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Multimodal LPS-Selective Hemoadsorption and Hemodiafiltration in the Intensive Care of Gram-Negative Sepsis Patients: a Multicenter Observational Study

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Summary

The aim of the study. To evaluate the effectiveness of multimodal selective lipopolysaccharide (LPS) hemoadsorption in combination with renal replacement therapy (RRT) in patients with gram-negative sepsis or septic shock.

Materials and methods. The study included 39 patients. In the main prospective group, patients received extracorporeal therapy in addition to standard of care (ET group, $N=10$). In the retrospective comparison group, patients received only standard therapy (ST group, $N=29$).

Results. In the ET group, the average SOFA score decreased by 3.4 [95% CI: 0.8; 5.2] scores after 72 hours of treatment, while in the ST group, the average SOFA value increased by 1.7 [95% CI: 0; 3.4] scores over the same period, $p_{adj}=0.002$. Hospital mortality was 1/10 (10%) in the ET group and 19/29 (66%) in the ST group, and OR = 0.06 [95% CI: 0.01; 0.4] $P=0.003$. The analysis, including consideration of severity of the condition at a baseline as a potential confounding factor, confirmed the robustness of the results: statistically significant differences in SOFA dynamics and mortality remained.

Conclusion. The use of selective hemoadsorption in combination with renal replacement therapy reduces the severity of organ dysfunction and mortality in patients with sepsis or septic shock.

Keywords: sepsis; septic shock; acute renal failure; endotoxins; hemoadsorption; renal replacement therapy

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Introduction

Sepsis is not only a problem, but also a serious challenge for international healthcare. Despite all efforts, the mortality rate in septic shock remains high, ranging from 40% to 60% [1]. The lack of significant progress is not only due to antibiotic resistance challenges, but also to the heterogeneity of sepsis, making it too demanding in terms of developing a universal treatment strategy [2]. It is believed that the release of endotoxin and inflammatory mediators into the systemic circulation plays a key role in the pathogenesis of gram-negative sepsis, causing mitochondrial and microcirculatory distress syndrome (MMDS) with associated tissue dysoxia. This is usually accompanied by massive immunocompetent cell death, which exacerbates multiple organ dysfunction syndrome (MODS) [3]. Intestinal paresis and splanchnic hypoperfusion contribute to gut barrier failure with subsequent translocation of bacteria, endotoxins, exotoxins, and microbial metabolites. Increasing concentration of sepsis-associated aromatic microbial metabolites (AMMs) indicates the progression of organ dysfunction and is associated with an increased risk of death [4]. Extracorporeal blood purification in sepsis is a powerful therapeutic tool, its' main goal is to remove pathogen-associated molecular patterns (PAMPs), such as endotoxin, toxic shock syndrome toxin-1 (TSST-1), aromatic microbial metabolites, and damage-associated molecular patterns (DAMPs), such as neutrophil extracellular traps (NETs), cytokines, ammonia, etc., from the systemic circulation.

Standard dialysis membranes and membranes with a high cutoff threshold do not have such properties [5, 6]. Despite the potential of continuous renal replacement therapy (CRRT) to reduce plasma concentrations of certain cytokines, its implementation leads to a loss in serum concentration of most water-soluble antibiotics, amino acids, and some micronutrients, which is very critical for the body [7, 8]. Other modern extracorporeal methods, such as cytokine hemoadsorption, are also being actively studied in critically ill patients. However, to date, the effectiveness of selective cytokine hemoadsorption in sepsis remains highly controversial in the absence of positive results from randomized studies [9, 10].

The most reasonable extracorporeal hemocorrection method in patients with sepsis is selective hemoadsorption of bacterial endotoxins (LPS-selective hemoadsorption) [11–13]. However, the role of lipopolysaccharide hemoadsorption (LPS-adsorption) in the treatment of sepsis has not been definitively established due to insufficient evidence of its positive influence on mortality [14–16].

Recently, a new device for hemoadsorption, Efferon LPS (PAO Efferon, Russia), has been introduced into clinical practice [12]. It is capable of multimodal removal of lipopolysaccharides (due to the LPS-selective ligand immobilized on the surface), excess cytokines, and cytolysis products (due to its internal porosity). The aim of this study was to evaluate the efficacy of multimodal selective LPS hemoadsorption in combination with renal replacement therapy in patients with gram-negative sepsis or septic shock.

Materials and Methods

Study design. The effectiveness of extracorporeal therapy (ET) was evaluated by comparing the prospective (main group, receiving extracorporeal therapy — ET) and retrospective (comparison group receiving standard therapy — ST) cohorts of patients with gram-negative sepsis or septic shock. Patients were recruited from 5 leading multidisciplinary medical institutions in the Republic of Kazakhstan (listed in the «Patients» section). The study was conducted under the supervision of employees of S. D. Asfendiyarov Kazakh National Medical University in the period from 09.2022 to 09.2023. The study was approved by the local Ethics Committee of the Research International Institute of postgraduate education (Almaty, Republic of Kazakhstan), Protocol No. 1 dated April 28, 2022.

Patients. The study included 39 patients with gram-negative sepsis or septic shock, according to the Sepsis-3 criteria [1]. Patients were recruited from the following medical facilities:

1) City Clinical Hospital No. 7, Almaty (ET group, $N=4$; ST group, $N=10$).

2) Aktobe Medical Center, Aktobe (ET group, $N=2$; ST group, $N=7$),

3) City Hospital No. 2, Shymkent (ET group, $N=2$; ST group, $N=6$),

4) City Multidisciplinary Hospital, Taraz (ET group, $N=1$; ST group, $N=4$),

5) Regional Perinatal Center, Kyzylorda (ET group, $N=1$; ST group, $N=2$).

All patients were admitted to intensive care units in a critical condition and received standard intensive care, in accordance with the recommendations of the Surviving Sepsis Campaign 2021 [16].

The main (prospective) group included patients receiving multimodal LPS-selective hemoadsorption (Efferon LPS device, Efferon PAO, Russia) and continuous venovenous hemodiafiltration (ET group, $N=10$) in addition to standard treatment for septic shock. The retrospective comparison group included patients who received only standard therapy (ST group, $N=29$). They were evaluated retrospectively up to 6 months before the first use of Efferon LPS.

Inclusion criteria. Compliance with the criteria for sepsis and septic shock according to the Sepsis-3 definitions at the time of inclusion in the study, followed by identification of pathogen through bacteriological tests; age $\geqslant 18$ years; patient's condition

allowing for the use of Efferon LPS hemoadsorption for at least 6 hours; and informed consent to participate in the study.

Exclusion criteria. Acute blood loss in the last 24 hours, severe granulocytopenia (white blood cell count < 500 cells/mm³) or severe thrombocytopenia (platelet count < 30,000 cells/mm³); HIV infection, terminal renal failure (GFR less than 15 ml/min/1.73 m²); severe congestive heart failure (IV NYHA class, ejection fraction < 35%); acute pulmonary embolism confirmed on CT; acute myocardial infarction within the last 4 weeks; acute cerebrovascular accident; transfusion reaction, anaphylactic reaction, dementia; more than 12 hours after septic shock onset according to Sepsis-3 criteria. Patients without bacteremia (confirmed gram-negative bacteria) were also excluded from the study.

Therapy. All patients received timely intravenous fluids, early treatment with broad-spectrum antibiotics, and vasopressor support as needed. The infusion load for patients in both groups was monitored using dynamic tests (passive leg elevation and pulse pressure variation).

In the ET group, multimodal LPS-selective hemoadsorption with Efferon LPS in combination with continuous venovenous hemodiafiltration (CVVHDF) was initiated within 12 hours from the diagnosis of sepsis or septic shock. Extracorporeal blood purification consisted of 2 consecutive sessions of multimodal LPS-selective hemoadsorption in combination with CVVHDF lasting 6–12 hr, and prescribed effluent fluid rate 30 ml/kg/hr. The second session was performed 24 hours after the first procedure.

A combined extracorporeal circuit with hemoadsorption and CVVHDF was assembled using the PrismaFlex system (Baxter, USA), and the prescribed effluent dose was 30 ml/kg/h. In the extracorporeal circuit, the adsorber was installed after the hemofilter. 2000 ml of saline solution with 5000 IU of unfractionated heparin (UFH) was added to the extracorporeal circuit. Before the procedure, heparin was also administered i/v in a bolus dose of up to 5,000 IU for anticoagulation. UFH was supplied at 500–2,000 IU per hour to maintain the activated partial thromboplastin time (APTT) at twice the normal value. When using Efferon LPS, the blood perfusion rate through the Efferon LPS column was maintained at 150–200 ml/min, and the average duration of perfusion was 6 hours.

No side effects such as intra-procedural hypotension, bleeding, or extracorporeal circuit thrombosis were revealed during the extracorporeal hemodiafiltration (HDF).

A clinical and laboratory examination of the patients was performed before the start of ET and 24 hours after its completion. To monitor the severity of inflammation and endogenous intoxication, the following parameters were assessed: SOFA score, blood, C-reactive protein (CRP), procalcitonin (PCT, measured by quantitative immunochemiluminescence), and the neutrophil-to-lymphocyte ratio (NLR). Blood culture tests were used to detect and identify the causative pathogen. The criteria for initiating RRT in both groups were in compliance with the KDIGO recommendations, 2012 [17].

Statistical analysis. RStudio 2023 and R version 4.2 were used for data analysis and plotting. Data with a normal distribution were presented as *M (SD)*. Data with a log-normal distribution were presented as *Me (Q1; Q3),* and the asymptotic estimation was applied to the log-normal distribution. The *n/N* (%) proportion was presented for categorical data, and for the chi-square test the bootstrapped *p*-values were used (B = 10000). A multi-response permutation procedure technique was used to analyze data with multiple traits (diseases and microbial pathogens). The variables in the groups were compared using Welch's *t*-test, and the log-normal data were logarithmically transformed. The distribution type was determined using the Shapiro–Wilk *W*-statistic. The dynamics of clinical and laboratory indicators over a 72-hour period were analyzed using linear regression with repeated measurements. The data were presented as the mean value and 95% confidence interval, *M* [95% CI]. Age and lactate were considered as covariates. Survival analysis was performed taking into account competing risks (discharge/death), using Fine-Gray regression and the tidycmprsk library. Mortality was also analyzed using logistic regression. Given the observational nature of the study and some baseline differences in patients, as part of the sensitivity analysis, all statistical calculations were repeated with adjustment for covariates. The resulting estimates are presented with the subscript adj. (adjusted).

Results

Clinical parameters before treatment.

The patient selection algorithm is presented in Fig. 1.

No statistically significant differences were found between the groups in terms of age, gender, or anthropometric data (Table 1).

The causes of sepsis or septic shock were infections after abdominal surgery, urological infections, obstetric infections, pulmonary infections, soft tissue infections, bloodstream infections, and infections of the central nervous system (Table 1). Both groups were comparable in terms of severity, although the ET group patients had slightly more severe cardiovascular, respiratory, and renal dysfunction, only the lactate concentration diverged significantly. At the time of inclusion in the study, 9/10 (90%) patients in the ET group and 26/29 (90%) patients in the ST group were diagnosed with septic shock.

Gram-negative bacteremia was documented in 90% of patients in the ET group, compared to 83% in

the ST group (Table 1). These results indirectly indicated the presence of endotoxin in the blood.

The groups were comparable in terms of concomitant diseases (Table 2). The cumulative fluid balance and central venous pressure dynamics in the ICU did not differ between the groups.

Dynamics of clinical parameters after treatment.

A significant improvement in clinical and laboratory parameters was documented in the ET group after the first Efferon LPS therapy session: a rapid decrease in the SOFA score, with an average change of –3.0 [–5.2; –0.8] scores over 72 hours of therapy, while the ST group demonstrated worsening of multiple organ failure — M=+1.3 [–0.6; +3.3], and the differences between the groups were statistically significant, $P=0.005$ (Table 3). Simultaneously, significant modifications in the doses of administered vasopressors were documented using VIS2020 scale [18], in the ET group it was –11 [–17; —5.5] in 72 hours, and in the ST group +11 [–4; +26], $P=0.008$. The decrease in lactate was more marked in the ET group vs the ST group: –3.2 [–4.6; –1.8] and –0.7 [–1.6; +0.2], respectively, $P=0.004$. Sensitivity analysis in multivariate linear regression taking into account covariates (age and lactate concentration) showed similar results (Table 3).

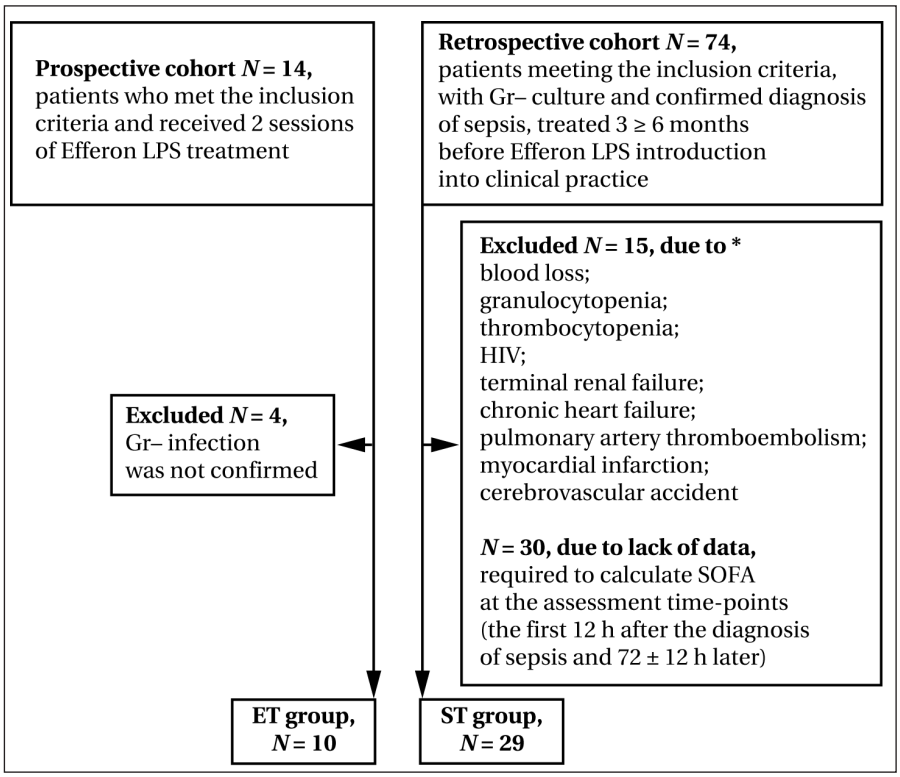

Fig. 1. Patient selection algorithm.
Note. * — a detailed description is provided in the «Materials and Methods» section.

Positive changes in the clinical picture included regression of the SOFA score, a decrease in body temperature to subfebrile values and the severity of pain syndrome, the appearance of peristaltic sounds, improved respiratory function and oxygenation with an increase in PaO_2/FiO_2, recovery of hemodynamic stability with reduced administration of vasopressors, and rebound diuresis, allowing to discontinue RRT after 3 days.

The dynamics of C-reactive protein and procalcitonin levels indirectly confirmed a decrease in endogenous intoxication (Table 3). Complete stabilization of laboratory parameters was documented by the 7th day of treatment.

In the ET group, 9 out of 10 patients had septic shock upon admission, one more patient developed shock on the third day after inclusion in the study. In the ST group, 90% (26/29) of patients had septic shock upon admission to the ICU, and the remaining 3 patients developed it later. Septic shock was resolved in 89% (8/9) of patients in the ET group and in 38% (10/26) of patients in the ST group, OR=13 [95% CI: 1.9; 257] $P=0.018$, $O_{Radj.}=30$ [95% CI: 3.4; 806] $P=0.010$, (Fig. 2, *a*). The incidence curves for the resolution of septic shock, acute kidney injury, transfer from the ICU, and ICU mortality differed significantly between the groups, both with and without adjustment for covariates (Fig. 2). The overall mortality rate was 20/29 (69%) in the ST group and 1/10 (10%) in the ET group, OR=0.06 [95% CI: 0.01; 0.4] $P=0.003$, $OR_{adj.}=0.03$ [95% CI: 0.01; 0.2] $P=0.005$. The duration of ICU stay did not differ statistically between the groups.

Discussion

The mortality rate for septic shock remains significant worldwide. According to a review, the 30-day mortality rate for patients with septic shock in Europe, North America, and Australia is 34.7% on average [19]. According to a meta-analysis by Chinese authors, the overall 28–30-day mortality rate for sepsis and septic shock was 37.3% [20].

According to our data, this is the first study in Kazakhstan to investigate the effectiveness of combined multimodal LPS-selective hemoadsorption and CVVHDF in patients with sepsis or septic shock. The 28-day mortality rate in the ST group was 66%, compared to 10% in the ET group.

Table 1. Patient characteristics at the time of inclusion in the study.

Parameters	Values in the groups, *M (SD) / n (%) / Me (IQR)*		*p*
	ET (*n* = 10)	ST (*n* = 29)	
Age, years	52 (14)	54 (18)	0.663
Body weight, kg	76 (14)	72 (14)	0.470
SOFA, scores	8 (3)	7 (4)	0.646
MAP, mmHg	74 (14)	78 (22)	0.504
Septic shock, *n/N* (%)	9/10 (90%)	26/29 (90%)	1
VIS 2020*, units	18 (12; 22)	10 (0.1; 17)	0.144
ARF, n/N (%)	8/10 (80%)	14/29 (48%)	0.14
MV, n/N (%)	4/10 (40%)	8/29 (28%)	0.702
PaO_2/FiO_2,	245 (89)	218 (71)	0.563
AKI, n/N (%)	10/10 (100%)	22/29 (76%)	0.234
Need for RRT, *n/N* (%)	10/10 (100%)	20/29 (69%)	0.116
Diuresis, ml/day	253 (34; 1847)	249 (41; 1493)	0.989
Creatinine, μmol/L	298 (141)	219 (184)	0.177
WBC, $\times 10^9$/L	19.9 (9.1)	17.9 (9.7)	0.563
Neutrophils, $\times 10^9$/L	17 (9)	15 (9)	0.470
Lymphocytes, $\times 10^9$/L	1.09 (0.7; 1.56)	1.06 (0.53;1.79)	0.926
NLR,	15.6 (8.4; 28.3)	13.9 (6.5; 28.7)	0.962
CRP, mg/L	258 (145)	178 (111)	0.140
Procalcitonin, ng/ml	14.1 (4; 44.2)	8.8 (2.4; 26.8)	0.483
Total bilirubin, μmol/L	39 (16; 94)	23 (12; 45)	0.265
Lactate, mmol/L	5.2 (2.1)	3.5 (2.2)	0.047
Platelets, $\times 10^9$/L	192 (108)	217 (124)	0.556
INR, units	1.37 (1.21; 1.54)	1.59 (1.26; 1.97)	0.077
Fibrinogen, g/L	5.9 (2)	4.7 (2.7)	0.164
Bacteremia, *n/N* (%)	9 (90%)	24 (83%)	1
Primary infectious site, *n/N* (%)			0.289
Acute pyelonephritis	2 (20%)	5 (17%)	
Acute pancreatitis	5 (50%)	3 (10%)	
Pneumonia	1 (10%)	9 (31%)	
Acute cholecystitis	0 (0%)	2 (7%)	
Acute intestinal obstruction	0 (0%)	2 (7%)	
Cellulitis	1 (10%)	3 (10%)	
Other	1 (10%)	5 (17%)	
Etiology of sepsis, *n/N* (%)			0.832
Gram-negative bacteria	10 (100%)	29 (100%)	
Klebsiella spp.	5 (50%)	16 (55%)	
Escherichia coli	3 (30%)	7 (24%)	
Acinetobacter spp.	1 (10%)	9 (31%)	
Pseudomonas aeruginosa	2 (20%)	6 (21%)	
Enterobacter spp.	1 (10%)	3 (10%)	
Proteus ssp.	0 (0%)	2 (7%)	
Gram-poisitive bacteria	2 (20%)	6 (21%)	
Staphylococcus aureus	1 (10%)	4 (14%)	
Streptococcus spp.	1 (10%)	1 (3%)	
Enterococcus spp.	1 (10%)	2 (7%)	

Note. Here and Table 3: *VIS2020 — Vasoactive Inotropic score [18]. *M (SD)* — mean value and standard deviation; *Me (Q1; Q3)* — median, 1 and 2 quantiles; SOFA — the Sequential Organ Failure Assessment scale; MAP — mean arterial pressure; NLR — neutrophil-to-lymphocyte ratio; INR — international normalized ratio; RRT — renal replacement therapy; ET — extracorporeal therapy; MV — mechanical ventilation; AKI — acute kidney injury.

Most of the patients included in the study had bacteremia, i. e. 83% in the ST group and 90% in the ET group. Microbiological examination of biological samples is a prerequisite for effective antibiotic therapy. Gram-negative pathogen was isolated and bacteriologically confirmed in 100% of patients in both groups. Gram-positive bacteria were found in 21% (ET group) and 20% (ST group), indicating a mixed type infection involving both Gram-positive and Gram-negative bacteria (Table 1). In the EUPHRATES study, isolated Gram-negative flora was found in 23.9% of cases in the selective LPS hemoadsorption group, compared to 13.3% in the comparison group [22].

Bacteremia in sepsis can worsen the prognosis for patients. For example, a 2023 review of the significance of bacteremia in 258 septic patients showed that bacteremia in patients with sepsis was associated with higher mortality rates and longer intensive care unit stays compared to patients without bacteremia, although this difference did not reach statistical significance [21].

The LASSO RCT (2021–2022 yrs, Russia) established an interesting fact of positive correlation between procalcitonin concentration, severity of endotoxemia, and SOFA score ($P < 0.05$) [12]. The LASSO data suggest that the main group patients had higher concentrations of endotoxin compared to the control group, based on documented in these patients higher levels of procalcitonin, CRP, and lactate at the time of inclusion [23].

The Efferon LPS machine is a multimodal device [24]. Due to immobilized on the surface of sorbent granules' LPS-binding ligand and granules' porous structure, the sorbent is capable of simultaneously removing both bacterial endotoxins and endogenous inflammatory mediators (cytokines and cytolysis products) [12].

A recent meta-analysis of the effects of extracorporeal blood purification methods on mortality, need for RRT, mechanical ventilation, and duration of hospital stay demonstrated that the use of continuous venovenous hemofiltration (CVVH) and concomitant use of CVVH and cytokine hemoadsorption led to reduced ICU stay [25]. In our study, the effect of eliminating LPS and DAMP molecules using Efferon LPS was potentiated by a 6-hour CVVHDF procedure.

In RCTs conducted before 2020 hemoadsorption was usually initiated in patients with average SOFA score of $\geqslant 10$ [26, 27]. An increase in survival and organ-support free days after the use of selective Polymyxin B hemoadsorption was demonstrated in 2191 patients out of 44177 analyzed sepsis cases from the National database (2018–2020 yrs) in a review by Japanese authors. [28]. The greatest advantages were documented in patients with baseline SOFA score of 7–12. The need for timely selective hemoadsorption using polymyxin B hemoperfusion was confirmed in a review describing studies in more than 2,000 patients [28]. According to the review, statistically significant positive results of extracorporeal treatment were obtained only when the SOFA score values of patients was within the range of 7–12 scores. In our study, the

Table 2. Distribution of chronic diseases.

Nosological diagnosis	Distribution in the groups	
	ET, N=10	ST, N=29
Diabetes mellitus	2 (20%)	9 (31%)
Arterial hypertension	3 (30%)	11 (38%)
Chronic kidney disease	4 (40%)	9 (31%)
Nephrolithiasis	1 (10%)	1 (3%)
Congestive heart failure/coronary artery disease	3 (30%)	5 (17%)
Chronic cholecystitis/gallstone disease	1 (10%)	1 (3%)
Anemia	3 (30%)	4 (14%)
Chronic gastric ulcer/gastritis	1 (10%)	2 (7%)
Chronic obstructive pulmonary disease/respiratory failure	2 (20%)	6 (21%)
Chronic cerebrovascular disease/strioke/discirculatory encephalopathy	1 (10%)	3 (10%)
Liver cirrhosis/hepatitis	1 (10%)	2 (7%)
Obesity	2 (20%)	2 (7%)
Other	2 (20%)	4 (14%)
p	0.439	

Table 3. Dynamics of parameters over 72 hours of treatment: ET group vs ST.

Parameters	Groups	Interval 0–72 hr			
		One-dimensional model M [95% CI]	p	Multi-dimensional model $M_{adj.}$ [95% CI]	p
SOFA	ET	–3.0 [–5.2; –0.8]	0.005	–3.4 [–5.2; –0.8]	0.002
	ST	+1.3 [–0.6; +3.3]		+1.7 [–0.0; +3.4]	
MAP	ET	+10.2 [+2; +18.4]	0.244	+7.8 [–2.1; 17.6]	0.476
	ST	+1.1 [–12.1; +14.3]		+3.4 [–3.4; 10.3]	
VIS2020	ET	–11.4 [–17.3; –5.5]	0.008	–13.7 [–30.6; 3.1]	0.005
	ST	+10.9 [–3.9; +25.6]		+19.2 [5.8; 32.7]	
PaO_2/FiO_2	ET	+108 [–8; +225]	0.081	+106.2 [–6.1; 218.5]	0.119
	ST	–5.5 [–61.7; +50.7]		–1 [–66.2; 64.2]	
Lactate	ET	–3.2 [–4.6; –1.8]	0.004	–2.6 [–3.6; –1.5]	0.02
	ST	–0.7 [–1.6; +0.2]		–1 [–1.7; –0.3]	
Total bilirubin	ET	–21.3 [–36; –6.7]	0.012	–16.8 [–31; –2.7]	0.067
	ST	+2.5 [–8.1; +13.2]		–0.4 [–10.1; 9.3]	
Diuresis	ET	+870 [+122; +1618]	0.352	+897 [+141; +1653]	0.245
	ST	+443 [–98; +984]		+325 [–265; +914]	
Creatinine	ET	–112.7 [–219.5; –6]	0.095	–93.8 [–174.2; –13.4]	0.084
	ST	–8.3 [–70.5; +53.9]		–6.8 [–61.9; +48.4]	
WBCs	ET	–7 [–12.6; –1.4]	0.403	–5.7 [–9.7; –1.8]	0.755
	ST	–4.3 [–7.6; –1]		–5 [–7.7; –2.3]	
NLR	ET	–5.9 [–18.1; +6.2]	0.625	–6.7 [–11.5; –1.9]	0.198
	ST	–9.3 [–16.2; –2.4]		–10.5 [–13.8; –7.2]	
Platelets	ET	–86 [–138; –33]	0.339	–89 [–130; –48]	0.147
	ST	–54 [–94; –15]		–52 [–79; –25]	
CRP	ET	–81.8 [–153.5; –10.2]	0.096	–61.4 [–107; –15.8]	0.169
	ST	–16.4 [–46.9; +14.1]		–21.8 [–53.9; +10.3]	
PCT	ET	–22.3 [–41.1; –3.6]	0.091	–15.2 [–24.3; –6.1]	0.320
	ST	–3.3 [–15.3; +8.8]		–9.3 [–16.3; –2.3]	
Lymphocytes	ET	–0.2 [–0.9; +0.5]	0.816	–0.2 [–0.9; 0.5]	0.320
	ST	–0.1 [–0.6; +0.5]		–0.1 [–0.6; +0.4]	
Neutrophils	ET	–6.4 [–12; –0.8]	0.471	–5.1 [–8.4; –1.7]	0.954
	ST	–4.2 [–6.9; –1.4]		–4.9 [–7.2; –2.6]	

Note. PCT — procalcitonin; MAP — mean arterial pressure.

average SOFA score in the ET group was 7.9, falling within the same SOFA range, when the hemoadsorption yields maximum efficiency.

The study had a number of limitations. Firstly, the ST comparison group was selected retrospectively, based on archived medical files therefore, cases were not initially adapted for the study, which made it impossible to compare a number of parameters. For example, the magnitude of multimodal LPS-selective hemoadsorption and CVVHDF positive effect on systemic blood pressure, on severity of vascular insufficiency, and cardiac index, due to the lack of invasive hemodynamic monitoring in ST group patients. Circulating endotoxin activity and concentrations were also not evaluated. Secondly, the statistical power was limited by the small sample size. Thirdly, the ST group patients did not receive CVVHDF, making it impossible to separate the effects of endotoxin sorption and CVVHDF. Additionally, the regression analysis used to adjust for the heterogeneity of patient baseline characteristics between groups has its own limitations.

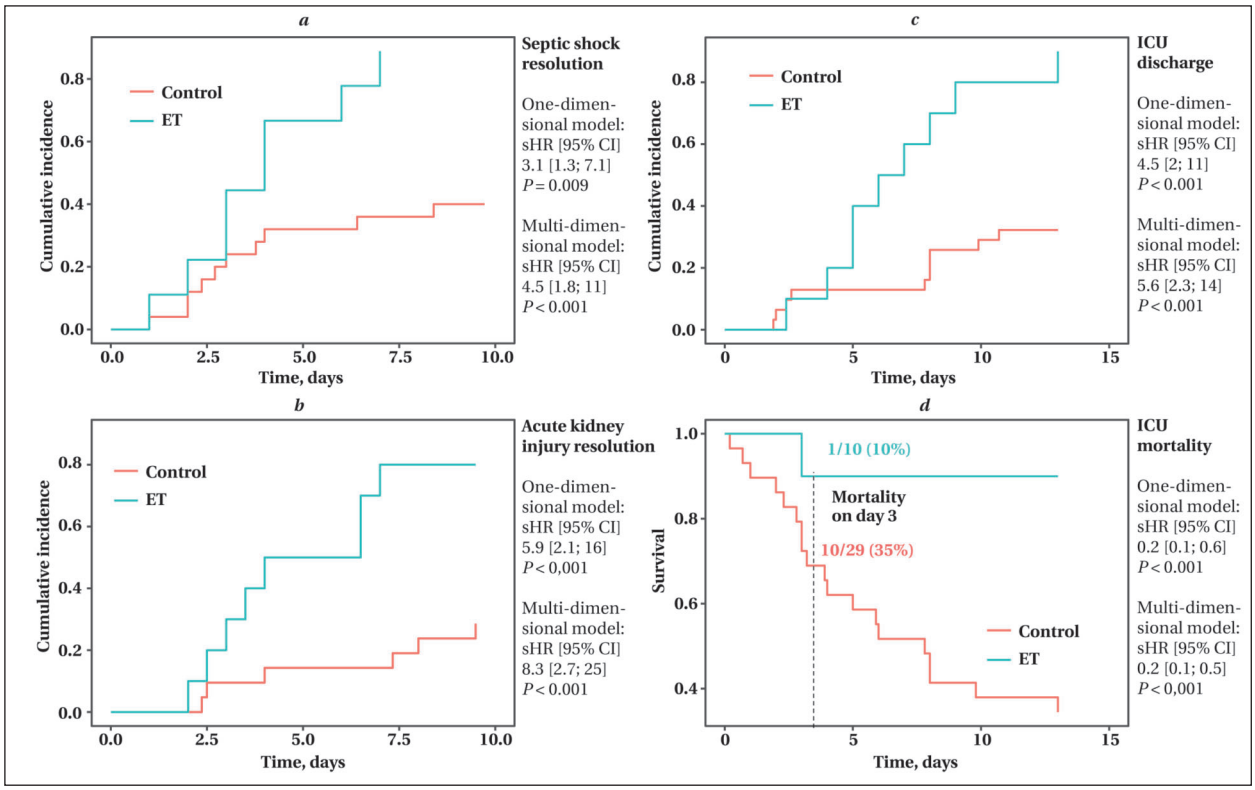

Fig. 2. Incident curves of septic shock resolution (*a*), acute kidney injury resolution (*b*), ICU discharge (*c*), and ICU mortality (*d*).

Conclusion

The concomitant use of selective hemoadsorption and hemodiafiltration in patients with sepsis or septic shock reduces the severity of organ dysfunction and mortality.

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