Managing Cirrhosis and Its Complications: Inpatient Strategies for Optimal Care

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Outline

- Why is it important to know about cirrhosis and complications?
- Management of cirrhosis-related complications (Package deal)
  - Hepatic encephalopathy, variceal bleeding, ascites, HRS-AKI
- Management of infections
  - SBP, other infections, consideration for MDROs and SBP prophylaxis
- Access and early consideration for liver transplant
- Diagnostic dilemmas related to cirrhosis
  - Missing a diagnosis of cirrhosis
  - Conflating ACLF with ALF
- Ensuring good outcomes at the time of discharge

Importance of cirrhosis

- Increasing in prevalence worldwide due to the obesity and alcohol pandemic with residual viral hepatitis.
- Long asymptomatic phase where it is often undiagnosed; diagnosis then requires a decompensating event or HCC.
- Greater burden from a clinical, and financial perspective compared to other chronic diseases.
- Very rapid progression from missed infection to acute on chronic liver failure and death if not acted upon.
- Needs early engagement with liver transplant teams and referral centers if not available in your center.

Obradović et al Hepatology 2025, Huang et al Nat Rev Gastro Hep 2023, ACG ACLF Guidelines 2022

- Mr. PS: 58-year-old Veteran with decompensated cirrhosis is on the floor.
- Stable HE on lactulose and rifaximin, ascites controlled on diuretics, and no variceal bleeding history. Last seen 1 month ago with MELD3.0 of 16.
- Seen in the hospital with mild confusion that is not responding to a higher lactulose dose by his wife. No signs of GI bleeding and SpO2>98% room air.

Labs	Outpatient 1M prior	On admission
WBC count	2.6	5.4
Creatinine	0.8	1.2
INR	1.5	1.7
Bilirubin	3.0	4.8
Sodium	139	134
Albumin	3.3	2.6
MELD3.0	16	23
Hematocrit	31	30
Ammonia	Not done because you know better	48 (ULN 32) (done in the ER)

Doubling of WBC count

New AKI: Creatinine↑ >0.3mg/dl over baseline

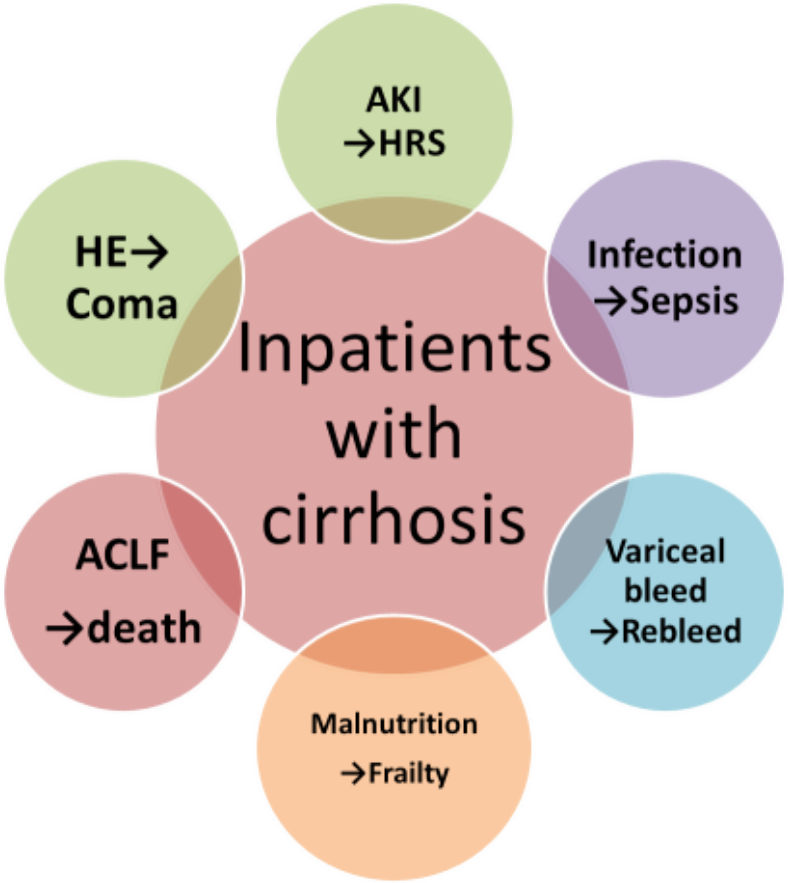
Worsening of the liver disease overall

With the confusion
=
Infection unless proven otherwise

So what to do now to prevent ACLF development?

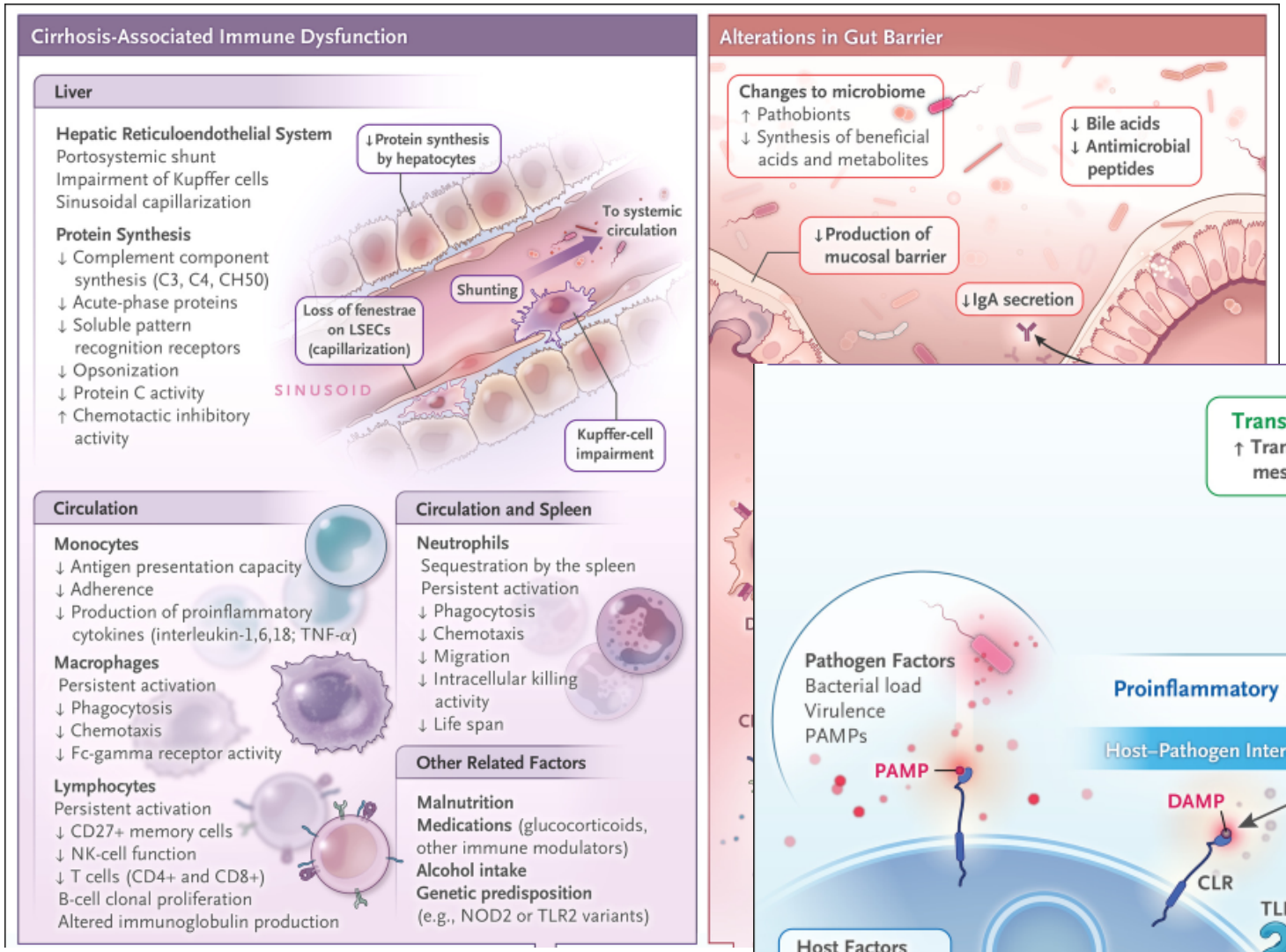
PACKAGE DEAL

- Diagnose and treat infections
- Avoid nosocomial infections
- Prevent HE worsening and aspiration
- Diagnose and treat AKI before ATN or HRS sets in
- Open lines of communication with families, transplant teams, and potential referral sites.



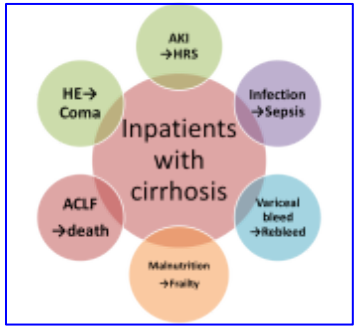
It is an infection unless proven otherwise!

Multiple levels where cirrhosis predisposes to infections



Bajaj et al, NEJM 2021

Clues that can indicate infections in cirrhosis

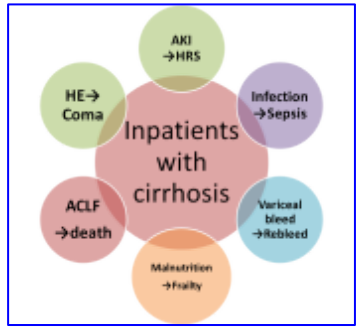


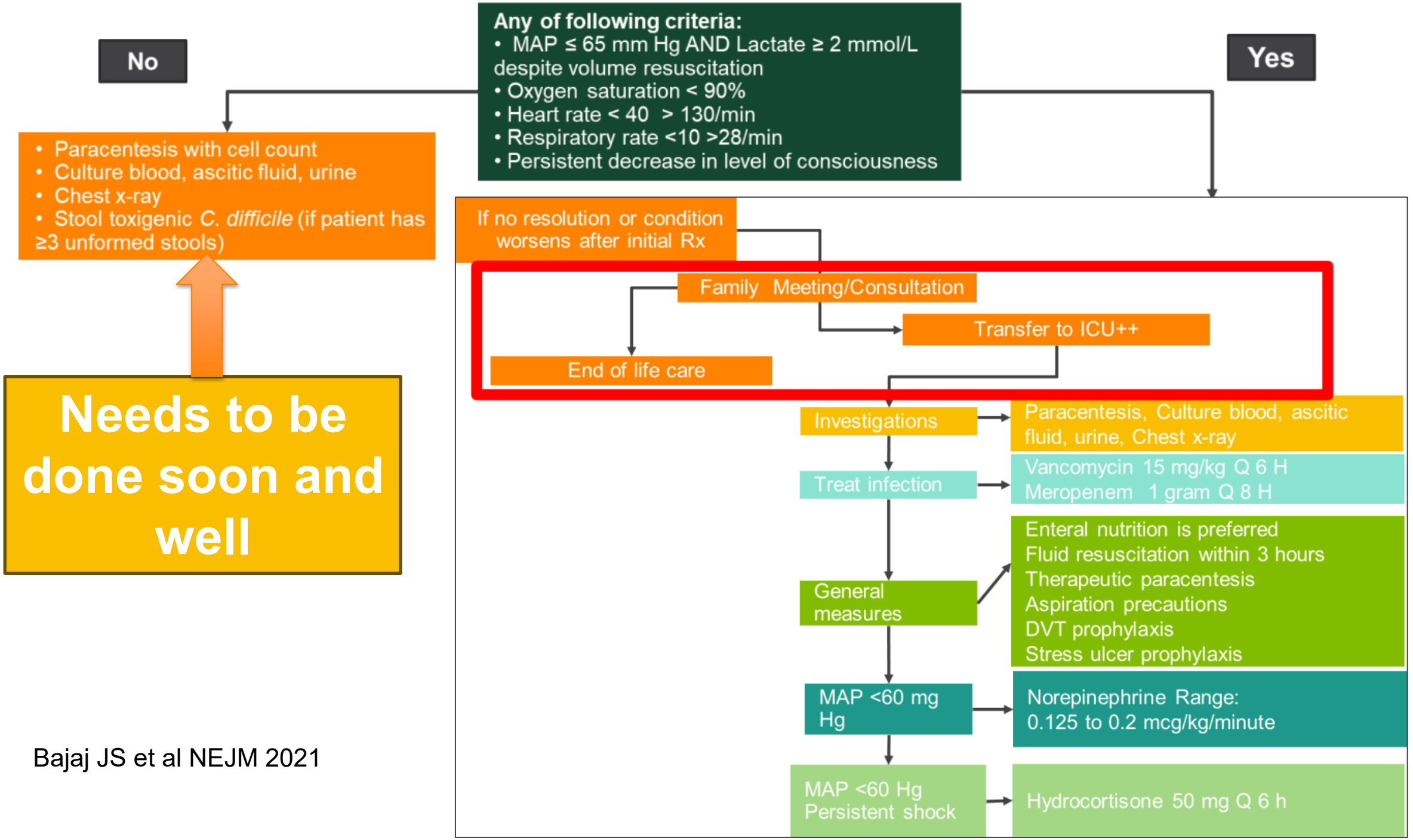
- Usual signs of infection may be absent
  - Altered mental status or hepatic encephalopathy ☑
  - Acute kidney injury ☑
  - Increase in WBC count may not be dramatic due to hypersplenism ☑

Important infections in cirrhosis:

- ✓ Spontaneous bacterial peritonitis
- ✓ UTI
- ✓ Respiratory tract infections
- ✓ Spontaneous bacteremia
- ✓ Skin and soft-tissue infections
- ✓ CDI

If infections are not dealt with soon→ dominoes start falling quickly!





Bajaj JS et al NEJM 2021

ACG ACLF Guideline Recommendations: Infections

- Check for infection in hospitalized patients.
- In suspected infection, we suggest early antibiotics
- In patients not responding to antibiotic therapy, we recommend suspicion of a resistant organism or fungal infection
- In SBP albumin with antibiotics to prevent AKI and subsequent organ failures but not in other infections.

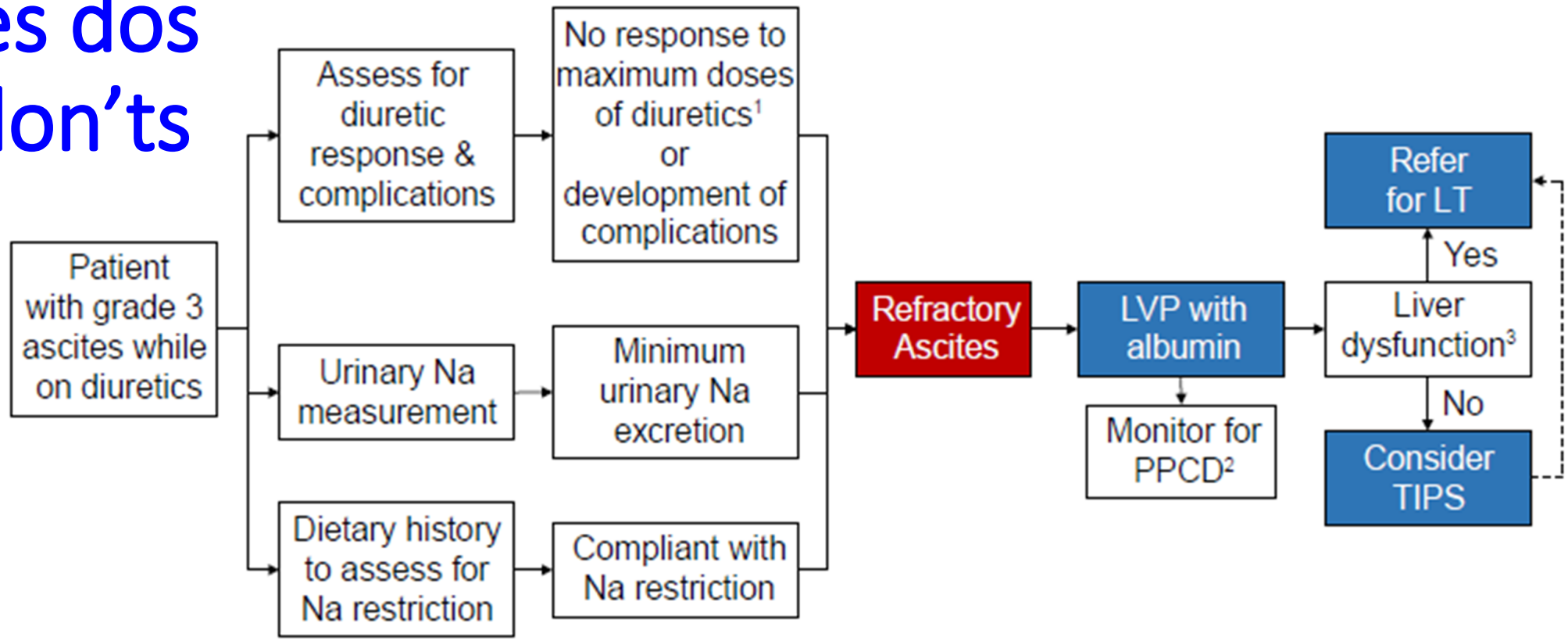
- ✓ Early broad-spectrum antibiotics following local sensitivities and after drawing cultures
  - ✓ Patient improving and sensitivities back? Narrow spectrum
  - ✓ Patient worsening? Broaden further, or add antifungal
- ✓ Avoid unnecessary albumin and be vigilant for nosocomial infections

Ascites, Refractory Ascites, AKI and HRS-AKI

A progression to avoid

Hint: teach house-staff how to do paracentesis!

Ascites dos and don'ts



- A timely tap to exclude SBP and ensure patients have relief is needed
- This will help avoid pneumonia, increase mobility, and improve nutrition
- Prevent PPCD by albumin infusion (6- 8 g/liter) during LVP of >5 L to avoid AKI
- LVP is the first- line treatment for RA but LT should be considered

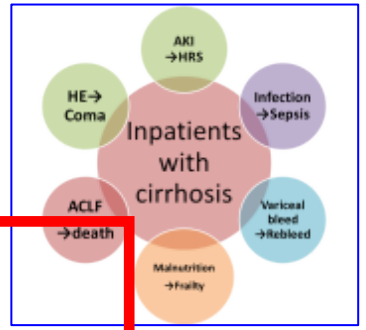
Biggins et al Hepatology 2021

Stages of AKI…very dynamic if ignored!

AKI Stage	Description
Stage 1	Increase of creatinine ≥0.3 mg/dL up to 2- fold of baseline
Stage 2	Increase in creatinine between 2- fold and 3- fold of baseline
Stage 3	Increase in creatinine >3- fold of baseline or creatinine >4 mg/dL (353.6 µmol/L) with an acute increase≥0.3 mg/dL (26.5 µmol/L) or initiation of RRT

Is all AKI HRS?....NO

- ✓ AKI + No response after diuretic withdrawal & albumin for 24 hours
- ✓ No shock, organic/structural renal disease or nephrotoxic druguse



AKI
Stage 2 or 3

Risk factor management

Full septic workup including diagnostic paracentesis

Infection suspected

Empirical antibiotics

Stop diuretics and beta blockers, adjust lactulose dose, or stop if necessary

Albumin at a dose of 1g/kg of body weight/day, max 100g, for 2 days

Resolution

Yes

Monitor

No

Meets the criteria for HRS

Vasoconstrictor therapy candidate? Assess respiratory status, ACLF grade, and creatinine level

No

Assess for liver transplant or palliation

Yes

Terlipressin and albumin

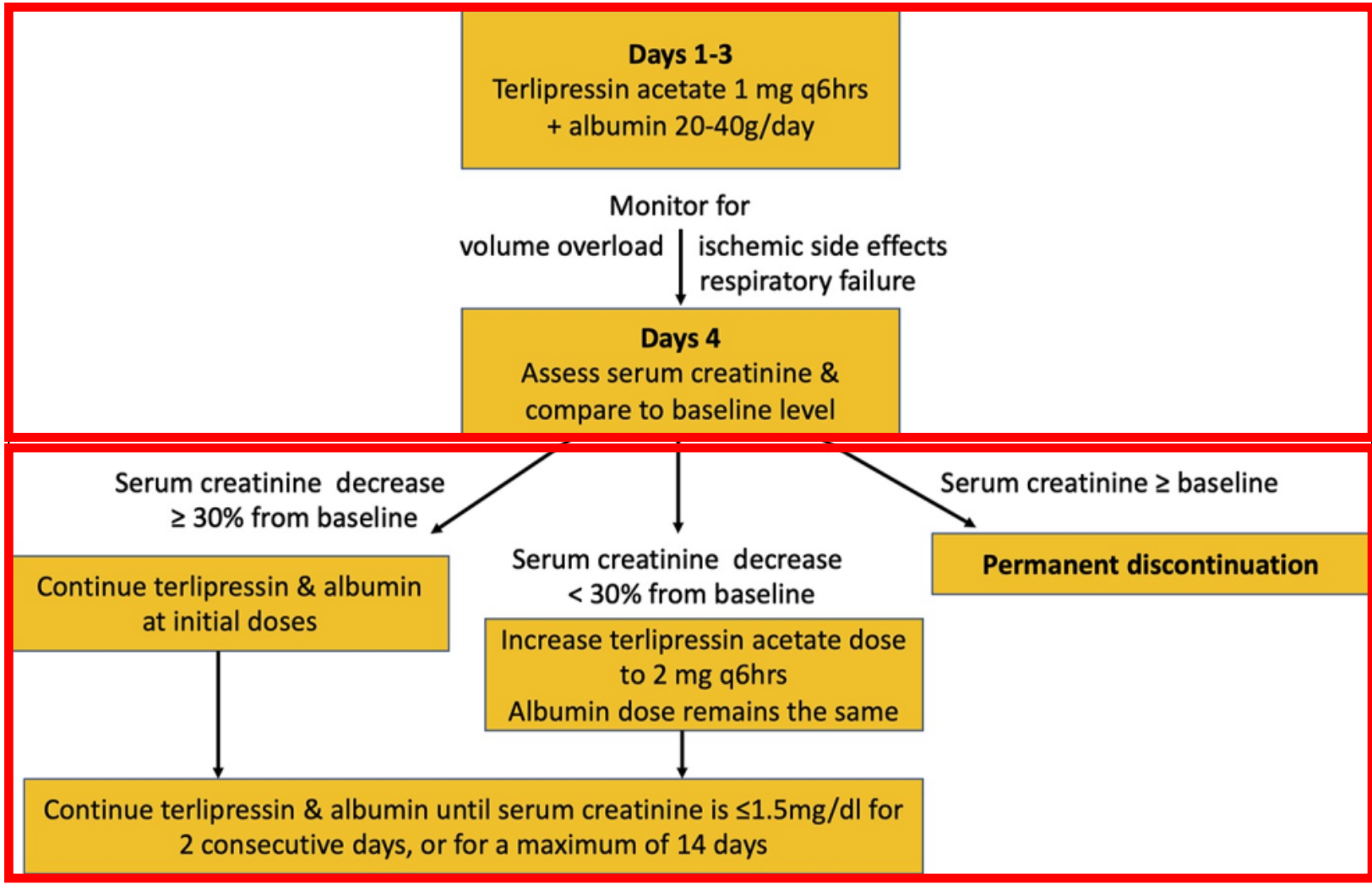
Assess for liver transplant

Wong and Kwo AJG 2023

Should everyone get terlipressin…not so fast!

Reconsider or is contraindicated

- ✓ Pre-Rx Creatinine >5mg/dl
- ✓ Pre-Rx Sp02<90%
- ✓ ACLF-3 or higher
- ✓ Ischemic conditions
- ✓ Unclear diagnosis of HRS-AKI



Wong and Kwo AJG 2023, Wong et al NEJM 2021

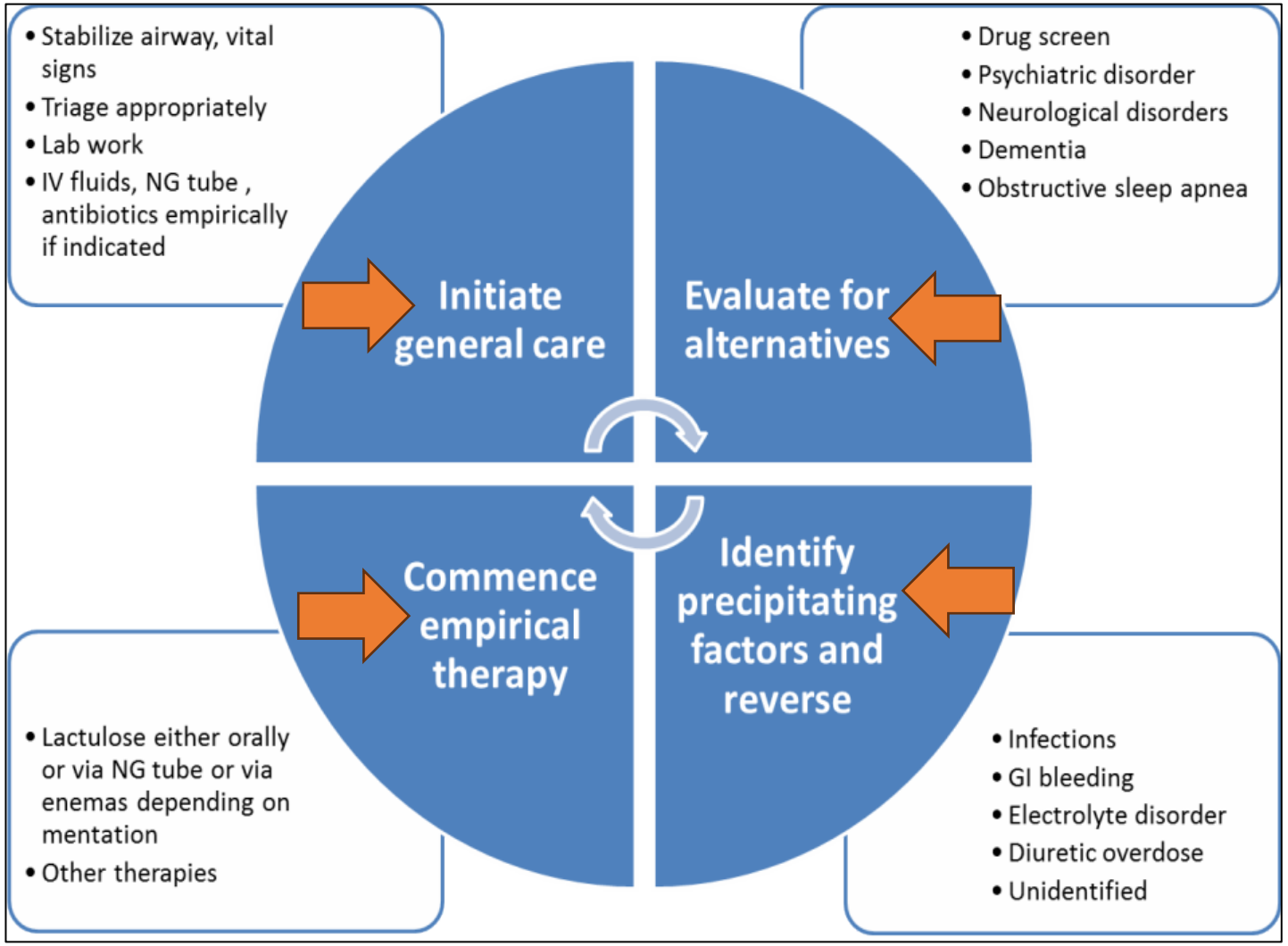
Confusion

Is it HE? Or not….?

Overt HE: Important Points During the Acute Episode

What to avoid

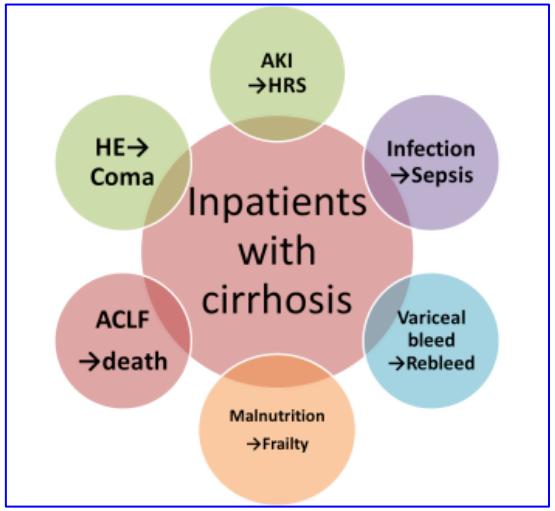
- Ammonia levels instead of clinical exam
- Unnecessary head imaging
- Aspiration pneumonia
- Too much lactulose → dehydration & hypernatremia
- Delaying advanced care planning & transplant evaluation.



Acharya et al Am J Gastro 2018, AASLD/EASL Guidelines 2014, Bajaj et al NACSELD APT 2018, Rahimi et al 2022

Expecting HE to improve without fixing the precipitant

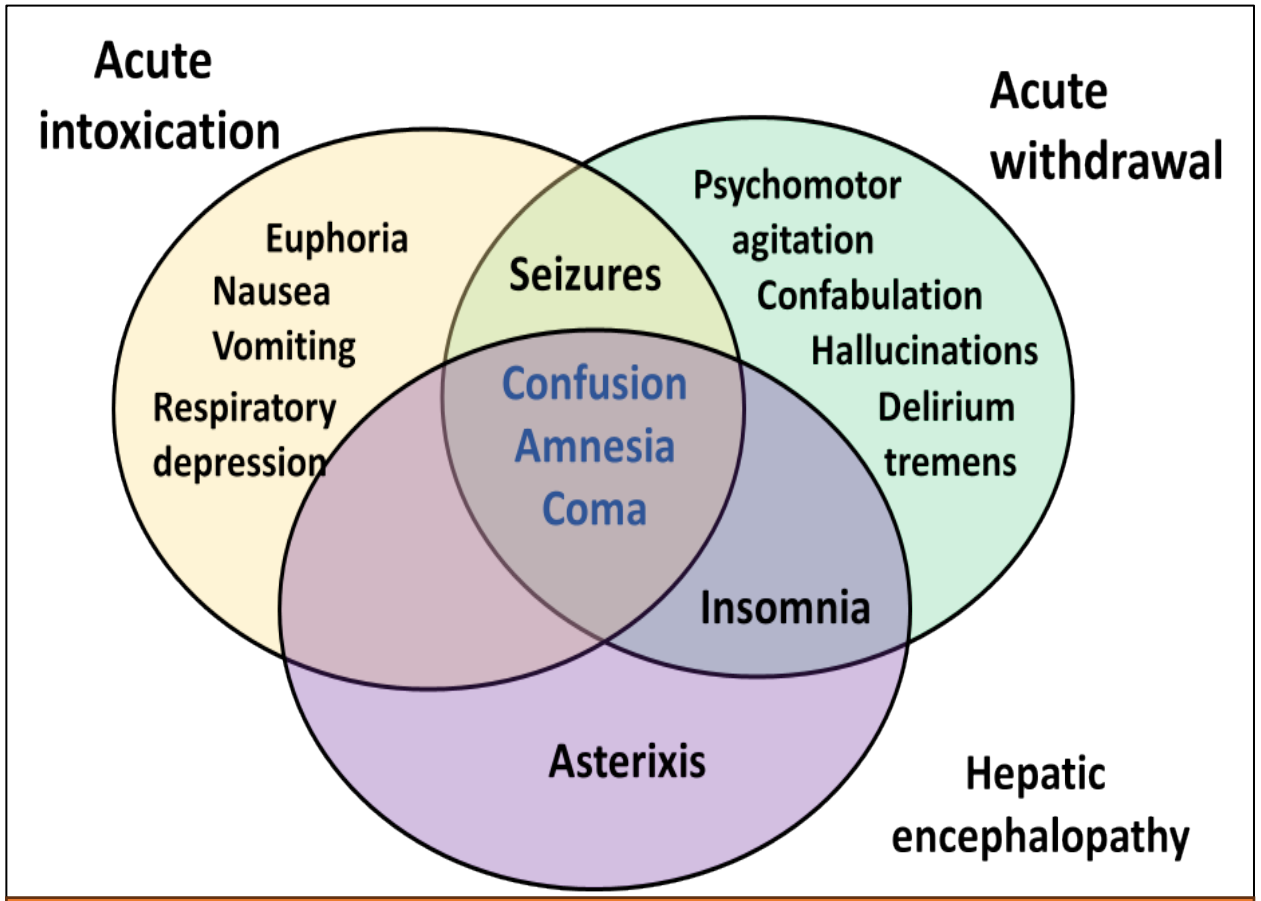
= Sisyphean task!



What is unlikely to be HE? Important role of Alcohol

Unlikely cirrhosis-related HE

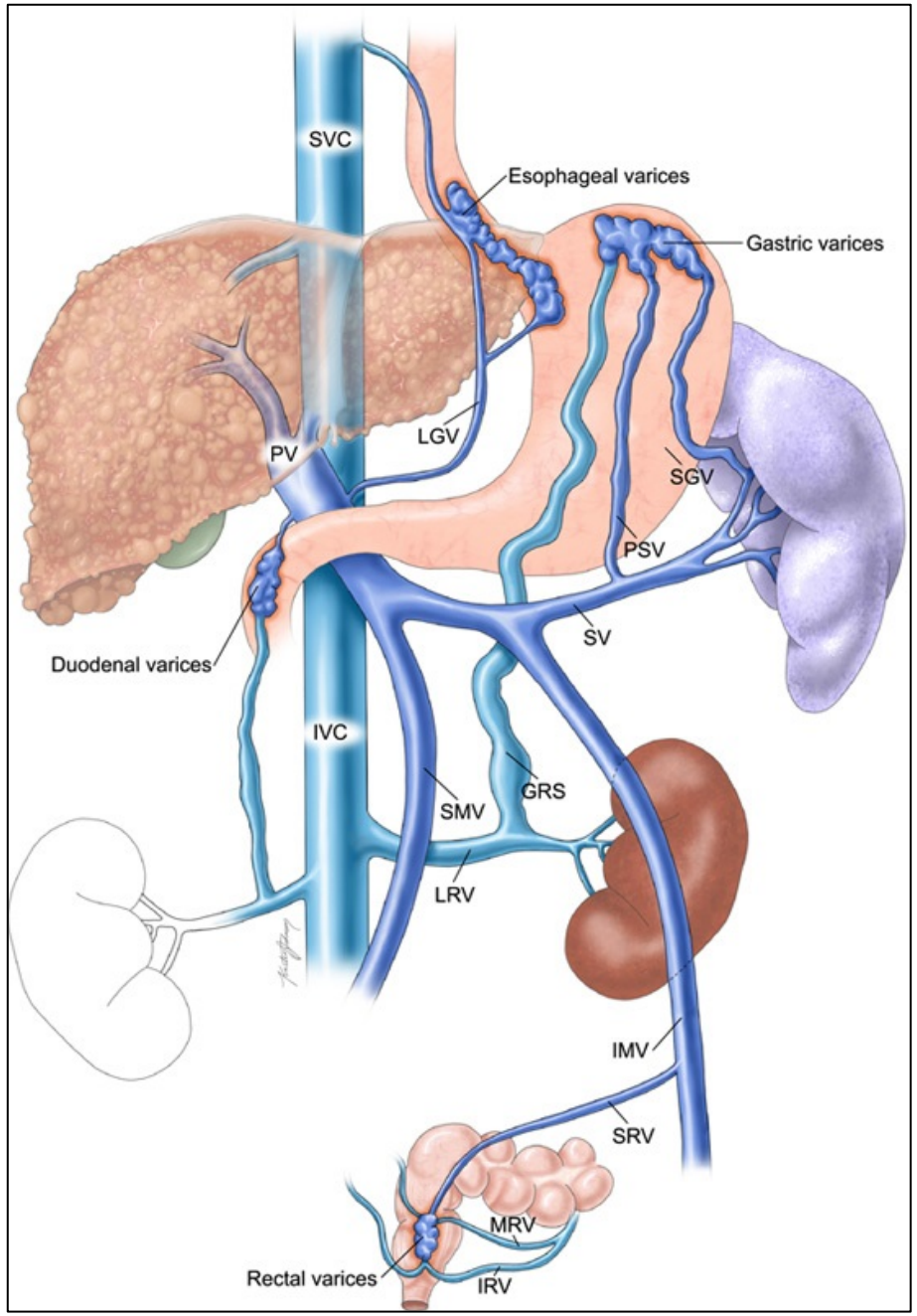
- Unclear history of cirrhosis
- Very rapid liver failure
- New-onset focal neurological deficits
- Seizures
- Recent/current alcohol or illicit drug use
- Other clinical situations where other conditions are more likely
- Normal ammonia levels in a comatose patient*



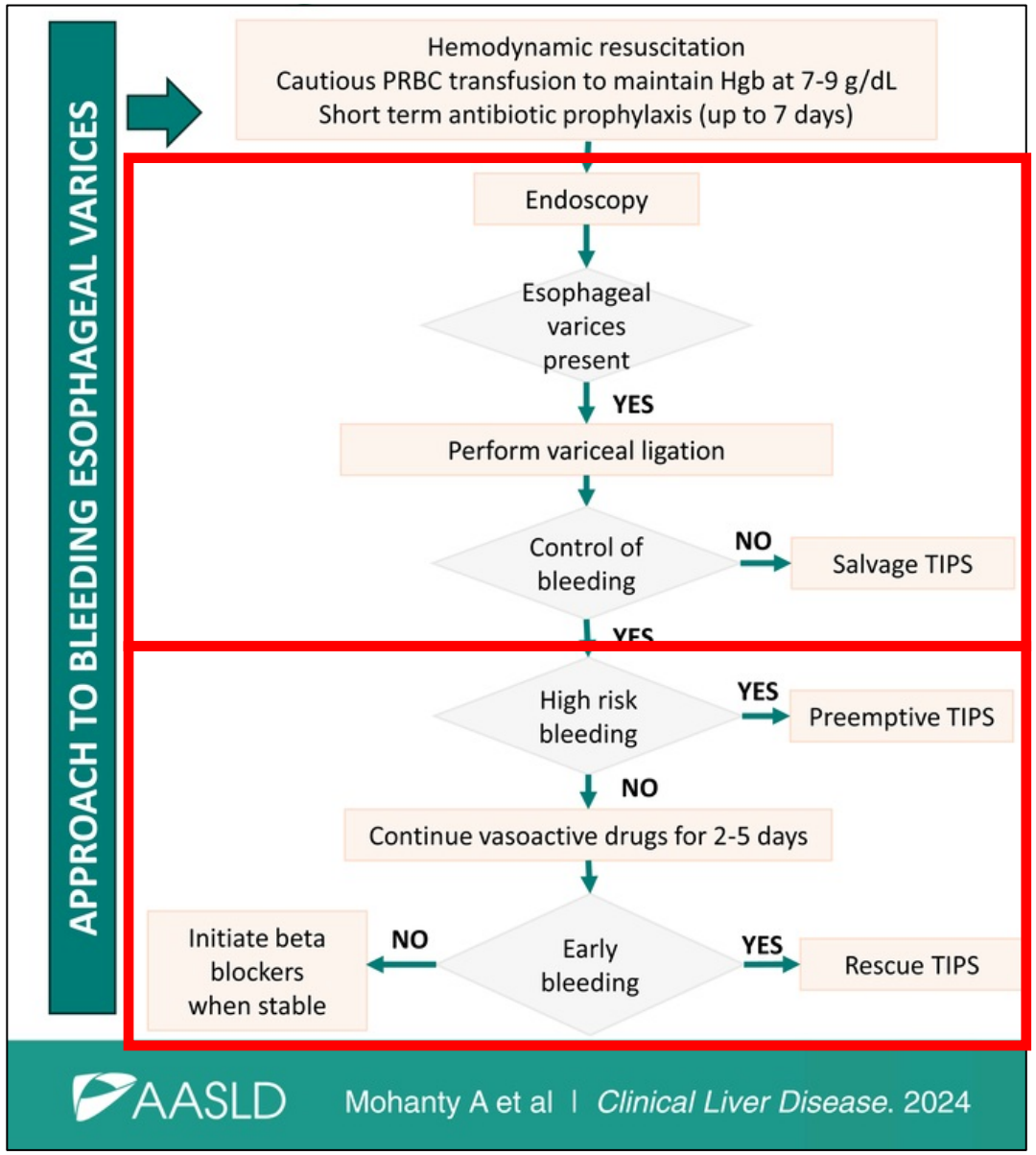
- Early involvement of mental health and substance abuse specialists
- CIWA protocol, and nutrition

Variceal bleeding…going but not totally gone!

Patients are also prone to acid peptic diseases



- Presentation: Melena, coffee grounds, or hematemesis
- Priorities
  - Airway support, intubate if needed.
  - Hemodynamic support with fluids
  - ICU or stepdown monitoring
- Differentials
  - Acid peptic disease
  - Mallory Weiss tears
- Pre-endoscopy medications
  - IV PPI
  - IV somatostatin analogues
  - IV ceftriaxone
  - IV erythromycin if high volume/clots suspected
- Transfuse cautiously till Hgb 7-9 g/dl



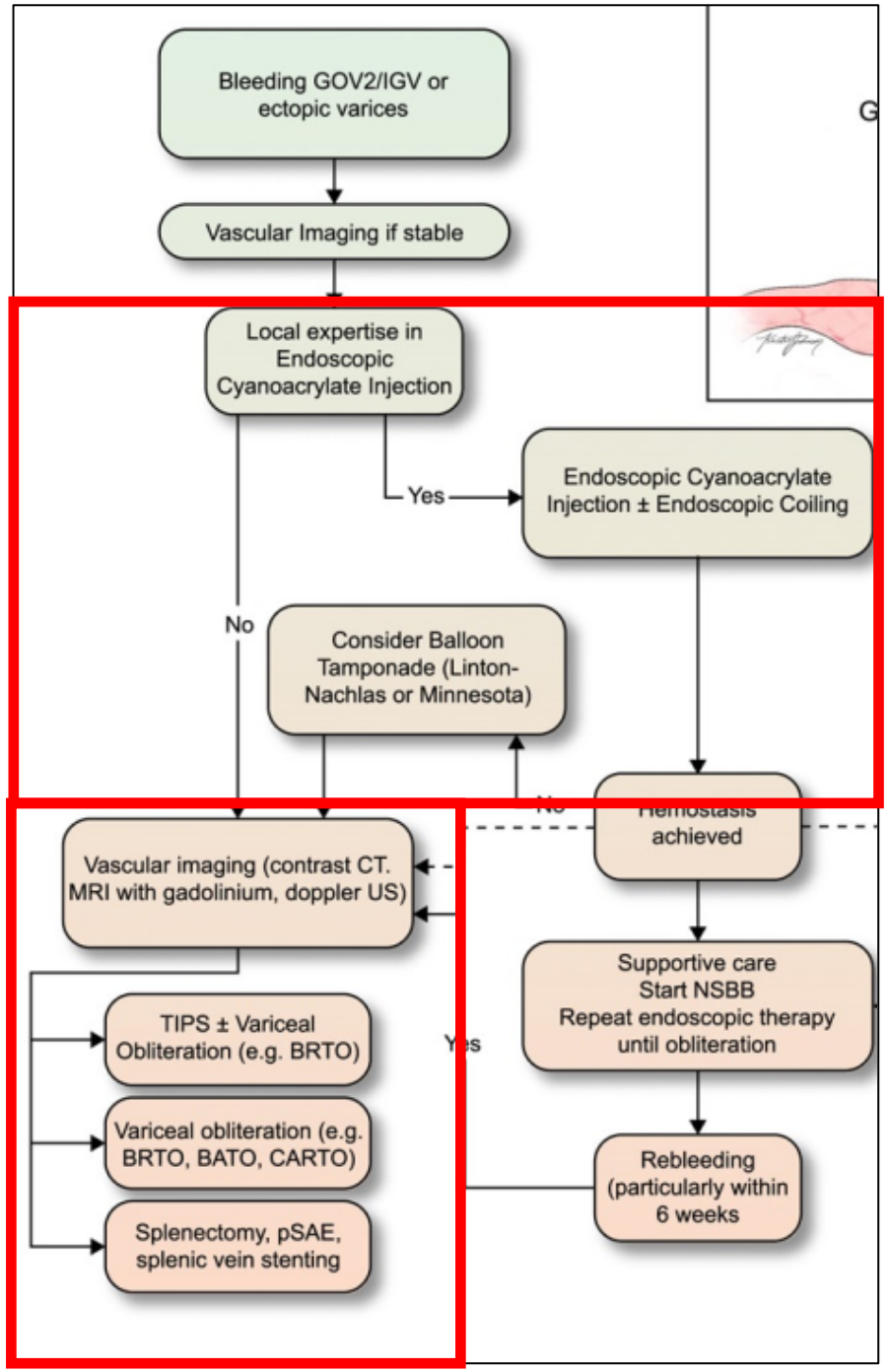
Esophageal variceal bleeding

- What if bleeding does not stop?
  - Balloon tamponade as a bridge to urgent TIPS
- TIPS in esophageal variceal bleeding?
  - Salvage: Initial treatment not working
  - Pre-emptive: initial treatment worked but still have high-risk stigmata for re-bleeding
  - Rescue: Early re-bleeding within 2-5 days

Mohanty et al CLD 2024, Kaplan et al Hepatology 2024 AASLD Guidelines

Gastro-fundal variceal bleeding

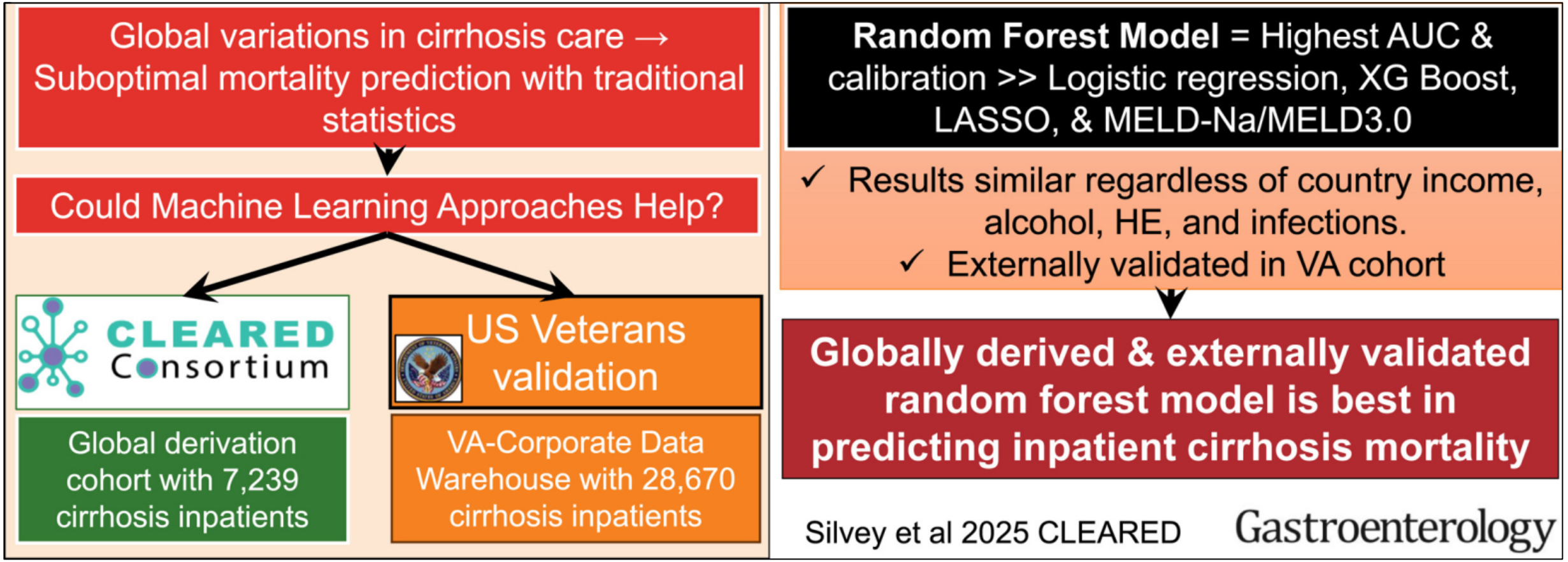
- Local expertise is key
- Comfort with cyanoacrylate injection / coil?
- Availability of TIPS/RTO
  - TIPS>>RTO when
    - Liver function maintained
    - Large varices & ascites
    - PVT
  - RTO>>TIPS when
    - Prior HE
    - Poor liver function



Mohanty et al CLD 2024, Kaplan et al 2024 AASLD Guidelines

Important issues, caveats and variations

Using clinical variables on day of admission: Machine learning >>> traditional statistics for mortality prediction



MODEL freely available: https://silveys.shinyapps.io/app_cleared/

Issue with diagnosis of cirrhosis in inpatients

Everyone's a suspect: MISSING IT

- Background prevalence is high
- 10-13% of patients with dementia had undiagnosed cirrhosis and ?HE
- Look for low platelet count and albumin and high FIB-4 in patients seen for other conditions
- Higher risk in
  - Diabetes
  - Other components of metabolic syndrome
  - Alcohol use disorder

Assumed: Acute liver failure vs ACLF

	Acute Liver Failure	ACLF
Background Liver Disease severity	**No chronic liver disease**	**Chronic Liver disease or cirrhosis**
Insults	Viral hepatitis, Medications,	Viral infection or flare, Infections, DILI, Alcohol, Surgery, TIPS
Hepatic failure required	Yes	Yes
Extra-hepatic Organ failure needed	No, even milder grades of HE are considered diagnostic	Yes
Course	High rate of death with infections and cerebral edema	High rate of death due to hepatic and extra-hepatic organ failure
Transplant suitability	Status 1 (UNOS US-based)	Priority based on MELD-Na score.

Huang et al Nat Rev Gastro Hep 2023,

Things to remember at the time of discharge, otherwise, patients will be readmitted

- General: Ensure follow-up appointment with GI/Hepatology
- HE: ensure medication(s) in hand, counsel patient and family, ensure underlying factor(s) behind episodes are addressed.
- Variceal bleeding: Complete Abx prophylaxis, Stop PPI, start carvedilol & schedule f/u EGD
- Ascites/SBP/AKI: Optimal diuretics, consideration for TIPS or taps as needed, re-evaluate prophylaxis
- Involve other team members: Substance abuse, nutrition, physical therapy, IR, PMD, liver transplant team

What happened to Mr. PS?

- **Responsive team**

✓ Rapid paracentesis found SBP, and blood/ascites cultures sent

✓

✓

✓

day 2 and was discharged day 4 with outpatient antibiotics sensitive to the cultures.

✓Transplant work-up initiated.

- **Team that needs more education**

×IR busy, paracentesis took >24 hours

AKI and hypoxia.

×Broad spectrum antibiotics started but patient needed intubation.

×Family meeting called, dialysis not initiated, and patient passed away.

A few hours and ensuring awareness can make all the difference!

Take home points

- Cirrhosis is often hidden in plain sight…do not miss it!
- Rapid, flexible, and team-based response is needed to prevent ACLF
- Early need for LT or palliative care input
- Complications come as an unfortunate “Package Deal”
- Everything is due to an infection unless proven otherwise
- It is better to de-escalate antibiotics than wait to escalate.
- Not all confusion is HE and not all high creatinine is HRS-AKI.
- UGI bleeding is not always variceal so change medicines accordingly
- Antibiotic resistance is a pandemic, and cirrhosis is the tip of the spear
- Our responsibility does not end at discharge
- Cirrhosis care is team-based, where communication and time are key

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