TIPS: When is the Appropriate Time?

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Disclosures

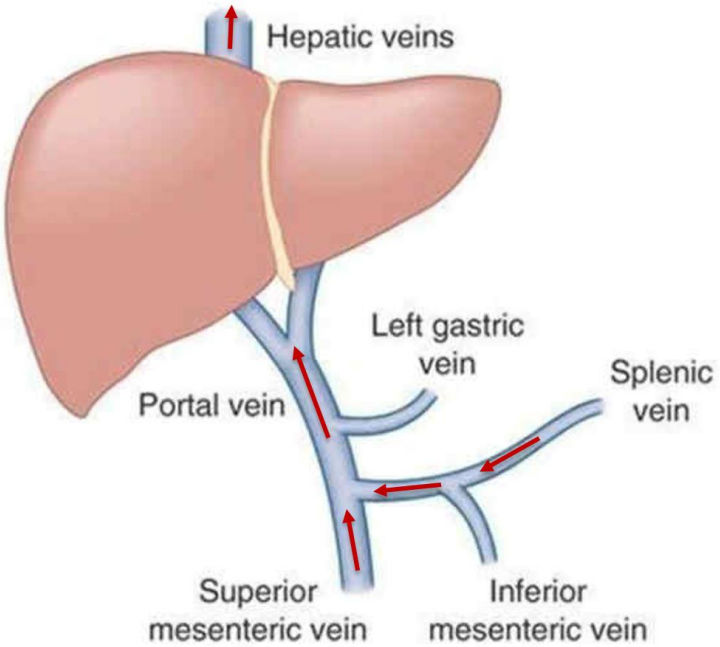
- I have received consulting fees and grant funding from W.L. Gore and Associates, Inc., manufacturer of transjugular intrahepatic portosystemic shunt (TIPS) endoprostheses which will be discussed.

Objectives

- Brief review of TIPS
- Timing of TIPS in Ascites
- Timing of TIPS in Varices
- When to avoid TIPS

Portal Hypertension in Cirrhosis

- Clinically Significant Portal Hypertension = HVPG >10mmHg
- Ascites and varices form when HVPG >10mmHg
- Varices at risk for bleeding when HVPG >12mmHg

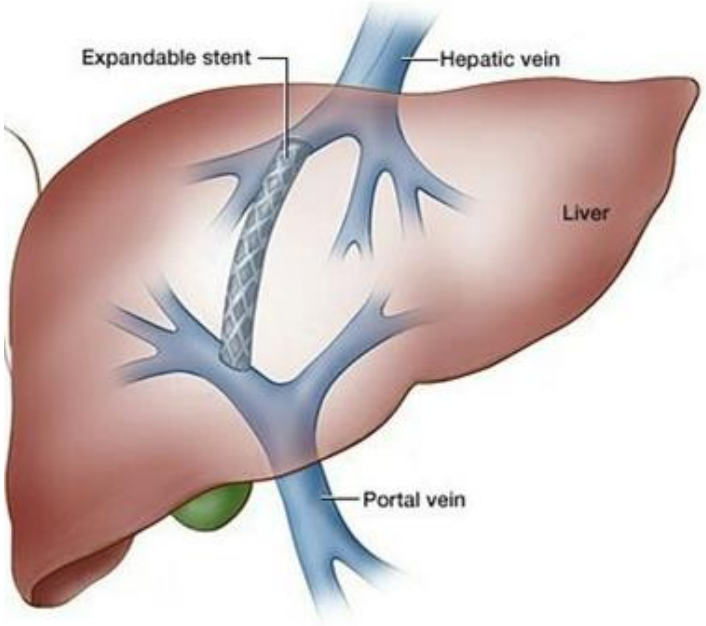


Garcia-Tsao G et al. *Hepatology. 2017.* 65(1), 310-335.

TIPS 101

Transjugular Intrahepatic Portosystemic Shunt

- TIPS effectively reduces portal pressure
- Benefits = resolution of ascites/bleeding varices
- Risks = Hepatic Encephalopathy >> liver decompensation



Hepatic Encephalopathy in TIPS

- Risk factors for HE after TIPS:
  - Sarcopenic / frailty
  - Advanced age (>70 y/o)
  - Unprovoked HE pre-TIPS
  - Advanced liver dysfunction (high MELD)
  - Larger TIPS stent diameter = increased shunting

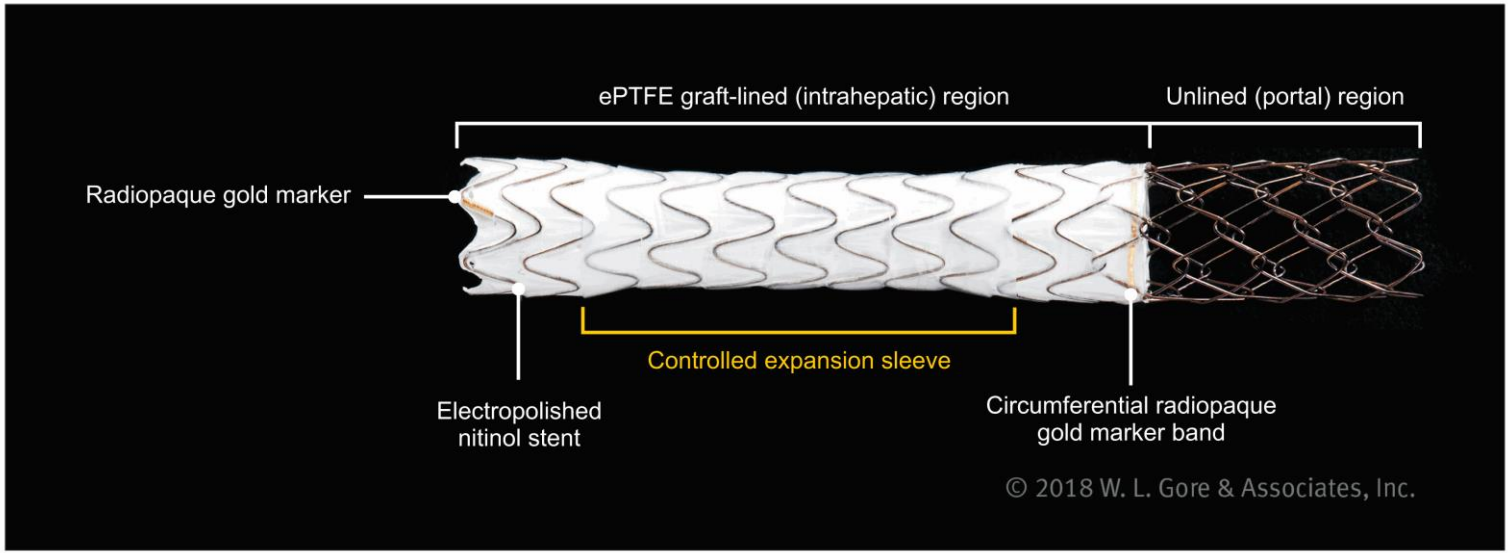
Q	Flow rate
P	Pressure
r	Radius
η	Fluid viscosity
l	Length of tubing

$$Q = \frac{\pi P r^4}{8 \eta l}$$

Boike, JR et al. *Clinical Gastroenterology and Hepatology.* 2021; DeFranchis R et al. *Journal of Hepatology.* 2021.

TIPS Stent Technology

- **Viatorr CX (Controlled Expansion) PTFE “covered” endoprosthesis**
  - Covered portion is intrahepatic / Uncovered in portal vein
  - Controlled Expansion = self expands to 8mm, can be dilated later to 10mm



Viatorr CX Stent

Traditional TIPS Indications

Variceal Bleeding

Ascites

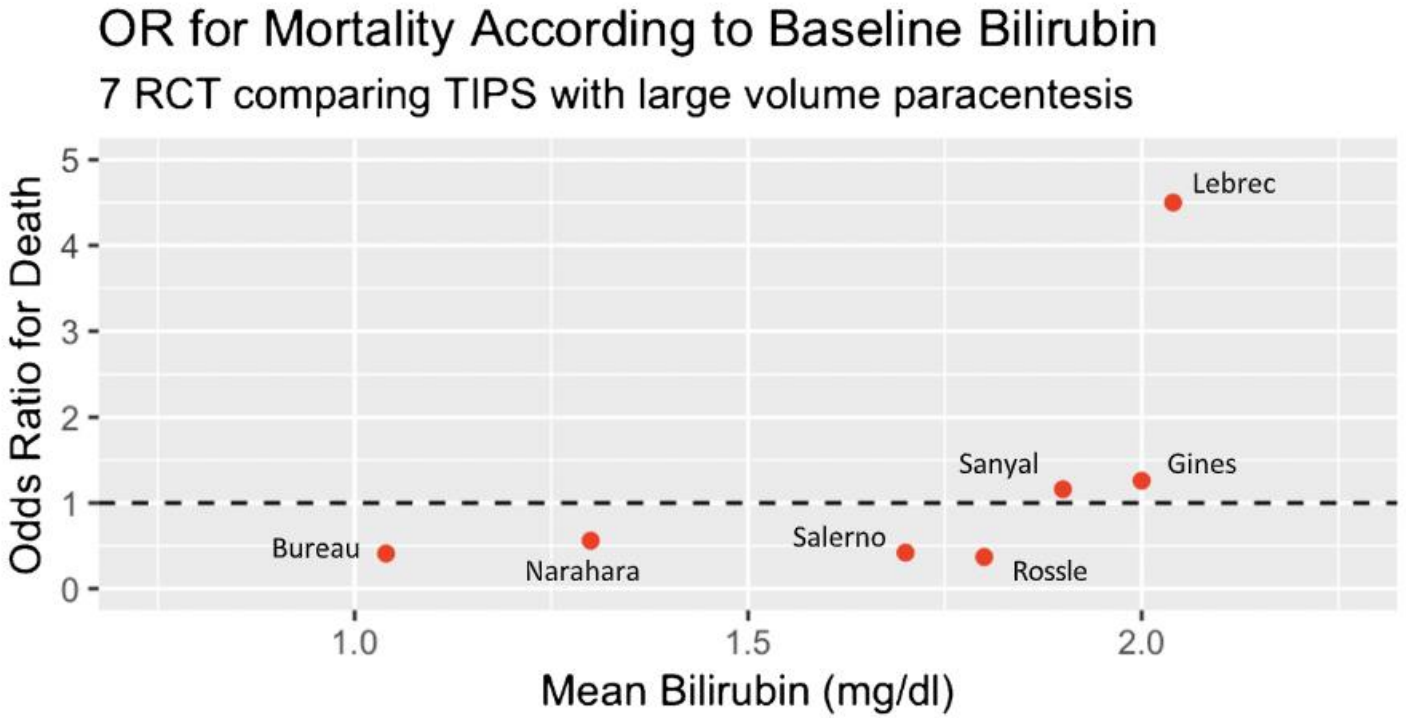
Garcia-Tsao G et al. *Hepatology. 2017.* 65(1), 310-335.

Ascites Management

- Onset of ascites ~ 50% mortality at 1 year
- Large volume paracentesis ≠ improve survival
  - LVP associated with worsening sarcopenia
- TIPS is >80-85% effective at controlling ascites…timing is key

Gines P et al. *N Engl J Med*. 2004; Gines P et al. *N Engl J Med*. 1991; Gines P et al. *Gastroenterology*. 2002.

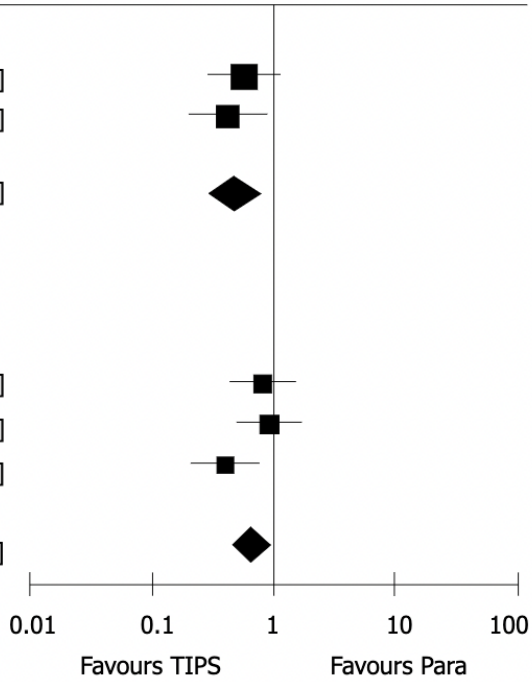
Timing of TIPS



Kok, Beverley, Juan Gonzalez Abraldes et al. *Current Hepatology Reports.* 2019.

TIPS Improves Transplant Free Survival Compared to LVP

Study or subgroup	log [HR]	SE	TIPS Total	Para Total	Weight	HR, 95%CI
Studies with both refractory and recidivant ascites patients						
Rössle, 2000	-0.52	0.32	29	31	54.5%	0.59 [0.32, 1.11]
Salerno, 2004	-0.80	0.35	33	33	45.5%	0.45 [0.23, 0.89]
Total	Fixed		62	64	100.0%	0.52 [0.33, 0.83]
Heterogeneity: $\chi^2 = 0.35$, $df = 1$ ($P = 0.55$); $I^2 = 0\%$						
Test for overall effect: $Z = 2.74$ ($P = 0.006$)						
Studies with only refractory ascites patients						
Ginès, 2002	-0.21	0.32	35	35	33.3%	0.81 [0.43, 1.52]
Sanyal, 2003	-0.09	0.31	52	57	35.4%	0.91 [0.50, 1.68]
Narahara, 2011	-0.92	0.33	30	30	31.3%	0.40 [0.21, 0.76]
Total	Fixed		117	122	100.0%	0.68 [0.47, 0.97]
Heterogeneity: $\chi^2 = 3.83$, $df = 2$ ($P = 0.15$); $I^2 = 48\%$						
Test for overall effect: $Z = 2.11$ ($P = 0.03$)						



Bai, Ming et al. *World Journal of Gastroenterology.* 2014.

CX TIPS vs. LVP in Ascites

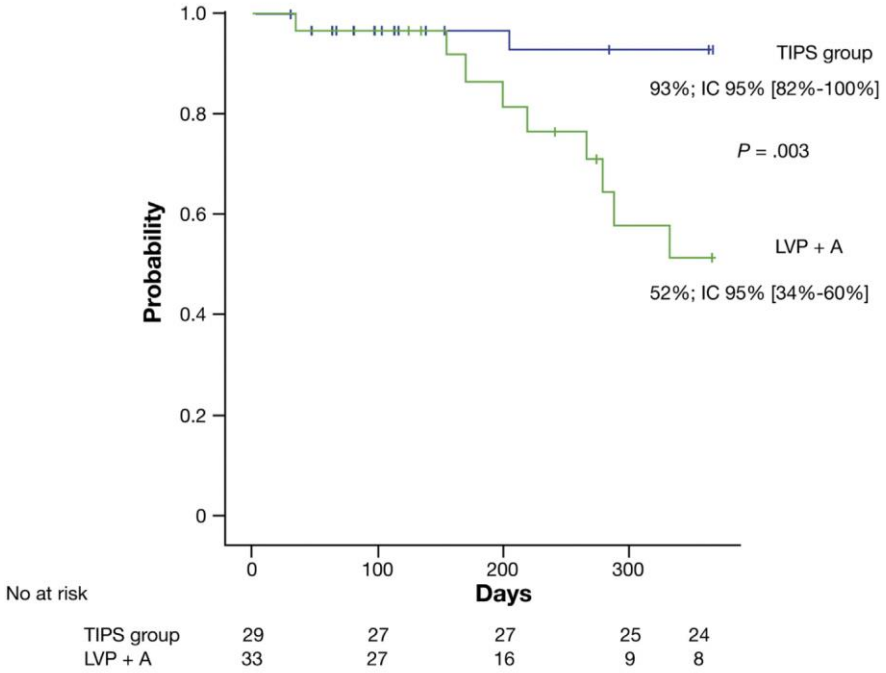


Figure 1. Probability of survival without liver transplantation in patients allocated to covered TIPS group and in those allocated to LVP+A group.

Inclusion:

- ≥2 LVPs in past 6 weeks

Exclusion:

- >6 LVPs in past 3 months

Patient Profile:

- MELD = 12
- Tbili = 1
- INR = 1.4
- Cr = 1.0

Bureau, C et al. *Gastroenterology.* 2017.

TIPS for Ascites

- **AASLD Guideline (2009)** – ascites refractory to diuretics or patient intolerant to diuretics
- **EASL Guideline (2018)** – recurrent of refractory ascites; utilize small caliber stent diameter
- **ALTA Consensus Guidance (2020) –** Consider TIPS for ascites after 3 LVPs in one year despite adequate diuretics
- **Baveno VII Consensus Guidance (2021)** - TIPS should be considered in patients with recurrent ascites ≥3 large-volume paracenteses within 1 year irrespective of the presence or absence of varices or history of variceal haemorrhage. **(GRADE A.1)**

Boyer, TD et al. *AASLD practice guideline update*. 2009; EASL *Journal of Hepatology.* 2018;
Boike, JR et al. *Clinical Gastroenterology and Hepatology.* 2021*;* DeFranchis R et al. *Journal of Hepatology.* 2021.

TIPS for Variceal Bleeding

- **Rescue TIPS:**
  - Variceal bleeding that fails endoscopic band ligation
- **Salvage TIPS:**
  - Uncontrolled variceal bleeding
- **Bleeding Gastric Varices**
  - Center specific; endoscopic gluing vs TIPS with embolization
- **”Early” or Preemptive TIPS…**

Boyer, TD et al. *AASLD practice guideline update*. 2009; EASL. *Journal of Hepatology.* 2018; Boike, JR on behalf of ALTA Consortium. *Clinical Gastroenterology and Hepatology.* 2021.

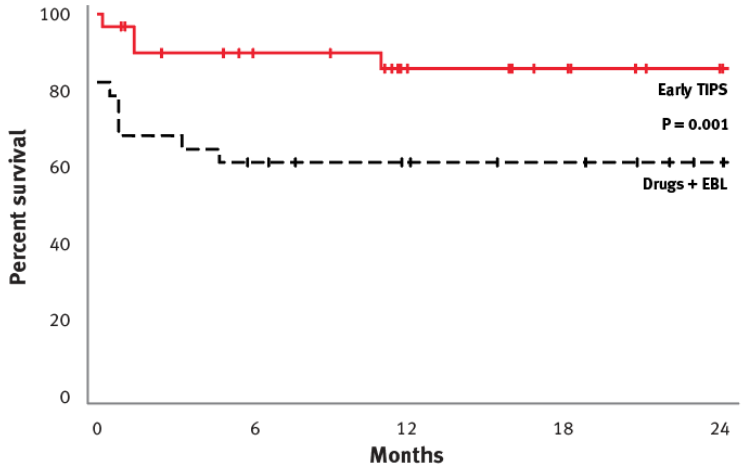
Early Use of TIPS in Patients with Cirrhosis and Variceal Bleeding

Juan Carlos García-Pagán, M.D., Karel Caca, M.D., Christophe Bureau, M.D., Wim Laleman, M.D., Beate Appenrodt, M.D., Angelo Luca, M.D., Juan G. Abraldes, M.D., Frederik Nevens, M.D., Jean Pierre Vinel, M.D., Joachim Mössner, M.D., and Jaime Bosch, M.D., for the Early TIPS (Transjugular Intrahepatic Portosystemic Shunt) Cooperative Study Group

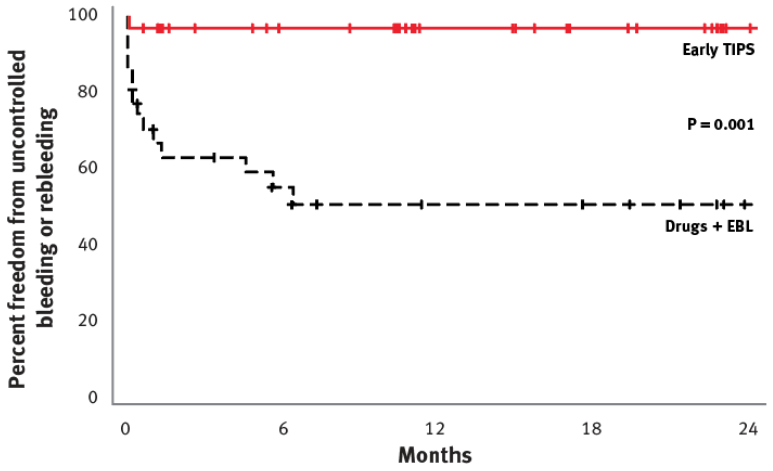
- TIPS within 72 hours in ”select” patients with high-risk for rebleeding
- High-Risk:
  - Childs C cirrhosis (CTP <14) at presentation
  - Childs B cirrhosis with active bleeding during endoscopy despite appropriate therapies (vasoactive medications)

García-Pagán JC et al. *NEJM.* 2010.

Early / Preemptive TIPS – RCT



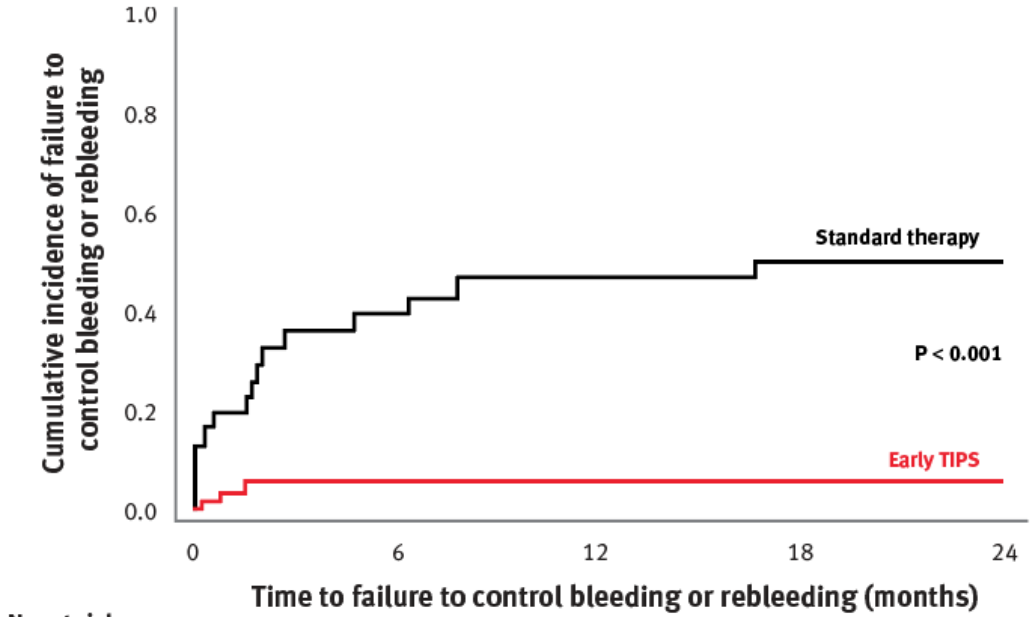
No. at risk					
Early TIPS	32	24	17	12	7
Drugs + EBL	31	18	13	10	5



No. at risk					
Early TIPS	32	24	15	11	5
Drugs + EBL	31	13	7	7	3

García-Pagán, J. C., et al. *NEJM.* 2010.

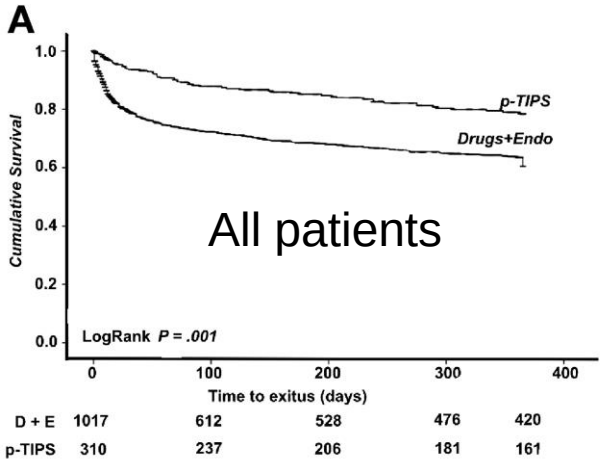
Early / Preemptive TIPS – Retrospective Data

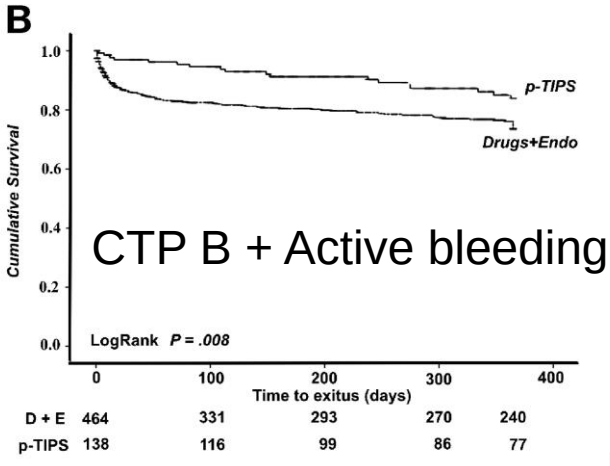


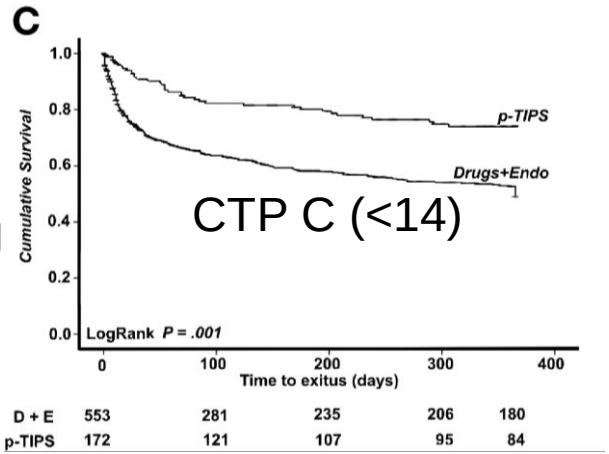
García-Pagán, J. C., et al. *NEJM.* 2010.

Meta-Analysis on Preemptive TIPS

3 RCTs and 4 observational studies to date (2021; 310 = pTIPS vs 1017 standard of care)







Childs B (score ≤ 7) = no difference in survival

Nicoară-Farcău, O. et al, *Gastroenterology.* 2021.

Caveats to Early/Preemptive TIPS

- Highly selected TIPS recipients:
  - Childs C cirrhosis (CTP <14) at presentation
  - Childs B cirrhosis (CTP >7) with active bleeding during endoscopy despite appropriate therapies (vasoactive medications)
  - Excluded patients with: CTP ≥14, gastric varices, HCC outside Milan, creatinine >3 mg/dL
- In clinical practice, ~30% of all variceal bleeding qualify however <10% receive “Early TIPS”

Thabut D et al. *Journal of Hepatology.* 2018.

Early TIPS in Variceal Bleeding

- **Early TIPS:**
  - TIPS within 72 hours of ”select” patients
    - Childs C cirrhosis (CTP <14) at presentation
    - Childs B cirrhosis (CTP >7) with active bleeding during endoscopy
- **AASLD Practice Guidance (2017)**
- **EASL Guidelines (2018) - Level I / Grade 2**
- **ALTA Guidance (2020) - Level 1c**
- **Baveno VII Guidance (2021) - Grade A.1**

Garcia-Tsao G et al. *Hepatology.* 2017; De Franchis R et al. *Journal of Hepatology.* 2015. EASL *Journal of Hepatology.* 2018; Boike JR et al. *Clinical Gastroenterology and Hepatology.* 2021.

When to think twice about TIPS…

- Cardiac
  - EF <50% or severe grade III diastolic dysfunction
  - Mod-severe pulmonary hypertension / RV dysfunction
  - Severe valvular heart dx (aortic stenosis)
- Anatomical
  - Prior hepatic resection, biliary obstruction/dilation
- Advanced hepatic dysfunction
  - MELD >20
  - Refractory HE

Boike JR et al. *Clinical Gastroenterology and Hepatology.* 2021.

Summary

Ascites

- Consider TIPS after ≥3 LVPs despite diuretics
- TIPS earlier in natural history of decompensation associated with improved transplant-free survival
- Utilize small caliber CX TIPS (8mm) to mitigate HE risk

Variceal Bleeding

- Childs C cirrhosis (CTP <14) at presentation
- Childs B cirrhosis (CTP >7) with active bleeding during endoscopy
- *Avoid TIPS in Childs C ≥14; advanced renal dysfunction

Questions?

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