Preventing First Decompensation *and* Further Decompensation in Cirrhosis (Some Tips from the Baveno VII Workshop)

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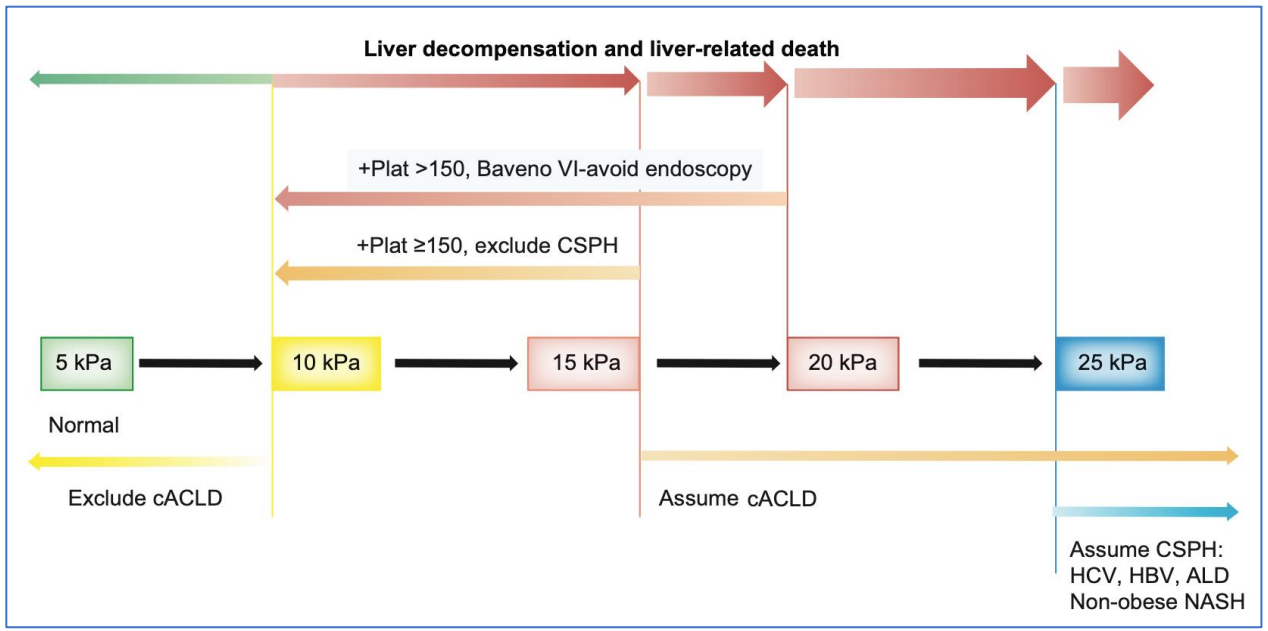
cACLD, CSPH, and the Rule of Five

- **Compensated advanced chronic liver disease (cACLD):** the continuum of severe fibrosis and cirrhosis in patients w/ chronic liver disease
- **Clinically significant portal hypertension (CSPH):** HVPG ≥10 mmHg in viral or EtOH related cirrhosis, and is associated w/ greater risk of decompensation in patients with compensated cirrhosis

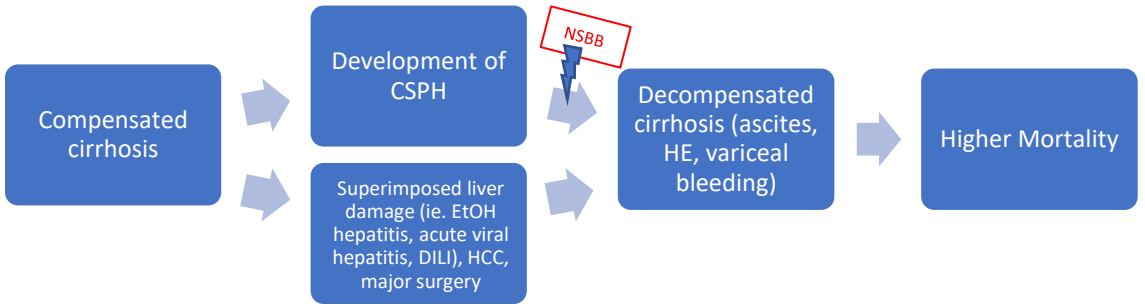
- **The Rule of Five for LSM by TE:** denotes the dose-response relationship between liver stiffness measurement (LSM) by transient elastography (TE) and higher risks of decompensation, liver related event, or mortality, *regardless of etiology of liver disease* (10-15-20-25 kPA)
- Using LSM, we can stratify risk of CSPH and decompensation



Citation: de Franchis R, Bosch J, Garcia-Tsao G, Reiberger T, Ripoll C; Baveno VII Faculty. Baveno VII - Renewing consensus in portal hypertension. J Hepatol. 2022 Apr;76(4):959-974. doi: 10.1016/j.jhep.2021.12.022. Epub 2021 Dec 30. PMID: 35120736.

Prevention of (first) decompensation

- **Decompensation events** refer to overt ascites (or pleural effusion w/ SAAG >1.1), overt hepatic encephalopathy, and variceal bleeding, and are complications of portal hypertension.
  - More evidence is needed to consider jaundice, minimal ascites, minimal hepatic encephalopathy, and portal hypertensive gastropathy as decompensation.
- **Why is preventing decompensation important?**
  - Transition from compensated to decompensated cirrhosis leads to increased mortality
  - ESPECIALLY important in compensated patients with CSPH and/or esophageal or gastric varices because of their increased risk of developing decompensation.

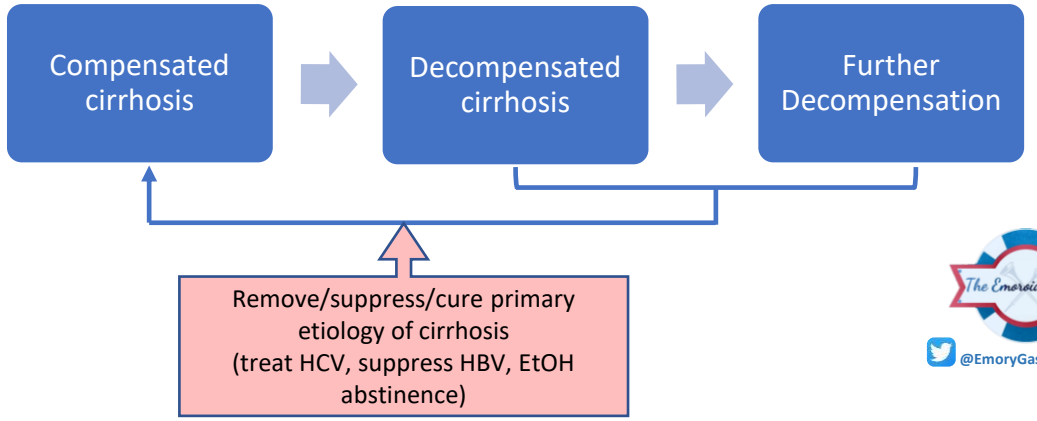


- **How can we prevent first clinical decompensation?**
  - **Nonselective β-blockers (NSBB)** reduce HVPG, prevent decompensation and improve survival
  - NSBB should be considered in patients with CSPH
- Carvedilol (6.25-25 mg QD) is preferred > propranolol (20-160 mg BID) or nadolol (20-160 mg QD), and is more effective in ↓ HVPG
- Compensated cirrhosis on NSBB do not need EGD for variceal screening, unless intolerant or CI to NSBB

- **WHAT is the evidence for NSBB in CSPH?**
  - *Villanueva et al.* in the ***PREDESCI trial*** investigated probability of developing decompensation or death in RCT comparing placebo vs **β-blockers** (carvedilol or propranolol) in patients with compensated cirrhosis and CSPH (HVPG ≥10 mmHg)
  - Endpoint of decompensation or death was 27% in placebo vs. 16% in β-blocker group (HR 0.51 w/ ARR 11%, NNT = 9)

Preventing Further Decompensation

- **What events define further decompensation?**
  - A 2nd portal hypertension driven decompensating event (ascites, variceal bleeding, or hepatic encephalopathy)
  - Recurrent variceal bleeding, recurrent ascites (requiring ≥3 large volume paracenteses in 1 year), or recurrent hepatic encephalopathy
  - SBP and/or HRS-AKI
  - Jaundice
  - New ascites, encephalopathy, or jaundice following recovery from prior variceal bleeding, provided these events were not present at time of hemorrhage
- **Further decompensation** in cirrhosis is associated w/ an **even higher mortality** than that associated with first decompensation.
- Bacterial infections may cause further decompensation and should be ruled out in patients hospitalized with decompensation. Antibiotics should be promptly started.
- Frailty and sarcopenia predict mortality in decompensated cirrhosis and efforts should be made to counsel patients on nutrition and regular exercise.



Goal in patients with decompensated cirrhosis is to prevent further decompensation and aim to achieve "recompensation".

Preventing further decompensation in patients with ascites

- Patients w/ decompensated cirrhosis should be considered for transplant
- Patients w/ ascites not on NSBB should undergo screening EGD
- Consider TIPS in patients w/ recurrent ascites (≥3 LVP in 1 year)
- Risk of variceal bleeding is increased in patients w/ ascites and high risk varices (Child C, large ≥5 mm varices, or red wale signs) and prevention of first variceal bleed w/ NSBB is preferred over endoscopic variceal ligation (EVL)
  - *McDowell et al. AP&T 2021.*, performed RCT comparing EVL vs carvedilol in preventing 1st variceal bleed
    - no difference in decompensation of liver disease, but carvedilol group had better survival compared to EVL
  - NSBB may be beneficial in patients w/ ascites and low risk varices (not Child C, <5 mm varices, no red wale sign)
- NSBB is not contraindicated in patients w/ ascites, but should be dose-reduced or discontinued in *refractory ascites* (*Tellez et al. J Hepatol 2020.*), persistently low BP (SBP <90 or MAP <65) and/or HRS-AKI.

Preventing recurrent variceal hemorrhage

- Combination of NSBB or carvedilol AND EVL is 1st line for prevention of recurrent variceal bleeding.
- TIPS is recommended if rebleeding occurs despite NSBB and EVL, or if patient is unable to tolerate NSBB

Preventing recurrent bleeding from PHG

- NSBB is 1st line for preventing recurrent bleeding from portal hypertensive gastropathy (PHG)
- Endoscopic therapy (APC or hemospray) may also be used
- TIPS can be considered in transfusion dependent PHG despite NSBB or endoscopy therapy

Recompensation

- Recompensation describes partial regression of structural and functional changes of cirrhosis following removal of etiology of cirrhosis.
- Must fulfill all of the following criteria:
  1. Removal/suppression/cure of primary etiology of cirrhosis
  2. Resolution of ascites (off diuretic), encephalopathy (off lactulose/rifaximin), and absence of recurrent variceal bleeding (for at least 12 months)
  3. Improvement in liver tests, including Albumin, INR, and bilirubin
- NSBB should not be discontinued despite recompensation because CSPH may persist. NSBB can be discontinued if CSPH resolves.
- Recompensation is NOT evident if there is resolution of ascites (due to diuretics or TIPS), absence of recurrent variceal bleeding (while on NSBB+EVL or after TIPS)