

Updated Guidelines for the Management of Portal Hypertension

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Disclosures

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- Lipocene (clinical trial site PI)

Practice Guidance



AASLD Practice Guidance on risk stratification and management of portal hypertension and varices in cirrhosis

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BOX 1 What's new

Recognition of the concept of compensated advanced chronic liver disease (cACLD), a shift away from the requirement of a histological or radiological diagnosis of cirrhosis for initial patient risk stratification

Codification of methodology to use noninvasive assessments to identify clinically significant portal hypertension (CSPH)

Endorsement of a change in paradigm with the recommendation of early utilization of nonselective beta-blocker therapy when CSPH is identified in order to decrease the risk of cirrhosis decompensation

Updated guidance on the use blood and blood products during initial resuscitation of acute variceal hemorrhage

Endorsement of preemptive TIPS in select patient subsets

Guidance on the use of upper endoscopy prior to transesophageal echocardiography

Two stages of cirrhosis

Compensated

- Absence of ascites, HE, or acute variceal hemorrhage

**Median survival
12 years**

Decompensated

- Overt ascites,
- Variceal hemorrhage, or
- Overt hepatic encephalopathy

**Median survival
1.5 years**



A New Entity :

“Advanced Chronic Liver Disease (ACL D)”

Non-invasive staging of chronic liver disease	No cACL D	Possible cACL D	Highly suggestive of cACL D	cACL D	
Liver stiffness (kPa)	<10	10-15	15-20	20-25	>25
Platelet count (K/mm ³)	NR	NR	If <110 = CSPH	If <150 = CSPH	CSPH**

“Rule of Five”

Risk of decompensation

Alternatives to transient elastography

Cut-offs to rule out cACL D
 MRE: <3.0 kPa
 pSWE/ARFI: <1.3-1.7 m/s
 2D-SWE: <7-8 kPa
 ELF: <7.7

Cut-offs to diagnose cACL D
 MRE: ≥3-4 kPa
 pSWE/ARFI: ≥1.7-2.1 m/s
 2D-SWE: 13-16 kPa
 ELF: ≥9.8

Cut-offs for prediction of varices, decompensation:
 MRE ≥4-5 kPa
 pSWE (ARFI): ≥2.4 m/s
 2D-SWE: ≥17-20 kPa
 ELF: ≥10.5-11.3

* CSPH = clinically significant portal hypertension

(HVPG ≥10 mmHg; varices on endoscopy; portosystemic collaterals; hepatofugal flow on imaging)

A New Entity :

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Non-invasive staging of chronic liver disease	No cACL D	Possible cACL D
Liver stiffness (kPa)	<10	10-15
Platelet count (K/mm ³)	NR	NR

Consider repeating this annually in whom underlying disease is not controlled

Risk of decompensation

* CSPH = clinically significant portal hypertension
(HVPG \geq 10 mmHg; varices on endoscopy; portosystemic collaterals; hepatofugal flow on imaging)

A New Entity :

“Advanced Chronic Liver Disease (ACL D)”

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Highly suggestive of cACL D	cACL D	
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Risk of decompensation

Manage portal hypertension!

* CSPH = clinically significant portal hypertension
(HVPG ≥ 10 mmHg; varices on endoscopy; portosystemic collaterals; hepatofugal flow on imaging)

Pharmacologic therapy for management of CSPH

Therapy	Mechanism of action	Starting dose
Propranolol	Decreased cardiac output; caused by decreased heart rate and contractility from beta-1 adrenergic blockade, plus	20–40 mg twice daily
Nadolol	Splanchnic arterial vasoconstriction; caused by beta-2 blockade leading to unopposed alfa-adrenergic vasoconstriction	20–40 mg at bedtime
Carvedilol	Above plus decreased intrahepatic vascular resistance; caused by anti-alpha-adrenergic activity	6.25 mg once daily

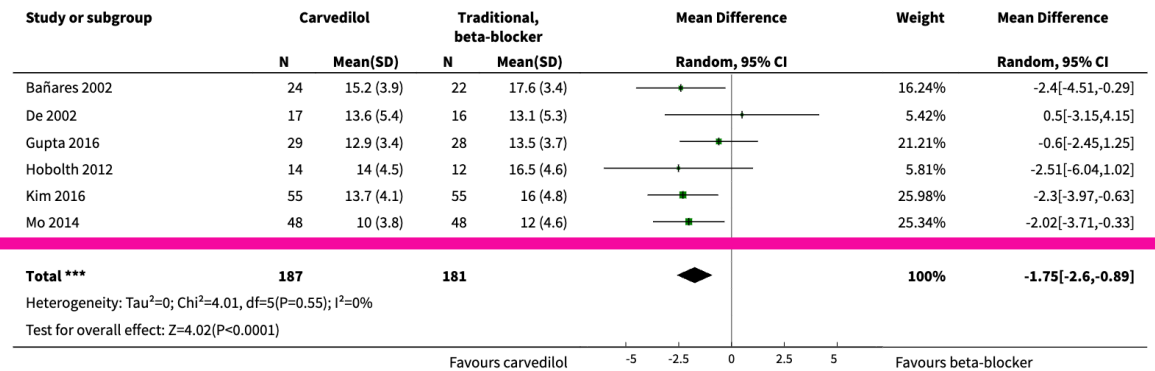
Cochrane comparison: Carvedilol vs. other NSBB for the outcome of HVPG



Trusted evidence.
Informed decisions.
Better health.

Cochrane Database of Systematic Reviews

Analysis 1.14. Comparison 1 Carvedilol versus non-selective beta-blockers, Outcome 14 Hepatic venous pressure gradient, end of treatment (mmHg) (overall).



Zacharias AP, et al. Cochrane Database Syst Rev. 2018

* CSPH = clinically significant portal hypertension
(HVPG ≥ 10 mmHg; varices on endoscopy; portosystemic collaterals; hepatofugal flow on imaging)

AASLD Guideline Statement



Guidance statements:

1. Carvedilol is recommended as the preferred NSBB for the treatment of PH in patients with cirrhosis.
2. The recommended maintenance dosage of carvedilol is 6.25–12.5 mg/day. Maintenance dosage can be given as a single daily dose or divided twice daily. In patients with concomitant arterial hypertension or cardiac disease, the dose of carvedilol may be further increased to address nonhepatic indications.

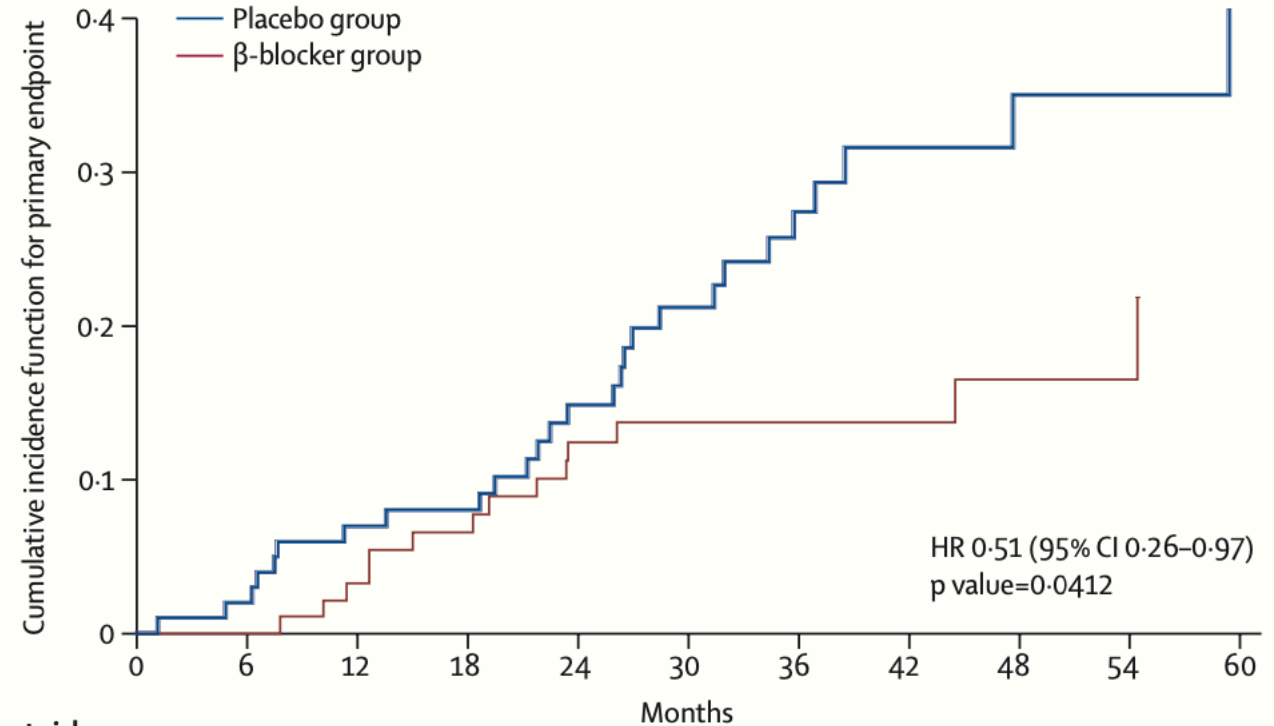


Patients with *compensated* cirrhosis
and clinically significant portal
hypertension

Prevent decompensation of cirrhosis with portal HTN (PREDESCI)

- 201 pts w/ compensated cirrhosis w/ CSPH without high-risk varices
- Randomized to: Propranolol/carvedilol vs. placebo
- Primary endpoint: death or decompensation
- 2 years follow-up

A



Patients at risk		0	6	12	18	24	30	36	42	48	54	60
β blockers	100	96	87	80	69	60	48	31	20	15	7	
Placebo	101	99	94	86	72	59	42	26	19	13	6	
Primary outcome (deaths)												
β blockers		1 (1)	3 (1)	4 (2)	5 (2)	1 (1)	0	0	1 (1)	0	1	
Placebo		2 (2)	5 (1)	1	6 (2)	5 (1)	4 (3)	2 (1)	1 (1)	0	1	



AASLD Guideline Statements

For cACLD with CSPH

NSBBs (preferably carvedilol 12.5 mg/day) should be considered for patients with cACLD with CSPH to prevent decompensation.*

[...use of NSBB] would obviate the need for further screening endoscopy.

Screening endoscopy is **not necessary** in pts on NSBB. Consider switching from selective to NSBB.

* Contraindications to NSBB: asthma, advanced heart block, bradyarrhythmias



AASLD Guideline Statements

For cACLD with CSPH *not on NSBB*

If TE not available for risk stratification or NSBB is contraindicated, endoscopic surveillance is recommended.

If not on NSBB, repeat endoscopy:

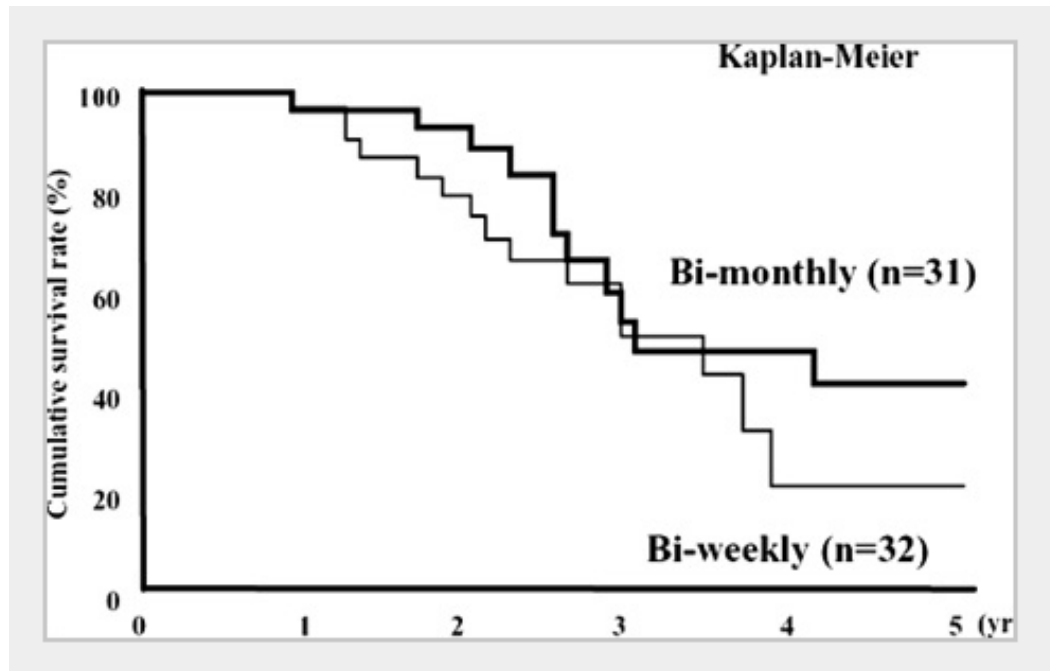
- Every 2 years if liver disease is active/uncontrolled
- Every 3 years if liver disease is controlled
- Annually if decompensated

Endoscopic variceal ligation for primary prophylaxis (in those with NSBB intolerance/contraindications)

Primary prophylaxis with EVL should be performed in patients with cACLD and CSPH and high-risk varices *who cannot receive NSBB.*

* High-risk varices: moderate/large varices, any size with red wale marks, CTP C

How often should to repeat EGD after EVL?



No difference in survival among bi-weekly vs. bi-monthly interval of EGD, *but* bi-weekly pts had more procedures and esophageal ulcers

Band ligation should be repeated every 2-4 weeks until obliteration...
And then at 6 months...
And then annually

And then at 6 months...

And then annually

Patients with *decompensated* ACLD

Annual endoscopy in those *not on*
NSBB to screen for EV

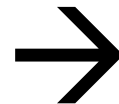
IF EV found, then need NSBB or EV
obliteration for primary
prophylaxis



NSBB in patients with decompensated cirrhosis

Carvedilol is preferred, but if the patient has low arterial blood pressure with low doses of carvedilol, consider switching to propranolol or nadolol (due to lesser effects on arterial blood pressure).

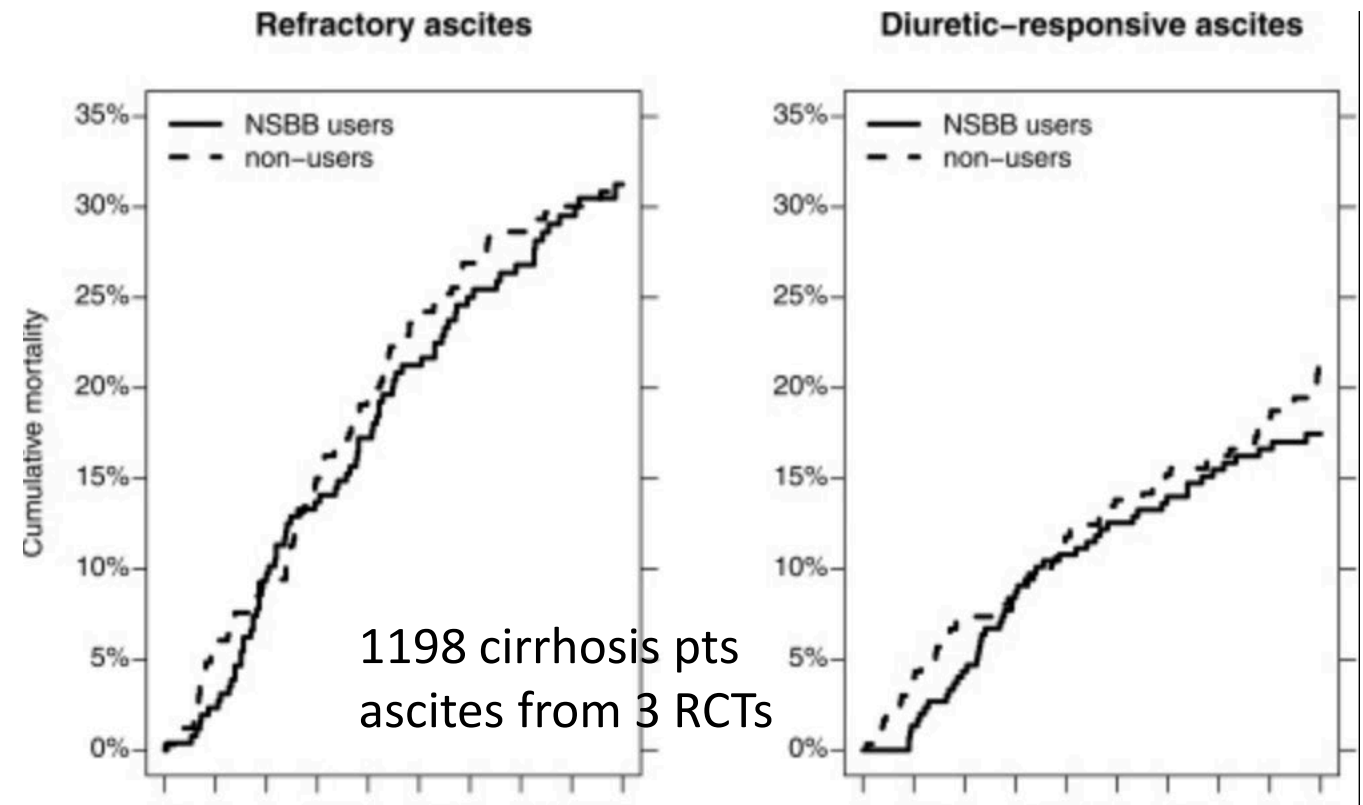
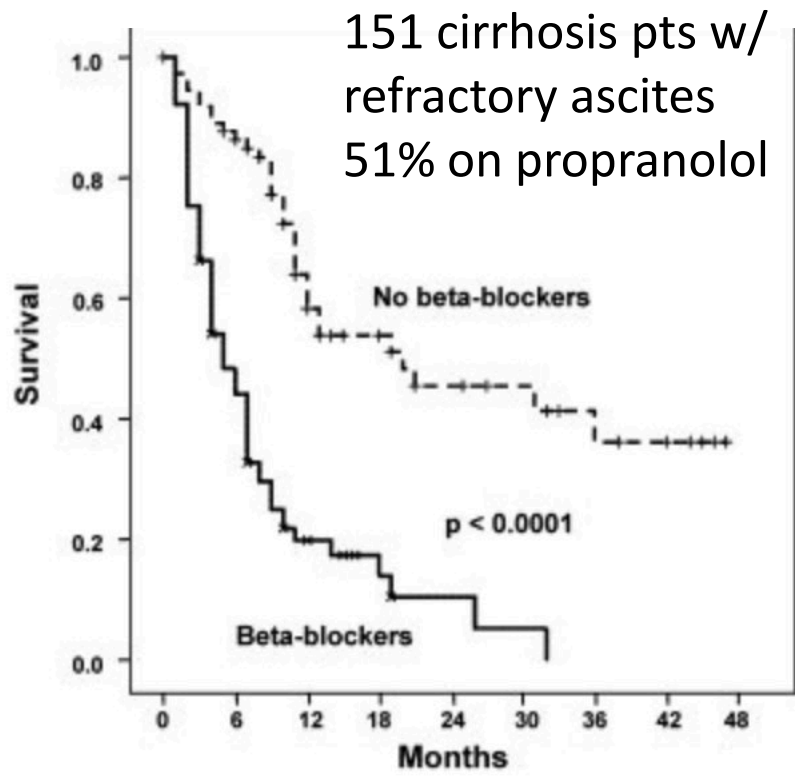
Reduce dose of NSBB with
SBP <90 mmHg



If discontinuing NSBB →
initiate annual endoscopic
surveillance

NSBB in patients with refractory ascites?

Concern: NSBB may limit the compensatory increase in cardiac output that is needed to maintain organ perfusion after LVP



Acute variceal hemorrhage



Acute variceal hemorrhage : Initial mgmt

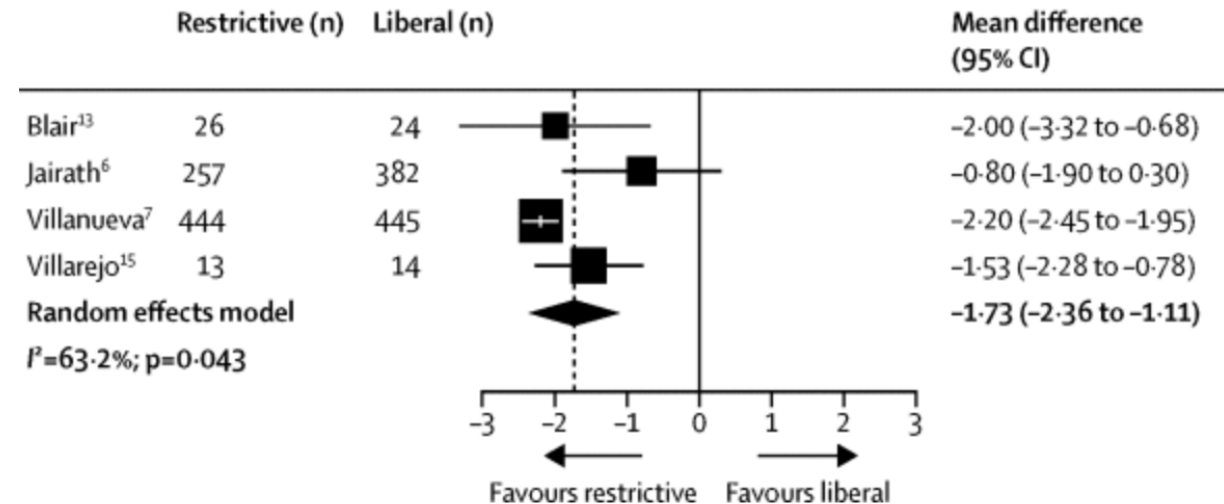
Checklist for management:

- ✓ Initiate vasoactive agent
- ✓ Initiate antibiotic prophylaxis
- ✓ Perform endoscopy *within 12 hours* of AVH presentation
- ✓ **Avoid use of routine FFP, platelet, or cryoprecipitate***
- ✓ **Transfuse to Hg >7g/dL**

Northup P, et al. Practice Guidance: Vasc d/o of the Liver. Hepatol 2021.

Meta-analysis: 5 RCTs with 1965 pts with cirrhosis + AVH randomized to “restrictive” vs. “liberal” RBC transfusion strategies

Number of RBC units transfused



Restrictive → lower rebleeding, no diff in ischemic events

Odutayo A, et al. Lancet Gastro & Hepatol 2017.

Acute variceal hemorrhage : Early (<72h) TIPS

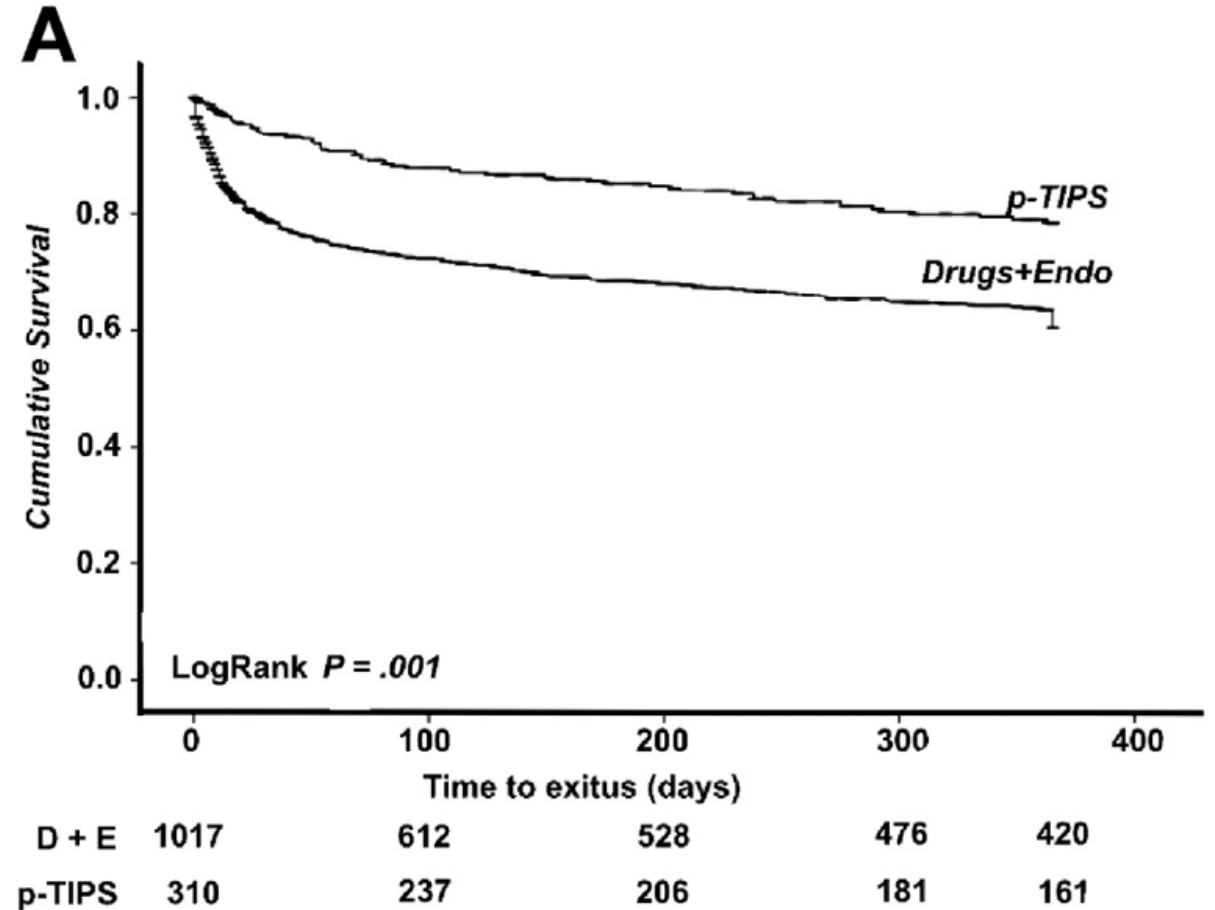
Meta-analysis:

1,327 patients with cirrhosis:

- 1) CTP 10-13
- 2) CTP B + active bleeding

Studies have excluded:

- Older adults
- Advanced HCC
- Acute or chronic kidney dz
- Prior hemorrhage
- Complete PVT



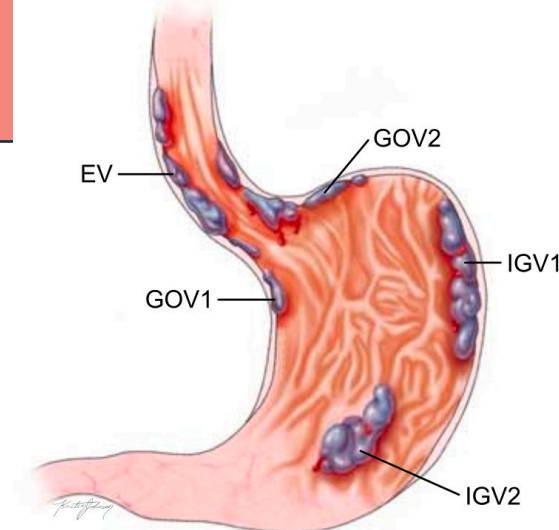
AASLD Guideline Statements



32. In patients with CTP class B score >7 and active bleeding on endoscopy or CTP class C score 10–13, preemptive TIPS creation (within 72 hours and ideally within 24 hours of initial upper endoscopy) should be recommended in absence of absolute contraindications to TIPS. If TIPS is not locally available, transfer to a center with the capacity to intervene should be considered.

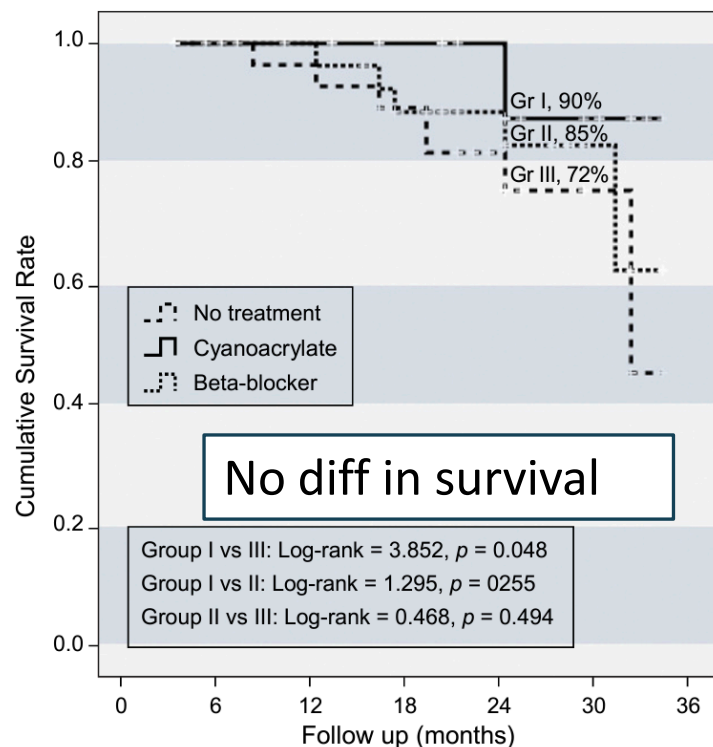
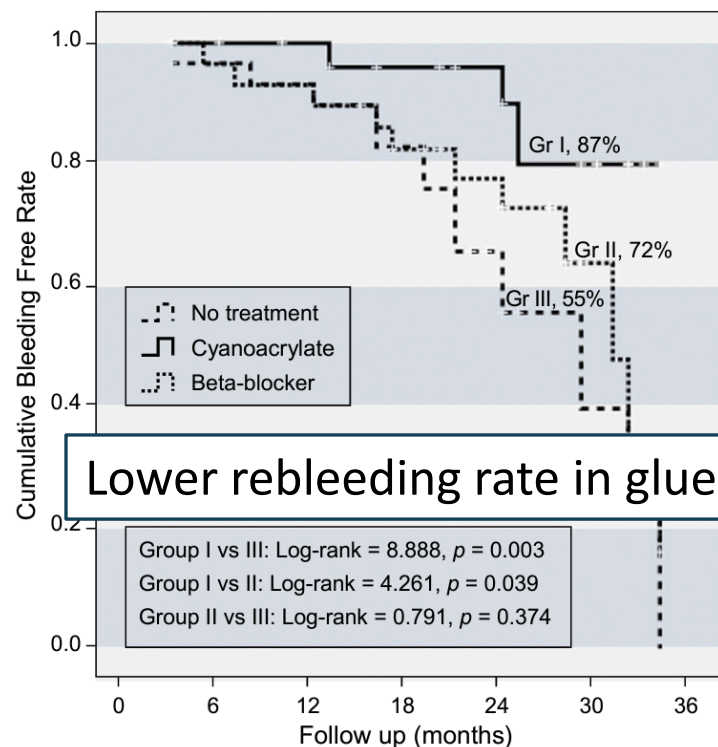
33. In patients presenting with AVH who do not undergo TIPS, NSBB should be initiated at discontinuation of vasoactive therapy.

Primary Px for Gastric varices



GV = CSPH → NSBB!

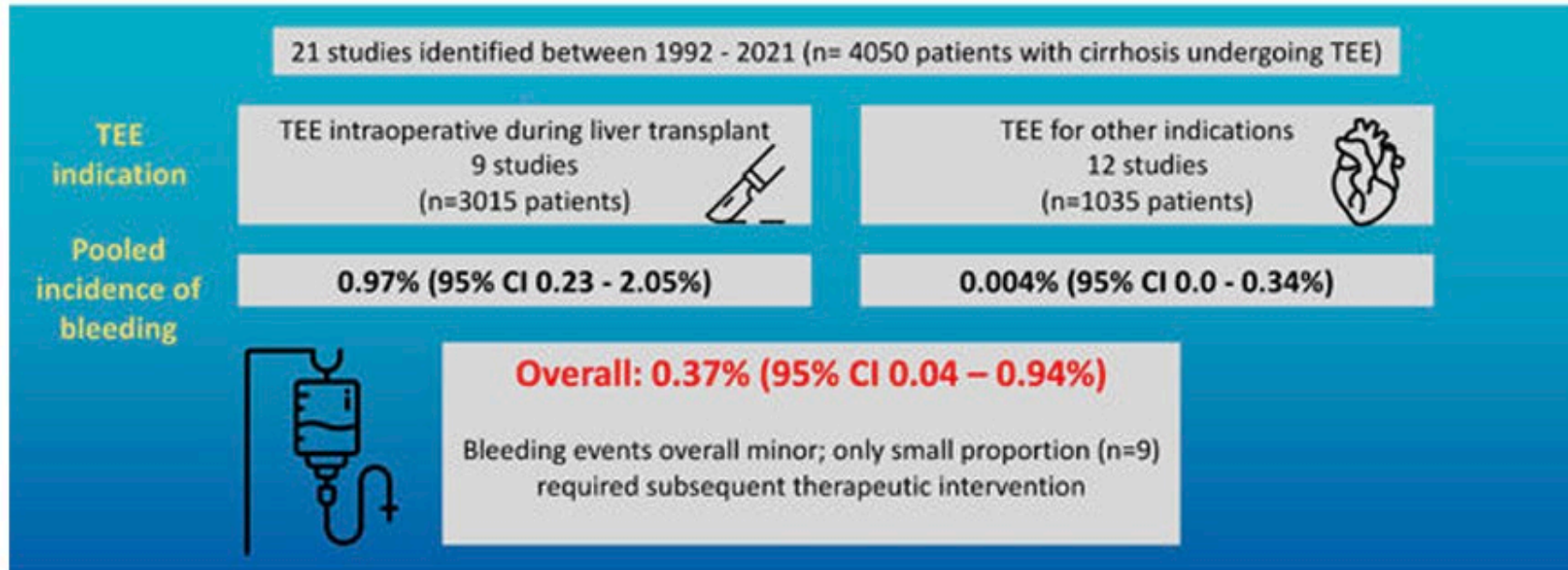
Glue? (Cyanoacrylate)



Patients with high-risk cardiofundal varices (≥ 10 mm, red wale signs, CTP B/C) who cannot receive NSBB may be considered for primary prophylaxis with endoscopic cyanoacrylate injection.

EGD prior to Transesophageal echocardiography?

Incidence of variceal hemorrhage in patients with cirrhosis undergoing transesophageal echocardiography: A systematic review and meta-analysis



Odewole M* and Sen A*, et al. *Aliment. Pharmacol. Ther.*

Guidance statement:

57. Routine upper endoscopy prior to TEE in patients with cirrhosis is not recommended.

Case #1

You are seeing a new patient with known MASH who has been referred to you because platelet count is 105 and ultrasound shows nodular liver with a splenorenal shunt. Do you:

- a) Order transient elastography to risk stratify
- b) Start propranolol
- c) Start carvedilol
- d) Schedule upper endoscopy to screen for esophageal varices



Case #2

You are seeing a new patient with known MASH who has been referred to you because platelet count is 130 and ultrasound shows nodular liver with a splenorenal shunt. Do you:

- a) Order transient elastography to risk stratify
- b) Start propranolol
- c) Start carvedilol
- d) Schedule upper endoscopy to screen for esophageal varices





Case #3

A 45 year old man with alcohol-associated liver disease presents to your ICU with an acute esophageal variceal hemorrhage. His MELD=15 and he is Child-Pugh C. What is the recommended next step?

- a) Band the varices and discharge to home when stable with plan for repeat EGD
- b) Do "A" but also add NSBB
- c) Do "B" and refer for outpatient TIPS evaluation
- d) Call IR now for TIPS placement prior to discharge



Grazie!

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- jennifer.lai@ucsf.edu

AVH: Immediate aftermath

- ✓ Continue vasoactive therapy for 2-5 days → initiate NSBB
- ✓ Continue antibiotic prophylaxis for 2-5 days
- ✓ **Restart nutrition as soon as AVH is controlled**
- ✓ Presence of variceal bands is *not* a contraindication to feeding tube placement
- ✓ Stop proton-pump inhibitor in the absence of specific indication (due to increased risk of infection and HE)

Two stages of cirrhosis

Compensated

- Absence of ascites, HE, or acute variceal hemorrhage

**Median survival
12 years**

Decompensated

- Overt ascites
- Variceal hemorrhage
- Overt hepatic encephalopathy

**Median survival
1.5 years**

