

ARTICLE

Predictive Value of Combined Urinary Sodium, Urinary FEK, and Urinary UK/Ucr Tests in Sepsis-Induced Early Acute Kidney Injury

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ABSTRACT

Objective: To explore the predictive value of the combined test of urinary sodium, urinary potassium excretion fraction (FEK), and urinary potassium concentration/urine creatinine concentration (UK/Ucr) in sepsis-induced early acute kidney injury (AKI). **Methods:** Sixty sepsis patients admitted to the Northern Hospital of National Pharmaceuticals from 2022.4 to 2024.4 were selected and divided into the AKI group (n=21) and the non-AKI group (n=39) according to whether AKI occurred or not, and another 20 health check-up subjects from our hospital were selected to be included in the control group during the same period of time, and we compared the urinary sodium, urinary FEK, and urinary UK/Ucr tests of the three groups, and analysed the urinary potassium concentration/urine creatinine concentration (UK/Ucr) in the early stage of sepsis-induced acute kidney injury (AKI) by plotting the working characteristics of the subjects (ROC) curve graph to analyse the predictive value of the combined detection of urinary sodium, urinary FEK and urinary UK/Ucr in sepsis-induced early AKI. **Results:** The levels of urinary FEK and urinary UK/Ucr in the non-AKI group were higher than those in the control group, and the levels of urinary sodium were lower than those in the control group ($P < 0.05$), while the levels of urinary FEK and urinary UK/Ucr in the AKI group were higher than those in the non-AKI group, and the levels of urinary sodium were lower than those in the non-AKI group ($P < 0.05$); the ROC was plotted and found that the combined test of urinary sodium, urinary FEK, and urinary UK/Ucr was useful for the prediction of early AKI caused by sepsis. The area under the curve (AUC) values ranged from 0.694-0.940, with high sensitivity and specificity, and the value of predicting sepsis-induced early AKI was high. **Conclusion:** Urinary sodium, urinary FEK and urinary UK/Ucr can be used as effective biomarkers for the early prediction of AKI, and the combined test has high value in predicting early AKI caused by sepsis.

Sepsis is a systemic inflammatory response syndrome caused by the host's immune response to infection losing control, leading to organ dysfunction. It is a significant cause of death in critically ill patients [1]. Sepsis-

related acute kidney injury (SA-AKI) is a common organ dysfunction complication associated with sepsis. Its pathogenesis is closely related to inflammatory immune responses, abnormal renal hemodynamics, and

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microcirculatory disorders, which can lead to varying degrees of structural and functional abnormalities in the kidneys. This condition is characterized by high incidence, high mortality, and poor prognosis [2]. Clinical data show that the incidence of AKI in sepsis patients is approximately 51% to 66.9%, with a mortality rate as high as 60%. Early diagnosis of SA-AKI is crucial for formulating targeted treatment plans, reducing mortality, and improving patient outcomes [3]. Serum creatinine (Scr) and urine output levels are commonly used laboratory biomarkers for diagnosing AKI, but their changes do not intuitively reflect the extent of kidney damage. Therefore, finding new biomarkers with higher sensitivity and specificity has become a hot topic in current clinical research [4]. Urine sodium, urine potassium excretion fraction (FEK), and urine potassium concentration to urine creatinine concentration ratio (UK/UCr) are important indicators for assessing kidney function and electrolyte balance. Changes in these levels are considered sensitive expressions of renal microcirculatory disorders. However, there is a lack of research in China on the predictive value of urinary sodium, urinary FEK, and urinary UK/UCr

in predicting SA-AKI. Based on this, our study selected patients with sepsis and healthy individuals undergoing physical examinations at our hospital to investigate the predictive value of combined detection of urinary sodium, urinary FEK, and urinary UK/UCr in early AKI caused by sepsis. This aims to provide theoretical support for further exploration of the pathogenesis of SA-AKI, early monitoring, and accurate assessment of renal function status in sepsis patients, guiding treatment decisions

1 Data and methods

1.1 General information

Sixty patients with sepsis admitted to the Northern Hospital of Sinopharm from April 2022 to April 2024 were selected, and they were divided into AKI group (n=21) and non-AKI group (n=39) based on whether AKI occurred. Additionally, 20 healthy individuals who underwent physical examinations at our hospital during the same period were included as the control group. The subjects were basically consistent in general information (P>0.05), see Table 1. This study has been reported to and approved by the ethics committee of our hospital.

Table 1. Comparison of general data (example)

index	sex		Age (years)	Body mass index (kg/m ²)	heart rate (次/min)	systolic pressure (mmHg)	diastolic pressure (mmHg)
	man	woman					
control group (n=20)	13	7	64.37±6.72	21.28±2.24	88.06±12.27	119.37±13.54	75.26±12.31
Non-AKI group (n=39)	25	14	63.65±6.58	20.75±2.12	92.46±11.83	114.29±12.79	72.75±11.58
AKI group (n=21)	12	9	67.24±6.91	20.96±2.08	91.67±11.59	116.58±13.11	71.84±12.14
<i>x2/F</i>	0.353		2.010	0.410	0.930	1.010	0.460
<i>P</i>	0.838		0.141	0.667	0.397	0.367	0.631

1.2 Inclusion and exclusion criteria

1.2.1 Inclusion and exclusion criteria of AKI group and non-AKI group

Inclusion criteria: (1) Pathological diagnosis meets the diagnostic criteria for sepsis as outlined in the “International Guidelines for the Management of Sepsis and Septic Shock 2021 Edition” [5] with a Sequential Organ Failure Assessment (SOFA) score>2; (2) Age between 18 to 75 years; (3) Expected survival period>6 months; (4) No history of chronic kidney disease, renal failure, or kidney surgery; (5) Informed consent from the patient and their family regarding the specifics of this study; (6) Normal cognitive function, willing to cooperate with communication and examinations.

Exclusion Criteria: (1) Patients with organic lesions or severe functional insufficiency of vital organs such as the liver and kidneys; (2) Patients with coagulation disorders or moderate to severe anemia; (3) Patients with renal vascular diseases or benign and malignant tumors; (4) Patients with severe infectious diseases or infections; (5) Patients with a recent history of glucocorticoid use or long-term immunosuppressive agent use; (6) Patients who have undergone imaging within 48 hours; (7) Patients with missing clinical data.

1.2.2 Inclusion and exclusion criteria for the health group

Inclusion criteria: (1) laboratory examination Scr is normal and urine volume is normal; (2) age is more than

18 years old; (3) all have undergone health examination in our hospital and obtained complete physical examination report; (4) good compliance.

Exclusion criteria: (1) patients with organic lesions of liver, kidney and other important organs; (2) patients with malignant tumors; (3) patients with history of radiotherapy and chemotherapy for tumors; (4) patients with joint trauma or inflammation.

1.3 Methodology

1.3.1 Diagnostic criteria for AKI related to sepsis

Clinical diagnosis in line with the ^[6]AKI diagnostic criteria of the Guidelines for Improving Global Renal Disease Prognosis (Summary) for Chronic Kidney Disease Anemia: (1) serum creatinine (Scr) $\geq 26.5 \text{ umol/L}$ (0.3 mg/dL) within 48h, and continued to rise to 1.5 times baseline, predicting occurrence within 7d; (2) urine volume $< 0.5 \text{ mL/(kg} \cdot \text{h)}$ for 6h or more;

1.3.2 Inspection method

Collect 6ml of mid-morning urine samples from healthy individuals and 6 ml of 24-hour urine samples from patients diagnosed with sepsis within 30 minutes. Centrifuge at 3000 r/min for 10 minutes using the Beckman Coulter 全自动生化分析仪 (Guangzhou Aolong Biotechnology Co., Ltd.; model: Au5800, radius 30 cm). Separate the sediment from the supernatant and store in EP tubes (Shanghai Xiyang Scientific Instruments Co., Ltd.; specification: 2 ml) in a-70°C incubator (Dongguan Kaiside Testing Instrument Co., Ltd.) for later use. Measure urinary sodium, urinary FEK, and urinary UK/UCr levels using the enzyme-

linked immunosorbent assay (ELISA) (Shanghai Debao Biotechnology Co., Ltd.).

1.4 Observation indicators

(1) Urinary sodium, urinary FEK and urinary UK/UCr levels: the levels of urinary sodium, urinary FEK and urinary UK/UCr were statistically compared.

(2) The predictive value of combined detection of urinary sodium, urinary FEK and urinary UK/UCr in early AKI caused by sepsis was analyzed using the subject work characteristic (ROC) curve.

1.5 Statistical processing

The data were analyzed by IBM SPSS 17.0 statistical software, and the count data were expressed as [n], with χ^2 test; the measurement data were expressed as ($\pm s$), with t-test, and $P < 0.05$ was considered to be statistically significant. In the ROC curve, $AUC > 0.6$ indicated predictive value.

2 Results

2.1 Comparison of urinary sodium, urinary FEK and urinary UK/UCr levels in three groups of subjects

The level of FEK and UK/UCr in urine was higher than that in the control group, and the level of sodium in urine was lower than that in the control group ($P < 0.05$); the level of FEK and UK/UCr in urine was higher than that in the non-AKI group, and the level of sodium in urine was lower than that in the non-AKI group ($P < 0.05$), as shown in Table 2.

Table 2. Comparison of urinary sodium, urinary FEK and urinary UK/UCr levels in three groups of subjects ($\pm s$)

group	UNa (mmol)	urine FEK (%)	urine UK/UCr
control group (n=20)	201.31 \pm 20.56	4.58 \pm 1.45	3.29 \pm 1.08
Non-AKI group (n=39)	185.39 \pm 19.32 [*]	6.03 \pm 1.68 [*]	4.41 \pm 1.25 [*]
AKI group (n=21)	162.87 \pm 18.94 ^{**}	9.46 \pm 2.17 ^{**#}	5.37 \pm 1.46 ^{**#}
<i>F</i>	20.200	38.920	13.760
<i>P</i>	< 0.001	< 0.001	< 0.001

Note: Compared with the control group, ^{*} $P < 0.05$; compared with the non-AKI group, ^{**#} $P < 0.05$

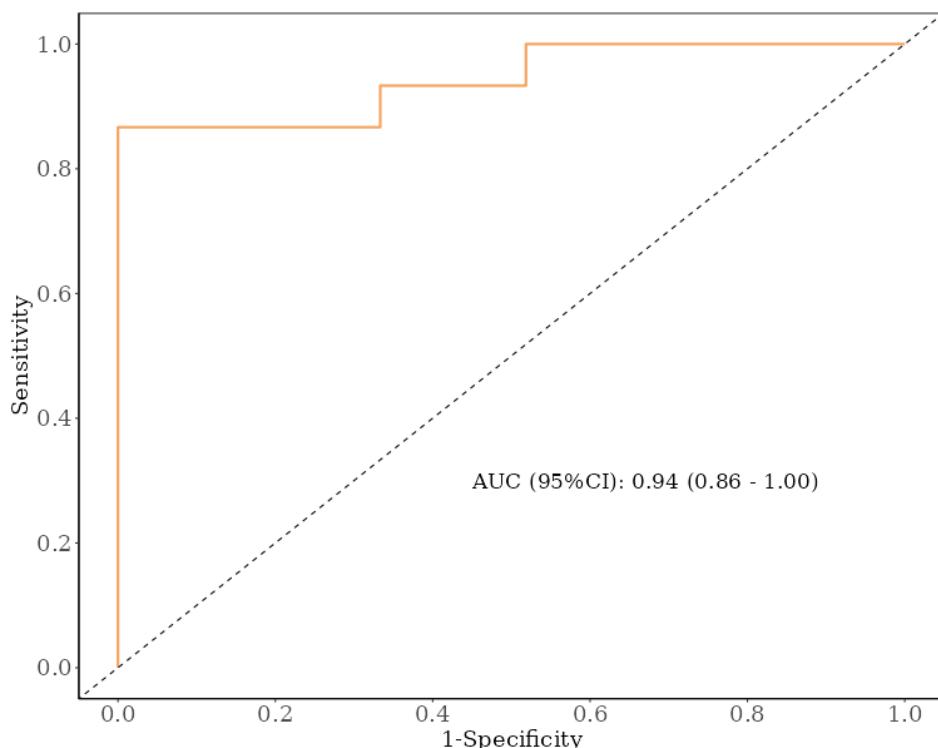
2.2 The predictive value of combined detection of urinary sodium, urinary FEK and urinary UK/UCr in early AKI caused by sepsis

As shown in Table 3 and Figure 1, the area under the curve (AUC) value of urinary sodium was 0.792, with a sensitivity of 0.795 and a specificity of 0.762; the AUC

value of urinary FEK was 0.887, with a sensitivity of 0.714 and a specificity of 0.974; the AUC value of urinary UK/UCr was 0.694, with a sensitivity of 0.476 and a specificity of 0.923; the combined prediction AUC value was 0.940, with a sensitivity of 0.920 and a specificity of 0.830.

Table 3. Predictive value of combined detection of urinary sodium, urinary FEK and urinary UK/UCr in early AKI caused by sepsis

feature	AUC price	sensitivity	specificity	Best threshold
UNa	0.792	0.795	0.762	172.180
urine FEK	0.887	0.714	0.974	8.290
urine UK/UCr	0.694	0.476	0.923	6.150
Joint projections	0.940	0.920	0.830	-

**Figure 1.** Predictive value of combined detection of urinary sodium, urinary FEK and urinary UK/UCr in early AKI caused by sepsis

3 Discussion

In recent years, with the intensification of population aging and the increase in invasive medical procedures, the incidence of sepsis has been on the rise. Globally, millions of new cases of sepsis are reported each year, with over one-quarter of these cases resulting in death^[7]. As a severe clinical complication of sepsis, early diagnosis and effective treatment of SA-AKI have become a hot topic of research both domestically and internationally^[8]. Previous diagnostic criteria based on urine volume and creatinine have had limitations in the early diagnosis and prognosis of AKI. Exploring novel biomarkers for AKI or optimal combinations of biomarkers is crucial for early clinical diagnosis of AKI, formulating targeted treatment plans, controlling disease progression, and improving patient survival outcomes.

Previous studies have found that^[9] and urinary sodium levels are closely related to microalbuminuria, with changes in these levels potentially increasing the risk of early kidney damage. The results of this study show that in the non-AKI group, urinary FEK levels and urinary UK/UCr were higher than those in the control group, while urinary sodium levels were lower ($P<0.05$). In the AKI group, urinary FEK and urinary UK/UCr levels were higher than those in the non-AKI group, but urinary sodium levels were lower ($P<0.05$). There were significant differences in urinary sodium, urinary FEK, and urinary UK/UCr during early SA-AKI detection. Studies by Yu Beilei et al.^[10] showed that as renal function declines in patients with kidney disease, urinary FEK levels tend to rise, possibly due to the body compensating for decreased glomerular filtration rate to maintain electrolyte balance. A clinical study conducted by Kumar N S et al.^[11]

confirmed a significant association between urinary potassium excretion levels and the risk of AKI, making it an effective biomarker for predicting early AKI. In this study, urinary FEK and urinary UK/UCr levels in the AKI group were significantly higher compared to non-AKI sepsis patients and healthy individuals, while urinary sodium levels were relatively lower. Urinary sodium, urinary FEK, and urinary UK/UCr can serve as effective biomarkers for predicting early AKI triggered by sepsis.

By plotting the ROC curve, the AUC values for the combined detection of urinary sodium, urinary FEK, and urinary UK/UCr were 0.792, 0.887, 0.694, and 0.940, respectively, indicating good specificity and sensitivity. This combination has significant value and guiding significance in predicting early AKI caused by sepsis. The excretion of urinary sodium and UK is closely related to renal filtration and reabsorption functions. As the primary pathway for UK excretion, its level is influenced by potassium balance within the body and renal function status. UK/UCr is an important indicator for assessing the kidney's concentrating and diluting capacity and the regulation of tubular acid-base balance, with changes in these indicators effectively reflecting the kidney's filtration function and electrolyte equilibrium state^[12]. Scholars such as Zhang Yawu et al.^[13] also believe that a decrease in glomerular filtration rate may be a significant factor leading to changes in urinary UK/UCr levels in SA-AKI patients, effectively reflecting the patient's ability to handle sodium and potassium and the overall renal function status. This study further compared the predictive value of urinary sodium, urinary FEK, and urinary UK/UCr in SA-AKI, showing that the combined detection had significantly higher predictive value than any single test.

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