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Comparing adsorptive blood purification modalities for sepsis patients: A systematic review and network meta-analysis

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ABSTRACT

Purpose: Hemoadsorption is a promising therapeutic modality for sepsis, however, the most effective approach is unknown. This meta-analysis aimed to compare the efficacy of different adsorptive blood purification (ABP) modalities in patients with sepsis.

Materials and methods: Randomized controlled trials (RCTs) investigating the clinical efficacy of ABP modalities in patients with sepsis were retrieved from English databases from inception up to October 14, 2024. The data were analyzed using Stata15 and R software. Quality assessment and publication bias were assessed using the Cochrane Risk of Bias Assessment Tool and funnel plots, respectively. The outcomes of the meta-analysis were hospital mortality, oxygenation index, ICU stay days, and blood lactate concentration.

Results: A total of 47 RCTs were identified, comprising 9 ABP modalities. In terms of cumulative ranking probability, the HA330 modality achieved the highest reduction in hospital mortality (99.5 %) and ICU stay days (97.2 %), whereas CPFA showed the highest reduction in oxygenation index (94.9 %) and oXiris had the highest reduction in lactate (95.7 %).

Conclusions: HA330 and PMX showed superior overall efficacy in sepsis patients compared with other modalities, although there was potential heterogeneity. However, further RCTs with large samples are advocated to test new approaches of hemosorption and validate the present findings.

1. Introduction

Sepsis (sepsis 3.0) is a life-threatening organ dysfunction caused by impaired immune response to infection [1]. Severe circulatory, cellular, and metabolic abnormalities induce septic shock in sepsis patients and may significantly increase morbidity and mortality. Most critically ill patients develop sepsis, which accounts for about 29.5 % of patients in intensive care units (ICUs) according to a worldwide survey. It has been reported that the in-hospital case fatality rate for these patients is as high as 35.3 % [2], and sepsis represents 19.7 % of all deaths globally. Studies have shown that the lung is a common site of infections that trigger sepsis [3,4], implying that the lung, especially in the context of lower respiratory tract infections, is a common origin of infections that trigger sepsis. This underscores the need to investigate sepsis across various disciplines including respiratory medicine. Although age-standardized morbidity and mortality rates have declined, sepsis continues to be a major cause of global health deterioration and is one of the serious challenges currently facing healthcare systems worldwide [4]. The conventional treatment regimen for sepsis consists of antibiotics which target to eliminate the infected foci, and symptomatic supportive therapy that controls inflammatory response in sepsis. Besides, extracorporeal blood purification therapy is often applied as an adjunctive therapy that corrects the immune imbalance. Theoretically, it has been suggested that blood purification can reduce the mortality rate of sepsis patients [5] by modulating the inflammatory cascade response as well as eliminating endotoxin and inflammatory mediators. Consequently, blood purification has become a popular research topic in the management of sepsis. However, it cannot completely cure sepsis treatment when applied alone. Randomized Controlled Trials (RCTs) have reported that continuous renal replacement therapy (CRRT) does not

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significantly reduce the plasma concentration of sepsis-associated inflammatory mediators, morbidity, and mortality [6–8]. Although high-dose CRRT can clear inflammatory factors, it has limited clinical efficacy in sepsis and does not significantly improve the prognosis of sepsis patients [9,10]. Although some studies have explored the timing of the initiation of blood purification modalities, such as CRRT, the results of such investigations are inconclusive. It is, however, speculated that the newly discovered ABP may be a promising therapeutic modality for sepsis. Among the modalities of CRRT, ABP involves the use of specific adsorbent materials to selectively remove harmful substances (such as toxins, inflammatory mediators, etc.) from the blood. The adsorbent materials exhibit specific affinity and binding capacity for target substances, promoting blood purification and restoration of the normal physiological state of the body. Basic and clinical studies have demonstrated that ABP can effectively improve sepsis, especially in patients with septic shock [11,12]. Several types of ABP such as oXiris, endotoxin adsorption with polymyxin (PMX), HA resin adsorption, and cytokine adsorption, have been applied in clinical practice. However, the optimal ABP treatment has not been clarified. In this retrospective study, we compared the efficacy of different ABP modalities in sepsis patients to provide an evidence-based basis to guide future decision-making regarding the application of ABP.

2. Material and methods

2.1. Inclusion criteria were

(1) RCTs; (2) Patients who met the diagnostic criteria for sepsis (considering differences in publication time, definitions of sepsis 1.0–3.0 were adopted), with no restriction on age, gender, or case origin; (3) Interventions: the treatment group included various ABP modalities (Table 1), and the control group included any one of the blood purification therapies (excluding ABP modalities) or standard therapy (ST). Standard therapy was defined as the application of fluid resuscitation, anti-infection, and other routine treatments that do not include blood purification. In renal replacement therapy (RRT) for sepsis patients, CRRT is often applied in combination with ABP. Therefore, in this systematic review, we included CRRT (such as CVVHD, CVVHDF, CVVH, without distinguishing treatment doses) as a separate intervention.

Table 1
Adsorptive blood purification (ABP) modalities.

Program	Blood adsorption
HA330HP	Adsorption of endotoxin and inflammatory factors by HA resin using polymer HA resin filters in tandem with CRRT or alone
PMXHP	Adsorption of endotoxin using an adsorbent cartridge (Toraymyxin) made of polystyrene fibers combined with polymyxin B.
CPFA	Combination of plasma perfusion, hemosorption, and hemofiltration, where plasma is first separated by a high retention membrane, and plasma is then passed through an adsorbent column for adsorption of inflammatory factors or endotoxins, and the adsorbed plasma is reintroduced into a second filter for filtration.
oXiris	Combining diffusion, convection, and adsorption; it is the only blood purification method that can simultaneously remove endotoxin and inflammatory factor.
Cytosorb	Cytokine adsorption column to adsorb cytokines and inflammatory mediators.
CRRT	Removal of water and small and medium molecular weight solutes by convection and diffusion, such as CVVH, CVVHDF, plasma exchange; bimodal plasma exchange were not included in the study.
OEAHP	other endotoxin adsorption hemoperfusion, including LPS, iHSA, Alteco, etc.
ST	Routine treatments for sepsis that do not include blood purification, such as fluid resuscitation, anti-infection, etc., categorizing STs that include CRRT in the original text as CRRT

Note: CRRT-related studies were also included to compare the differences between CRRT modalities with the addition of ABP and conventional CRRT since most adsorption-based treatment modalities are often used in combination with CRRT.

Adoption of this literature search method allowed us to compare the indicators in the absence and presence of ABP; (4) Primary outcome indicators: hospital mortality was defined as patient death while receiving treatment during the RCT study. (5) Secondary outcome indicators: oxygenation index, ICU hospitalization days and blood lactate.

2.2. Exclusion criteria

(1) Studies with no full text and studies with unclear diagnostic criteria and efficacy evaluation criteria; (2) Duplicate studies, literature reviews, case reports, animal experiments, conference abstracts, dissertations, etc.

2.3. Search strategy and data extraction

The search was conducted using a combination of subject terms + free words. The key subject terms included "Sepsis, Adsorption, Hemoperfusion, Blood-purification, oXiris, Cytosorb". Two investigators (Xing and Wei) independently searched the PubMed, Embase, Cochrane Library, and Web of Science databases to identify relevant RCTs, as well as reviews and meta-analyses related to the topic. The search was conducted from database inception up to October 14, 2024. (The details of the search strategy are presented in Supplementary Material 1). Literature screening and data extraction were independently conducted after the literature search, and any disagreements were resolved by discussion. The main data extracted from the studies were the authors, country, year of publication, number of cases, age, sex, interventions and controls, blood creatinine, sepsis type, and outcome indicators.

2.4. Literature acquisition and quality evaluation

(1) The extracted data were imported into Endnote literature management software. The two investigators screened the studies independently by reading the titles and abstracts, followed by full-text reading to extract and organize the relevant data. Any discrepancies were solved through discussion or by seeking help from a third person. (2) The quality of the included literature was evaluated using the Cochrane Risk of Bias Assessment Tool (Cochrane Handbook of Systematic Evaluation). This tool uses the following; randomization method; whether allocation concealment was applied correctly; whether subjects and implementers were blinded; whether the evaluators of the results were blinded; the completeness of the data and the results; the selective reporting; and the other bias situations.

2.5. Statistical analysis

Stata15 and the GeMTC package in R software were used for data analysis. The odds ratio and mean difference were selected as the effect size for dichotomous variables and continuous variables, respectively (expressed by 95 % confidence interval (CI)). The odds ratio and mean difference were statistically significant when the 95 % CI of the OR value did not include the effect line 1 or the 95 % CI of the MD value did not include the effect line 0, depending on the OR value. Heterogeneity among studies was evaluated using the I^2 test. If $I^2 < 50\ \%$ and $P > 0.1$ indicated no statistical heterogeneity among studies, and a fixed-effects model was used for analysis, otherwise a random-effects model was used. The area under the cumulative ranked probability map (SUCRA) was calculated to predict the efficacy ranking of each intervention. A network plot was constructed to display the comparison results between various intervention measures. In the network plot, each circle represents an intervention measure and the edges represent existing comparisons. The size of the circles is proportional to the number of patients included. Inconsistency between direct and indirect evidence was detected using the node-splitting method when there was a closed loop in the network plot. Finally, funnel plots were established to explore potential publication bias.

3. Results

3.1. Literature search

The initial search identified 1213 relevant studies, which contained 354 duplicates. After the removal of the duplicates, an additional 762 studies were eliminated after reading the titles and abstracts, retaining 97 studies for further screening. Moreover, we identified 11 additional studies from other sources. The full texts of the remaining studies were screened, which led to the identification of 47 studies suitable for the final analysis. The screening process is presented in Fig. 1.

3.2. Basic characteristics of the included studies

The included studies [13–58] were published between 1995 and 2024, and contained 3229 cases involving 9 interventions. The detailed basic information is shown in Table S1 of Supplementary Material 2. Among the included studies, 5 articles investigated the use of HA330, with 3 articles involving a combination of this approach with CRRT. Four studies explored the application of OEAHP, including 2 on LPSHP, 1 on ISHA, and 1 on Alteco. Due to the small sample size and considering that all were based on endotoxin adsorption but with different products from various companies, the interventions were merged for analysis.

3.3. Quality evaluation

The overall quality of the 47 studies was classified as high, and there was no follow-up bias. One [56] did not mention the randomization method used. In addition, most studies did not clarify whether blinding was performed and whether there were other biases. The specific risk of bias assessment is detailed in Figs. 2 and 3.

3.4. Reticulated meta-analysis

3.4.1. Hospital mortality

A total of 37 studies (involving 7 interventions and 941 patients) reported hospital mortality. Analysis of the network plot (Fig. 4A) identified a closed loop in the network, necessitating the use of local inconsistency test in the analysis. It was observed that there was no difference in direct comparison, indirect comparison, and network comparison between HA330, CRRT, ST, and CPFA ($P>0.05$) (Figure S1 of Supplementary Material 2). High heterogeneity ($I^2>50\ \%$) was observed among the studies that compared CRRT and ST with CPFA, HA330 with CRRT, PMX with ST, but no heterogeneity ($I^2<50\ \%$) was found among studies comparing CRRT, CytoSorb, HA330, and OEAHP with ST (Figure S2 of the Supplementary Material 2). Compared with standard treatment, the application of PMX [OR = 0.74, 95 % CI (0.57,0.94)] and HA330 [OR = 0.34, 95 % CI (0.17,0.61)] achieved a more significant reduction in in-hospital mortality (Fig. 4B). In the cumulative ranking probability of the comparison network, HA330 (99.5 %) was ranked the highest, followed by PMX (71.3 %), CRRT (58.1 %), CPFA (52.6 %), ST (33.8 %), OEAHP (28.7 %), CytoSorb (5.9 %). The cumulative probability plot (Fig. 4C) exhibited a large area under the curve suggesting higher cumulative ranking probability and good intervention effect. Results of the pairwise comparison results between different intervention measures are presented in the in-hospital mortality league table (Table 2), with shaded areas indicating $P < 0.05$. Notably, HA330 showed the best performance among the intervention measures, while PMX showed significantly better effects on CytoSorb and ST.

3.4.2. Oxygenation index

Overall, 12 studies comprising 7 interventions and 444 patients investigated the oxygenation index(Fig. 5A). High heterogeneity was found between studies comparing CRRT and ST ($I^2>50\ \%$), but no heterogeneity was detected among other studies ($I^2<50\ \%$) (Figure S3 of Supplementary Material 2). Compared to standard treatments, CPFA [OR = 109.93, 95 % CI (58.57, 158.92)], CRRT [OR = 41.14, 95 % CI (31.28, 50.88)], HA330 [OR = 33.70, 95 % CI (11.39, 56.16)] significantly improved the oxygenation index (Fig. 5B). In the cumulative ranking probability of the comparison network, CPFA (94.9 %) had the highest performance, followed by CytoSorb (77.6 %), HA330 (71.7 %), CRRT (64.9 %), PMX (27.9 %), ST (19.6 %), OEAHP (9.3 %). Analysis of the cumulative probability plot (Fig. 5C) and league table (Table S2 of Supplementary Material 2) revealed that CPFA was superior to CRRT, HA330, PMX, and ST; CRRT was superior to PMX and ST; and HA330 was superior to PMX and ST.

3.4.3. ICU hospitalization days

In the analysis of ICU hospitalization days, 17 studies comprising 8 interventions and 823 patients were identified (Fig. 6A). High heterogeneity was found between studies comparing HA330 and ST ($I^2>50\ \%$), but no heterogeneity was detected among other studies ($I^2<50\ \%$) (Figure S4 of Supplementary Material 2). Compared with standard treatments, HA330 [MD = −5.64, 95 % CI, (−6.87, −4.41)] and CRRT [MD = −4.71, 95 % CI, (−4.99, −4.36)] significantly reduced ICU stay, whereas PMX [MD = 2.38, 95 % CI, (0.87, 3.90)] significantly increased the ICU stay (Fig. 6B). In the cumulative ranking probability of network

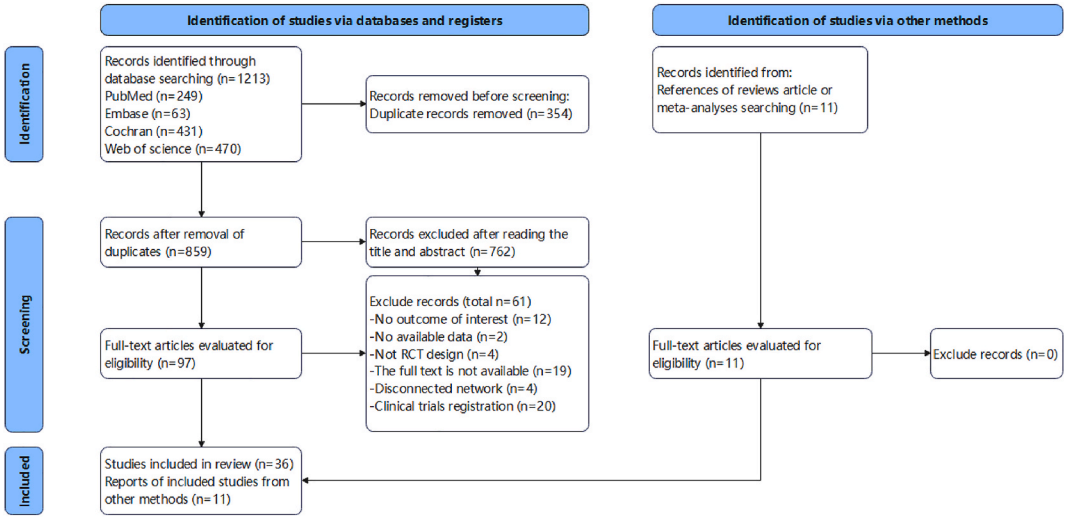

Fig. 1. Flow chart showing the screening process.

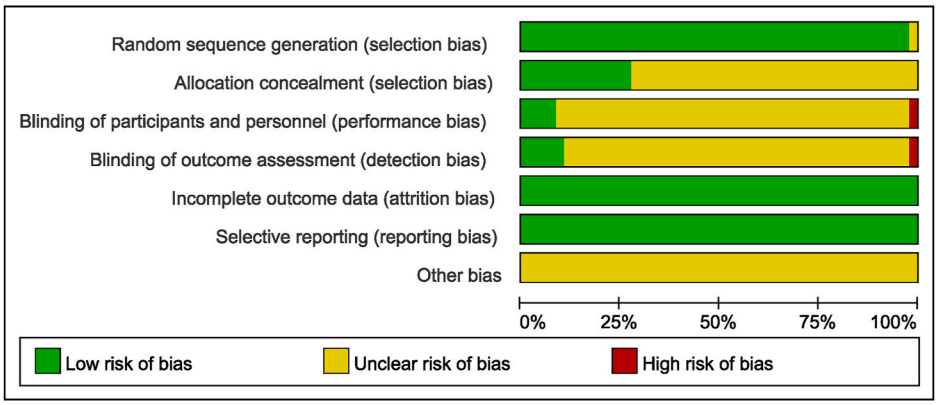

Fig. 2. Risk of bias graph.

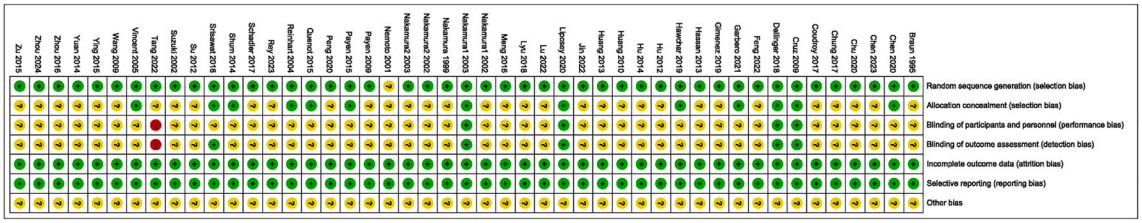

Fig. 3. Risk of bias summary.
Note: Different colors (green, red, yellow) and symbols ("+", "-", "?") are used in the figure to represent "low-risk bias", "high-risk bias", and "unclear", respectively. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

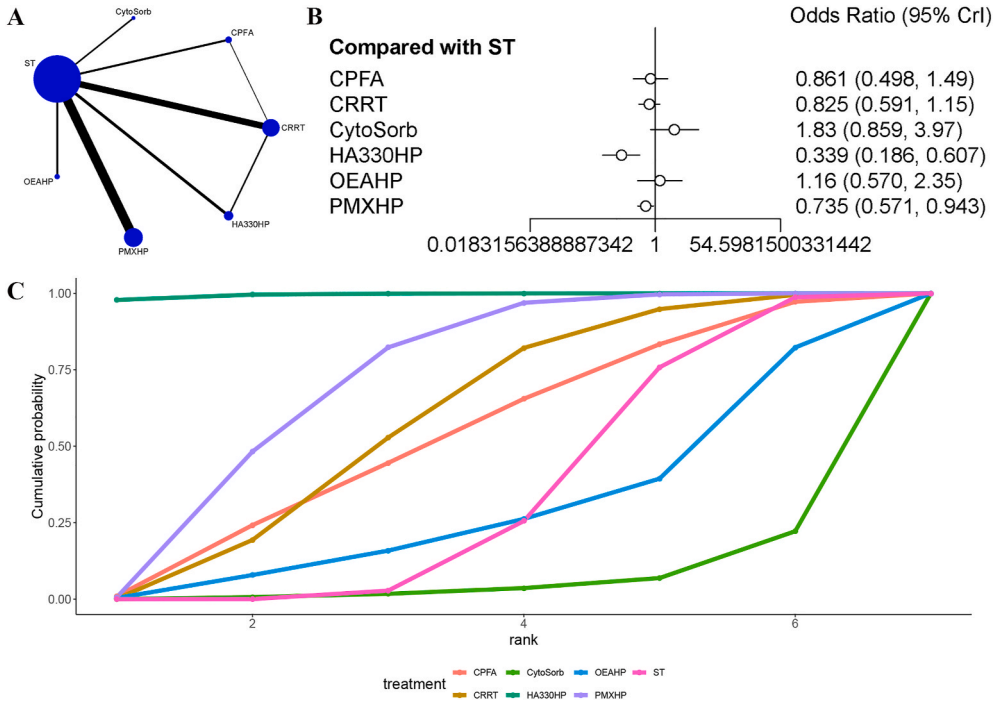

Fig. 4. **(A)** The network plot of hospital mortality. Each circle corresponds to an intervention measure and the edges represent existing comparisons. The size of the circles is proportional to the number of patients included. **(B)** The forest plot of hospital mortality. If OR>1, it indicates that the efficacy is better than standard treatment. The vertical line in the figure is an invalid line, and if the 95 % CI intersects with the invalid line, the result is not statistically significant. **(C)** The cumulative probability plot of hospital mortality. Each colored line represents an intervention measure, and the larger the area under the curve, the higher the cumulative ranking probability and the better the intervention effect.

comparison, the HA330 was the best (97.2 %), followed by CRRT (77.8 %), HA330 (87.6 %), CPFA (60.7 %), OEAHP (49.7 %), CytoSorb (30.9 %), ST (29.3 %), PMX (4.4 %). Further examination of the cumulative probability plot (Fig. 6C) and league table (Table S3 of Supplementary Material 2) demonstrated that HA330, CRRT, CPFA, OEAHP, and ST were superior to PMX; HA330 was superior to OEAHP and ST; CRRT was

Table 2
The league table of hospital mortality. OR = Odds Ratio.

OR(95%CI)						
CRRT	CPFA 1.04 (0.56, 1.94)	CRRT				
CytoSorb	0.47 (0.18, 1.2)	0.45 (0.19, 1.03)	CytoSorb			
HA330HP	2.54 (1.15, 5.68)	2.43 (1.3, 4.64)	5.42 (2.07, 14.37)	HA330HP		
OEAHP	0.74 (0.3, 1.82)	0.71 (0.33, 1.55)	1.58 (0.56, 4.51)	0.29 (0.12, 0.73)	OEAHP	
PMXHP	1.17 (0.64, 2.13)	1.12 (0.74, 1.71)	2.5 (1.12, 5.63)	0.46 (0.24, 0.87)	1.58 (0.75, 3.33)	PMXHP
ST	0.86 (0.5, 1.49)	0.83 (0.59, 1.15)	1.83 (0.86, 3.97)	0.34 (0.19, 0.61)	1.16 (0.57, 2.35)	0.73 (0.57, 0.94)

Note: Each data item in the table represents the comparison results of two intervention measures. If the data is greater than 1, it indicates that the intervention measures on the left side of the data are better than those at the top of the data, and the shadow indicates that the comparison results between the two are statistically significant.

better than ST.

3.4.4. Lactate

Ten studies involving 8 interventions and 367 patients investigated blood lactate levels as shown in Fig. 7A. There was no heterogeneity among the studies ($I^2 < 50\ \%$) (Figure S5 of the Supplementary Material 2). Compared to standard treatments, OXiris [MD = −7.24, 95 % CI (−12.59, −1.86)], AN69 [MD = −6.51, 95 % CI, (−12.11, −0.89)], CRRT [MD = −2.73, 95 % CI, (−3.93, −1.54)], HA330 [MD = −2.33, 95 % CI, (−3.67, −0.99)], OEAHP [MD = −0.92, 95 % CI, (−1.78, −0.07)] significantly reduced blood lactate level (Fig. 7B). In the cumulative ranking probability of network comparison, oXiris was the best (95.7 %), followed by AN69 (85.3 %), CRRT (71.5 %), HA330 (58.8 %), OEAHP (39.7 %), ST (18.8 %), Cytosorb (16.2 %), and PMX (14.0 %). In the cumulative probability plot (Fig. 7C) and league table (Table S4 of Supplementary Material 2), the OXiris outperformed CytoSorb, OEAHP, PMX, and ST; AN69 was superior to CytoSorb, PMX, and ST; HA330 was better than PMX and ST; OEAHP was better than ST and inferior to CRRT.

3.5. Publication bias

Comparison-corrected funnel plots revealed the existence of slopes in studies investigating oxygenation indexes, hospital mortality, ICU days of hospitalization, and blood lactate, indicating the possibility of publication bias and small-sample effects (Fig. 8).

4. Discussion

The ABP modalities are increasingly considered as important treatment strategies for sepsis in current clinical practice. In this meta-analysis, ABP showed superior efficacy to simple CRRT in terms of improving in-hospital mortality and ICU length of stay, which is consistent with findings from previous studies. This indicates that ABP can effectively treat sepsis.

A previous meta-analysis compared the effectiveness and safety of all blood purification options in sepsis and severe infections. The analysis reported that plasma exchange and PMX showed promising potential to improve the prognosis of sepsis [59]. However, previous meta-analyses and RCT studies have not clarified the best ABP modality in the management of sepsis patients. In the present study, we compared the effects of different ABP modalities. Methodologically, we combined CVVH, CVVHDF, and CVVHD without ABP to determine whether the addition of ABP will provide additional benefits, as well as identify the most optimal modality. Moreover, we have incorporated a broader range of literature, including studies on HA330 hemoadsorption from Chinese-language sources. This inclusion allows for a more comprehensive analysis of regional differences in adsorption therapies. By comparing the findings of both studies, while acknowledging the

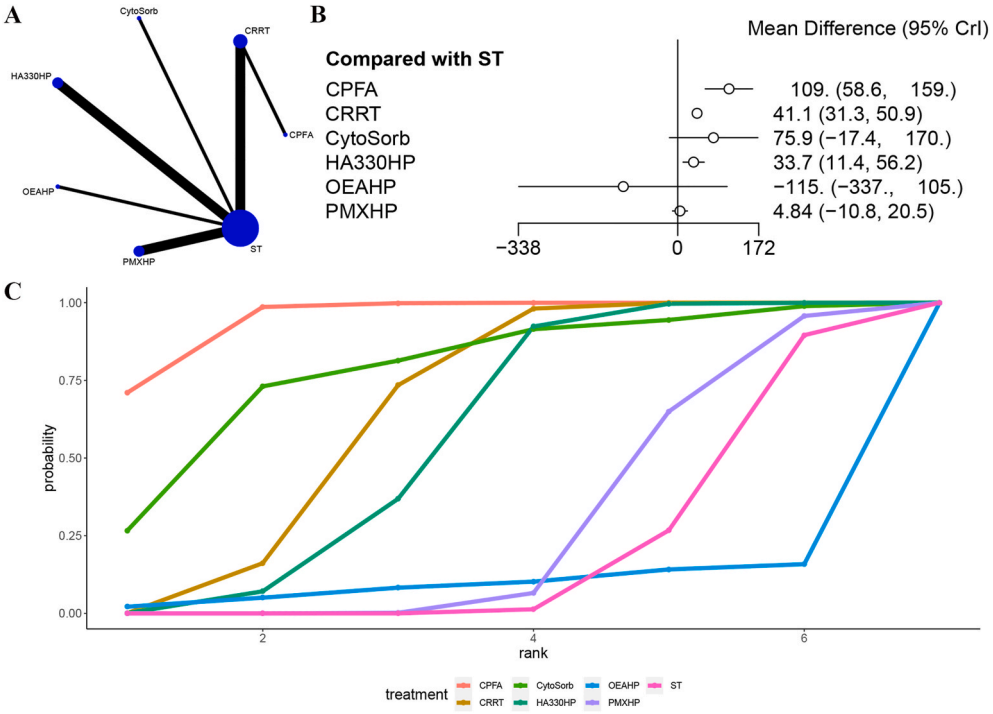

Fig. 5. **(A)** The network plot of oxygenation index. **(B)** The forest plot of oxygenation index. **(C)** The cumulative probability plot of oxygenation index.

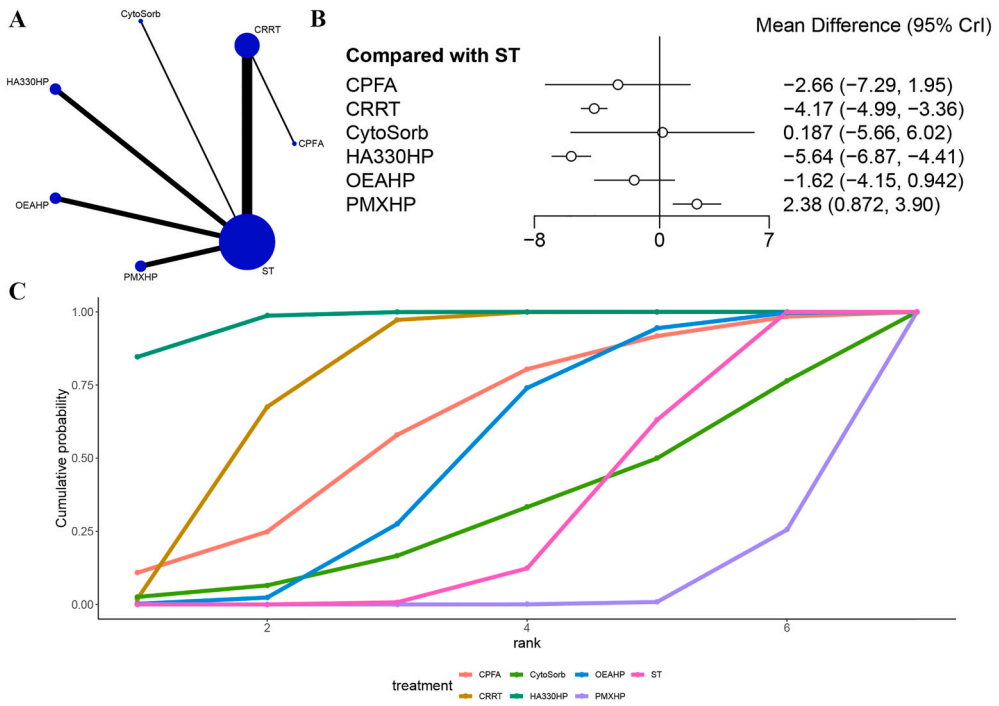

Fig. 6. **(A)** A network plot of ICU stay days. **(B)** Forest plot of ICU stay days. **(C)** The cumulative probability plot of ICU stay days.

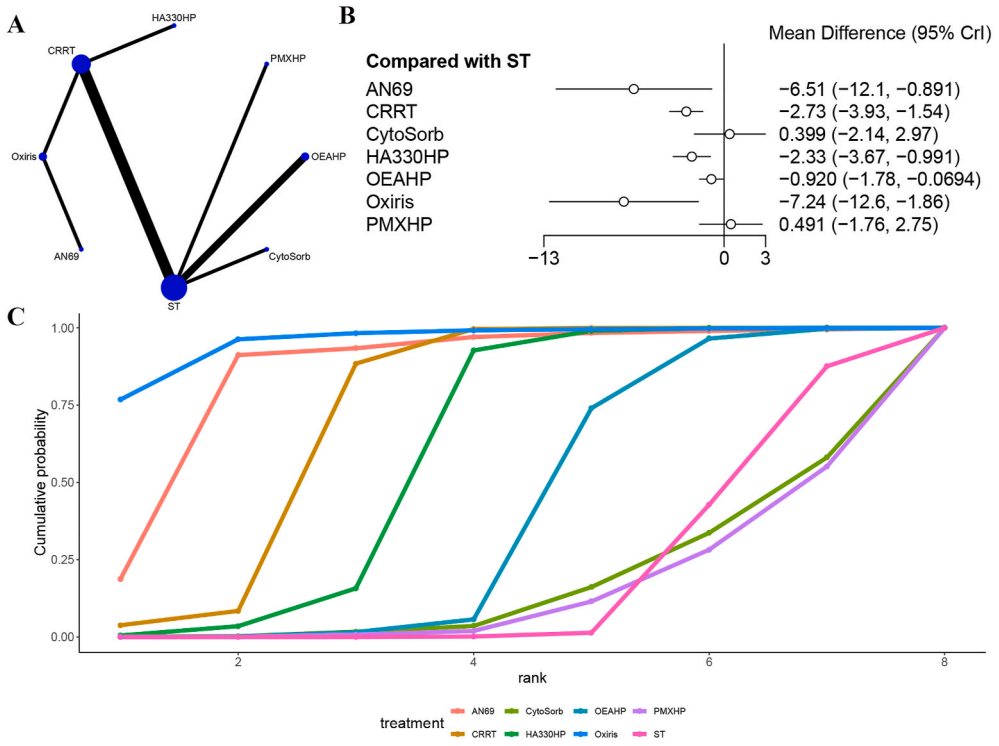

Fig. 7. **(A)** The network plot of lactate. **(B)** The forest plot of lactate. **(C)** The cumulative probability plot of lactate.

limitations associated with the absence of large-scale RCTs for various emerging adsorption therapies, we reaffirm the advantages of PMX in sepsis blood purification. The American Therapeutic Plasma Exchange Guideline provides a weak recommendation for plasma exchange in sepsis management [60]. Given that plasma exchange is excluded, the value of HA330 becomes pronounced. The present study helps to clarify the significance of different ABP modalities in the treatment of sepsis.

The in-hospital mortality rate is a critical outcome measure for researchers. Although there was potential heterogeneity among the studies, our analysis suggests that PMX and HA330 may effectively reduce in-hospital mortality. However, it is important to acknowledge that the evidence supporting PMX, a pre-coated polymyxin blood perfusion column manufactured in Japan, is primarily derived from Japanese studies. These studies predominantly focus on sepsis cases associated with abdominal infections or severe peritonitis, which may introduce potential biases related to ethnicity and disease-specific

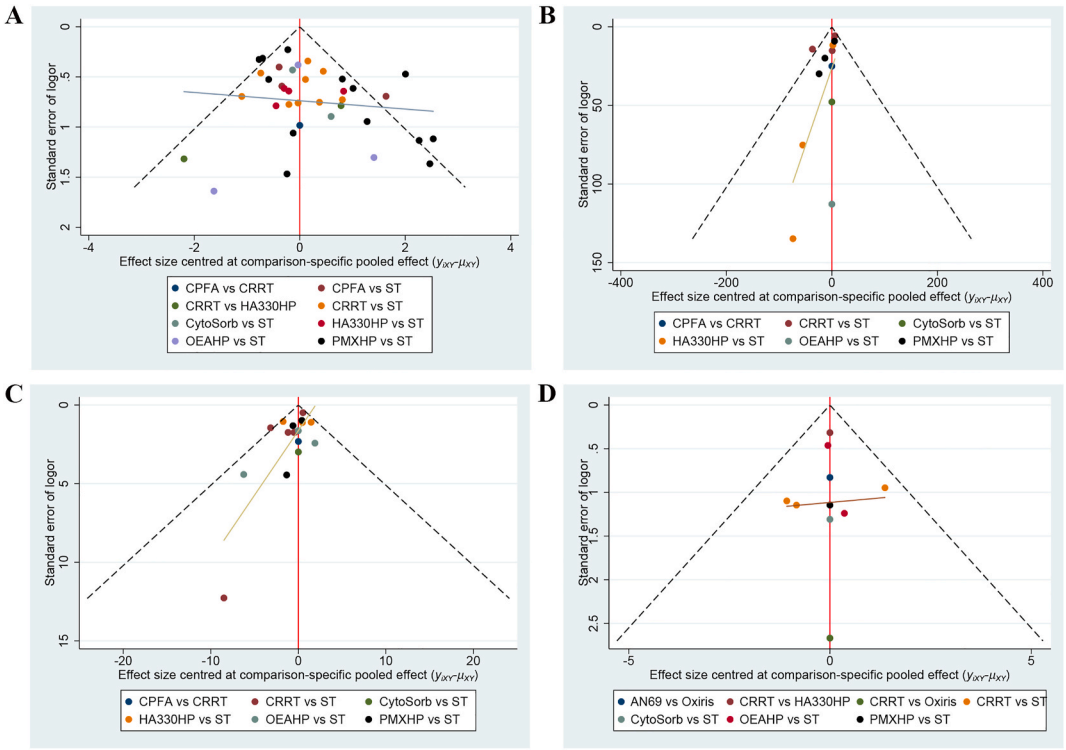

Fig. 8. (A) The comparison-corrected funnel plots of hospital mortality. **(B)** The comparison-corrected funnel plots of oxygenation index. **(C)** The comparison-corrected funnel plots of ICU stay days. **(D)** The comparison-corrected funnel plots of lactate.
Note: Each dot in the figure represents a comparison of two intervention measures. The more symmetrical the dots in the figure, the smaller the publication bias. Conversely, the more symmetrical the dots, the larger the publication bias.

characteristics. However, based on the current meta-analyses, it is considered the best intervention, highlighting its potential for widespread application in clinical practice.

Despite the EUPHRATES study by Dellinger RP et al. [29] demonstrating no significant reduction in 28-day mortality among patients with endotoxin activity exceeding 0.6 treated with PMX, the 2021 international guidelines for sepsis and septic shock management [61] do not endorse the use of this therapy for sepsis. However, the study enrolled a large number of critically ill sepsis patients, which may have masked the benefits of PMX. Recently, a post-hoc analysis demonstrated that for patients to be included in the EUPHRATES study, stratification was performed using machine-learning methods. The study found that EAA (endotoxin activity assay) between 0.60 and 0.90 improved the 28-day mortality risk, indicating that this therapy is suitable for a specific group of patients [62]. The discrepancy between our findings and those of previous PMX studies may be attributable to differences in patient inclusion criteria. Nevertheless, our data, coupled with the meta-analysis by Chen et al. [59], suggests that PMX holds potential clinical benefits and warrants further investigation.

The HA330 hemoperfusion device manufactured in China has also shown an advantage in reducing in-hospital mortality. It is a neutrally charged macroporous adsorption resin treated with a unique process, and its coating material is collodion. It can adsorb endotoxin and inflammatory factors. Many clinical experts from countries outside of China have used HA330 blood perfusion in patients with severe COVID-19 [63], demonstrating advantages in reducing the risk of death and potentially serving as a supplementary option.

The OXiris filter for filtration-based hemoadsorption is an interesting new type of polyacrylonitrile membrane [64]. Based on the original AN69 membrane, it is surface-modified with polyethyleneimine cationic polymer and can simultaneously adsorb cytokines and endotoxins. Several studies have compared the effects of OXiris on the AN69 membrane, which is produced by the same manufacturer. Compared with the AN69 membrane, OXiris has shown better advantages in RCT studies, mainly due to its better adsorption characteristics. However, few RCT studies have compared the OXiris with other treatment modalities, with some reporting that it has no advantages compared to other modalities. Another meta-analysis that included several studies besides RCT studies [64] found that this treatment modality was more effective in reducing the 28-day mortality rate of patients. Although this inclusion strategy may limit the strength of evidence from the meta-analysis, it highlights the potential benefits of this intervention. A significant number of Oxiris studies are based on cohort or retrospective designs, which do not meet our inclusion criteria, thereby limiting the comprehensive evaluation of its efficacy. To establish the effectiveness of Oxiris with greater certainty, further high-quality RCTs are essential.

Cytosorb is a cytokine adsorption column that uses polystyrene divinylbenzene polymer microspheres as adsorbents. This material has a high surface area and porous structure, providing a large number of adsorption sites. This technology can remove cytokines generated by the inflammatory storm in sepsis patients. *In vivo*, *ex vivo*, and *in vitro* studies have demonstrated that Cytosorb can clear IL-1β, IL-6, IL-8, and TNF α. Currently, there is limited evidence to support the clinical use of this technology. A meta-analysis investigating the potential of Cytosorb to remove IL-6. However, no conclusive finding was obtained due to the limited data. We speculate that Cytosorb may clear inflammatory factors, thereby improving clinical outcomes. Therefore, it may be applied in various clinical scenarios, especially in conditions where excessive inflammation plays a crucial role in disease progression. A 2023 study [65] that incorporated both observational studies and RCTs concluded that this technology does not significantly improve patient mortality. These findings are consistent with the results of our meta-analysis. Therefore, caution is warranted when considering the adoption of this treatment modality. Continuous Plasma Filtration Adsorption (CPFA) works by first separating plasma from whole blood. The plasma is then passed through an adsorbent material that can bind and remove various

inflammatory mediators, endotoxins, and other harmful substances. This purified plasma is then returned to the patient. Although pioneer studies [66] suggested potential benefits in reducing inflammatory markers and improving organ function, our current meta-analysis does not support the efficacy of this modality.

We also note that in other countries, there are some potentially promising products. They have a common characteristic in that they all fall within the category of endotoxin adsorption. We integrate them as "other endotoxin adsorption", including LPSHP, ISHA, and Alteco. Although individual RCTs have suggested potential advantages over standard care, meta-analyses have not consistently shown a clear benefit compared to other treatment modalities.

In our analysis of secondary indicators, AN69 and Oxiris demonstrated greater efficacy in reducing lactic acid levels. We hypothesize that this advantage may be attributed to their dual function as both filters and adsorbers, enabling the continuous removal of small molecules such as lactic acid. With respect to the oxygenation index, although CPFA exhibited certain benefits, these findings may be influenced by the higher proportion of ARDS patients included in this subset of the study population. However, these modalities have not been found to offer significant benefits in most studies. In the analysis of ICU length of stay, a cautious interpretation is warranted regarding the potential prolongation associated with PMX use. Based on the study by I. Osawa et al. [62], we hypothesize that this finding may be attributed to the inclusion of a higher proportion of critically ill patients in PMX-related studies. This baseline heterogeneity could partially account for the observed outcome. Future large-scale RCTs are needed to further elucidate the underlying relationship.

In the present studies, publication bias and heterogeneity were detected in the included studies. We speculate that this may be due to the following reasons: (1) We adopted a relatively strict data retrieval scheme and excluded non-randomized studies. Although this may have increased the level of evidence, it may also lead to the exclusion of many high-quality retrospective analyses. OXiris adsorption hemofiltration exemplifies this limitation. Further RCTs are required to definitively establish the efficacy and safety of this modality. In addition, the broad definition of sepsis presents challenges in standardizing patient populations and treatment protocols. Different infection sources and severity levels may contribute to the observed heterogeneity. The most obvious example is PMX. Targeting specific patient subgroups, particularly those with less severe disease, may reveal the potential benefits of PMX perfusion. However, future studies should employ rigorous research designs to further validate these findings.

5. Conclusion

In summary, ABP combined with CRRT treatment may significantly reduce mortality in sepsis patients. Overall, PMX and HA330 decrease hospital mortality, ICU stay days, and oxygenation index in sepsis patients, and their effect may be better when combined with CRRT. However, well-designed RCT studies with larger sample sizes and newer modalities of ABP are needed to validate the present findings.

CRediT authorship contribution statement

Huameng Xing: Writing – original draft. **Yuxuan Wei:** Writing – review & editing. **Dongmei Zhang:** Conceptualization. **Zheng Jiang:** Investigation, Formal analysis. **Jianhua Qin:** Funding acquisition. **Santao Ou:** Resources. **Weihua Wu:** Supervision, Methodology.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.rmed.2025.107994.

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