TABLE 3 Diagnostic criteria of AKI in cirrhosis[267]

Parameter	Definition
Baseline sCr	Stable sCr in ≤3 mo If not available, a stable sCr closest to the current one If no previous sCr at all, use admission sCr
Definition of AKI	Increase in sCr by ≥0.3 mg/dL (26.4 μmol/L) in <48 h or 50% increase in sCr from baseline
Staging	Stage 1: increase in sCr by ≥0.3 mg/dL (26.4 μmol/L) in <48 h or increase in sCr of 1.5 to two times or greater from baseline Stage 2: increase in sCr of more than two to three times from baseline Stage 3: increase in sCr of more than three times from baseline or sCr >4 mg/dL (352 μmol/L) with an acute increase of ≥0.3 mg/dL (26.4 μmol/L) or the initiation of renal replacement therapy
Course of AKI Progression Regression	Progression of AKI to a higher stage or need for renal replacement therapy Regression of AKI to a lower stage
Response to Rx None Partial Complete	No regression of AKI Regression of AKI stage with final sCr ≥0.3 mg/dL (26.4 μmol/L) from baseline Regression of AKI stage with final sCr <26.4 μmol/L (0.3 mg/dL) from baseline
Diagnostic criteria for HRS-AKI	• Cirrhosis with ascites • Diagnosis of Stage 2 AKI or higher according to IAC-AKI criteria • No response after 2 consecutive days of diuretic withdrawal and plasma volume expansion with albumin 1 g/kg of body weight to a maximum of 100 g/day • Absence of shock • No current or recent treatment with nephrotoxic drugs • Absence of parenchymal kidney disease as indicated by absence of proteinuria >500 mg/day, microhematuria (>50 red blood cells per high power field) and normal renal ultrasonography

Abbreviations: AKI, acute kidney injury; HRS, hepatorenal syndrome; IAC, International Ascites Club; Rx, treatment; sCr, serum creatinine.

structural causes of AKI. Biomarkers such as neutrophil gelatinase-associated lipocalin and fractional excretion of sodium or fractional excretion of urea can differentiate ATN from functional causes of AKI.[107] Although a diagnosis of exclusion, HRS-AKI only occurs in patients with cirrhosis and ascites and is often associated with systemic hypotension and hyponatremia; a lack of these clinical features makes the diagnosis of HRS-AKI unlikely.

Management of AKI

The initial management of AKI in patients with cirrhosis follows three broad principles: identify the phenotype of the AKI, remove or treat the precipitating factor, and perform a trial of fluid challenge (Figure 3). As bacterial infection is a common precipitating factor for HRS-AKI, it is imperative that all patients be monitored for evidence of infection. For every hour delay in the start of antibiotics, there is an increase in mortality by 1.86 times from multiorgan failure, including kidney failure. Therefore, in patients suspected of having a bacterial infection, early administration of empiric antibiotics is recommended once all the cultures from appropriate sites have been taken.[108] Antibiotic therapy can be stopped or tailored as culture data become available. In patients who have SBP, the use of albumin in conjunction with antibiotics can prevent the development of kidney dysfunction, especially in patients with high baseline sCr or with liver dysfunction.[109] Consider avoiding radiographic dye, which may worsen the renal ischemia. In patients with ACLF with abnormal hemodynamics, diuretics or nephrotoxic drugs should be withdrawn and fluid challenge given.[110]

The recommended fluid challenge is 25% albumin for both its oncotic and anti-inflammatory properties[111] at a dose of 1 g/kg of body weight to a maximum of 100 g/day for 48 h. Patients should be monitored closely for signs of volume overload/pulmonary edema while receiving albumin. Furthermore, they should also be monitored for progression of kidney dysfunction, emergence of infections or other complications of cirrhosis, or organ failure and treated accordingly.

Pharmacotherapy for HRS-AKI

The mainstay of treatment for HRS-AKI that is not responsive to volume challenge is vasoconstrictor therapy together with albumin (20–40 g/day). The optimal duration of albumin administration is unclear. In the most recent clinical trial using terlipressin for the treatment of HRS1,[112] respiratory failure was observed in 8% of patients who received terlipressin, especially in those with ACLF-3, but not in those who received placebo,[112] and there was a trend toward higher incidence of respiratory failure in those who received a higher volume of albumin in the pretreatment period. Patients should be carefully monitored for pulmonary edema, as some of these patients may have a degree of cirrhotic cardiomyopathy or diastolic dysfunction. In addition, the total amount of albumin administered prior to initiation of terlipressin should also be considered. The published literature so far has only reported on results of vasoconstrictor use in patients with HRS1. There are no studies of