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Efficacy of CA330 hemoadsorption combined with CRRT in sepsis-associated acute kidney injury

A retrospective cohort study

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Abstract

Hemoadsorption regulates sepsis-related inflammatory mediators. The CA330 cartridge, a cross-linked divinylbenzene/polyvinylpyrrolidone (DVB/PVP) adsorbent, is approved in China but no prospective or retrospective clinical studies have validated the efficacy of the CA330 in the context of sepsis-associated acute kidney injury (SA-AKI). This single-center retrospective study (January 2022–December 2024) enrolled 60 SA-AKI patients (SEPSIS-3 criteria, AKI stage II): 30 received CA330 + continuous renal replacement therapy (CRRT), 30 CRRT alone. Key outcomes included hemodynamics, interleukin-6 (IL-6) levels, renal recovery, and mortality. The CA330 group had higher baseline severity (APACHE II score, norepinephrine (NE) requirements, IL-6). After 24h, it showed 60.2% lower NE (P <.01), 21.2% higher mean arterial pressure (P <.001), 66.0% lower IL-6 (P <.01), and higher renal recovery (33.33% vs 16.67%, P = .0221) versus CRRT alone. Intensive care unit mortality was higher in CA330 group (43.33% vs 10%), but APACHE II score (not CA330) independently predicted mortality. Gram-negative bacilli subgroup had more pronounced hemodynamic benefits. No device-related adverse events occurred. CA330 + CRRT improves hemodynamics, cytokine clearance, and renal recovery in SA-AKI, especially in gram-negative infections. Baseline severity explains mortality differences, prospective RCTs are needed to confirm efficacy.

Abbreviations: CRRT = continuous renal replacement therapy, ICU = intensive care unit, IL-6 = interleukin-6, MAP = mean arterial pressure, NE = norepinephrine, PCT = procalcitonin, PLT = platelet, SOFA = sequential organ failure assessment.

Keywords: acute kidney injury, CA330 hemoadsorption, sepsis, septic shock

1. Introduction

1.1. Background

Sepsis is characterized as a life-threatening dysregulated immune response to infection, leading to severe multiple organ dysfunction, and is among the leading causes of mortality globally.[1–3] Despite substantial advancements in antibiotic therapy, hemodynamic management, and ventilation strategies, the mortality rate associated with septic shock remains alarmingly high, ranging from 30 to 50%.[4–6] Within the sepsis patient population, those experiencing acute kidney injury (AKI) exhibit the highest mortality rates.[7] It is hypothesized that a "cytokine storm" exacerbates the progression of sepsis to septic shock.[8] This hyperinflammatory response is triggered not only by the release of endogenous cytokines, such as interleukin-1β (IL-1β), interleukin-6 (IL-6), interleukin-12 (IL-12), and tumor necrosis factor-alpha (TNF-α), but also by exogenous factors, including pathogen-associated molecular patterns and damage-associated molecular patterns.[9–14]

The CA330 cartridge is a hemoperfusion device that uses cross-linked divinylbenzene/polyvinylpyrrolidone as its adsorbent, and it can trap inflammatory mediators using its pore structure, the hydrophobic and lipophilic characteristics of benzene rings, and the van der Waals forces of the adsorbent. Unlike HA series,[15] CA330 utilizes a chemical polyvinylpyrrolidone (PVP) coating, while HA series employs collodion. Additionally, CA330's larger surface area (53,880 m^2) and PVP coating enables a higher endogenous toxins removal rate.

1.2. Objectives

Despite its approval in China in 2021, there still have not been any studies supporting the efficacy of the absorbers. The primary objective of our analysis was to examine whether the

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Our study was approved by the ethics committee (IRB approval number: hkuszh2023115) of the University of Hong Kong, Shenzhen Hospital.

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implementation of CA330 hemoadsorption in patients with SA-AKI would influences norepinephrine (NE) requirements and mean arterial pressure (MAP). The second objective was the influence on IL-6 level.

2. Methods

2.1. Study design and setting

Following the approval from the ethics committee (IRB approval number: hkuszh2023115) of the University of Hong Kong, Shenzhen Hospital, we conducted a data collection in the adult intensive care unit (ICU) of a tertiary hospital in Shenzhen, China, spanning from January 2022 to December 2024.

2.2. Participants

The CA330 hemoadsorption was employed for patients who met the following criteria: a diagnosis of sepsis in accordance with the SEPSIS-3 criteria; fulfillment of the minimum criteria for AKI stage II, characterized by serum creatinine levels 2.0 to 2.9 times the baseline and urine output of <0.5 mL/kg/h for more than 12 hours.[16,17] Additionally, we conducted a retrospective analysis of a cohort of patients from our adult ICU, treated between January 2022 and December 2024, who met the same clinical inclusion criteria to serve as a historical control group. Consequently, our study was designed as a single-center retrospective study utilizing historical controls.

All patients were treated in accordance with the local sepsis treatment protocol, which was based on the actual guidelines valid during each treatment period.[16,18] Despite the standard treatments including fluid loading, NE therapy to achieve MAP more than 65 mm Hg, antibiotics in a minimum of 1 hour after diagnosis of sepsis, corticoid treatment and respiratory support. If there was no decrease in NE requirement, CA330 (Jafron Biomedical Co. (divinylbenzene/polyvinylpyrrolidone), Zhuhai, Guangdong Province, China) in combination with continuous renal replacement therapy (CRRT) (Ultraflux® AV 600S, Fresenius Polysulfone, St. Wendel, Saarland, Germany) was initiated. CRRT (Ultraflux® AV 600S, Fresenius Polysulfone, Germany) was performed in veno-venous hemodialysis-filtration mode with a blood flow rate of 150 mL/min, a dialysis and filtration dose of 30 mL/kg/h, and a citrate-based anticoagulation protocol. A CA330 adsorber was integrated into the CRRT circuit in a pre-hemodiafilter position for 6 hours per session. Each patient received 1 CA330 hemoperfusion treatments within 24 hours.

2.3. Variables and data measurement

The collected data included patients' characteristics, and NE requirements, lactic acid levels, MAP, platelet (PLT) count, procalcitonin (PCT) levels, IL-6 levels, and sequential organ failure assessment (SOFA) scores, both prior to and following each CA330 hemoperfusion combined with CRRT or only CRRT treatment. Additionally, the analysis included metrics such as mortality rates at 28 days, in the ICU, and during hospitalization.

2.4. Bias

To mitigate selection bias, control patients were matched by disease severity (APCHEII score), though residual confounding may exist due to the retrospective design. The Acute Physiology and Chronic Health Evaluation II (APACHE II) scores were calculated 24 hours prior to the initiation of continuous renal replacement therapy (CRRT) or CA330 hemoadsorption, as stipulated by the registry protocol.

All laboratory indicators (such as IL-6, PCT, lactic acid, PLT) were uniformly tested by the hospital's clinical laboratory using the same detection reagents and instruments to ensure the consistency of the detection methods for indicators in both groups. Hemodynamic indicators (MAP, NE dosage) were recorded in real-time by the ICU bedside monitor, and the average value of data before treatment and every hour within 24 hours of treatment was taken to reduce single measurement errors.

In the multivariate regression analysis, potential confounding factors such as APACHE II score, IL-6 level, PCT level, NE dosage, Charlson comorbidity index, age, gender, SOFA score, and lactic acid level were included. These factors were identified as key influencing factors for the prognosis and treatment response of sepsis patients based on previous studies.[3,7]

Data extraction was independently completed by 2 trained researchers (training content included interpretation of the research protocol, standards for variable definitions, and specifications for filling out data extraction forms). The extracted results were cross-checked, and inconsistencies were resolved by reviewing original medical records and communicating with clinicians to ensure data accuracy. Blinding was used for extracting outcome indicators (such as mortality), and the extractors were unaware of the patient grouping to avoid subjective judgment bias.

2.5. Study size

The determination of the sample size in this study was based on data from previous retrospective studies on the treatment of sepsis-associated acute kidney injury (SA-AKI) using similar blood adsorption devices.[10,19–27] Preliminary experimental results showed that CRRT combined with blood adsorption therapy could reduce patients' NE demand by approximately 68%. With α set at 0.05 (two-tailed test) and test power (1-β) at 0.8, calculations using Prism 10 software indicated that each group required at least 26 samples. Considering potential missing medical record data in retrospective studies (with an estimated missing rate of approximately 13%), it was finally determined that 30 patients would be included in each group, resulting in a total sample size of 60 cases to ensure the validity of statistical tests.

2.6. Quantitative variables and data acquisition and statistical analysis

The analysis and processing methods of quantitative variables in this study are as follows: Continuous outcome variables (such as NE dosage, MAP, IL-6 level, lactic acid level): Normality test (Shapiro–Wilk test) was first performed, and the results showed that the above variables did not conform to the normal distribution (P <.05). Therefore, the median (interquartile range; M [IQR]) was used for description, and the Mann–Whitney U test was used for comparison between groups; the Wilcoxon signed-rank test was used for the analysis of changes before and after treatment, and the magnitude of change (such as the percentage decrease in NE dosage, the absolute value of the decrease in IL-6 level) was calculated to intuitively reflect the therapeutic effect. Statistically significant results and differences are indicated with an asterisk (*) in Tables 1 and 2. Within this article, the term "significant" refers to statistical significance, defined as P <.05.

3. Results

3.1. Participants and descriptive data

From January 2022 to December 2024, a total of 645 sepsis patients were admitted to the ICU of our hospital, among which 72 patients met the diagnostic criteria for SA-AKI stage II. Finally, 60 patients were included (30 in the intervention group and 30 in the control group). The reasons for excluding 12 patients are as follows: Incomplete medical record data (6

Table 1

Demographics of the study population (control group vs hemoadsorption therapy).

Characteristic	Cytokine-absorbing filter and CRRT (n = 30)	CRRT alone (n = 30)	*P* value
Age, years, median (IQR)	69.50 (59.75, 83.50)	73.00 (65.00, 84.00)	.34
Gender, male (n%)	23 (76.66%)	16 (53.33%)	.10
BMI, median (Q1, Q3)	20.73 (17.66, 22.87)	22.18 (18.27, 27.14)	.16
Infection source, n (%)			
Pulmonary	16 (53.33%)	23 (76.67%)	
Abdominal	8 (26.66%)	3 (10.00%)	
Urogenital	4 (13.33%)	2 (6.67%)	
Skin, muscle, bone infection	0	2 (6.67%)	
Other	2 (9.52%)	0	
APACHEII	33.50 (25.00, 39.25)	27.50 (22.00, 30.25)	.0105*
SOFA	12.00 (9.75, 14.00)	12.50 (11.00, 15.00)	.34
Time from sepsis diagnosis to therapy initiation (min)	465.00 (232.50, 1515.00)	194.00 (133.80, 489.80)	.0124*
MAP before CRRT (mm Hg)	68.50 (64.00, 81.25)	74.50 (62.75, 84.50)	.27
Noradrenaline before CRRT (μg/kg/min)	0.615 (0.217, 1.165)	0.175 (0.085, 0.307)	.0007*
Lactate before CRRT (mmol/L)	5.05 (3.05, 9.22)	2.23 (1.53, 3.55)	.0001*
PCT before CRRT (ng/L) (n = 27 vs 30)	23.59 (6.41, 42.47)	2.06 (0.68, 8.38)	.002*
IL-6 before CRRT (pg/mL) (n = 27 vs 30)	3145 (1026, 18,237)	201.10 (77.30, 558.25)	<.001*

APACHEII = acute physiology and chronic health evaluation II, BMI = body mass index, CRRT = continuous renal replacement therapy, IL-6 = interleukin-6, MAP = mean arterial pressure, SOFA = sequential organ failure assessment, PLT = platelet, PCT = procalcitonin.

*$P \leq .05$.

Table 2

Treatment and outcome of control and CA330 group.

	Cytokine-absorbing filter and CRRT (n = 30)	CRRT alone (n = 30)	*P* value
Norepinephrine dependency, median (IQR) (μg/kg/min)			
Before treatment	0.615 (0.217, 1.165)	0.175 (0.085, 0.307)	.0007*
After 24 h	0.255 (0.06, 0.94)	0.05 (0.01, 0.25)	.0176*
P	.0037*	.31	
Δ Norepinephrine dependency	−0.17 (−0.36, −0.04)	−0.02 (−0.22, 0.06)	.066
MAP (mm Hg)			
Before treatment	68.50 (64.00, 81.25)	74.50 (62.75, 84.50)	.27
After 24 h	83.00 (73.00, 90.25)	74.50 (68.00, 85.25)	.0404*
P	.0009*	.5473	
Δ MAP	8.00 (−3.25, 21.25)	0.50 (−11.50, 7.00)	.0036*
Lactate, median (IQR) (mmol/L)			
Before treatment	5.05 (3.05, 9.22)	2.23 (1.53, 3.55)	<.001
After 24 h	4.45 (1.86, 8.06)	2.01 (1.30, 3.56)	.007
P	.29	.53	
Δ Lactate	−0.89 (−2.39, 0.45)	−0.22 (−1.06, 0.53)	.12
IL-6 levels (pg/mL)			
Before treatment, (n = 27 vs 30)	3145 (1026, 18,237)	201.10 (77.30, 558.25)	<.001*
After 24 h, (n = 28 vs 30)	797.5 (179.3, 2897.0)	70.50 (25.93, 148.00)	<.001*
P	.004*	<.001*	
Δ IL-6	−2077.00 (−15,167.20, −107.70)	−106.75 (−443.90, −30.42)	.008*
Platelet level (10^9/L)			
Before treatment	145.50 (102.50, 219.80)	128.50 (75.75, 187.25)	.28
After 24 h	86.00 (56.25, 154.50)	94.50 (60.50, 185.75)	.65
P	<.0001*	.0053*	
Δ Platelet level	−53.50 (−89.25, −24.75)	−11.50 (−61.75, 0.25)	.006*
Renal recovery rate	9 (33.33%)	5 (16.67%)	.0221*
ICU mortality, n (%)	13 (43.33%)	3 (10.0%)	.0035*
Hospital mortality, n (%)	17 (56.66%)	14 (46.7%)	.43
28-d mortality, n (%)	13 (43.33%)	9 (30.0%)	.28

Δ values represent changes from baseline to 24 h post-treatment.

CRRT = continuous renal replacement therapy, ICU = intensive care unit, IL-6 = interleukin-6, MAP = mean arterial pressure.

*$P \leq .05$.

cases): Key indicators were mainly missing (such as incomplete records of pretreatment IL-6 levels and APACHE II scores), making it impossible to perform baseline matching and outcome analysis; Inconsistent treatment plans (4 cases): Among them, 2 cases adopted anticoagulant-free CRRT due to active bleeding, 1 case had CRRT treatment duration <24 hours, and 1 case did not use NE, which did not meet the research intervention and outcome evaluation criteria; Family members refused to participate (2 cases): Although they met the inclusion criteria, their family members refused to provide informed consent and authorization for the use of medical record data, so they were excluded (Fig. 1).

The endpoint of follow-up in this study was defined as the patient's discharge from the ICU or death. The follow-up period was from the patient's enrollment to their discharge from the ICU or death. All patients in both groups completed the entire

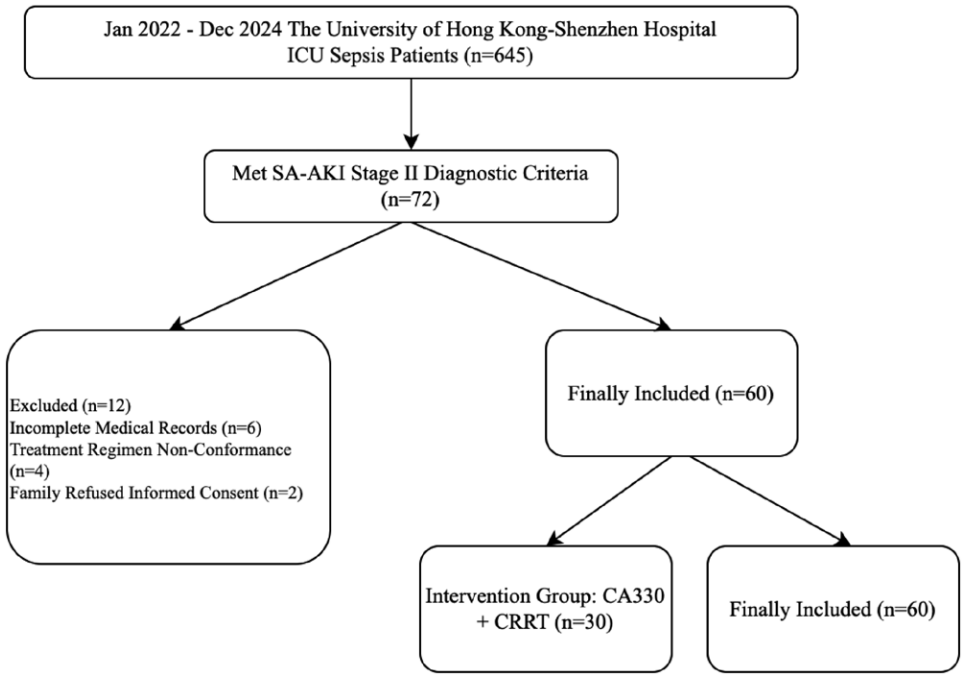

Figure 1. Research subject selection and inclusion process.

follow-up period, with no cases of loss to follow-up. The average ICU follow-up time was (12.5 ± 4.2) days in the intervention group and (10.8 ± 3.6) days in the control group. Among the 30 patients in the intervention group, 13 cases (43.33%) died during their ICU stay, and 17 cases (56.67%) were transferred out of the ICU. Among the 30 patients in the control group, 3 cases (10.00%) died during their ICU stay, and 27 cases (90.00%) were transferred out of the ICU. All patients transferred out of the ICU were further followed up until discharge. The average hospital follow-up time was (28.3 ± 7.5) days in the intervention group and (25.6 ± 6.8) days in the control group, with no loss to follow-up during hospitalization. There were 3 cases with missing IL-6 levels and 1 case with missing PCT, all of which were patients in the intervention group.

The baseline demographic and clinical characteristics of the patients are detailed in Table 1. In both cohorts, the majority of patients were male, with 23 (76.66%) in the CA330 hemoadsorption group and 16 (53.3%) in the CRRT group ($P = .10$). Pulmonary infections were the most prevalent in both groups, while abdominal infections were more frequently observed in the CA330 hemoadsorption group (26.66% compared to 10.00%). Prior to the initiation of CRRT, the patient characteristics, including age, gender, BMI, SOFA score and MAP, were comparable across the groups (refer to Table 1). Notable differences between the 2 groups included significantly higher APACHE II scores ($P = .041$), NE requirements ($P < .001$), IL-6 levels ($P < .001$), PCT levels ($P = .002$), lactate levels ($P = .001$), and the time delay from sepsis diagnosis to the commencement of therapy ($P = .024$) in the CA330 hemoadsorption group (see Table 1).

3.2. Outcome data and main results and other analyses

The alterations in NE requirements, MAP, lactate levels, SOFA scores, IL-6 levels, and PLT counts before and after the administration of CA330 in combination with CRRT, or with CRRT alone, are detailed in Table 2. At the initiation of CRRT, MAP was comparable between the 2 groups. However, NE requirements were significantly higher in the CA330 hemoadsorption group compared to the CRRT alone group ($P = .007$). After 24 hours of treatment, there were no significant changes in MAP and NE requirements in the CRRT alone group (74.50 [IQR: 62.75, 84.50] vs 74.50 [IQR: 68.00, 85.25], $P = .27$; 0.175 [IQR: 0.085, 0.307] vs 0.05 [IQR: 0.01, 0.25], $P = .31$). Conversely, the CA330 hemoadsorption group exhibited a significant increase in MAP (68.50 [IQR: 64.00, 81.25] vs 83.00 [IQR: 73.00, 90.25], $P = .0009$) and a significant decrease in NE requirements (0.615 [IQR: 0.217, 1.165] vs 0.255 [IQR: 0.06, 0.94], $P = .0037$).

Prior to treatment, the IL-6 levels were significantly elevated in the CA330 hemoadsorption group compared to the CRRT group ($P < .001$). Following 24 hours of treatment, both groups exhibited a significant reduction in IL-6 levels. The magnitude of change in IL-6 levels was significantly greater in the CA330 hemoadsorption group compared to the CRRT group (−2077.00 [−15,167.20, −107.70] vs −106.75 [−443.90, −30.42], $P = .008$). Additionally, both groups experienced a significant reduction in PLT count, with the CA330 hemoadsorption group showing a significantly greater change (−53.50 [−89.25, −24.75] vs −11.50 [−61.75, 0.25], $P = .006$). No adverse events related to the device were reported.

Regarding renal function recovery, a key outcome indicator for SA-AKI patients, the CA330 hemoadsorption combined with CRRT group achieved a significantly higher renal recovery rate compared to the CRRT alone group (33.33% [9/30] vs 16.67% [5/30], $P = .0221$), as shown in Table 2.

Patients who received a combination of CA330 hemoadsorption therapy and CRRT exhibited higher ICU and hospital mortality rates compared to those who received CRRT alone, with rates of 43.33% versus 10% ($P = .0035$) and 56.66% versus 46.7% ($P = .43$), respectively, as shown in Table 2.

A multivariate regression analysis, which controlled for variables such as APACHE II score, IL-6 levels, PCT levels, NE dosage, Charlson Comorbidity Index, age, gender, SOFA score, and lactate levels at the initiation of treatment, identified the APACHE II score as independently associated with lower ICU mortality rates (odds ratio [OR]: 1.144, 95% confidence interval [CI]: 1.044–1.466, $P = .0221$). The coefficient for CA330 hemoadsorption was not statistically significant in the models

(OR: 4.307, 95% CI: 0.3877–42.99, $P = .2886$). The model demonstrated a c-index of 0.9007 (95% CI: 0.7788–1.000), as illustrated in Figure 2.

3.3. Subgroup analysis

To further explore the effect of CA330 hemoadsorption combined with CRRT in different patient subgroups, we performed subgroup analyses based on the type of pathogenic infection (Gram-negative bacilli vs Non Gram-negative bacilli). The results are presented in Tables 3 and 4, which details the changes in NE dependency, MAP, and 28-day mortality in each subgroup before and after treatment.

NE dependency: In the Gram-negative bacilli subgroup, both treatment modalities reduced NE dependency, but only the CA330 + CRRT group achieved a statistically significant reduction ($P = .0151$), with a median decrease from 0.63 to 0.32 μg/kg/min. Although the CRRT alone group showed a numerical decrease (from 0.21 to 0.065 μg/kg/min), the change was not statistically significant ($P = .7646$). In the Non Gram-negative bacilli subgroup, the baseline NE dependency was significantly higher in the CA330 + CRRT group than in the CRRT alone group ($P = .002$). After 24 hours of treatment, both groups exhibited reduced NE requirements, with a significant difference in the magnitude of reduction between the 2 groups ($P = .0378$). The CA330 + CRRT group showed a substantial reduction from 0.60 to 0.19 μg/kg/min, while the CRRT alone group had a modest decrease from 0.13 to 0.05 μg/kg/min.

MAP:In the Gram-negative bacilli subgroup, the CA330 + CRRT group demonstrated a significant increase in MAP after treatment (from 75.00 to 89.00 mm Hg, $P = .0173$), and the post-treatment MAP was significantly higher than that in the CRRT alone group ($P = .0083$). In contrast, the CRRT alone group showed no significant change in MAP ($P = .3687$). In the Non Gram-negative bacilli subgroup, both groups showed numerical increases in MAP after treatment, but the changes were not statistically significant (CA330 + CRRT group: $P = .0754$; CRRT alone group: $P = .3687$), and there was no significant difference in post-treatment MAP between the 2 groups ($P = .6412$).

28-day mortality: In the Gram-negative bacilli subgroup, the 28-day mortality rates were 40.00% in the CA330 + CRRT group and 46.15% in the CRRT alone group, with no statistically significant difference ($P = .7428$). In the Non Gram-negative bacilli subgroup, the CA330 + CRRT group had a higher numerical mortality rate (53.33%) compared to the CRRT alone group (35.29%), but the difference did not reach statistical significance ($P = .3047$). This discrepancy may be attributed to the higher baseline disease severity in the CA330 + CRRT subgroup, as indicated by elevated APACHE II scores and IL-6 levels in the overall cohort analysis.

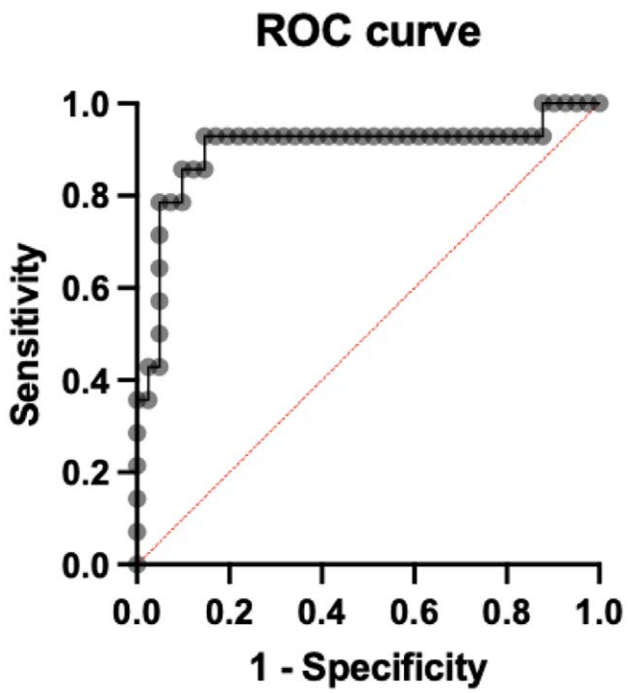

Figure 2. Forest plot of multivariate logistic regression for ICU mortality predictors. APACHE II score (OR: 1.144, 95% CI: 1.044–1.466, $P = .022$) was independently associated with mortality, while CA330 use was not (OR: 4.307, 95% CI: 0.388–42.99, $P = .289$).

4. Discussion

4.1. Key results

This retrospective study evaluated the clinical efficacy of combining CA330 hemoadsorption with CRRT in patients with sepsis-associated acute kidney injury (SA-AKI). The key findings demonstrate that CA330 hemoadsorption significantly reduced NE requirements, improved MAP, and achieved a more pronounced reduction in IL-6 levels, and enhanced renal function recovery compared to CRRT alone.

The observed reduction in NE requirements and improvement in NE dependency and MAP align with the proposed mechanism of CA330, which effectively adsorbs inflammatory mediators such as IL-6 through its polyvinylpyrrolidone (PVP)-coated divinylbenzene matrix. The greater decline in IL-6 levels in the CA330 group (−2077.00 vs −106.75 pg/mL, $P = .008$) supports its capacity to mitigate the "cytokine storm," a hallmark of septic shock progression. These findings are consistent with prior studies on hemoadsorption devices like CytoSorb, which similarly reported hemodynamic stabilization in sepsis.[19,21,22]

Table 3

Subgroup analysis of therapeutic outcomes by pathogenic infection type of gram-negative bacilli.

Gram-negative bacilli (n = 28)	Cytokine-absorbing filter and CRRT (n = 15)	CRRT alone (n = 13)	*P* value
Norepinephrine dependency, median (IQR) (μg/kg/min)			
Before treatment	0.63 (0.21, 2.13)	0.21 (0.13, 0.49)	.0949*
After 24 h	0.32 (0.04, 0.93)	0.065 (0.025, 0.925)	.3279
P	.0151*	.7646	
MAP (mm Hg)			
Before treatment	75.00 (61.00, 83.00)	69.00 (58.75, 77.75)	.3662
After 24 h	89.00 (77.00, 94.00)	70.00 (60.25, 75.00)	.0083*
P	.0173*	.3687	
28-d mortality, n (%)	6 (40.00%)	6 (46.15%)	.7428

CRRT = continuous renal replacement therapy, MAP = mean arterial pressure.

*$P \leq .05$.

Table 4

Subgroup analysis of therapeutic outcomes by pathogenic infection type of non gram-negative bacilli.

Non gram-negative bacilli (n = 32)	Cytokine-absorbing filter and CRRT (n = 15)	CRRT alone (n = 17)	*P* value
Norepinephrine dependency, median (IQR) (μg/kg/min)			
Before treatment	.60 (.24, 1.15)	.13 (.035, .28)	.002*
After 24 h	.19 (.07, 0.97)	.05 (.00, .255)	.0378*
P	.0769	.7846	
MAP (mm Hg)			
Before treatment	66.00 (64.00, 79.00)	83.00 (71.00, 93.50)	.27
After 24 h	78.00 (72.00, 83.00)	79.00 (71.00, 89.50)	.6412
P	.0754	.3687	
28-d mortality, n (%)	8 (53.33%)	6 (35.29%)	.3047

CRRT = continuous renal replacement therapy, MAP = mean arterial pressure.

*$P \leq .05$.

However, unlike CytoSorb®, CA330's unique PVP coating and larger surface area (53,880 m^2) may enhance endogenous toxins removal, though this requires further validation.

Notably, the CA330 hemoadsorption combined with CRRT group achieved a significantly higher renal recovery rate (33.33% [9/30] vs 16.67% [5/30], $P = .0221$) compared to the CRRT alone group. This finding holds particular clinical significance for SA-AKI patients, as renal function recovery is a core therapeutic target in this population – impaired renal function not only exacerbates hemodynamic instability and toxin accumulation but also increases long-term morbidity and mortality.

The elevated mortality rate observed in the CA330 group is likely attributable to baseline disparities in illness severity. Patients administered CA330 exhibited significantly higher APACHE II scores (33.5 vs 27.5, $P = .0105$), NE requirements (0.615 vs 0.175 μg/min, $P < .001$), and IL-6 levels (3145 vs 201.1 pg/mL, $P < .001$), indicating a more advanced disease state at the time of enrollment. Multivariate analysis identified the APACHE II score as an independent predictor of mortality (OR: 1.144, $P = .0221$), whereas CA330 itself was not significantly associated with an increased risk of mortality (OR: 4.307, $P = .2886$). These findings suggest that the observed mortality differences were due to confounding by severity rather than the intervention itself. Our findings are in line with the existing RCTs, where the authors stated that no mortality reduction could be found in CytoSorb hemoadsorption group.[19,23] Furthermore, the delayed initiation of therapy in the CA330 group (465 vs 194 minutes, $P = .0124$) may have further worsened outcomes, highlighting the critical importance of timely intervention in the management of sepsis.[24,25]

An additional finding warrants further examination. The CA330 group exhibited a more pronounced decrease in PLT counts (−53.50 vs −11.50, $*P* = .006$), a trend previously associated with hemoadsorption devices due to sepsis and nonspecific adsorption.[21,26,27] Although no bleeding events were observed, this finding underscores a potential safety concern.

The subgroup analysis reveals that the therapeutic benefit of CA330 hemoadsorption combined with CRRT is more pronounced in patients with Gram-negative bacilli infection. Specifically, this combination therapy significantly improves hemodynamic stability (as reflected by reduced NE dependency and increased MAP) in Gram-negative bacilli-infected patients, which may be related to the robust "cytokine storm" induced by Gram-negative pathogens (e.g., lipopolysaccharide release). The CA330 cartridge, with its large surface area (53,880 m^2) and polyvinylpyrrolidone (PVP) coating, effectively adsorbs proinflammatory mediators such as IL-6, thereby mitigating the dysregulated immune response and improving vascular reactivity. These findings suggest that CA330 hemoadsorption combined with CRRT may be a more favorable therapeutic option for SA-AKI patients with Gram-negative bacilli infection, particularly those with severe hemodynamic instability.

4.2. Limitations, interpretation, generalizability

This study is subject to several limitations. The retrospective, single-center design limits causal inference and generalizability. The limited sample size (n = 30 per group) and the single-center nature of the study constrain the generalizability of the findings. Furthermore, the exclusive focus on IL-6 neglects the potential impact of other cytokines, such as tumor necrosis factor-alpha (TNF-α) and interleukin-1 beta (IL-1β), which could influence the outcomes. Lastly, the lack of long-term follow-up data, such as 90-day mortality rates, hinders the evaluation of sustained benefits. Future prospective studies should stratify patients by pathogen type to further validate the subgroup-specific efficacy of CA330 hemoadsorption and identify optimal candidates for this therapy.

5. Conclusions and future directions

In summary, CA330 hemoadsorption combined with CRRT exhibits significant advantages in improving hemodynamic stability and reducing cytokine load in SA-AKI patients, especially in those with Gram-negative bacilli infection and severe hemodynamic instability. Notably, the renal recovery rate was significantly higher in the CA330 hemoadsorption combined with CRRT group compared to the CRRT alone group. Given the limitations of this study, including its retrospective, single-center design, limited sample size, and exclusive focus on IL-6, future multicenter randomized controlled trials should emphasize the early enrollment of well-matched cohorts, stratify patients by pathogen type to validate the subgroup-specific efficacy of CA330 hemoadsorption, include comprehensive cytokine profiling (such as TNF-α and IL-1β), and assess long-term outcomes (such as 90-day mortality) to further clarify the therapeutic value and optimal application population of CA330 hemoadsorption in the management of SA-AKI. Additionally, investigating the role of CA330 in specific subgroups with gram negative bacteria infection phenotypes may further enhance its therapeutic applicability.

Supplemental Digital Content "20251220OA_Supplemental Digital Content" is available for this article (https://links.lww.com/MD/R282).

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