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ORIGINAL ARTICLE

Clinical efficacy of oXiris-continuous hemofiltration adsorption in septic shock patients: A retrospective analysis

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KEYWORDS
Septic shock;
oXiris-continuous hemofiltration adsorption;
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Clinical prognosis

Abstract
Objective: This study aimed to assess the clinical impact of oXiris-continuous hemofiltration adsorption on patients with septic shock and their prognosis.
Design: A retrospective study.
Participants: Septic shock patients.
Interventions: The oXiris group underwent hemofiltration adsorption using oXiris hemofilters and septic shock standard treatment, while the control group received septic shock standard treatment.
Main variables of interest: The changes in inflammatory indicators and short-term mortality rate were evaluated. Propensity score matching (PSM) was conducted based on the 1:2 ratio between the oXiris and control groups to account for any baseline data differences.
Results: Results showed that after 24 h, 48 h, and 72 h of treatment, PCT, IL-6, and hs-CRP levels in the oXiris group were significantly lower than those in the control group ($P < 0.05$). However, there were no significant differences in norepinephrine equivalents and organ function status (APACHE II score, SOFA score, Lac) between the two groups at the same time points. The 72-h mortality rate (21.88% vs. 34.04%) and the 7-day mortality rate (28.12% vs. 44.68%) were lower in the oXiris group compared to the control group, but not statistically significant. The 28-day mortality rate did not show a significant difference between the two groups (53.19% vs. 56.25%).
Conclusions: oXiris continuous hemofiltration adsorption technology may reduce the levels of inflammatory factors in patients with septic shock; however, it does not appear to enhance organ function or improve the 28-day mortality rate in these patients.

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PALABRAS CLAVE
Shock séptico;
Absorción continua de hemofiltración oxiris;
CRRT;
Pronóstico clínico

Análisis retrospectivo de la eficacia clínica de la adsorción continua de hemofiltración de oxiris en el tratamiento del shock séptico

Resumen
Objetivo: Este estudio tiene como objetivo evaluar el impacto clínico y el pronóstico de la adsorción continua de hemofiltración de oxiris en pacientes con shock séptico.
Diseño: Estudio retrospectivo.
Participantes: Pacientes con shock séptico.
Intervención: El Grupo oxiris utiliza un filtro de sangre oxiris para la absorción de hemofiltración y recibe el tratamiento estándar de shock séptico, mientras que el grupo control recibe el tratamiento estándar de shock séptico.
Variables de interés principales: Evaluación de indicadores inflamatorios y cambios en la mortalidad a corto plazo.La coincidencia de puntuación de predisposición se realizó de acuerdo con la tasa 1: 2 entre el Grupo oxiris y el grupo control para explicar cualquier diferencia en los datos de referencia.
Resultados: Los resultados mostraron que después de 24, 48 y 72 horas de tratamiento, los niveles de pct, IL - 6 y HS - CRP en el Grupo oxiris fueron significativamente más bajos que en el grupo control ($p < 0,05$). Sin embargo, al mismo tiempo, no hubo diferencias significativas en el equivalente de noradrenalina y el Estado funcional de los órganos (puntuación Apache ii, puntuación sofa, lac) entre los dos grupos. Las tasas de mortalidad a 72 horas (21,88% frente al 34,04%) y a 7 días (28,12% frente al 44,68%) fueron más bajas en el Grupo oxiris que en el Grupo control, pero no estadísticamente significativas. La mortalidad a 28 días no mostró diferencias significativas entre los dos grupos (53,19% frente al 56,25%).
Conclusión: La tecnología de absorción de hemofiltración continua de oxiris puede reducir los niveles de factores inflamatorios en pacientes con shock séptico; Sin embargo, no parece haber mejorado la función orgánica de estos pacientes ni haber aumentado la mortalidad a los 28 días.

Introduction

Sepsis is distinguished by organ dysfunction that could be life-threatening, originating from the host's abnormal response to infection. Septic shock is essentially sepsis that is compounded by severe circulatory, metabolic, and cellular dysfunction, carrying a higher mortality risk in comparison to uncomplicated sepsis.[1] A comprehensive meta-analysis conducted from 2009 to 2019 across regions such as North America, Europe, and Australia discovered that the 90-day mortality rates were 32.2% for sepsis and 38.5% for septic shock.[2] Similarly, a cross-sectional study in China indicated that sepsis accounted for 20% of ICU patient diagnoses, with 90-day mortality rates observed at 35.5% for sepsis and 51.9% for septic shock.[3]

The methods for treating sepsis include antibiotics, infection source control, hemodynamic optimization. Anti-endotoxin antibodies have been used in clinical practice, but have not shown significant therapeutic effects.[4] Scholars are continuously investigating new treatment approaches based on the pathological and physiological mechanisms of sepsis, particularly for septic shock with a high mortality rate. It is widely accepted that an excessive inflammatory response in sepsis patients can lead to organ dysfunction and early death.[5] Continuous hemofiltration dialysis was first reported in 1993 by Bellomo et al.'s study as a method to clear inflammatory mediators.[6] Subsequent studies have confirmed that the adsorption or filtration modes of continuous renal replacement therapy (CRRT) may effectively remove pro-inflammatory and anti-inflammatory cytokines in sepsis patients,[7–11] helping to maintain a stable immune balance.[12]

Currently, China and several Western countries have started using the oXiris hemofilter for treating septic shock patients.[4,13] The oXiris hemofilter combines the functions of CRRT, endotoxin adsorption, and cytokine adsorption, effectively suppressing the inflammatory response in septic shock patients.[6] Preliminary small-scale clinical trials have indicated that oXiris can notably decrease endotoxin levels and remove inflammatory mediators in hyperendotoxemia patients.[14–18] However, it remains uncertain whether oXiris hemofilter can enhance circulatory status, organ function, clinical outcomes in patients experiencing septic shock. Therefore, this study retrospectively analyzes the clinical outcomes from our center to offer additional insights into the application of oXiris hemofilter in septic shock patients.

Materials and methods

Participants and grouping

The study involved patients who were admitted to the ICU (The Third Hospital of Mianyang, Sichuan Province, China) with septic shock from December 2020 to December 2023. The criteria for inclusion were: 1) individuals aged 18 years or older, 2) diagnosed with septic shock according to Sepsis 3.0 criteria, and 3) received antibiotics and sufficient fluid resuscitation following the onset of septic shock. To diagnose septic shock, the following criteria were used: 1) confirmed or suspected infection, 2) an increase in the SOFA score by more than 2 points compared to the baseline, 3) requirement of vasopressor medications to maintain a mean arterial pressure of at least 65 mmHg after fluid resuscitation, and 4) blood lactate levels exceeding 2 mmol/L. Patients were excluded if they had: 1) stage 5 chronic kidney disease (glomerular filtration rate less than 15 mL/min/1.73 m^2) or were on maintenance dialysis, 2) primary illnesses with a poor prognosis (e.g., cardiogenic shock), 3) previously received ECMO treatment, 4) malignant tumors with an expected lifespan of less than six months, 5) were organ transplant recipients, 6) had family members unwilling to pursue aggressive treatment choices (DNI, DNR, refusal of invasive procedures), or 7) lacked medical records.

Participants were grouped based on whether they received oXiris hemofilter CRRT or conventional hemofilter CRRT. Those who received oXiris hemofilter CRRT were categorized into the oXiris group, while those who did not receive oXiris hemofilter CRRT or only received conventional hemofilter CRRT (ST 100) were placed in the control group. In this study, the baseline time point (0 h) for the oXiris group was defined as the first instance of oXiris hemofilter CRRT on the machine after septic shock was diagnosed. For the control group, the baseline time point (0 h) was when the patient was diagnosed with septic shock. Subsequent time points were marked as 24 hours (24 h), 48 hours (48 h), and 72 hours (72 h) after the baseline.

Data collection

Data collection included information on patients' general situation upon entering the group such as name, sex, age, height, ideal weight, underlying diseases, main diagnosis, site of infection, use of antibiotics, vital signs, and use of vasoactive drugs (measured as norepinephrine equivalent). Underlying diseases were assessed using the aCCI score[19] (see Table S4 in Supplemental digital content). The study also gathered data on parameters for oXiris treatment, indicators of inflammation, organ function, and evaluation of prognosis. This included specifics such as time on the oXiris machine, duration of hemofilter usage, alterations in infection markers (white blood cells, procalcitonin (PCT), Interleukin-6 (IL-6), high-sensitivity C-reactive protein (hs-CRP)), levels of lactate, equivalent amount of norepinephrine (NE), Acute Physiology and Chronic Health Evaluation II (APACHE II) score, Sequential Organ Failure Assessment (SOFA) score at 0 h, 24 h, 48 h, and 72 h. Subsequent evaluations up to 28 days post admission documented overall hospital stay, length of ICU hospitalization, time on mechanical ventilation, and mortality rate after 28 days. Norepinephrine dose equivalences were estimated based on previous studies[20] (refer to Table S5 in Supplemental digital content).

Statistical analysis

Mean ± standard deviation or median (lower quartile-upper quartile) described continuous variables, while examples (percentage) depicted classified variables. To compare continuous variables, t-tests or nonparametric tests were utilized, and χ^2 analysis or Fisher's exact test were employed for classified variables. Matching variables with statistically significant differences ($P < 0.05$) in baseline data (such as age, sex, aCCI, and various physiological measurements) between the control group and the oXiris group underwent propensity score matching (PSM) at a 1:2 ratio. Subsequent comparisons between groups were conducted on observed differences in indicators. Kaplan-Meier survival analysis curve was used to assess 28-day mortality between the groups. A univariate logistic regression analysis was employed to assess the influencing factors on 28-day mortality in two groups of patients. Since the baseline data for both groups had already undergone PSM, the multivariate analysis was conducted based on previously reported risk factors, as well as those factors that demonstrated statistical significance in the univariate analysis, which were subsequently included in the model. Statistical analysis was performed using IBM SPSS version 26.0 (IBM SPSS, Armonk, N.Y., USA) and R language 3.5.3.

Results

General characteristics

A total of 271 individuals diagnosed with sepsis were admitted to the ICU between December 2020 and December 2023. Among them, 216 patients exhibited signs of septic shock, while 36 individuals were excluded for various reasons: 11 cases were in the late stage of tumors, 2 cases were complicated by severe cardiogenic shock, 4 cases had stage 5 chronic kidney disease, and 19 cases were discontinued by family members. The median age of the group was 70.00 years (IQR: 60.00–79.00), with a median aCCI of 4.00 (IQR: 2.00–5.00), a median APACHE II score of 24.00 (IQR: 20.00–30.00), and a median SOFA score of 11.00 (IQR: 9.00–13.00). The most common infection locations were the lungs (44.4%), abdomen (48.9%), bloodstream (14.4%), and other regions (17.2%). Some individuals had multiple sites of infection, such as simultaneous lung and bloodstream infections.

The study included a control group (n = 138) and an oXiris group (n = 42). Baseline data comparison between the two groups showed differences in heart rate (111.50 [92.25, 132.75] vs. 124.50 [112.00, 138.00] per min), norepinephrine equivalent (0.59 [0.29, 1.66] vs. 2.87 [1.03, 3.94]mcg/kg/min), SOFA score (10.00 [8.00, 13.00] vs. 13.00 [10.00, 14.75]), arterial blood lactate (3.40 [2.20, 5.68] vs. 5.10 [3.12, 8.45] mmol/L), creatinine (121.00 [78.75, 233.25] vs. 190.00 [132.00, 244.00] umol/L), procalcitonin (16.64 [5.20, 50.00] vs. 50.36 [18.97, 100.00] ng/ml), and

Table 1 Baseline characteristics of patients in two groups before and after adjusting for the groups using the Propensity Score Matching.

Variable	Before PSM				After PSM			
	Control group (n = 138)	oXiris group 1 (n = 42)	P	SMD	Control group (n = 47)	oXiris group 1 (n = 32)	P	SMD
Age[a], years	69.00 (59.25, 80.00)	70.50 (66.00, 77.75)	0.765	−0.084	71.00 (65.00, 79.00)	72.00 (66.75, 78.00)	0.940	−0.061
Male[b], (n,%)	90 (65.22)	31 (73.81)	0.299	0.195	34 (72.34)	24 (75.00)	0.793	0.061
aCCI[a]	3.50 (2.00, 5.00)	4.00 (3.00, 5.00)	0.462	0.106	4.00 (2.00, 5.00)	3.50 (3.00, 5.00)	0.883	−0.048
HR[a], per min	111.50 (92.25, 132.75)	124.50 (112.00, 138.00)	0.028	0.399	116.00 (99.50, 131.00)	123.00 (111.00, 129.25)	0.451	0.139
MAP[a], mmHg	68.50 (56.17, 83.67)	61.17 (53.42, 76.83)	0.063	−0.259	64.33 (54.50, 80.00)	61.17 (53.08, 75.17)	0.542	−0.103
RR[a], per min	23.00 (18.00, 30.00)	28.00 (20.00, 32.00)	0.124	0.141	23.00 (16.00, 32.00)	28.00 (20.00, 32.00)	0.190	0.288
NE[a], mcg/kg/min	0.59 (0.29, 1.66)	2.87 (1.03, 3.94)	<.001	0.948	1.92 (0.58, 3.27)	2.52 (0.99, 3.56)	0.281	0.229
APACHE II[a] Score	24.00 (20.00, 29.00)	23.50 (20.25, 31.00)	0.224	0.271	24.00 (20.50, 31.00)	23.50 (21.00, 30.00)	0.865	0.053
SOFA[a] Score	10.00 (8.00, 13.00)	13.00 (10.00, 14.75)	<.001	0.704	12.00 (10.00, 14.50)	12.00 (10.00, 13.00)	0.813	0.004
P/F[a], mmHg	196.25 (120.00, 284.23)	177.50 (136.57, 220.93)	0.333	−0.263	182.00 (116.50, 273.00)	177.50 (136.98, 223.00)	0.838	−0.067
Lac[a], mmol/L	3.40 (2.20, 5.68)	5.10 (3.12, 8.45)	0.003	0.406	4.10 (2.75, 7.15)	4.65 (3.03, 7.78)	0.772	0.027
WBC[a], 10^9 /L	9.48 (5.42, 15.19)	11.77 (6.85, 17.56)	0.293	0.133	11.01 (3.21, 19.55)	13.10 (7.06, 17.22)	0.447	−0.048
BUN[a], mmol/L	12.79 (8.83, 20.66)	15.81 (11.13, 19.81)	0.182	−0.119	14.12 (9.52, 21.10)	15.81 (11.38, 19.62)	0.611	−0.222
Cr[a], umol/L	121.00 (78.75, 233.25)	190.00 (132.00, 244.00)	0.003	0.256	163.00 (106.00, 291.50)	191.50 (131.00, 238.00)	0.772	−0.189
PCT[a], ng/ml	16.64 (5.20, 50.00)	50.36 (18.97, 100.00)	<.001	0.670	52.22 (16.70, 86.86)	50.36 (18.00, 85.80)	0.774	0.035
IL-6[a], pg/ml	351.97 (66.73, 1964.20)	4000.00 (589.60, 4000.00)	<.001	0.779	2234.50 (348.97, 4000.00)	1103.42 (434.55, 4000.00)	0.640	−0.017
hs-CRP[a], mg/L	113.22 (48.21, 233.42)	139.14 (55.15, 245.55)	0.443	0.146	115.10 (64.34, 227.54)	134.38 (59.03, 243.85)	0.723	0.078

aCCI: age-adjusted Charlson Comorbidity Index; HR: heart rate; MAP: mean arterial pressure; RR: respiratory rate; NE: norepinephrine equivalent; APACHE II: Acute Physiology and Chronic Health Evaluation II; SOFA: Sequential Organ Failure Assessment; P/F: Arterial oxygen tension/Inspired oxygen fraction; Lac: lactate; WBC: leukocyte; BUN: blood urea nitrogen; Cr: creatinine; PCT: procalcitonin; IL-6: Interleukin-6; hs-CRP: high-sensitivity C-reactive protein.

p Value <0.05 was considered as a significant difference.

[a] Mann-Whitney test for comparison between three groups.

[b] Chi-square test for comparison between two groups.

interleukin-6 (351.97 [66.73, 1964.20] vs. 4000.00 [589.60, 4000.00] pg/ml). Due to the larger sample size in the control group, matching variables were used to balance the groups at a 1:2 ratio after propensity score matching, resulting in 47 cases in the control group and 32 cases in the oXiris group. The characteristics of baseline data before and after matching can be found in Table 1.

Following PSM, there were no notable variances in infection sites and etiological data between the two cohorts, the antibiotic usage rate for both groups of patients was 100% (Table 2). Within the oXiris cohort, A total of 22(68.75%) patients were diagnosed with septic shock and received oXiris hemofilters treatment within 24 hours, while an additional 10(31.25%) patients received oXiris hemofilters treatment between 24 and 48 hours. The hemofilter typically underwent replacement after a specific timeframe (12 or 24 hours) or upon achieving the desired results. The majority of hemofilters received anticoagulation with regional citrate (n = 26), followed by heparin anticoagulation (n = 2), and no anticoagulation (n = 4). On average, 2 (range: 1–4) oXiris hemofilters were utilized during hospital stay in the oXiris cohort, with the mean duration of hemofilter use being 26.7 hours. In the control group, a total of 5 patients (10.6%) received CRRT treatment utilizing conventional filters (ST100). The CRRT parameters were configured as follows: Blood flow rate (120–150 ml/h) and CRRT mode set to continuous venovenous hemodiafiltration (CVVHDF), with a prescribed treatment dose of 30 ml/kg/h. Bicarbonate replacement solution (produced by Chengdu Qingshan Likang Pharmaceutical Co., Ltd., Chengdu, China) was administered utilizing a post-dilution technique (fluid replacement/dialysate ratio of 1:1).

Infection indexes and inflammatory mediators

Changes in infection indicators and inflammatory markers were observed in both the control group and the oXiris group. Both groups experienced a slight decrease in white blood cell count up to 72 hours after admission, compared to levels upon admission, although this distinction was not statistically significant. Additionally, procalcitonin (PCT), interleukin-6 (IL-6), and high-sensitivity C-reactive protein (hs-CRP) all showed a decline in levels within the 72-h period for both groups. Significantly, the oXiris group exhibited markedly lower levels of PCT, IL-6, and hs-CRP compared to the control group at 24, 48, and 72 hours post-admission ($P < 0.05$) (Fig. 1 and Table S5).

NE equivalent and organ function status

Changes in the equivalent of noradrenaline (NE) and the status of organ function were assessed in both the control and oXiris groups. At the start of the study (0 hours), the NE equivalent was 1.92 (0.58, 3.27) mcg/kg/min in the control group and 2.52 (0.99, 3.56) mcg/kg/min in the oXiris group. Similarly, after 48 hours, the NE equivalent was 1.66 (0.68, 3.20) mcg/kg/min in the control group and 2.00 (1.22, 2.89) mcg/kg/min in the oXiris group. By the 72-h mark, the NE equivalent was 1.04 (0.32, 2.94) mcg/kg/min in the control group compared to 1.89 (0.67, 3.12) mcg/kg/min in the oXiris group, with no statistically significant difference between the groups. The Acute Physiology and Chronic Health Evaluation (APACHE) II scores were compared at different time points (0 h, 24 h, 48 h, 72 h) along with Sequential Organ Failure Assessment (SOFA) scores (0 h, 24 h, 48 h, 72 h), showing no significant differences between the control and oXiris groups. Additionally, the levels of lactate (0 h, 24 h, 48 h, 72 h) did not differ significantly between the control and oXiris groups as depicted in Fig. 2 and Table S7.

Prognosis analyses

Comparing the prognosis of the two groups revealed that the mortality rates at 72 hours and 7 days were greater in the control group than in the oXiris group (16 (34.04%) vs. 7 (21.88%) and 21 (44.68%) vs. 9 (28.12%), respectively, with no significant variation noted. The mortality rate at 28 days was comparable between the two groups (25 (53.19%) vs. 18 (56.25%)), also lacking statistical significance (Table 3). Examination of Kaplan-Meier survival data revealed no notable contrast in the 28-day mortality rates between the oXiris and control groups ($p = 0.594$) (Fig. 3). Univariate logistic analysis revealed a statistically significant difference ($P < 0.05$) in the distribution of 28-day mortality rates between the NE equivalent and SOFA scores of the two patient groups. Treating 28-day mortality as the dependent variable (survival = 0, death = 1) and utilizing the independent variables that demonstrated statistically significant differences in the univariate analysis, the results indicated that the NE equivalent greater than 1.0 mcg/kg/min was an independent risk factor for 28-day mortality (Table S8). The duration of ICU hospital stay was significantly lengthier in the oXiris group than in the control group (8.00 (3.75, 13.00) vs. 4.00 (2.00, 8.50), showing a significant difference ($P < 0.05$). Moreover, the periods of mechanical ventilation, ICU expenses, and total hospitalization costs were elevated in the oXiris group compared to the control group, albeit lacking statistical significance (Table 3).

Discussion

Our study found that the oXiris hemofilters significantly reduced levels of PCT, hs-CRP, and IL-6 compared to the control group. Although the 72-h and 7-day mortality rates were lower in the oXiris group, these differences were not statistically significant. Additionally, there was no significant difference in 28-day mortality between the two groups. Furthermore, the oXiris group exhibited longer hospital stays, increased mechanical ventilation times, and higher ICU and total hospitalization costs compared to the control group; however, these differences were also not statistically significant.

Endotoxin, a lipopolysaccharide present in the cell wall of Gram-negative bacteria, is released into the bloodstream upon bacterial death in significant quantities. This release triggers the activation of the monocyte-macrophage system through endotoxin stimulation, leading to the generation of several inflammatory markers like C-reactive protein, procalcitonin, tumor necrosis factor-α (TNF-α), and IL-6. This sequence initiates an immune inflammatory cascade, promoting the binding of neutrophils to endothelial cells. At

Table 2 The conditions of the infection in two groups.

Variables	Control group (n = 47)	oXiris group (n = 32)	*P*
Site of infection			
Pulmonary (n,%)	22 (46.81)	10 (31.25)	0.167
Intra-abdomen (n,%)	25 (53.19)	19 (59.38)	0.587
Urinary (n,%)	2 (4.26)	3 (9.38)	0.655
Blood (n,%)	6 (12.77)	8 (25.00)	0.162
Skin or tissue (n,%)	1 (2.13)	0 (0.00)	1.000
Culture-proven infection			
Gram positive (n,%)	5 (10.64)	1 (3.12)	0.421
Gram negative (n,%)	25 (53.19)	18 (56.25)	0.789
Gram positive and negative (n,%)	6 (12.77)	6 (18.75)	0.683
Fungal infection (n,%)	4 (8.51)	5 (15.62)	0.538
Pathogen			
Staphylococcus aureus (n,%)	7 (14.89)	1 (3.12)	0.186
Pseudomonas aeruginosa (n,%)	1 (2.13)	5 (15.62)	0.073
Acinetobacter baumannii (n,%)	13 (27.66)	9 (28.12)	0.964
Escherichia coli (n,%)	9 (19.15)	12 (37.50)	0.070
Klebsiella (n,%)	16 (34.04)	8 (25.00)	0.391
Candida Albicans (n,%)	4 (8.51)	5 (15.62)	0.538
Others	3 (6.38)	4 (12.50)	0.592
Antimicrobial treatment (n,%)	47(100%)	32(100%)	–

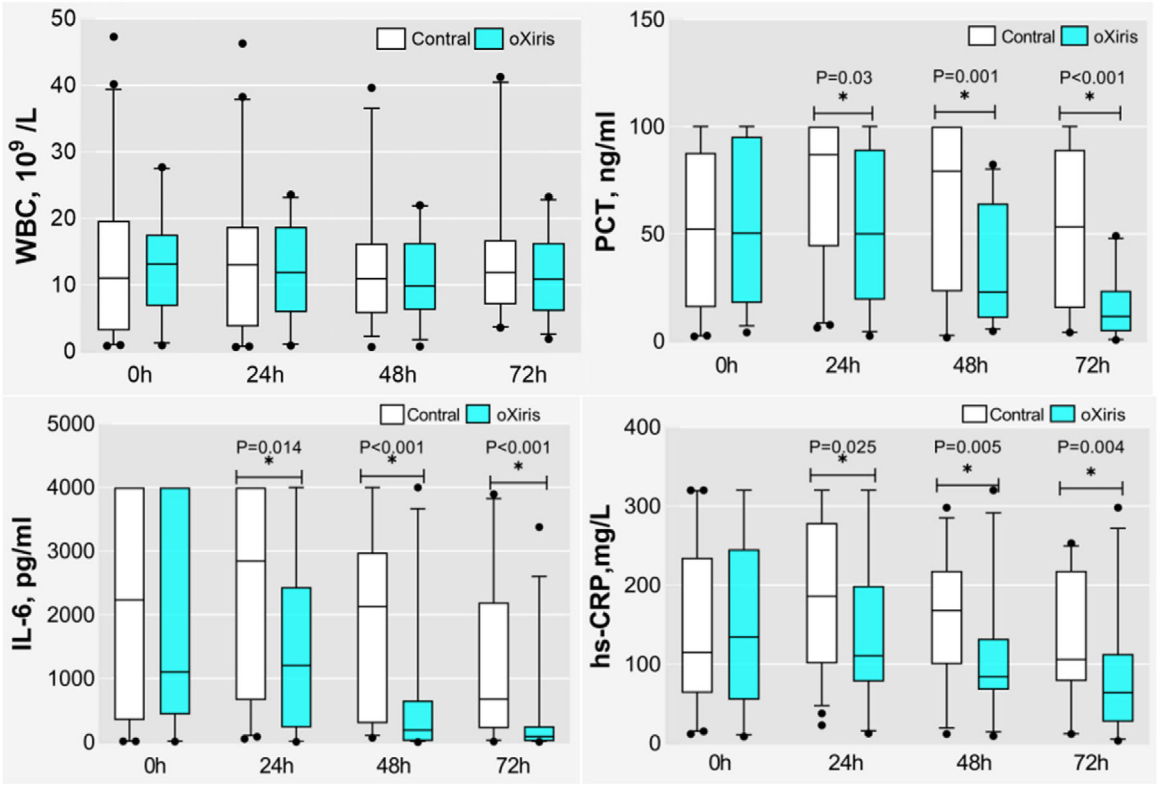

Figure 1 Changes in WBC, PCT, IL-6 and hs-CRP at baseline, 24 h, 48 h and 72 h in two groups. *P < 0.05.

the same time, the excessive release of protease due to lysosome membrane breakdown causes damage to vascular endothelial cells, microvascular dysfunction, and irregular contractions, eventually resulting in septic shock.[21] Oxidative stress can trigger molecular pathways, initiating inflammatory responses and causing tissue injury, a critical mechanism in the development of multiple organ failure in septic shock.[22] Conventional CRRT membrane

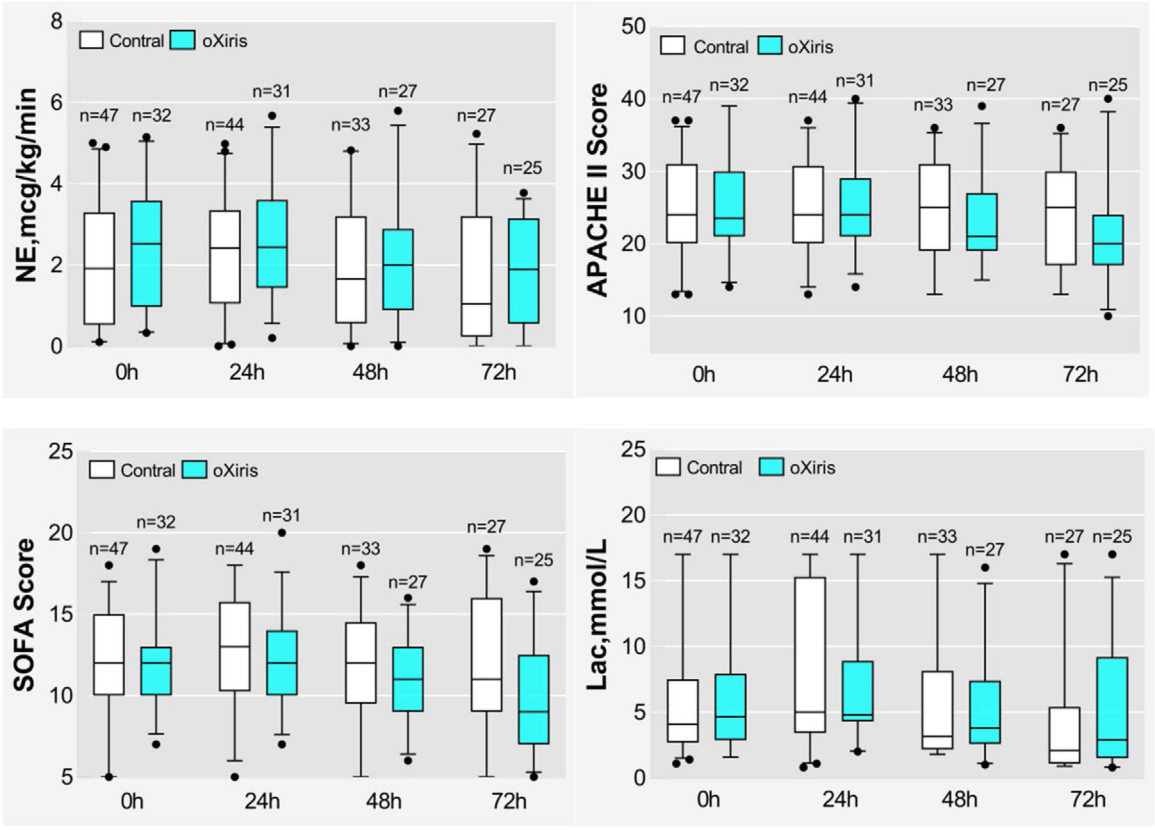

Figure 2 Changes in NE dosage, APACHE II score, SOFA score and Lac at baseline, 24 h, 48 h and 72 h in two groups.

Table 3 The outcomes in two groups.

Variables	Control group (n = 47)	oXiris group (n = 32)	*P*
72 h death[b], n(%)	16 (34.04)	7 (21.88)	0.243
7 days death[b], n(%)	21 (44.68)	9 (28.12)	0.137
28 days death[b], n(%)	25 (53.19)	18 (56.25)	0.789
ICU days[a]	4.00 (2.00, 8.50)	8.00 (3.75, 13.00)	0.030
Hospital Days[a]	10.00 (3.00, 15.50)	13.00 (7.75, 15.25)	0.243
Mechanical ventilation time[a](hours)	41.00 (18.50, 89.50)	98.50 (17.50, 201.00)	0.242
Hospitalization expenses[a], CNY	63196.95 (32247.11, 108122.24)	79291.03 (33249.99, 134161.16)	0.368
ICU expenses[a], CNY	33581.00 (19859.93, 90673.63)	59541.24 (28937.14, 112613.71)	0.055

CNY: Chinese Yuan.
[a] Mann-Whitney test for comparison between three groups.
[b] Chi-square test for comparison between two groups.

materials primarily provide kidney support, while adsorptive CRRT membrane materials like AN69/AN69ST/PMMA not only offer traditional CRRT functions but also have the ability to adsorb inflammatory mediators. The latest AN69 series product, the oXiris membrane material, is an advancement that not only absorbs inflammatory mediators but also endotoxins, while still providing kidney support. PMX adsorption columns target endotoxins through perfusion, and CytoSorb absorbs cytokines through hemoperfusion. Among current blood purification products, the oXiris membrane material stands out for its comprehensive functionality.[23]

Research conducted in laboratory settings has shown the effectiveness of the oXiris hemofilter in the elimination of inflammatory mediators and endotoxin.[24] A small trial that involved random assignment of participants to different groups found that the oXiris hemofilters successfully removed inflammatory mediators including TNF- α, IL-6, IL-8, and IFN-γ.[25] Additional studies have pointed out that patients with sepsis who survived exhibited a more rapid reduction in IL-6 levels post-treatment in comparison to patients who did not survive.[14] The findings of this investigation indicated a substantial decrease in infection markers PCT, hs-CRP, and IL-6, with a particular focus on the sig-

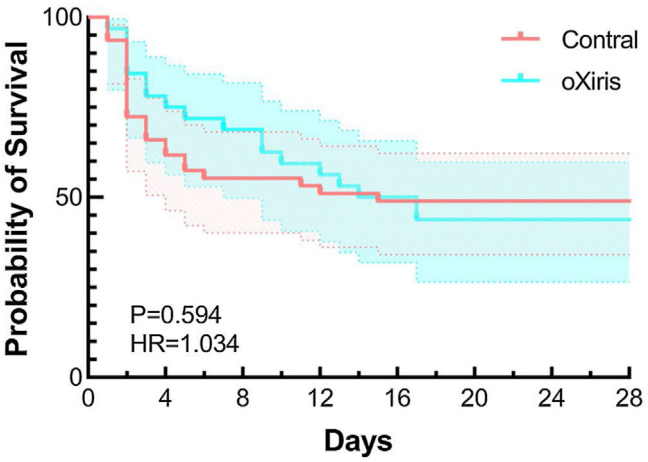

Figure 3 Twenty-eight-day survival probability in two groups.

nificant decrease in IL-6 compared to the control group, thereby suggesting the effectiveness of the oXiris hemofilter in eliminating inflammatory mediators.

Several clinical trials have suggested that oXiris might enhance hemodynamic parameters, reduce the necessity for norepinephrine, improve lactic acid clearance, decrease the need for resuscitation fluids,[26,27] and decrease the SOFA score.[28–30] Our study presents results that are in contrast to prior investigations. It was noted that patients in the oXiris group, following 24 to 72 hours of treatment, did not display a decrease in demand for NE equivalents or lactate levels compared to the control group. While there was a decline in APACHEII score and SOFA score in the oXiris group in comparison to the control group, this difference did not achieve statistical significance. We attribute the aforementioned results to the severe shock experienced by the selected patients, 10 of whom (31.25%) initiated oXiris treatment within 24 hours of being diagnosed with septic shock. It is possible that these patients experienced a deterioration in their condition, necessitating higher doses of vasopressors. This study show that the 28-day mortality rates between the two groups were comparable (56.25% vs. 53.19%). This result contradicts several prior investigations.[13,31] Pooling data from 14 studies with 695 patients, a meta-analysis discovered that septic patients using the oXiris hemofilter had lower 28-day mortality rates [odds ratio (OR) 0.53; 95% confidence interval (CI) 0.36–0.77, $p = 0.001$] and reduced ICU stays [weighted mean difference (WMD) −1.91; 95% CI −2.56 to −1.26, $p < 0.001$].[32] However, concerns have been expressed by some researchers about the statistical techniques utilized, and most of the studies included were retrospective, with insufficient cases to definitively confirm the benefits of oXiris.[33] These results prompt the inquiry as to why prognosis is not enhanced. One possible rationale is that although the oXiris hemofilter can eliminate endotoxins and inflammatory mediators, it may impact only a fraction of the inflammatory network, leaving the overall network unaffected. Another consideration is that the removal of certain cytokines and inflammatory mediators might overly suppress the immune response in sepsis patients. Emphasizing the significance of antibiotics in septic shock treatment is crucial. Not only do membranes for hemofiltration absorb endotoxins and inflammatory mediators but they also have the capability to capture antibiotics. At present, there are no set protocols for altering antibiotic levels in oXiris hemofilter CRRT, and the ideal antibiotic concentration is still unknown. It is crucial to acknowledge that utilizing blood hemofilters such as oXiris could potentially reduce the effectiveness of antibiotics, potentially accelerating the decline of the patient. This highlights the importance of ongoing clinical surveillance and evaluation.

There is currently no agreement on the use of oXiris in critically ill individuals with AKI. A recent randomized controlled trial conducted across multiple countries showed that initiating treatment with oXiris promptly can result in enhanced kidney function, reduced CRRT duration, and shortened ICU stay.[34] In our study of the oXiris group, patients had high APACHEII and SOFA score, the dose of vasoactive drugs at the beginning of oXiris treatment was very large, indicating severe conditions. Further research is needed to determine if inflammatory adsorption therapy should be initiated when vasoactive drug doses reach a certain level (such as NE > 0.5 μg/kg/min or 1.0 μg/kg/min). Our study used an average of 2.5 oXiris hemofilters per patient, with an average hemofilter use time of 26.7 hours. The optimal number of hemofilters and timing for their use remains unclear, considering both clinical efficacy and economic factors. Notably, patients in the oXiris group incurred higher costs and longer hospitalization and ICU stays compared to the control group, possibly influenced by early mortality rates and limited control group cases.

The study comes with several limitations. Primarily, standardized clinical guidelines for the utilization of oXiris are lacking, including explicit directions for commencing and ceasing treatment, alongside inconsistencies in CRRT parameters and the simultaneous utilization of traditional hemofilters. Furthermore, this retrospective study was conducted at a singular center with a restricted number of cases. Even though PSM was utilized to account for differences in fundamental characteristics and disease severity, potential biases stemming from unobserved confounding variables remain plausible. The demographic of the study exhibited notable diversity, encompassing various infection locations (such as the abdominal cavity, lungs, blood, urine, skin, and soft tissue) and diverse pathogens (including gram-negative bacteria, gram-positive bacteria, and fungi). Solely IL-6 levels were recorded, with pivotal cytokines like endotoxin level, IL-1, IL-8, and TNF-α, which play vital roles in sepsis progression, not being evaluated, thereby limiting the substantiation endorsing the efficacy of oXiris in removing inflammatory mediators. Given the limited number of cases, our study did not analyze the differences between the two patient groups using conventional filters and oXiris filters.Moreover, essential hemodynamic information, such as cardiac output and vascular resistance, was not gathered, raising uncertainties regarding whether CRRT, by eradicating inflammatory mediators and enhancing vascular tone, amplified circulatory function in patients with septic shock. Furthermore, the study's follow-up duration was brief, precluding insights into the enduring effects of oXiris usage on the prognosis of septic shock patients.

Conclusion

The oXiris-continuous hemofiltration adsorption has shown promise in reducing inflammatory mediators in septic shock patients, yet it has not demonstrated significant improvements in organ function or patient prognosis. Further randomized controlled trials are necessary to validate its clinical efficacy.

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Contribution of the authors

Yuxin Yang: Formal analysis, Investigation, Data Curation, Writing the Original Draft. Qionglan Dong: Conceptualisation, Methodology, Project administration, Funding acquisition. Jianpeng Su, Hongjun Xiao, Dan Zan, Jinfeng Chen, Xue Chen, Qibing Tang, Cheng Zeng, Yanyan Yong, Investigation, Data Curation. All authors reviewed, revised, and approved the final version of the manuscript and agreed to the submission of this manuscript.

Conflict of 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 manuscript.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.medin.2024.09.001.

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