Comparative efficacy of hemodynamic resuscitation strategies in severe sepsis: a systematic review of impact on mortality and complications in critically ill patients

Eficacia comparada de las estrategias de reanimación hemodinámica en la sepsis grave: una revisión sistemática del impacto sobre la mortalidad y las complicaciones en pacientes críticamente enfermos

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ABSTRACT

Introduction: Severe sepsis and septic shock present significant challenges in critical care, requiring effective hemodynamic resuscitation strategies to improve patient outcomes. This review aims to assess the comparative efficacy of hemodynamic resuscitation strategies—including fluid resuscitation, vasopressors, and advanced therapeutic interventions—on mortality, ICU stay, and complications in patients with severe sepsis and septic shock. Methods: A systematic literature search was conducted across PubMed, Embase, and Cochrane Library for studies published between 2019 and 2024. Eligible studies focused on the effects of different hemodynamic strategies in severe sepsis patients. A total of 3138 articles were identified, and after screening, 14 studies met the inclusion criteria. The quality of included studies was evaluated using the Cochrane Collaboration tool and the Newcastle-Ottawa Scale. Results: Fourteen studies were included, encompassing various strategies such as EGDT, vasopressor use, and fluid resuscitation. Notably, EGDT did not show significant mortality reduction compared to protocolized resuscitation care, with vasopressor demand 20% lower in the EGDT group. Balanced crystalloids significantly reduced 30-day mortality compared to saline. Early norepinephrine improved shock control rates and reduced mortality compared to standard care. Fluid resuscitation strategies showed mixed outcomes; while higher fluid resuscitation rates were linked to faster shock reversal and lower 28-day mortality, medium-volume fluid resuscitation (20-30 mL/kg) was most effective in reducing 28-day mortality. Prehospital hemodynamic optimization also demonstrated a significant reduction in 30-day mortality. Conclusion: Hemodynamic strategies such as balanced crystalloids and early norepinephrine may improve outcomes in severe sepsis and septic shock, although further studies are needed to determine optimal treatment protocols.

Keywords: Severe sepsis, hemodynamic resuscitation, fluid resuscitation, vasopressors, early goal-directed therapy (EGDT), mortality.

RESUMEN

Introducción: La sepsis grave y el shock séptico presentan desafíos importantes en cuidados críticos y requieren estrategias efectivas de reanimación hemodinámica para mejorar los resultados de los pacientes. Esta revisión tiene como objetivo evaluar la eficacia comparativa de las estrategias de reanimación hemodinámica (incluida la reanimación con líquidos, vasopresores e intervenciones terapéuticas avanzadas) sobre la mortalidad, la estancia en la UCI y las complicaciones en pacientes con sepsis grave y shock séptico. Métodos: se realizó una búsqueda bibliográfica sistemática en PubMed, Embase y la Biblioteca Cochrane de estudios publicados entre 2019 y 2024. Los estudios elegibles se centraron en los efectos de diferentes estrategias hemodinámicas en pacientes con sepsis grave. Se identificaron un total de 3138 artículos y, después de la selección, 14 estudios cumplieron los criterios de inclusión. La calidad de los estudios incluidos se evaluó mediante la herramienta de Colaboración Cochrane y la Escala de Newcastle-Ottawa. Resultados: Se incluyeron catorce estudios que abarcan diversas estrategias como EGDT, uso de vasopresores y reanimación con líquidos. En particular, la EGDT no mostró una reducción significativa de la mortalidad en comparación con la atención de reanimación protocolizada, con una demanda de vasopresores un 20 % menor en el grupo de EGDT. Los cristaloides equilibrados redujeron significativamente la mortalidad a los 30 días en comparación con la solución salina. La norepinefrina temprana mejoró las tasas de control del shock y redujo la mortalidad en comparación con la atención estándar. Las estrategias de reanimación con líquidos mostraron resultados

mixtos; Si bien las tasas más altas de reanimación con líquidos se relacionaron con una reversión más rápida del shock y una menor mortalidad a los 28 días, la reanimación con líquidos de volumen medio (20-30 ml/kg) fue más efectiva para reducir la mortalidad a los 28 días. La optimización hemodinámica prehospitalaria también demostró una reducción significativa de la mortalidad a los 30 días. Conclusión: Las estrategias hemodinámicas como los cristaloides equilibrados y la norepinefrina temprana pueden mejorar los resultados en la sepsis grave y el shock séptico, aunque se necesitan más estudios para determinar los protocolos de tratamiento óptimos.

Palabras clave: Sepsis grave, reanimación hemodinámica, reanimación con líquidos, vasopresores, terapia temprana dirigida por objetivos (EGDT), mortalidad.

INTRODUCTION

Severe organ failure resulting from an uncontrolled host reaction to an infection is known as sepsis. Although sepsis on its own does not represent a larger risk of death than septic shock, which is a subtype of sepsis with underlying circulatory, cellular, and metabolic abnormalities (Singer et al., 2016). The rising prevalence of sepsis and septic shock, together with its considerable pathophysiological, molecular, genetic, and clinical complexity, provide a significant worldwide burden and a challenge to emergency doctors (Rhodes et al., 2017). Approximately 49 million instances of sepsis and 11 million fatalities linked to sepsis were reported globally in 2017 (Chiu & Legrand, 2021). The frequency of sepsis and septic shock has been steadily rising since the initial consensus definition (Sepsis-1) was developed in 1991. Due to these findings, sepsis was designated as a worldwide health priority by the World Health Organisation (WHO). The concerning rise in occurrences can be ascribed to various factors: (i) patients' advanced average age, particularly in western nations; (ii) a rise in invasive procedures; (iii) the widespread use of chemotherapy and immunosuppressive medications; and (iv) antibiotic resistance (Vakkalanka et al., 2018). When combined, these two illnesses account for about 20% of all cause deaths worldwide, making septic patients one of the highest-mortality conditions seen in the emergency department (ED) (Yealy et al., 2021) (Seymour et al., 2012). This is true even with major advances in therapeutic management.

In order to effectively treat severe sepsis and septic shock, haemodynamic resuscitation must be initiated promptly. There are other resuscitation techniques that have been suggested, such as early-goal guided treatment (EGDT), the use of vasopressors, and fluid resuscitation. As it may raise intravascular volume, enhance cardiac output, and enhance tissue perfusion, fluid resuscitation is one of the key therapies for septic shock (Chang & Holcomb, 2016). Resuscitation fluids come in a variety of forms, however, and it's still unclear which is the best. Crystalloid or colloid solutions are the two general categories into which resuscitation fluids fall. Balanced solutions (Ringer lactate, Ringer acetate, and Plasma-Lyte) with various concentrations of sodium, chloride, and other electrolytes make up the former. The latter include gelatin solutions, dextran, and hydroxyethyl starch (HES), which have a molecular weight greater than crystalloids. The first fluids that patients with sepsis and septic shock should be given are crystalloids, according to current recommendations. Nonetheless, since the release of this guideline, a number of randomised controlled studies (RCTs) have been conducted to examine the effectiveness of different resuscitation fluids in patients with severe or septic shock, potentially yielding new data (Self et al., 2017)(Rochwerg et al., 2017)(Hammond et al., 2017). Rochwerg et al, conducted a network meta-analysis, which provided evidence that resuscitation using albumin or balanced crystalloids seems to be related with a lower death rate among sepsis patients when compared to other fluids (Rochwerg et al., 2014).

Increasing systemic and regional/microcirculatory flow is a crucial step in treating individuals with septic shock. When a patient is hypotensive, the input pressure that drives organ perfusion is improved by raising arterial blood pressure using vasopressors.Norepinephrine is recommended as the first-line vasoactive drug in patients presenting with septic shock by the Surviving Sepsis Campaign (SSC) guidelines (Rhodes et al., 2017). The SSC recommends vasopressin as a second-line vasopressor. Given that a major randomised experiment comparing vasopressin vs norepinephrine in patients undergoing septic shock (VASST) found no difference in mortality when vasopressin was added to norepinephrine (Russell et al., 2008). But because vasopressin wasn't started until almost 12 hours after the study's requirements were satisfied, it's possible that this had a negative effect on the way patients fared.

Patients presenting to the emergency department with severe sepsis and septic shock had a lower mortality rate if they received a specific 6-hour bundle of early-goal directed therapy (EGDT) for resuscitation; the absolute risk reduction was 16%, according to a 2001 randomised, non-blinded, controlled trial, conducted by Rivers (Rivers et al., 2001). Based on this, the surviving sepsis campaigning (SSC) recommendations from 2004 to 2012 supported EGDT (Dellinger et al., 2013)(Dellinger et al., 2004)(Dellinger et al., 2008). Three multicenter randomised controlled studies, ProCESS, ARISE, and ProMISe, raised doubts about the effectiveness of EGDT, nevertheless. EGDT did not lower the death rate of patients with septic shock and severe sepsis when compared to standard treatment, according to the authors' reports (DM Yealy, 2014)(SL Peake, 2014)(Mouncey et al., 2015).

The effectiveness of several hemodynamic resuscitation strategies for severe sepsis and septic shock has been the

subject of many systematic reviews in the literature. Jiang et al, discovered, for example, that patients with severe sepsis and septic shock did not have reduced death rates when they received Early Goal-Directed Therapy (EGDT)(Jiang et al., 2016). According to Nagendran et al, vasopressin outperformed dopamine regarding mortality in septic shock (Nagendran et al., 2016). Furthermore, Li et al. concluded that balanced solutions (BS) were the best resuscitation fluid (Li et al., 2020). Some fluids, like high-molecular-weight hydroxyethyl starch (H-HES), showed a higher risk of unfavorable outcomes, including the need for renal replacement therapy (RRT) and acute kidney injury (AKI). None of the reviews that have already been done have thoroughly examined the combined effects of different hemodynamic resuscitation approaches—including both vasopressors and fluid management strategies—on mortality and complications in severe sepsis and septic shock. These reviews have mostly concentrated on either particular resuscitation strategies like EGDT or the relative effectiveness of vasopressors and fluids. Moreover, recent evidential studies are also not included in them. This systematic review aims to bridge the gap by evaluating the comparative efficacy of different hemodynamic resuscitation strategies—including fluid types, vasopressors, and advanced therapeutic approaches—on mortality, ICU stay, and complications in patients with severe sepsis and septic shock by providing evidence from the most recent studies. The goal is to provide an updated and comprehensive understanding of optimal resuscitation strategies in this critically ill population.

METHODOLOGY

Study Design

This systematic review evaluated the comparative efficacy of hemodynamic resuscitation strategies in severe sepsis, focusing on their impact on mortality and complications in critically ill patients.

Sample Selection

The objective of the search was to systematically identify relevant studies examining hemodynamic resuscitation strategies and their outcomes in severe sepsis. The search was performed using a combination of keywords and MeSH terms with Boolean operators (AND, OR) across databases such as PubMed, Embase, and Cochrane Library. Search terms included "severe sepsis," "hemodynamic resuscitation," "fluid resuscitation," vasopressor," "EGDT" "mortality," and "complications."

Inclusion Criteria

•   Studies assessing the efficacy of hemodynamic resuscitation strategies in patients with severe sepsis.

•   Research articles published in English.

•   Studies involving human subjects.

•   Publications from 2019 to 2024.

•   Articles published in peer-reviewed journals.

•   Studies providing comprehensive methodologies and outcomes related to hemodynamic resuscitation.

Exclusion Criteria

•   Review articles, surveys, editorials, letters, and conference abstracts.

•   Studies that did not focus on hemodynamic resuscitation strategies or outcomes in severe sepsis.

•   Non-English publications.

•   Studies with insufficient or unclear methodologies and outcomes.

Study Method

In addition to the electronic search, identified studies were screened based on their titles and abstracts. Full texts of selected articles were then assessed for eligibility, applying the established inclusion and exclusion criteria. The review included only those articles that met the inclusion criteria.

Sample Size

A total of 14 articles were included in the final analysis for data extraction, covering a diverse range of hemodynamic resuscitation strategies and their impacts.

Quality Assessment

Using suitable evaluation tools, such as the Cochrane Collaboration's tool for randomised controlled trials and the Newcastle-Ottawa Scale (NOS) for cohort studies, the methodological quality of the included studies was assessed. Two reviewers separately completed quality evaluations; differences were discussed or resolved with the assistance of a third reviewer.

Data Extraction

Data were extracted from the selected studies using a standardized form. Key information recorded included study characteristics (e.g., author, year of publication), patient demographics, intervention details, outcomes assessed (mortality, ICU stay, vasopressor use), and findings relevant to hemodynamic resuscitation strategies.

Data Analysis

A qualitative synthesis of the findings was conducted, summarizing the effects of various hemodynamic resuscitation strategies on mortality and complications. Heterogeneity among studies was assessed, and a narrative synthesis was performed to discuss the implications of the findings in the context of clinical practice for severe sepsis management.

RESULTS

In the first literature search, 3138 articles were found. 223 articles were found to be relevant after a thorough review of the abstracts and titles; their whole texts were then obtained for further analysis. The research that was excluded either did not meet the requirements for inclusion or did not specifically look at the relative effectiveness of different hemodynamic approaches in cases of severe sepsis. After a rigorous screening process, 14 publications were deemed suitable for the systematic review and meta-analysis.

Figure 1 - Prisma Flow Diagram
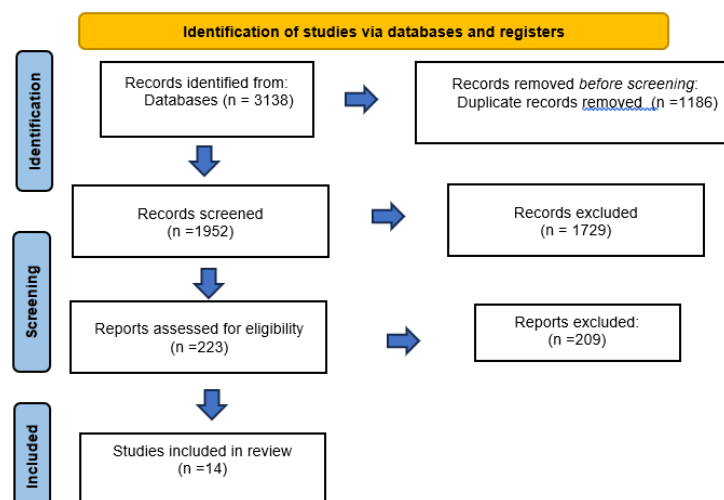
Source: the authors.

Study characteristics

The systematic analysis of 14 papers assessing hemodynamic resuscitation techniques in cases of septic shock and

severe sepsis was included. The study included a wide variety of study designs, such as historical cohort studies (n = 1, 7%), randomized controlled trials (n = 3, 21%), prospective cohort studies (n = 2, 14%), retrospective cohort studies (n = 7, 50%), and secondary analyses of randomised controlled trials (n = 1, 7%). These investigations, which mirrored actual treatment situations for septic patients, were carried out in a variety of clinical settings, including emergency rooms, intensive care units (ICUs), and prehospital mobile ICUs (mICUs).

From as few as 71 individuals in certain trials to as many as 2227 people in bigger cohort studies, the research included a variety of groups. Patients with septic shock, severe sepsis, and special subgroups including obese patients, patients with chronic heart failure (CHF), and post-EGDT sepsis cohorts were among the patient populations. Even prehospital settings were the subject of one research, which highlighted the differences in the management of septic patients there.

The majority of the therapies that were looked at were fluid resuscitation techniques. These included both conventional fluid boluses (such as 30 mL/kg) and customised dosage based on ideal body weight (IBW), actual body weight (ABW), or high-versus low-volume methods. In order to improve outcomes including 30-day mortality, ICU stay, and time to shock reversal, further strategies included the use of early norepinephrine, balanced crystalloids against saline, and advanced haemodynamic optimisation.

The trials' results varied greatly, with several concentrating on important clinical outcomes including death, duration of stay in the intensive care unit, and haemodynamic stability. While some studies assessed the requirement for organ support measures like mechanical breathing or days without a vasopressor, others looked at the development to septic shock. While one randomised study focused on the use of selepressin to lessen the need for ventilator support and vasopressors, another examined the precise effects of EGDT deployment in sepsis treatment.

Mortality

According to the research, individuals with severe sepsis have a range of death outcomes. While the early goal-directed treatment (EGDT) group had higher mortality than the protocolised resuscitation care (PRC) group, Elsayed (2021) concluded that the difference was not statistically significant ($p = 0.405$). The use of ideal body weight (IBW) vs non-IBW fluid resuscitation procedures did not significantly alter the in-hospital death rates, according to Kaseer's (2021) research. In contrast, underweight individuals had a greater death rate from underdosing, whereas obese patients did not exhibit any significant changes (Ward et al., 2022). The 28-day mortality rate did not change significantly ($p > 0.05$) between the IBW and non-IBW groups, according to Antal et al. (2019). A higher death rate (OR 1.52, 95% CI 1.03-2.24) was associated with not meeting the 30 mL/kg fluid dosage in Kuttab et al. (2019). Jouffroy et al. (2021) observed a substantial reduction in 30-day mortality (HRa = 0.52; $p = 0.01$) with prehospital haemodynamic optimisation. Comparably, patients receiving balanced crystalloids as opposed to saline had a decreased 30-day death rate ($p = 0.01$), according to Brown et al. (2019). A tendency towards reduced 28-day mortality with early norepinephrine was seen by Permpikul et al. (2019); the difference was not statistically significant ($p = 0.15$). There was no discernible variation in the 90-day death rate ($p = 0.77$) according to Pierre-Francois Laterre et al.(2019). According to Mohammed Abdel Gabbar & Amr Hassan (2020), the use of EGDT decreased death rates (12% vs. 25%, $p < 0.05$). Bo Hu and colleagues (2020) demonstrated a correlation between lower 28-day mortality and greater initial fluid resuscitation rates (HR=0.71, $p<0.001$). More patients who did not comply with fluids died after a year (HR 2.18, $p = 0.01$), according to Andreas H. Taenzer et al. (2020). The last finding was that a higher rate of intravenous fluid resuscitation was linked to a decreased rate of in-hospital mortality (AOR 0.87, 95% CI 0.76-0.99) by Gladis Kabil et al. (2022). The authors Hua-Ling Wang et al. (2021) observed a correlation between a lower 28-day mortality rate and a medium-volume fluid resuscitation dosage (20–30 mL/kg).

ICU Stay

The duration of stay in the intensive care unit varied according to the research' findings. ICU stays did not vary significantly, according to Elsayed (2021) ($p = 0.091$). Moreover, Kaseer (2021) found no discernible variation in the median length of ICU stay ($p = 0.13$). According to Ward et al. (2022), ICU stays were lengthier for patients who received ABW-based dosing regimens. Kuttab et al. (2019) emphasised the correlation between an extended ICU stay (~2 days, $\beta = 2.0$, 95% CI 0.5-3.6) and the inability to fulfil the 30 mL/kg fluid dose. Jouffroy et al. (2021) observed that prehospital optimisation may have an effect on ICU stay. According to Permpikul et al. (2019), early norepinephrine administration may lessen problems and hence shorten ICU stays. Bo Hu et al. (2020) noted that longer ICU stays might potentially be impacted by greater fluid resuscitation rates. Furthermore, Hua-Ling Wang et al. (2021) hypothesised that the medium-volume fluid resuscitation strategy could affect the length of hospital stay.

Table 1 - Characteristics and results of the studies

| Author	Year	Study Design	Population Type & Number	Setting	Intervention	Comparison	Outcomes Assessed	Results	Conclusion
Elsayed et al.(Elsayed et al., 2022)	2022	Randomized controlled trial	100 adult patients with septic shock	Emergency Department and ICU (Alexandria University Hospital)	Early goal-directed therapy (EGDT)	Protocolized resuscitation care (PRC)	Mortality, vasopressor use, ICU stay, mechanical ventilation days	Vasopressor demand was 20% lower in the EGDT group (p = 0.001), mortality was lower in the PRC group but there was no significant difference (p = 0.405); there were no significant changes in the length of the vasopressor (p = 0.372), days of mechanical ventilation (p = 0.243), or ICU stay (p = 0.091).	PRC may be beneficial compared to EGDT with a non-significant trend to decrease mortality.
Kaseer et al. (Kaseer et al., 2021)	2021	Retrospective observational	72 obese patients with severe sepsis	Academic tertiary care center	Fluid resuscitation dosing: 30 mL/kg/ideal body weight (IBW)	Non-IBW dosing strategy (30 mL/kg/non-IBW)	Progression to septic shock, ICU and hospital length of stay, mortality	There was no significant difference in the median ICU stay (p = 0.13) or hospital length of stay (p = 0.07); in-hospital death rates were comparable between the IBW and non-IBW groups with regard to the progression to septic shock (18% vs. 26%; p = 0.54).	IBW-based fluid resuscitation did not affect progression to septic shock in obese septic patients.
Ward et al. (Ward et al., 2022)	2022	Retrospective cohort study	1,032 adults with severe sepsis or septic shock	Urban tertiary care ED	30 mL/kg fluid dosing (ABW vs IBW)	ABW vs IBW-based fluid dosing	Mortality, ICU stay, 30by3 fluid administration	Underweight: failure to reach ABW-based 30by3 increased mortality (OR 1.78, 95% CI 1.18-2.69). Obese patients had no significant mortality differences. Longer ICU stay with ABW (β = 2.40, 95% CI 0.84-3.95) and IBW (β = 1.58, 95% CI 0.07-3.08).	Underweight patients had higher mortality with under-dosing; no impact for obese patients.
Antal et al. (Antal et al., 2019)	2019	Observational prospective study	71 patients with sepsis or septic shock	ICU	Fluid resuscitation with IBW adjustment	IBW-adjusted fluid load vs non-IBW dosing	Renal outcome, hemodynamic parameters, 28-day mortality	Significant difference in fluid load before and after IBW adjustment No significant differences in 28-day mortality or urinary output between IBW and non-IBW groups (p > 0.05).	IBW-adjusted dosing was supported, but no significant difference in clinical outcomes.
Kuttab et al. (Kuttab et al., 2019)	2019	Retrospective cohort study	1,032 patients with severe sepsis or septic shock	Urban tertiary care ED	30by3 fluid administration	30by3 dosing vs failure to reach 30by3	Mortality, hypotension, ICU stay	Failure to meet 30by3 was associated with higher mortality (OR 1.52, 95% CI 1.03-2.24), delayed hypotension (OR 1.42, 95% CI 1.02-1.99), and increased ICU stay (~2 days, β = 2.0, 95% CI 0.5-3.6).	Failure to meet 30by3 linked to increased mortality and ICU stay.
Jouffroy et al. (Jouffroy et al., 2021)	2021	Retrospective cohort study	337 patients with septic shock	Prehospital mICU	Prehospital hemodynamic optimisation (MAP >65 mmHg or >75 mmHg)	No hemodynamic optimisation	30-day mortality	Prehospital optimisation significantly decreased 30-day mortality (HRa = 0.52; 95% CI [0.31–0.86]; p = 0.01).	Prehospital hemodynamic optimisation is associated with decreased 30-day mortality in septic shock.
Brown et al. (Brown et al., 2019)	2019	Secondary analysis of RCT (SMART)	1,641 sepsis patients	ICU	Balanced crystalloids	Balanced crystalloids vs saline	30-day mortality, kidney events, vasopressor use	30-day mortality: 26.3% (balanced) vs. 31.2% (saline) (aOR, 0.74; 95% CI 0.59–0.93; p = 0.01). Major kidney events: 35.4% (balanced) vs. 40.1% (saline) (aOR, 0.78; 95% CI 0.63–0.97).	Balanced crystalloids were associated with lower 30-day mortality and reduced adverse kidney events.
Permpikul et al. (Permpikul et al., 2019)	2019	Randomized double-blind trial	310 adults with sepsis and hypotension	Emergency Room	Early norepinephrine	Early norepinephrine vs standard care	Shock control, 28-day mortality	Shock control: 76.1% (early norepinephrine) vs. 48.4% (standard care) (p < 0.001). 28-day mortality: 15.5% (early norepinephrine) vs. 21.9% (standard care) (p = 0.15). Lower cardiogenic pulmonary edema and new-onset arrhythmia (p < 0.05).	Early norepinephrine significantly increased shock control, with potential for lower complications.
Pierre-Francois Laterre et al. (Laterre et al., 2019)	2019	Randomized Clinical Trial	868 patients with septic shock	ICU	Selepressin (1 of 3 dosing regimens)	Placebo	Ventilator- and vasopressor-free days; 90-day mortality; kidney replacement therapy-free days; ICU-free days	No significant difference in ventilator- and vasopressor-free days (15.0 vs 14.5, P=0.30); 90-day mortality (40.6% vs 39.4%, P=0.77)	Selepressin did not improve vasopressor- and ventilator-free days compared with placebo. Further research is needed.
Mohammed Abdel Gabbar (Gabbar & Hassan, 2024)	2024	Retrospective Observational	220 sepsis patients (120 pre-EGDT, 100 post-EGDT)	ICU (Hospital in Cairo, Egypt)	Early Goal-Directed Therapy (EGDT) implementation	Pre-EGDT	Mortality rate	EGDT group had lower mortality (12% vs 25%, P<0.05)	Implementation of the EGDT protocol reduced mortality in sepsis patients in the hospital ICU.
Bo Hu et al. (Hu et al., 2020)	2020	Historical Cohort Study	1052 patients with septic shock	MICU	Higher fluid resuscitation rate (≥0.25 ml/kg/min)	Lower fluid resuscitation rate (<0.17 ml/kg/min)	Time to shock reversal; 28-day mortality	Faster fluid rate shortened time to shock reversal (HR=0.78, P=0.01); reduced 28-day mortality (HR=0.71, P<0.001)	Higher initial fluid resuscitation rates were associated with earlier shock reversal and lower 28-day mortality.
Andreas H. Taenzer et al. (Taenzer et al., 2020)	2020	Retrospective cohort study	Sepsis patients with CHF, 211 patients	Emergency Department (ED)	30 mL/kg crystalloid fluid bolus	No fluid bolus	1-year mortality	NFBC patients had higher 1-year mortality (HR 2.18, 95% CI 1.2-4.0, P = 0.01)	Fluid resuscitation in CHF patients with sepsis improved mortality compared to non-fluid compliant patients.
Gladis Kabil et al. (Kabil et al., 2022)	2022	Retrospective cohort study	Patients with suspected sepsis or septic shock (n=2227)	ED & Intensive Care Unit (ICU)	Intravenous fluids (>3600 mL)	<3600 mL within 24 hours	In-hospital mortality	Increased IV fluids reduced mortality (AOR 0.87, 95% CI 0.76-0.99); septic shock had stronger association (AOR 0.44, 95% CI 0.22-0.91)	Increased fluid resuscitation (>3600 mL) in septic shock/sepsis patients was associated with lower in-hospital mortality.
Hua-Ling Wang et al. (Wang et al., 2021)	2021	Prospective observational study	Septic shock patients, 302 patients	ICU	30 mL/kg crystalloid fluids	High-volume (>30 mL/kg), low-volume (<20 mL/kg)	28-day mortality	Medium-volume fluid group had the lowest 28-day mortality (OR 0.507, 95% CI 0.310-0.828, P = 0.007). Kaplan-Meier showed significant difference in mortality rates (P=0.0016).	A medium-volume fluid resuscitation dose (20-30 mL/kg) within the first 1-2 hours was associated with reduced 28-day mortality in septic shock patients.

Source: the authors.

Análisis: Con respecto al factor de asociación funcionalidad familiar vinculada al sobrepeso, es buena en el 28% (14 estudiantes), 22% tienen disfunción leve (11), 16% disfunción moderada (8) y 12% disfunción severa (6), en relación a la obesidad grado I, tienen disfunción leve el 14% (7 estudiantes) buena funcionalidad familiar, el 6% (3) disfunción moderada el 2% (1), se deduce que existe mayor predominio de funcionalidad familiar buena vinculada al sobrepeso y disfuncional leve asociada a la obesidad grado I.

Table 2- Quality assessment of the reviewed studies by New Castle Ottawa Scale

Study	Representative ness of the exposed cohort（1）	Selection of the non-exposed cohort（1）	Ascertainment of exposure （1）	Demonstration that outcome of interest wasnot present at start of study（1）	Compare ability of cohorts on the basis ofthe design or analysis （2）	Assessment of outcome （1）	Was follow-up long enough for outcomes to occur（1）	Adequacy of follow up of cohorts（1）	Representativen ess of the exposed cohort（1）
Kaseer et al. (Kaseer et al., 2021)	1	1	1		2	1	1	1	1
Ward et al. (Ward et al., 2022)	1	1	1	1	2	1	1	1	1
Antal et al. (Antal et al., 2019)	1	1	1		2	1	1	1	1
Kuttab et al. (Kuttab et al., 2019)	1		1		1	1	1	1	1
Jouffroy et al. (Jouffroy et al., 2021)	1		1		1	1	1	1	1
Mohammed Abdel Gabbar (Gabbar & Hassan, 2024)	1	1	1		2	1	1	1	1
Bo Hu et al. (Hu et al., 2020)	1	1	1	1	2	1	1	1	1
Andreas H. Taenzer et al. (Taenzer et al., 2020)	1	1	1		2	1	1	1	1
Gladis Kabil et al. (Kabil et al., 2022)	1	1	1	1	1	1	1	1	1
Hua-Ling Wang et al. (Wang et al., 2021)	1		1	1	1	1	1	1	1

Source: the authors.

Figure 2 - Quality assessment of RCTs by RoB 2.0
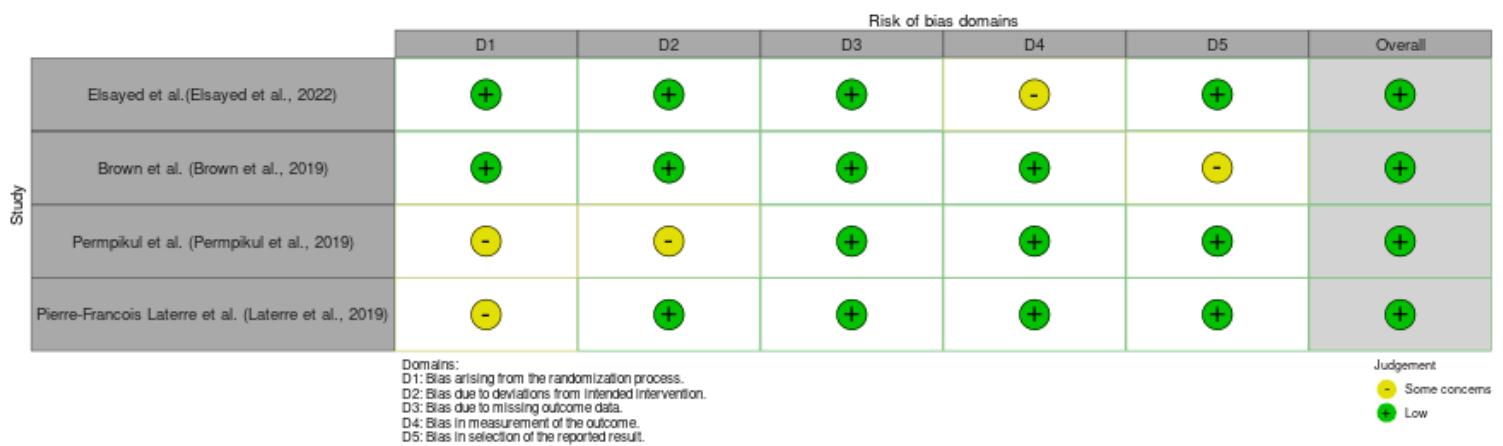
Source: the authors.

DISCUSSION

A number of studies have assessed fluid resuscitation tactics in the treatment of severe sepsis, with an emphasis on the amount and kind of fluid used, as well as the comparison between ideal and actual body weights (ABW and IBW). While Ward

et al. (2022) observed higher mortality rates among underweight patients who were under-dosed based on ABW, Kaseer (2021) and Ward et al. (2022) found no significant difference in mortality outcomes between IBW and non-IBW dosing strategies. However, there was no significant mortality impact observed in obese patients. Similarly, when comparing IBW-adjusted fluid dosage to non-IBW dosing, Antal et al. (2019) found no significant difference in renal outcomes or 28-day mortality.

Some research, meanwhile, stressed the significance of fluid volume. In contrast to lower fluid resuscitation rates, Bo Hu et al. (2020) showed that a greater fluid resuscitation rate (≥0.25 mL/kg/min) was linked to quicker shock reversal and decreased 28-day mortality. According to Kabil et al. (2022), patients who received more intravenous fluid quantities (>3600 mL) had a lower in-hospital death rate, especially if they were suffering from septic shock. Wang et al.'s (2021) findings further emphasise the significance of the ideal fluid volume in resuscitation. They discovered that medium-volume fluid resuscitation (20–30 mL/kg) during the first 1-2 hours was linked to the lowest 28-day mortality.

These data from our research are consistent with previous research, such as retrospective analyses by Zhang et al. (2021) and Messina et al. (2024), which showed that early ICU days with positive fluid balances are associated with a notably higher risk of death (Messina et al., 2024)(Zhang et al., 2021). More evidence for this came from Mele et al, who demonstrated that progressive fluid overload causes harmful renal events and increased mortality (Mele et al., 2022). But according to a prospective research by Nagi et al. (2021), the IVC collapsibility index may be able to minimise overload and improve fluid responsiveness (Nagi et al., 2021). However, an RCT by Shapiro et al, revealed no statistically significant difference in 90-day mortality between the liberal and restricted fluid regimens, suggesting that the use of liberal fluids may not necessarily be detrimental(NI et al., 2023). Nevertheless, a research conducted in South Korea by Hyun et al., confirmed that beyond the first ICU day, prolonged positive fluid balances were associated with a higher risk of death, indicating the need of careful fluid control throughout time (Hyun et al., 2023).

When it came to fluid type, Brown et al. (2019) discovered that balanced crystalloids were linked to fewer adverse renal events and a lower 30-day mortality when compared to saline. According to this, fluid amount and type might affect how a patient does in cases of severe sepsis; balanced crystalloids and patient-specific dosage are preferred.

Permpikul et al. (2019) provided evidence about the use of vasopressors and showed that early norepinephrine administration improved shock management (76.1% vs. 48.4% with standard care). However, the changes in 28-day mortality were not statistically significant. The advantages of early vasopressor beginning in enhancing haemodynamic stability and lowering cardiogenic consequences, such as arrhythmias and pulmonary oedema, were emphasised in this research. Similarly, Jouffroy et al. (2021) found that patients with septic shock saw a substantial 30-day mortality reduction with prehospital haemodynamic optimisation, which included keeping mean arterial pressure (MAP) above 65 mmHg. According to these results, prompt and purposeful use of vasopressors may improve sepsis outcomes by bringing about haemodynamic stabilisation quickly.

While Laterre et al. (2019) assessed the vasopressor Selepressin in patients experiencing septic shock, they were unable to detect any statistically significant variation in ventilator- or vasopressor-free days, 90-day mortality, or other outcomes when compared to placebo. The lack of effect seen with clepressin suggests that not all vasopressors are equally effective and that their use should be customised based on specific clinical conditions. Early norepinephrine use was linked to better shock control, and prehospital vasopressor strategies improved mortality.

Early Goal-Directed Therapy (EGDT) has been studied in relation to managing sepsis. In comparison to Protocolised Resuscitation Care (PRC), Elsayed et al. (2021) observed that while EGDT resulted in a 20% decrease in vasopressor usage, there was no discernible change in mortality or duration of stay in the intensive care unit. Similar to this, Mohammed Abdel Gabbar and Amr Hassan (2020) found that EGDT decreased mortality in patients in intensive care units, indicating that it may be useful in raising survival rates in critical care environments.

Comparing EGDT to other techniques, however, revealed contradictory results. While EGDT decreased the requirement for vasopressors, Elsayed et al. (2021) found that the advantages of EGDT in terms of mortality were not statistically significant when compared to PRC. This suggests that the benefits of EGDT may vary depending on the context or be impacted by other variables such as patient characteristics and timing. EGDT adoption, on the other hand, was shown to clearly reduce mortality in the research conducted by Mohammed Abdel Gabbar and Amr Hassan (2020), highlighting the significance of early, protocol-based treatments in lowering sepsis-related fatalities.

All of these studies point to the possibility that fluid resuscitation techniques with balanced crystalloids and appropriate fluid volumes—especially medium to higher volumes—are linked to better outcomes, such as decreased mortality and fewer complications (Bo Hu et al., 2020; Kabil et al., 2022; Wang et al., 2021; Brown et al., 2019). Vasopressors may greatly enhance shock management and minimise consequences when used early in the course of sepsis, especially when norepinephrine delivery is initiated (Permpikul et al., 2019; Jouffroy et al., 2021). Some research (Elsayed et al., 2021; Mohammed Abdel Gabbar and Amr Hassan, 2020) suggest that EGDT is helpful in lowering the usage of vasopressors and

increasing survival; nevertheless, its effect on mortality in comparison to other resuscitation techniques is still unclear.

There were inconsistent results mostly concerning IBW vs ABW-based fluid dosing regimens, which did not consistently affect the course of sepsis or death (Kaseer, 2021; Ward et al., 2022; Antal et al., 2019). Furthermore, as not all vasopressor medications seem to be equally effective in septic patients, the lack of effectiveness shown with selepressin emphasises the need of carefully choosing vasopressors depending on the clinical setting (Laterre et al., 2019).

There are a few limitations on this review. The heterogeneity in the results may have been caused by the included studies' inconsistent research designs, patient demographics, and resuscitation techniques. Not all research accounted for confounding variables such comorbidities or baseline illness severity, and a large number of studies were observational or retrospective in nature, which might add bias. Non-English articles were also disregarded in the review as they could have omitted pertinent international evidence. Furthermore, it was difficult to do a thorough meta-analysis since several of the interventions—like the kind and timing of vasopressors—were reported inconsistently in different trials. Large-scale, multicenter randomised controlled studies that assess haemodynamic techniques in a range of patient groups should be the main focus of future research. To improve result comparison, more standardised methods are required for the administration of vasopressors and fluid resuscitation. Novel technology including sophisticated monitoring systems might improve personalised haemodynamic care in septic shock. More research on the long-term effects of various resuscitation techniques, such as quality of life and recovery of organ failure, will provide more light on the best ways to treat severe sepsis and septic shock.

CONCLUSION

In the treatment of severe sepsis and septic shock, haemodynamic resuscitation techniques vary widely and are complicated, as this comprehensive review makes clear. No one technique has consistently outperformed others in lowering mortality or improving clinical outcomes across all patient categories, despite the potential benefits of treatments like fluid resuscitation, vasopressor usage, and early goal-directed therapy (EGDT). Vasopressor demand was shown to be lower with EGDT; nevertheless, fluid resuscitation techniques, especially those that used balanced crystalloids, were linked to better results in terms of renal events and mortality. The results highlight the significance of customising haemodynamic therapies to the unique characteristics of each patient as well as the various therapeutic contexts. To provide precise recommendations for the best mix of fluids, vasopressors, and cutting-edge treatments in this very sick patient group, more excellent, large-scale research is yet required.

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