Nephrol Dial Transplant (2012) 27: 2248–2254
doi: 10.1093/ndt/gfr705
Advance Access publication 29 December 2011

The fallacy of the BUN:creatinine ratio in critically ill patients

Jean-Sebastien Rachoin[1], Ralph Daher[2], Charles Moussallem[3], Barry Milcarek[4], Krystal Hunter[4], Christa Schorr[1], Mariam Abboud[3], Patricia Henry[3] and Lawrence S. Weisberg[5]

[1]Division of Critical Care Medicine, Department of Medicine, Cooper University Hospital, Camden, NJ, USA, [2]Division of Nephrology, Department of Medicine, Johns Hopkins Bayview Medical Center, Baltimore, MD, USA, [3]Department of Medicine, Cooper University Hospital, Camden, NJ, USA, [4]Cooper Research Institute, Cooper University Hospital, Camden, NJ, USA and [5]Division of Nephrology, Department of Medicine, Cooper University Hospital, Camden, NJ, USA

Correspondence and offprint requests to: Lawrence S. Weisberg; E-mail: Weisberg-Lawrence@CooperHealth.edu

Abstract

Background and objectives. Acute kidney injury (AKI) is common in critically ill patients and is associated with a high mortality rate. Pre-renal azotemia, suggested by a high blood urea nitrogen to serum creatinine (BUN:Cr) ratio (BCR), has traditionally been associated with a better prognosis than other forms of AKI. Whether this pertains to critically ill patients is unknown.

Methods. We conducted a retrospective observational study of two cohorts of critically ill patients admitted to a single center: a derivation cohort, in which AKI was diagnosed, and a larger validation cohort. We analyzed associations between BCR and clinical outcomes: mortality and renal replacement therapy (RRT).

Results. Patients in the derivation cohort ($N = 1010$) with BCR >20 were older, predominantly female and white, and

more severely ill. A BCR >20 was significantly associated with increased mortality and a lower likelihood of RRT in all patients, patients with AKI and patients at risk for AKI. Patients in the validation cohort ($N = 10\,228$) with a BCR >20 were older, predominantly female and white, and more severely ill. A BCR >20 was associated with increased mortality and a lower likelihood of RRT in all patients and in those at risk for AKI, BUN correlated with age and severity of illness.

Conclusions. A BCR >20 is associated with increased mortality in critically ill patients. It is also associated with a lower likelihood of RRT, perhaps because of misinterpretation of the BCR. Clinicians should not use a BCR >20 to classify AKI in critically ill patients.

Keywords: acute kidney injury; critical illness; hospital mortality; renal replacement therapy

Introduction

Acute kidney injury (AKI) is common among hospitalized patients [1] and most common among critically ill patients [2, 3]. AKI is strongly associated with adverse clinical outcomes, including mortality [2, 4–11].

The differential diagnosis of AKI classically includes pre-renal, renal and post-renal causes [12]. Pre-renal azotemia results from a reduction in glomerular filtration rate (GFR) in response to a degree of renal hypoperfusion that exceeds the autoregulatory capacity of the kidney [12]. In pre-renal azotemia, the structural integrity of the kidney is assumed to be unscathed since resolution of the azotemia rapidly follows restoration of normal renal perfusion.

Urea and creatinine both undergo glomerular filtration. Unlike creatinine, however, urea undergoes tubular reabsorption. Therefore, in states of renal hypoperfusion with intact tubular function and augmented tubular reabsorption, the blood urea nitrogen (BUN) concentration tends to rise out of proportion to the serum creatinine concentration (S_{Cr}) [13]. This is thought to account for the observation of a high BUN:creatinine ratio (BCR) in patients with pre-renal azotemia. A recent study, for example, showed an average BCR of 26–30 in patients with pre-renal azotemia compared with a BCR of 11 in patients with intrinsic renal failure [14].

Consistent with its proposed pathogenesis, pre-renal azotemia is associated with better clinical outcomes than intrinsic renal failure [15]. One study showed that patients with pre-renal azotemia had a mortality rate of only 7% compared with 55% in patients with intrinsic renal failure [16], and Liaño and Pascual [17] demonstrated a similarly lower mortality in hospitalized patients with pre-renal azotemia compared with those with acute tubular necrosis.

Therefore, a diagnosis of pre-renal azotemia based on a high BCR would seem to offer clinicians some reassurance about the patient's prognosis. But such reassurance may be unfounded, particularly in critically ill patients. Patients with pre-renal azotemia tend to have a high BCR, but a high BCR does not necessarily imply pre-renal azotemia. The BUN may increase not just because of tubular reabsorption of urea but due to an increase in urea generation rate (from exogenous or endogenous protein catabolism). Critically ill patients are prone to accelerated protein catabolism, which may cloud the implications of what might otherwise appear to be a 'benign' high BCR. Moreover, as a ratio, the BCR may rise from a low rate of creatinine generation (from low muscle mass). One study reported a very high BUN (average BCR of 36) in a small group of critically ill patients who had high protein catabolism and low muscle mass. Fifty-eight percent of the patients died but in that study, no comparison was made with outcomes in patients with a low BCR [18].

In this study, we aimed to clarify the prognostic implications of a high BCR in critically ill patients. We hypothesized that a BCR >20 is not associated with lower mortality or reduced need for renal replacement therapy (RRT) in critically ill patients.

Materials and methods

Study design

We conducted a retrospective, single center observational study of patients of critically ill patients. The study was approved by the Institutional Review Board of Cooper University Hospital.

Record selection

We included patients aged at least 18 years, admitted to the mixed medical–surgical intensive care unit (ICU) or the trauma ICU at Cooper University Hospital, a 550-bed tertiary referral center. For purposes of the study, we refer to the two ICUs collectively as the ICU. We excluded patients who were receiving RRT before admission to the ICU.

We analyzed patient records in two independent sets: (i) a derivation cohort admitted to the ICU between 1 May 2004 and 31 December 2004 and (ii) a validation cohort admitted to the ICU between 1 January 2005 and 30 September 2008.

The derivation cohort included patients who survived >24 h in the ICU and had at least two measurements of S_{Cr}. The derivation cohort was used to identify a S_{Cr} cut-point defining a range of values predictive of AKI. This S_{Cr} cut-point was validated in the second cohort as a predictor of mortality and RRT.

If patients were admitted to the ICU more than once during the study period, only the last admission was considered for analysis.

Data collection

Patients in both cohorts were identified from the Project Impact® (PI) database [19], which houses prospectively collected clinical information about all critically ill patients in our institution.

For the derivation cohort, we retrieved additional laboratory data from the electronic medical information system. We recorded the first simultaneous BUN and S_{Cr} of the day for each of the first three calendar days of their ICU stay. For the validation cohort, we recorded only the highest BUN and S_{Cr} during the first 24 h of their ICU stay.

Demographic information, length of stay, complications while in hospital, APACHE II score, use of mechanical ventilation and vasopressors and use of RRT were recorded prospectively and entered into the PI database. In addition, the following comorbid conditions were recorded and entered prospectively: chronic kidney disease (CKD), hypertension (HTN), congestive heart failure (CHF) and chronic obstructive pulmonary disease (COPD).

We defined AKI as any change (increase or decrease [20]) in S_{Cr} of $\geq$0.3 mg/dL during the first 2 days [21].

Data analysis

Outcomes of interest were new in-hospital RRT and in-hospital mortality. We tested proportion differences within cohorts for significance by Pearson chi-square or Mann–Whitney *U*-tests. We analyzed correlations using Spearman coefficient. To identify S_{Cr} ranges on the day of ICU admission (S_{Cr1}) most predictive of ARF status, we applied a chi-square automatic interaction detection (CHAID) recursive segmentation model [22]. The CHAID algorithm enabled up to 20 cut-points to be defined for continuous

S_{Cr} values on Day 1 (S_{Cr1}) with Bonferroni adjustment of recursive significance tests used to determine distinct S_{Cr1} values minimizing within-range and maximizing between-range variation.

A stepwise multivariable logistic regression (backward elimination based on likelihood ratio) was used to adjust mortality and new RRT associations with BCR >20 and S_{Cr1} for the following risk factors: age, gender (female), race (Caucasian versus other), APACHE II score, use of vasopressors, use of mechanical ventilation, diabetes mellitus, CKD, CHF, HTN and COPD.

We performed a Kaplan–Meier survival analysis for new RRT and in-hospital mortality separately. In the survival analysis, the events (death within 30 days and new RRT within 30 days) were analyzed using a log-rank test (Mantel-Cox).

We divided the distribution of BCR and S_{Cr} in the validation cohort by decile (10 equal groups) and compared mortality in all groups with that in the index decile (that with the lowest mortality rate).

SPSS version 13.0 (Chicago, IL) was used for all analyses.

Results

Derivation cohort

During this study period, 1240 patients were admitted to the ICU. Of these, 230 records were excluded: 29 because they had fewer than two S_{Cr} measurements; 180 due to repeat admissions; 20 because of missing data on risk factors and 1 patient on RRT before admission to the ICU. A total of 1010 patients are included in the derivation cohort (Figure 1a).

Recursive segmentation (CHAID) analysis revealed that a S_{Cr} on the day of ICU admission (S_{Cr1}) of at least 1.0 mg/dL was associated with increased group homogeneity with respect to the development of AKI; that is, patients with $S_{Cr1} \geq 1.0$ mg/dL were significantly more likely to develop AKI than patients with $S_{Cr1} < 1.0$ mg/dL [odds ratio (OR) 4.8 (3.6–6.3)], $P < 0.001$].

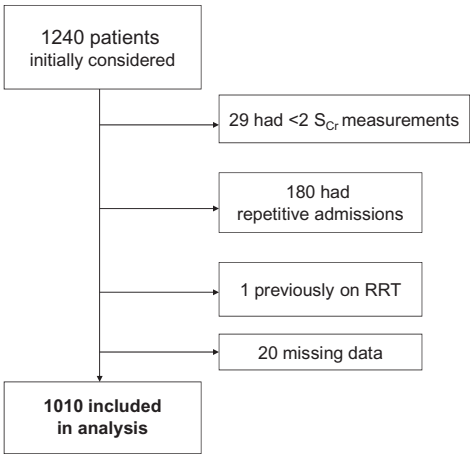
Table 1 shows the baseline data for the derivation cohort. The BCR was >20 in 518 patients (51%). These patients were more likely to be older, female, white and have a higher APACHE II score. In addition, they had a higher prevalence of diabetes mellitus, HTN and COPD. The group of patients with a BCR >20 had both a higher average BUN and a lower average S_{Cr} on admission to the ICU.

Clinical outcomes for the derivation cohort are shown in Table 2. Patients with a BCR >20, in the group as a whole and in and both 'high-risk' subgroups (AKI and S_{Cr1} >1.0 mg/dL), had a higher mortality, before and after adjusting for differences between groups. Patients in the group as a whole with a BCR >20 were less likely to undergo RRT [unadjusted OR 0.27 (0.1–0.74), $P = 0.008$ and adjusted OR 0.3 (0.1–0.9), $P = 0.047$]. The same tendency was observed in patients with S_{Cr1} >1.0 mg/dL and AKI, although the results did not achieve statistical significance.

Validation cohort

There were 12 746 admissions to the ICU during this study period, of which 11 416 represented unique patients. We excluded 438 records because the patients were receiving RRT before admission to the ICU and 750 because of missing data, leaving 10 228 records in the validation cohort (Figure 1b). Of those, 4296 (42%) had a BCR >20. Baseline characteristics of this cohort, by BCR cut-point, are shown in Table 3.

a. Acquisition of the derivation cohort



b. Acquisition of the validation cohort

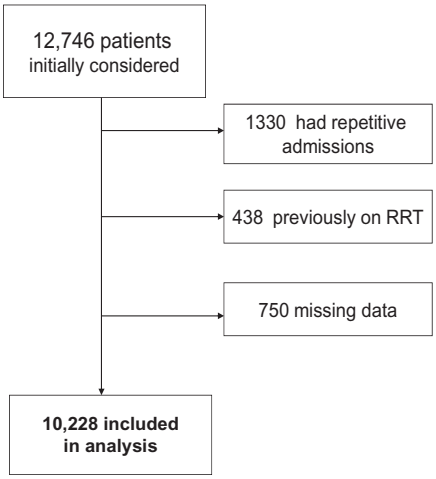


Fig. 1. (**a**) Schematic of acquisition of the derivation cohort. (**b**) Schematic of acquisition of the validation cohort.

Again, patients with a BCR >20 were more likely to be female, older and white, and to have a higher APACHE II score. This larger cohort revealed associations of a BCR >20 with a variety of underlying chronic conditions, including diabetes mellitus, HTN, CHF and COPD. The use of vasopressors and mechanical ventilation was more common among patients with a BCR >20. Once again, the group with a BCR >20 had both a higher average BUN and a lower average S_{Cr}. We found significant correlations between BUN and APACHE II score ($P = 0.19$, $P < 0.001$) and age ($P = 0.40$, $P < 0.001$).

Mortality in the validation cohort as a whole was 13.5, and 2.4% of the cohort underwent RRT.

We applied the S_{Cr1} cut-point of 1.0 mg/dL—found in the derivation cohort to increase the likelihood of AKI—to define a high-risk subgroup in the validation cohort. We identified 4201 in this high-risk subgroup. A BCR >20 in the cohort as a whole, and in the high-risk subgroup, was associated with increased mortality and lower likelihood of RRT, both before and after adjustment (Table 4).

Table 1. Baseline characteristics, derivation cohort[a]

	BCR ≤20 ($N = 492$)	BCR >20 ($N = 518$)	P-value	Total ($N = 1010$)
Age (year)	57 [43–71]	67.5 [57–76]	<0.001	64 [50–74]
Female	30%	49.4%	<0.001	40%
White	62%	75%	<0.001	68.5%
APACHE II	14 [10–17]	15 [11–19]	0.002	14 [11–18]
Vasopressors	21.1%	24.1%	0.331	23%
Mechanical ventilation (%)	60%	60%	0.797	60%
BUN	14 [11–21]	21 [15–30]	<0.001	17 [13–26]
S_{Cr}	1.0 [0.7–1.4]	0.7 [0.6–1]	<0.001	0.9 [0.6–1.2]
BCR	15 [12–19]	27 [24–35]	<0.001	21 [16–28]
DM	24%	35%	<0.001	30%
HTN	53%	61%	0.009	57%
CKD	1.6%	0.8%	0.253	1.2%
COPD	7%	11%	0.037	9%
CHF	7.7%	10.6%	0.127	9.2%

[a]DM, diabetes mellitus. Continuous data are shown as median [IQR].

Table 2. Clinical outcomes for patients in the derivation cohort

			Unadjusted OR		Adjusted OR	
	BCR ≤20	BCR >20	OR (95% CI)	P-value	OR (95% CI)	P-value
(a) Mortality						
All patients	3.5%	8.7%	2.7 (1.5–4.7)	0.001	2.4 (1.2–4.9)	0.015
S_{Cr1} ≥1.0 mg/dL	6.0%	14.8%	2.7 (1.3–5.4)	0.006	3.2 (1.4–7.6)	0.007
Patients with ARF	3.5%	10.6%	3.3 (1.5–7.3)	0.003	3.4 (1.3–8.6)	0.010
(b) New RRT						
All patients	3.5%	1.0%	0.2 (0.1–0.74)	0.008	0.3 (0.1–0.99)	0.047
S_{Cr1} ≥1.0 mg/dL	6.8%	2.8%	0.4 (0.1–1.2)	0.106	0.49 (0.13–1.8)	0.280
Patients with ARF	5.8%	2.3%	0.4 (0.1–1.1)	0.068	0.47 (0.14–1.6)	0.230

Table 3. Baseline characteristics, validation cohort[a]

	BCR ≤20 ($N = 5932$)	BCR >20 ($N = 4296$)	P-value	Total ($N = 10\ 228$)
Age (year)	57 (44–70)	67 (54–77)	<0.001	61 (48–74)
Female	35%	51%	<0.001	42%
Caucasian	59%	69%	<0.001	63%
APACHE II	9 (0–15)	12 (0–17)	<0.001	10 (0–16)
Vasopressors	18%	21%	<0.001	19%
Mechanical ventilation	46%	43%	0.003	44%
BUN	14 (10–19)	23 (17–34)	<0.001	17 (12–26)
S_{Cr}	0.9 (0.7–1.2)	0.8 (0.6–1.2)	<0.001	0.9 (0.7–1.2)
BCR	16 (13–18)	27 (23–33)	<0.001	19 (15–25)
DM	25%	34%	<0.001	29%
HTN	54%	64%	<0.001	58%
CKD	7%	6%	0.219	6.4%
COPD	8%	15%	<0.001	11%
CHF	9%	17%	<0.001	12%

[a]See Table 1 for abbreviations and data representation.

Table 4. Clinical outcomes for patients in validation cohort

	Unadjusted OR				Adjusted OR	
	BCR ≤20	BCR >20	OR (95% CI)	P-value	OR (95% CI)	P-value
(a) Mortality						
All patients	10.6	17.5	1.8 (1.6–2)	<0.001	1.6 (1.4–1.8)	<0.001
S_{Cr1} ≥1.0 mg/dL	16.7	25	1.7 (1.4–1.9)	<0.001	1.7 (1.4–2.0)	<0.001
(b) New RRT						
All patients	3.2	1.4	0.4 (0.3–0.6)	<0.001	0.5 (0.3–0.7)	<0.001
S_{Cr1} ≥1.0 mg/dL	6.5	3.2	0.4 (0.3–0.5)	<0.001	0.4 (0.3–0.8)	<0.001

We analyzed mortality across deciles defined by BCR in the group as a whole. This revealed a J-shaped relationship between BCR and mortality (Figure 2), with the lowest mortality (9.7%) seen in Decile 3 (BCR 13.75–15.5). Dividing the cohort into deciles defined by S_{Cr} revealed a similar J-shaped relationship with mortality (Figure 3), with the lowest mortality (7%) seen in Decile 3 (S_{Cr} 0.6–0.7).

The time to death and time to RRT are represented by Kaplan–Meier survival curves (Figures 4 and Figure 5, respectively). The log-rank test showed significant differences between the BCR groups for both in-hospital mortality within 30 days {hazard ratio 1.5 [95% confidence interval (CI)], 1.3–1.6} and new RRT within 30 days [hazard ratio 0.5 (95% CI, 0.4–0.7)] (both $P < 0.001$). The curve for cumulative incidence of RRT flattens substantially ~15 days, whereas that for survival shows a linear decline over time. The median [interquartile range, IQR] time to death was significantly shorter in the BCR >20 group than in the BCR <20 group (7 [3–15] days versus10 [5–20] days, $P < 0.001$). Conversely, the median [IQR] time to dialysis was significantly longer in the BCR >20 group than in the BCR <20 group (6 [1.5–10] days versus 4 [1–14] days, $P < 0.001$).

Discussion

We examined mortality and new RRT in critically ill patients stratified by BCR. BCR >20 has long been viewed as indicative of pre-renal azotemia, which is generally thought to have a more benign prognosis than other causes of AKI [15]. Contrary to this conventional wisdom, however, results from this study of critically ill patients show that a BCR >20 is associated with higher mortality than in patients with a low BCR. How can we explain this paradoxical observation?

The patients in our study with a BCR >20 had both a higher average BUN and a lower average S_{Cr} than patients with a BCR ≤20. To begin to understand the relationship between BCR and clinical outcomes in our study, we will first examine the factors that tend to raise the BUN, to see if those factors are associated with the higher mortality.

Classically, a high BCR in AKI implies pre-renal azotemia based on the pathophysiologic construct of intact tubular function and enhanced urea reabsorption, in the setting of renal hypoperfusion [13]. This conception might be valid if other conditions affecting the BUN were held constant. Such is not the case in critically ill patients, however. Critical illness is associated with increased protein catabolism and increased urea generation rate [23]. One might

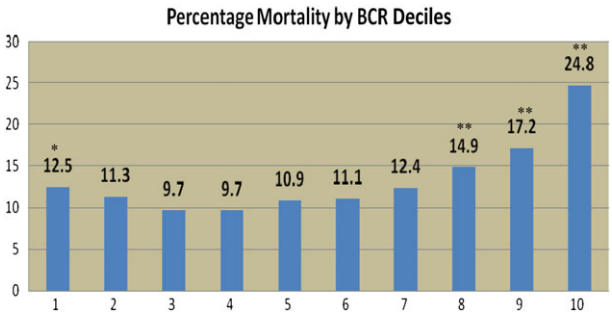


Fig. 2. Mortality in the validation cohort, by deciles of BCR. Deciles: 1 [<11.5], 2 [11.5–13.75], 3 [13.75–15.5], 4 [15.5–17.3], 5 [17.3–18.9], 6 [18.9–21.1], 7 [21.1–23.3], 8 [23.3–27], 9 [27–33.3], 10 [>33.3]. *P = 0.047; ** P < 0.001, versus index Decile 3.

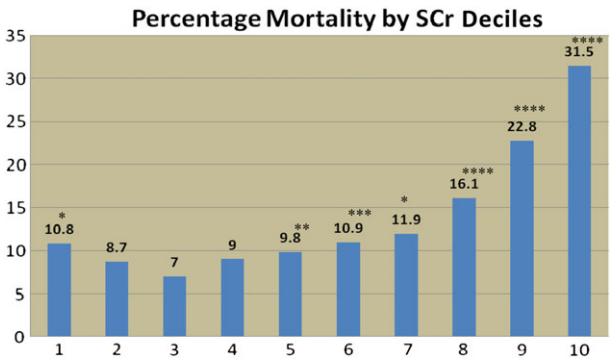


Fig. 3. Mortality in the validation cohort, by deciles of S_{Cr}. Deciles: 1 [≤0.5]; 2 [0.5–0.6], 3 [0.6–0.7], 4 [0.7–0.8], 5 [0.8–0.9], 6 [0.9–1], 7 [1–1.1], 8 [1.1–1.3], 9 [1.3–1.9], 10 [>1.9]. *P = 0.001; **P = 0.015; ***P = 0.002; ****P < 0.001, versus index Decile 3.

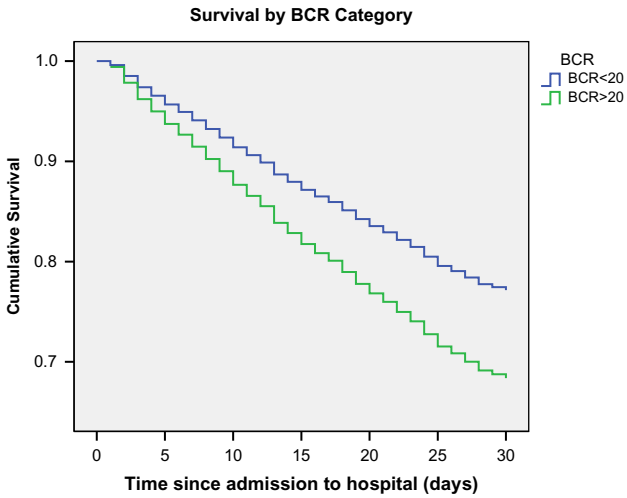


Fig. 4. Survival by BCR status.

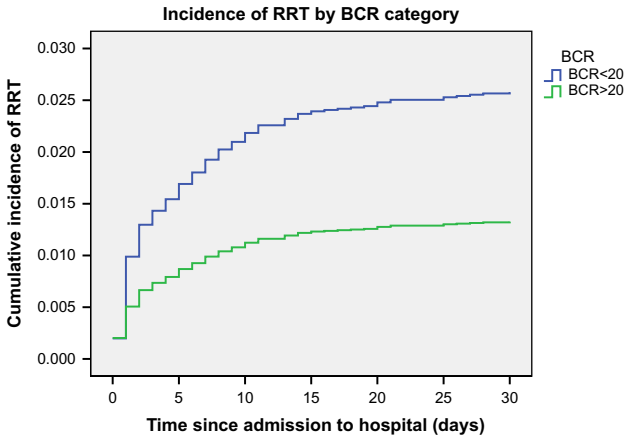


Fig. 5. Cumulative hazard of new RRT within 30 days.

logically assume that the severity of illness correlates with the intensity of protein catabolism. Furthermore, advancing age is associated with resistance to protein anabolism, perhaps by way of insulin resistance [24]. Patients with a BCR >20 in our study were older, and their APACHE II score was higher than patients in the low BCR group. Both APACHE II (our data show a correlation between APACHE II score and BUN, but this is confounded by the inclusion of another measure of renal function, S_{Cr}, in the calculation of the APACHE II) and age correlate significantly with BUN in our population. Thus, we suspect that at least part of the reason for the high BCR in this critically ill population is a higher protein catabolic rate. The very factors that lead to the high protein catabolic rate—severity of illness and age—are clearly associated with increased mortality in critically ill patients [25–27].

BCR being a ratio, the denominator, S_{Cr}, must be considered for its possible contribution to the high BCR and to mortality. At any given GFR, S_{Cr} is a function of muscle turnover, itself a function of muscle mass. Muscle mass declines steadily with age, and at any age, women tend to have less muscle mass than men [28]. Furthermore, whites tend to have less muscle mass and generate less creatinine than blacks [29]. Patients in our study with a BCR >20 had a lower average S_{Cr} than patients in the lower BCR group. They were significantly older. Moreover, the high BCR group had a significantly higher proportion of whites and women. These factors could account for the lower S_{Cr}.

To what extent might these same factors track with mortality? Clearly, age is associated with increased mortality among critically ill patients [30–32]. Female gender was also associated with higher mortality rate in a large study of critically ill patients [33]. Indeed, creatinine generation rate has been inversely associated with severity of illness in patients with ARF [34, 35].

Thus, both the high BUN and lower S_{Cr} are explicable by factors other than a 'pre-renal' state, and those factors are associated with increased mortality.

Our findings are concordant with those of other trials. A retrospective study of 11 291 critically ill patients showed that low baseline serum creatinine was independently associated with increased mortality [36]. Analysis of data from the BEST Kidney study showed that patients with sepsis-associated AKI who had impaired pre-morbid kidney function (and thus a higher baseline SC_r) had a trend towards lower mortality [37].

We also found that patients with a high BCR were less likely to undergo RRT than patients with a low BCR. The reasons for this are not obvious, mainly because the study design does not allow us to discriminate between, on one hand, RRT that was indicated but withheld and, on the other hand, unnecessary RRT. The Kaplan–Meier survival curve analyses of time to death and time to RRT suggest that there was ample opportunity to initiate RRT before death. It is interesting to speculate that the high BCR may have led the clinicians to think the AKI was pre-renal and would resolve with restoration of renal perfusion. This, in turn, may have encouraged them to withhold RRT. Insofar, as the relatively low S_{Cr} in this group may have led the clinicians to underestimate the severity of the AKI, it might have had an effect similar to the high BCR. The role of gender in regard to initiating RRT is unknown, but somewhat disturbing to contemplate. A large study of critically ill patients showed that women are less likely to undergo technical or invasive procedures than men with identical APACHE II scores and yet had a higher mortality [33]. (In that study, however, there was no disparity in the use of hemodialysis [33].) The detailed chart review that would have been required to support or refute such speculation is beyond the scope of this study.

If the BCR is a poor indicator of pre-renal azotemia in critically ill patients, as it appears to be, is there a better method to diagnose pre-renal azotemia in this population? The answer to this question is not readily apparent. Low urinary sodium concentration and a low fractional excretion of sodium, commonly accepted indices of renal hypoperfusion, are unreliably associated with pre-renal azotemia and, indeed, are commonly reported in sepsis-associated AKI [38, 39]. Physical assessment of volume status may be equally unreliable [40], especially in critically ill patients where the usual indices (such as edema and vital signs) are frequently misleading rendering such an endeavor quite challenging. The surest way to diagnose pre-renal azotemia is to observe prompt improvement in renal function with restoration of normal hemodynamics, which often requires fluid administration to a patient thought to be volume depleted. Even this is frought with uncertainty, however, since failure of the renal function to improve could reflect either an inadequate 'fluid challenge' or volume-unresponsive kidney failure. Thus, the BCR appears to be another of a number of unreliable tools for the diagnostic evaluation of a patient with AKI.

Interpretation of our results is limited by the fact that we did not analyze chart-level information. This is particularly germane to the issue of RRT, as discussed above. The use of recursive segmentation (CHAID) analysis to define a high-risk subgroup based on the initial S_{Cr} alone might be judged overly simplistic. It did, however, define a subgroup with roughly 5-fold likelihood of developing AKI, and it allowed us to construct a similar high-risk subgroup in the larger validation cohort. Fractional excretion of sodium (FENa) was not recorded, but we believe this would shed little light on our results, for reasons we discussed above [38, 39]. Underlying CKD could influence the propensity for AKI and may influence its outcome. We did not estimate GFR in this population because we lacked a reliable stable 'baseline' S_{Cr}. All patients in all groups, however, were susceptible to this limitation. Lastly, in the validation cohort, although the recorded BUN and creatinine were each the highest in the first 24 h of the ICU stay, they were not necessarily drawn simultaneously. While we are unable to estimate the impact of this possible time discrepancy on the BCR, it applied to all patients in the validation cohort.

In conclusion, contrary to the conventional wisdom that associates BCR >20 with pre-renal azotemia and a more benign prognosis, we found a high BCR to be associated with increased mortality in critically ill patients. We also found that a high BCR was associated with a lower likelihood of undergoing RRT. Based on these findings, we recommend abandoning the BCR as an adjunct to the diagnosis of pre-renal azotemia in critically ill patients.

Acknowledgements. Funded in part by a grant from the National Kidney Foundation serving the Delaware Valley.

Conflict of interest statement. None declared.

References

1. 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
2. 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
3. Uchino S, Kellum JA, Bellomo R *et al.* Acute renal failure in critically ill patients: a multinational, multicenter study. *JAMA* 2005; 294: 813–818
4. Ricci Z, Cruz D, Ronco C. The RIFLE criteria and mortality in acute kidney injury: a systematic review. *Kidney Int* 2008; 73: 538–546
5. 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
6. Ali T, Khan I, Simpson W *et al.* Incidence and outcomes in acute kidney injury: a comprehensive population-based study. *J Am Soc Nephrol* 2007; 18: 1292–1298
7. Chen YC, Jenq CC, Tian YC *et al.* Rifle classification for predicting in-hospital mortality in critically ill sepsis patients. *Shock* 2009; 31: 139–145
8. Bagshaw SM, George C, Dinu I *et al.* A multi-centre evaluation of the RIFLE criteria for early acute kidney injury in critically ill patients. *Nephrol Dial Transplant* 2008; 23: 1203–1210
9. Dasta JF, Kane-Gill SL, Durtschi AJ *et al.* Costs and outcomes of acute kidney injury (AKI) following cardiac surgery. *Nephrol Dial Transplant* 2008; 23: 1970–1974
10. 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
11. Covic A, Schiller A, Mardare NG *et al.* The impact of acute kidney injury on short-term survival in an Eastern European population with stroke. *Nephrol Dial Transplant* 2008; 23: 2228–2234
12. 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
13. Blantz RC. Pathophysiology of pre-renal azotemia. *Kidney Int* 1998; 53: 512–523
14. Carvounis CP, Nisar S, Guro-Razuman S. Significance of the fractional excretion of urea in the differential diagnosis of acute renal failure. *Kidney Int* 2002; 62: 2223–2229
15. Lee VWS, Harris D, Anderson RJ *et al.* Acute renal failure. In: Schrier RW (ed). *Diseases of the Kidney and Urinary Tract*. Philadelphia, PA: Lippincott Williams & Wilkins, 2007
16. Kaufman J, Dhakal M, Patel B *et al.* Community-acquired acute renal failure. *Am J Kidney Dis* 1991; 17: 191–198
17. 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
18. 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
19. Cook SF, Visscher WA, Hobbs CL *et al.* Project IMPACT: results from a pilot validity study of a new observational database. *Crit Care Med* 2002; 30: 2765–2770
20. Ostermann M, Chang R. Correlation between the AKI classification and outcome. *Crit Care* 2008; 12: R144
21. Mehta RL, Kellum JA, Shah SV *et al.* Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury. *Crit Care* 2007; 11: R31
22. Magidson J. *The CHAID Approach to Segmentation Modeling: Chi-squared Automatic Interaction Detection*. Oxford, UK: Blackwell, 1994
23. Mizock BA. Metabolic derangements in sepsis and septic shock. *Crit Care Clin* 2000; 16: 319–336, vii
24. Rennie MJ. Anabolic resistance in critically ill patients. *Crit Care Med* 2009; 37 (10 Suppl): S398–S399
25. Ho KM, Dobb GJ, Knuiman M *et al.* A comparison of admission and worst 24-hour Acute Physiology and Chronic Health Evaluation II scores in predicting hospital mortality: a retrospective cohort study. *Crit Care* 2006; 10: R4
26. Esteban A, Anzueto A, Frutos-Vivar F *et al.* Outcome of older patients receiving mechanical ventilation. *Intensive Care Med* 2004; 30: 639–646
27. Vosylius S, Sipylaite J, Ivaskevicius J. Determinants of outcome in elderly patients admitted to the intensive care unit. *Age Ageing* 2005; 34: 157–162
28. Doherty TJ. Invited review: aging and sarcopenia. *J Appl Physiol* 2003; 95: 1717–1727
29. Levey AS, Bosch JP, Lewis JB *et al.* A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. *Ann Intern Med* 1999; 130: 461–470
30. Carson SS, Garrett J, Hanson LC *et al.* A prognostic model for one-year mortality in patients requiring prolonged mechanical ventilation. *Crit Care Med* 2008; 36: 2061–2069
31. Douglas SL, Daly BJ, O'Toole EE *et al.* Age differences in survival outcomes and resource use for chronically critically ill patients. *J Crit Care* 2009; 24: 302–310
32. Bagshaw SM, Webb SA, Delaney A *et al.* Very old patients admitted to intensive care in Australia and New Zealand: a multi-centre cohort analysis. *Crit Care* 2009; 13: R45
33. Fowler RA, Sabur N, Li P *et al.* Sex-and age-based differences in the delivery and outcomes of critical care. *CMAJ* 2007; 177: 1513–1519
34. Clark WR, Mueller BA, Kraus MA *et al.* Quantification of creatinine kinetic parameters in patients with acute renal failure. *Kidney Int* 1998; 54: 554–560
35. Pesola GR, Akhavan I, Carlon GC. Urinary creatinine excretion in the ICU: low excretion does not mean inadequate collection. *Am J Crit Care* 1993; 2: 462–466
36. Cartin-Ceba R, Afessa B, Gajic O. Low baseline serum creatinine concentration predicts mortality in critically ill patients independent of body mass index. *Crit Care Med* 2007; 35: 2420–2423
37. Bagshaw SM, Uchino S, Bellomo R *et al.* Septic acute kidney injury in critically ill patients: clinical characteristics and outcomes. *Clin J Am Soc Nephrol* 2007; 2: 431–439
38. Bagshaw SM, Bellomo R. Urine abnormalities in acute kidney injury and sepsis. *Contrib Nephrol* 2010; 165: 274–283
39. Bagshaw SM, Langenberg C, Bellomo R. Urinary biochemistry and microscopy in septic acute renal failure: a systematic review. *Am J Kidney Dis* 2006; 48: 695–705
40. Chung HM, Kluge R, Schrier RW *et al.* Clinical assessment of extracellular fluid volume in hyponatremia. *Am J Med* 1987; 83: 905–908

Received for publication: 31.3.11; Accepted in revised form: 9.11.11