

The Diagnostic Value of Spot Urine Sodium-to-Potassium (UNa/K) Ratio Compared to 24-hour Urine Sodium (24-hr UNa) for the Management of Cirrhotic Patients with Ascites

Pusadee Rojpalakorn, M.D.
Panida Thong-U-thaisri, M.D.
Chutima Pramoolsinsap, M.D.

ABSTRACT

Background: Management of cirrhotic patients with ascites is based on improving excretion of sodium (24-hr UNa excretion >78 mmol/d) with diuretics and dietary Na restriction. The spot UNa/K ratio may replace the cumbersome 24-hr urine collection but only few data have been confirmed.

Objective: To compare the diagnostic value of spot UNa/K ratio ≥ 1 with 24-hr UNa ≥ 78 mmol/day in cirrhotic patients with ascites.

Patients and Methods: Seventy-three cirrhotic outpatients with ascites were recruited in the study. Cirrhotic patients were classified as Child A 8.3%, Child B 61.7% and Child C 30.0%. 24-hr UNa, urine creatinine and spot UNa/K ratio were measured and analyzed.

Results: Sixty urine specimens were (82%) collected and completely analyzed. Mean of 24-hr UNa was 146.7 ± 92.7 mmol (range 22-404 mmol). Forty-five (75%) of 24-hr urine specimens contained ≥ 78 mmol of Na/d. Fifty one (85%) of specimens had UNa/K ratio ≥ 1 . When compared with 24-hr UNa ≥ 78 mmol, sensitivity, specificity, PPV, NPV of spot UNa/K ratio ≥ 1 was 82%, 6%, 72% and 11%, respectively. From the ROC curve, the best cut off point was UNa/K ratio = 3. We found that the sensitivity was 44% and specificity was 73%.

Conclusions : The spot UNa/K ratio ≥ 1 has a good sensitivity but very low specificity to predict adequate 24-hr UNa excretion. Even at the best cut off point at 3, it still had low sensitivity and specificity. Therefore, 24-hr UNa collection remains the gold standard for the management of cirrhotic patients with ascites.

Key words : Spot urine Sodium-to-Potassium, Cirrhotic, Ascites

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BACKGROUND

Ascites is one of the most three common complications of cirrhosis; other complications are hepatic encephalopathy and variceal hemorrhage.⁽¹⁾ Approximately 50% of compensated cirrhosis patients develop ascites during 10 years of observation. And 50% of these patients succumb in 2 years.⁽¹⁾

The main treatment of cirrhotic ascites include dietary sodium restriction (2 gm per day or 88 mmol per day)⁽²⁾. Only 10-15% of patients can control ascites by dietary sodium restriction alone⁽³⁾. While, others require additional oral diuretics.⁽³⁾ When weight loss is less than desired, measurement of 24 hours urinary sodium excretion is a helpful parameter.⁽²⁾ The goal of treatment is to increase urinary excretion of

sodium to be more than 78 mmol per day (88 mmol intake per day - 10 mmol nonurinary excretion per day). Patients who are excreting sodium more than 78 mmol per day with unchanged or increasing weight are presumed to have sodium intake more than 88 mmol per day. These patients should be counsulted for dietary sodium restriction.

Patients who do not lose weight and excrete less than 78 mmol per day should receive a higher dose of diuretics.⁽³⁾ If the patient is not respond to a high dose of diuretic treatment (400 mg per day of spironolactone and 160 mg per day of furosemide). These patients are defined as diuretic-resistance and should proceed to second-line therapy such as serial therapeutic paracentesis, TIPS, peritoneovenous shunt, or liver transplantation.⁽⁴⁻⁶⁾

Generally, 24-hr urinary sodium excretion required a full-day collection, there by it is cumbersome and incomplete collection can not be used for interpretation.

The use of Na/K ratios obtained from random urine specimens has proposed as an alternative to 24-hr collection, but only few data have been published.^(7,8)

The aim of this study was to compare the diagnostic value of spot UNa/K ratio ≥ 1 with 24-hr UNa ≥ 78 mmol in cirrhotic patients with ascites.

PATIENTS AND METHODS

Patients

Uncomplicated cirrhotic patients from any cause with ascites in outpatient clinic at Ramathibodi hospital were enrolled between Febuary and October 2005. Patients were 18-80 years of age and received diuretic

(spironolactone and/or furosemide). The diagnosis of cirrhosis was either biopsy proven or clinically and laboratories suspected. Exclusion criteria included patients with serum creatinine greater than 1.5 mg/dl, patient taking NSAIDS, ACEI or KCl, and patient with fever or diarrhea on the day that the urine specimen was collected.

Methods

All Cirrhotic patients with ascites underwent history taking and physical examination and then were checked for baseline laboratories including CBC, coagulogram, LFT, BUN, Cr, electrolytes, urine analysis and upper abdominal ultrasonography.

Twenty-four hour urine specimen collection had been begun in the morning until completed collection and then spot urine specimen was collected from the next void. The urine specimens were sent to laboratory for 24-hr UNa, 24-hr UCr, spot UNa, spot UK. Specimens were considered complete if 24-hr UCr was ≥ 10 mg/kg/day in female or ≥ 15 mg/kg/day in male.⁽⁹⁾ (Figure 1)

Statistical analysis

Statistical analysis was performed using the SPSS package statistical programs (version 13 ; SPSS Inc., Chicago, IL, USA) and stata. Results were expressed as mean \pm SD, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). Chi-square or Fishers test were used to compare discrete variable, wherever applicable. The level of significant was set at $p = 0.05$. A receiver operating characteristic (ROC) curve was made using the spot UNa/K ratios as the variable to find out an appropriate

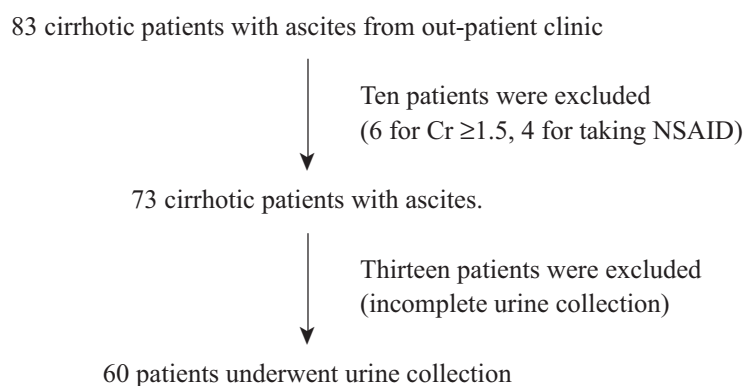


Figure 1 Chart flow of cirrhotic patients who enrolled in the study.

cut off point that had 24-hr UNa ≥ 78 mmol/day. Sensitivity and specificity of the cut off value were calculated.

RESULTS

Eighty-two percents of 73 specimens were completed. Baseline clinical and biochemical characteristics were summarized in the Table 1. The majority of patients in this study were; cirrhotic with child B (61.7%) and cirrhotic with child C (30%). Alcoholic cirrhosis was the most common population (30%). Fifty-five percents were taking spironolactone alone, 43% spironolactone combined with furosemide and only 3% furosemide alone. The median dosage of spironolactone and furosemide were 85.3 ± 64.4 mg/day, and 40 ± 23.1 mg/day respectively.

Table 2 showed the results of 24-hr and spot urine collection.

Table 3 showed the diagnostic value of spot UNa/K ratio ≥ 1 with 24-hr UNa ≥ 78 mmol/day. Forty-five

Table 1 Baseline characteristic of the patients

	Number
Sex	
Male	25 (41.7%)
Female	35 (58.3%)
Age, Mean \pm SD (range)	59.2 ± 11.8 (32.87)
Child Turcot Pugh grade	
A	5 (8.3%)
B	37 (61.7%)
C	18 (30.0%)
Cause of cirrhosis	
Alcohol	18 (30.0%)
HBV	15 (25.0%)
HCV	13 (21.7%)
Cryptogenic	8 (13.3%)
HBV/HCV	2 (3.3%)
AIH	2 (3.3%)
HBV/alcohol	1 (1.7%)
Wilson	1 (1.7%)
Diuretics	
Spironolactone	32 (53.3%)
Furosemide	2 (3.3%)
Combination	26 (43.3%)
Dose of diuretics (mg), Mean \pm SD (range)	
Spironolactone	85.3 ± 64.4 (25-300)
Furosemide	40.0 ± 23.1 (20-120)

Table 2 The results of 24-hr and spot urine collection.

Variables	Mean \pm SD (range)
24 hr. urine volume (ml)	$1,827 \pm 869$ (600 - 3,990)
24 hr. UNa (mmol)	146.7 ± 92.7 (22-404)
24 hr UNa	
>78 mmol/day	45 (75%)
<78 mmol/day	15 (25%)
Spot UNa/K ratios	2.9 ± 2.0 (0.4-9.1)
Spot UNa/K ratio	
≥ 1	51 (85%)
< 1	< 19 (15%)

Table 3 Diagnostic value of spot UNa/K ratio with 24-hr UNa collection

		24 hr Urine (mmol/day)		
		>78	<78	total
Spot urine Na/K	>1	37	14	51
	<1	8	1	9
	Total	45	15	60

Sensitivity	82%
Specificity	6%
PPV	72%
NPV	11%

Table 4 Spot UNa/K ratios

Cut point	Sensitivity (%)	Specificity (%)	ROC area
0.5	97.78	0.00	0.4889
1.0	82.22	13.33	0.4778
1.5	66.67	40.00	0.5333
2.0	60.00	46.67	0.5333
2.5	55.56	46.67	0.5111
3.0	44.44	73.33	0.5889
3.5	40.00	73.33	0.5667
4.0	31.11	73.33	0.5222
4.5	20.00	80.00	0.5000
5.0	20.00	80.00	0.5000
5.5	11.11	80.00	0.4556
6.0	8.89	80.00	0.4444
6.5	4.44	93.33	0.4889
7.0	2.22	93.33	0.4778
7.5	2.22	100.00	0.5111
8.0	2.22	100.00	0.5111
8.5	2.22	100.00	0.5111
9.0	2.22	100.00	0.5111

patients had 24-hr UNa ≥ 78 mmol/day. In this group, 37 had spot UNa/K ratio ≥ 1 and 8 had spot UNa/K ratio < 1 . Fifteen patients had 24-hr UNa < 78 mmol/day, 14 had spot UNa/K ratio ≥ 1 and 1 had spot UNa/K ratio < 1 . Therefore sensitivity of spot UNa/K ratio ≥ 1 in predicting 24-hr UNa ≥ 78 mmol/day was 82% (specificity 6%, PPV 72%, NPV 11%).

An ROC curve was showed in table 4 and figure 2. The spot UNa/K ratio of each patient as the independent variable and 24-hr UNa ≥ 78 mmol/day as the dependent variable was made. The area under the ROC curve was 0.59. A spot UNa/K ratio ≥ 3 was found to be 44.4% sensitive and 73.3% specific for a prediction of 24-hr UNa ≥ 78 mmol/day.

Table 4 showed effect of diuretic and result of urine Na and K excretion. 24-hr UNa excretion did not depend on type of diuretic (spironolactone alone or a combination of spironolactone and furosemide).

DISCUSSION

According to the AASLD guideline in Hepatology

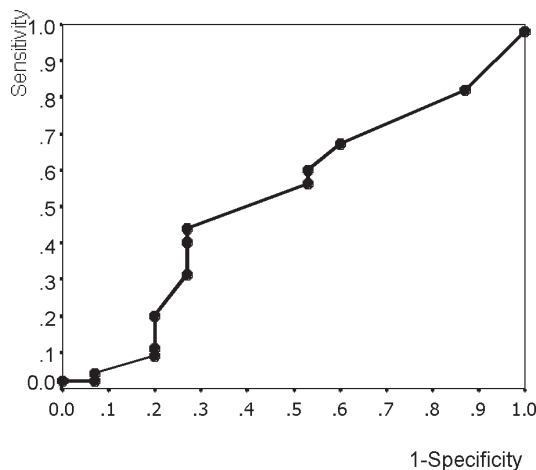


Figure 2 ROC curve

Table 5

	24 hr urine ≤ 78	24 hr urine < 78	Total
UNa / K > 1	22	9	31
UNa / K < 1	1	0	1
	23	9	32

Sensitivity	95.65%	
Specificity	0%	P = 1.000
PPV	70.95%	
NPV	0%	

2004⁽³⁾, recommend that urine sodium / potassium ratio may replace the 24-hr urine collection. But only few data have been published on the efficacy of spot UNa/K ratio^(7,8). The majority of our patients (82%) collected complete 24-hr urine specimen. Seventy-five present had 24-hr UNa ≥ 78 mmol/day. If weight loss was less than desired, it reflected that they consumed more than 2 gm of sodium per day. The dosage of diuretic in the present study was slightly low 85.3 ± 64.4 mg/day for spironolactone and 40 ± 23.1 mg/day for furosemide.

Sensitivity of spot UNa/K ratio ≥ 1 was good (82%) but it had very low specificity (6%) to predict 24-hr UNa ≥ 78 mmol/day and NPV was also very low (11%). By using ROC curve, the best cut off point was at spot UNa/K ratio = 3, it also had low sensitivity (44%) and low specificity (73%).

Although type of diuretic can interfere the result of spot UNa/K ratio, in our study it had no effect on the result of 24-hr UNa. Both spironolactone and furosemide induced urinary sodium excretion but it had difference effect on urine potassium. Spironolactone is a potassium sparing diuretic and, it reabsorbed potassium from renal tubule and excreted small amount of potassium in the urine. While furosemide was a loop diuretics, it excreted potassium in the urine. This effect explains why diuretics can interfere the Na/K ratio. From the result of the present study, patient who was taking spironolactone alone had spot UNa/K ratio ≥ 1 more than patient who was taking a combination of diuretics.

From our study, we concluded that spot UNa/K ratio ≥ 1 had a good sensitivity but had a low specificity to predict 24-hr UNa ≥ 78 mmol/day. Twenty-four hr UNa collection remains the gold standard for the management of cirrhotic patients.

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