Research letter

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Fractional excretion of sodium or urea as prognostic indicators for acute kidney injury in the emergency department

Gregor Lindner[a], Adrian Wolfensberger[a], Aristomenis K. Exadaktylos[b], Christoph Schwarz[c], Georg-Christian Funk[d] and Svenja Ravioli[a], [a]Department of Internal and Emergency Medicine, Buergerspital Solothurn, Solothurn, [b]Department of Emergency Medicine, Inselspital, University Hospital Bern, Bern, Switzerland, [c]Department of Nephrology, Pyhrn-Eisenwurzenklinikum, Steyr and [d]Karl-Landsteiner-Institute for Lung Research and Pulmonary Oncology, Klinik Ottakring, Vienna, Austria

Correspondence to Gregor Lindner, EBCEM, FSSERM, Director Dept. of Internal and Emergency Medicine, Bürgerspital Solothurn, Schöngrünstrasse 42, 4500 Solothurn, Switzerland
Tel: +41 (0) 32 627 3805; e-mail: lindner.gregor@gmail.com

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In a recent study in emergency department (ED) patients, prevalence of acute kidney injury (AKI) was described to be 8% [1]. Calculation of fractional excretion of solutes has been suggested in the past to discriminate the etiology of AKI as well as whether it is permanent or transient [2]. Potentially, it could be of significant importance to the emergency physician to obtain prognostic information on the course of AKI in order to decide whether treatment on in- or outpatient basis is required.

The aim of this study was to identify the prognostic value of fractional excretion rates of either sodium or urea for a course of AKI during the first 7 days of hospitalization after initial emergency consultation.

In this retrospective analysis, all patients admitted to the ED between 1 January 2017 and 31 December 2018 with AKI, defined by the Kidney Disease Improving Global Outcomes (KDIGO) Clinical Practice Guideline AKI, with available urine and serum parameters to calculate FeNa and or FeUrea were included [3] Patients with AKI were classified according to the AKIN classification [4].

FeNa and FeUrea were calculated on admission or latest on day 1 after admission:

$$FE_{Na} = \frac{Na_{Urine} \text{ x } Creatinine_{Plasma}}{Na_{Plasma} \text{ x } Creatinine_{Urine}}$$

$$FE_{Urea} = \frac{Urea_{Urine} \text{ x } Creatinine_{Plasma}}{Urea_{Plasma} \text{ x } Creatinine_{Urine}}$$

The course of renal function was evaluated calculating the percent-decline of serum creatinine until day 7 compared to on-admission serum creatinine. Renal function recovery was defined as reaching at least one serum creatinine level within baseline serum creatinine ±25% during the first 7 days after emergency consultation.

Mann–Whitney *U* test, χ^2 test or Fisher's exact test as well as logistic regression were used to analyze data and explore the association of categories of urine parameters and their derivatives with course of renal function (recovery of renal function yes/no). Linear regression was used to explore the association of urine parameters and their derivatives with maximum serum creatinine. Receiver operator characteristic (ROC) curves were constructed to quantify the predictive abilities of urine parameters in relation to the course of kidney function. A two-sided *P* value <0.05 was considered statistically significant.

The study was approved by the local ethics committee (www.eknz.ch; Project-.ID 2020-02097).

A total of 111 patients fulfilled the criteria for AKI and had measurements of serum and urine parameters. Mean age was 78 years (±14) and 69% were women. Median length of stay was 7 days (interquartile range (IQR): 5–12). Fifty-six patients (51%) had loop diuretics on admission to the ED while 39 (35%) had thiazide diuretics. Twenty-seven patients (24%) had known CKD among them 7 (6.3%) with CKD KDIGO stage 2, 16 (14.4%) with stage 3 and 4 (3.6%) with stage 4. Mean baseline creatinine level of all patients was 99 µmol/L (±36). 41 patients (36.9%) had AKIN stage 1 on admission, 37 (33.3%) AKIN stage 2 and 33 (29.7%) AKIN stage 3.

FeNa was calculated for 79 patients (71%) and FeUrea for 109 (98%). Median decline in serum creatinine until day 7 compared to on-admission creatinine was -28% (IQR: –50 to –12). 51 patients (46%) were considered reaching renal function recovery until day 7, defined as a serum creatinine level within baseline serum creatinine ±25%. Patients who experienced renal function recovery until day 7 were younger with an age of 79 years (IQR: 68–85) compared to 85 (IQR: 78–88), *P* = 0.01. Significantly more patients in the nonrecovery group died during hospitalization (9.0 versus 1.8%, *P* = 0.036). Maximum decline in serum creatinine was significantly higher in patients with renal function recovery (–46% (IQR: –59 to –31%) versus –15% (IQR: –28 to –7%), *P* = 0.0001). Moreover, urine creatinine, urine urea as well as urine potassium were significantly higher in patients with renal function recovery (Table 1).

Table 1 Characteristics of patients stratified for recovery of renal function until day 7

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		Median	Quartile 1	Quartile 3	Percent	Median	Quartile 1	Quartile 3	Percent	*P* value
Age		85	78	88		79	68	85		0.01
Sex (men)	0				35.1%				33.3%	0.42
	1				18.9%				12.6%	
Length of stay		7.3	4.9	12.7		7.9	5.0	11.6		0.99
Death	0				45.0%				44.1%	0.036
	1				9.0%				1.8%	
ACE-I	0				43.2%				37.8%	0.81
	1				10.8%				8.1%	
ARB	0				36.9%				27.0%	0.33
	1				17.1%				18.9%	
RI	0				53.2%				45.9%	0.99
	1				0.9%				0.0%	
KSDI	0				41.4%				36.0%	0.99
	1				12.6%				9.9%	
LODI	0				27.0%				22.5%	0.99
	1				27.0%				23.4%	
TIDI	0				36.0%				28.8%	0.69
	1				18.0%				17.1%	
Beta-blockers	0				27.9%				19.8%	0.45
	1				26.1%				26.1%	
NSAID	0				47.7%				37.8%	0.42
	1				6.3%				8.1%	
CKD	0				43.2%				32.4%	0.27
	1				10.8%				13.5%	
CKD stage	0				43.2%				32.4%	0.29
	2				1.8%				4.5%	
	3				8.1%				6.3%	
	4				0.9%				2.7%	
AKIN Stage	1				19.8%				17.1%	0.58
	2				16.2%				17.1%	
	3				18.0%				11.7%	
FeNa		1.71	1.13	3.55		1.11	0.50	2.29		0.098
FeUrea		37.24	25.76	45.73		32.25	22.31	42.96		0.204
Max. creatinine decline		−15%	−28%	−7%		−46%	−59%	−31%		0.0001
$Creatinine_{Serum}$		197	140	268		180	132	270		0.39
eGFR		24	17	34		27	17	34		0.33
$Urea_{Serum}$		15.7	10.9	19.2		16.3	11.5	20.6		0.61
K_{Serum}		4.40	3.90	4.65		4.20	3.40	4.80		0.26
Na_{Serum}		137	134	139		136	131	140		0.8
$Creatinine_{Urine}$		6142	3851	7994		7282	5647	11 310		0.009
$Urea_{Urine}$		157	92	217		222	151	276		0.0001
Na_{Urine}		66	37	103		62	38	83		0.48
K_{Urine}		21	12	25		38	31	60		0.0001

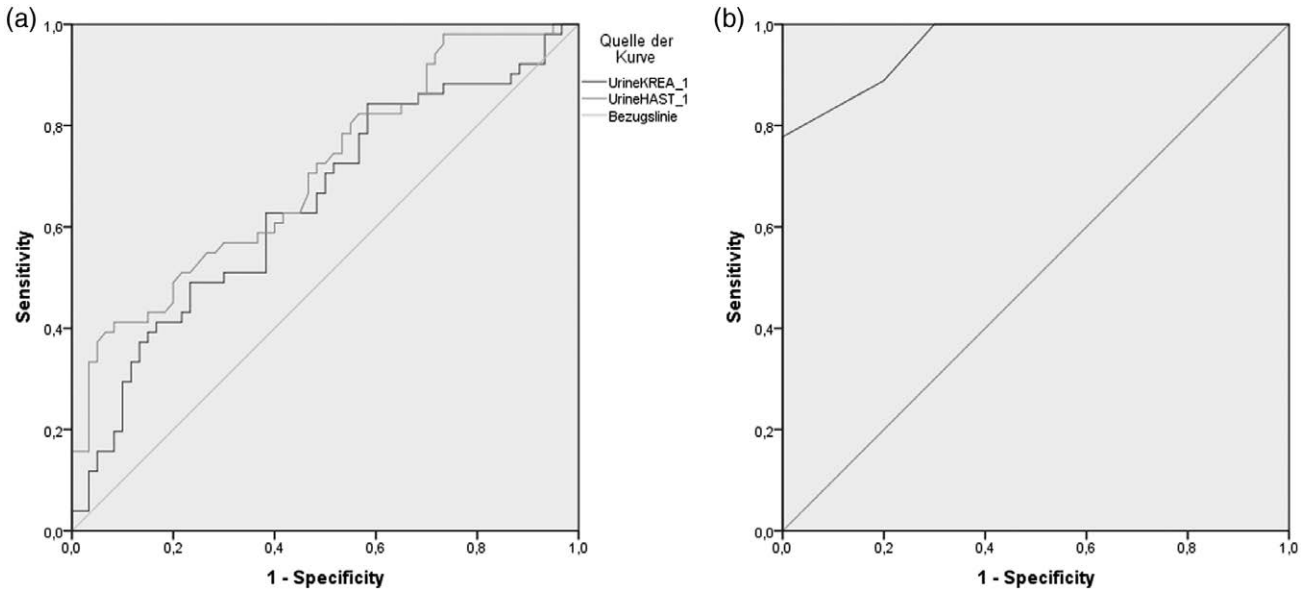
ACE-I, ACE-inhibitors; AKIN, acute kidney injury network; ARB, angiotensin-receptor blockers; CKD, chronic kidney disease; KSDI, potassium-sparing diuretics; LODI loop diuretics; NSAID, nonsteroidal anti-inflammatory drugs; RI, renin inhibitors; TIDI, thiazide diuretics.

While FeNa as a continuous variable was not predictive for renal function recovery (regression coefficient −0.17; standard error 0.127; $P = 0.181$), an FeNa <1% as a binary variable was predictive for renal function recovery in the chi-square test (FeNa <1% in 17 of 47 patients in the nonrecovery versus 15 of 24 in the recovery group; $P = 0.045$) as well as in the binary logistic regression analysis corrected for use of loop diuretics (regression coefficient 1.097; standard error 0.520; $P = 0.036$). FeNa <0.5%, other cut-offs for FeNa as well as a FeNa corrected for eGFR of patients did not result in a predictive value for renal function recovery.

FeUrea with a cut-off of 35% was not predictive for renal function recovery neither in the chi-square test (FeUrea <35% in 22 of 55 in the nonrecovery versus 28 of 53 in the recovery group; $P = 0.25$) nor in the binary logistic regression analysis (regression coefficient −0.015; standard error 0.014; $P = 0.289$). In the area under the receiver operating characteristic, urine creatinine (AUC 0.645; standard error 0.053; $P = 0.009$) and urine urea (AUC 0.705; standard error 0.049; $P < 0.0001$) were predictive of renal function recovery until day 7. Urine creatinine inversely correlated with the maximum decline in creatinine until day 7 (regression coefficient −15.9; standard error 4.6; $P = 0.001$). Urine urea also correlated inversely with the maximum decline of serum creatinine compared to creatinine on admission (regression coefficient −10.3; standard error 3.86; $P = 0.009$). Urine potassium concentration proved to be predictive of renal function recovery (AUC 0.961; standard error 0.039; $P = 0.001$). Figure 1 gives the ROC curves for urine creatinine, urine urea as well as urine potassium.

The present study is limited by its retrospective design as well as the low sample size with available urine potassium values. Moreover, it should be of note, that the definition of renal function recovery used in the present study is not uniformly accepted. Also, the risk of confounder bias (e.g. diuretic medication, comorbidities) has to be kept in mind.

Fig. 1



ROC curves for urine creatinine (UrineKREA) and urine urea (UrineHAST) on the left as well as for urine potassium on the right side.

In conclusion, the preliminary findings of this study suggest that FeNa <1% but not FeUrea in any form may predict renal function recovery until day 7 in patients with AKI diagnosed in the ED. Interestingly, urine creatinine, as well as urea, predicted renal function recovery more precisely. Also, higher urine potassium was associated with renal function recovery. These new findings should be evaluated in more detail in future studies.

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Conflicts of interest

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