



# Acute kidney injury in patients with decompensated cirrhosis: knowing the cause is often difficult

Mohammed Faisal Rahman, Harold M. Szerlip

Baylor University Medical Center at Dallas, Dallas, USA

Correspondence to: Harold M. Szerlip, MD. Baylor University Medical Center at Dallas, 3600 Gaston Ave, Suite 904 Barnett Tower, Dallas, TX 75246, USA. Email: harold.szerlip@BSWHealth.org.

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Acute renal failure (AKI), which occurs in up to 20–50% of patients hospitalized with decompensated cirrhosis is an important predictor of poor outcomes and mortality (1,2). The etiology of AKI in these patients has been divided into a functional decrease in renal function; as is in pre-renal azotemia (PRA) and Hepato-renal syndrome (HRS) or structural abnormalities as is in acute tubular necrosis (ATN). Because the gold standard “kidney biopsy” is rarely performed the ability to distinguish between these etiologies is based on clinical criteria that lack specificity and sensitivity. Patidar *et al.* (3) has examined the diagnostic accuracy of fractional excretion of urea (FEUrea) as a tool for differentiating between the etiologies of AKI within 24 hours of admission in patients with decompensated cirrhosis and ascites.

This was a retrospective single centered study. Patients with cirrhosis and ascites admitted from February 2012 to September 2013 were screened and total of 50 patients were included. AKI was defined according to acute injury network criteria (AKIN), and AKI phenotype was determined after adjudication between nephrologist and hepatologist using International Club of Ascites and AKIN guidelines. FEUrea was able to distinguish between: (I) ATN *vs.* non-ATN: FEUrea greater than 33.41% predicted ATN with 100% sensitivity and 85% specificity; (II) HRS *vs.* non-HRS: FEUrea greater than 28.16% predicted non-HRS with a sensitivity of 75% and specificity of 83%; (III) PRA *vs.* HRS: FEUrea greater than 21.35% predicted PRA; if FEUrea is less than 21.35%, the diagnoses of HRS

is likely (sensitivity of 91% and specificity of 61%). The diagnostic accuracy was 96% for ATN versus non-ATN, 87% for HRS versus non-HRS, and 81% PRA versus HRS. The findings were validated in an independent cohort of 50 patients. The authors postulate that the lower FeUrea in HRS as compared to PRA is due to “tubular damage” in HRS causing decreased filtration of urea but that distal reabsorption in the inner medullary collecting duct remains intact. Although FeUrea has been historically used as a sensitive biomarker to separate PRA from ATN, the data supporting its specificity are lacking (4,5).

The authors are to be commended on their efforts to identify a valid biomarker to identify the etiology of AKI in patients with decompensated cirrhosis. However, there are several major problems with the conclusions and the study should be interpreted in the context of its limitations. This is a single centered-retrospective study with low power (n=50). More importantly the authors provide no conclusive data that the clinical adjudication of the cause of the AKI was correct. The concept that HRS is just a severe form of prerenal azotemia without structural damage is being challenged (1,6,7). It is becoming more evident that inflammatory changes occur within the kidney including areas of tubular damage and necrosis. The fact that infection is the most common precipitating cause of HRS supports the role of inflammation. Despite using currently recommended therapy reversal of renal dysfunction does not occur in up to 40% of patients diagnosed with HRS (8). In addition, it is likely that HRS often transitions to ATN.

The authors speculate that it is important to quickly identify the underlying cause of the AKI to promptly provide treatment but as just pointed out treatment is often futile, and the judicious use of albumin and pressor agents is unlikely to seriously harm patients with ATN. Furthermore, outcomes of patients with cirrhosis and AKI from any etiology has a poor outcome (9,10).

Novel plasma and urinary biomarkers may help in correct diagnosis of AKI phenotype but they are expensive, not widely available and currently being used mostly for research purposes (11,12). However, because of the overlap between HRS and ATN, biomarkers may serve more as predictors of outcomes rather than identifiers of disease pathology. Even if in larger prospective trials FEUrea shows promise as an objective test that might help in prompt diagnosis, early initiation of specific treatment and avoidance of unnecessary interventions; unless the use of this biomarker improves clinical outcomes, will it become a useful tool. Unfortunately, that has yet to be established.

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### Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

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