, and Web of Science databases from their establishment to April 16, 2022, without restrictions on language, country, or region. We also searched the Cochrane Central Register of Controlled Trials and the Chinese Clinical Trials Registry. The following terms were used to search the literature: "fluid therapy"; "resuscitation"; "resuscitation orders"; "ultrasonography"; "diagnostic imaging"; "ultrasonography, Doppler"; "ultrasonography, interventional"; "echocardiography"; "echocardiography, Doppler, pulsed"; "echocardiography, Doppler, color"; "echocardiography, Doppler"; "echocardiography, transesophageal"; "heart-lung machine"; "lung"; "vena cava, inferior"; "sepsis"; "shock, septic"; "randomized controlled trial." The literature was managed using EndNote X9 software (Clarivate Analytics).

Inclusion and exclusion criteria

The inclusion criteria were as follows: (1) randomized controlled trials (RCTs); (2) adult patients (>18 years of age) with a definitive diagnosis of septic shock; (3) initial fluid resuscitation in the emergency department or ICU; (4) the intervention group was directed by ultrasound during initial resuscitation, including hemodynamics, fluid responsiveness, and interstitial syndrome; (5) usual care arms that received fluid resuscitation goals recommended by the SSC guidelines; and (6) other treatments between the 2 groups were comparable. Case reports, retrospective studies, observational studies, animal studies, repeated studies, and those irrelevant to the outcomes of interest were excluded.

Study selection

Two authors (Chen Z and Han X) independently screened the titles and abstracts of the articles and further evaluated the eligible articles. Any disputes were discussed with a third author (Wang B).

Outcomes and data extraction

The primary outcome was mortality during the study period. Secondary outcomes included 24-hour fluid volume, dose or duration of vasoactive drugs, length of hospital stay, and ICU stay. Two authors (Chen Z and Han X) independently extracted all the data and a third author (Wang B) checked the data. These data included the first author, year of publication, country, type of study design, number of cases, treatment versus control groups, and primary outcomes. The relevant data were collected using Microsoft Excel (Microsoft Office 2019, Microsoft Corporation). Quantitative data were presented as mean and standard deviation (mean ± standard deviation [SD]; $\bar{X} \pm S$), while binary data were expressed as frequencies or percentages. Medians and quartiles were converted to mean and SD using the method provided by McGrath et al.[24] The quality of the included studies was evaluated in terms of the random allocation method, concealment of the allocation scheme, blinding, incomplete outcome data, selective reporting of outcomes, and other sources of bias, as recommended by the Cochrane Collaboration. These data were classified as low, moderate, or high quality and are presented in green, yellow, and red, respectively.[25]

Statistical analysis

Dichotomous and continuous data were calculated using the Mantel-Haenszel risk ratio (RR) and inverse variance (IV) mean difference (MD), respectively, with 95% confidence intervals (CI). Estimates of the effects were summarized using forest plots. Except for adverse events, all results were evaluated in the meta-analysis. The heterogeneity between studies was assessed using Cochran's Q-statistic ($P < 0.10$ considered statistically significant), I^2, and visual inspection of forest plots. A fixed-effects model was used when $I^2 < 50\%$; otherwise, a random-effects model was used. Additionally, funnel plots were used to assess the potential publication bias in the outcomes of the 12 included studies. Subgroup analysis was performed according to different ultrasound strategies with significant heterogeneity. A qualitative analysis was performed during the subgroup analysis. A sensitivity analysis was also performed. All relevant data were analyzed using RevMan 5.4.1 (The Cochrane Collaboration, 2020) and STATA 17.0 (StataCorp, 2021).

Grading of Recommendations Assessment, Development, and Evaluation assessment of evidence quality

Grading of Recommendations Assessment, Development, and Evaluation (GRADE) Profiler 3.2.2 was used to evaluate the quality of evidence for outcome indicators. RCTs were set as the highest level of evidence in the GRADE quality evaluation system. The grade of evidence quality was then evaluated based on 5 downgrade conditions (study limitations, publication bias, study inconsistency, study indirectness, and study imprecision) and 3 upgrade conditions (large effect, plausible confounding that would change the effect, and dose-response gradient).

Results

Literature selection and characteristics

A total of 1309 articles were initially obtained after searching, and 23 relevant studies were found on the clinical trial registration Web site. A total of 89 articles were duplicates and were excluded. After reading the article titles and abstracts, 1,218 irrelevant articles were excluded. After reading the complete text, the same research team published 4 similar studies, 2 did not have relevant endpoints, 1 was in children, 3 did not use ultrasound-guided fluid resuscitation, 1 did not include septic shock, and 2 did not compare ultrasound guidance with the usual care strategy. Finally, 12 studies were included (Fig. 1).

Study characteristics

A total of 947 participants, of whom 473 were treated with ultrasound-guided fluid resuscitation, were included in the study (Table 1).[20,21,26–35]

Nine studies reported fluid volume, of which 6 reported 24-hour fluid volume as mean ± SD [26,35] and median with interquartile range,[21,30,32,33] 1 reported 24-hour fluid balance,[29] 1 reported target titration of fluids,[27] and 1 reported 6-hour infusion volumes.[31] Three studies reported the dose of norepinephrine as "μg/kg/h" [26,27] and the maximum dose,[31] 1 reported the duration of norepinephrine,[33] and 1 reported the total dose of norepinephrine over 24 hours.[35] Two studies reported the dose of dobutamine [26,27] and the number of participants.[30,31] Three studies reported the duration of vasopressin,[26,27,31]

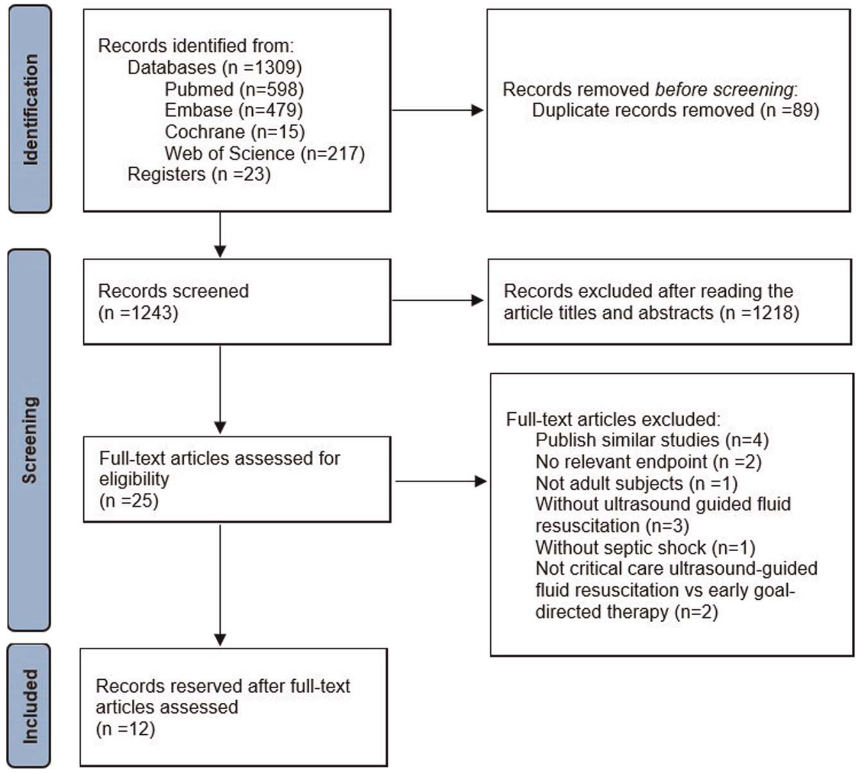

Figure 1. Flowchart of the search strategy in this systematic review and meta-analysis.

1 did not report the duration of the infusion,[21] and 1 reported patients who received vasopressin in the first 6 hours.[32] The length of stay was expressed as mean ± SD in 2 studies [20,27] and median with interquartile range in 3 studies.[21,26,32] The length of ICU stay was expressed as median with interquartile range in 3 studies,[26,31,33] as the median in 1 study,[29] and as the mean ± SD in 1 study.[27] The length of the free ICU stay was reported in 2 studies.[21,30] The fluid management and hemodynamic optimization indicators of the research are shown in Supplemental Table 1 (http://links.lww.com/ECCM/A63).

Primary outcome

Mortality was analyzed using a fixed-effects model (Fig. 2). Ultrasound-guided fluid resuscitation was associated with a lower mortality rate (RR: 0.78; 95% CI: 0.65–0.94; $P = 0.007$). The heterogeneity between the studies was low ($I^2 = 29\%$, $P = 0.21$). The funnel plot analysis did not indicate a significant publication bias for mortality (Supplemental Fig. 1, http://links.lww.com/ECCM/A64). The sensitivity analysis showed that mortality was reliable (Supplemental Fig. 2, http://links.lww.com/ECCM/A64).

Secondary outcomes and subgroup analysis

The 24-hour fluid volume was analyzed using a fixed-effects model (Fig. 3A). Fluid volume at 24 hours was significantly reduced in ultrasound-guided fluid resuscitation patients (MD: –1.02; 95% CI: –1.28 to –0.75; $P < 0.001$) with low heterogeneity ($I^2 = 0\%$, $P = 1$).

The norepinephrine dose was analyzed using a fixed-effects model (Fig. 3B). The dose of norepinephrine was increased during ultrasound-guided fluid resuscitation (MD: 0.07; 95% CI: 0.02–0.11; $P = 0.002$), with low heterogeneity ($I^2 = 45\%$, $P = 0.18$). The dose of dobutamine was analyzed using a fixed-effects model (Fig. 3C). The dose of dobutamine was increased (MD: 2.2; 95% CI: 0.35–4.04; $P = 0.02$) with low heterogeneity ($I^2 = 0\%$, $P = 0.61$). Ultrasound-guided fluid resuscitation did not reduce the risk of dobutamine use (RR: 1.67; 95% CI: 0.52–5.36; $P = 0.39$) (Fig. 3D), with low heterogeneity ($I^2 = 0\%$, $P = 0.86$). The duration of vasopressin infusion was analyzed using a random-effects model (Fig. 3E). The duration of vasopressin infusion was not significantly changed by ultrasound-guided fluid resuscitation (MD: –5.46; 95% CI: –38.78 to 27.86; $P = 0.75$), with high heterogeneity ($I^2 = 98\%$, $P < 0.001$). Because of the small number of included studies, a single-study effect analysis was adopted. Taking IVC-related measures during ultrasound may be advantageous for the duration of vasopressin infusion.[26,27]

The length of hospital stay was analyzed using a random-effects model (Fig. 3F). Ultrasound-guided fluid resuscitation did not shorten the length of hospital stay (MD: –2.19; 95% CI: –6.28 to 1.91; $P = 0.29$), with high heterogeneity ($I^2 = 91\%$, $P < 0.001$). Therefore, we performed a subgroup analysis (Fig. 4). Based on the different ultrasound indicators for monitoring, the patients were divided into 2 groups: IVC-related measures and echocardiography. After removing this factor, the results showed that IVC-related measures reduced the length of hospital stay (MD: –2.91; 95% CI: –5.2 to –0.62; $P = 0.01$), with low heterogeneity ($I^2 = 8\%$, $P = 0.34$). However, the heterogeneity in the echocardiography group was high ($I^2 = 97\%$, $P < 0.001$). Qualitative analysis showed that the use of the passive leg-raising test combined with echocardiography to assess fluid reactivity showed superiority for the length of hospital stay.[20] The length of the ICU stay was analyzed using a random-effects model (Fig. 3G). Ultrasound-guided fluid resuscitation did not reduce the length of ICU stay (MD: –0.71; 95% CI: –4.43 to 3.02; $P = 0.71$), with high heterogeneity ($I^2 = 85\%$, $P < 0.001$). Therefore, we also performed a subgroup analysis of ICU stays using different ultrasound strategies (Fig. 5). The results showed

Table 1

The Characteristics of Studies Included

Studies	Country, SC/MC	No. Patients	Intervention	Male (%)	Mean Age, y	APACHE II/SOFA Score at Baseline	Primary Outcome/ Primary End Points
Alhabashy et al.[26] (2021)	Ireland	87	UGFR	57.1	42.33 ± 8.96	(A) 23.95 ± 3.45	30-Day mortality
	SC		UCS	51.1	44.44 ± 7.65	24.76 ± 4.26	
Elsayed Afandy et al.[27] (2020)	Egypt	60	UGFR	56.7	38.6 ± 3.3	(A) 25.4 ± 3.7	30-Day mortality
	SC		UCS	53.3	39.4 ± 3.7	25.5 ± 3.7	
Garg et al.[28] (2016)	India	36	UGFR	55.6	37.39 ± 15.53	(A) 21.38 ± 9.61	IVCCI <20%; MAP of ≥65 mm Hg and CVP >12 mm Hg
	SC		UCS	44.4	44.5 ± 18.73	20.66 ± 7.39	
Ismail et al.[29] (2018)	Egypt	80	UGFR	55	56	—	Reaching score of 16 according to ultrasound scoring system CVP of 8–12 mm Hg
	SC		UCS	42.5	58	—	
Lanspa et al.[30] (2018)	United States	30	UGFR	47	69 (61–77)	(A) 29 (23–41)	Changing in SOFA score at 48 hours
	SC		UCS	53	64 (49–75)	33 (31–41)	
Li et al.[20] (2019)	China	74	UGFR	46	62.1 ± 15.3	—	CVP of 8–12 mm Hg, MAP ≥65 mm Hg, urine volume ≥0.5 mL/kg/h, and $ScvO_2$ ≥0.7 within 6 h
	SC		UCS	48.6	64.2 ± 17.5	—	
Li et al.[31] (2021)	China	94	UGFR	49	54.5 ± 15.2	(A) 20.8 ± 8.2	28-Day mortality
	SC		UCS	62.2	56.7 ± 11	21.8 ± 6.7	
Musikatavorn et al.[32] (2021)	Thailand	202	UGFR	52.5	65.3 ± 20.1	—	30-Day mortality
	SC		UCS	62.4	63.7 ± 16.8	—	
Qi et al.[33] (2020)	China	68	UGFR	77.8	65.5 (50–72)	(A) 18 (18–20.5)	In-hospital mortality rate, 90-Day survival rate
	SC		UCS	75	67 (50.5–73)	19.5 (18–24.5)	
Sricharoenchai et al.[34] (2019)	Thailand	90	UGFR	—	—	(SO) 4 (3–6)	30-Day all-cause mortality
	SC		UCS	—	—	4 (3–6)	
Yu et al.[21] (2022)	China	86	UGFR	71.4	54.1 ± 15.4	(A) 22.2 ± 6.1	LCR at 6 hours
	SC		UCS	63.6	57.8 ± 15.7	23.6 ± 5.5	
Zhuang et al.[35] (2020)	China	40	UGFR	40	71.6 ± 11.3	(SO) 12.2 ± 5.1	6-Hour blood pressure achieved rate (MAP ≥65 mm Hg), 24-h resuscitation fluid volume
	SC		UCS	55	71.6 ± 19.2	14.3 ± 5	

All results are present in mean (median if not reported).

(A) APACHE II, acute physiology and chronic health evaluation II; CVP, central venous pressure; IVCCI, inferior vena cava collapsibility index; LCR, lactate clearance rate; MAP, mean arterial pressure; MC, multicenter; SC, single-center; $ScvO_2$, systemic central venous blood oxygen saturation; (SO), SOFA score, sepsis-related organ failure score; UCS, usual care strategy; UGFR, ultrasound-guided fluid resuscitation.

that IVC-related measures reduced the length of ICU stay (MD: −2.77; 95% CI: −4.51 to −1.02; P = 0.002) with low heterogeneity (I^2 = 0%, P = 0.57). The length of the free ICU stay was analyzed using a fixed-effects model (Fig. 3H). Ultrasound-guided fluid resuscitation did not significantly change the length of the free ICU stay (MD: 1.5; 95% CI: −3.81 to 6.81; P = 0.58), with low heterogeneity (I^2 = 0%, P = 0.55).

Sensitivity analysis showed that secondary outcomes, including 24-hour fluid volume, norepinephrine dose, dobutamine dose, number of dobutamine users, length of hospital stay, length of ICU stay, and free ICU stay, were credible (Supplemental Figs. 3–6, 8–10, http://links.lww.com/ECCM/A64), while the duration of vasopressin infusion was not (Supplemental Fig. 7, http://links.lww.com/ECCM/A64). The funnel plot analysis did not indicate significant publication

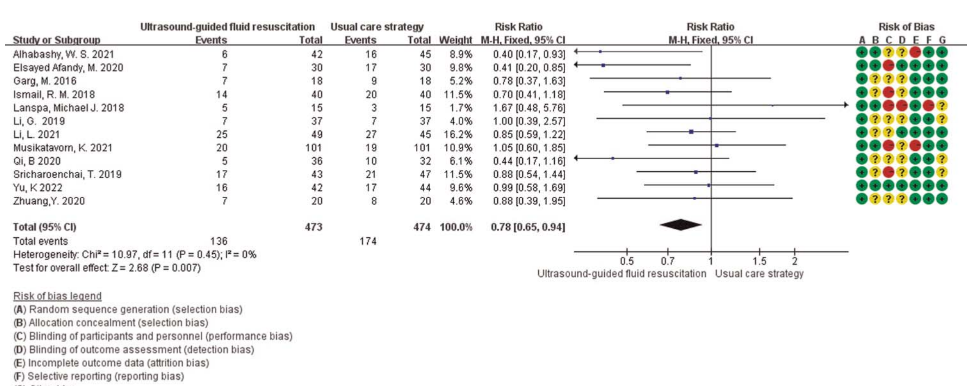

Figure 2. Mortality of septic shock patients based on ultrasound-guided fluid resuscitation treatment. Pooled effects are calculated using the M-H method with the fixed-effects model. CI, confidence interval; M–H, Mantel–Haenszel.

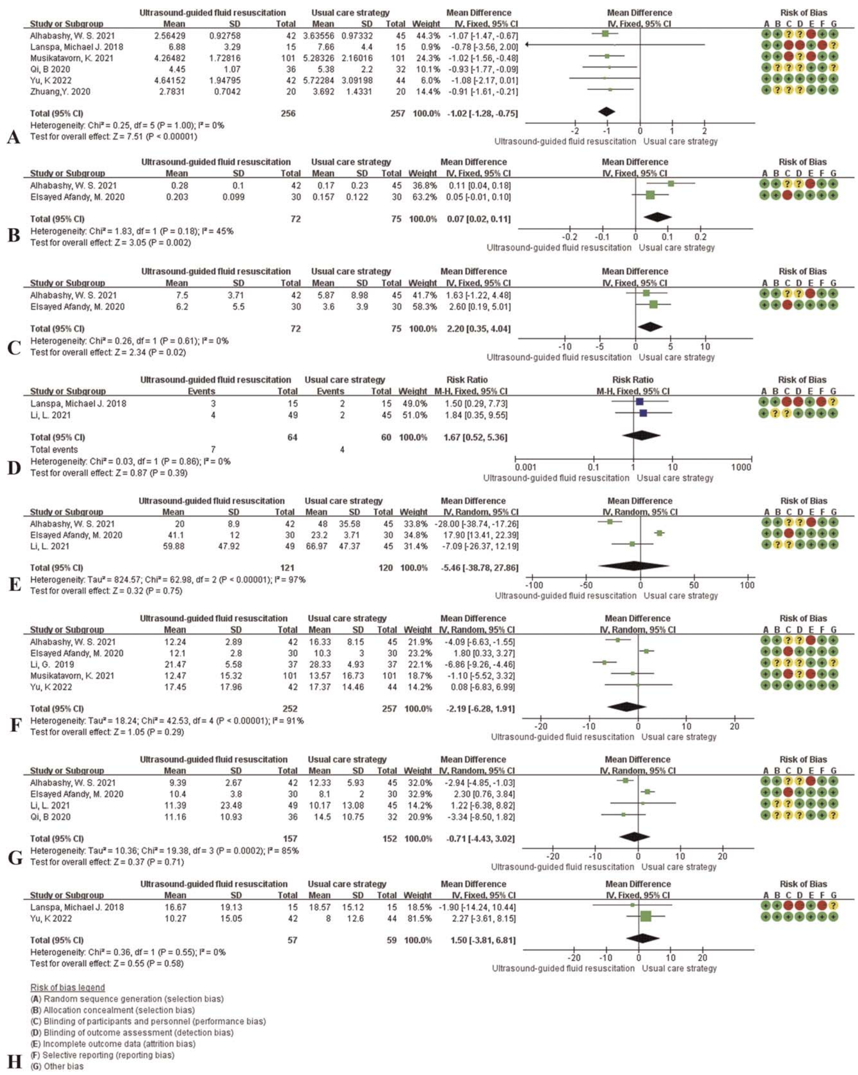

Figure 3. The 24-hour fluid administration. (A) Norepinephrine dose. (B) Dobutamine dose. (C) Number of dobutamine users. (D) Duration of vasopressin infusion. (E) Length of hospital stays. (F) ICU stays. (G) Free ICU stays. (H) Septic shock patients based on ultrasound-guided fluid resuscitation treatment. The pooled effects are calculated by the M-H or IV method with the fixed-effects or random-effects model. CI, confidence interval; IV, inverse variance; M–H, Mantel–Haenszel; SD, standard deviation.

bias for the 24-hour fluid volume (Supplemental Fig. 11, http://links.lww.com/ECCM/A64). However, other studies were not evaluated because only a small number of patients were included in the secondary outcomes.

GRADE assessment for evidence quality

The level of evidence for each outcome index included in the meta-analysis was evaluated. The results showed that mortality, 24-hour fluid administration, norepinephrine dose, dobutamine dose, number of dobutamine users, duration of vasopressin infusion, and free ICU stay were moderate-quality evidence, while the outcome indicators of the length of hospital and ICU stay were low-quality evidence. The main downgrading factors are shown in Supplemental Fig. 12 (http://links.lww.com/ECCM/A64).

Discussion

Few meta-analyses have compared ultrasound-guided fluid resuscitation with the usual care strategies in patients with septic shock. In a systematic review, ultrasound-guided fluid resuscitation was found to be useful and practical for septic shock patients within 7 days after admission compared with EGDT; however, it did not reduce the 28-day mortality rate, duration of mechanical ventilation, or length of ICU stay.[36] These findings contrast with the results of this study. Our systematic review and meta-analysis of 12 studies comprehensively reviewed RCTs published in recent years, and subgroup analyses or qualitative assessments were performed for outcomes with greater heterogeneity. We found that ultrasound-guided fluid resuscitation in patients with septic shock could reduce mortality during the management of homogeneity. In secondary outcomes, ultrasound-guided fluid resuscitation in patients with septic shock reduced 24-hour fluid volume and increased doses of norepinephrine and dobutamine but did not reduce the number of patients using dobutamine. Furthermore, IVC-related measures were advantageous in reducing the duration of vasopressin use. Increasing the dose of vasoactive drugs in the ultrasound-guided fluid resuscitation group, which may maintain organ tissue perfusion by reducing the amount of fluid, may have more adverse effects. Vasoactive drugs also play an essential role in the treatment of septic shock.

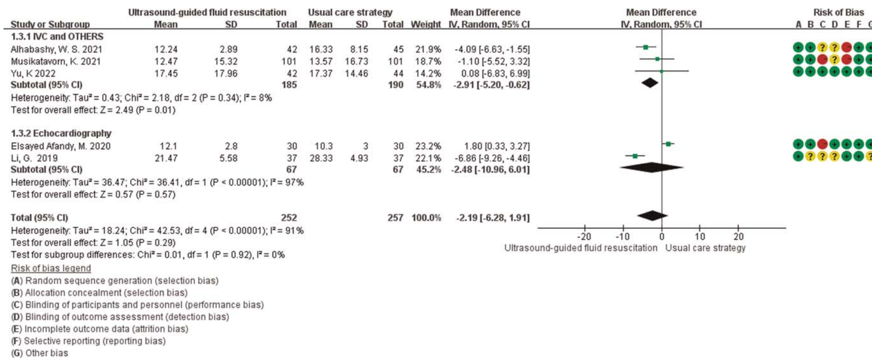

Figure 4. The subgroup in the total length of hospital stay in septic shock patients based on ultrasound-guided fluid resuscitation treatment. Pooled effects are calculated using the IV method with the random-effects model. CI, confidence interval; IV, inverse variance; SD, standard deviation.

In clinical practice, vasoactive drugs are required when blood pressure cannot maintain organ and tissue perfusion even with adequate fluids. Vasoactive drugs regulate vascular tone through receptors to improve fluid distribution and tissue perfusion and avoid fluid overload.[37]

We found no significant advantage of ultrasound-guided fluid resuscitation in the length of hospital and ICU stay. However, these results were heterogeneous, which may be related to the use of different ultrasound strategies. Therefore, we divided the ultrasound measurements into 2 groups: with and without IVC-related indicators. In subgroup analyses, an ultrasound study with IVC-related measures significantly reduced the length of hospital and ICU stays. The use of dynamic indicators, including echocardiography, to guide fluid resuscitation was weakly recommended in the surviving sepsis campaign, and the quality of the evidence was deficient. Other organ and volume responsiveness indicators have not yet been proposed for monitoring.[11] Subgroup analysis showed that IVC-related measures, such as the diameter and morphological variability of the IVC, when combined with other measures to guide fluid resuscitation, had a better prognosis.

Early identification of sepsis, especially septic shock, and timely treatment are essential to reduce mortality and complications.[11] Compared with the 2016 SSC guidelines, the 2021 SSC guidelines did not change the initial fluid resuscitation for patients with septic shock. However, it downgraded the recommendation of fluid volume for early resuscitation in sepsis from strong to weak.[11,38] Initial fluid resuscitation is a highly controversial issue, and most recommendations are based on clinical practice in multiple extensive studies. The need for early fluid resuscitation in patients with sepsis-induced hypotension or septic shock is based on pathophysiological changes. The requirement for fluid resuscitation is related to the early hypovolemic state of the patient, which is caused by systemic vasodilation and increased vascular permeability. Therefore, fluid resuscitation can restore intravascular volume, increase cardiac output, and improve oxygen delivery, thus improving tissue perfusion.[39] Therefore, physicians should consider using guidelines to individualize therapy.

Not all volume expansion effects were expected. Because of individual differences in patients, organ function and volume responsiveness are essential to determining whether fluid resuscitation has a therapeutic or detrimental effect.[40] Personalized management of these patients should include close monitoring of their responses to interventions.[41] In recent years, ultrasound has played an increasingly important role in the whole process of diagnosing and treating critically ill patients and has become a standard practice in the ICU.[42] As a noninvasive monitoring method, ultrasound can effectively assess the patient's organ function and volume responsiveness.[43] In the present study, patients' hemodynamics were analyzed using ultrasound, which allowed assessment of the advantages and disadvantages of fluid therapy and vasoactive medication and the selection of the most suitable treatment. As a dynamic indicator for monitoring volume responsiveness, IVC-related measures can provide right atrial pressure and an indication of cardiopulmonary interactions to guide fluid therapy with greater accuracy. However, IVC-related monitoring measures

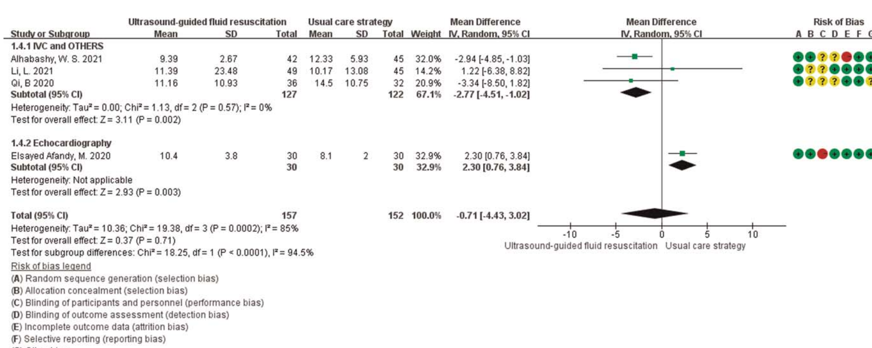

Figure 5. The subgroup in the length of ICU stays in septic shock patients based on ultrasound-guided fluid resuscitation treatment. Pooled effects are calculated using the IV method with the random-effects model. CI, confidence interval; IV, inverse variance; SD, standard deviation.

are also affected by many factors, including diseases that alter blood flow to the right heart, venous thrombosis, and blood vessel compression.[44] Left ventricular outflow tract velocity time integral is an ultrasound method for hemodynamic assessment that uses a Doppler-derived measure of cardiac output and stroke volume.[45] Although several studies have reported that the LVOT-VTI can predict fluid responsiveness, it has some limitations, including severe aortic regurgitation or obstruction, arrhythmias, and severe measurement errors.[46,47] However, Vignon et al.[48] compared several ultrasound indicators to monitor fluid responsiveness in mechanically ventilated patients and found that LVOT-VTI had the highest sensitivity to measure the diameter of the superior vena cava, while respiratory variability had the highest specificity, which was better than IVC-related measures and LVOT-VTI. For improved accuracy, appropriate measures should be taken according to their characteristics, and more than one measure should be used to assess fluid responsiveness.

Limitations

This systematic review and meta-analysis had some limitations. Despite our literature search, most of the RCTs were single-center studies (ie, no high-quality RCTs). Furthermore, some secondary outcome results were based only on 2–3 RCTs and only 1 study. Because of the limited number of quantitative studies, it is difficult to highlight the definite outcomes of ultrasound-guided fluid resuscitation. In addition, heterogeneity was observed between some of the included studies, and the same outcome may have been expressed differently. It was challenging to combine these studies, resulting in fewer studies with secondary outcomes and limited certainty.

Conclusion

Ultrasonography has the advantage of requiring fluid resuscitation. To the best of our knowledge, this systematic review and meta-analysis is the most comprehensive to date and compares ultrasound-guided fluid resuscitation with the usual care strategy in patients with septic shock. We found that ultrasound-guided fluid resuscitation, especially the measurement of IVC-related indicators in patients with septic shock, is beneficial due to reductions in mortality, 24-hour fluid volume, duration of vasopressin use, and length of hospital and ICU stay.

Conflict of interest statement

The authors declare no conflict of interest.

Author contributions

Chen Z conceived and designed the study, acquired the data, and drafted the manuscript. Han X conceived the study, extracted the data, and performed the statistical analysis. Liu Y and Wang M interpreted the data and drafted the manuscript. Wang BB collected the data and designed the study. Wang L contributed to the study design, and Jin HX edited and examined the manuscript. All authors have read and approved the final manuscript.

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Ethical approval of studies and informed consent

All studies included in this study followed the principles of the Declaration of Helsinki as revised in 2013.

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