ACG Acute-on-Chronic Liver Failure Clinical Guidelines
By Tina Hang

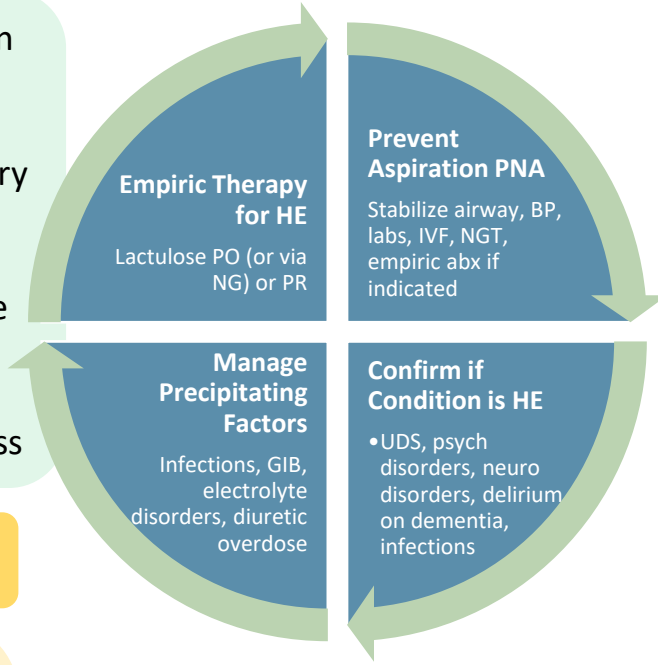
ACLF Definition

- 3 major definitions ⇒ Asian Pacific Association for the Study of the Liver (APASL) vs. European Association for the Study of Liver-Chronic LIver Failure (EASL-CLIF) vs. North American Consortium for the Study of End-Stage Liver Disease (NACSELD)
- Essentially ACLF= possibly reversible condition in those with CLD (± cirrhosis) w/ potential for **multiple organ failure** or **mortality** w/in 3 months without treatment of underlying liver disease, liver support, or liver transplantation
- Admitted patients → NACSELD score a/w futility, EASL-CLIF sequential organ failure assessment score a/w 28d prognostication

		APASL	EASL CLIF-C	NACSELD
ACLF Definition		Liver failure + ascites or HE w/in 4 weeks	Hepatic & extrahepatic organ failure	Extrahepatic organ failure
Organ Failure	**Liver**	T bili ≥ 5mg/ dl +INR ≥ 1.5	T bili > 12 mg/dL	--
	Kidney	AKI Network criteria	Cr ≥ 2.0 mg/dL or RRT	Need for dialysis or other forms RRT
	Brain	West-Haven HE grade 3-4	West-Haven HE grade 3-4	West-Haven HE grade 3-4
	Circulatory	↑lactate	Use of vasopressor	Shock (MAP <60 mmHg or ↓40 mmHg baseline SBP despite adequate fluid resuscitation & CO)
	Respiratory	--	PaO_2/FiO_2 ≤200, SPO_2/FiO_2 ≤ 214, or need for mechanical ventilation	Need for mechanical ventilation

Brain Failure

- Use **dexmedotomidine** for sedation (shorten time to extubation)
- Cirrhosis w/ ACLD requiring mechanical ventilation 2/2 brain conditions or respiratory failure despite optimal therapy ⇒ ⊘ liver transplant listing
- Ventilation in absence of AMS ≠ brain failure
- Discuss **GOC** before onset HE whenever possible
- Monitor for critical care post-traumatic stress



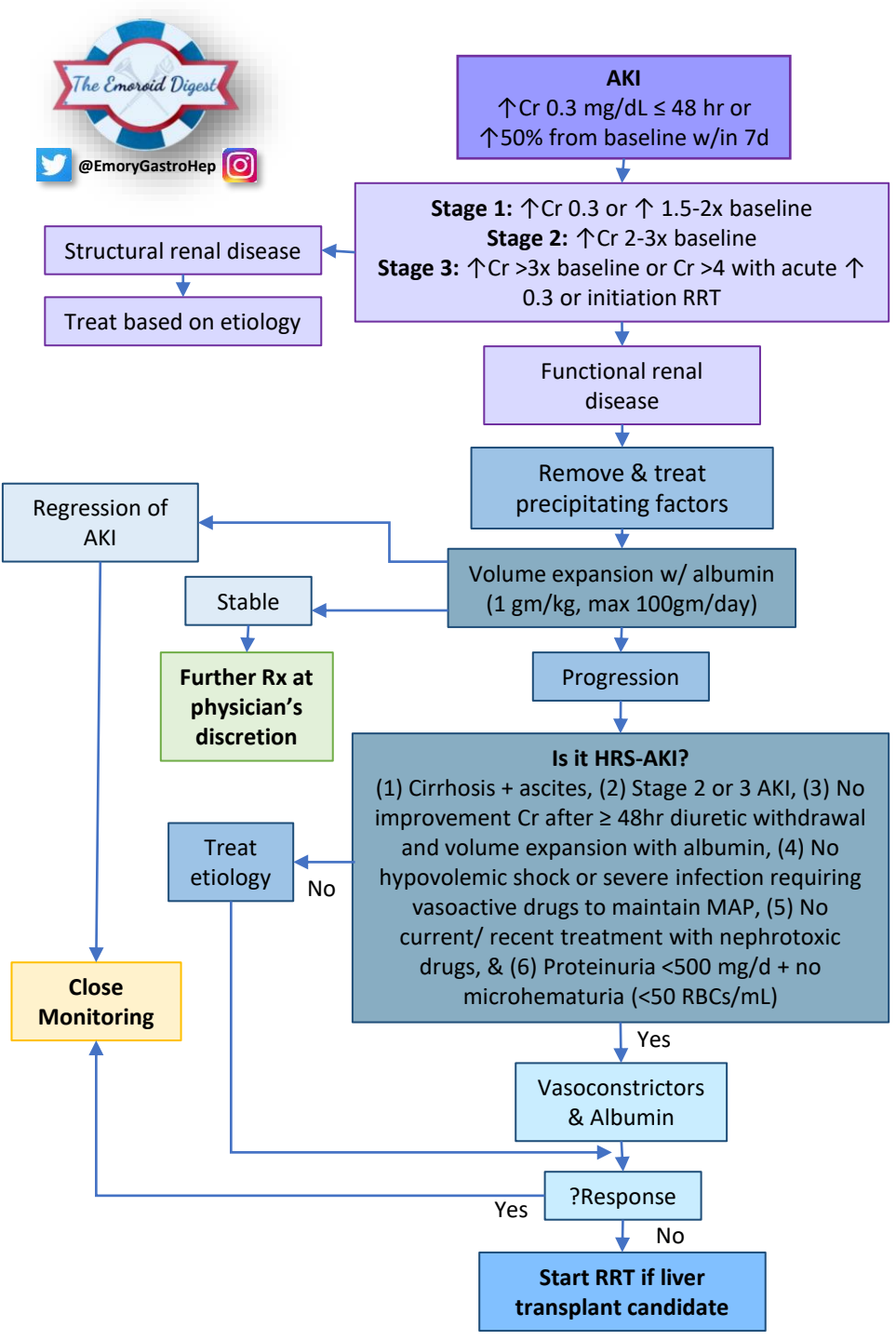
Lung Failure

- Respiratory failure= PaO_2/FiO_2 ≤200, SPO_2/FiO_2 ≤ 214, or need for mechanical ventilation
- Grade 3-4 HE ⇒ intubate for airway management, prevent aspiration, & control ventilation
- ↓ Risk VAP with 30-45° head-end elevation & subglottic suction
- ⊘ Prophylactic abx for VAP
- ⊘ Routine sedatives in grade 3-4 HE
- **PPI** > H2B for stress ulcer ppx in cirrhosis

Circulation Failure

- >MAP may ↓ risk ACLF
- **NE**= vasopressor of choice
- Hyperdynamic state in ACLF a/w ↑risk death

Bajaj, Jasmohan S. MD, MS, FACG1; O'Leary, Jacqueline G. MD, MPH, FACG2; Lai, Jennifer C. MD, MBA3; Wong, Florence MD, FACG4; Long, Millie D. MD, MPH, FACG (Methodologist)5; Wong, Robert J. MD, MS, FACG (Methodologist)6; Kamath, Patrick S. MD7 Acute-on-Chronic Liver Failure Clinical Guidelines, The American Journal of Gastroenterology: February 2022 - Volume 117 - Issue 2 - p 225-252. doi: 10.14309/ajg.0000000000001595



Kidney Failure

- Bacterial infections = most common precipitant for AKI in those w/ cirrhosis + ascites
- Stage 2/3 AKI ⇒ **IV albumin + vasoconstrictors** > albumin alone
- Don't use biomarkers to predict renal failure development
- If ↑Cr when admitted, monitor closely ⇒ ↑ baseline Cr a/w worse renal outcomes & 30-day survival
- HRS-AKI w/o high grade ACLF or disease ⇒ **terlipressin or NE** to ↑ renal function
- Albumin + abx in SBP to prevent HRS-AKI and subsequent organ failures, but ⊘ albumin for non-SBP infections
- Refer for LT assessment early in course of AKI. LT= definitive treatment for HRS-AKI.
- SLK recommended for prolonged hx AKI, RRT >90 days before LT, >60 years old, underlying CKD, & hereditary renal conditions

Coagulation Failure

- **INR ≠ coagulation risk**
- ↑ risk VTE in cirrhosis ⇒ ppx unless contraindication (recent bleed or platelets <50K)
- ⊘ Transfusion in absence of bleeding or planned procedure
- Use thromboelastography (TEG) or rotational TEG (ROTEM) to assess transfusion needs → if not available, can use fibrinogen & platelet levels
- Cryoprecipitate or PCC > FFP (high volume ⇒ ↑ portal HTN, also has anticoagulants)
- Hypercoagulation on TEG/ROTEM= poor prognosis

Infections

- Infections= #1 cause ACLF in West
- Look for infections ⇒ **early treatment** is 🔑
- Nosocomial & fungal infections → ↑risk ACLF & mortality
- ⊘ Foleys to monitor UOP or only for limited mobility → ↑ risk UTI
- If bacterial infection not responding to abx ⇒ think **MDR or fungal infection**
- De-escalate abx once cultures available
- Hx SBP ⇒ abx for 2° SBP ppx
- 1° SBP ppx w/ daily norfloxacin, ciprofloxacin, or trimethoprim- sulfamethoxazole
- **Avoid PPI unless clear indication**
- NSBBs ↓ bacterial translocation, but those with ACLF can't tolerate adequate doses

Alcohol-Associated Hepatitis (AAH)

- Severe AAH (MDF ≥ 32 or MELD >20) ⇒ prednisolone or prednisone 40mg/d PO to ↑ 28-day mortality if no contraindications
- ⊘ pentoxifylline
- **ETOH abstinence** essential for survival >6 mo
- Consider LT in highly selected patients

Drug-Induced Liver Injury (DILI)

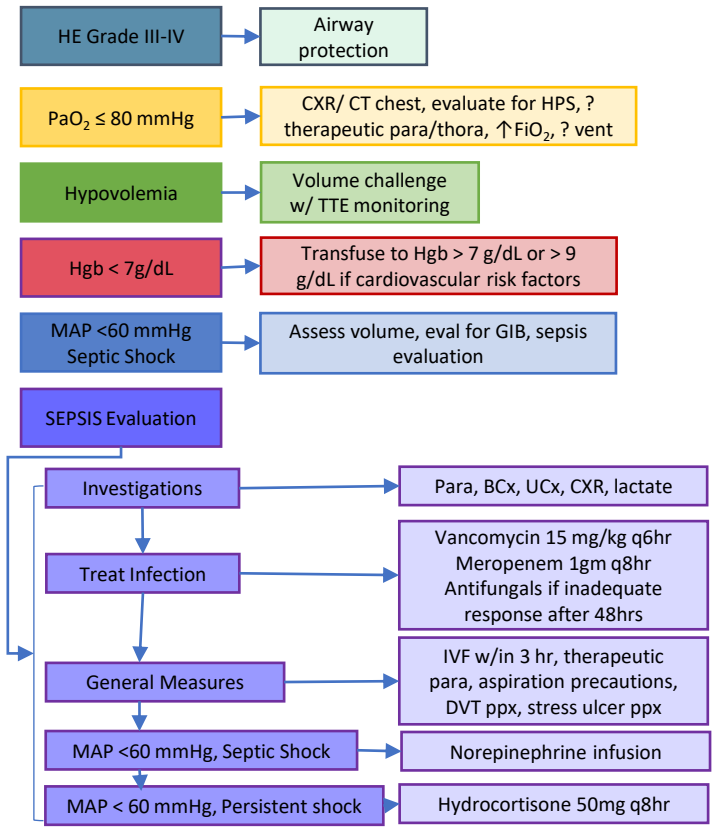
- Most common prescription DILI= **antimicrobials**
- 👀 Complementary and alternative medicine (CAM)
- Onset ACLF ~1 month after taking offending med, but can be delayed for up to 3 months
- >50% mortality for DILI-related ACLF

Viral Hepatitis

- HBV flares= common cause ACLF in Asia ⇒ can present like ALF
- Hepatitis B flare can be spontaneous, due to antiviral discontinuation, antiviral resistance, or from chemotherapy
- Vaccinate CLD patients against hepatitis A & B!
- 👀 HAV & HEV superimposed on CLD or HDV superimposed on HBV

Procedures

- Assess surgical mortality with Mayo Clinic score and VOCAL PENN score
- ACLF RFs after surgery= acute hepatic decompensation + infection
- Can get ACLF with nonsurgical interventions (ie, therapeutic paracentesis, TIPS, endoscopies)
- MELD ≥ 15 ⇒ high risk ACLF with ERCP



Management

- 🔑 Early goal-directed therapy, intravascular volume resuscitation, broad-spectrum antibiotics w/in 1 hour presentation, monitoring of tissue oxygenation, support of failing organs including consideration of artificial liver support and LT in select patients
- **MAP goal ≥ 60 mmHg** in cirrhosis (rather than 65)
- Septic shock in cirrhosis ⇒ empiric **meropenem + vancomycin**
- MAP ≤ 60mm Hg despite volume resuscitation ⇒ +NE ⇒ if still not >60, **+ hydrocortisone 50mg q6**hr
- ⊘ *Routine* use of parenteral nutrition, enteral nutrition, or oral supplements to improve mortality
- ⊘ Daily albumin infusion to maintain serum albumin >3 g/dL
- 5% albumin for rapid volume expansion vs 25% albumin for sustained volume expansion
- ⊘ Strong evidence for artificial liver support systems (ie, MARS and single-pass albumin dialysis)
- Plasma exchange improves survival in ALF, but ?ACLF
- ⊘ Granulocyte colony-stimulating factor to improve mortality
- Insufficient evidence for stem cell therapy
- Cirrhosis + ACLF + ongoing mechanical ventilation for ARDS or brain-related conditions despite optimal therapy ⇒ ⊘ LT
- 🔑 Discuss GOC early in ESLD admissions
- MELD-Na underestimates 1 & 3 mo mortality risk in ACLF