# Efficacy of Hemoadsorption Therapy in Patients With Sepsis-associated Acute Kidney Injury: A Systematic Review and Meta-analysis

Behrad Saeedian,[1] Nastaran Babajani,[2] Monir Sadat Hakemi,[3] Fatemeh Jodeiri,[4,5] Mohammad Amin Aslani,[6,7] Ilad Alavi Darazam,[8] Amir Kasaeian,[1,9] Antoine Schneider,[10,11] Amir Ahmad Nassiri[12]

[1]Liver and Pancreatobiliary Diseases Research Center, Digestive Diseases Research Institute, Tehran University of Medical Sciences, Tehran, Iran
[2]Digestive Diseases Research Center, Digestive Diseases Research Institute, Tehran University of Medical Sciences, Tehran, Iran
[3]Department of Nephrology, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran
[4]Digestive Diseases Research Institute, Tehran University of Medical Sciences, Tehran, Iran
[5]School of Medicine, Islamic Azad University, Tehran Medical Branch, Tehran, Iran
[6]School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
[7]Vascular Disease and Thrombosis Research Center, Rajaie Cardiovascular Institute, Tehran, Iran
[8]Department of Infectious Diseases and Tropical Medicine, Loghman Hakim Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[9]Research Center for Chronic Inflammatory Diseases, Tehran University of Medical Sciences, Tehran, Iran
[10]Service de médecine intensive adulte, Centre Hospitalier Universitaire Vaudois (CHUV), Rue du Bugnon 46, Lausanne, 1011, Switzerland
[11]Faculty of Biology and Medicine, University of Lausanne, Lausanne, Switzerland
[12]Department of Nephrology, Imam Hossein Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

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**Introduction.** Sepsis-associated acute kidney injury (SA-AKI) is a frequent and severe complication of sepsis with high mortality. Hemoadsorption has been increasingly used as an adjunct to continuous renal replacement therapy (CRRT) to remove inflammatory mediators, but its clinical efficacy in SA-AKI remains uncertain. We conducted a systematic review and meta-analysis to evaluate the effects of hemoadsorption added to CRRT in critically ill patients with SA-AKI.

**Methods.** Following PRISMA guidelines, we systematically searched PubMed, EMBASE, Web of Science, Scopus, Cochrane Library, ClinicalTrials.gov, and WHO ICTRP through December 1, 2025. Comparative studies evaluating hemoadsorption plus CRRT versus standard CRRT in septic patients with AKI were included. The primary outcome was mortality (28-, 60-, 90-day, ICU, and in-hospital). Secondary outcomes included ICU and hospital length of stay, CRRT duration, changes in SOFA score, vasopressor dose, lactate, IL-6, and procalcitonin. Random-effects meta-analyses were performed.

**Results.** Fifteen studies involving 3,093 patients (1,509 hemoadsorption plus CRRT; 1,584 CRRT alone) were included. Overall, hemoadsorption was not associated with a significant reduction in 28-day mortality (RR = 0.79, 95% CI: 0.61 to 1.02) or other mortality endpoints. However, hemoadsorption significantly reduced SOFA score at 48 hours (MD = −2.79, 95% CI: −4.00 to −1.58), IL-6 levels at 24 hours, and lactate levels at 24 and 48 hours compared with CRRT alone. It also did not affect ICU or hospital length of stay or CRRT duration. Subgroup analyses suggested a significant reduction in 28-day mortality with specific adsorption modalities (oXiris, oXiris plus CytoSorb, and HA330-II), but not with polymyxin B.

**Conclusions.** In critically ill patients with SA-AKI, adding hemoadsorption to CRRT improves short-term markers of organ dysfunction and metabolic derangement but does not confer a clear mortality benefit. Future large, multicenter trials with standardized protocols are needed to determine whether specific patient subgroups or adsorption modalities derive meaningful survival benefit.

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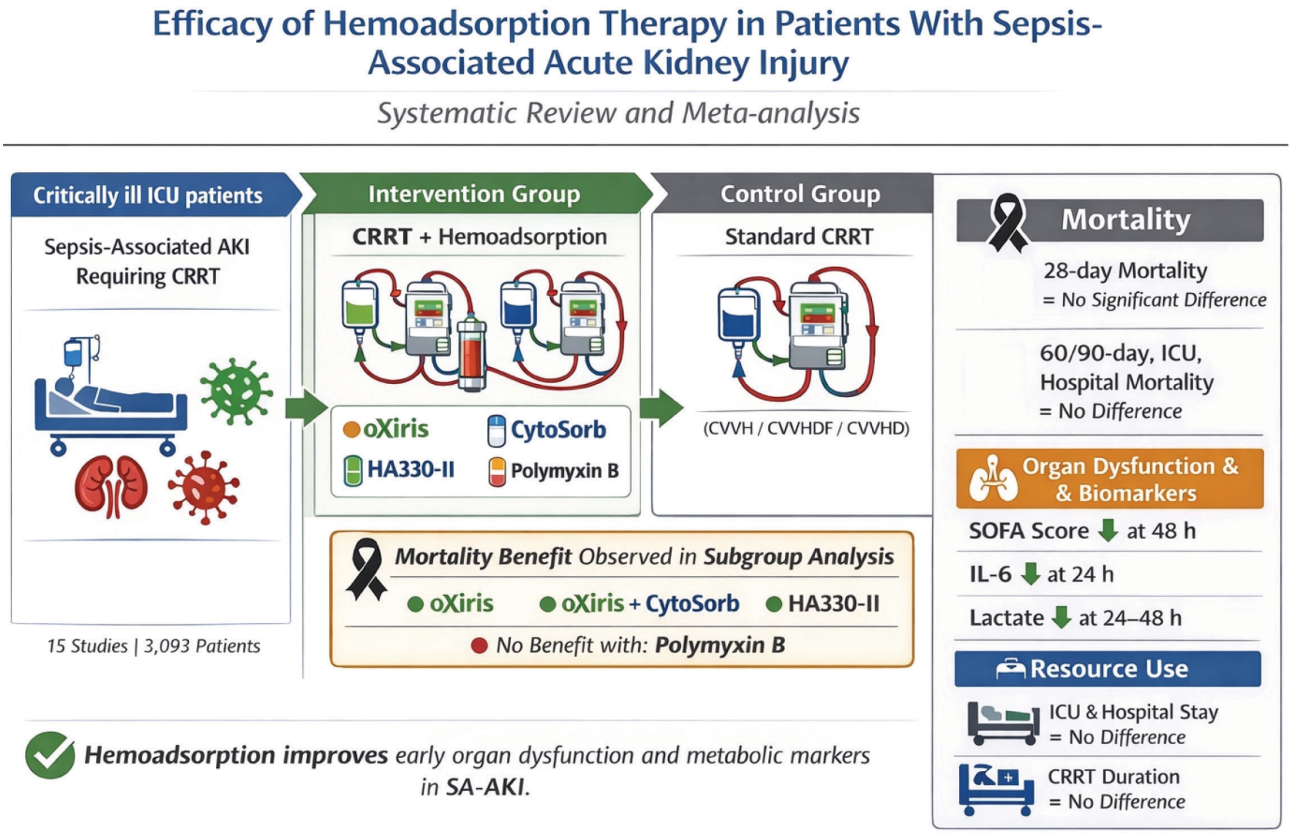



**Graphical Abstract**

## INTRODUCTION

Sepsis is a life-threatening condition caused by a dysregulated response to an infectious source in the body, which can lead to subsequent organ injury.[1] Sepsis-associated acute kidney injury (SA-AKI) is one of the serious complications of the mentioned organ injury. It is estimated that AKI occurs in 60% of patients admitted with sepsis, and it is a leading cause of mortality and morbidity in these patients.[2] A recent cohort study in France by Monard *et al.* reported that nearly 30% of patients with SA-AKI died during the disease course. They also found that compared to isolated sepsis patients, the occurrence of AKI increased the hospital length of stay (LOS) by about 33%, and the cost of treatment by 38%. Around 14.5% of SA-AKI patients required renal replacement therapy (RRT).[3]

The basic principles of SA-AKI rely on early recognition, administration of appropriate antibiotics for source control, fluids and vasopressors to maintain organ perfusion, and renal replacement therapy (RRT) to remove accumulated products.[4,5] Several RRT modalities are investigated to optimize clinical outcomes in SA-AKI, each with a distinct physiological mechanism.[6] Continuous renal replacement therapy (CRRT) modalities, including continuous Veno-venous hemofiltration (CVVH), continuous Veno-venous hemodialysis (CVVHD), and continuous Veno-venous hemodiafiltration (CVVHDF), work based on extracorporeal blood purification strategies in which uremic waste products and inflammatory mediators are removed simultaneously.[7] They can also be combined with other therapeutic measures. For example, CVVH can be used in combination with recombinant alkaline phosphatase (rALP), functioning as a dephosphorylating agent of lipopolysaccharide, which is the main pathogenic component of gram-negative bacterial endotoxins.[8]

Hemoadsorption has gained attention as RRT in SA-AKI management in recent years, which is an extracorporeal blood purification strategy designed for the removal of inflammatory mediators and pathogenic substances from the blood. Hemoadsorption can be beneficial for SA-AKI patients by regulating microcirculatory

oxygenation in the kidneys, protecting the kidneys from tubular cell injury, and facilitating rapid hemodynamic restoration, which leads to reduced vasopressor administration.[9,10] It has also been shown to be effective in critically ill COVID-19 patients.[11] CytoSorb is one of the most studied hemoadsorption devices, primarily used in conjunction with CRRT, which removes a wide range of inflammatory mediators non-specifically.[12] oXiris® Hemofilter is another unselective hemoadsorption modality in which both cytokines and endotoxins are removed simultaneously.[13] Seraph 100® is also an unselective device used for the direct removal of infectious pathogens like viruses or bacteria from the circulation.[14] Polymyxin B, a selective hemoadsorption modality mainly used for the removal of endotoxins, is highly useful in cases of endotoxemia.[15] Jafron® HA is a recent hemoadsorption modality with different models for different purposes (HA130, HA230, and HA330). HA130 is mainly used in combination with hemodialysis, while HA230 is usually used in drug, pesticide, or industrial poisoning.[16] HA330-II is used in the context of an acute hyperinflammatory state, such as SA-AKI, which removes a broad spectrum of inflammatory mediators and bacterial toxins from the bloodstream.[17]

Despite the increase in usage of hemoadsorption techniques in septic and SA-AKI patients in recent years, many uncertainties remain in this field. Moreover, direct comparison of hemoadsorption addition to CRRT with standard CRRT therapy in this population has not been made. This study aims to do a systematic review and meta-analysis in order to evaluate the efficacy of hemoadsorption in the SA-AKI clinical context.

## MATERIALS AND METHODS

### Eligibility Criteria

This systematic review and meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines.[18] Studies reporting the use of hemoadsorption in septic patients with AKI were eligible for inclusion. Case reports, review articles, non-English manuscripts, protocols, non-comparative studies, and conference abstracts were dismissed. The protocol of our study was registered in PROSPERO (registration number = CRD420251270537).

### Search Strategy

We systematically searched the following electronic databases: PubMed, EMBASE, Web of Science, Scopus, Cochrane Library, Clinicaltrials.gov, and WHO's International Clinical Trials Registry Platform (ICTRP) until December 1, 2025. No language restrictions or search filters were applied. Keywords and search terms were: "Hemoadsorption", "Hemoperfusion", "Blood Purification", "Sepsis", "Acute Kidney Injury", and "AKI". We also screened the reference list of eligible studies and relevant reviews on the topic.

### Study Selection

The results of the systematic search were imported into EndNote software version 21.2 (Clarivate PLC, London, United Kingdom). Two independent authors (BS, NB) screened them using titles and abstracts of the studies. Disagreements were resolved by a third reviewer (AAN).

### Data Collection

Full texts of selected studies were retrieved, and data were extracted according to a predesigned sheet. One of the reviewers (BS) did the data extraction, while a second reviewer (NB) cross-checked it. If any needed information was unavailable, we contacted the authors. From each trial, the following information was extracted: the first author's name, study year, country of origin, trial design, population and baseline characteristics, exclusion criteria, details on the CRRT protocol, sample size of each comparison group, and prespecified outcomes. Reported data only in the plots were extracted using the WebPlotDigitizer tool.[19] Our primary outcome was mortality (including 28-, 60-, 90-day, ICU, and hospital mortality). Secondary outcomes were: 1) ICU and hospital stay (days), 2) duration of CRRT (days), 3) Changes in lactate, IL-6, and PCT levels, and 4) Changes in SOFA score and norepinephrine dose.

### Risk of Bias Assessment

The quality of the included randomized controlled trials (RCTs) was assessed using version 2.0 of the Cochrane Risk of Bias Assessment Tool

for Randomized Trials (RoB2).[20,21] Observational studies were rated using the Newcastle-Ottawa Scale (NOS) tool for cohort and case-control studies.[22] Lastly, the critical appraisal of case series studies was done using the JBI's critical appraisal tool.[23]

### Data Synthesis and Statistical Analysis

We performed all statistical analyses using the R Programming language[24] and R Studio version 2025.09.1+401,[25] utilizing the "meta"[26] and "dmetar"[27] statistical packages. The random-effects model for the meta-analysis used the inverse-variance method (IV) for continuous outcomes and the Mantel-Haenszel method (MH) for dichotomous outcomes. Due to insufficient data, a survival meta-analysis of reported hazard ratios was not possible. Mean and standard deviation (SD) were used to calculate the mean difference (MD) with a 95% confidence interval (CI) for continuous variables or risk ratios (RR) with a 95% CI for dichotomous variables. For outcomes with different units (such as µg/h and µg/Kg/h for norepinephrine dose), standardized mean difference (SMD) with 95% CI was calculated. Median and interquartile range (IQR) were converted to mean and SD using the methods developed by Luo *et al*.[28] and Wan *et al*.[29] We calculated the change from baseline values from final and baseline measurements, assuming a correlation coefficient of 0.5. The restricted maximum likelihood (REML) model was used to estimate the between-study variance. Heterogeneity was evaluated using Higgin's $I^2$ test, with thresholds defined as ≤ 25% for low, 26 to 75% for moderate, and > 75% for high.[30] Meta-regression, subgroup, and leave-one-out sensitivity analyses were conducted to identify sources of heterogeneity. Publication Bias was evaluated using funnel plot visual assessments, and a trim-and-fill analysis was performed afterwards.[31] We utilized Egger's test[32] to check the significance of publication bias for continuous variables reported in more than ten studies. Due to the low number of studies in the analyses (< 10), performing a meta-regression using baseline SOFA or APACHE-II score was not feasible.

## RESULTS

### Study Characteristics

The selection process for the included studies is illustrated in the PRISMA flow diagram (Figure 1). Following the screening, 15 studies met the eligibility criteria and were included in the analysis.[13,36-49] Details of the included studies are presented in Table 1. Studies were published from 2002 to 2025, encompassing 1509 patients on hemoadsorption therapy and 1584 patients on standard CRRT therapy. All studies compared hemoadsorption plus CRTT with CRRT alone; four studies used polymyxin B, seven used oXiris, two used CytoSorb, one used a combination of oXiris and CytoSorb, and one used HA330-II. Seven studies performed CRRT using CVVHDF, six used CVVH, one used CVVHD, and in one study, the modality was not specified.[38] Further details of the CRRT protocols used in the included studies, including treatment duration and intervals, effluent flow rate, ultrafiltration, replacement flow rate, and blood flow rate, are presented in Table 2.

### Risk of Bias in Studies

By using the RoB2 tool, of the four included RCTs, one was judged to have a low overall risk of bias, one had some concerns, and two were at a high risk. Cohort and case-control studies were evaluated using the NOS tool, and all received a low risk of bias except one.[41] One case series study with a historical control group was assessed using the case-series JBI tool and was deemed suitable for inclusion in the analysis.

### Meta-analysis

*Comparison of mortality rates between CRRT plus hemoadsorption and standard CRRT treatment.* Compared to CRRT standard therapy, CRRT plus hemoadsoroption therapy was not associated with a significantly lower 28-day mortality rate (RR = 0.79, 95% CI: 0.61 to 1.02; $I^2$ = 65.6%, Figure 2). We performed subgroup analyses based on hemoadsorption type, CRRT modalities, and study design. oXiris, the combination of oXiris/CytoSorb, and HA330-II significantly reduced 28-day mortality, whereas PMX did not. Additionally, no significant differences were observed between studies using CVVH versus CVVHDF ($P$ = .29) or between clinical trials and observational studies ($P$ = .08). Sensitivity leave-one-out analysis revealed that excluding either the study by Suzuki *et al*.[36]

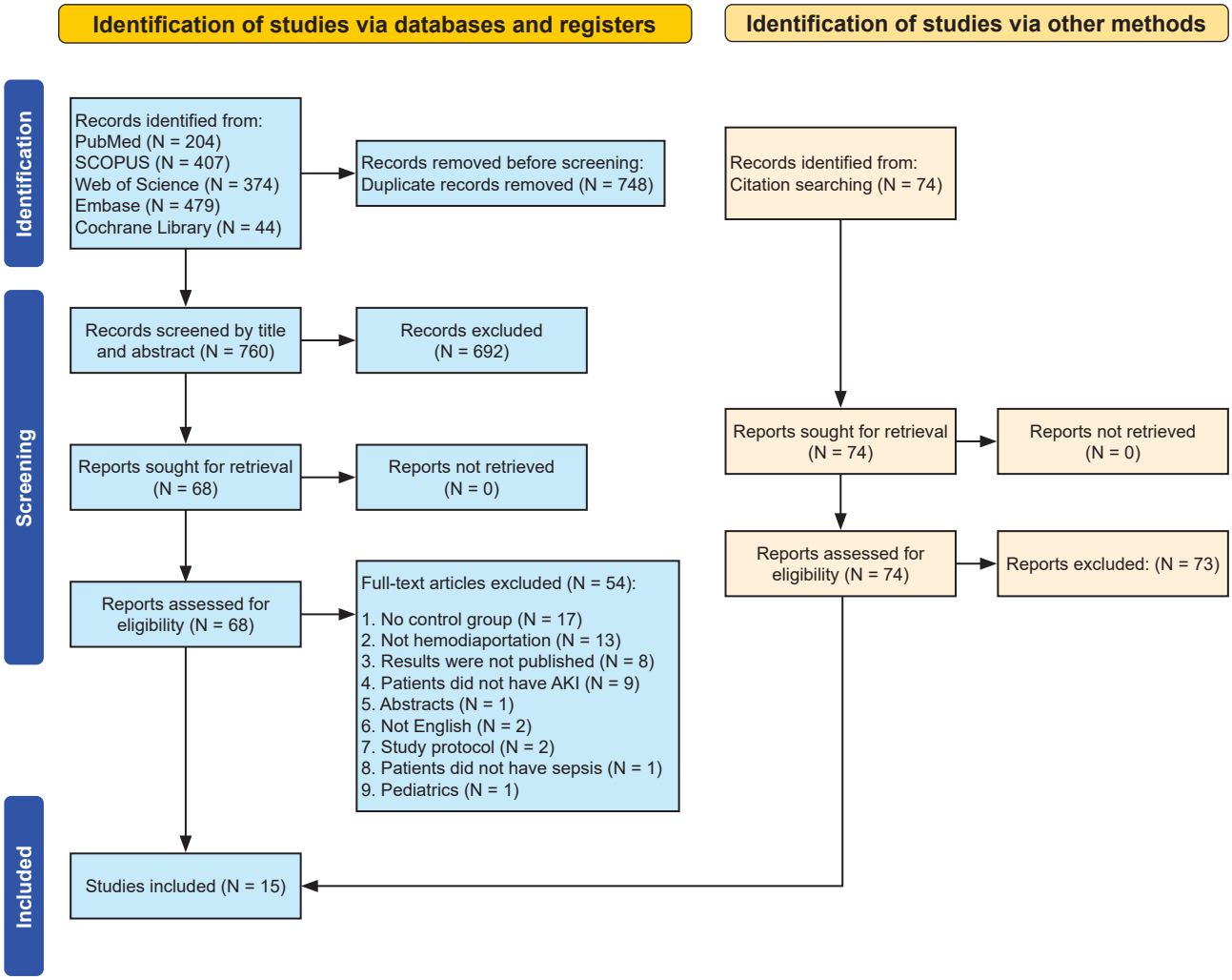



**Figure 1.** The PRISMA Flow Diagram of the Screening Process

or Lee *et al.*[42] would make the 28-day mortality reduction by hemoadsorption statistically significant (RR = 0.87, 95% CI: 0.81 to 0.94; RR = 0.85, 95% CI: 0.78 to 0.91; respectively). The visual assessment of the funnel plot did not indicate the presence of publication bias, and the Trim-and-Fill analysis did not alter the significance of the findings. Further analyses showed that adding hemoadsorption to CRRT did not significantly reduce 60-day, 90-day, ICU, or hospital mortality.

*Comparison of secondary outcomes between CRRT plus hemoadsorption and standard CRRT treatment.* Adding hemoadsorption to standard CRRT did not significantly affect ICU or hospital length of stay, nor CRRT duration (Figure 3). Sensitivity analyses, funnel plots, and Trim-and-Fill analyses confirmed the robustness of these results.

Compared to CRRT alone, the combination of CRRT and hemoadsoprtion demonstrated a significant reduction of the SOFA score 48 hours after CRRT (MD = -2.79, 95% CI: -4.00 to -1.58, $I^2$ = 0%), although no significant difference was found after 24 hours (Figure 4). Moreover, no significant differences in norepinephrine dose reduction 24 and 48 hours after CRRT were observed between the two groups (Figure 4).

Hemoadsorption significantly lowered IL-6 levels at 24 hours (MD = -593.59, 95% CI: -728.57 to -458.61, $I^2$ = 80.4%) and lactate levels at both 24 and 48 hours (MD = -0.88, 95% CI: -1.66 to -0.11, $I^2$ = 48.3%; MD = -0.72, 95% CI: -1.33 to -0.1, $I^2$ = 7.2%; respectively) compared with the control group (Figure 5). However, no significant difference was found in PCT reduction 24 hours

**Table 1.** Study Characteristics of the Included Studies

| Author | Year | Country | Design | Population | Exclusion Criteria | Group 1, n | Group 2, n | SOFA1 | SOFA2 | APACHE1 | APACHE2 | Male% | Age | Main Findings |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Suzuki et al. | 2002 | Japan | Randomized controlled double-blind | Patients with a clinical diagnosis of septic shock (ACCP-SCCM 1997) and ARF. Gram-negative sepsis was confirmed for most patients, while In a small number of patients, gram-negative infection was only suspected and no infection site was found despite an aggressive search. | Patients who were less than 18 years old, pregnant, and organ-transplant recipients, if informed consent from the patient's family was not granted, if they were experiencing acute organ transplant rejection, or if they were in a chronic vegetative state. | CVVHDF + PMX, 24 | CVVHDF, 24 | | | 25 ± 2.1 | 25 ± 2.3 | 72.9 | 64.5 ± 2 | At 28 days, survival was 25% with CHDF alone compared with 75% when CHDF was combined with PMX. The combination therapy led to a marked reduction in plasma endotoxin and interleukin-6, both relative to baseline and to CHDF alone. |
| Shum et al. | 2013 | China | Single-center Prospective case series with historical controls | Adult patients with sepsis-induced (ACCP-SCCM 2001) acute kidney injury due to gram-negative bacteria | Documented chronic kidney disease stage 5 (glomerular filtration rate <15 mL/min/1.73 $m^2$), End-stage renal failure on long-term dialysis, Those treated with renal replacement therapy prior to intensive care unit admission | CVVH + oXiris, 6 | CVVH (FX80), 24 | 12 (9, 15) | 13 (10, 15) | 36 (28, 41) | 34 (31, 37) | 63.3 | 72.3 ± 12.7 | The mean oXiris circuit lifespan was approximately 61 hours. At 48 hours, SOFA scores decreased by 37% in the oXiris-CVVH group, whereas a 3% increase was observed in controls. No significant adverse effects were reported, and mortality did not differ between groups. |
| Iwagami et al. | 2016 | Japan | Multicenter, retrospective cohort | Patients aged 18 or older satisfying all the following inclusion criteria were selected: 1) diagnosis of sepsis due to Haemophilus influenza, Gram-negative organisms, or unspecified; 2) started CRRT in ICU; and 3) required noradrenaline and/or dopamine on the day of CRRT initiation. | (i) ESRD at admission and/or the use of maintenance hemodialysis or peritoneal dialysis; (ii) records of cardiac intervention; (iii) started PMX before or after the day of CRRT initiation; (iv) diagnosis of viral, fungal, or Gram-positive bacterial infection; (v) received intermittent RRT (IRRT) before CRRT, and (vi) received plasma exchange before CRRT; (vii) acute pancreatitis and (viii) acute hepatic condition; (ix) interstitial pneumonia | CRRT + PMX, 978 | CRRT, 978 | | | | | 59.1 | 70.5 ± 12.1 | Logistic regression showed that PMX use was independently linked to lower 28-day mortality (adjusted OR 0.75; 95% CI 0.62–0.91). |
| Navas et al. | 2018 | Spain | Prospective case-control | Adult patients with acute septic shock and suspected gram-negative bacteria infection (an abdominal, biliary, or renal focus of infection), with acute kidney injury requiring CRRT and with elevated plasma endotoxin activity, defined as > 0.6 EU/ml on the Endotoxin Activity Assay | | CVVH + PMX, 9 | CVVH (AN69), 9 | 11 ± 2.4 | 11.6 ± 2.9 | 20.1 ± 4.3 | 21.2 ± 5.3 | 33.3 | 67.55 ± 9.6 | Abdominal infections were the main source, with half of patients presenting with peritonitis. Compared with controls, the hemoperfusion group had longer durations of mechanical ventilation and CRRT. Both groups showed reductions in noradrenaline requirements and inflammatory markers. By day 5, endotoxin activity was significantly lower with hemoperfusion, but other biomarkers and ICU mortality were comparable. No hemoperfusion-related adverse events were reported. |

**Table 1.** Continued

| Author | Year | Country | Design | Population | Exclusion Criteria | Group 1, n | Group 2, n | SOFA1 | SOFA2 | APACHE1 | APACHE2 | Male% | Age | Main Findings |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Broman et al. | 2019 | Sweden | Randomized crossover double-blind | Adult patients in ICU with septic shock, a blood culture positive for a Gram-negative bacteria or suspected to be caused by a Gram-negative agent, and associated KDIGO stage 3 acute renal failure. Patients with a plasma endotoxin level >0.03 EU/ml were enrolled. | Age <18 years and/or known human immunodeficiency virus (HIV) or hepatitis B/C infection. | CVVHDF + oXiris, 8 | CVVHDF (ST150), 8 | | | | | 62.5 | 69.4 ± 11.16 | During the treatment period, endotoxin levels fell in 78% of patients using the oXiris filter versus 17% with a standard filter (P = 0.02). Reductions in TNF-α, IL-6, IL-8, and IFN-γ were also greater with oXiris. Lactate decreased significantly with oXiris but not with the standard filter, and norepinephrine requirements declined only in the oXiris group. |
| Schittek et al. | 2020 | Germany | Prospective cohort with a historical control group | sepsis-associated acute kidney injury (KDIGO stage 3) in adult patients treated in ICU | | CVVHDF + CytoSorb, 43 | CVVHDF (M150), 33 | | | 39 (36, 42) | 35 (33, 40) | 21.1 | 62.4 ± 15.2 | Patients receiving haemoadsorption had higher APACHE II scores, but risk-adjusted ICU mortality (O/E ratios) was similar between groups. Although haemoadsorption was associated with shorter ICU stay and reduced need for catecholamines and RRT, these differences were not confirmed after multivariate adjustment, where neither mortality nor LOS differed significantly between groups. |
| Lee et al. | 2021 | South Korea | Single-center retrospective cohort | Patients with septic shock and AKI | Patients with chronic dialysis, prior solid organ transplantation, and stage IV malignancy and patients aged younger than 18 years. | CVVHDF + PMX, 66 | CVVHDF (ST-100), 66 | 13.7 ± 4.1 | 14.1 ± 2.6 | | | 58.4 | 60.9 ± 14.66 | Both crude 28-day and 90-day mortality rates were higher in the PMX-HP plus CRRT group than with CRRT alone. After propensity score matching for illness severity and key clinical variables, 66 matched pairs confirmed significantly higher 28-day and 90-day mortality in the PMX-HP with CRRT group. |
| Guan et al. | 2022 | China | Single-center retrospective cohort | Patients who met the following criteria were eligible to participate: (I) CRRT ≥ 24 h; (II) septic shock (Sepsis-3); (III) AKI stage 2 or 3 (KDIGO 2012); (IV) cardiovascular SOFA score ≥ 3; (V) sepsis due to GNB infection (or suspected GNB infection). | AKI associated with chronic kidney disease; immunosuppressive treatment or steroids (prednisone > 0.5 mg/kg/day or equivalent); autoimmune disorder; coexisting illness with a high probability of death (<6 months); pregnancy; other modalities of blood purification were used; and inclusion in another ongoing study within the last 30 days. | CVVHDF + oXiris, 70 | CVVHDF (ST150), 66 | 16.97 ± 3.56 | 14.98 ± 3.15 | | | 72.1 | 55.4 ± 13.97 | Early mortality at 7 and 14 days was significantly lower with oXiris than with the ST150 filter (47.1% vs 74.2% and 58.5% vs 80.3%), though 90-day mortality did not differ. The oXiris group showed faster reductions in SOFA and VIS scores at 24–72 hours, as well as greater declines in procalcitonin. In multivariate Cox analysis, oXiris use was independently associated with improved prognosis (HR 0.50, 95% CI 0.28–0.89). |

**Table 1.** Continued

| Author | Year | Country | Design | Population | Exclusion Criteria | Group 1, n | Group 2, n | SOFA1 | SOFA2 | APACHE1 | APACHE2 | Male% | Age | Main Findings |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Feng et al. | 2022 | China | Single-center randomized controlled trial | Surgical septic shock with AKI patients admitted in the ICU. The inclusion criteria consisted of (1) Diagnosis of Septic shock (Sepsis-3); (2) Any culture (such as blood, sputum, or drainage fluid) positive for bacteria or suspected to be caused by a Gram-negative agent; (3) Diagnosis of KDIGO Stage 3 AKI. | (1) Patient age <18 years old; (2) Weight ≤ 30 kg; (3) Patients with highly contagious infectious diseases such as open tuberculosis; (4) Previous renal replacement therapy; and (5) Patients that underwent cardio-pulmonary resuscitation (CPR) | CVVH + oXiris, 8 | CVVH (AN69 ST), 8 | 9.9 ± 2.9 | 9 ± 1.5 | 19.9 ± 6.6 | 23.1 ± 4.2 | 68.8 | 65.75 ± 15.1 | In the oXiris group, the first CRRT session significantly reduced PCT (p = 0.046) and IL-6 (p = 0.043) compared with pre-treatment levels. Lactate also decreased by 1.70 mmol/L (p = 0.028). Norepinephrine infusion rates were lower at 4, 6, and 8 hours post-treatment compared with the ST group. |
| Liu et al. | 2022 | China | Single-center retrospective cohort | Adult patients with septic shock (Sepsis-3) complicated with AKI (stage 2 or 3 KDIGO) admitted to the ICU | Pregnant or lactating women; survival time < 24 hours; those who had received CRRT before admission to ICU. | CVVH + oXiris, 15 | CVVH (ST-100), 15 | 13.27 ± 2.28 | 12.00 ± 3.59 | 20.60 ± 3.83 | 19.27 ± 3.28 | 56.7 | 64 + 13.1 | At 48 hours after CRRT, the oXiris group showed significant reductions in WBC count, hs-CRP, and PCT. Compared with controls, SOFA scores, lactate levels, and norepinephrine requirements were also lower. The duration of vasoactive support and CRRT was shorter with oXiris, while mechanical ventilation duration, ICU and hospital length of stay, and ICU or in-hospital mortality did not differ between groups. |
| Epstein et al. | 2024 | Israel | Single-center retrospective cohort | Adult patients admitted with severe septic shock or those who developed severe septic shock during their ICU stay and required CRRT (Sepsis-3). | Presence or suspicion of cardiogenic shock, haemorrhagic shock, obstructive shock, or anaphylactic shock; and initiation of blood purification or CRRT treatment more than 48 h after the diagnosis of septic shock. | CVVHDF + CytoSorb/ Oxiris, 47 | CVVHDF (M150), 29 | 15 (13, 17) | 13 (11, 14) | | | 72.4 | 64.35 ± 14.7 | Compared with CRRT alone, the haemoadsorption group showed greater 24-hour reductions in lactate and VDI. Mortality was lower with haemoadsorption in the ICU (34.0% vs 65.5%), and at 30 and 60 days. Adjusted analyses upheld its association with reduced ICU and 30-day mortality, but not 60-day mortality. |
| Zheng et al. | 2024 | China | Single-center retrospective cohort | (1) Age > 18, (2) Met the diagnostic criteria of Sepsis-3; (3) matched the diagnostic criteria for AKI from KDIGO 2012; (4) CRRT for at least 24 h. | (1) Other factors contributing to AKI, including prior use of nephrotoxic medications, contrast-induced nephropathy, and urinary blockages; (2) pre-existing CKD; (3) pregnancy; (4) treatment with immunosuppressive drugs; (5) active neoplasia; (6) insufficiency clinical data; (7)coexisting disease with a high probability of death (< 6 months). | CVVH + oXiris, 88 | CVVH (M150), 155 | 10.02 ± 2.48 | 9.70 ± 2.55 | 27.35 ± 8.15 | 27.66 ± 8.42 | 65 | 68.1 ± 14.9 | In the oXiris group, complete recovery, partial recovery, and dialysis dependence occurred in 60.3%, 13.6%, and 26.1% of patients, compared with 63.9%, 15.5%, and 20.6% in controls. Twenty-eight-day mortality did not differ. The oXiris group showed greater reductions in VIS scores at 24 and 48 hours, and lower lactate levels at 48 hours. Although baseline IL-6 levels were higher in the oXiris group, post-CRRT levels were comparable between groups. Multivariable Cox analysis indicated that oXiris use, along with SOFA score and inflammatory markers, was independently associated with reduced 28-day mortality (HR 0.466, 95% CI 0.233–0.934). |

**Table 1.** Continued

| Author | Year | Country | Design | Population | Exclusion Criteria | Group 1, n | Group 2, n | SOFA1 | SOFA2 | APACHE1 | APACHE2 | Male% | Age | Main Findings |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Zhou et al. | 2024 | China | Randomized controlled single-blind | Adult patients with septic shock (Sepsis-3) complicated with AKI (KDIGO 2012) | Patients who died or abandoned treatment within 24 h, with underlying chronic kidney disease or malignant tumor, with immunodeficiency diseases, or taking immunosuppressants. | CVVHDF + HP (HA330-II machine), 10 | CVVHDF, 10 | 12.10 ± 4.61 | 14.10 ± 1.91 | 17.00 ± 5.83 | 16.30 ± 6.22 | 65 | 67.4 ± 13.97 | IL-6 and PCT levels were significantly lower in the treatment group, while decreases in IL-1β, TNFα, and CRP were not statistically significant. Lactate, SOFA scores, and norepinephrine requirements differed significantly between groups. Survival analysis demonstrated a significantly higher 28-day survival rate in the treatment group. |
| He et al. | 2025 | China | Single-center retrospective cohort | Adult SA-AKI patients (Sepsis-3, KDIGO stage 2 or 3) | Age < 18 years, pregnancy, end-stage renal disease (ESRD), and a history of renal transplantation | CVVH + oXiris, 126 | CVVH (M150), 135 | 12 (8.5, 14) | 12 (9, 15) | 22.27 ± 7.11 | 20.89 ± 7.83 | 64.4 | 58.68 ± 16.34 | After CRRT, the oXiris group demonstrated significant improvements compared with baseline, including increased MAP ($p < 0.001$) and decreased SI ($p < 0.001$), lactate ($p < 0.001$), and IL-6 ($p = 0.045$). No comparable changes were seen in the M150 group. The total norepinephrine dose was also lower in the oXiris group ($p = 0.020$). Mortality at 7, 14, 30, 60, and 90 days did not differ significantly between groups. |
| Mariano et al. | 2024 | Italy | Single-center retrospective cohort | Burn patients who developed AKI-associated septic shock (Sepsis-3) receiving CRRT for more than 72 h | All patients included in the study were without brain injury at Burn Center admission | CVVHD + CytoSorb, 11 | CVVHD, 24 | 12 (11, 12) | 12 (11, 13) | | | 91.4 | 64.66 ± 25.36 | 7 of 11 patients initiated adsorption concurrently with CRRT. Compared with controls, the sorbent group showed a significant reduction in norepinephrine requirements and clinical improvement over the first four days, including a marked decrease in vasopressor use by day 4. In-hospital mortality was lower in the sorbent group (45.4% vs. 70.8%), with superior long-term survival on Kaplan–Meier analysis. All survivors in both groups recovered renal function at discharge, whereas nonsurvivors did not. |

**Table 2.** Details of the CRRT Protocols Used in the Included Studies

| Author | Year | Country | Design | Group 1 | Group 2 | n1 | n2 | CRRT protocol | Effluent flow rate | Ultrafilteration | replacement flow rate | blood flow rate |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Suzuki et al. | 2002 | Japan | Randomized controlled double-blind | CVVHDF + PMX | CVVHDF | 24 | 24 | HP: 4h, CHDF was started after that for at least 24h | | 20 mL/kg/ h | | 100 to 150 mL/min |
| Shum et al. | 2013 | China | Single-center Prospective case series with historical controls | CVVH + oXiris | CVVH (FX80) | 6 | 24 | | | HP: 32.0 mL/kg/h (IQR, 29.3 to 38.1) contorl: 35.7 mL/ kg/h (IQR, 32.7 to 37.7) | 2500 mL/h | 150 mL/min |
| Iwagami et al. | 2016 | Japan | Multicenter, retrospective cohort | CRRT + PMX | CRRT | 978 | 978 | HP: 2h per session, the PMX sessions performed was 1 or 2 on consecutive days | | | | 80–120 mL/ min |
| Navas et al. | 2018 | Spain | Prospective case-control | CVVH + PMX | CVVH (AN69) | 9 | 9 | 2h hemoperfusion on two consecutive days, starting within 24 h of ICU admission. | 35 mL/kg/h | | | |
| Broman et al. | 2019 | Sweden | Randomized crossover double-blind | CVVHDF + oXiris | CVVHDF (ST150) | 8 | 8 | 24h | | | | |
| Schittek et al. | 2020 | Germany | Prospective cohort with a historical control group | CVVHDF + CytoSorb | CVVHDF (M150) | 43 | 33 | | | | | |
| Lee et al. | 2021 | South Korea | Single-center retrospective cohort | CVVHDF + PMX | CVVHDF (ST-100) | 66 | 66 | Two sessions of 2h hemoperfusion with an interval of 24 h | | | 20 mL/kg/h | CRRT: 150 mL/min PMX-HP: 100 mL/min |
| Guan et al. | 2022 | China | Single-center retrospective cohort | CVVHDF + oXiris | CVVHDF (ST150) | 70 | 66 | oXiris was replaced with ST150 hemofilter when patients became stable. | 30–35 mL/ kg/h | | | 150-200 mL/ min |
| Feng et al. | 2022 | China | Single-center randomized controlled trial | CVVH + oXiris | CVVH (AN69 ST) | 8 | 8 | | | | 30–35 mL/ kg/h | 150-200 mL/ min |
| Liu et al. | 2022 | China | Single-center retrospective cohort | CVVH + oXiris | CVVH (ST-100) | 15 | 15 | HP: 48h, then conventional hemofilter was replaced | | 35 mL/kg/h | | 150 mL/min |
| Epstein et al. | 2024 | Israel | Single-center retrospective cohort | CVVHDF + CytoSorb/ Oxiris | CVVHDF (M150) | 47 | 29 | 72hr, after that CVVHDF as long as an indication for RRT existed. | 30–35 mL/ kg/h | | | 150-200 mL/ min |
| Zheng et al. | 2024 | China | Single-center retrospective cohort | CVVH + oXiris | CVVH (M150) | 88 | 155 | 72hr, after that the M150 filter was replaced | | | 35 mL/kg/h | 150–180 ml/ min |

**Table 2.** Continued

| Author | Year | Country | Design | Group 1 | Group 2 | n1 | n2 | CRRT protocol | Effluent flow rate | Ultrafilteration | replacement flow rate | blood flow rate |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Zhou et al. | 2024 | China | Randomized controlled single-blind | CVVHDF + HP (HA330-II HP machine) | CVVHDF | 10 | 10 | 4hr, CVVHDF for the rest of the day. patients received 3–5 HP treatments. | | | 3000–4000 mL/h | 180–200 mL/min |
| He et al. | 2025 | China | Single-center retrospective cohort | CVVH + oXiris | CVVH (M150) | 126 | 135 | 24h | 20–30 mL/kg/h | 20–35 mL/kg/h | | 150–200 mL/min |
| Mariano et al. | 2024 | Italy | Single-center retrospective cohort | CVVHD + CytoSorb | CVVHD | 11 | 24 | a minimum cycle of 2 sessions, and a maximum of 6 sessions. The indications for CytoSorb® were evaluated daily after 2 sessions | 20–25 mL/kg/h | | | |

and 48 hours after CRRT (Figure 5).

## Qualitative Synthesis

*Kidney Function and Prognosis.* Utilizing multiple regression models, some studies found the use of oXiris hemoadsorption to be significantly and independently associated with reduction of ICU, 30-day, and 90-day mortality.[13,45] On the contrary, other studies found no association between the use of oXiris and 60- or 90-day mortality.[45,48] Moreover, He *et al.* found no interaction between the use of oXiris and age, AKI stage, or SOFA score in predicting 90-day mortality.[48] The use of PMX treatment was also found to have conflicting results regarding the association with 28-day mortality,[38,42] with no interaction found between PMX use and underlying malignancy, site of infection, previous surgery, ventilation support, or use of norepinephrine.[38] Regression models also showed CytoSorb not to have a significant association with ICU and hospital mortality.[41] Complete recovery of kidney function had no significant difference between CRRT standard therapy and using oXiris.[13,46] or CytoSorb.[49] This complete recovery was defined as a return of serum creatinine to baseline levels and a normal urine test[13,46] or recovery from CRRT need.[49] With hemoadsorption using oXiris, creatinine levels did not differ significantly between the two groups.[39,44] HA330-II decreased creatinine levels in the treatment group; still, the difference was not clinically significant.[47]

*Hemodynamics.* Two studies demonstrated that mean arterial pressure (MAP) values were identical in the oXiris and standard filter groups,[40,43] while another reported significant improvements in the oXiris group.[48] In a study by Epstein *et al.*, the vasopressor dependency index (VDI) showed a slight increase in the standard CRRT group, while patients receiving hemoadsorption (CytoSorb/Oxiris) experienced a significant reduction.[45] The reduction in vasoactive-inotropic score (VIS) was also found to be greater in the oXiris group than in the control group.[13,46] Patients receiving hemoadsorption via CytoSorb[41] or oXiris[44] were on a significantly shorter duration of catecholamine administration compared to standard filters. On the other hand, no significant differences in

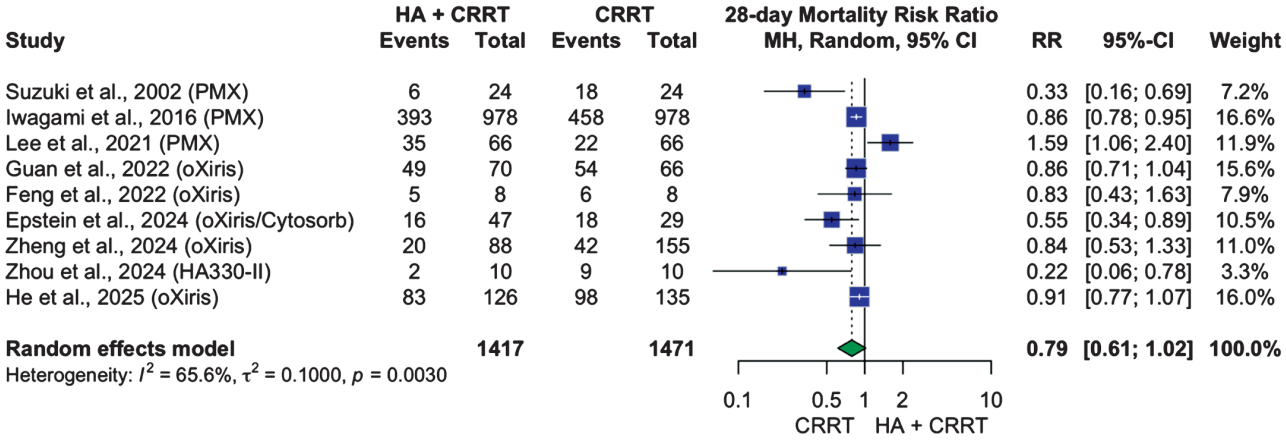
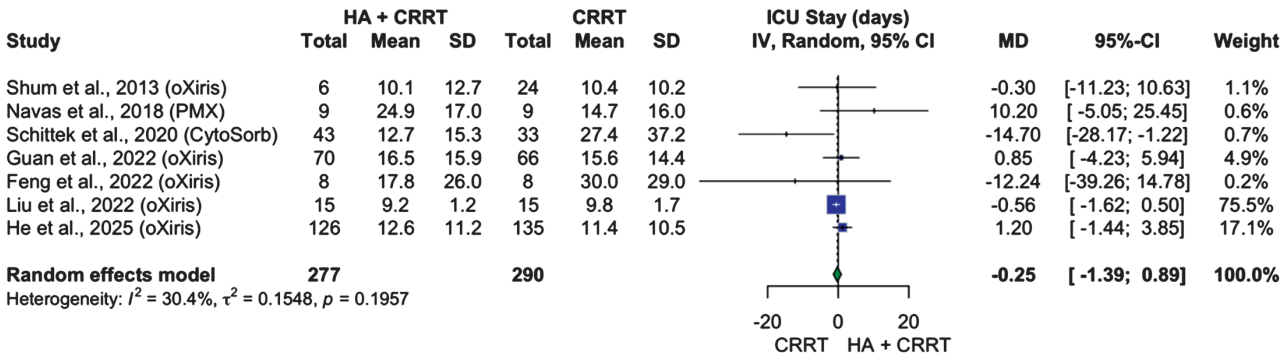
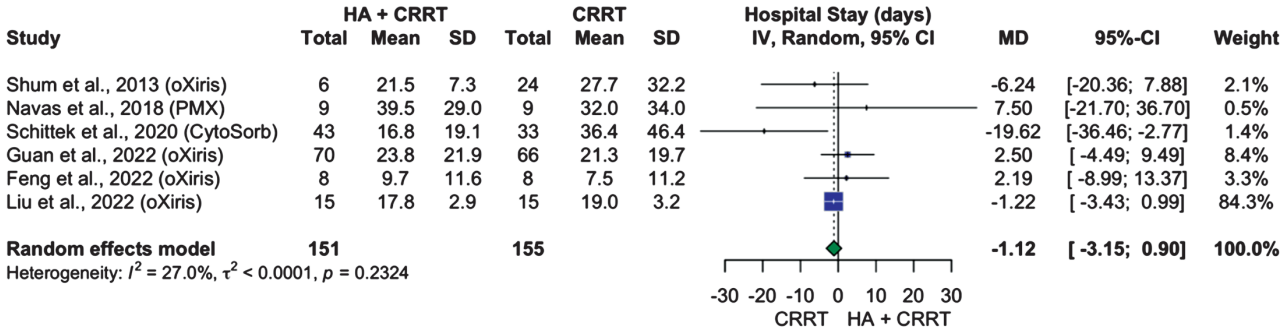



**Figure 2.** Forest Plot of the 28-day Mortality Risk Ratio Between hemoadsorption + CRRT and CRRT



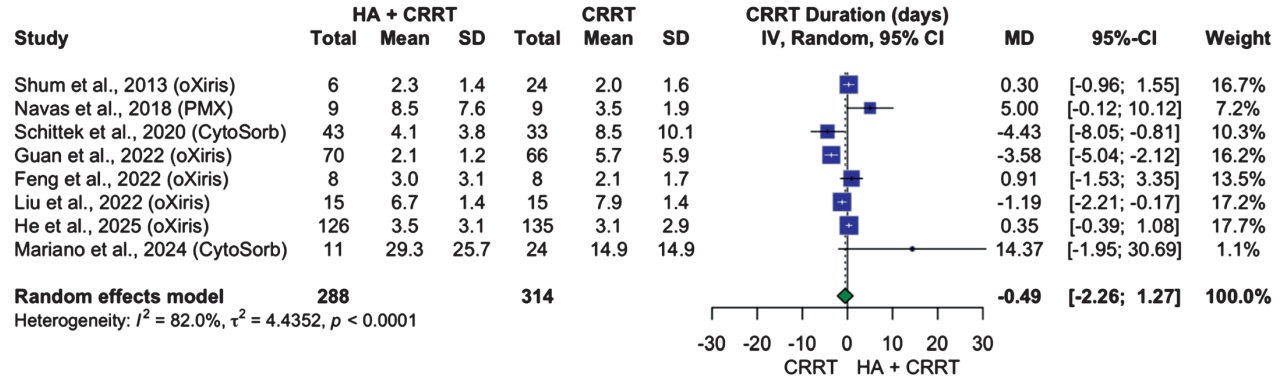




**Figure 3.** Forest Plot of ICU Stay, Hospital Stay, and CRRT Duration Mean Difference Between Hemoadsorption + CRRT and CRRT

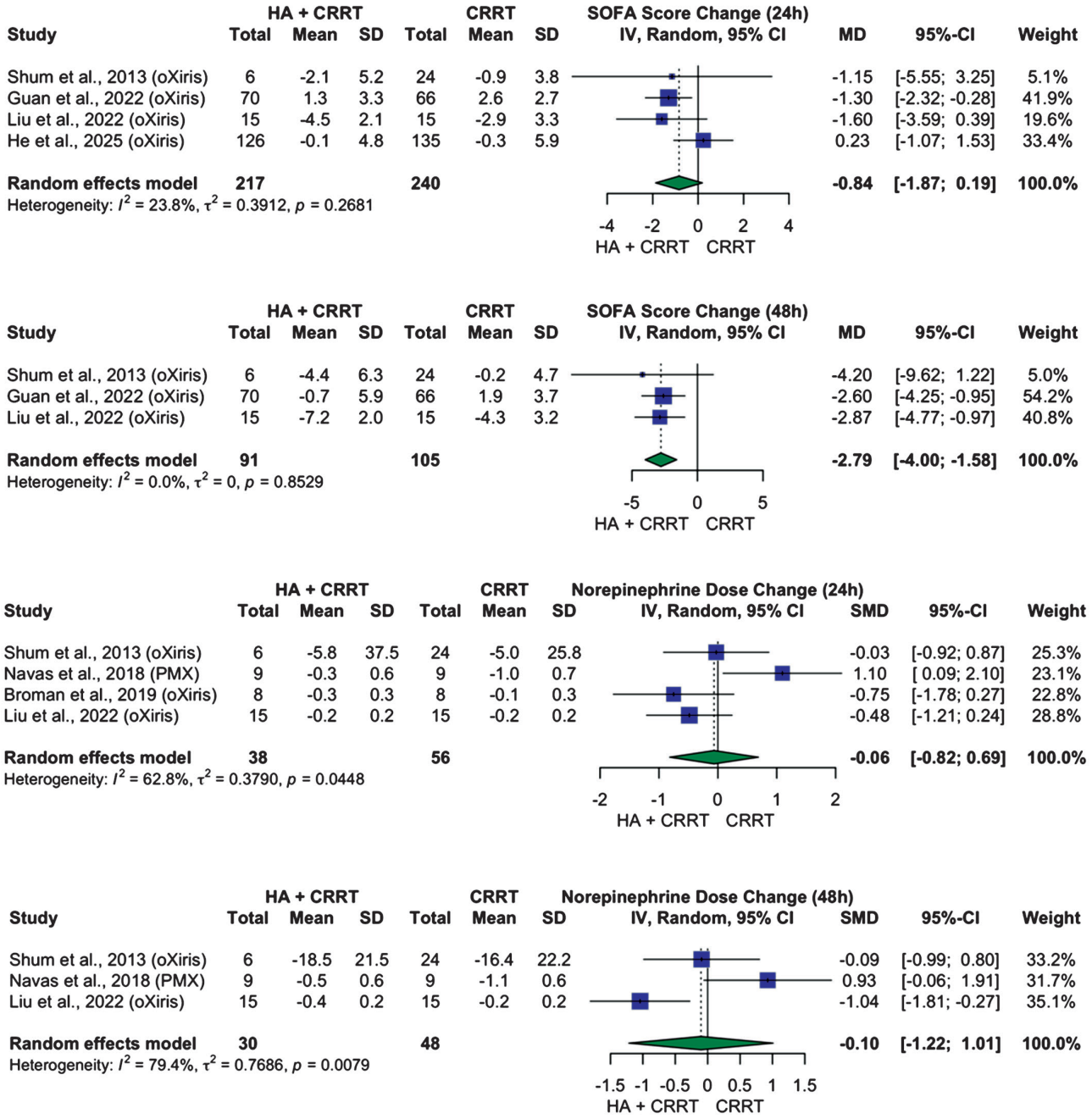



**Figure 4.** Forest Plot of the SOFA Score and Norepinephrine Dose Changes Mean Difference, 24 and 48 Hours After CRRT, Between hemoadsorption + CRRT and CRRT

mechanical ventilation duration between CVVH + oXiris and CVVH alone were found.[44] Notably, patients in the hemoadsorption with PMX group required a longer duration of mechanical ventilation compared to controls.[39] The changes in CRP levels were contradictory between studies.[13,39,43,44,47,48]

*Endotoxin and Cytokine Levels.* Only two studies measured endotoxin levels and reported that endotoxin levels had a significantly greater decline in the oXiris[40] and PMX group[36] compared to the standard filter group. Broman *et al.* revealed that TNF-α levels declined more rapidly and to a greater extent in the oXiris group (70% reduction), compared with the standard CRRT therapy (20% reduction).[40] Zheng *et al.* showed that TNFα and IL-10 levels were lower in the oXiris group compared

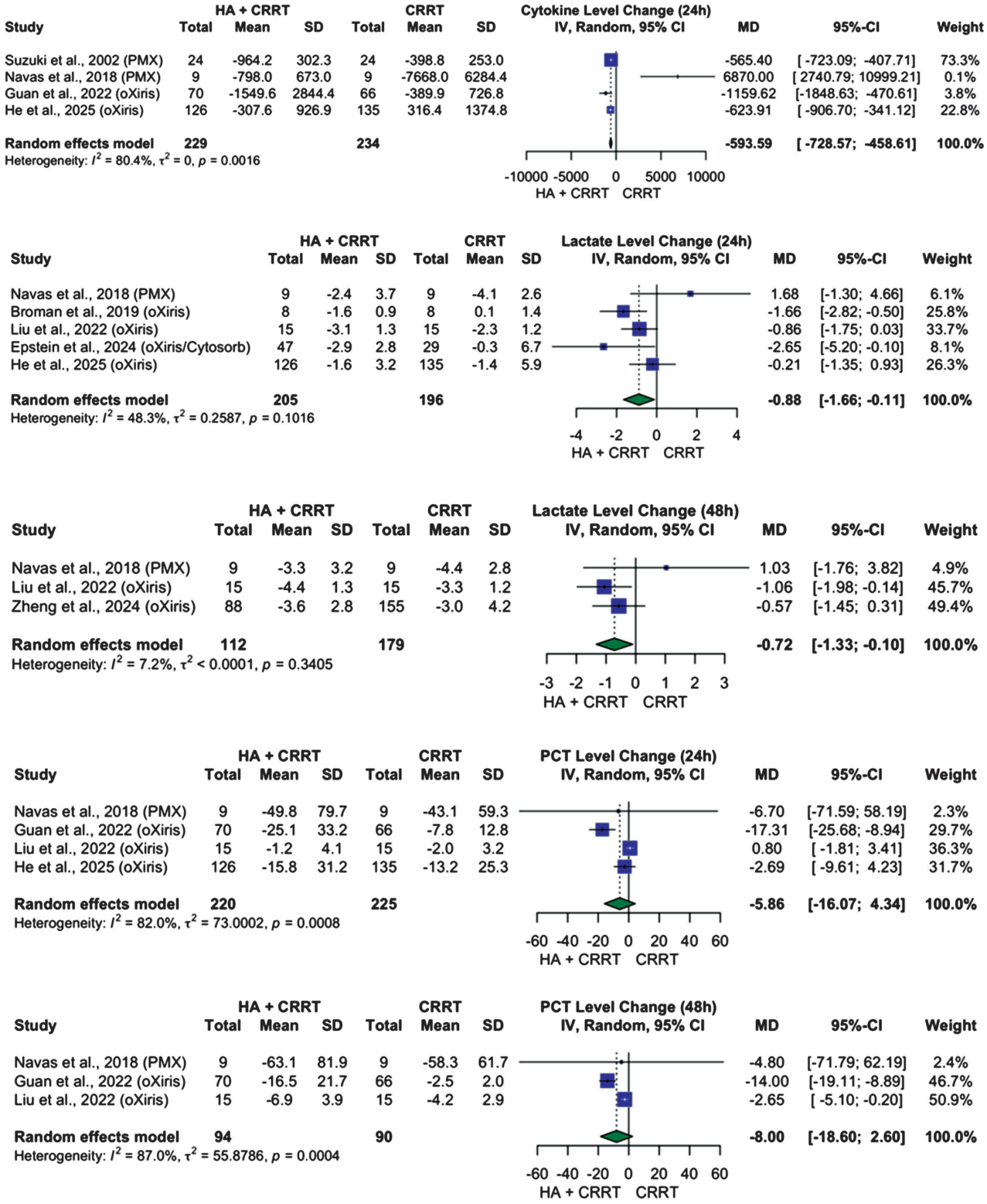



**Figure 5.** Forest Plot of IL-6, Lactate, and PCT Level Changes Mean Difference, 24 and 48 Hours After CRRT, Between hemoadsorption + CRRT and CRRT

to the control group.[46] However, other studies reported no significant differences between the two groups in changes of IL-2, IL-10, and TNF-α after the first treatment with oXiris,[43] IL-1β, IL-8, IL-10, and TNF-α after treatment with PMX,[39] and IL-1β and TNFα after treatment with HA330-II.[47]

## DISCUSSION

In our analysis of SA-AKI patients requiring intensive care, the use of hemoadsorption techniques, when added to CRRT, did not demonstrate a statistically significant difference across primary mortality outcomes compared to conventional CRRT alone. No significant differences were observed in primary endpoints, including 28-, 60-, and 90-day mortality, as well as ICU and in-hospital mortality. Similarly, secondary outcomes, such as length of ICU stay, total hospital length of stay, and duration of CRRT, were comparable between patients treated with hemoadsorption-based strategies and those receiving standard CRRT. Importantly, our analysis demonstrated that adding hemoadsorption to CRRT was associated with a significant reduction in SOFA score at 48 hours and a significant decrease in IL-6 concentrations at 24 hours, alongside significant reductions in lactate levels at both 24 and 48 hours. Subgroup analyses further suggested a significant reduction in 28-day mortality with specific adsorption modalities, including oXiris, the combination of oXiris with CytoSorb, and HA330-II. Moreover, when combined with hemoadsorption, no difference was found between CVVH and CVVHDF modalities for CRRT.

Non-significant differences in primary mortality outcomes may be due to short follow-up durations and multifactorial drivers of mortality in SA-AKI, which are strongly influenced by disease severity and comorbidities. Also, secondary outcomes, including ICU length of stay, hospital length of stay, and CRRT duration, were not inferior to CRRT alone, suggesting that the addition of hemoadsorption did not increase treatment duration or healthcare resource use and may therefore be feasible without increasing healthcare burden. This finding was further supported by subgroup analysis, which showed no improved efficacy of CVVHDF compared to CVVH and no need for higher costs. Also, our analysis demonstrated that the addition of hemoadsorption to CRRT was associated with a significant reduction in SOFA score at 48 hours, suggesting a more rapid short-term improvement in organ dysfunction compared with CRRT alone. This early stabilization effect is biologically plausible, given that hemoadsorption membranes can clear circulating cytokines and endotoxins, key drivers of sepsis-related vasodilation and impaired tissue perfusion.[50] This interpretation is supported by prior studies reporting similar early improvements in organ function and hemodynamics using adsorptive filters like oXiris.[50-2]

In parallel, lactate levels were significantly lower at both 24 and 48 hours in the hemoadsorption group. Lactate is a core component of the current definition of septic shock and represents an objective marker of tissue hypoperfusion that is less influenced by clinician judgment than vasopressor titration. Experimental and clinical data have linked persistent hyperlactatemia in sepsis to microcirculatory dysfunction, endothelial injury, and impaired oxygen utilization, highlighting its relevance as a surrogate of microvascular recovery.[53] In contrast, no significant differences were observed in vasopressor dose reduction between groups, a finding that may reflect the subjective nature of vasopressor management, which depends on physician preference, different protocols, and target blood pressure strategies. Taken together, these findings suggest that hemoadsorption may preferentially improve objective markers of perfusion, such as lactate, and early organ dysfunction, which may help limit early progression from sepsis toward septic shock.

Hemoadsorption is an extracorporeal blood purification strategy designed to remove circulating inflammatory mediators and pathogenic substances involved in the dysregulated immune response of sepsis and SA-AKI.[9,10] Broad-spectrum adsorption devices such as oXiris, CytoSorb, and HA330-II can remove a wide range of cytokines, pathogen-associated and damage-associated molecular patterns, and selected toxins, thereby addressing multiple inflammatory pathways beyond renal solute clearance alone.[16,51,54] In contrast, polymyxin B hemoperfusion is primarily intended to selectively bind circulating lipopolysaccharide and is therefore most relevant in endotoxemia related to gram-

negative bacterial infections.[10,16] These mechanistic differences are reflected in our subgroup findings, which demonstrated a significant reduction in 28-day mortality with oXiris, the combination of oXiris plus CytoSorb, and HA330-II, but not with polymyxin B hemoperfusion. Consistently, sensitivity analyses showed that exclusion of either the Suzuki *et al.* or Lee *et al.* studies resulted in a statistically significant reduction in 28-day mortality, a finding that is plausibly explained by the predominant use of polymyxin B in those trials. Taken together, these observations suggest that inclusion of PMX-based studies where efficacy may be confined to a narrower, endotoxin-driven septic phenotype can dilute pooled mortality effects in heterogeneous SA-AKI populations, whereas broader adsorption modalities may be better suited to the complex inflammatory environment of critically ill patients.

Our findings align with the most recent meta-analyses and reviews focused on CytoSorb or similar broad-spectrum hemoadsorption in sepsis, which have not demonstrated a significant mortality reduction despite improvements in inflammatory mediator clearance or hemodynamics.[55,56] Notably, these studies also described inconsistent effects on secondary clinical outcomes, with some reporting modest or transient reductions in lactate levels or vasopressor requirements, while others found no meaningful differences in ICU length of stay or duration of organ support.[17,55,56] Similarly, we observed significant improvements in objective metabolic and organ dysfunction markers, such as lactate reduction and SOFA score at 48 hours, without corresponding changes in vasopressor dose or ICU length of stay. In contrast, a network meta-analysis of blood purification techniques in septic patients reported heterogeneous results across modalities, suggesting that potential benefits in clinical or surrogate outcomes may be driven by specific adsorption filters rather than hemoadsorption as a uniform intervention.[17]

Most of the previous studies focused on individual hemoadsorption devices, mostly CytoSorb, and enrolled heterogeneous septic populations without specifically focusing on patients with SA-AKI.[52,55,56] In contrast, our meta-analysis exclusively evaluated ICU patients with SA-AKI undergoing CRRT and systematically assessed hemoadsorption as an adjunctive therapy across short-term and intermediate-term mortality endpoints.

## LIMITATIONS

This meta-analysis has several limitations. Most included studies were conducted in Asia, with limited representation from North America, Africa, and other regions, which may restrict generalizability. The majority of studies were single-center with relatively small sample sizes, and hemoadsorption dose and duration were not consistently reported. In addition, study populations were largely restricted to ICU patients, and outcomes predominantly focused on short-term mortality, particularly 28-day mortality, with limited data on long-term outcomes.

## CONCLUSION

In critically ill patients with sepsis-associated AKI, the addition of hemoadsorption to CRRT was associated with significant short-term improvements in organ dysfunction and metabolic markers, including reductions in SOFA score, IL-6, and lactate levels. However, it didn't cause significant improvements in short- or intermediate-term mortality, nor did they affect ICU or hospital length of stay or CRRT duration. Larger, well-designed multicenter trials with standardized hemoadsorption protocols and longer follow-up are needed to clarify whether specific patient subgroups or adsorption modalities may derive meaningful clinical benefit.

## CONFLICT OF INTEREST

Amir Ahmad Nassiri and Ilad Alavi Darazam serve as members of the RJCCN editorial team. The authors had no involvement in the peer-review or editorial decision-making processes for this manuscript.

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Correspondence to:
Amir Ahmad Nassiri, MD
Associate Professor of Nephrology, Department of Nephrology, Imam Hossein Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
ORCID ID: 0000-0002-3748-1181
E-mail: nassirimorad@yahoo.com



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