Varices en complicaties

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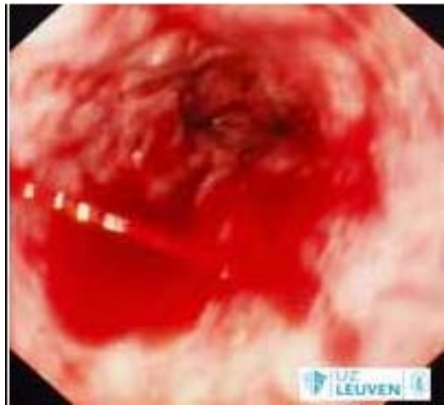
Een patient met cirrose en een hoge gastrointestinale bloeding



- Man 35 j VG angstaanvallen en alcolmisbruik
- 27-05-2019: Braken rood bloed
  Terlipressine en 2 ligaturen (verwijzend ziekenhuis)
  30-05-2019:

  - INR 2,7; Bilirubine 18,7 mg/dl (<1,2); Creatinine 1,4 mg /dl

  - WBC 16 000 (neutrofielen 81% en lymfocyten 6%); CRP 69

  - Gamma GT 325 ; ALT 137 en AST 33

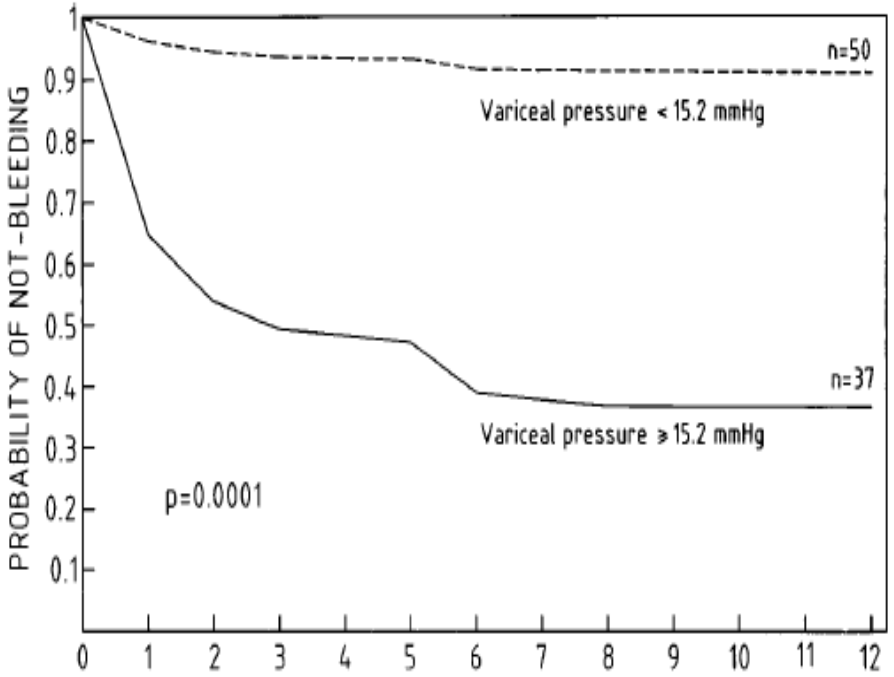
- -Echografie: hepatomegalie, indirecte tekens van cirrose, geen ascites, open vena porta

Complicaties van cirrose en pathophysiologie

- Varices : PH (portale hypertensie)
- Ascites : PH + synthese probleem
- Encefalopathie: PH (shunting) + synthese probleem
- Acuut op chronisch leverfalen: PH + immunologisch defect

Link tussen varices ruptuur en druk

- Risk of variceal rupture is directly linked with portal pressure



Variables Predictive of a First Variceal Bleed Retained in the Multivariate Cox Proportional Hazards Regression Model

Variable	Parameter Estimate	SE	*P*	Risk Ratio	95% Confidence Limits
VP	0.939	0.338	0.005	2.558	1.317-4.968
NIEC index	0.378	0.157	0.016	1.460	1.073-1.987
Time since varices known	−0.020	0.009	0.033	0.980	0.962-0.998

Nevens F, Hepatology 1998

Behandeling van portale hypertensie

Table 2. Treatment of portal hypertension

Mechanism	Treatment
Invasive reduction of portal pressure	TIPS
Reduction of increased portal inflow	Acute conditions: – Terlipressin, somatostatin and analogues Chronic conditions: – NSBB – Carvedilol
Reduction of intrahepatic resistance	Intrahepatic NO donors: – Nitrates in combination with NSBB – Simvastatin – FXR agonists? Prevention of intrahepatic vascular thrombosis: – Enoxaparin Antifibrotic: – Simvastatin – FXR agonists? Prevention of bacterial translocation: – FXR agonists?

Nevens F, Dig Dis 2017

Mortaliteits risico door slokdarmvarices bloeding

- Variceal vs non-variceal bleeding

Crude mortality by endoscopic diagnosis

Endoscopic diagnosis (n)	Crude mortality rate (%) Total* (5004) % (n)	New admissions (4109) % (n)	Inpatients (833) % (n)
Peptic ulcer	8.9 (162/1826)	5.8 (81/1403)	22 (70/322)
Varices	15 (82/544)	11 (51/469)	41 (29/70)

Hearnshaw S, Gut 2011

Bij welke patienten dient men te screenen naar slokdarmvarices ?

Table 1. Non-invasive methods to rule-in clinical significant portal hypertension [5]

In patients with viral induced cirrhosis:
Transelastography ≥20–25 kPa (≥2 measurements on different days in fasting conditions)
In patients with all etiologies:
Collateral circulation on imaging

Baveno consensus, J Hepatol 2015
Nevens F, Dig Dis 2017

Preventie van slokdarmvarices bloeding

- Niet-Selectieve β blockers zijn de standaard

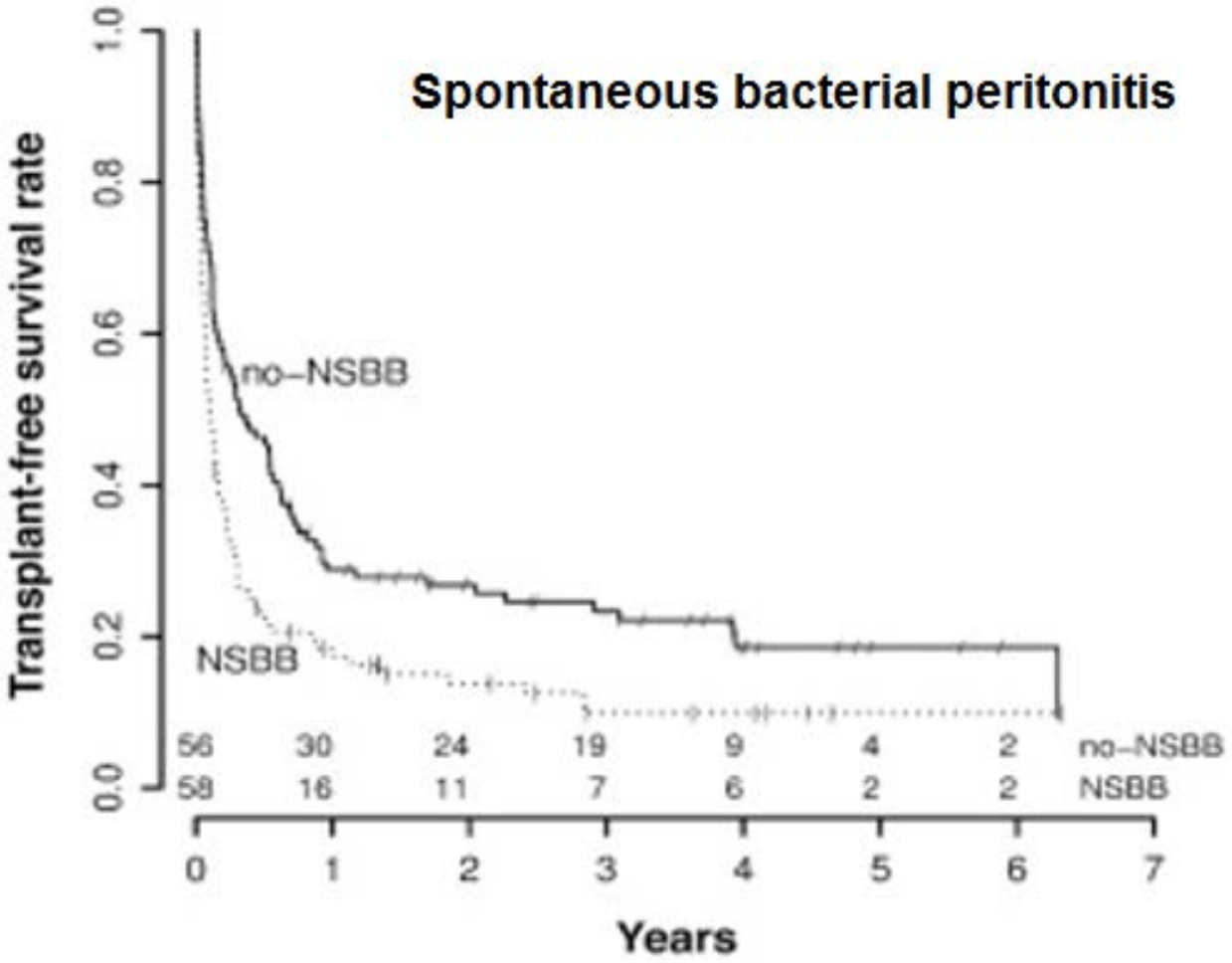
Meta-analytical data on the efficacy of NSBBs for primary and secondary prophylaxis treatment of variceal bleeding

Study	Intervention	Number of trials	Number of patients	Rebleeding	Mortality	Adverse events
Primary prevention						
Gluud and Krag[6]	EBL vs NSBB	19	1504	OR 0.62, CI (0.44 to 0.87)	OR 1.12, CI (0.87 to 1.44)	OR 0.47, CI (0.26 to 0.88)
Secondary prevention						
Laine and Cook[11]	EBL vs Scl	7	547	OR 0.52, CI (0.37 to 0.74)	OR 0.67, CI (0.46 to 0.98)	OR 0.10, CI (0.03 to 0.29)
Bernard *et al*[12]	NSBB vs NT	12	769	OR 0.36, CI (0.24 to 0.53)	OR 0.60, CI (0.42 to 0.87)	OR 3.69, CI (1.81 to 7.54)
Li *et al*[13]	EBL vs NSBB	6	687	OR 0.86, CI (0.43 to 1.76)	OR 1.43, CI (1.00 to 2.05)	OR 0.92, CI (0.66 to 1.28)
Thiele *et al*[5]	Combined EBL and NSBB vs EBL	5	495	OR 0.55, CI (0.39 to 0.78)	OR 0.86, CI (0.58 to 1.27)	OR 1.69, CI (0.95 to 2.99)

Data were obtained from various meta-analyses.
EBL, endoscopic band ligation; NSBB, non-selective β-blockers; NT, no treatment; Scl, sclerotherapy.

Krag A, Gut 2014

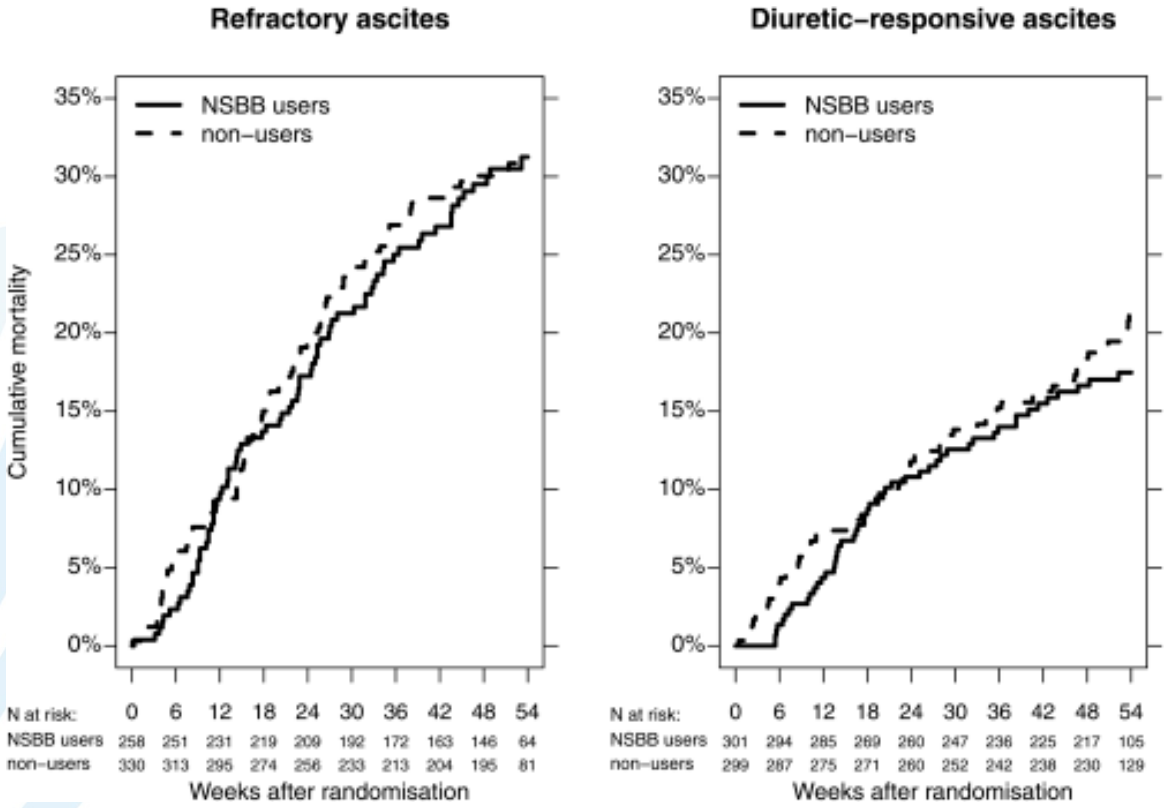
Niet-selectieve betablockers and mortaliteit bij patienten met ascites



Sersté T, Hepatology 2010
Mandorfer M, Gastroenterology 2014

- **Geen toegenomen mortaliteit**

Posthoc analysis of 3 randomized controlled trials (n=1198)



Bossen L, Hepatology 2016

Study on 28-day mortality in 624 consecutive patients with decompensated cirrhosis and ascites

RESULTS

- Mortality was numerically lower with Non-selective betablockers(NSBB)

  But survival benefit was lost with MAP <65 mmHg (p=0.5)
  - Similar results in ACLF and Spontaneous Bacterial Peritonitis patients(SBP)

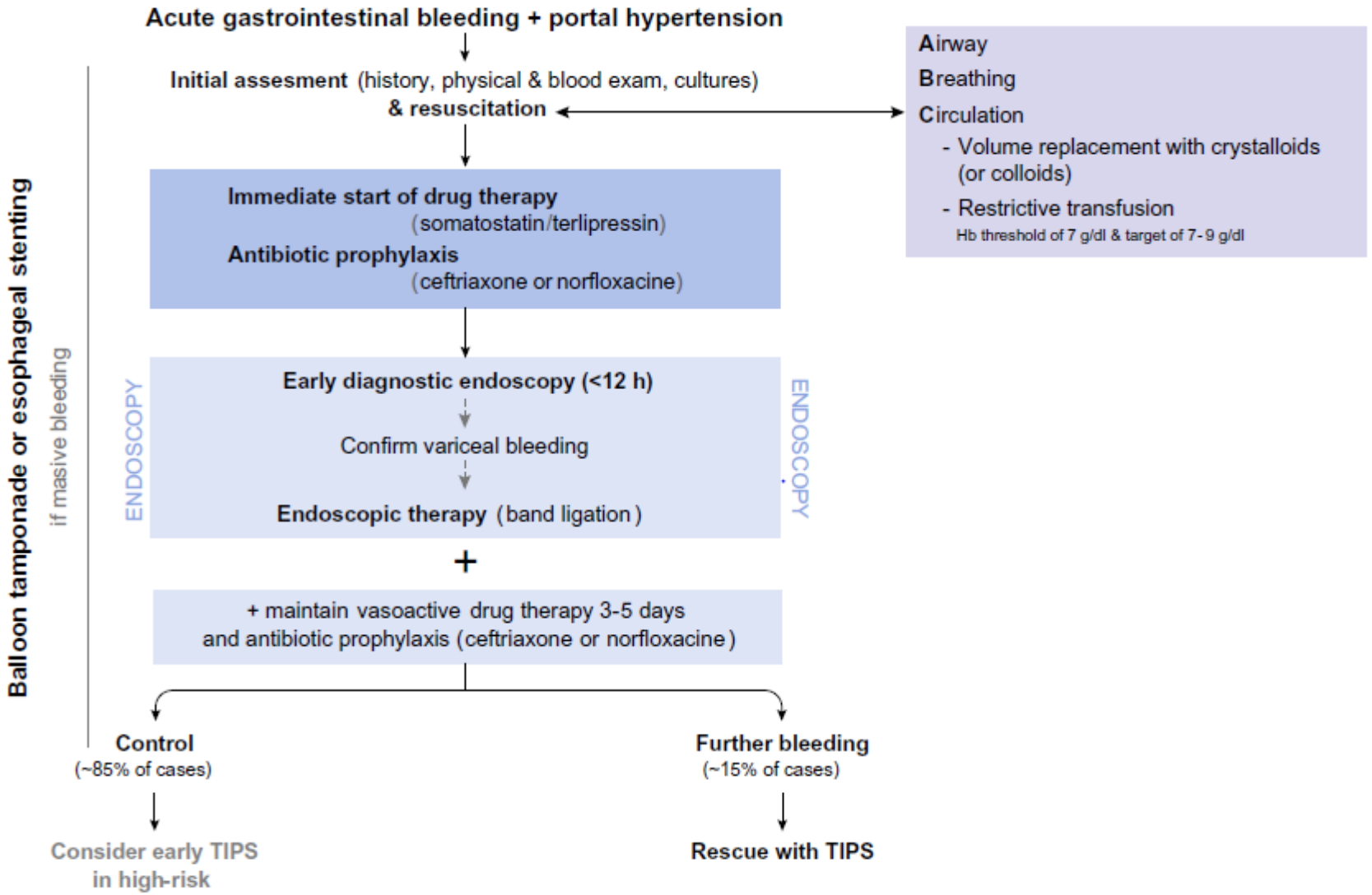
CONCLUSIONS

Neither the degree of Ascites, ACLF nor SBP *per se* seem to limit the safe usage of NSBB in patients with cirrhosis.

In contrast, a low MAP might be a more valid indicator to determine the therapeutic window of NSBB treatment.

Tergast TL A , ILC 2019; PS-081

Behandeling van slokdarmvarices bloeding



EASL guidelines, J Hepatol 2019

Terlipressin and Hyponatremie

Incidence of hyponatremia in recent studies using terlipressin for acute variceal bleeding

	number	Hyponatremia
Solà et al (ref 8)	58	21 (36%)*
Seo et al (ref 7)	261	30 (11%)**
Yim et al (ref 12)	151	29 (19%)

* decrease > 10 mEq/l

** vs 3 (1.5 %) with somatostatin and 2 (1.2 %) with octreotide

Nevens F, Baveno meeting 2015

Optimale timing van endoscopie bij vermoeden van slokdarmvarices bloeding

BACKGROUND & AIMS

- Guidelines recommend endoscopy 12–24 hours from hospital admission, but evidence is limited
- Aim: to investigate the link between endoscopy timing and 42-day mortality in variceal bleeding

METHODS

Prospective data on patients admitted with variceal bleeding at 34 centres in Europe and Canada

Association between endoscopy timing and 42-day mortality

Population characteristics (n=1,373†)	
Mean age, years	59
Mean Child–Pugh score	8.2
Endoscopy timing, %:	
<6 hours	69
6–12 hours	18
12–24 hours	8
>24 hours	5
42-day mortality, %	26.2

Laursen SB, ILC 2019; PS-022

Optimale timing van de endoscopie bij vermoeden van slokdarmvarices bloeding

RESULTS

- Endoscopy within 24 hours of admission was associated with lower mortality in:
  - Patients with Child–Pugh A or B cirrhosis
  - Patients with with Systemic blood pressure <90 mmHg

- Endoscopy within 6–12 hours was not associated with further reduction in mortality

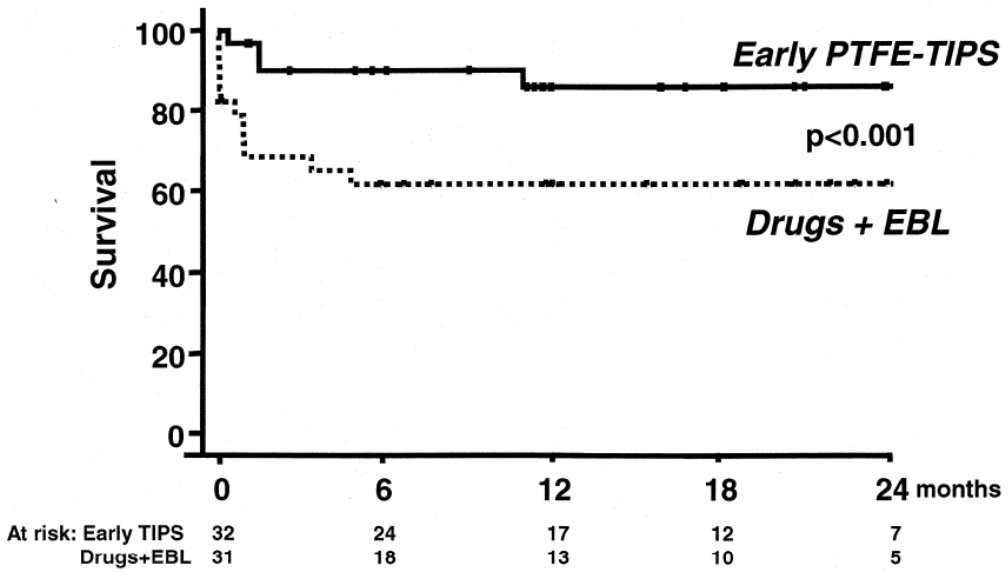
Laursen SB, ILC 2019; PS-022

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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



Garcia Pagán JC, New Eng J Med 2010

Early TIPS with covered stent vs. standard treatment for variceal bleeding in patients with advanced cirrhosis: A randomized controlled trial

BACKGROUND & AIMS

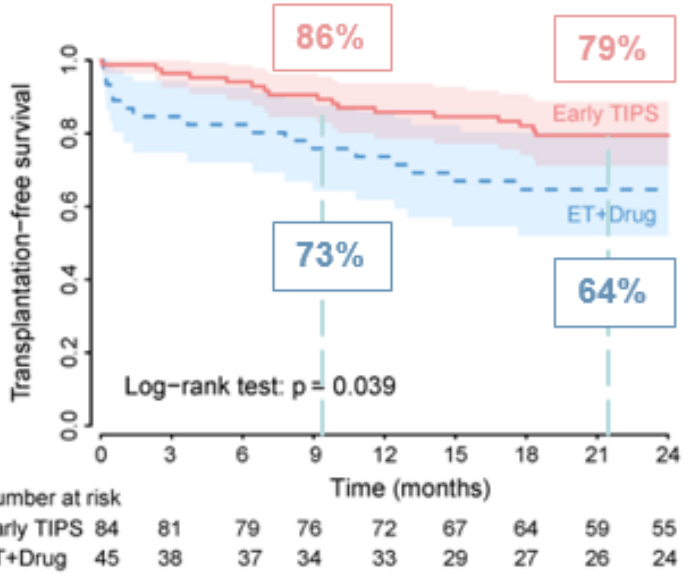
- Early TIPS improves survival in high-risk patients with cirrhosis and variceal bleeding (ABV)
- Whether the same can be achieved in a broader population remains to be assessed

METHODS

- Consecutive patients with advanced cirrhosis (Child–Pugh B or C) and AVB

RESULTS

- 129 patients were randomized (early TIPS, n=84; Endotherapy (ET) + Drug group, n=45)
- Transplant-free survival was higher with early TIPS vs ET+ Drug



Lv Y, ILC 2019; PS-024

Early TIPS with covered stent vs. standard treatment for acute variceal bleeding in patients with advanced cirrhosis: A randomized controlled trial

RESULTS (Cont.)

Beneficial in most subgroups (*Figure*)

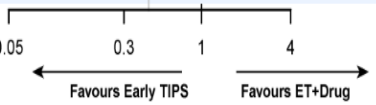
Early TIPS was associated with:

- Decreased risk of failure to control bleeding/rebleeding
- New/worsening ascites

No increase in frequency/severity of hepati encephalopathy and other adverse events

C

Subgroups	Early TIPS Events/Total, (%)	ET+Drug Events/Total, (%)	Adjusted Hazard Ratio (95% CI)	P for interaction
Early TIPS criteria *				0.770
Low risk	8/48 (17)	7/25 (28)	0.50 (0.18 to 1.40)	
High risk	9/36 (25)	9/20 (45)	0.41 (0.16 to 1.06)	
Child-Pugh class				0.913
B	11/65 (17)	11/35 (31)	0.46 (0.20 to 1.07)	
C	6/19 (32)	5/10 (50)	0.44 (0.13 to 1.50)	
Child-Pugh class and active bleeding				0.807
Child B without active bleeding	8/48 (17)	7/25 (28)	0.50 (0.18 to 1.40)	
Child B + active bleeding	3/17 (18)	4/10 (40)	0.38 (0.08 to 1.72)	
Child C	6/19 (32)	5/10 (50)	0.44 (0.13 to 1.50)	
MELD score				0.811
≤11	2/16 (13)	1/10 (10)	1.25 (0.11 to14.06)	
12–18	10/60 (17)	12/31 (39)	0.37 (0.16 to 0.87)	
≥19	5/8 (63)	3/4 (75)	0.74 (0.17 to 3.22)	
All patients	17/84 (20)	16/45 (36)	0.44 (0.22 to 0.88)	



Outcome = Death or transplantation

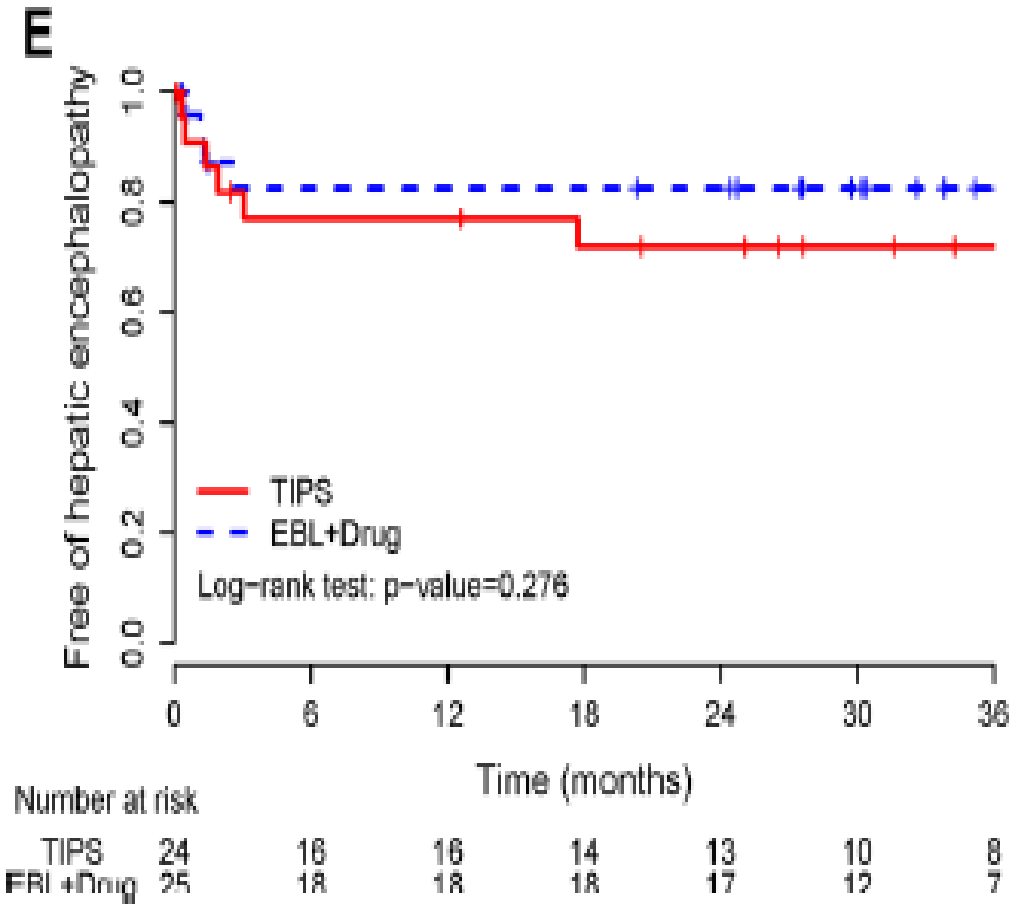
* Early TIPS criteria: low risk: Child-Pugh B without active bleeding at initial endoscopy; high risk: Child B with active bleeding at endoscopy and Child-Pugh class C <14

CONCLUSIONS

Confirmation of the superiority of early TIPS for variceal bleeding

Lv Y, ILC 2019; PS-024

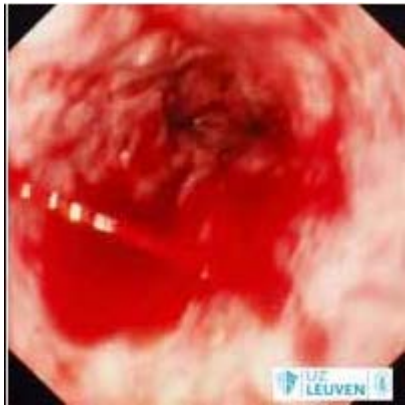
Vroegtijdig TIPS voor slokdarmvaricesbloeding en encefalopathie



Yong Lv, Gut 2017
Garcia Pagan JC, J Hepatol 2013 and NEJM 2010

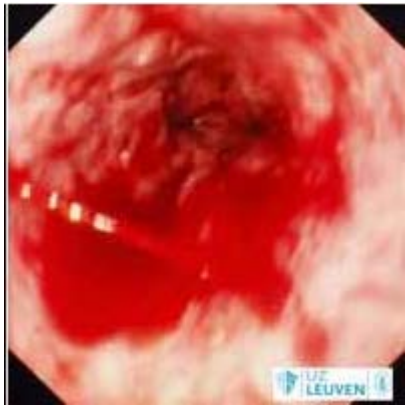
Een patient met cirrose en een hoge gastrointestinale bloeding

- Hoe noem je dit syndroom ?



- alcoholische cirrose
- gedecompenseerde cirrose
- alcoholische hepatitis
- ACLF

Een patient met cirrose en een hoge gastrointestinale bloeding



- Behandeling van de bloedende slokdarmvarices:

  - 5 dagen terlipressine en na 3-4 weken ligaturen
  - TIPS

Besluit en leerstoelstellingen

- Slokdarmvarices (en bloeding) worden veroorzaakt door overdruk
- Slokdarmvarices bloeding heeft nog steeds een hoge mortaliteit en primaire en secundaire preventie is een ‘must’
- Transelastografie kan ons helpen wie we moeten screenen naar de aanwezigheid van varices
- Alleen in geval van hypotensie dienen beta- blokkers gestopt te worden
- Bij hoog risico patienten, om te falen aan vasoactieve medicatie en endotherapie, dient met spoed een TIPS uitgevoerd te worden