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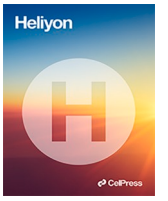

Research article

Sequential respiratory support in septic patients undergoing continuous renal replacement therapy: A study based on MIMIC-III database

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ABSTRACT

Objective: Oxygen and hemodynamic management are important for providing a sufficient adequate oxygen-containing blood to the organs for septic patients. In present study, we aimed to explore the application of sequential respiratory support (SRS) and the association of SRS with the outcome of septic patients who needed continuous renal replacement therapy (CRRT).

Methods: We extracted the medical information of septic patients who received CRRT within 24 h of intensive care unit (ICU) admission from the MIMIC-III v1.4. SRS was defined as receiving firstly oxygen therapy followed by mechanical ventilation (MV) within 24 h of admission to ICU. The *propensity score matching (PSM)* was performed to compare the differences in clinical characteristics and outcomes of patients with or without SRS. Finally, we developed *logistic* regression models to analyze the effects of SRS on hospital mortality.

Results: A total of 181 patients entered in this study, and there were 80 patients undergoing MV including SRS group (n = 61) and non-SRS group (n = 19). In the multivariate *logistic* regression, the value of SRS was associated with the lower risk of hospital mortality adjusted by minimum systolic BP (SBP), maximum lactate, vasopressor use, and sequential organ failure assessment (SOFA) score or Logistic Organ Dysfunction System (LODS) scores within the first 24 h of ICU stay. After *PSM* adjusted by SBP, maximum lactate, vasopressor use, SOFA, and LODS, there were 31 patients in SRS group with a and 18 cases in non-SRS group, displaying a significantly lower hospital mortality in SRS group than that in patients without *SRS* (19.4 % *vs.* 83.3 %, $P < 0.001$). In addition, age, qSOFA, necessitating the administration of vasopressor, and duration of vasopressor were significantly correlated with the hospital mortality in septic patients undergoing CRRT and SRS.

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Conclusions: Receiving SRS within the first 24 h upon admission to the ICU was independently associated with the hospital mortality in patient with sepsis undergoing CRRT, and patients who were directly received MV had a high risk of death.

1. Introduction

Sepsis is a life-threatening disease in intensive care units (ICUs) with high mortality. About 1.7 million adults hospitalize due to sepsis per year and 270,000 deaths in America [1]. In children, the pooled case-fatality rates (CRF) of severe sepsis and septic shock were 31.7% in developing countries, comparing with a CRF of 19.3% in developed countries [2]. Usually, the common site of infection is the respiratory tract [3], and sepsis-associated acute respiratory distress syndrome (ARDS) requiring mechanical ventilation (MV) would suffer the modest excess risk of mortality [4]. In pediatric patients with sepsis-associated ARDS, the hospital mortality was 24.6% and severity of hypoxemia accurately stratified the patient outcomes [5]. Either adult or children, elucidating the risk factors of prognosis should be helpful for the personalized management of patients with sepsis complicated by ARDS or respiratory failure.

Hemodynamic instability is a common problem and high risk factor in septic patient developing ARDS, which leads to tissue hypoxia either in lung or extra-pulmonary organs [6,7]. Liberal oxygen therapy increases mortality, and the recommendation about conservative administration of oxygenation is raised [8]. In regard of quality of life, lung injury, or the occurrence of sepsis-associated cardiovascular events, there are no differences between higher and lower oxygenation strategies [9]. Until now, the application of conservative oxygen therapy is still controversial, and the evidence-based research is not enough to make recommendations [10,11]. The surviving sepsis campaign (SSC) recommendations of international guideline suggest that continuous replacement renal therapy (CRRT) is used in sepsis or septic shock [12],. Recently, CRRT has become a preferred application to manage fluid overload during ARDS, leading to improved dynamic lung compliance (Cdyn) and oxygenation index (OI) in pediatric patients with ARDS [13]. Early extubation following non-invasive MV is feasible to cope with respiratory failure in children [14] or patients with difficult weaning off MV [15]. Sequential respiratory support (SRS) was defined as receiving firstly oxygen therapy followed by MV within 24 h of admission to ICU. However, there is little information about the effect of SRS in septic patients undergoing CRRT.

In the present study, septic patients received CRRT within 24 h of admission to ICU were selected from the public database of Martin Intensive Care (MIMIC)-III database v1.4 as described in our previous study [16]. The medical records about the application of respiratory support of these selected patients were collected, and we found that the application of SRS within 24 h of ICU hospitalization was significantly associated with the decreased hospital mortality in patient with sepsis undergoing CRRT.

2. Materials and methods

2.1. Study design

Referenced to our previous study [16], the patients met sepsis 3.0 and their medical recorded information were collected [17]. The application for access permission to the MIMIC-III database was authorized by Institutional Review Boards of BIDMC and Massachusetts Institute of Technology.

2.2. Study population

This is a secondary analysis of detailed information about 181 patients as reported in our previous study [16]. In the present study, SRS group and non-SRS group were included according to whether the patients received SRS during hospitalization. Hospital mortality was the primary outcome, and both length of ICU and hospital stay were the secondary outcomes.

2.3. Ethics approval

The MIMIC database is a well-known freely accessible database. In this study, 4 authors (Wang C, Zheng J, Zhao Y, and Liu T) completed the web-based course and obtained permission to access the dataset. Because all personal information was listed anonymously, informed consent and ethical approval were waived.

2.4. Data collection

All variables were collected from MIMIC III database as reported in our previous study [16]. In this study, we selected demographics, sequential organ failure assessment (SOFA), quick SOFA (qSOFA), systemic inflammatory response syndrome (SIRS), logistic organ dysfunction system (LODS), the values of clinical and laboratory indexes on the first service, the status of blood infection, the minimum values of systolic BP (SBP) and mean arterial pressure (MAP), oxyhemoglobin saturation (SpO_2) and PaO_2/FiO_2, the minimum levels of platelet or albumin, the maximum levels of creatinine, bilirubin, blood urea nitrogen (BUN), or lactate, the maximum values of international normalized ratio (INR), and the minimum and maximum of white blood cells (WBCs). In addition, the ratio of vasopressor needed, vasopressor duration, the mode of oxygen therapy, and duration of ventilation were accessed.

2.5. Statistical analysis

Continuous variables were summarized as the mean ± standard deviation (SD) for normal distribution, and the median (interquartile range, IQR) were used for continuous variables with non-normal distribution. Accordingly, student's *t*-test or Mann-Whitney *U* test was used to compare the group differences according to data characteristics, respectively. Numbers or percentage were used to describe categorical variables, with the *chi-square* test for detecting the group differences. *P* value less than 0.05 was considered as statistically significant.

Bi-variable crude odds ratio and 95% confidence interval (*CI*) ($P < 0.05$) were used to select candidate variables for entering multivariable analysis. Then, selected variables were entered into *Multivariate logistic* regression to assess the association with the prognosis, and the results presented as the *odd* ratio (*OR*) and 95% confidence intervals (*CI*). STATA 15.0 MP (College Station, Texas, USA) were used to conduct all data analyses.

To avoid the differences in baseline characteristics, we performed *propensity score matching (PSM)* between patients with or without SRS. After *PSM*, confounders are evenly distributed, and it is more feasible to conduct the targeted comparisons of the two groups [18]. A *PSM* model ($cal = 0.05$ and $k = 4$) was used to minimize or reduce the confounding effect of covariate when estimating the effects of SRS on the outcome of hospital mortality. In this *PSM* model, minimum systolic BP, maximum lactate, vasopressor, SOFA, and LODS were considered to match. Based on the *logistic* regression, the propensity score for receiving oxygen therapy was assessed, and the correspondingβ coefficients and *P*-values for selected variables in the full propensity score model were shown in Supplemental Table S1.

3. Results

3.1. Baseline characteristics

Among 181 patients selected as described in our previous study [16], there were 101 cases without MV [MV (−)] and 80 patients received MV [MV (+)] during ICU stay. No significant differences were found in age, gender, ethnicity, the ratio of first service, and blood infection (all $P > 0.05$). In MV (−) subgroup, the length of both ICU and hospital stay was shorter in non-survivors compared with survivors (Table 1). In addition, the scores of SOFA, qSOFA, and LODS were significantly higher in non-survivors of MV (+) group (all $P < 0.05$), but not in non-survivors of MV (−) group (Table 1).

Table 1
Baseline characteristics in patients with sepsis received CRRT.

Parameters		MV (−) (n = 101)		P		MV (+) (n = 80)		P
	Total (n = 101)	Survivors (n = 95)	Non-survivors (n = 6)		Total (n = 80)	Survivors (n = 55)	Non-survivors (n = 25)	
Demographic variables								
Gender male, n (%)	63 (62.2)	60 (63.2)	3 (50)	0.519	46 (57.5)	29 (52.7)	17 (68)	0.200
Age, year, mean (SD)	62.6 (15.1)	62.0 (15.1)	72.5 (12.7)	0.098	61.7 (13.8)	61.0 (14.3)	63.2 (12.8)	0.517
Ethnicity, n	101	95	6	0.605		55	22	0.605
White	49	46	3			35	17	
Black	28	26	2			7	0	
Hispanic	8	8	0			1	0	
others	16	15	1			12	5	
Severity, median (IQR)								
SOFA	6 (5, 7)	6 (4, 7)	7 (5, 8)	0.359	10.7 (4.3)	9.5 (3.7)	13.3 (4.5)	<0.001
qSOFA, **mean (SD)**	1.7 (0.7)	1.7 (0.7)	2.3 (0.5)	0.022	2.1 (0.7)	1.9 (0.7)	2.3 (0.7)	0.021
SIRS	2 (2 , 3)	2 (2 , 3)	7 (5 , 8)	0.928	3 (3, 4)	3 (3, 4)	4 (3, 4)	0.461
LODS, **mean (SD)**	4.9 (2.3)	4.8 (2.2)	6.7 (2.6)	0.051	8.8 (3.4)	7.9 (2.6)	10.7 (4.1)	<0.001
First service, n	101	95	6	0.962	80	55	25	0.744
CMED	10	9	1		14	9	5	
MED	96	81	5		65	45	20	
NMED	2	2	0		1	1	0	
Others	3	3	0		0	0	0	
Blood Infection, n (%)	35 (34.7)	34 (35.8)	1 (16.7)	0.340	33 (41.3)	20 (36.4)	13 (52)	0.188
Mechanical ventilation, n (%)	0 (0)	0 (0)	0 (0)		80 (100)	55 (68.8)	25 (31.2)	
Length of ICU stay, days, median (IQR)	2 (2, 3)	2 (2, 3)	3 (3, 7)	0.093	5 (3 , 10)	7 (3 , 12)	3 (2, 5)	0.011
Length of hospital stay, days, median (IQR)	7 (4, 11)	7 (5, 11)	4 (2, 7)	0.117	11 (4 , 21)	13 (8, 22)	3 (2, 10)	<0.001

SOFA: sequential organ failure assessment; *qSOFA:* Quick SOFA; *SIRS:* systemic inflammatory response syndrome; *LODS:* Logistic Organ Dysfunction System.

3.2. Clinical and laboratory parameters

Among 80 patients in MV (+) group, there were significantly different between survivors and non-survivors in aspect of SBP, MAP, lactate, bilirubin, or INR, platelet or albumin, and the ratio of vasopressor needed or receiving SRS (Table 2).

Table 2
Indexes within 24 h after ICU admission in patients with sepsis received CRRT and MV.

Parameters	Total (n = 80)	Survivors (n = 55)	Non-survivors (n = 25)	*P*
Vital signs, median (IQR) if not otherwise specified				
Maximum heart rate (/min), mean (SD)	110 (22)	110 (22)	110 (22)	0.979
Minimum systolic BP (mmHg), mean (SD)	82 (19)	87 (17)	72 (19)	0.001
Systolic BP group, (mmHg)				0.070
Systolic BP ≥ 100, n (%)	16 (20)	14 (25.5)	2 (8)	
Systolic BP < 100, n (%)	64 (80)	41 (74.5)	23 (92)	
Minimum diastolic BP (mmHg)	39 (31, 47)	41 (34, 47)	35 (30, 44)	0.174
Diastolic BP group, (mmHg)				0.909
Diastolic BP ≥ 60, n (%)	6 (7.5)	4 (7.3)	4 (16)	
Diastolic BP < 60, n (%)	74 (92.5)	51 (92.7)	23 (84)	
Minimum MAP (mmHg)	51 (45, 58.5)	53 (48, 61)	47 (44, 51)	0.018
MAP group, (mmHg)				0.303
MAP ≥70, n (%)	6 (7.5)	3 (5.5)	3 (12)	
MAP <70, n (%)	74 (92.5)	52 (94.5)	22 (88)	
Maximum respiratory rate (/min) mean (SD)	30 (8)	30 (8)	32 (7)	0.197
Respiratory rate group, (/min)				0.782
Respiratory rate ≤20, n (%)	4 (5)	3 (5.5)	1 (4)	
Respiratory rate >20, n (%)	76 (95)	52 (94.5)	24 (96)	
Maximum temperature (°C),	37.6 (36.9, 384)	37.7 (37.1, 38.2)	37.2 (36.6, 38.9)	0.306
Serum laboratory variables, median (IQR) if not otherwise specified				
Maximum lactate (μmol/L)	2.75 (1.8, 6.9)	2.6 (1.6, 4.6)	5.6 (2, 9.9)	0.008
Lactate group, (μmol/L)				0.021
Lactate <4, n (%)	44 (55)	35 (63.6)	9 (36)	
Lactate ≥4, n (%)	36 (45)	20 (36.4)	16 (64)	
Maximum creatinine (μmol/L)	4.6 (3.3, 7)	4.55 (3.3, 7.6)	4.7 (3, 5.5)	0.584
Maximum glucose (mg/dL)	198.5 (130.5, 305)	193 (123, 301)	240 (136, 331)	0.332
Maximum bilirubin (mg/dL)	0.7 (0.4, 2.25)	0.7 (0.4, 1.5)	2.05 (0.6, 4.1)	0.042
Bilirubin group, (mg/dL)				0.946
Bilirubin <4, n (%)	58 (72.5)	40 (72.7)	18 (72)	
Bilirubin ≥4, n (%)	22 (27.5)	15 (27.3)	7 (28)	
Minimum platelet ($\times 10^9$/L)	143 (85, 218)	181 (105, 227)	109 (74, 158)	0.014
Platelet group, ($\times 10^9$/L)				0.091
Platelet ≥ 100, n (%)	58 (72.5)	43 (78.2)	15 (60)	
Platelet < 100, n (%)	22 (27.5)	12 (21.8)	10 (40)	
Maximum INR	1.5 (1.2, 2.2)	1.4 (1.2, 1.8)	2 (1.4, 2.7)	0.017
INR group				0.115
INR < 1.5, n (%)	44 (55)	27 (49.1)	17	
INR ≥ 1.5, n (%)	36 (45)	28 (50.9)	8	
Maximum BUN, (mmol/L)	54 (43, 79)	58.5 (43, 83)	49 (44, 71)	0.438
Minimum WBC ($\times 10^9$/L)	10.8 (6.9, 14.9)	11.05 (7.9, 15.4)	9.5 (5.4, 14)	0.166
Maximum WBC ($\times 10^9$/L) mean (SD)	16.6 (8.0)	17.1 (8.4)	15.3 (7.2)	0355
Minimum albumin (g/dL), mean (SD)	2.9 (0.7)	3.0 (0.7)	2.6 (0.5)	0.043
Albumin group, (g/dL)				0.652
Albumin ≥ 4, n	26	17	9	
Albumin < 4, n	54	38	16	
Pulmonary parameters, median (IQR) if not otherwise specified				
SpO_2	95 (90.5, 97)	95 (92, 97)	93 (86, 97)	0.235
PaO_2/FiO_2, mmHg	111.5 (73.5, 191)	122 (75, 196.7)	90 (63, 140)	0.151
Impaired pulmonary function group				0.272
$PaO_2/FiO_2 \geq 300$, n	22	17	5	
$300 < PaO_2/FiO2 \leq 200$, n	7	4	3	
$200 < PaO_2/FiO_2 \leq 100$, n	23	18	5	
$PaO_2/FiO_2 < 100$, n	28	16	12	
Ventilation durations, hours	65.6 (27.9, 167.5)	82 (30.8, 189.8)	60 (27.4, 98.2)	0.338
Vasopressor				0.004
No, n (%)	24 (30)	22 (40)	2 (8)	
Yes, n (%)	56 (70)	33 (60)	23 (92)	
Vasopressor duration, hours	44.8 (26.2, 122.4)	42.0 (20.5, 135.0)	59.6 (27.6 ， 109.8)	0.459
SRS, n (%)	61 (76.3)	51 (92.7)	10 (40)	<0.001

SD: standard deviation; *IQR:* Inter Quartile Range; BP: blood pressure; SpO_2: Pulse Oxygen Saturation; *PaO_2/FiO_2*: the ratio of the partial pressure of oxygen in arterial blood (PaO_2) to the inspired oxygen fraction (FiO_2); INR: International Normalized Ratio; SRS, sequential respiratory support.

3.3. Risk factors of hospital mortality

The univariate *logistic* regression analysis was performed using the variables with statistically significant differences according to the results of Tables 1 and 2. SOFA, qSOFA, LODS, SBP, lactate, vasopressor needed, and SRS were significantly correlated with hospital mortality in 80 septic patients undergoing CRRT and MV (all $P < 0.05$) (Supplementary Table S2). Moreover, multivariate *logistic* regression model adjusted by SOFA or LODS displayed that SRS was a protective factor of hospital mortality in 80 septic patients undergoing both CRRT and MV support (Table 3).

To further analyze the significant association of SRS and hospital mortality in 80 septic patients received CRRT and MV, we compared the difference of critical variables between patients with or without SRS. The severity as shown as SOFA and LODS, the values of lactate, bilirubin, INR, the ratio of vasopressor needed, the length of ICU and hospital stay, as well as hospital mortality were significantly different (Table 4). After *PSM*, the hospital mortality in patients without SRS was still high compared with patients received SRS (83.3 % *vs.* 19.4 %, $P < 0.001$). In addition, all these patients without SRS had a shorter length of hospital or ICU stay (Table 4).

After comparing the outcomes and the clinical characteristics of patients received SRS, the age of non-survivors was significantly larger than that of survivors ($P = 0.008$), and the qSOFA score was relatively higher in non-survivors than survivors, but without statistical significance ($P = 0.062$). The ratio of vasopressor support in non-survivors was 90% comparing 58.8% in survivors ($P = 0.060$). The levels of lactate, platelet, INR, and vasopressor duration displayed slight differences but without statistical significance (all $P > 0.05$) (Table 5). Due to the small size of non-survivors (n = 10), if we defined P value < 0.1 as statistically significant, the variables of age, qSOFA, vasopressor need, and vasopressor duration were associated with the hospital mortality of septic patients received CRRT with SRS (Supplementary Table S3).

4. Discussion

Patients with sepsis with respiratory support receive non-invasive oxygen therapy or MV when complicated with respiratory failure. However, until now, there is still little information variable of detailed criteria for respiratory support [10,19–21]. Though oxygen support significantly increases survival in animal sepsis model [22], but it is ambiguous for the clinical benefits in different mode of respiratory support in patients [10,20]. In the present study, we firstly get evidence that SRS could get clinical benefits in septic patients received CRRT.

Acute respiratory failure is risk factor for the worse outcome of sepsis. The patients with sepsis induced by pulmonary infection displayed a lower in-hospital mortality than that in nonpulmonary source of sepsis [23]. There were metabolically different between sepsis-induced direct and indirect ARDS [24], and there are two phenotypes identified as hyperinflammatory phenotype with worse clinical outcomes and hypoinflammatory phenotype with a longer duration of MV [25]. In our present study, the total mortality of 80 septic patients undergoing both CRRT and MV support was 31.3% (16.4% in the SRS group *vs.*78.9% in the non-SRS group). The differences of hospital mortality could be mainly related to the subtype of sepsis because the results after PSM still showed the worse outcome of patients with sepsis receiving CRRT and MV (42.9% in the SRS group *vs.* 83.3% in the non-SRS group). High-flow nasal cannula, one of kind of non-invasive ventilation (NIV), significantly decreased the respiratory drive and effort in septic patients of nonpulmonary origin [26], and NIV failure was associated with the severity of sepsis [27]. Considering that the advantage of CRRT in improving hemodynamics in patients with septic shock, SRS could be favorable for early oxygen delivery to improve the microcirculation and organ function. It was possible that the critical emergency led to direct MV. However, after PSM, SRS was still significantly associated with the better outcome of septic patients receiving CRRT. It may be worth noting that the importance of oxygen supplement for extrapulmonary requirement.

A recent meta-analysis indicated that both SOFA score and pulmonary sepsis were associated with ARDS [28]. In our present study, it could be related to the limitation of included septic patients with CRRT, and there were no significantly association of MBP, maximum lactate, vasopressor, SOFA, or LODS. We speculated that the support of CRRT could contribute the outcome of these

Table 3
Multivariate *Logistic* analysis of factor related to hospital mortality.

Parameters	*OR* (95% *CI*)	*P*
Model 1		
SRS	0.047 (0.009–0.260)	<0.001
Minimum systolic BP	0.967 (0.924–1.012)	0.144
Maximum lactate	1.022 (0.858–1.218)	0.803
Vasopressor	4.956 (0.390–62.910)	0.217
SOFA	1.020 (0.831–1.252)	0.852
Model 2		
SRS	0.052 (0.010–0.255)	<0.001
Minimum systolic BP	0.985 (0.937–1.034)	0.538
Maximum lactate	1.004 (0.849–1.186)	0.966
Vasopressor	7.447 (0.378–146.810)	0.187
LODS	1.218 (0.898–1.652)	0.204

OR: odds ratio; *CI:* confidence interval; *BP:* blood pressure; SOFA: sequential organ failure assessment; SRS, sequential respiratory support.

Table 4
Comparison of the clinical characteristics and outcomes in septic patients received CRRT with (SRS) or without SRS (non-SRS).

Parameters	*Before PSM*				*After PSM*			
	Total (n = 80)	SRS (n = 61)	non-SRS (n = 19)	*P*	Total (n = 49)	SRS (n = 31)	non- SRS (n = 18)	*P*
Gender male, n (%)	46 (57.5)	33 (54.1)	13 (68.4)	0.270	32 (65.3)	19 (61.3)	13 (72.2)	0.438
Age, year, mean (SD)	61.7 (13.8)	62.9 (14.3)	57.7 (11.5)	0.150	60.5 (13.7)	62.7 (14.7)	56.8 (11.1)	0.144
SOFA, **mean (SD)**	10.7 (4.3)	9.7 (3.7)	14.2 (4.5)	<0.001	13.1 (3.3)	12.2 (2.4)	14.7 (4.0)	0.031
qSOFA, **mean (SD)**	2.1 (0.7)	2.0 (0.7)	2.1 (0.8)	0.700	2.2 (0.6)	2.3 (0.4)	2.2 (0.8)	0.604
SIRS, **median (IQR)**	3 (3, 4)	4 (3, 4)	3 (3, 4)	0.230	3.4 (0.7)	3.4 (0.7)	3.5 (0.7)	0.553
LODS, **mean (SD)**	8.8 (3.4)	8.1 (2.7)	10.8 (4.5)	0.002	10.2 (3.2)	9.7 (1.9)	11.1 (4.5)	0.136
Maximum lactate (μmol/L)	2.75 (1.8, 6.9)	2.6 (1.7, 5.05)	5.75 (2, 10.6)	0.017	4.2 (2, 8.4)	3.4 (2, 7.1)	5.75 (2, 10.6)	0.202
Maximum creatinine (μmol/L)	4.6 (3.3, 7.0)	4.65 (3.3, 7.6)	4.6 (3, 5.7)	0.419	4.6 (3.2, 5.7)	4.5 (3.2, 6.7)	4.65 (3, 5.7)	0.885
Maximum glucose (mg/dL)	198.5 (130.5, 305)	193 (136, 284)	279 (121, 408)	0.237	241 (142, 319)	213 (143, 296)	284.5 (132, 408)	0.246
Maximum bilirubin (mg/dL)	0.7 (0.4, 2.25)	0.7 (0.4, 1.6)	2.15 (0.7, 4.5)	0.022	1.1 (0.5, 2.95)	0.7 (0.4, 1.8)	2.15 (0.7, 4.5)	0.052
Minimum platelet ($\times10^9$/L)	143 (85, 218)	158 (101.5, 223.5)	102 (80, 172)	0.067	139 (80, 193)	158 (78, 246)	101.5 (80, 168)	0.097
Maximum INR	1.5 (1.2, 2.2)	1.4 (1.2, 1.8)	2.1 (1.7, 3.7)	0.002	1.8 (1.3, 2.4)	1.5 (1.3, 2.2)	2.05 (1.7, 3.1)	0.059
Maximum BUN, (mmol/L)	54 (43, 79)	58 (44, 92)	47 (37, 66)	0.179	49 (39, 66)	56 (41, 92)	46 (37, 63)	0.299
Minimum WBC ($\times$109/L)	10.8 (6.9, 14.9)	10.7 (7.35, 15.45)	11.1 (4.3, 13.8)	0.273	10.8 (6.9, 14.8)	10.4 (7.5, 15.9)	11.2 (4.3, 13.8)	0.481
Maximum WBC ($\times10^9$/L), mean (SD)	16.6 (8.0)	16.8 (8.1)	15.9 (7.9)	0.667	17.1 (8.2)	17.6 (8.5)	16.3 (7.9)	0.618
Minimum albumin (g/dL), mean (SD)	2.9 (0.7)	3.0 (0.7)	2.6 (0.6)	0.117	2.8 (0.7)	2.9 (0.8)	2.4 (0.6)	0.231
SpO_2	95 (90.5, 97)	95 (92, 97)	94 (86, 96)	0.185	93 (87.5, 96)	93 (89, 95)	94 (86, 96)	0.856
PaO_2/FiO_2, mmHg	111.5 (73.5, 191)	112.9 (75, 190)	101.5 (63, 192)	0.407	94 (63, 152)	94 (73, 133.3)	101.5 (63, 192)	0.654
Vasopressor				0.034				0.691
No, n (%)	24	22	2		2	1	1	
Yes, n (%)	56	39	17		47	30	17	
Vasopressor duration, hours	44.8 (26.2, 122.4)	47.0 (20.5, 178.6)	40.8 (29.8, 59.6)	0.539	47.0 (26.5, 135.0)	58.8 (20.5, 178.6)	40.8 (29.8, 59.6)	0.319
Ventilation durations, hours	65.6 (27.9, 167.5)	93.9 (27.3, 236.3)	37.7 (28.3, 82)	0.115	86.1 (36.3, 228.2)	149.9 (60.6, 288))	44.3 (28.3, 82)	0.319
Length of ICU stay, days, median (IQR)	5 (3, 10)	7 (4, 14)	2 (1, 4)	<0.001	5.7 (3.1, 12.0)	9.2 (5.5, 19.4)	2.2 (1.4, 3.9)	<0.001
Length of hospital stay, days, median (IQR)	11 (4, 21)	13 (8, 23)	2 (1, 4)	<0.001	11.2 (3.2, 20.7)	18.6 (11.2, 24.3)	2.5 (1.5, 4.2)	<0.001
Hospital mortality, n (%)	25 (31.3)	10 (16.4)	15 (78.9)	<0.001	21 (42.9)	6 (19.4)	15 (83.3)	<0.001

SOFA: sequential organ failure assessment; *qSOFA:* Quick SOFA; *SIRS:* systemic inflammatory response syndrome; *LODS:* Logistic Organ Dysfunction System.

patients. Moreover, the higher non-respiratory pediatric logistic organ dysfunction (PELOD-2) score and $PaO_2/FiO_2 < 100$ at diagnosis were independently associated with NIV failure in pediatric ARDS, and use of NIV at diagnosis of mild to moderate hypoxemia resulted in shorter exposure to MV in children [29]. It is interesting that the hospital mortality of 61 patients with SRS was significantly lower than that of patients without SRS. Consistently, it has been proved that conservative oxygen therapy decreased the MV duration, new organ failure, and the risk of RRT application during ICU hospitalization [30]. So, we propose that SRS support within 24 h of admission to ICU could be of great advantage in septic patients undergoing CRRT support. From another view, conventional therapy would leave high ratio of patients exposed to hyperoxemia compared to conservative oxygen group (44.5% *vs.* 11.4%) [31]. To avoid the harmful effect of hyperbaric oxygenation, conservative oxygen supplement should be suggested.

This study has several limitations. First, it is a database study with a lack of detailed information about SRS, and the clinical features including sepsis-causing origin organ, pathogen strain, *etc*. Second, the sample size was small due to the limited septic patients receiving the support of CRRT. The protective roles of SRS in patients under CRRT were firstly reported in this study; however, it is more important to conduct a prospective study in well-designed clinical research.

5. Conclusions

It is still ambiguous to clearly demonstrate the clinical benefits of different mode of respiratory support in septic patients undergoing CRRT. In this study, this is the first report to get evidence that septic patients received CRRT could obtain clinical benefits from SRS within the first 24 h of ICU stay, which is an independently protective factor of hospital mortality in septic patient undergoing CRRT.

Table 5
Comparison of the clinical characteristics in septic patients received CRRT with SRS.

Parameters	Total (n = 61)	Survivors (n = 51)	Non-survivors (n = 10)	*P*
Gender male, n (%)	33 (54.1)	27 (52.9)	6 (60)	0.682
Age, year, mean (SD)	62.9 (14.3)	60.8 (14.5)	73.8 (7.0)	0.008
SOFA, mean (SD)	9.7 (3.7)	9.5 (3.6)	10.5 (4.1)	0.519
qSOFA, mean (SD)	2.0 (0.7)	2.0 (0.7)	2.4 (0.5)	0.062
SIRS, median (SD)	3.2 (0.8)	3.2 (0.8)	3.0 (0.8)	0.369
LODS, mean (SD)	8.1 (2.7)	7.9 (2.6)	8.9 (2.7)	0.301
Maximum lactate (μmol/L)	2.6 (1.7, 5.1)	2.6 (1.6, 4.6)	5 (2, 7.1)	0.129
Maximum creatinine (μmol/L)	4.7 (3.3, 7.6)	4.6 (3.3, 7.8)	5.1 (3.8, 6.7)	0.923
Maximum glucose (mg/dL)	193 (136, 284)	196 (140, 309)	160 (122, 240)	0.231
Maximum bilirubin (mg/dL)	0.7 (0.4, 1.6)	0.7 (0.4, 1.5)	1.4 (0.4, 2.9)	0.381
Minimum platelet ($\times 10^9$/L)	158 (10.1.5, 223.5)	188.5 (105, 227)	128 (74, 158)	0.110
Maximum INR	1.4 (1.2, 1.8)	1.4 (1.2, 1.6)	1.8 (1.4, 2.7)	0.170
Maximum BUN, (mmol/L)	58 (44, 92)	58.5 (41, 83)	54 (46, 98)	0.552
Minimum WBC ($\times 10^9$/L)	10.7 (7.4, 15.5)	10.9 (7.9, 15.9)	9.7 (6.7, 14.6)	0.558
Maximum WBC ($\times 10^9$/L), mean (SD)	16.8 (8.1)	17.0 (8.5)	15.6 (6.2)	0.601
Minimum albumin (g/dL), mean (SD)	3.0 (0.7)	3.0 (0.7)	2.8 (0.6)	0.658
SpO_2	95 (92, 97)	95 (91, 97)	95 (93, 98)	0.826
PaO_2/FiO_2, mmHg	113 (75, 190)	119 (75, 193)	101 (84, 140)	0.744
Vasopressor, n (%)	39 (63.9)	30 (58.8)	9 (90)	0.060
Vasopressor duration, hours	47.0 (20.5, 178.6)	41.8 (15.5, 139.4)	109.8 (68.0, 218.0)	0.134
Ventilation durations, hours	93.9 (27.3, 236.3)	93.9 (27.9, 226.5)	95.3 (25.5, 408)	0.671
Length of ICU stay, days, median (IQR)	6.7 (3.6, 13.7)	6.7 (3.6, 13.2)	8.0 (3.4, 24.1)	0.726
Length of hospital stay, days, median (IQR)	13.0 (7.8, 23.0)	13.7 (9.7, 23.0)	8.1 (3.2, 24.0)	0.205

SOFA: sequential organ failure assessment; *qSOFA:* Quick SOFA; *SIRS:* systemic inflammatory response syndrome; *LODS:* Logistic Organ Dysfunction System.

Data availability statement

Datasheet used in this study were submitted as supplementary materials, which can be made available.

CRediT authorship contribution statement

Chunxia Wang: Writing – original draft, Supervision, Investigation, Data curation, Conceptualization. **Jianli Zheng:** Software, Investigation, Funding acquisition, Formal analysis, Data curation. **Yilin Zhao:** Methodology, Investigation, Data curation. **Tiantian Liu:** Methodology, Investigation, Conceptualization. **Yucai Zhang:** Writing – review & editing, Supervision, Funding acquisition, Conceptualization.

Declaration of competing interest

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

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e27563.

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