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SYSTEMATIC REVIEW

The Effect of Extracorporeal Hemopurification Combined With Conventional Anti-Infection on Clinical Prognosis and Immune Function in Sepsis: A Meta-Analysis

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Abstract

Aims/Background Sepsis remains a major cause of mortality in intensive care units (ICUs) worldwide, with conventional treatments showing limited efficacy. Extracorporeal hemopurification (EH) techniques have emerged as promising adjunctive therapies. This study aims to explore the impact of EH techniques, including hemofiltration, hemoperfusion, hemodialysis, and hemosorption, on the clinical prognosis and immune function of patients with sepsis.

Methods We searched relevant literature describing patients with a precise clinical diagnosis of sepsis, severe sepsis, or septic shock across various databases, including MEDLINE, AMED, Cochrane Library, Embase, PubMed, China National Knowledge Infrastructure (CNKI), Weipu, and Wanfang, published from January 2010 to October 2023. Both randomized controlled trials and observational studies were included to compare those receiving EH and conventional anti-infective treatment. Meta-analysis was performed using RevMan 5.3 software after two evaluators independently screened the literature, extracted information, and evaluated the methodological quality of the included studies. The primary outcome indicators included in-hospital mortality (IHM) and length of ICU stay (LOS-ICU). Furthermore, the changes in T-helper 1/T-helper 2 (Th1/Th2) levels were analyzed and expressed as relative risk (RR), odds ratio (OR), or mean difference (MD) with corresponding 95% confidence interval (CI) as appropriate for the type of outcome measure.

Results This analysis included 30 studies (n = 2262) (1267 in the EH group and 995 in the conventional treatment group). We observed that EH treatment, such as hemopurification, hemofiltration, hemoperfusion, hemodialysis, and hemoadsorption, significantly reduced IHM in sepsis patients (RR = 0.75, 95% CI: 0.68–0.84, $p < 0.00001$). However, there was no significant impact on LOS-ICU (MD = –0.44, 95% CI: –2.29–1.41, p = 0.64). Subgroup analyses suggested that cytokine adsorption (OR = 0.69, p = 0.17) or polymyxin B blood perfusion (OR = 0.73, p = 0.06) did not reduce IHM in sepsis patients. Similarly, EH did not improve IHM in patients with septic acute renal failure (RR = 0.82, p = 0.27) and IHM in patients with burn-induced sepsis (RR = 0.59, p = 0.07). For sepsis patients with improved Th1/Th2 value of immune factor levels by EH, IHM was not significantly reduced (RR = 0.61, p = 0.08), and LOS-ICU also showed no significant difference (MD = 0.34, 95% CI: –5.92–6.60, p = 0.92).

Conclusion For sepsis patients without relevant contraindications, EH holds promise as an adjunctive therapy, but the modulation of immune factor levels during treatment does not consistently influence the LOS-ICU.

Key words: sepsis; extracorporeal hemopurification; intensive care units; T-helper 1; T-helper 2

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Introduction

Sepsis is a systemic inflammatory response syndrome induced by infection (Fleischmann-Struzek et al, 2020). Traditional treatment approaches for sepsis primarily include early goal-directed therapy, appropriate antimicrobial therapy, source control, and supportive care for organ dysfunction. Despite these conventional treatments, the sepsis-related mortality rate remains high (Markwart et al, 2020). Sepsis commonly originates from severe infections such as burns, trauma, severe pneumonia, or diffuse peritonitis. Without timely and effective treatment, it can develop into severe sepsis or even septic shock (Font et al, 2020). Primary death in patients often results from early complications of infection, such as metabolic acidosis, coagulation disorders, and hypoxemia, while secondary death is significantly associated with systemic inflammatory response syndrome, compensatory anti-inflammatory response syndrome, and ultimately multiple organ dysfunction syndrome (Zou et al, 2022). Effective modulation of the inflammatory response during the progression of sepsis proves effective in treating sepsis and serves as an efficient strategy to reduce in-hospital mortality (IHM).

Extracorporeal hemopurification (EH) has become a common clinical adjunctive therapy for sepsis. EH reduces sepsis-associated inflammatory mediators and cytokines levels through biological clearance (Zhang et al, 2021). Moreover, EH can attenuate the systemic inflammatory disorder induced by sepsis, thus helping to maintain the body's metabolic balance within a manageable range (Vorobii et al, 2019). In recent years, a range of novel EH treatments have emerged following the classical principle of EH, such as high-volume hemofiltration (Bilgrami et al, 2010), coupled plasma filtration and adsorption (Li et al, 2022), and polymyxin B blood perfusion.

The present study aims to explore treating sepsis patients using EH, a technology that has not been fully integrated into routine clinical practice. The options for EH modalities are vast; however, although the effectiveness of novel EH approaches has been demonstrated, their ability to improve IHM in septic patients remains controversial (Terayama et al, 2017). The main objective of this study is to examine the effect of EH on both overall IHM and immune function in septic patients by means of conducting a meta-analysis according to the PRISM 2020 checklist (**Supplementary Material**).

Methods

Literature Search

We searched relevant literature across multiple databases, including MEDLINE, AMED, Cochrane Library, Embase, PubMed, China National Knowledge Infrastructure (CNKI), Weipu, and Wanfang, published from January 2010 to October 2023. We focused on literature concerning EH and its impact on prognosis and immune cytokines in patients with sepsis. Search keywords include "hemopurification", "hemofiltration", "hemoperfusion", "hemodialysis", "hemoadsorption", "sepsis", "severe sepsis", "septic shock", "mortality", "in-hospital stay length", and "immunity function". To ensure comprehensive coverage of the literature, a secondary expanded search of the references of the included literature was conducted to incorporate additional relevant literature in this analysis.

Inclusion and Exclusion Criteria

The included article must satisfy the following criteria: (1) All selected studies used at least one type of EH treatment; (2) The research subjects had a precise clinical diagnosis of sepsis, severe sepsis, or septic shock based on the diagnostic criteria outlined in the 2019 American College of Thoracic Physicians/Consultative Conference on Critical Care Medicine (Hunt, 2019); (3) Randomized controlled trials and observational studies (prospective and retrospective cohort studies) that compared patients receiving EH combined with conventional anti-infective treatment versus conventional treatment alone were included; (4) The study subjects were divided into two groups: an EH group and an antibiotic treatment control group, with clear documentation of clinical prognosis; (5) The studies clearly reported the changes in immune-related cytokine levels among patients receiving EH treatment. However, studies were excluded from this meta-analysis if they fulfilled the criteria below: (1) Studies including patients with limited clinical infection lesions that have not progressed to sepsis; and (2) Studies demonstrating proportional models or survival curves as clinical prognosis data, making it impossible to precisely assess the relevant survival data.

Data Extraction

Two researchers independently performed literature search based on the predefined searching strategy. Subsequently, they reviewed and determined the inclusion of eligible studies. A third researcher was responsible for extracting relevant data for summarization and organization. The specific details were extracted, including the first author's name, publication years, patient numbers, EH methods, death rates, length of intensive care unit (ICU) stay (LOS-ICU), changes in immune function-related cytokine levels, and other relevant information.

Statistical Methods

For data with dichotomous outcomes, relative risks (RRs) or odds ratios (ORs) and corresponding 95% confidence intervals (CIs) were calculated as appropriate. For continuous outcomes, mean differences (MDs) and corresponding 95% CIs were calculated. For continuous outcomes, MDs and corresponding 95% CIs were calculated. The heterogeneity of $I^2 > 50\%$ was considered significant. Moreover, the fixed-effect model was utilized to combine outcome data if $I^2 < 50\%$, whereas the random-effect model was employed to combine outcome data when $I^2 > 50\%$. A p-value < 0.05 was considered statistically significant, unless otherwise stated. Statistical analyses were performed using Review Manager software (RevMan version 5.3, Cochrane Collaboration, Cambridge, UK).

Results

Literature Retrieval Process

An initial screening identified a total of 1770 articles. Finally, 30 articles that met the predefined inclusion criteria were included in the meta-analysis (Fig. 1). Out of the included studies, there were 25 articles related to EH and clinical prognosis (e.g., Zuccari et al, 2020; Mitaka et al, 2022) and 13 articles related to EH and LOS-ICU (e.g., Peng et al, 2010; Paul et al, 2021). Subgroup analysis was conducted on different EH treatment methods. Particularly, 5 articles (Friesecke et al, 2019; Hawchar et al, 2019; Kobashi et al, 2018; Shiga et al, 2014; Zuccari et al, 2020) reported the association between cytokine absorption and IHM, and 5 articles (Dellinger et al, 2018; Ichiyasu et al, 2017; Kim et al, 2019; Maynar et al, 2013; Srisawat et al, 2018) explored the correlation between polymyxin B blood fusion and IHM. Subgroups of patients with sepsis were analyzed based on their underlying comorbidities. Among these, 3 articles (Jin et al, 2022; Miao et al, 2018; Shiga et al, 2014) reported the association between EH and IHM in patients with sepsis combined with acute kidney injury, and 3 articles (Chung et al, 2017; Srisawat et al, 2018; Xu et al, 2014) revealed the association between EH and IHM in patients with burn-induced sepsis. Furthermore, 9 articles were included regarding the association between T-helper 1/T-helper 2 (Th1/Th2) values and clinical prognosis (Boss et al, 2021; Friesecke et al, 2019; Kobashi et al, 2018; Meng et al, 2018; Regiroli et al, 2023; Shiga et al, 2014; Wu et al, 2019; Xu et al, 2014; Zuccari et al, 2020), of which 3 articles (Jin et al, 2022; Meng et al, 2018; Wu et al, 2019) pertained to the association between Th1/Th2 values and LOS-ICU (Table 1).

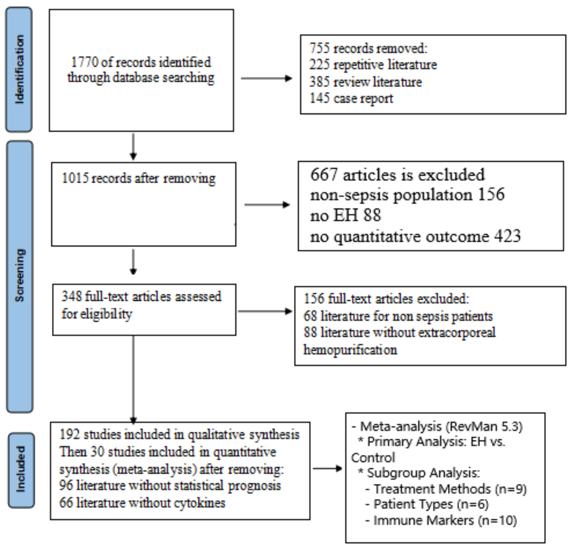

Fig. 1. PRISMA flow diagram for studies in this meta-analysis. EH, extracorporeal hemopurification.

Table 1. Clinical characteristics of the study population.

Studies	*n*	Average age (years)	Gender		Blood purification technique	Therapeutic method		In-hospital mortality		Th1/Th2 improvement		Length of ICU stay	
			Male	Female		Blood purification	Traditional treatment	Blood purification	Traditional treatment	Blood purification	Traditional treatment	Blood purification	Traditional treatment
Zuccari et al, 2020	9	–	5	4	Cytokine adsorption	6	3	2	2	1	–	–	–
Peng et al, 2010	155	56.0	110	65	High-volume hemofiltration	93	62	35	32	–	–	11.7	15.4
Wu et al, 2019	106	48.6	66	40	High-volume hemofiltration	78	28	25	18	35	–	13.8	14.6
Srisawat et al, 2018	22	73.6	9	13	Polymyxin B blood perfusion	15	7	3	4	–	–	5.6	6.7
Shum et al, 2014	15	74.3	–	–	Blood adsorption	7	8	1	3	–	–	12.5	5.3
Quenot et al, 2015	60	66.6	42	18	High-volume hemofiltration	29	31	6	10	–	–	21.6	20.7
Kim et al, 2019	40	67.3	24	16	Polymyxin B blood perfusion	20	20	10	10	–	–	10.9	14.6
Dellinger et al, 2018	450	59.9	273	177	Polymyxin B blood perfusion	224	226	78	85	–	–	–	–
Hawchar et al, 2019	20	65.6	13	7	Cytokine adsorption	10	10	1	3	–	–	10.2	10.0
Xu et al, 2014	22	31.3	19	3	Hemodialysis	11	11	1	4	6	8	–	–
Miao et al, 2018	155	56.0	110	45	High-volume hemofiltration	93	62	26	21	–	–	15.7	16.8
Vassallo et al, 2019	98	75.8	75	28	Coupled plasma filtration and adsorption	48	50	7	6	–	–	–	–
Regiroli et al, 2023	10	58.1	6	4	Hemofiltration	7	3	4	1	5	2	–	–
Boss et al, 2021	65	63.5	44	21	Hemofiltration	50	15	40	3	33	–	–	–
Friesecke et al, 2019	38	68.7	25	13	Cytokine adsorption	19	19	10	10	7	9	–	–
Jin et al, 2022	150	69.0	85	65	High volume hemofiltration	105	45	20	40	32	30	18.5	12.5
Kobashi et al, 2018	142	70.0	88	54	Cytokine adsorption	70	72	25	29	38	31	–	–
Maynar et al, 2013	21	74.3	9	12	Polymyxin B blood perfusion	14	7	3	3	–	–	5.4	6.1
Meng et al, 2018	76	60.3	50	26	High-volume hemofiltration	55	21	10	16	43	15	31.2	35.6
Livigni et al, 2014	184	65.3	121	63	Coupled plasma filtration and adsorption	91	93	41	44	–	–	65.6	66.2
Chung et al, 2017	48	46.5	35	13	High-volume hemofiltration	30	18	10	8	–	–	–	–
Ichiyasu et al, 2017	77	59.6	53	24	Polymyxin B blood perfusion	39	38	12	25	–	–	–	–
Ren et al, 2016	15	58.6	10	5	High-volume hemofiltration	8	7	2	3	–	–	–	–
Mitaka et al, 2022	103	65.0	68	35	Hemofiltration	50	53	20	32	–	–	–	–
Shiga et al, 2014	34	63.9	23	11	Cytokine adsorption	18	16	5	8	10	8	–	–
Paul et al, 2021	45	54.3	36	9	Cytokine adsorption	24	21	–	–	20	16	16.88	19.74
Franchi et al, 2016	21	62.1	15	6	Coupled plasma filtration and adsorption	10	11	–	–	8	8	–	–
Servillo et al, 2013	20	63.0	12	8	Hemofiltration	12	8	–	–	10	6	–	–
Guo et al, 2017	48	64.8	35	13	High-volume hemofiltration	24	24	–	–	20	20	–	–
You et al, 2018	13	66.2	8	5	High-volume hemofiltration	7	6	–	–	4	3	–	–

Th1/Th2, T-helper 1/T-helper 2; ICU, intensive care unit.

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Quality Assessment of the Included Literature

Quality assessment was performed using tools appropriate for each study design. For randomized controlled trials (RCTs), the Cochrane risk of bias assessment tool was applied, while the Newcastle-Ottawa Scale (NOS) was used for non-randomized studies. All 30 papers included in the review underwent quality evaluation.

Cochrane Risk of Bias Assessment Results

Twelve RCTs were evaluated using the Cochrane risk of bias assessment tool. Among them, four multicenter RCTs demonstrated a relatively low overall risk of bias: Dellinger et al (2018), Livigni et al (2014), Chung et al (2017), and Quenot et al (2015). Most RCTs showed high risk of bias in participant and personnel blinding, primarily due to the procedural nature of blood purification therapies that precluded effective blinding. Dellinger et al (2018) reduced blinding-related bias by employing sham treatment controls. The majority of studies exhibited low risk of bias in random sequence generation and incomplete outcome data, but information regarding allocation concealment and outcome assessment blinding was often insufficient, resulting in "unclear" risk ratings. Fig. 2 illustrates the bias risk map for these studies, while Fig. 3 provides a summary chart of the overall bias risk.

NOS Scores Results

Eighteen non-randomized studies were assessed using the NOS scoring system. Quality assessment results were as follows: high-quality studies (8–9 points) included Mitaka et al (2022), Kim et al (2019), Wu et al (2019), Miao et al (2018), Ren et al (2016), and Zuccari et al (2020); moderate-quality studies (6–7 points) included Kobashi et al (2018), Ichiyasu et al (2017), Paul et al (2021), Franchi et al (2016), Maynar et al (2013), Friesecke et al (2019), Boss et al (2021), and Xu et al (2014); lower-quality studies ($\leq$5 points) included Servillo et al (2013), Shiga et al (2014), Regiroli et al (2023), and Vassallo et al (2019). The detailed results of the NOS assessment are shown in Table 2.

Associations of EH With IHM and LOS-ICU

The association between different EH treatment methods and IHM was investigated in 24 studies. Our forest plot analysis revealed that EH treatment significantly reduced the overall IHM (RR = 0.75, 95% CI: 0.68–0.84, $p < 0.00001$, with moderate heterogeneity among studies [I^2 = 47%], Fig. 4). Additionally, 13 articles reported the impact of different EH treatment methods on LOS-ICU, indicating that EH treatment did not affect the overall LOS-ICU (MD = –0.44, 95% CI: –2.29–1.41, $p = 0.64$, with high heterogeneity [I^2 = 86%], Fig. 5).

Subgroup Analysis

The impact of cytokine absorption therapy on IHM was investigated in 5 studies. The results showed that compared to the conventional hemofiltration techniques, cytokine absorption therapy did not improve the clinical prognosis of pa-

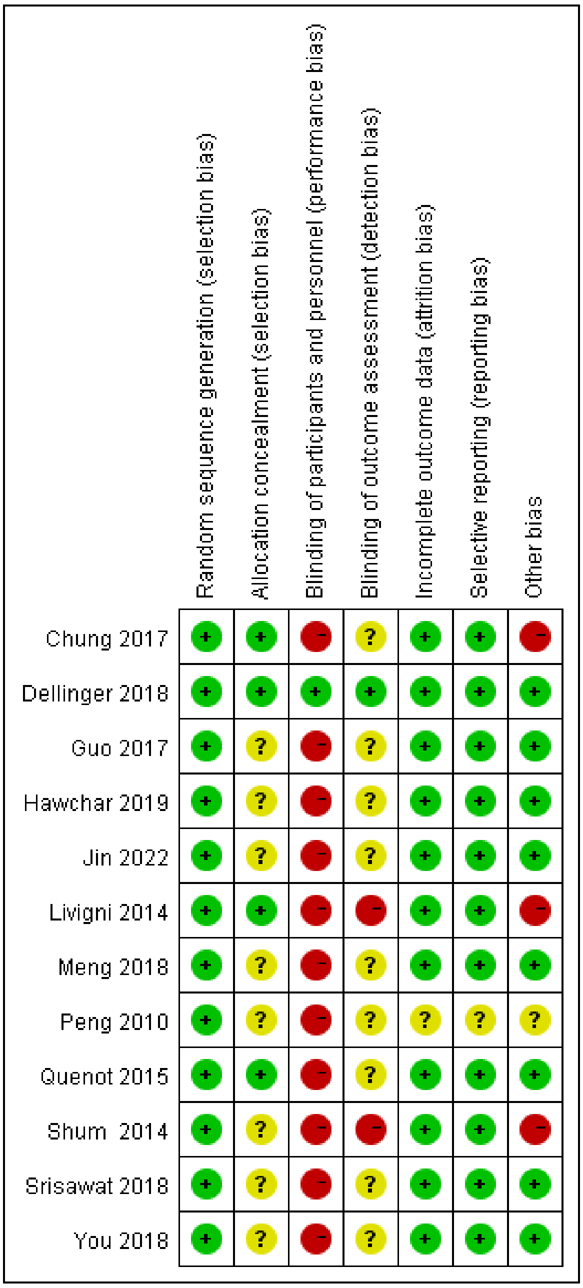

Fig. 2. The bias risk map of this meta-analysis.

tients (OR = 0.69, 95% CI: 0.41–1.17, p = 0.17, Fig. 6). Furthermore, five studies that examined the association between polymyxin B blood perfusion treatment and IHM indicate that the addition of polymyxin B blood perfusion is not effective in reducing IHM compared to conventional hemoperfusion techniques (OR = 0.73, 95% CI: 0.53–1.02, p = 0.06, Fig. 7). Moreover, three research papers focusing on patients with sepsis combined with renal injury showed that EH did not effectively improve the clinical prognosis of patients in this subgroup (RR = 0.82, 95% CI: 0.58–1.16, p = 0.27, Fig. 8). Furthermore, three studies reported that EH did not significantly reduce the IHM among burn-induced sepsis patients (RR = 0.59, 95% CI: 0.33–1.04, p = 0.07, Fig. 9). Additionally, ten studies have investigated the changes in cytokine Th1/Th2 value during EH treatment, along with the correla-

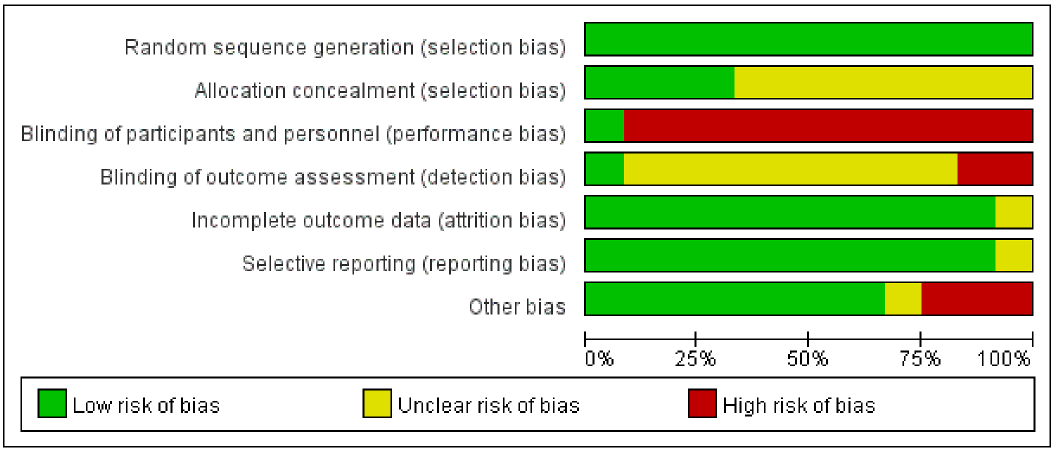

Fig. 3. A summary chart of bias risk.

tion between the levels of changes and IHM. After treatment, IHM in patients with improved Th1/Th2 values did not show significant improvement (RR = 0.61, 95% CI: 0.36–1.05, p = 0.08, Fig. 10). The relationship between changes in Th1/Th2 values during EH treatment and overall LOS-ICU was examined in 3 studies. The analysis demonstrated that patients with improved Th1/Th2 values did not show a significant difference in LOS-ICU (MD = 0.34, 95% CI: –5.92–6.60, p = 0.92, Fig. 11). A random-effect model was used for this analysis due to the high heterogeneity observed (I^2 = 94%).

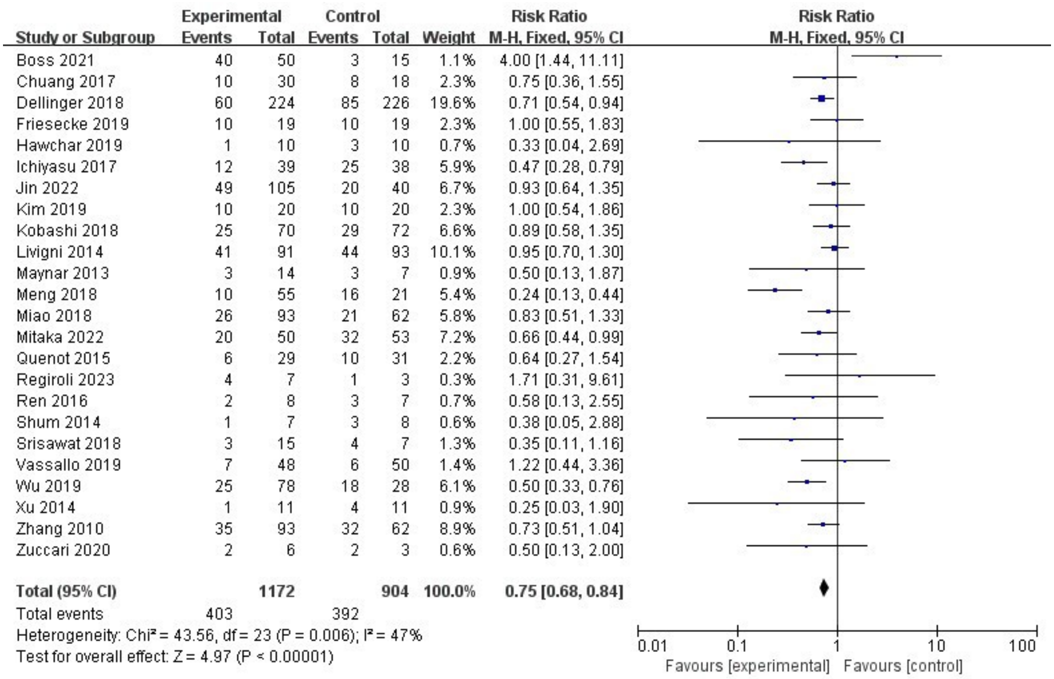

Fig. 4. Association between extracorporeal hemopurification and in-hospital mortality in sepsis patients. CI, confidence interval.

Table 2. Detailed Newcastle-Ottawa Scale (NOS) quality assessment results.

Study	Selection bias (max 4)	Comparability bias (max 2)	Outcome bias (max 3)	NOS score	Quality category
Mitaka et al, 2022	3	2	3	8	High quality
Kim et al, 2019	3	2	3	8	High quality
Wu et al, 2019	3	2	3	8	High quality
Miao et al, 2018	3	2	3	8	High quality
Ren et al, 2016	3	2	3	8	High quality
Kobashi et al, 2018	2	2	3	7	Moderate quality
Ichiyasu et al, 2017	3	1	3	7	Moderate quality
Paul et al, 2021	3	2	2	7	Moderate quality
Franchi et al, 2016	3	2	2	7	Moderate quality
Maynar et al, 2013	3	1	2	6	Moderate quality
Friesecke et al, 2019	2	2	3	7	Moderate quality
Boss et al, 2021	2	2	3	7	Moderate quality
Zuccari et al, 2020	3	2	3	8	High quality
Xu et al, 2014	2	1	3	6	Moderate quality
Servillo et al, 2013	2	1	2	5	Low quality
Shiga et al, 2014	2	1	2	5	Low quality
Regiroli et al, 2023	2	1	1	4	Low quality
Vassallo et al, 2019	2	1	2	5	Low quality

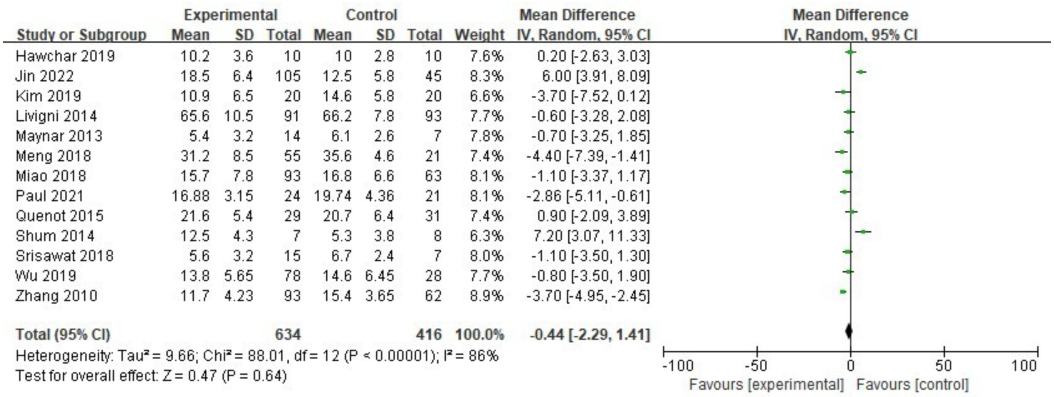

Fig. 5. Association between extracorporeal hemopurification and length of intensive care unit (ICU) stay (LOS-ICU) in sepsis patients.

Discussion

In recent years, various studies have investigated whether patients with sepsis can benefit from EH treatment, yielding diverse results. One study has shown that EH treatment significantly improves clinical prognosis, reduces IHM, and improves patients' clinical symptoms. Jin et al (2022) used high-volume hemofiltration to treat patients with sepsis complicated with acute kidney injury. The results showed that high-volume hemofiltration significantly increased the Th1 percentage and the Th1/Th2 ratio, reduced mortality, significantly reduced the Sequential Organ Failure Assessment (SOFA) score, and shortened the LOS-ICU. Furthermore,

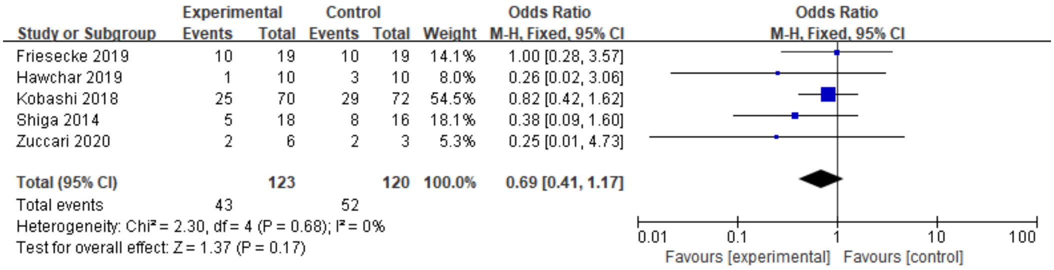

Fig. 6. Effect of cytokine adsorption therapy on in-hospital mortality in sepsis patients receiving extracorporeal hemopurification.

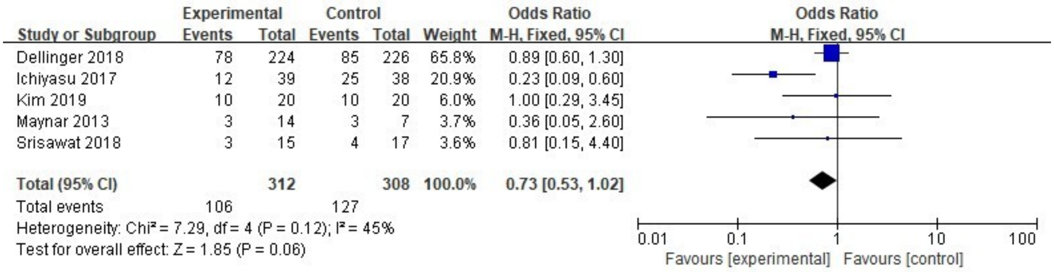

Fig. 7. Effect of polymyxin B blood perfusion on in-hospital mortality in sepsis patients receiving extracorporeal hemopurification.

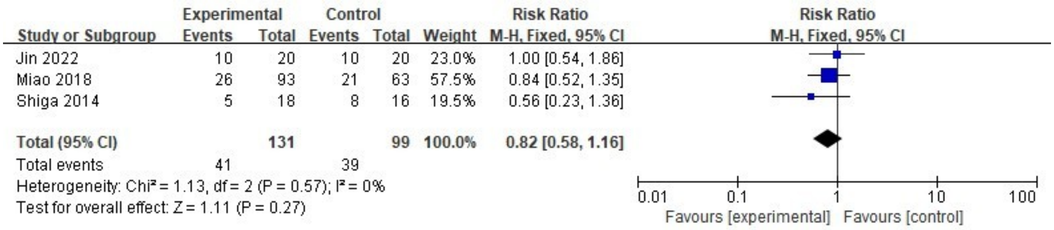

Fig. 8. In-hospital mortality in sepsis patients with acute kidney injury receiving extracorporeal hemopurification.

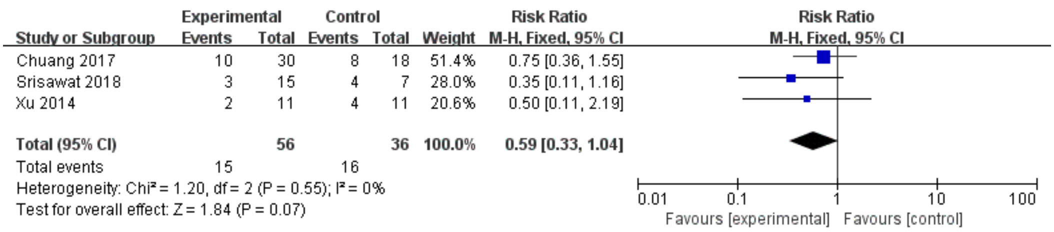

Fig. 9. In-hospital mortality in patients with burn-induced sepsis receiving extracorporeal hemopurification.

Friesecke et al (2019) confirmed that cytokine absorption can improve the immune function of patients with sepsis. Dellinger et al (2018) used polymyxin B blood perfusion to treat patients with septic shock, revealing a significant reduction in the incidence of multiple organ dysfunction syndrome and lower death rates. Additionally, in their study of organic immune imbalance, Guo et al (2017) found

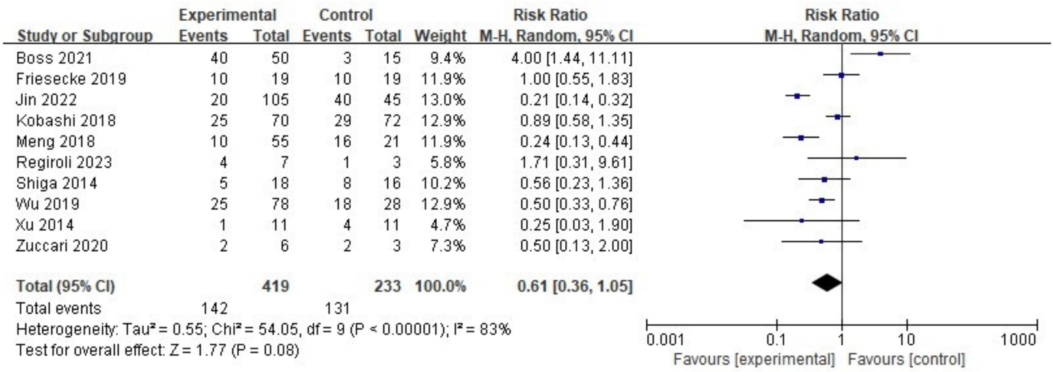

Fig. 10. Association between Th1/Th2 value improvement and in-hospital mortality in sepsis patients receiving extracorporeal hemopurification.

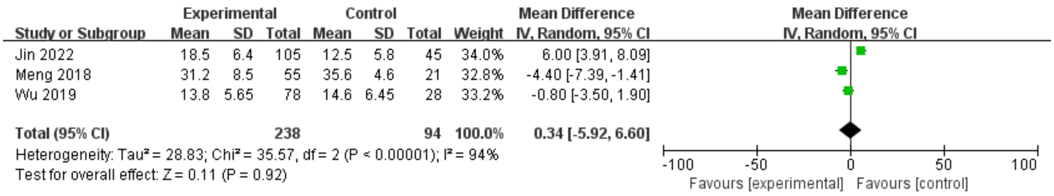

Fig. 11. Association between Th1/Th2 value improvement and length of ICU stay in sepsis patients receiving extracorporeal hemopurification.

a significant decrease in SOFA scores in sepsis-induced multiple organ dysfunction syndrome patients receiving high-volume hemofiltration. Meng et al (2018) demonstrated that high-volume hemofiltration significantly reduced the level of inflammatory factors, shortened LOS-ICU, and improved patients' immune function. You et al (2018) showed that high-volume hemofiltration significantly improved 90-day survival rates among patients with burn-induced sepsis.

On the contrary, some studies have demonstrated that EH treatment does not affect the prognosis of sepsis patients. Possible hypotheses for these outcomes include: (1) The "threshold immune regulation hypothesis": EH treatment may eliminate cytokines from the blood, leading to an imbalance in the ratio of cytokines between tissue and blood, thereby promoting the transfer of cytokines from the tissue to the blood. Consequently, the concentration of harmful cytokines in the body fluid cycle does not decrease. (2) The "peak clearance hypothesis": EH treatment eliminates harmful components from the blood, accompanied by the clearance of therapeutic elements such as nutrients and antibiotics, resulting in no significant change in the proportion of various components in the overall body fluid circulation. Kim et al (2019) indicated that polymyxin B blood fusion treatment for septic shock could reduce serum inflammatory factor levels; however, it did not have a significant effect on IHM and LOS-ICU. Hawchar et al (2019) found that early extracorporeal cytokine adsorption therapy is a safe method for treating individuals with septic shock and has a significant impact on norepinephrine demand, procalcitoninogen and big endothelin-1 concentrations, instead of on LOS-ICU and IHM. Numerous studies have compared novel EH method with classical EH therapy in the treatment of sepsis and have revealed that the former has limited efficacy in improving long-term survival. Particularly, multiple studies have suggested that cytokine adsorption therapy failed to reduce overall IHM (Boss et al, 2021; Friesecke et al, 2019; Hawchar et al, 2019; Kobashi et al, 2018; Zuccari et al, 2020). Furthermore, studies related to polymyxin B blood perfusion therapy showed that it did not significantly improve IHM (Dellinger et al, 2018; Ichiyasu et al, 2017; Kim et al, 2019; Maynar et al, 2013; Srisawat et al, 2018).

In this study, the impact of EH on patients with sepsis was investigated, particularly in terms of clinical prognosis using IHM and LOS-ICU as the relevant parameters. We also analyzed outcomes among patients receiving various types of novel EH methods, encompassing those with underlying comorbidities, and independently studied the impact of the change in cytokine Th1/Th2 levels. The findings showed that in patients with sepsis, although EH intervention did not reduce LOS-ICU, their judicious use of EH therapy significantly reduced overall IHM and improved long-term prognosis. Recently, the use of standardized EH treatments has proven to be sufficiently effective, yet the clinical use of novel EH still needs to be validated. In patients with sepsis and comorbidities, EH treatment is not yet sufficient to improve their clinical prognosis, and active treatment of the primary disease and control of comorbidities remain the focus of treatment for this group of patients. Moreover, among patients with improved values of the immune cytokine Th1/Th2 during EH treatment, their LOS-ICU was not significantly shortened, neither were the IHM rates being substantially reduced. Results from other individual studies are also highly heterogeneous, with some reporting increased LOS-ICU while others showing decreased LOS-ICU. This suggests that the impact of immune modulation in patients receiving EH on their hospitalization- and mortality-related prognosis may be influenced by additional factors not captured in the current analysis.

Several limitations of this study need to be acknowledged: (1) Only studies focusing on cytokine adsorption and polymyxin B blood perfusion were included in this meta-analysis as novel EH treatments. High-volume hemofiltration and hemofiltration were not included in the analysis due to incomplete data and limited literature. (2) In the present analysis, quantitative changes in Th1/Th2 concentration were not captured; instead, only the number of cases associated with the ordinally stratified categories of Th1/Th2 levels was analyzed. (3) Heterogeneity tests were not performed, and the literature included in the analyses only contains a small number of heterogeneous studies.

Conclusion

In summary, for patients with sepsis, EH treatment offers significant benefits as an adjunctive therapy to the standardized treatment. Nevertheless, the current meta-analysis was unable to demonstrate a consistent effect of immune cytokine modulation on patients' LOS-ICU, despite that such a beneficial impact is theoretically possible.

Key Points

- Extracorporeal hemopurification significantly reduces overall in-hospital mortality in sepsis patients.
- The relationship between immune factor modulation during EH treatment and length of ICU stay remains inconclusive, due to high heterogeneity among studies included.
- Novel EH approaches show promise but require further optimization for clinical implementation.

Availability of Data and Materials

The data underlying this meta-analysis were retrieved from systematic searches of eight databases: MEDLINE, AMED, Cochrane Library, Embase, PubMed, China National Knowledge Infrastructure (CNKI), Weipu, and Wanfang (January 2010 to October 2023). The detailed research strategies are provided in the the Methods section. Reference lists of included studies were also searched.

Author Contributions

JQ, KKW, JJL made substantial contributions to conception and design. FFZ performed the acquisition and analysis of data. KKW drafted the manuscript. All authors contributed to important editorial changes in the manuscript. All authors gave final approval of the version to be published. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://www.magonlinelibrary.com/doi/suppl/10.12968/hmed.2024.0651.

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