



Multidisciplinary Management of Extrahepatic Organ Failures in Patients with Advanced Liver Disease

Glossary, Acronyms and Show Notes

Acute-on-Chronic Liver Failure (ACLF): A potentially reversible condition in patients with chronic liver disease, with or without cirrhosis, that is associated with the potential for multiple organ failure and mortality within 3 months in absence of treatment of the underlying liver disease, liver support, or liver transplantation. ACLF is recognized by the presence of chronic liver disease along with elevation in the serum bilirubin and prolongation of the INR. The presence of kidney, lung, circulatory, or brain failure supports the diagnosis. [Bajaj JS, et al. *Am J Gastroenterol* 2022;117:225–252](#)

Acute Kidney Injury (AKI): Acute kidney injury (AKI) is a sudden decline in kidney function that can range from minor to complete kidney failure. AKI is defined as an increase in serum creatinine (SCr) by ≥ 0.3 mg/dL within 48 hours or a rise of $\geq 50\%$ from baseline. [KDIGO AKI Practice Guideline 2012.](#)

Acute Tubular Necrosis (ATN): a form of AKI caused by damage to tubular epithelial cells, typically from ischemia or nephrotoxins, characterized by high FENa ($>2\%$) and muddy brown casts in urinalysis. Recovery usually occurs within 1-3 weeks with supportive care and addressing the underlying cause, though temporary dialysis may be needed and some patients may not recover full kidney function.

Albumin: plays a critical role in cirrhosis by maintaining oncotic pressure and vascular function, while also binding toxins, with levels below 3.5 g/dL associated with poorer patient prognosis. Its therapeutic administration is specifically guideline-recommended for large-volume paracentesis ($>5L$), spontaneous bacterial peritonitis, and HRS/AKI, where it helps prevent complications and improve survival. [Biggins SW, et al. *Hepatology*. 2021;74:1014-1048](#)

Arginine vasopressin (AVP): AVP is inappropriately elevated in cirrhosis due to arterial underfilling and baroreceptor activation, leading to increased water retention and dilutional hyponatremia. This contributes to the formation of ascites and edema.

Ascites: The pathologic accumulation of fluid within the peritoneal cavity, commonly caused by conditions like liver cirrhosis, heart failure, or certain cancers that disrupt the balance of hydrostatic and oncotic pressures. The condition typically presents with abdominal distention, discomfort, and shortness of breath, and can significantly impact a patient's quality of life while also serving as an important diagnostic indicator of underlying disease severity. [Biggins SW, et al. *Hepatology*. 2021;74:1014-1048](#)



Central Venous Pressure (CVP): The pressure in the right atrium and great veins combined, which serves as an indicator of right heart preload and volume status, with normal values ranging from 2-6 mmHg. In cirrhosis, despite total body volume overload, CVP often remains normal or low due to splanchnic vasodilation and venous pooling, making it an unreliable indicator of volume status in these patients, but is a key factor in calculating SVR.

Chronic Kidney Disease (CKD): A progressive loss of kidney function over months to years, defined by a glomerular filtration rate <60 mL/min/1.73m² or evidence of kidney damage for ≥ 3 months, and is typically caused by diabetes, hypertension, or glomerular diseases. CKD is staged from 1-5 based on GFR, with stage 5 (<15 mL/min/1.73m²) representing end-stage kidney disease requiring replacement therapy.

Crystalloid Therapy: Intravenous administration of solutions containing water and electrolytes (like normal saline or lactated Ringer's) that freely cross capillary membranes and distribute throughout the extracellular space. These solutions are used for fluid resuscitation and volume expansion, with the choice between balanced (like lactated Ringer's) versus unbalanced (like normal saline) solutions depending on the clinical scenario and concern for acid-base disturbances.

Damage-Associated Molecular Patterns (DAMPs): Endogenous molecules normally found inside cells but released into the extracellular space when cells are damaged or die through non-programmed cell death pathways like necrosis. Upon release, these molecules bind to pattern recognition receptors on immune cells to trigger inflammatory responses and tissue repair mechanisms, essentially serving as "danger signals" that alert the immune system to tissue damage. *Cullaro G, et al. Liver Transpl. 2020;26:283-293*

Esophageal/Gastric Varices: Abnormally dilated submucosal veins in the lower esophagus and stomach that develop as a complication of portal hypertension, serving as portosystemic collaterals to decompress the high-pressure portal system. These vessels can rupture and cause life-threatening hemorrhage, particularly when they become large (>5 mm) or develop high-risk features like red wale signs. *Garcia-Tsao G, et al. Hepatology. 2017;65:310-335*

Fractional Excretion of Sodium (FENa): The percentage of filtered sodium excreted in urine, calculated using the formula: $(UNa \times PCr)/(PNa \times UCr) \times 100$, where U and P represent urine and plasma concentrations respectively. A value of $<1\%$ suggests prerenal



AKI with appropriate sodium retention, while values $>2\%$ typically indicate ATN or other intrinsic renal causes of kidney injury where sodium handling is impaired.

Fractional Excretion of Urea (FEUrea): the percentage of filtered urea excreted in urine, calculated as $(U_{\text{urea}} \times P_{\text{Cr}}) / (P_{\text{urea}} \times U_{\text{Cr}}) \times 100$, and serves as an alternative to FENA for patients on diuretics. A value $<35\%$ suggests prerenal acute kidney injury, while values $>50\%$ typically indicate acute tubular necrosis, making it potentially useful in differentiating causes of acute kidney injury in patients taking diuretics.

Hepatic Encephalopathy (HE): A neuropsychiatric syndrome that occurs in patients with liver dysfunction, characterized by a spectrum of symptoms ranging from subtle cognitive impairment to coma, caused by the accumulation of neurotoxic substances (particularly ammonia) that would normally be cleared by a healthy liver. *Vilstrup H, et al. Hepatology. 2014;60:715-735*

Hepatic Venous Pressure Gradient (HVPG): The difference between the wedged and free hepatic venous pressures, serving as the gold standard measurement for portal pressure and an important prognostic indicator in liver disease. HVPG values above 10 mmHg indicate clinically significant portal hypertension associated with increased risk of complications like variceal bleeding. *De Franchis R, et al. J Hepatol. 2022;76:959-974*

Hepatorenal Syndrome (HRS): The old name for HRS/AKI. A specific etiology of AKI observed in patients with advanced liver disease. The PH arising from cirrhosis generates a state of systemic vasodilation; to prevent hyperfiltration, renal bed vasculature undergoes hyperconstriction, resulting in a form of functional AKI that typically cannot be recovered by volume re-expansion.

International Normalized Ratio (INR): Standardized measurement of blood coagulation that specifically reflects the activity of the extrinsic pathway and vitamin K-dependent factors, calculated by comparing a patient's prothrombin time to a standardized control value. The INR is particularly useful for monitoring warfarin therapy and assessing liver synthetic function.

Kidney Replacement Therapy (KRT): Otherwise known as renal replacement therapy (RRT). Treatment modalities that artificially perform the essential functions of the kidneys, primarily including hemodialysis, peritoneal dialysis, and kidney transplantation. The utility of KRT in AKI associated with cirrhosis is limited, as longer time spent on dialysis prior to liver transplantation is linked to poorer outcomes post-surgery

Large-Volume Paracentesis (LVP): Therapeutic removal of $>5\text{L}$ of ascitic fluid, requiring intravenous albumin replacement (6-8g per liter removed) to prevent post-paracentesis



circulatory dysfunction. The procedure provides rapid symptom relief of abdominal distention and respiratory compromise, though it doesn't address the underlying cause of ascites formation; per guidelines, LVP is reserved for refractory or tense (Grade 2-3) ascites. [Biggins SW, et al. Hepatology. 2021;74:1014-1048](#)

Mean Arterial Pressure (MAP): Average arterial pressure during a complete cardiac cycle, calculated as one-third systolic pressure plus two-thirds diastolic pressure, or more simply as $(\text{systolic} + 2 \times \text{diastolic})/3$. A normal MAP ranges from 70-100 mmHg and represents the perfusion pressure driving blood flow to organs, with values below 65 mmHg typically indicating inadequate tissue perfusion and requiring intervention in critically ill patients. A MAP of >75 mmHg is a typical target in patients with HRS/AKI in the ICU.

Model for End-Stage Liver Disease (MELD) score: The MELD score (V3.0 currently in use by OPTN) uses serum bilirubin, creatinine, sodium, albumin, and INR to predict 90-day mortality in patients with cirrhosis. A higher MELD score (ranging from 6 to 40) indicates worse liver function and greater mortality risk, with the score being particularly useful for prioritizing liver transplant allocation. <https://www.mdcalc.com/calc/10437/model-end-stage-liver-disease-meld>

Membranoproliferative glomerulonephritis (MPGN): a classification of CKD with a pattern of glomerular injury, characterized by thickening of the glomerular basement membrane, mesangial cell proliferation, and subendothelial deposits. MPGN typically presents with nephrotic syndrome, nephritic syndrome, or both, and can be either primary (idiopathic) or secondary to various conditions including infections, autoimmune diseases, and monoclonal gammopathies. <https://kdigo.org/guidelines/gd/>

Organ Procurement and Transplantation Network (OPTN): OPTN is currently the unified transplant network in the United States that manages organ allocation policies and maintains the national transplant waiting list. The OPTN sets policies for matching deceased donor organs with recipients, collects transplant data, and develops standards for organ recovery and transportation in an attempt to ensure equitable and efficient organ distribution. <https://optn.transplant.hrsa.gov/>

Portal Hypertension: An elevated pressure gradient occurring between the portal vein and inferior vena cava that typically occurs when liver cirrhosis creates resistance to portal blood flow, though it can also be caused by pre-hepatic obstruction or post-hepatic venous congestion. This increased pressure leads to serious complications including the development of varices, ascites, and hepatic encephalopathy, as the body attempts to decompress the portal system through the formation of portosystemic collaterals. [De Franchis R, et al. J Hepatol. 2022;76:959-974](#)



Prerenal Azotemia (PRA): A rapid decline in kidney function caused by decreased renal perfusion due to volume depletion, heart failure, or other causes, characterized by low urine sodium (<20 mEq/L) and FENa <1% as the kidneys attempt to retain sodium and water. The condition is typically reversible with restoration of adequate renal perfusion, distinguishing it from intrinsic AKI etiologies like ATN.

Renin-angiotensin-aldosterone system (RAAS): a hormonal cascade that regulates blood pressure, fluid volume, and electrolyte balance, initiated when low renal perfusion triggers renin release, leading to the conversion of angiotensinogen to angiotensin I and then to angiotensin II, which causes vasoconstriction and stimulates aldosterone release. This system works to increase blood pressure through vasoconstriction, including the renal bed, along with sodium retention and water reabsorption.

Serum Creatinine (SCr): Waste product of muscle metabolism that is freely filtered by the kidneys and serves as a key biomarker of kidney function, with elevated levels indicating decreased glomerular filtration rate and kidney dysfunction.

Spontaneous Bacterial Peritonitis (SBP): A serious infection of ascitic fluid in patients with cirrhosis, typically caused by bacterial translocation from the gut and diagnosed when the ascitic fluid neutrophil count exceeds 250 cells/mm³, even if cultures are negative. SBP presents with fever, abdominal pain, and worsening encephalopathy in about two-thirds of cases, and it carries a high mortality rate if not promptly treated with empiric antibiotics.

Biggins SW, et al. Hepatology. 2021;74:1014-1048

Steatotic Liver Disease (SLD) Classification: Newly updated by the AASLD in 2023, SLD can be classified into four types. Metabolic dysfunction-associated SLD (MASLD) replaces what used to be nonalcoholic fatty liver disease (NAFLD); this can progress into what used to be termed NASH but is now Metabolic dysfunction-associated steatohepatitis (MASH). MetALD is a newer term for patients with MASLD who consume significant quantities of alcohol weekly, and then Cryptogenic SLD, where the cause is unknown.

Sympathetic Nervous System (SNS): In cirrhosis, systemic vasodilation triggers compensatory sympathetic activation, leading to increased heart rate, cardiac output, and renal vasoconstriction with sodium retention. This sympathetic overactivation contributes to portal hypertension, ascites formation, and HRS/AKI.

Systemic Vascular Resistance (SVR): Resistance to blood flow offered by all systemic vasculature except the pulmonary vessels, calculated as (MAP - CVP)/cardiac output, with normal values ranging from 800-1200 dyne·sec·cm⁻⁵. In conditions like cirrhosis, SVR is typically decreased due to pathologic vasodilation.



Vasoconstrictor Therapy for AKI: Therapies used in conjunction with volume expansion to maintain or restore kidney function in patients with functional AKI etiologies such as HRS/AKI in advanced liver disease.

Relevant Practice Guidelines on Cirrhosis, ACLF and Extrahepatic Complications

American Association for the Study of Liver Diseases (AASLD)

- 1) Ascites, SBP and HRS/AKI

https://journals.lww.com/hep/fulltext/2021/08000/diagnosis_evaluation_and_management_of_ascites,.38.aspx

- 2) ACLF

https://journals.lww.com/hep/fulltext/2024/06000/aasld_practice_guidance_on_acute_on_chronic_liver.25.aspx

European Association for the Study of the Liver (EASL)

[https://www.journal-of-hepatology.eu/article/S0168-8278\(18\)31966-4/fulltext](https://www.journal-of-hepatology.eu/article/S0168-8278(18)31966-4/fulltext)

American College of Gastroenterology (ACG)

https://journals.lww.com/ajg/citation/2022/06000/acute_on_chronic_liver_failure.4.aspx

Acute Disease Quality Initiative (ADQI)

[https://www.journal-of-hepatology.eu/article/S0168-8278\(24\)00214-9/fulltext](https://www.journal-of-hepatology.eu/article/S0168-8278(24)00214-9/fulltext)

American Gastroenterological Association

[https://www.cghjournal.org/article/S1542-3565\(22\)00829-1/fulltext](https://www.cghjournal.org/article/S1542-3565(22)00829-1/fulltext)