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Defining renal failure in cirrhosis -Acute kidney injury classification or traditional criteria?

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Article commented

Piano S, Rosi S, Maresio G, Fasolato S, Cavallin M, Romano A, Morando F, et al. Evaluation of the Acute Kidney Injury Network criteria in hospitalized patients with cirrhosis and ascites. *J Hepatol* 2013; 59: 482-9.

Comment

Renal failure in cirrhosis has been arbitrarily defined as an increase in serum creatinine (SCr) over 1.5 mg/dL which corresponds to a glomerular filtration rate (GFR) of approximately 30 mL/min.[1-3] This definition (conventional criteria), proposed in 1996 by the International Ascites Club for has been widely accepted one among the hepatology community.[3] Although hepatologists have accepted this definition, the nephrology community has been more skeptical mainly because SCr is a suboptimal marker for renal function because it may overestimate GFR, mainly due to decreased creatinine production or reduced muscle mass. Furthermore, a SCr level below 1.5 mg/dL does not necessarily exclude renal dysfunction.[4] Therefore the concept of acute kidney injury (AKI) which was proposed by critical care and nephrology societies to define kidney failure has been also studied in patients with cirrhosis. The AKI definition stems from studies correlating changes in SCr *vs*. morbidity and mortality in ICU patients.[5] Therefore as its name implies it defines an abrupt decrease in kidney function. This definition does not take into account the classification of prerenal, intrinsic, or post-renal renal failure; instead the AKI definition is based on small changes in SCr AKI is defined as an increase in SCr of > 50% from baseline or a rise in SCr of ≥ 0.3 mg/dL in less than 48 h.[5] AKI is graded into three stages according to the magnitude of increase in SCr:

- **Stage 1.** 150-200%.
- **Stage 2.** > 200-300%.
- **Stage 3.** > 300% or of at least 0.5 dL in patients with baseline SCr of ≥ 4 dL or renal replacement therapy. Morbidity and mortality increase in parallel with the AKI stages from no AKI to AKI stage 3.

New attempts at defining renal failure in cirrhosis using the AKI definition have been proposed by different authors.[6,7] In theory, this new definition has the advantage of detecting earlier phases of kidney dysfunction with the goal of implementing early therapy. A limited number of studies have shown that minor increases in SCr detected by the AKI definition are independently associated with increased mortality in hospitalized patients with cirrhosis.[8-10] However, until now there was no information comparing accuracy and outcomes of the traditional or conventional classification *vs*. the new AKI definition in patients with cirrhosis.

Therefore, the aim of the study authored by Piano, *et al*. was to compare AKI criteria and conventional criteria in the prediction of in-hospital mortality in a cohort of patients with cirrhosis and ascites. The authors included 233 consecutive patients with cirrhosis and ascites admitted to the hospital. In the study, Scr was obtained at admission (baseline value) and followed daily during hospitalization. Patients with AKI stage-1 were subdivided into two groups, those with an increase in SCr ≥ 0.3 mg/dL but without reaching 1.5 mg/dL and those in whom SCr reached a peak over 1.5 mg/dL.

AKI was diagnosed in 26% and 12% patients, according to AKI criteria and conventional criterion, respectively. Most patients (72%) had initial AKI stage 1 whereas the rest were stage 2 and 3. Resolution of AKI during the hospitalization was seen in more than half of the patients who fulfilled AKI

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criteria while an improvement of AKI diagnosed on the basis of the conventional criteria was observed in 36% of patients. In the study only SCr ≥ 1.5 mg/dL at the time of fulfillment of the AKI criteria was found to be a predictor of AKI stage progression. Finally, patients with initial AKI stage 1 and SCr < 1.5 mg/dL showed a lower rate of progression and a higher rate of resolution than patients with AKI stage 1 and SCr ≥ 1.5 mg/dL, as expected this latter group had a worse prognosis.

The study showed marked differences between the two groups. The in-hospital mortality of patients with AKI-1 was higher, although not significant, than that of patients without AKI. However, progression of AKI and mortality were significantly higher in patients with AKI-1 and SCr ≥ 1.5 than in patients with AKI-1 and SCr < 1.5 mg/dL. The study therefore suggests that patients with AKI-1 and serum creatinine <1.5 mg/dL have a benign course and that only the progression of renal impairment which leads to a significant reduction of GFR (i.e. SCr >1.5 mg/dL) is what determines a poor prognosis.

This study is one of the first to compare the prognostic value of AKI defined by AKI criteria and conventional criteria in patients with cirrhosis and ascites. In the study, AKI defined by AKI criteria was found as accurate as AKI defined by conventional criteria for the prediction of hospital mortality. The conventional criteria for the diagnosis of AKI applied by hepatologists performed well, which reassures us that we indeed did a good job in the past with the conventional criteria and perhaps are ok if we keep using it. That said, given the above data it is difficult to conclude if the AKI classification improves the conventional diagnostic criteria of renal failure in cirrhosis in terms of prediction of morbidity and mortality. AKI-stage 1 is associated with increased mortality only in patients with significant decrease in GFR and peak serum creatinine >1.5 mg/dL. Further data comparing these two definitions will help clarify the role of the traditional criteria *vs.* the AKI criteria for the diagnosis of renal failure in patients with cirrhosis.

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