AKTET
Journal of Institute Alb-Shkenca
Reviste Shkencore e Institutit Alb-Shkenca

ISSN 2073-2244
www.alb-shkenca.org

EVALUATION OF SERUM UREA-TO-CREATININE RATIO IN ACUTE KIDNEY INJURY PATIENTS
VLERËSIMI I RAPORTIT UREMI-KREATININEMI NË PACIENTËT ME DËMTIM RENAL AKUT

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AKTET V, 1: 48 - 52, 2013

PËRMBLEDHJE
Një tregues biokimik për diferencimin e azotemisë prerenale (APR) dhe nekrozës tubulare akute (NTA) është raporti uremi-kreatininemi (RUKR)>20. Qëllimi është të vlerësojmë RUKR në lidhje me të dhënat klinike dhe prognozën. **Metoda:** Pacientët u ndanë në dy grupe: RUKR I ulët (nëse RUKR ≤20), RUKR I lartë (nëse RUKR >20). **Rezultatet:** 53 (57%) pacientë plotësuan kriteret RIFLE për DRA. Midis këtyre pacientëve, 4 (7.5%) kishin RUKR<20 dhe 49 (92.5%) kishin RUKR >20. Karakteristikat për grupin me RUKR të ulët kundrejt RUKR të lartë janë: median [IKR] kreatininemi në dalje nga spitali ose vdekje: 6,1 [2,4-7,4] vs 1,7 [1,1-2,6], P=0.04; mosrekuperim i funksionit renal sipas RIFLE: 4 (100%) vs 36 (73.5%), P=0.219; mortaliteti: 3 (75%) vs 34 (69.3%), P=0.772. **Konkluzione:** Më shumë se gjysma e pacientëve me RUKR të lartë kishin mosrekuperim të funksionit renal sipas RIFLE duke e bërë këtë parametër biokimik të papërshtatshëm për diferencimin e azotemisë prerenale.
Fjalë çelës. uremia, kreatininemia; azotemia prerenale.

SUMMARY
A biochemical parameter for differentiation of prerenal azotemia (PRA) and acute tubular necrosis (ATN) is a serum urea-to-creatinine ratio (BCR) >20. Aim was to evaluate BCR in correlation with clinical data and outcome. **Methods**: 93 adults (≥14 years) admitted in an ICU, during 2007 were reviewed retrospectively. Patients were divided: low BCR (BCR≤20), high BCR (BCR>20). **Results**: 53 (57%) patients reached RIFLE criteria for AKI. Among these patients, 4 (7.5%) had a BCR<20 and 49 (92.5%) had a BCR >20. For the two groups low BCR versus high BCR: median [IQR] sCr at hospital discharge or death was: 6,1 [2,4-7,4] versus 1,7 [1,1-2,6], P=0.04; non recovery of renal function according to RIFLE: 4 (100%) versus 36 (73.5%); mortality: 3 (75%) versus 34 (69.3%). **Conclusions**: More than half of patients with high BCR had non recovery of renal function, which makes this biochemical parameter not appropriate for differentiation of PRA.
Keywords: serum urea, creatinine; prerenal azotemia

INTRODUCTION

Applying RIFLE and AKIN criteria many studies showed a high occurrence of acute kidney injury (AKI) among hospitalized patients [15] and especially among critically ill patients [1, 8, 9]. They found also strong correlation between severity of AKI and worse outcome [1. 8, 9, 15]. Almost 50 % of AKI patients in intensive care unit (ICU) have prerenal azotemia [7], resulting from a reduction in glomerular filtration rate (GFR) in response to renal hypoperfusion that exceeds the autoregulatory capacity of the kidney [5]. In pre-renal azotemia, the structural integrity of the kidney is assumed to be unchanged and

resolution of the azotemia happened rapidly following restoration of normal renal perfusion. Urea is the principle finale product of protein catabolism and creatinine is an important intermediate metabolite. Urea and creatinine both undergo glomerular filtration.

Unlike creatinine, however, urea undergoes tubular reabsorption, depending on renal perfusion and urinary flux. From 40 to 80 % of filtered urea can be reabsorbed mostly on proximal tubule. A high BUN:creatinine ratio (BCR) in patients with pre-renal azotemia is one of the common laboratory tests used to distinguish it from ATN [13].

Usually pre-renal azotemia has a better outcome than ATN [12]. Even though some studies have found that even small changes of creatinine are independently associated with mortality [4, 11]. A low creatinine concentration associated with high tubular reabsorption of urea may give a high BCR but not necessarily better outcome.

In this study, we aimed to observe the association of a high BCR with outcome in critically ill patients.

MATERIALS AND METHODS

This is a retrospective observational study of 93 adult patients (≥14 years) admitted in a medical surgical ICU at University Hospital Centre "Nënë Tereza" in Tirana, during 2007. Patients were excluded if they were younger than 14 years old, if they were on chronic dialysis or had a kidney transplant or if their length of hospital stay was shorter than 24 h. If a patient had more than one admission during the study period, each admission was included as a new case in the study. The study was approved by the Research Ethics Committee. Serum creatinine and BUN values for all included patients during their hospital stay were obtained from the medical notes. AKI was classified according to maximum Risk, Injury, Failure, Loss and End-stage kidney disease (RIFLE) criteria [3]. For patients with no data on the baseline creatinine before admission, was estimated using the MDRD equation [14], as recommended by the ADQI workgroup (assuming an average GFR of 75 mL/min in this age group) [3]. The peak creatinine was defined as the highest creatinine during their hospital admission.

Patients were divided into three groups: 'low BCR' if BCR when AKI developed was ≤20, 'high BCR' if BCR when AKI developed was >20 and 'no AKI' if patients did not reach any of the RIFLE criteria for AKI during hospitalization.

Demographic information, age, gender, complications while in hospital, SOFA score, use of mechanical ventilation and vasopressors were recorded prospectively. Use of renal replacement therapy (RRT), length of stay and hospital mortality, the following comorbid conditions were recorded and entered: chronic kidney disease (CKD), hypertension (HTN), congestive heart failure (CHF), diabetes mellitus (DM). Complete recovery of renal function was defined as a serum creatinine<1.5 x basal level at discharge.

Demographic data are presented as medians (25th –75th quartiles) or percentages. The demographics were compared between 'low BCR' and 'high BCR' with the chi square or Fisher's exact test for nominal values and Mann–Whitney test for numerical variables. A statistical package was used (SPSS Statistics 15). A P-value of <0.05 was considered statistically significant.

RESULTS

Among 93 patients included in the study, 53 (57 %) had AKI according to RIFLE. Among these patients, 4 (7.5%) had a BCR of ≤20 when AKI was diagnosed ('low BCR') and 49 (92.5%) were classified as 'high BCR'.

Table 1 shows the demographics of patients compared between the two groups. There was no difference for those patients according to age, gender, SOFA score, prevalence of diabetes mellitus, HTN, CKD and CHF. Compared with 'low BCR' group, patients in the 'high BCR' had a lower average sCr max. (6.5±4.1 vs. 2.6±1.8; P < 0.0001).

Table 2 shows characteristics of patients according to RIFLE class. Serum urea and serum creatinine grows with severity of AKI, but there is no correlation between BCR and the severity of

AKI. The average BCR for each class was: Risk 41,82±15,67, Injury 52,13 ±14,95, Failure 32,65±10,82. Complete recovery correlate inversely with the severity of AKI.

Table 1. Demographics of patients

Characteristic	BCR≤20 (N=4)	BCR>20 (N=49)	P-value
Age (year)	70,0± 15,9	67,1± 13,2	0,678
Male(%)	4 (7.4)	30 (55.6)	0.111
SOFA score	8.0±1.8	9.3±3.8	0.507
Vasopressors(%)	2 (3.7)	19 (35.2)	0.636
Mechanical ventilation (%)	3 (56.6)	30 (5.7)	0.585
Serum urea	123.6± 70.9	115.2± 59.1	0.790
SCr	6.5±4.1	2.6±1.8	0.001
SUCR	42.1± 14.7	18.2± 3.2	0.002
DM(%)	1 (1.9)	9 (16.7)	0.675
HTN(%)	2 (3.7)	9 (16.7)	0.675
CKD(%)	0	2 (3.7)	0.675
CHF(%)	0	1 (1.9)	0.675

Table 3 shows renal and hospital outcomes. Patients in the 'high BCR' group had lower sCr at discharge [1,7 (1,1-2.6) vs. 6,1 (2,4-7,4); p= 0,038] but complete recovery during their hospital stay was low, just 14 (28.5%) patients. Hospital mortality was no significantly different between the groups [34 (69.3%) versus 3 (75%); p= P=0.772]. Both groups had no difference on duration of AKI (7.9±7.1 vs. 6.0±4.8).

Figure 2 shows the negative correlation between BCR and sCr at hospital discharge found in this group of AKI patients.

Table 2. Characteristics of patients according to RIFLE class

Characteristic	Risk	Injury	Failure
Nr. patients	11	15	27
Serum urea	76.8±29.6	111.0±66.7	139.6±57.3
SCr	1.4±0.1	1.9±0.4	4.3±2.7
BCR	41,8±15,6	52,1±14,9	32,6±10,8
Complete recovery	7 (63.6%)	5 (33%)	2 (7.4%)
BCR≤20 (%)	1 (9.15)	0	3 (11.5)
BCR>20 (%)	10 (90.9)	15 (100)	24 (88.5)

DISCUSSION

AKI in hospitalized patients is usually caused by hypoperfusion (prerenal azotemia) or acute tubular necrosis (ATN). Simple clinical indices may help distinguish prerenal azotemia from ATN. The blood urea nitrogen (BUN)/creatinine ratio (BCR) is one of the common laboratory tests used to distinguish PRA and ATN. A BCR ≤20 has been used as indices of ATN. Patients with pre-renal azotemia tend to have a high BCR. Urinary flux influence tubular urea reabsorption, but also other factors may increase BUN, particularly in critically ill patients. Critically ill patients are prone to accelerated protein catabolism, which will increase urea generation rate.

Table 3. Renal and hospital outcomes

Characteristic	BCR≤20 (N=4)	BCR>20 (N=49)	P-value
sCr at recovery or death	6,1 (2,4-7,4)	1,7 (1,1-2.6)	0,038
Complete recovery (%)	0	14(28.5)	0,219
Mortality (%)	3(75)	34(69.3)	0.772

Length of stay	6.0±4.8	7.9±7.1	0.592

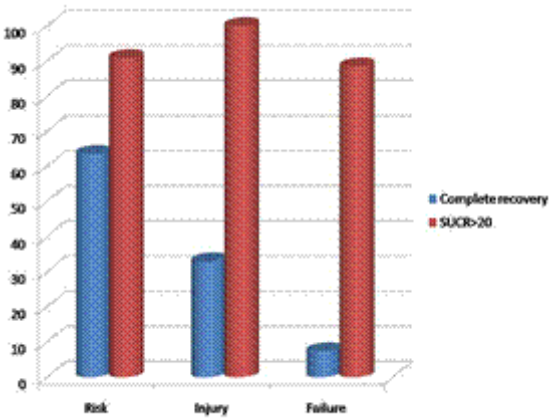

Figure 1. BCR and complete recovery according to RIFLE.

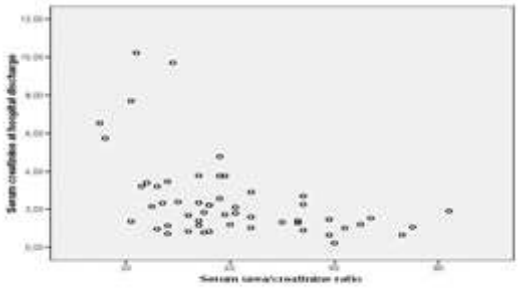

Figure 2. Correlation between BCR and sCr at hospital discharge.

In our study of critically ill patients we found that the best part of AKI patients had a high BCR 92.5%. An interesting founding was that peak serum creatinine was lower in high BCR group. The causes for that in critically ill patients may be related to the low muscle mass, or low concentration as result of overhidration.

In this study we had a look of correlation between the BCR and complete recovery. Pre-renal failure, also called prerenal azotemia, is described as a reversible increase in serum creatinine and urea concentrations resulting from decreased renal perfusion, which leads to a reduction in the glomerular filtration rate (GFR) [10]. We found a negative correlation between high BCR and low sCr at discharge, but only 28.5% patients of "high BCR" group had complete recovery, showing that this index is not appropriate for diagnosis of PRA in critically ill patients. Mortality was another clinical outcome observed between the two groups. ATN carries a worse prognosis than PRA [12], but we didn't found significant difference on mortality between high and low BCR group patients. An explanation for that may be related of other than renal factors, associated with increased mortality.

A recent study [16], performed on a large database of patients admitted to hospital found that patients with a high BCR had a higher morality rate than those with low BCR and the results of the multivariable logistic regression analysis for hospital mortality showed the odds ratio (OR) for mortality among 'high-BCR' patients (5.732) was higher than for 'low-BCR' patients (3.321). Recent studies [2, 6] suggest that BUN is modulated by a number of mechanisms and is a marker of illness severity. In our study (table 4) multivariable logistic regression analysis for hospital mortality showed advanced age and SOFA score as significant factors associated with worse outcome.

Table 4. Multivariable logistic regression analysis for hospital mortality

Characteristic	Sig.	Exp(B)	95.0% C.I.for EX	
			Lower	Upper
Age	0.388	1.029	.965	1.098
SOFA score	0.004	1.759	1.201	2.576
Oliguria	0.719	0.624	0.048	8.094
sCr max	0.733	0.907	0.517	1.592
Uremia	0.667	0.995	0.971	1.019

This study contains several limitations. This is a single-center study and with a small number of patients, but we found interesting information about recovery of renal function and BCR.

CONCLUSIONS

In conclusion we found that the best part of AKI ICU patients had a BCR >20. A negative correlation between BCR and sCr at hospital discharge was found in this group of AKI patients, but evaluating recovery according to RFLE less than half "high BCR" patients had complete recovery of renal function. Maximal sCr was lower in the "high BCR" group, but mortality not different with the "low BCR" group. Independent factors associated with mortality were advanced age and severity illness score SOFA. These findings make the biochemical BCR parameter not appropriate for differentiation of prerenal azotemia.

REFERENCES

1. Bagshaw SM, George C, Bellomo R. A comparison of the RIFLE and AKIN criteria for acute kidney injury in critically ill patients. Nephrol Dial Transplant 2008; 23: 1569–1574

2. Beier K, Eppanapally S, Bazick HS et al. Elevation of blood urea nitrogen is predictive of long-term mortality in critically ill patients independent of ''normal'' creatinine. Crit Care Med 2011; 39: 305–313

3. Bellomo R, Ronco C, Kellum JA et al. Acute renal failure—definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. Crit Care 2004; 8: 204–212

4. Chertow GM, Burdick E, Honour M, et al. Acute kidney injury, mortality, length of stay, and costs in hospitalized patients. J Am Soc Nephrol 2005; 16: 3365–3370.

5. Clarkson MR, Friedewald JJ, Eustace JA et al. Acute kidney injury. In: Brenner BM (ed). Brenner and Rector's the Kidney. Philadelphia, PA: Saunders, 2007.

6. Feinfeld DA, Bargouthi H, Niaz Q et al. Massive and disproportionate elevation of blood urea nitrogen in acute azotemia. Int Urol Nephrol 2002; 34: 143–145.

7. Garzotto F, Piccinni P, Cruz D,Ronco C; NEFROINT investigation group. RIFLE-based data collection/management system applied to a prospective cohort multicenter Italian study on the epidemiology of acute kidney injury in the intensive care unit. Blood Purif. 2011;31(1-3):159-71.

8 Gjyzari A, Thereska N. Acute kidney injury according to rifle classification in the intensive care unit: occurrence, risk factors, outcome and predictive factors. Nephrol. Dial. Transplant. *2012 May*; *27(Suppl 2): 1-549.*

9. Hoste EA, Clermont G, Kersten A, et al: RIFLE criteria for acute kidney injury are associated with hospital mortality in critically ill patients: A cohort analysis. Crit Care 2006; 10:R73.

10. Lameire N, Van Biesen W, Vanholder R. Acute renal failure. Lancet 2005; 365: 417–430.

11. Lassnigg A, Schmidlin D, Mouhieddine M, et al. Minimal changes of serum creatinine predict prognosis in patients after cardiothoracic surgery: a prospective cohort study. J Am Soc Nephrol 2004; 15: 1597–1605.

12. Liano F, Pascual J. Epidemiology of acute renal failure: a prospective, multicenter, community-based study. Madrid Acute Renal Failure Study Group. Kidney Int 1996; 50: 811–818.

13. Miller TR, Anderson RJ, Linas SL, et al: Urinary diagnostic indices in acute renal failure: A prospective study. Ann Intern Med 1978;89:47-50.

14. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis 2002; 39 (2 Suppl 1): S1–S266.

15. Uchino S, Bellomo R, Goldsmith D et al. An assessment of the RIFLE criteria for acute renal failure in hospitalized patients. Crit Care Med 2006; 34: 1913–1917.

16. Uchino S, Bellomo R, Goldsmith D. The meaning of the blood urea nitrogen/creatinine ratio in acute kidney injury. Clin Kidney J (2012) 5: 187–191.