

Predictors for acute kidney injury in patients with sepsis and septic shock

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Summary

Objective: This study aimed to determine the risk factors for acute kidney injury (AKI) in patients with sepsis and septic shock. **Subject and method:** A prospective descriptive study with longitudinal follow-up of 201 patients with sepsis and septic shock admitted to Emergency Department - 108 Military Central Hospital. **Result:** The proportion of patients with AKI was 64.7%. In univariate analysis of risk factors for AKI, six potential risk factors identified: Hypertension, APACHE II score ≥ 20 , SOFA score > 8 , MOD score > 8 , lactate $\geq 2\text{mmol/L}$, and $\text{HCO}_3^- < 15\text{mmol/L}$. However, in multivariate analysis, only hypertension, APACHE II score ≥ 20 , and SOFA score > 8 emerged as independent risk factors for AKI. **Conclusion:** In patient with sepsis and septic shock, hypertension, APACHE II score ≥ 20 and the SOFA score > 8 were the key risk factors for acute kidney injury.

Keywords: Sepsis, acute kidney injury, risk factor.

I. BACKGROUND

Acute kidney injury (AKI) and sepsis share a bidirectional relationship. AKI, a multifactorial syndrome, often stems from sepsis and septic shock. Epidemiological studies indicate that AKI occurs in 11%–60% of septic patients¹. AKI prevalence increases with the severity of sepsis, with rates of 19% in sepsis, 23% in severe sepsis, and 51%–64% in septic shock patients².

According to some authors, the risk factors of sepsis-associated acute kidney injury (S-AKI) can be categorized into three groups: (1) Pre-septic risk factors: These include concurrent chronic diseases, gender, age, smoking history, etc. (2) Factors related to sepsis: Symptoms, types of sepsis, sources of infection, and bacterial characteristics. (3) Factors related to sepsis treatment: Mechanical ventilation, antibiotic use, duration of ICU stay, etc.

This study aimed to identify the risk factors for AKI in patients with sepsis and septic shock.

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II. SUBJECT AND METHOD

2.1. Subject

This study was conducted on 201 patients who enrolled from the Emergency Department at the 108 Military Central Hospital between January 2021 and August 2023.

Inclusion criteria: Patients aged ≥ 18 years and diagnosed with sepsis or septic shock as per SCCM/ESICM 2016 guidelines³. Consent was obtained from patients and/or their families for participation and adherence to treatment.

Exclusion criteria: Patients admitted with cardiac arrest, brain death, chronic kidney disease, or those treated for less than 24 hours or patients lacking proper monitoring/ laboratory tests. Patients whose families did not consent were also excluded.

2.2. Method

Study design and methodology.

This was a prospective descriptive study with longitudinal follow-up. Data were collected from all eligible patients using standardized medical records.

Research methodology:

Patients meeting the inclusion criteria were enrolled.

Clinical examinations and laboratory tests were conducted upon admission to the Emergency Department.

Data collected included age, gender, underlying diseases, clinical signs, and test results to calculate scores, the percentage of AKI cases, mechanical ventilation use, kidney replacement therapy, and in-hospital deaths.

Logistic regression analysis was performed to determine risk factors for AKI.

Variables and algorithms:

AKI diagnosis: Based on KDIGO 2012 guidelines:

Serum creatinine: An increase of at least 0.3mg/dL within 48 hours or an increase of at least 1.5 times baseline within the last 7 days.

Urine output: Less than 0.5mL/kg/h for at least 6 hours.

Sepsis and septic shock diagnosis: As per Sepsis-3 guidelines:

Sepsis: Defined as an acute change in the total SOFA score ≥ 2 points consequent to infection.

Septic shock: A subset of sepsis with persisting hypotension requiring vasopressors to maintain MAP ≥ 65 mmHg and a serum lactate level > 2 mmol/L despite adequate volume resuscitation.

Statistical analysis:

Analysis was performed using SPSS version 23.0. Continuous variables were presented as mean $\pm$ standard deviation, and categorical variables as percentages. Correlation among variables was assessed using univariate and multivariate logistic regression analysis. Statistical significance was determined when the p-value < 0.05 .

III. RESULT**Table 1. Characteristics of patients**

Characteristics		Number (n = 201)	Percentage %
Age (year)	X $\pm$ SD (min-max)	66.43 $\pm$ 16.42 (19-99)	
	< 41	14	7
	41 -50	16	8
	51-60	34	17
	61-70	52	26
	> 70	85	42
Gender	Female	81	40.3
	Male	120	57.7
Renal replacement therapy (RRT)		14	7.0
In-hospital mortality		95	47.3

Comment: The study group of patients ranged in age from 19 to 99 years, with a median age of 66.43 $\pm$ 16.42 years. Patients were primarily concentrated in the age group over 70 years (85/201 patients, 42.3%). The proportion of patients aged 40 years and under accounted for 7%. The ratio of male to female patients was 1.48:1, indicating a higher number of male patients compared to females. The percentage of patients who required renal replacement therapy (RRT) was 7.0%, while the in-hospital mortality rate was 47.3%.

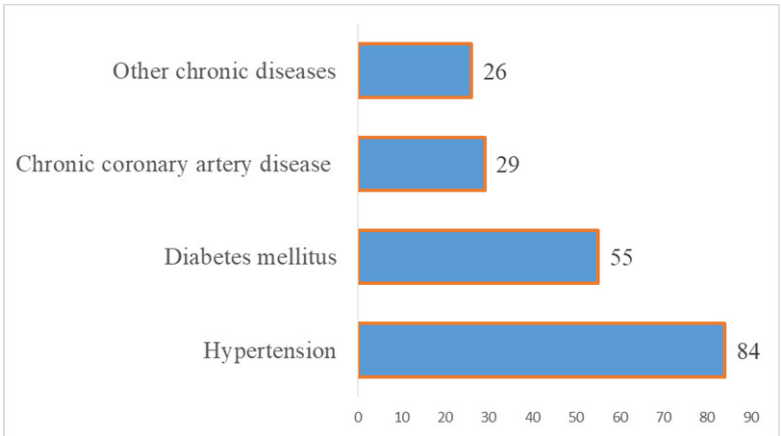


Figure 1. Patient's medical history

Comment: In the study, 68.2% of patients had chronic diseases, with diabetes and hypertension being the most common conditions.

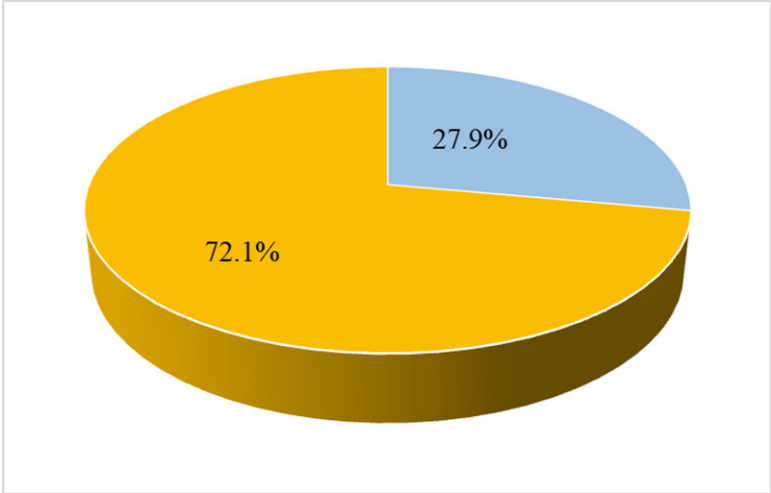


Figure 2. Ratio of sepsis and septic shock in the study

Comment: In the study, 56 out of 201 patients had SEPSIS accounted for 27.9%.

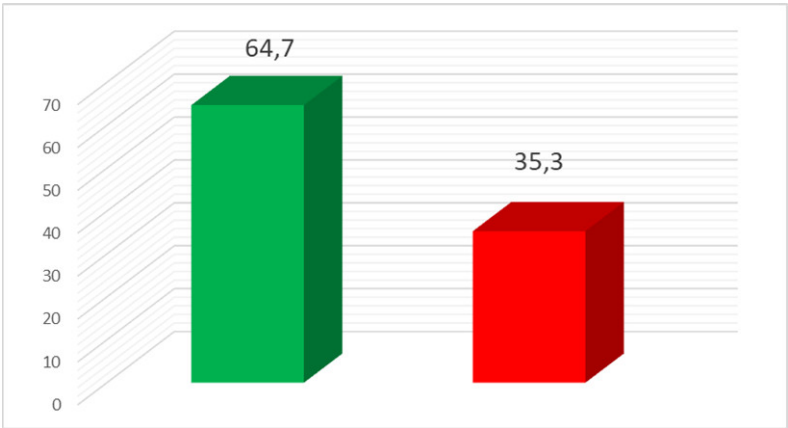


Figure 3. Rate of acute kidney injury

Comment: The proportion of patients with AKI was 64.7%, while those without accounted for 35.3%. The ratio of patients with AKI to those without AKI was 1.8/1.

Table 2. Univariate analysis of risk factors for AKI

Variables		AKI (n = 130)	Non AKI (n = 71)	Univariate analysis		
				OR	95% CI	p
Medical history						
1	Age > 60 (years)	94	44	1.60	0.87-2.96	>0.05
2	Men	83	38	1.53	0.85-2.76	>0.05
3	Hypertension	61	23	2.01	1.07-3.78	<0.05
4	Diabetes mellitus	41	14	1.98	0.98-4.00	>0.05
5	Smoking			1.23	0.59-2.62	>0.05
6	Chronic coronary artery disease	20	9	1.29	0.55-3.02	>0.05
7	Have at least 1 chronic disease	94	43	2.19	1.08-4.42	<0.05
Clinical and subclinical symptoms						
8	Glasgow score ≤ 13	21	18	1.41	0.63-3.14	>0.05
9	Breathing rate > 22	17	19	1.12	0.51-2.37	>0.05
10	Systolic blood pressure < 90mmHg	61	23	1.99	0.76-5.21	>0.05
11	qSOFA ≥ 2	24	22	1.18	0.53-2.61	>0.05
12	Septic shock	97	48	1.41	0.75-2.66	>0.05
13	APACHEII score ≥ 20	48	6	6.34	2.56-15.74	<0.05
14	SOFA Score ≥ 9	70	24	2.28	1.25-4.17	<0.05
15	MOD Score ≥ 9	39	11	2.36	1.10-5.09	<0.05
16	Total serum bilirubin >34 mmol/l	34	13	1.72	0.83-3.57	>0.05
17	pH ≤ 7.2	11	2	3.19	0.69-14.8	>0.05
18	Lactate ≥ 2 mmol/L	95	41	2.23	1.16-4.28	<0.05
19	HCO ₃ ⁻ < 15 mmol/L	30	6	3.23	1.27-8.21	<0.05
20	Platelet count < 50G/L	23	6	2.22	0.86-5.75	>0.05
21	Positive blood cultures	52	28	1.02	0.57-1.85	>0.05
22	Gram-negative infections	50	32	0.61	0.27-1.40	>0.05
23	Source of the infection: Digestive system	60	28	1.31	0.73-2.37	>0.05
24	Source of the infection: Urinary system	19	10	1.05	0.46-2.48	>0.05
25	Unknown source of the infection	15	6	1.41	0.52-3.82	>0.05
Treatment						
26	Ventilator	55	22	0.61	0.33-1.13	>0.05
27	ICU stay over 3 days	89	44	1.33	0.72-2.48	>0.05

Comment: There were six risk factors for AKI: Hypertension, APACHE II score ≥ 20, SOFA score > 8, MODS score > 8, lactate ≥ 2mmol/L, and HCO₃⁻ < 15mmol/L.

The factors identified in the univariate analysis with p<0.05 were included in the logistic regression analysis, yielding the following results:

Table 3. Multivariate analysis of risk factors for AKI

Variables		Multivariate analysis		
		OR	95% CI	p
1	Hypertension	2.80	1.26-6.20	<0.05
2	APACHE II score $\geq$ 20	4.74	1.43-15.70	<0.05
3	SOFA score > 8	2.35	1.01-5.48	<0.05
4	MODs Score > 8	0.90	0.32-2.49	>0.05
5	Lactate $\geq$ 2mmol/L	1.54	0.67-3.55	>0.05
6	HCO ₃ ⁻ < 15mmol/L	1.85	0.59-5.81	>0.05

Comment: Multivariate analysis showed that hypertension, an APACHE II score $\geq$ 20, and a SOFA score > 8 were the three independent risk factors for acute kidney injury.

IV. DISCUSSION

Our research identified six risk factors for acute kidney injury (AKI) in patients with sepsis and septic shock: Hypertension, APACHE II score $\geq$ 20, SOFA score > 8, MOD score > 8, lactate $\geq$ 2mmol/L, and HCO₃⁻ < 15mmol/L. However, multivariate analysis revealed that only three independent risk factors for AKI were significant: Hypertension, APACHE II score $\geq$ 20, and SOFA score > 8.

Several studies have investigated risk factors for AKI in patients with sepsis and septic shock, with results varying due to factors such as geography, study design, and patient monitoring methods.

Liu J et al conducted a meta-analysis that included 31 risk factors, identifying 20 statistically significant ones. The most common risk factors for S-AKI were (OR, 95% CI and prevalence in patients with S-AKI): Septic shock [2.88 (2.36–3.52), 60.47%], hypertension [1.43 (1.20–1.70), 38.39%], diabetes mellitus [1.59 (1.47–1.71), 27.57%], abdominal infection [1.44 (1.32–1.58), 30.87%], vasopressor use [2.95 (1.67–5.22), 64.61%], mechanical ventilation [1.64 (1.24–2.16), 68.00%], positive blood culture results [1.60 (1.35–1.89), 41.19%], and a history of smoking [1.60 (1.09–2.36), 43.09%]. Other risk factors included cardiovascular disease, coronary artery disease, liver disease, infections with unknown

access, diuretic and ACEI/ARB use, gram-negative bacterial infections, and post-transplant⁵. We knowed that the pathogenesis of AKI associated with sepsis is relatively complex and includes hemodynamic abnormalities due to inflammatory response, oxidative stress, and shock, which subsequently cause a decrease in renal perfusion pressure and eventually lead to ischemia and hypoxia in renal tissue⁶. The kidneys of people with hypertension were more sensitive to changes in blood pressure. Moreover, high blood pressure could damage and narrow renal blood vessels, making hypertension a significant risk factor for AKI.

Pinheiro KHE et al studied 320 ICU patients and found that the length of stay in the ICU for the S-AKI group was twice as long as for non-AKI patients. Each additional day in the ICU increased the likelihood of developing S-AKI by 33%⁷. Furthermore, the absence of nephrologist support increased the risk of S-AKI by 211%.

Research by Shen Hejin et al showed that mechanical ventilation was a risk factor for S-AKI. Observing that after 24 hours of invasive ventilation, patients experienced significant declines in glomerular filtration rate, creatinine clearance, and urea clearance. These outcomes may result from improper ventilator use, leading to reduced renal perfusion and kidney failure. At the same time, in patients on long-term invasive mechanical ventilation, insufficient pain relief and sedation activate the renin-angiotensin-aldosterone system, reducing kidney blood flow and leading to damage to renal function^{8, 9}. Hypoxemia, hypercapnia and

excessive PEEP during mechanical ventilation were also identified as AKI risk factors.

Currently, there is no universally effective method to prevent or reduce AKI associated with mechanical ventilation. However, studies suggest that adjusting ventilator settings—such as minimizing hypoxia, avoiding prolonged hypercapnia, and using lower PEEP—can mitigate AKI risk. A meta-analysis found that invasive mechanical ventilation may be associated with a three-fold increase in the incidence of AKI in ICU patients, though tidal volume (TV), PEEP did not alter this risk¹⁰.

Xin Wang's 2014 analysis of 3,107 patients in 30 ICU departments identified 21 risk factors, with six independent risk factors: Age, APACHE II score, duration of mechanical ventilation, duration of MAP < 65mmHg, time to initiation of renal replacement therapy, and the disease stage based on KDIGO criteria¹¹.

V. CONCLUSION

In patients with sepsis and septic shock: Hypertension, the APACHE II score ≥ 20 , and the SOFA score > 8 were identified as predictors for acute kidney injury.

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