2023
SCSG
LIVER SYMPOSIUM
DECEMBER 9-10, 2023

Updates in the Management of Portal Hypertension

AASLD 2023 Guidance

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AASLD Practice Guidance on Risk Stratification and Management of Portal Hypertension and Varices in Cirrhosis

Best practices for:

- Identification of portal hypertension
- Prevention of initial hepatic decompensation
- Management of acute variceal hemorrhage
- Reduction in risk of recurrent variceal hemorrhage

- In alignment with Baveno VII recommendations (J Hepatol 2022;76:959)

David Kaplan, Jaime Bosch, Cristina Ripoll, Maja Thiele, Brett Fortune, Douglas Simonetto, Lupe Garcia-Tsao. *Hepatology.* 2023 PMID: 37870298.

New Concepts

Advanced chronic liver disease (ACLD)

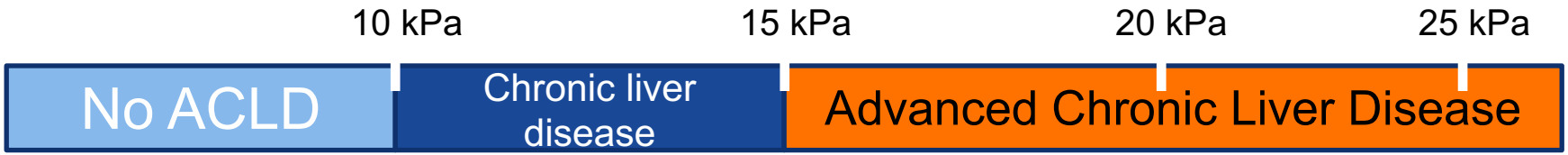
Clinically significant portal hypertension (non-invasive diagnosis)

Carvedilol to prevent decompensation

Further decompensation

New Concepts: Advanced Chronic Liver Disease (ACLD)

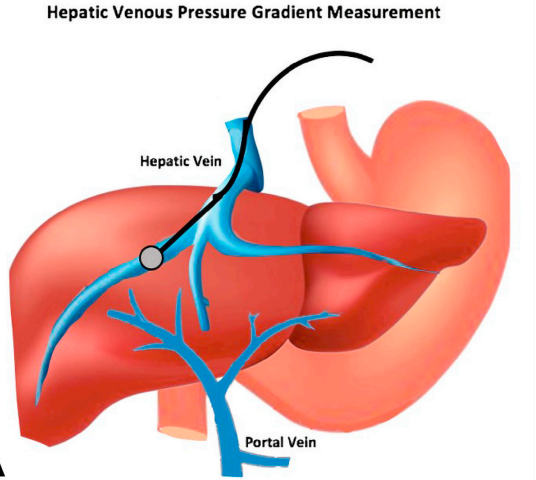
- Advanced chronic liver disease (ACLD)
  - A **clinical diagnosis of cirrhosis** or near cirrhosis (F3/4) based on liver stiffness measurement
  - Replaces liver biopsy and/or imaging (eg, US, CT, MRI) to diagnose patients at risk of complications of cirrhosis (eg, variceal bleeding, ascites, etc.)
- cACLD: *compensated* advanced chronic liver disease
  - Replaces compensated cirrhosis
- dACLD: *decompensated* advanced chronic liver disease
  - Ascites, variceal bleeding, hepatic encephalopathy, HRS-AKI, jaundice
  - Replaces decompensated cirrhosis



ACLD=Advanced Chronic Liver Disease (F3 or F4)

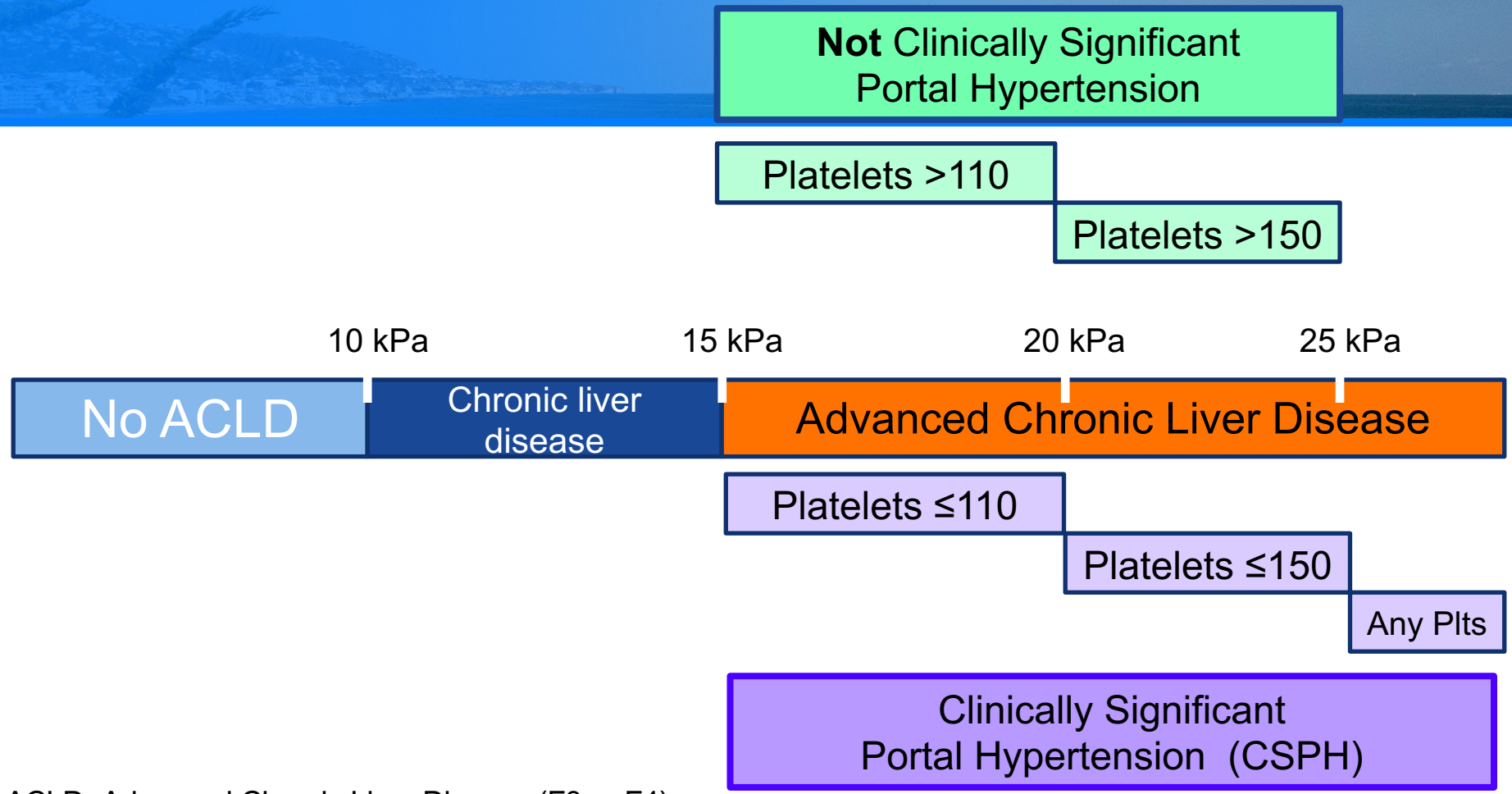
New Concepts: Clinically Significant Portal Hypertension (CSPH)

- Portal hypertension: WHVP ≥6 mm Hg
- Clinically significant portal hypertension (CSPH)
  - WHVP ≥10 mm Hg
  - ↑ Risk of variceal bleeding and decompensation events
  - Non-invasive diagnosis based on liver stiffness and platelet count



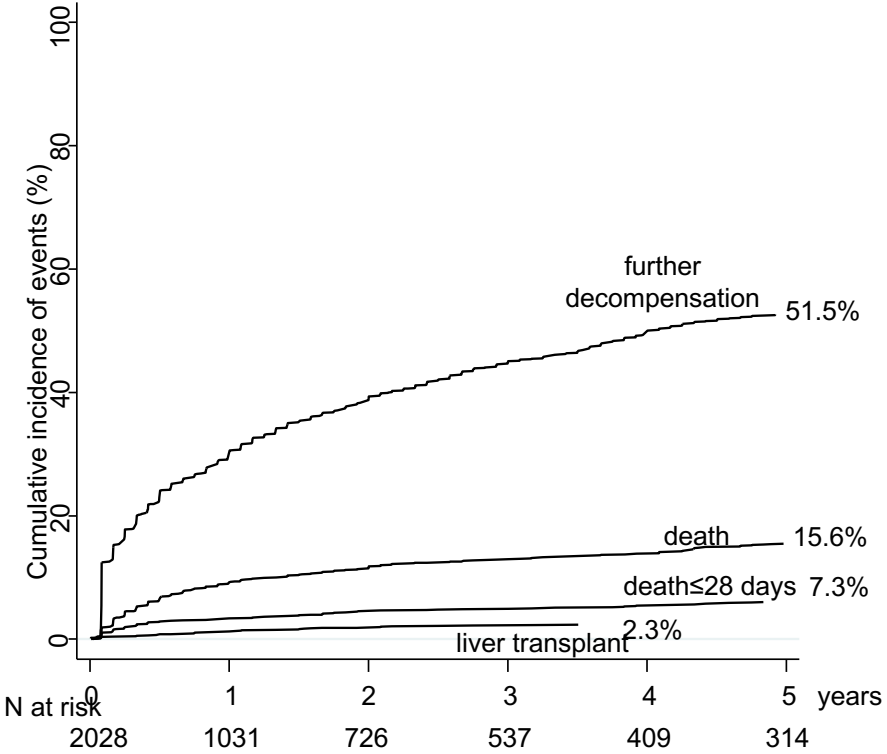
Clinically Significant Portal Hypertension is present if
- Clinical decompensation
- Gastroesophageal varices on endoscopy
- Collaterals or hepatofugal flow on abdominal imaging

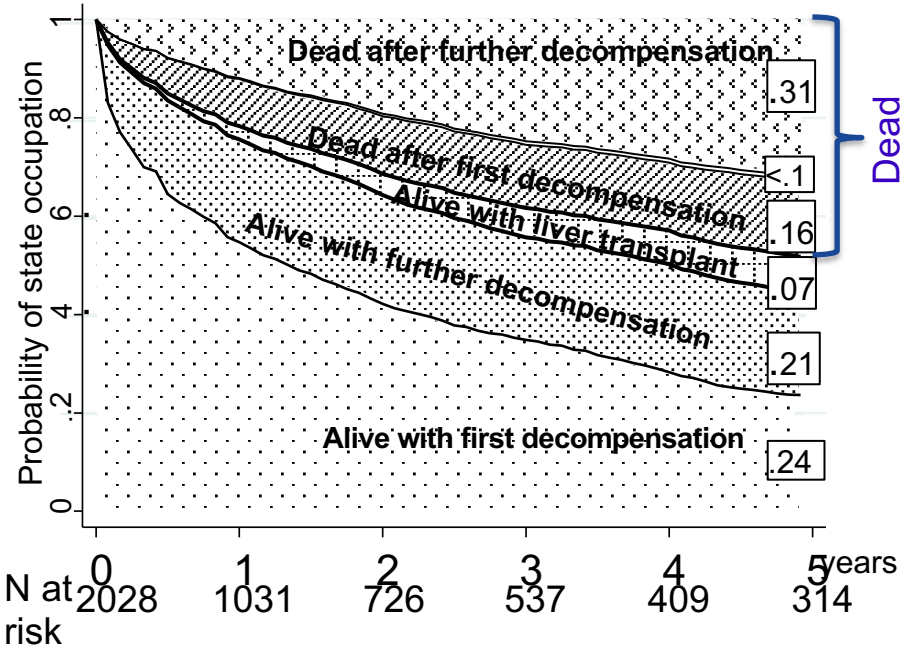
Based on liver stiffness measurement and platelet count
- LSM ≥25 kPa irrespective of platelet count
- LSM 20 – 24.9 kPa and platelet count <150,000/mm^3
- LSM 15 – 19.9 kPa and platelet count <10,000/mm^3



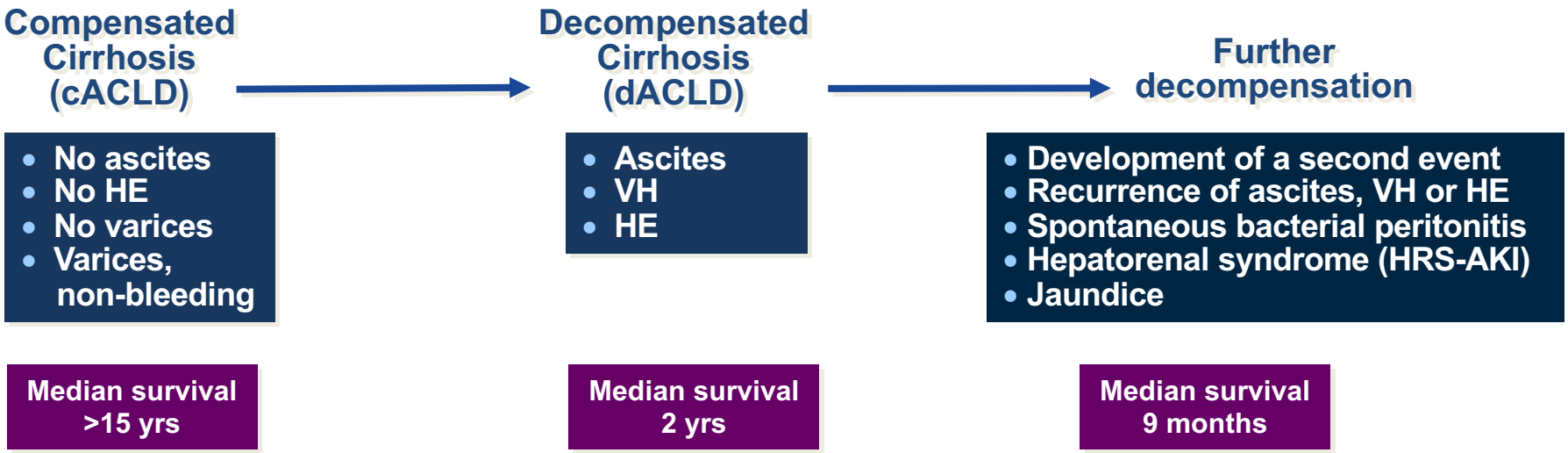
ACLD=Advanced Chronic Liver Disease (F3 or F4)

Further Decompensation: 2028 patients with first decompensation (5-year follow up)





In Cirrhosis/ACLD, There Are 3 Prognostic Stages, Each Associated With a Higher Mortality

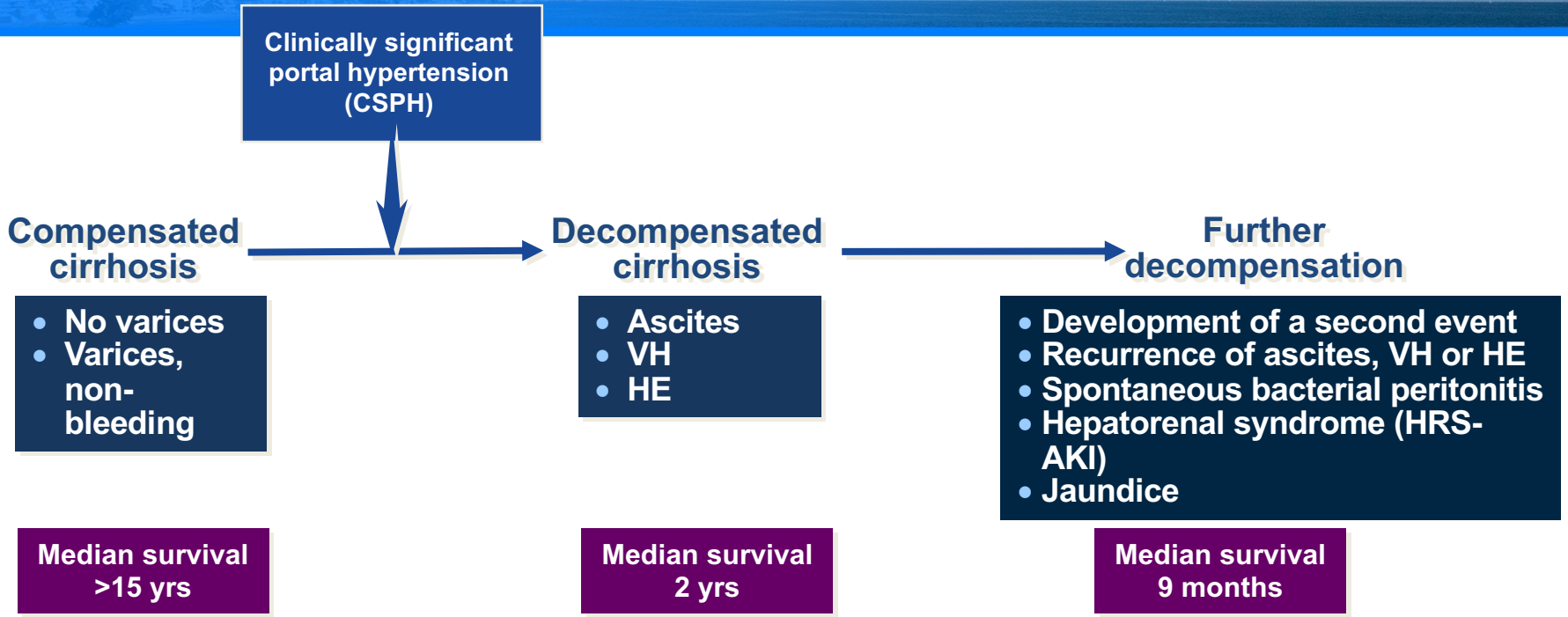


VH=variceal hemorrhage; HE= hepatic encephalopathy.

D'Amico, Garcia-Tsao, *J Hepatol*. 2006;44:217-31; Baveno VII consensus. *J Hepatol.* 2022;76:959; D'Amico, Garcia-Tsao. *Hepatology.* [in press].

Modified from Dr. Garcia-Tsao.

The Main Driver of Decompensation Is Portal Hypertension



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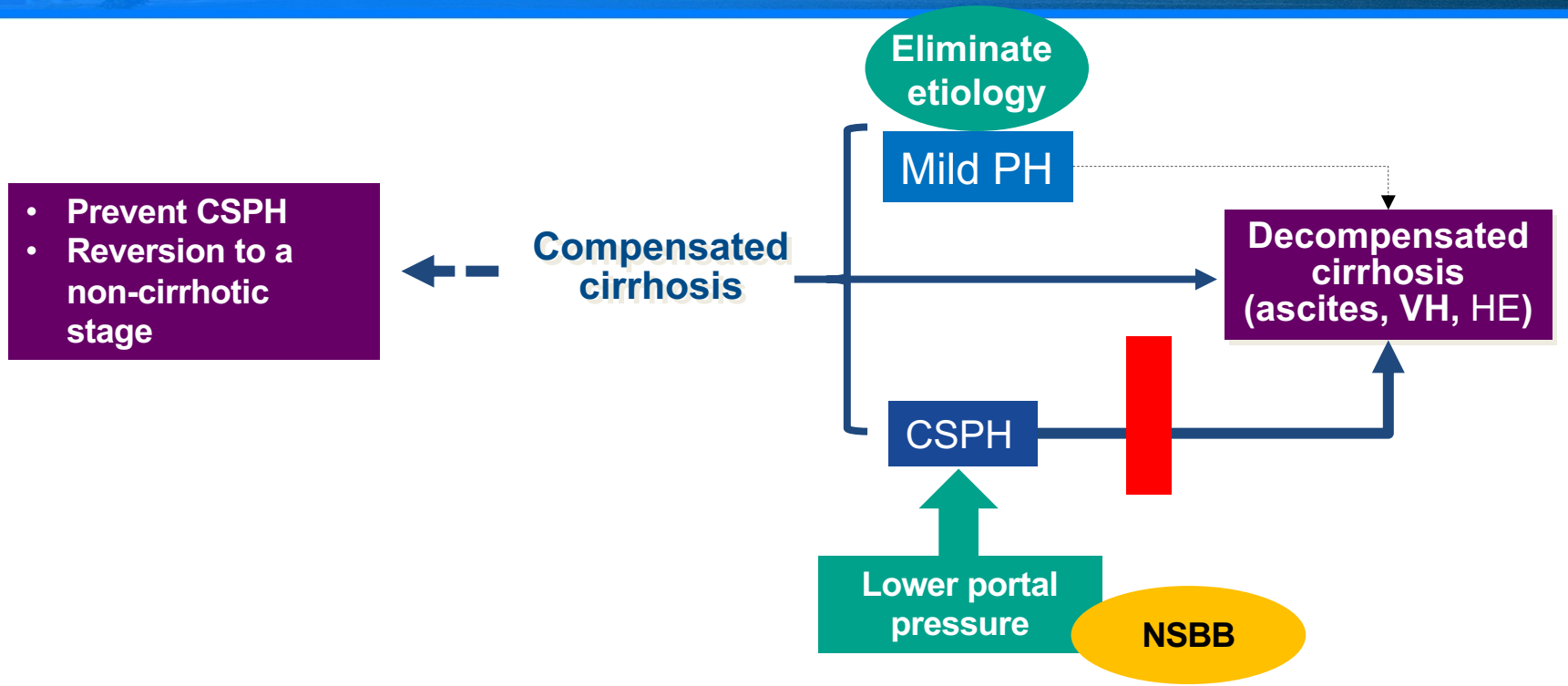
Modified from Dr. Garcia-Tsao.

In Patients With Compensated Cirrhosis, Preventing Decompensation (Ascites, VH) Is a Loftier Goal Than Just Preventing VH



CSPH= clinically significant portal hypertension; VH = variceal hemorrhage; HE = hepatic encephalopathy; NSBB=non-selective beta-blockers.
Modified from Dr. Garcia-Tsao.

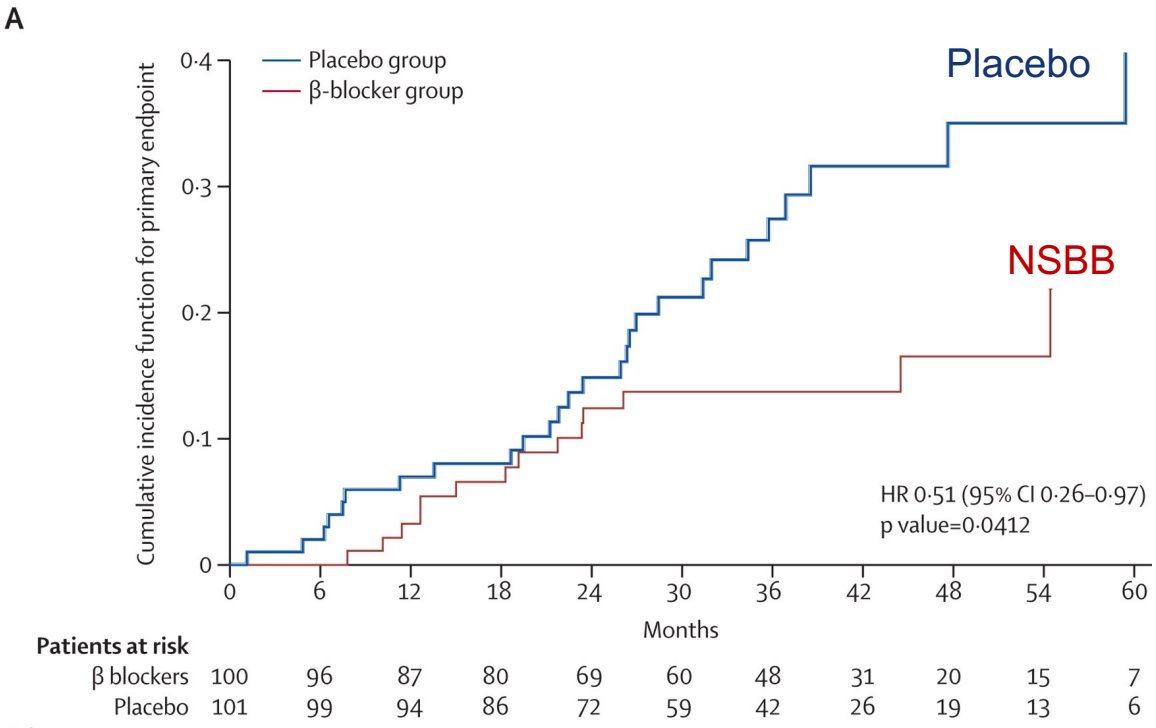
NSBBs Prevented Decompensation and/or Death in Patients With Compensated Cirrhosis and WHVP≥10 mmHg (No or Small Varices)

Probability of developing any decompensation or death

Ascites, variceal hemorrhage, Overt HE, HRS-AKI

Decompensation or death
- 27% of placebo vs
- 16% of NSBB

11% reduction; NNT=9



NSBB= nonselective beta-blocker; CSPH= clinically-significant portal hypertension; HVPG= hepatic venous pressure gradient

Villanueva et al (PREDESCI trial). *Lancet.* 2019;393:1597-1608.

Carvedilol, Compared to Propranolol, Is More Effective in Reducing HVPG and Significantly Reduces Decompensation and Death Compared with Placebo/EVL

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

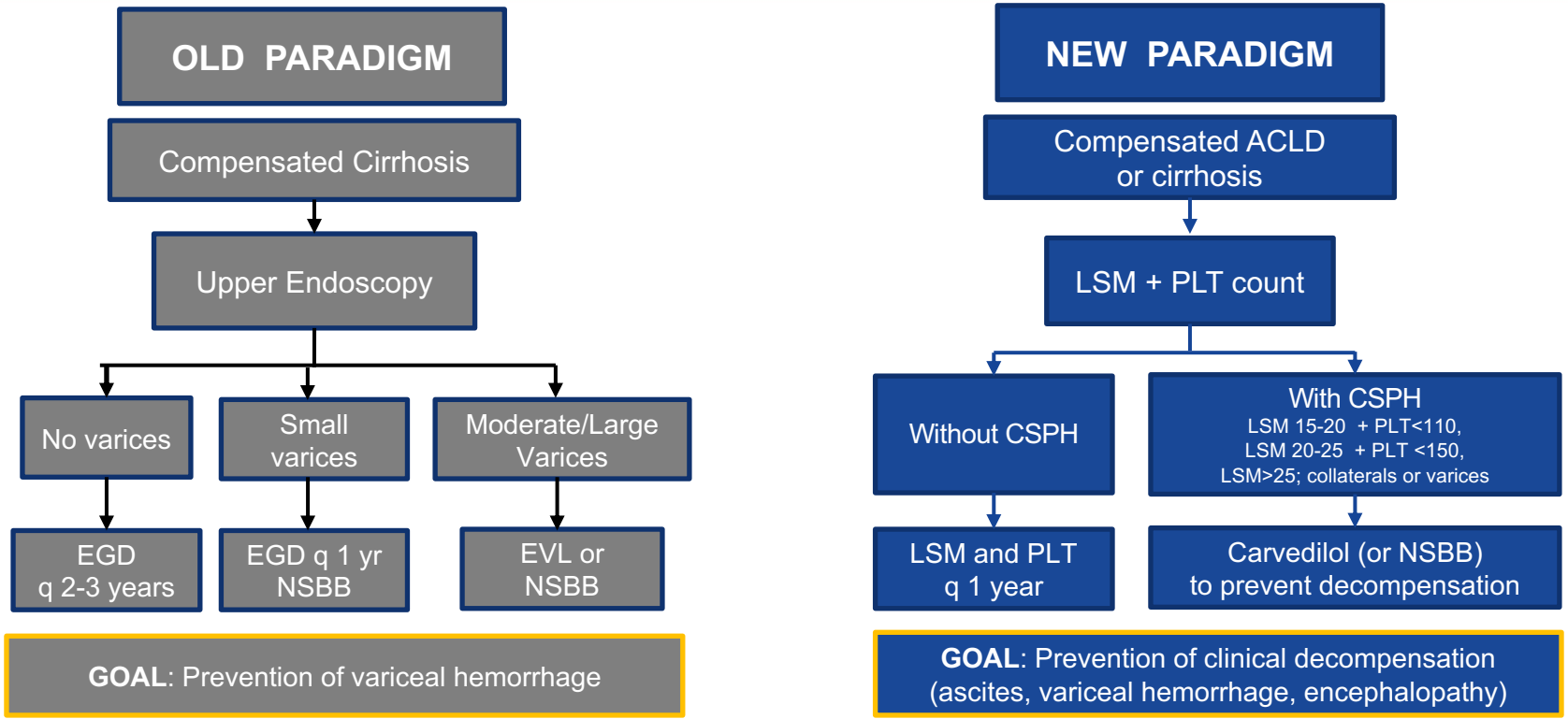
Study or subgroup	Carvedilol N	Carvedilol Mean(SD)	Traditional, beta-blocker N	Traditional, beta-blocker Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Bañares 2002	24	15.2 (3.9)	22	17.6 (3.4)		16.24%	-2.4[-4.51,-0.29]
De 2002	17	13.6 (5.4)	16	13.1 (5.3)		5.42%	0.5[-3.15,4.15]
Gupta 2016	29	12.9 (3.4)	28	13.5 (3.7)		21.21%	-0.6[-2.45,1.25]
Hobolth 2012	14	14 (4.5)	12	16.5 (4.6)		5.81%	-2.51[-6.04,1.02]
Kim 2016	55	13.7 (4.1)	55	16 (4.8)		25.98%	-2.3[-3.97,-0.63]
Mo 2014	48	10 (3.8)	48	12 (4.6)		25.34%	-2.02[-3.71,-0.33]
Total ***	**187**		**181**			**100%**	**-1.75[-2.6,-0.89]**

- **Carvedilol is recommended as the preferred NSBB for the treatment of portal hypertension in patients with cirrhosis**
- **The recommended maintenance dosage of carvedilol is 6.25–12.5 mg/day, after initiating treatment for 2 days with only 6.25 mg at bedtime**
- **Maintenance dosage can be given as a single dose**
- **In patients with concomitant arterial hypertension or cardiac disease, the dose of carvedilol may be further increased to address non-hepatic indications**

Study	Control		95% CI)	Weight (%)
Tripathi 2009	16(1)/26 [53]		-1.812)	32%
Shah 2014	5(4)/53 [54]		-1.962)	28%
Bhardwaj 2017	9(5)/59 [73]		-2.073)	18%
Villanueva 2019	4(3)/33 [90]		-1.856)	22%
Pooled	34(13)/171 [270]	2	-0.896)	100%

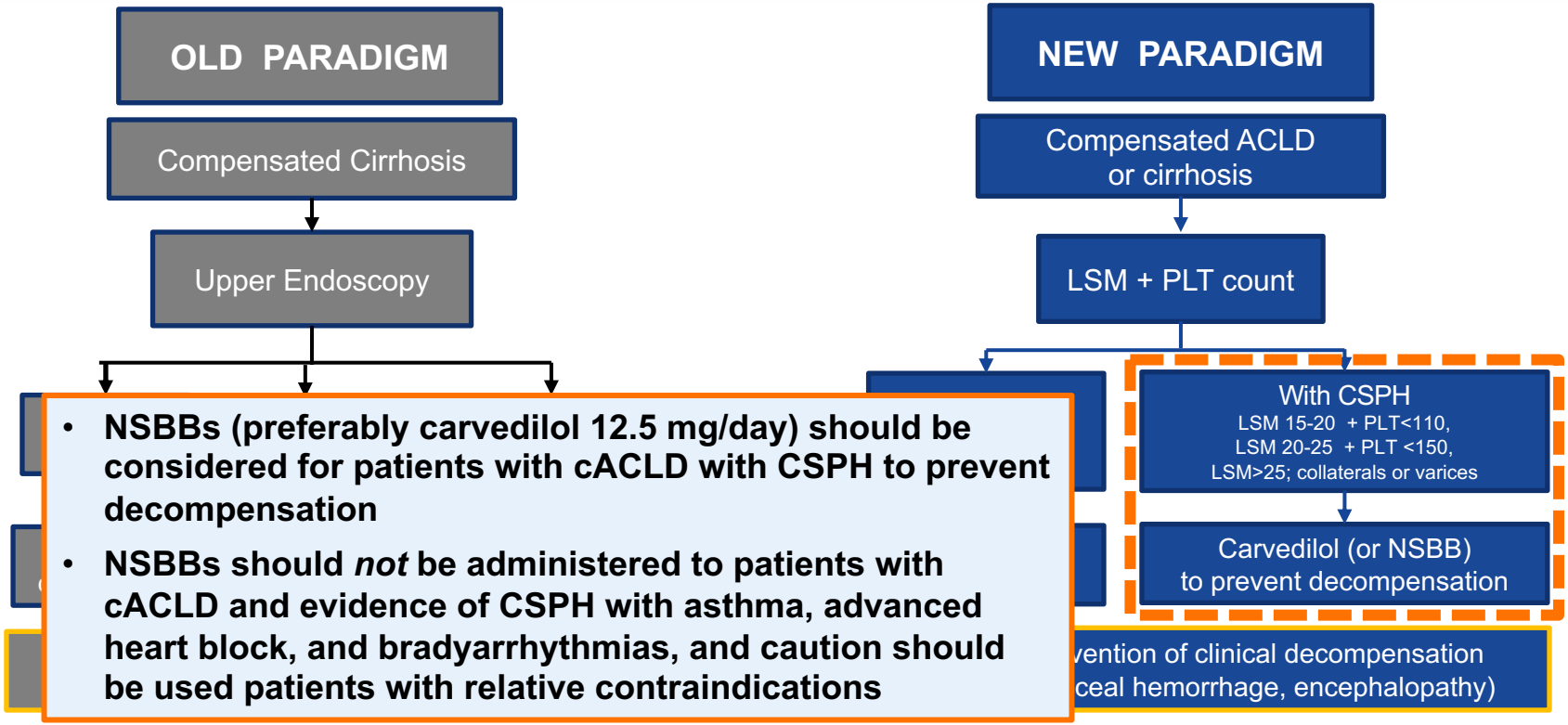
Zacharias AP et al. *Cochrane Database Syst Rev.* 2018;10:CD011510; Villanueva et al. Baveno Cooperation meta-analysis. *J Hepatol*. 2022; 77:1014-25; Modified from Dr. Garcia-Tsao.

New Paradigm for cACLD and CSPH: Carvedilol to Prevent Decompensation



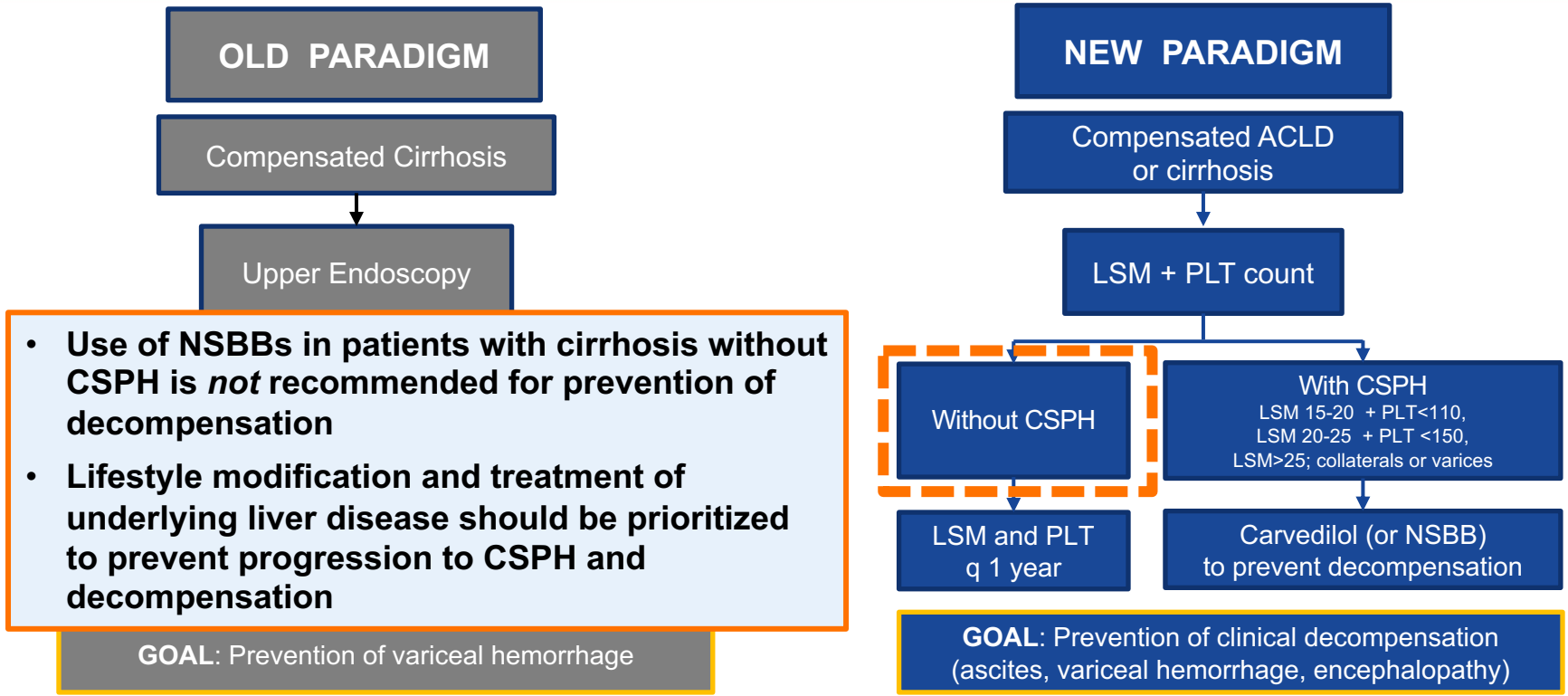
Modified from Dr. Garcia-Tsao.

New Paradigm: cACLD With CSPH



Modified from Dr. Garcia-Tsao.

New Paradigm: cACLD without CSPH



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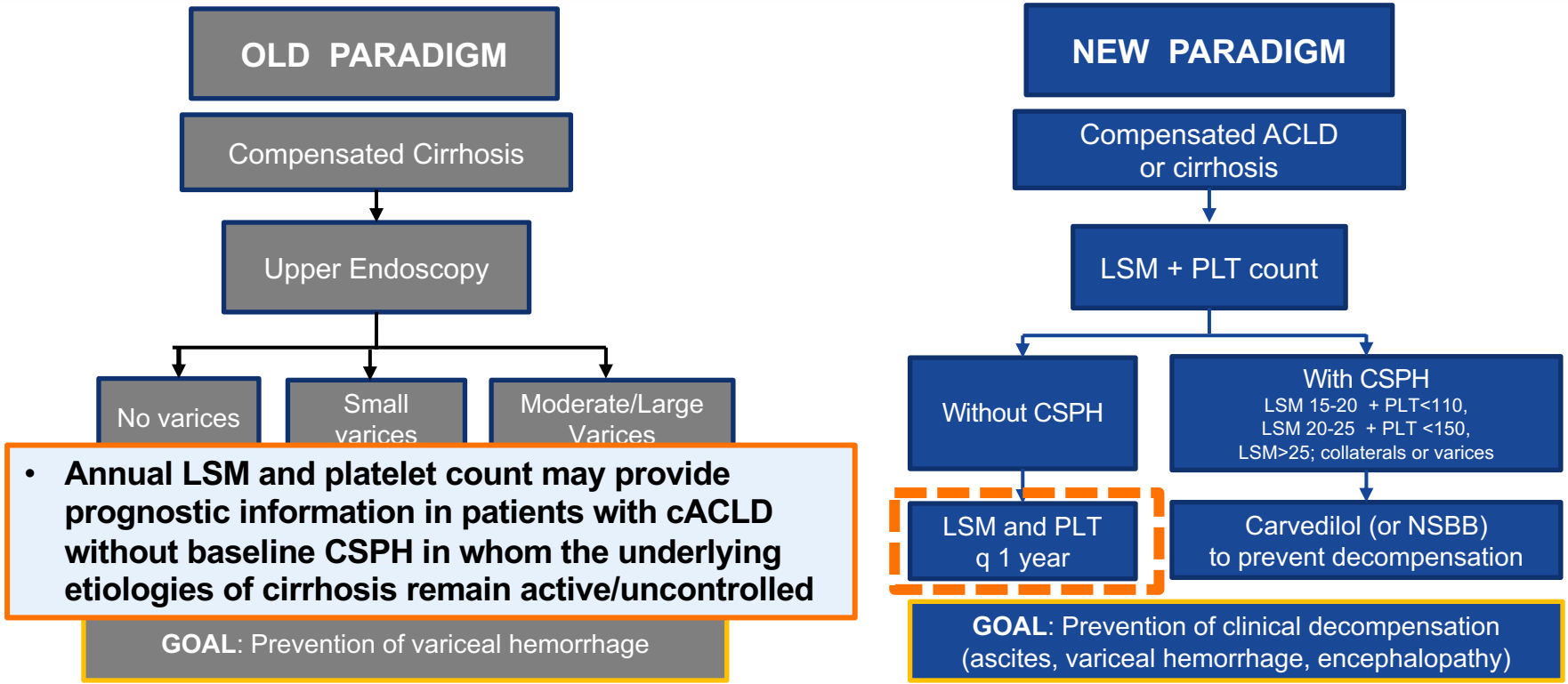
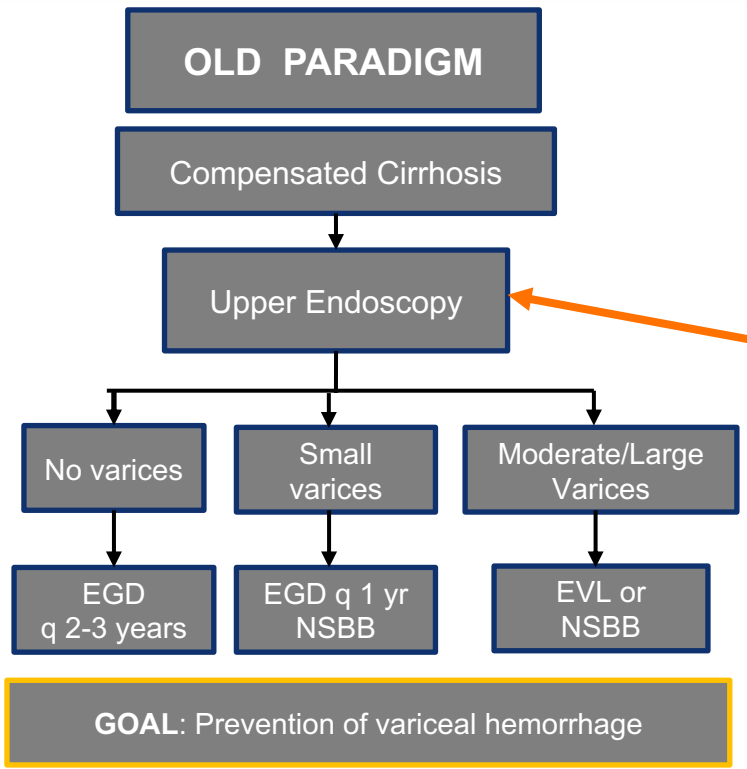
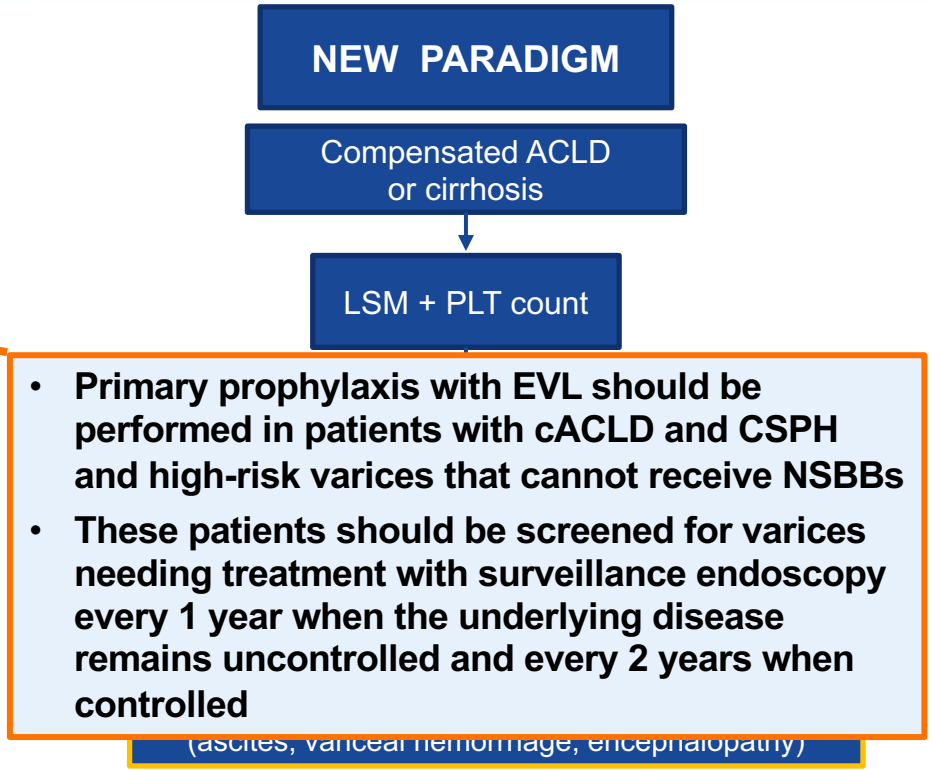


Modified from Dr. Garcia-Tsao.

New Paradigm: cACLD + CSPH Intolerant to NSBB





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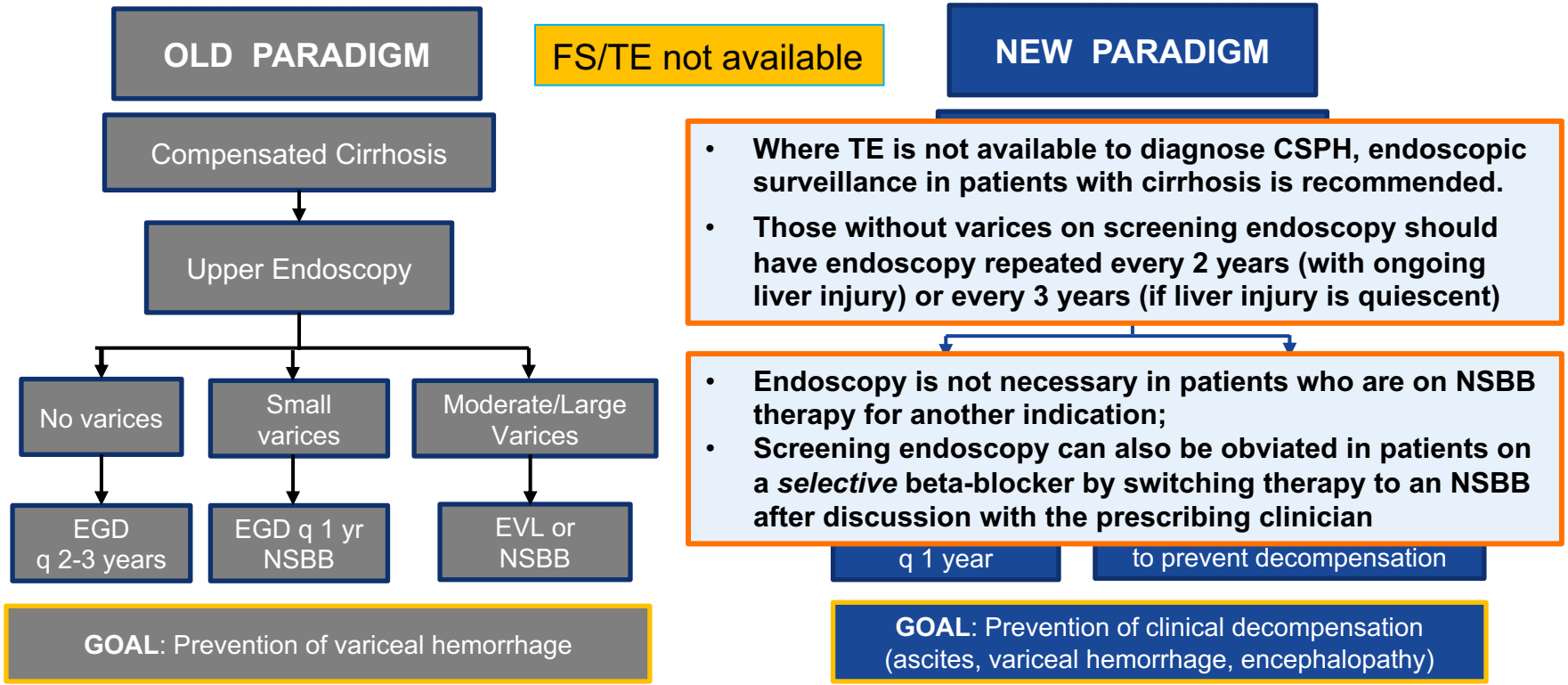
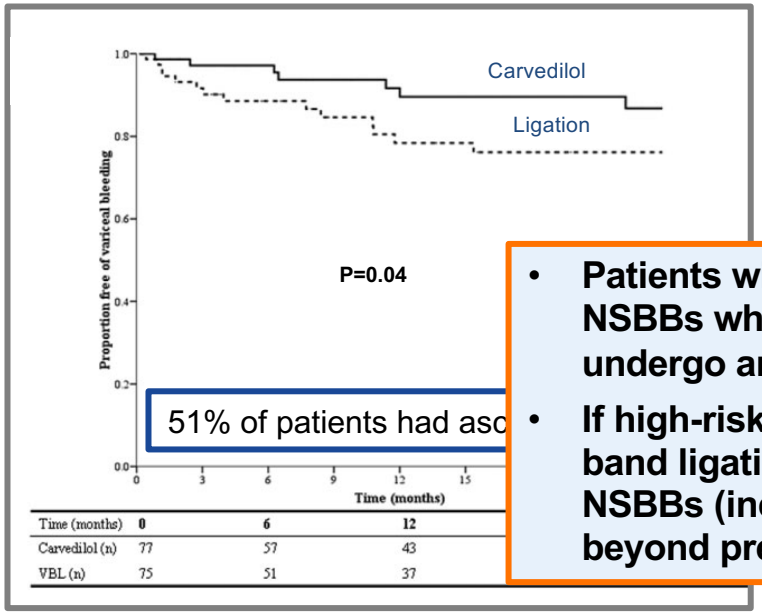
New Paradigm: FibroScan not available



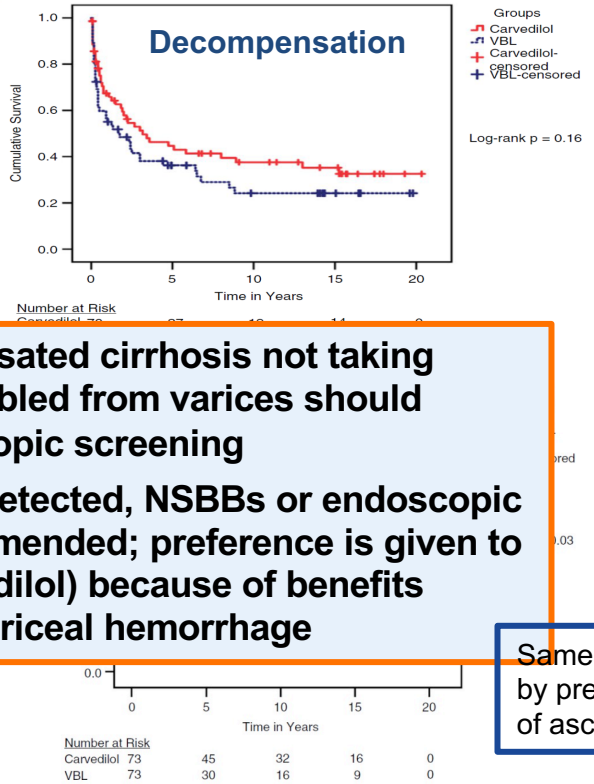
Modified from Dr. Garcia-Tsao.

In Patients With Ascites (Already Decompensated) Who Have Not Bled, The Objective Is to Prevent First Variceal Hemorrhage

First variceal hemorrhage



51% of patients had asc

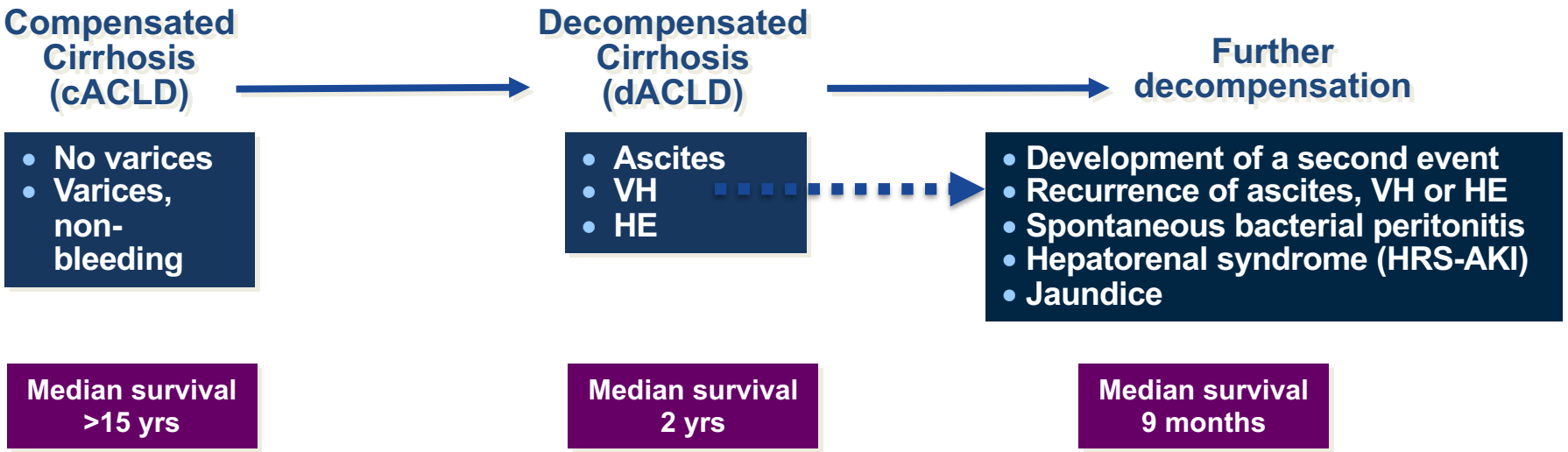


- **Patients with decompensated cirrhosis not taking NSBBs who have never bled from varices should undergo annual endoscopic screening**
- **If high-risk varices are detected, NSBBs or endoscopic band ligation are recommended; preference is given to NSBBs (including carvedilol) because of benefits beyond prevention of variceal hemorrhage**

Same results stratifying by presence or absence of ascites

Tripathi et al. *Hepatology.* 2009;50:825-833; McDowell et al. *Aliment Pharmacol Ther.* 2021;53(4):531-539.

In Patients With Variceal Hemorrhage Goals of Therapy are to Control Hemorrhage and to Prevent Recurrent Hemorrhage and Death



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Modified from Dr. Garcia-Tsao.

Control of Acute Variceal Hemorrhage in Patients With Cirrhosis

- **IV vasoactive drug as soon as VH is suspected**
- **Antibiotic prophylaxis (ceftriaxone 1 g/d)**
- **Cautious PRBC transfusion: target Hgb 7 g/dL**

Unchanged from previous guidance

- **Upper endoscopy** should be performed **within 12 hours** of presentation with AVH
- If esophageal variceal bleeding is confirmed, **endoscopic variceal ligation (EVL)** should be performed

- **Fresh frozen plasma and platelet transfusions should not be administered based on INR or platelet count targets, respectively, because there is no evidence of benefit of such transfusions in acute variceal hemorrhage, and in the case of fresh frozen plasma, there is evidence of potential harm**
- **Proton pump inhibitors should be discontinued once acute variceal hemorrhage has been confirmed as the bleeding source in the absence of other specific indications**
- **Enteral feeding should be started once acute variceal hemorrhage episode has been controlled. The presence of variceal bands does not contraindicate placement of a feeding tube if indicated.**

Modified from Dr. Garcia-Tsao.

AASLD Practice Guidance on the Use of TIPS, Variceal Embolization, and Retrograde Transvenous Obliteration in the Management of Variceal Hemorrhage

Edward Wolfgang Lee[1] | Bijan Eghtesad[2] | Guadalupe Garcia-Tsao[3,4] | Ziv J. Haskal[5] | Virginia Hernandez-Gea[6] | Hamed Jalaeian[7] | Sanjeeva P. Kalva[8] | Arpan Mohanty[9] | Dominique Thabut[10] | Juan G. Abraldes[11]

The present document aims to equip care providers with an in-depth understanding of the use of TIPS and other variceal embolization/obliteration in the management of variceal hemorrhage. The goal is to facilitate multidisciplinary discussions between hepatologists, gastroenterologists, interventional radiologists, and surgeons in the selection of endovascular treatment for patients with variceal hemorrhage.

Hepatology. 2023 PMID: 37390489.

TIPS and Retrograde Transvenous Obliteration (RTO)

Pre-emptive TIPS: TIPS in a high-risk patient who has bleeding at endoscopy in whom banding stops the bleeding

Salvage TIPS: TIPS in a patient in whom banding is not successful (ie, continued bleeding)

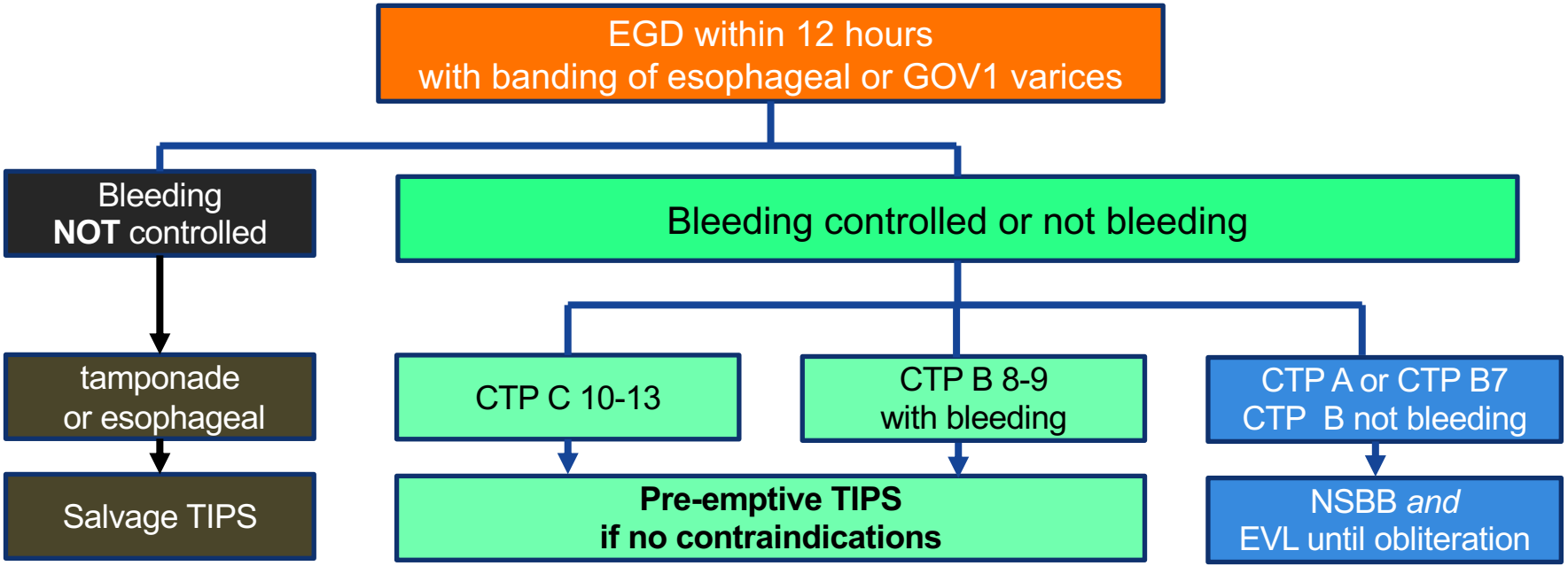
Rescue TIPS: TIPS in a patient who re-bleeds following initial banding

Retrograde Transvenous Obliteration (RTO)
IR procedure to treat varices in the stomach and GI tract (eg, rectal varices)

Acute UGI bleeding in a patient with ACLD/cirrhosis

Airway protection if AMS
Admit to ICU
CT/MRI/US when stable

Vasoactive agents (octeotride, somatastatin, terlipressin)
Antibiotics (ceftriaxone 1g/d) for 5 days or discharge
Transfuse to Hgb ~7 g/dL; avoid platelets or FFP



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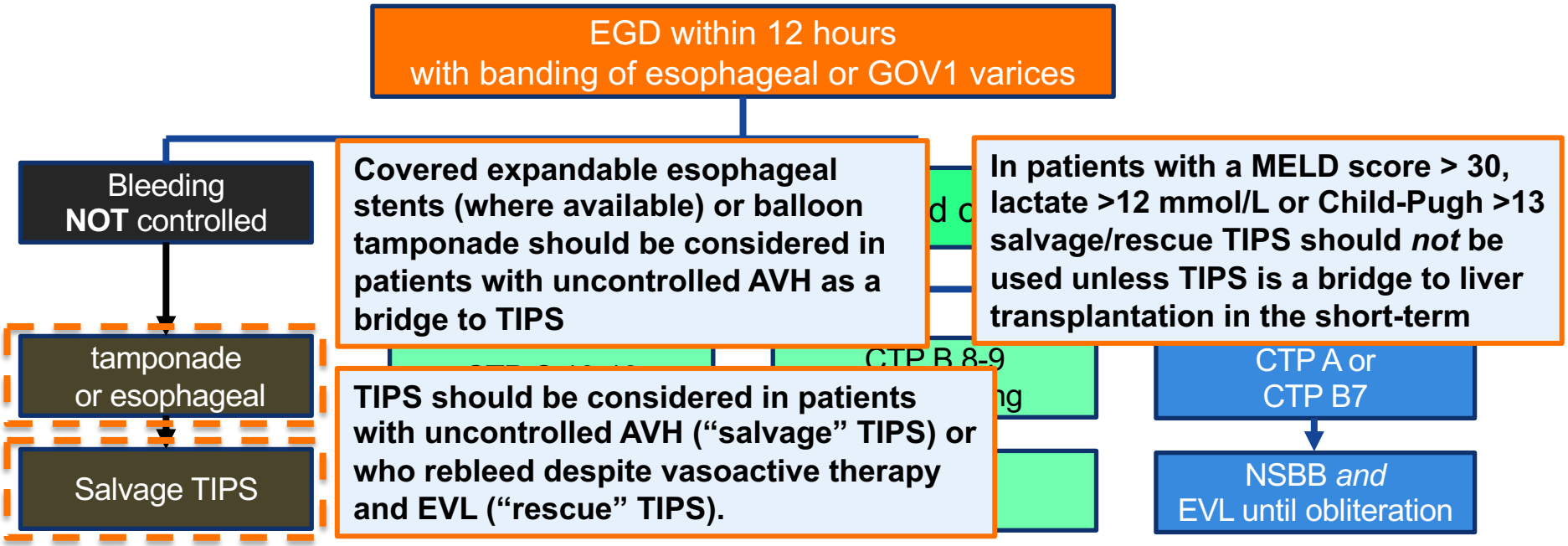
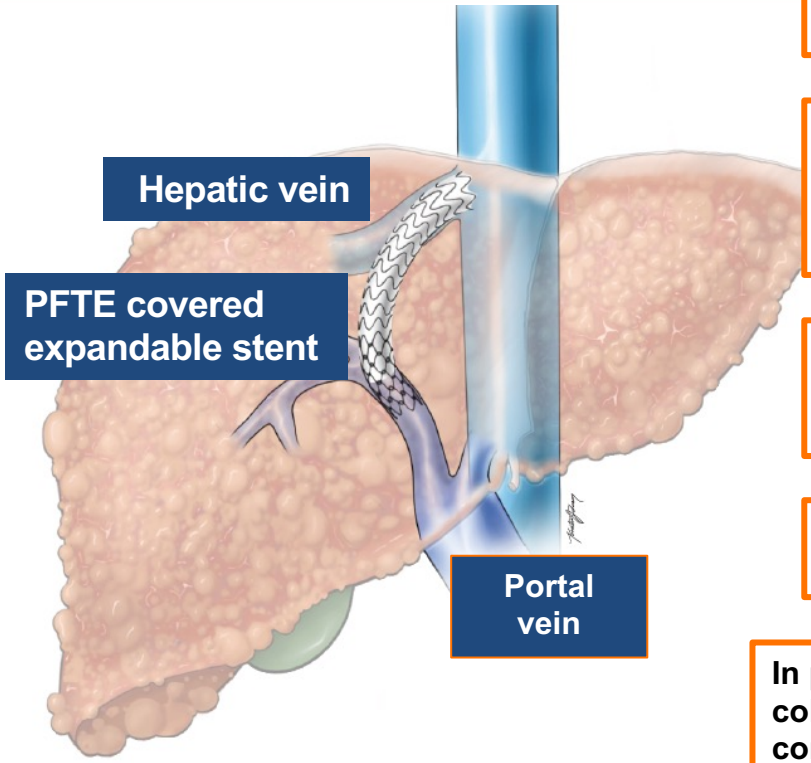


Transjugular Intrahepatic Portosystemic Shunt (TIPS)



Modified from Dr. Garcia-Tsao.

PTFE-coated TIPS stents should be considered standard of care

When the indication for TIPS is variceal hemorrhage, TIPS should be progressively dilated (starting at 8 mm of diameter) to the minimum diameter needed to achieve a portosystemic pressure gradient (gradient between PV and IVC) below 12 mmHg

In patients whose portosystemic pressure gradient does not decrease below 12 mmHg despite maximum dilation of TIPS (10 mm), NSBB should be added to further decrease portal pressure

Bland portal vein thrombosis does not preclude creation of a TIPS. Referral to experienced centers should be considered

In patients with large spontaneous portal systemic collaterals, collateral embolization at the time of TIPS placement may be considered since it may decrease the risk of hepatic encephalopathy

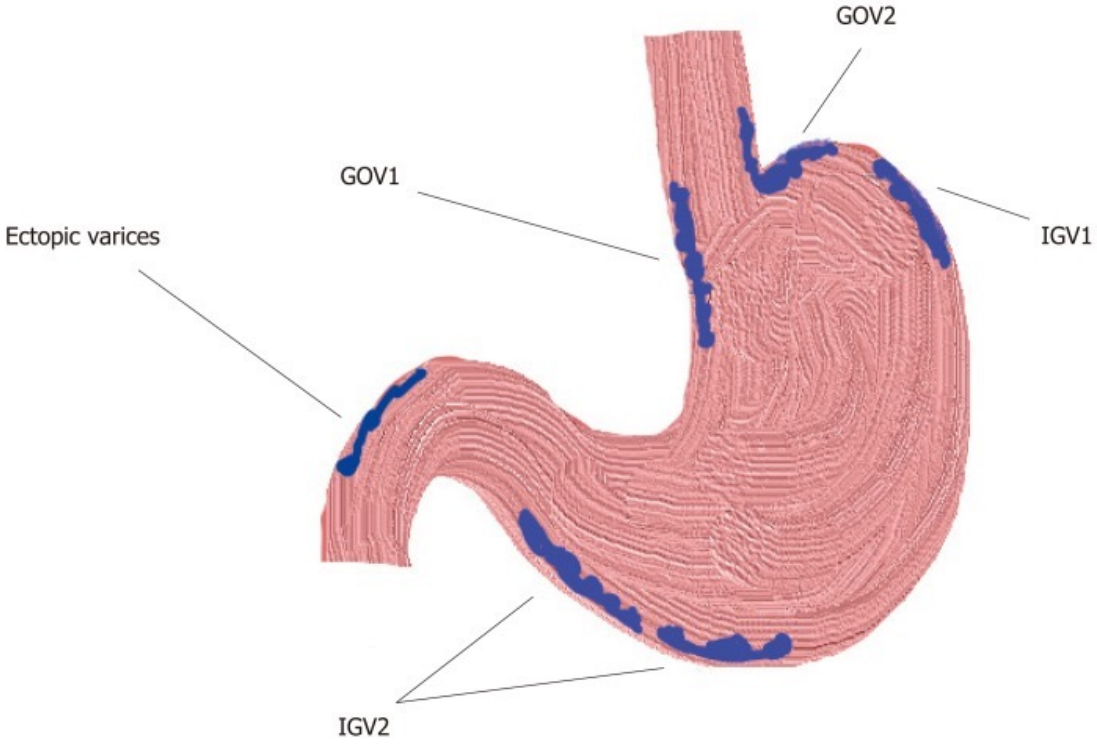
Contraindications for TIPS

Absolute

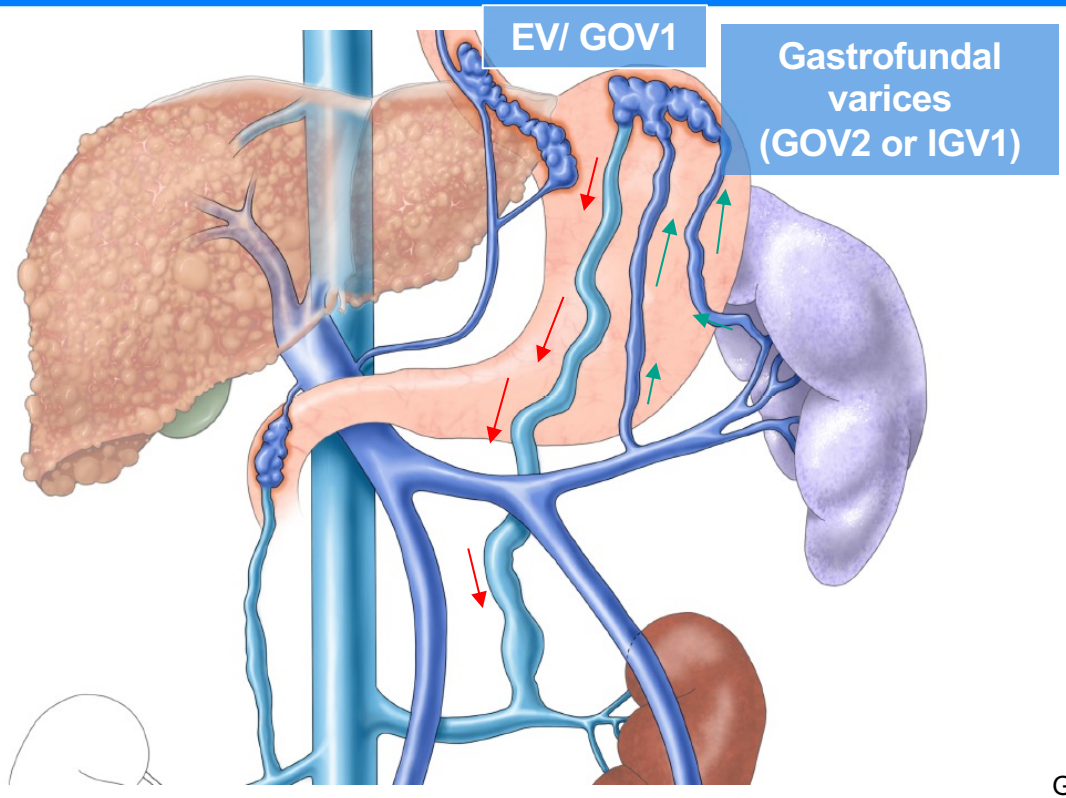
- Congestive heart failure (Stage C/D or EF <50%)
- Severe pulmonary hypertension with mPAP >45 mm Hg
- Severe uncontrolled hepatic encephalopathy
- Uncontrolled sepsis

Relative

- **Balance of risks and benefits is different in uncontrolled bleeding vs. other indications**
- No specific MELD threshold can be recommended to contraindicate TIPS
- Most trials in TIPS for variceal bleeding excluded patients with a Child-Pugh >13
- Patients >75 excluded from RCTs. A recent study suggests acceptable outcomes of TIPS in highly selected patients over 70 years old


GOV2
GOV1
Ectopic varices
IGV1
IGV2

Cardiofundal Varices Drain Through Gastrorenal Shunts, “Stealing” Blood From the Portal Vein into the Systemic Circulation (Decreased Flow to the Liver)



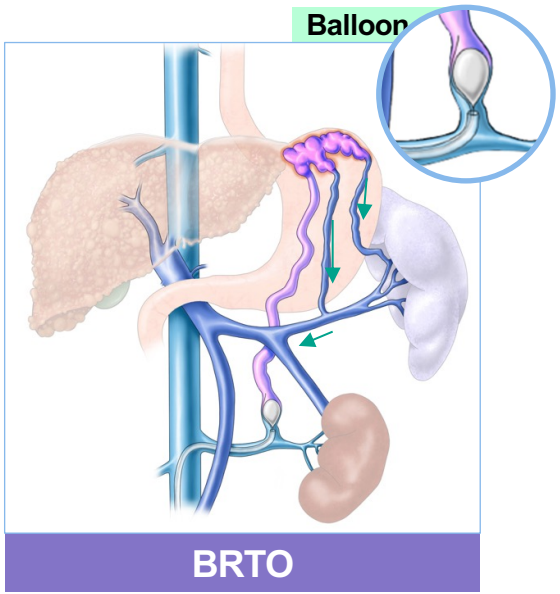
Considerations

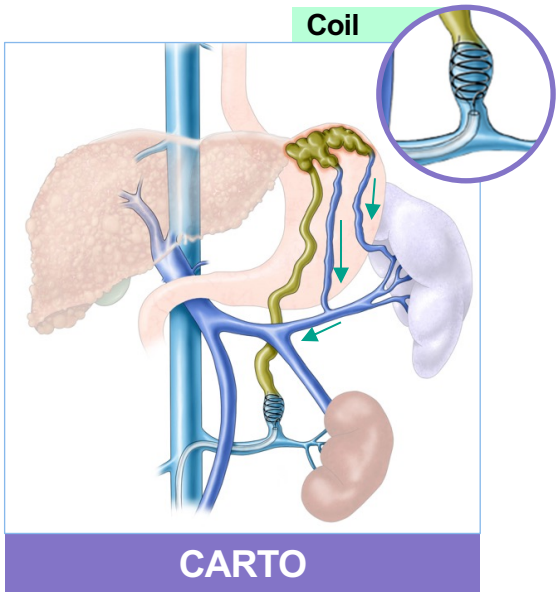
- **Location of the varices**
- **Anatomy of efferent and afferent vessels**
- **Presence of shunts**
- **Flow dynamics of circuit**
- **Splenic vein thrombosis**
- **Liver function (Child Pugh score)**

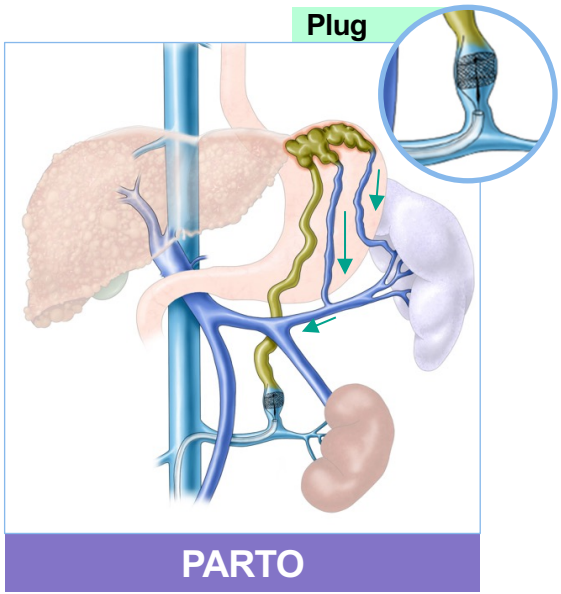
Indication for pre-emptive TIPS and salvage/rescue TIPs are similar to EV/GOV1

GOV=gastro-*o*esophageal varices; IGV= isolated gastric varices
Modified from Dr. Garcia-Tsao..

Gastrorenal Shunts Can Be Obliterated With Sclerosant (BRTO), Coils (CARTO) or Vascular Plugs (PARTO). Blood Flow to Liver Increases.



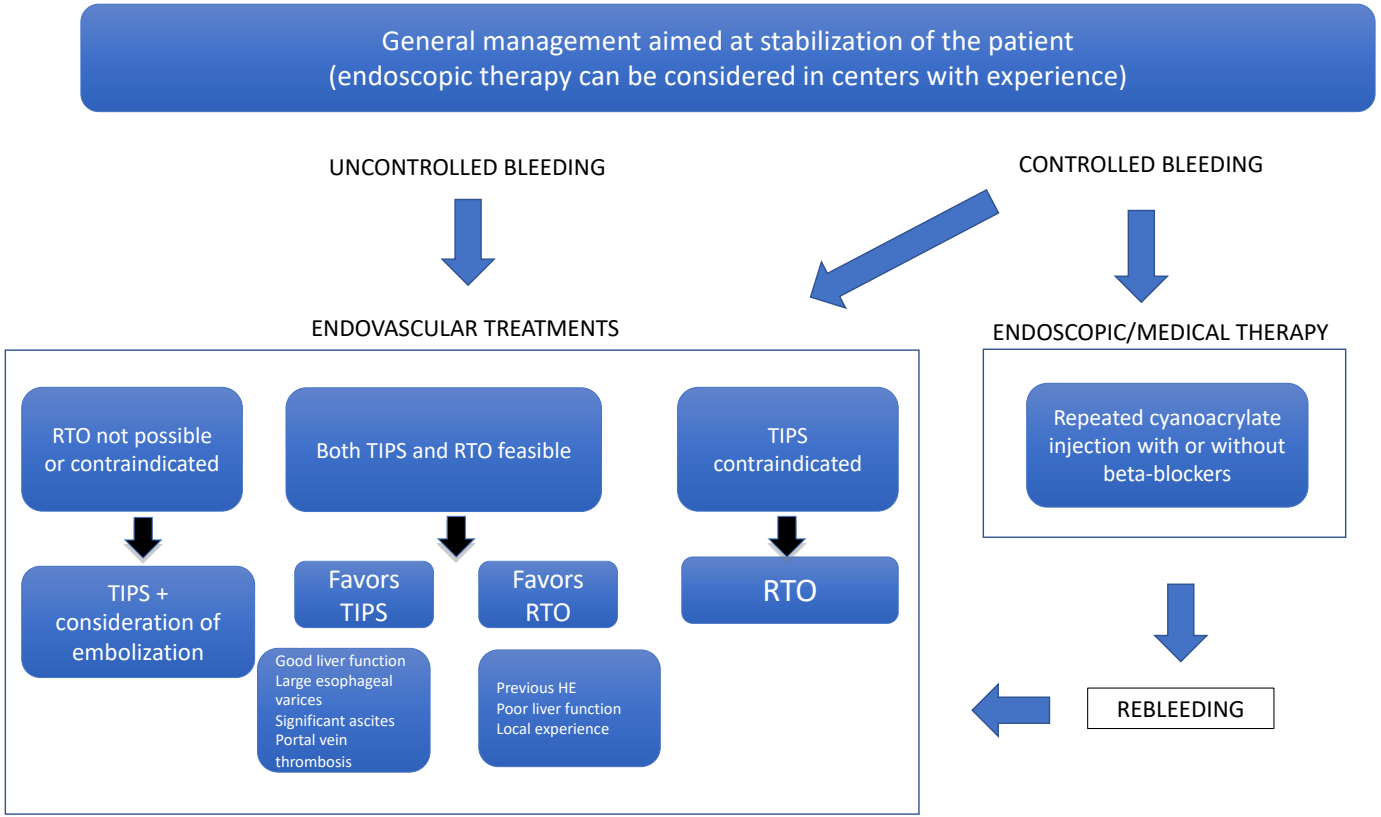




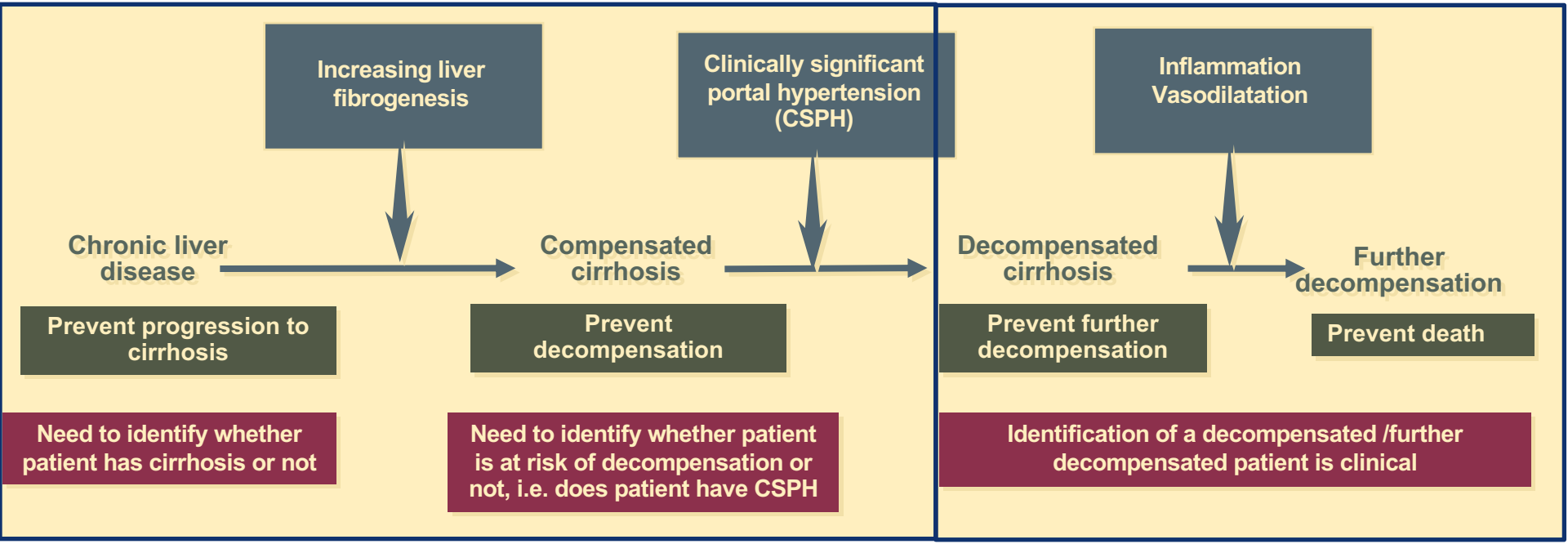
CARTO or PARTO have lower complication profiles compared with traditional BRTO or mBRTO and may be the preferred methods at experienced institutions

Modified from Dr. Garcia-Tsao

Management Algorithm for Variceal Hemorrhage From Gastrofundal Varices (GOV2 or IGV1)



Main Goals in the Management of Chronic Liver Disease Depend on Disease Stage and Type of Complication



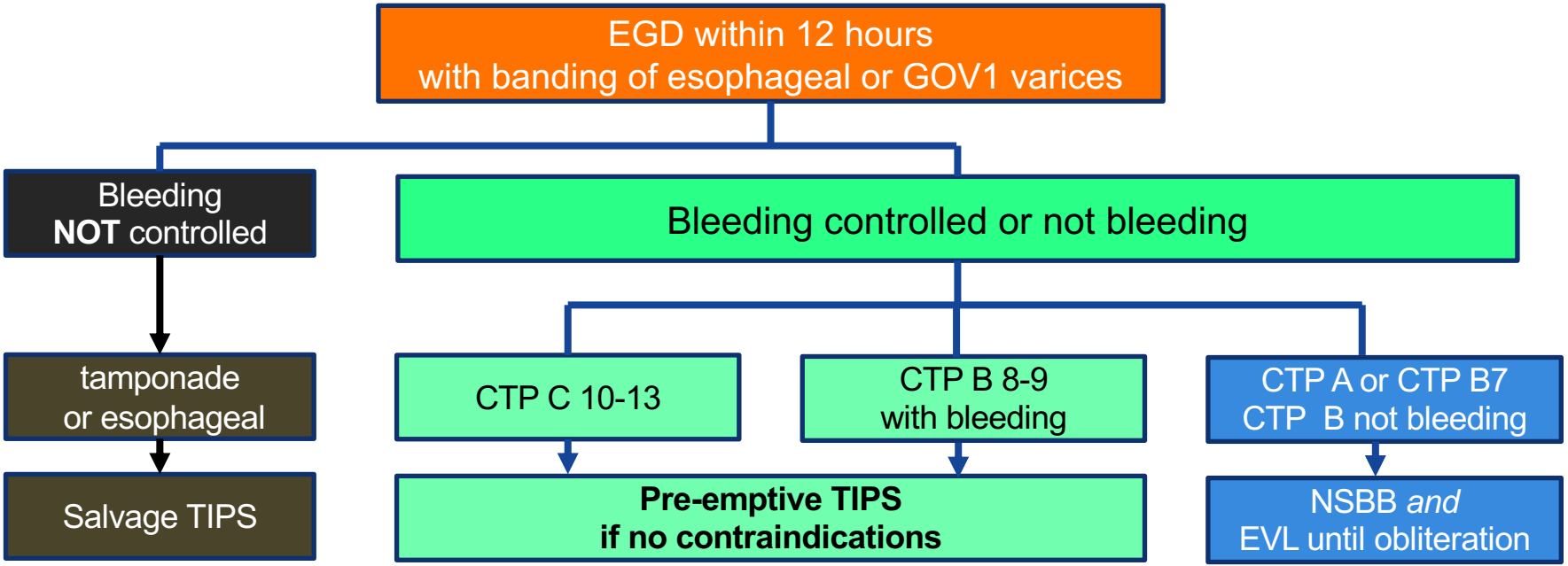
In compensated cirrhosis/cACLD and CSPH, consider starting carvedilol, to prevent decompensation

In patients with first variceal hemorrhage, think of preemptive TIPS to prevent further decompensation/death

Baveno VII consensus. J Hepatol 2022;76:959 and AASLD guidance 2023 [in press].

Modified from Dr. Garcia-Tsao.

Acute UGI bleeding in a patient with ACLD/cirrhosis

Airway protection if AMS
Admit to ICU
CT/MRI/US when stable

Vasoactive agents (octeotride, somatastatin, terlipressin)
Antibiotics (ceftriaxone 1g/d) for 5 days or discharge
Transfuse to Hgb ~7 g/dL; avoid platelets or FFP