Management of difficult ascites: TIPS?

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Organised by: Pr Patrick MARCELLIN
Association for the Promotion of Hepatologic Care (APHC)

CONFLICT OF INTEREST

Abbvie, Gilead, Gore

Clinical Vignette 1: Mr FC, 51 years old

- Outpatient clinics in Aug 2019
- Cirrhosis + NASH
  - with ascites, one paracentesis/week of 8 liters for one year
  - Last EOGD: grade 1 EV (July 2019)
  - US exam: dysmorphia, no nodule, ascites (April 2019)
  - Treatment: spironolactone 75 mg/d, furosemide 40 mg/j
  - No history of HE

- Plt 65G/L, BiliT 55 µmol/L, PT 65%, INR 1.4, Creat 127 µmol/L, Na+ 134 mmol/L, Albumin 32 g/L, Child-Pugh B8, MELD 18

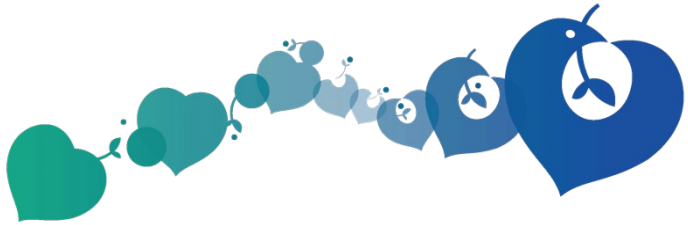
- Wants a paracentesis

Clinical Vignette 1:
Mr FC, 51 years old

- Large volume paracentesis is the best option
- The patient should be referred to a liver transplant unit ASAP
- Increase of diuretics is the best option
- TIPS should be indicated
- It is probably too late for TIPS

What is (are) the correct answer(s) ?

Clinical Vignette 2: Mr MA, 62 years old



- First outpatient visit
- Cirrhosis with active OH consumption, multiple withdrawals and relapses, Child A until then
- Diagnosis of ascites 4 months ago
  - Tx with Spironolactone 300 mg/d, furosemide 160 mg/d (Na+ 137, creat 62)
  - Persistence of tense ascites, Na+ 128, creat 89, decrease diuretics
  - 3 paracentesis within 2 months
  - No HE

- Plt 123G/L, BiliT 16 µmol/l, PT 73%, INR 1.0, Creat 78 µmol/l, Na+ 134 mmol/l, Albumin 33 g/l, Child B8, MELD 6

Clinical Vignette 2: Mr MA, 62 years old

- Large volume paracentesis is the best option
- The patient should be referred to a liver transplant unit ASAP
- Alcohol withdrawal is the best option
- TIPS should be indicated
- It is probably too late for TIPS

What is (are) the correct answer(s) ?

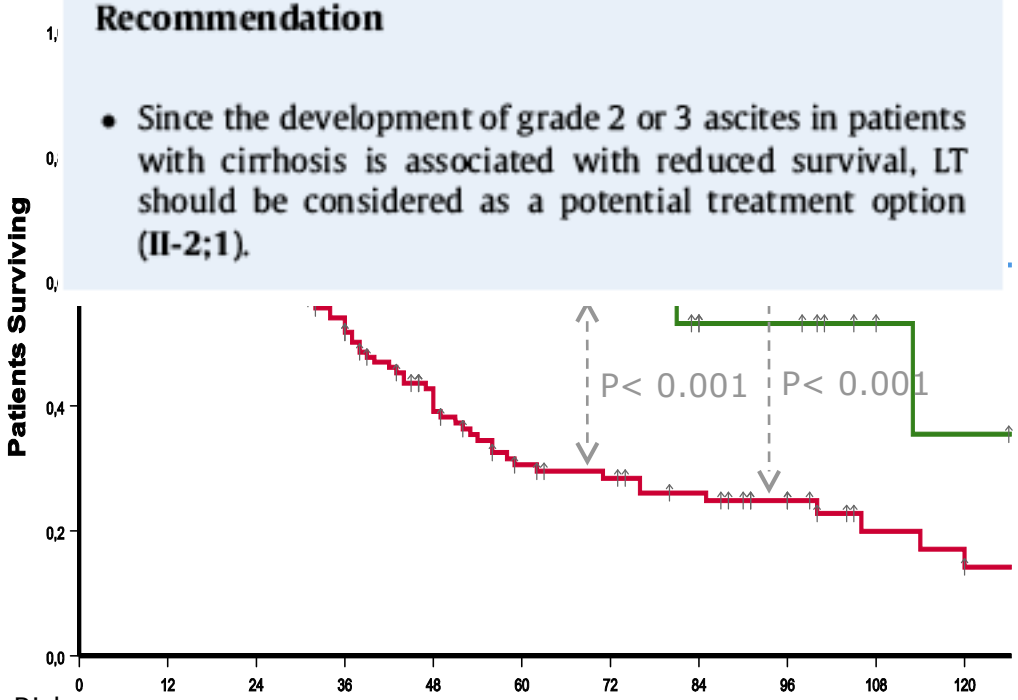
Prognostic value of different stages of cirrhosis

Different substages of decompensated cirrhosis:

- Bleeding without any other decompensation
- Ascites without bleeding
- Bleeding and any other decompensation

Recommendation

- Since the development of grade 2 or 3 ascites in patients with cirrhosis is associated with reduced survival, LT should be considered as a potential treatment option (II-2;1).



N=398

Bleeding alone

Ascites(±HE)

Bleeding & Ascites(±HE)

Patients at Risk

Bleeding	90	79	66	55	43	31	19	7	7	4	2
Ascites	131	120	108	96	84	71	60	48	36	24	12
Bleeding+Ascites	177	166	153	142	130	118	106	93	82	70	58

Garcia-Guix M et al., EGTSS
C Villanueva AASLD 2016
D'Amico , AP&T 2014

Refractory ascites:
Therapeutic options

- **Liver transplantation**
- **LVP + albumin**
- **TIPS**
- **Peritoneo-vesical shunt = Alfapump®**

EASL CPG: refractory ascites

Clinical Practice Guidelines

JOURNAL OF HEPATOLOGY

EASL Clinical Practice Guidelines for the management of patients with decompensated cirrhosis☆

European Association for the Study of the Liver*

- Repeated LVP plus albumin (8 g/L of ascites removed) are recommended as first line treatment for refractory ascites (I;1).
- Diuretics should be discontinued in patients with refractory ascites who do not excrete >30 mmol/day of sodium under diuretic treatment (III;1).

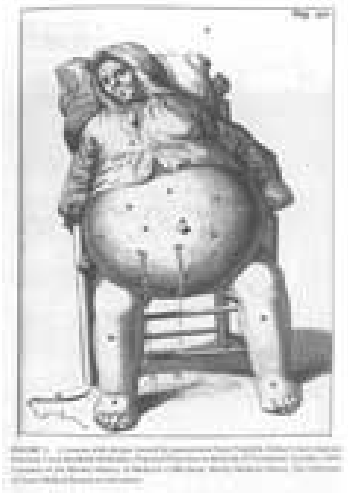
- TIPS insertion is recommended in patients with recurrent ascites (I;1) as it improves survival (I;1) and in patients with refractory ascites as it improve the control of ascites (I;1).
- The use of small-diameter PTFE-covered stents in patients is recommended to reduce the risk of TIPS dysfunction and hepatic encephalopathy with a high risk of hepatic encephalopathy is recommended (I;1).

- Careful selection of patients for elective TIPS insertion is crucial, as is the experience of the centre performing this procedure. TIPS is not recommended in patients with serum bilirubin > 3 mg/dl and a platelet count lower than 75 x 10^9/L, current hepatic encephalopathy grade ≥2 or chronic hepatic encephalopathy, concomitant active infection, progressive renal failure, severe systolic or diastolic dysfunction, or pulmonary hypertension (III;1).

J Hepatol 2018

BLIPS

Refractory ascites:
LVP or TIPS ?



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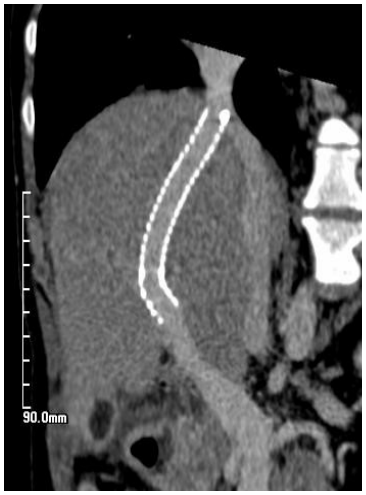


6 Randomized controlled trials

Lebrec D et al., J Hepatol 1996
Rössle M et al., NEJM 2000*
Gines P et al., gastroenterology 2002
Sanyal A et al., Gatsroenterology 2003
Salerno F et al., Hepatology 2004*
Narahara Y et al., J Gastroenterol 2011

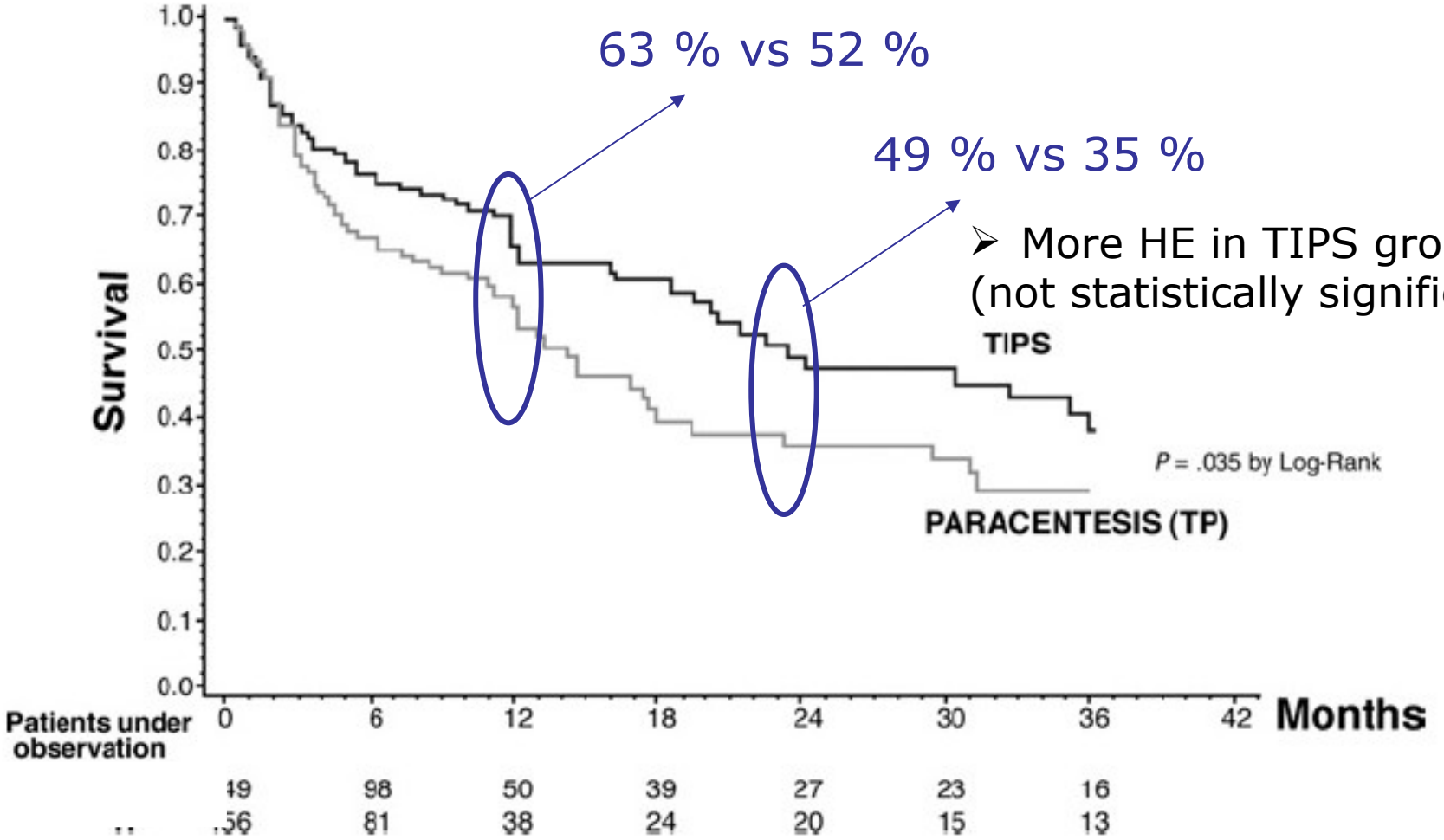
7 meta-analyses

Deltenre P et al., Liv Int 2005
Albillos A et al., J Hepatol 2005
D'Amico G et al., Gastroenterology 2005
Saab S et al., Cochrane 2006
Salerno F et al., Gastroenterology 2007
Chen RP et al., J Clin Gastroenterol 2014
Bai M et al., WJG 2014

- *including recurrent ascites
- Bare-metal stents
- Some rather severe patients (Bili 5-10 mg/dl)

TIPS and refractory ascites: meta-analyse of 4 RCT, individual data

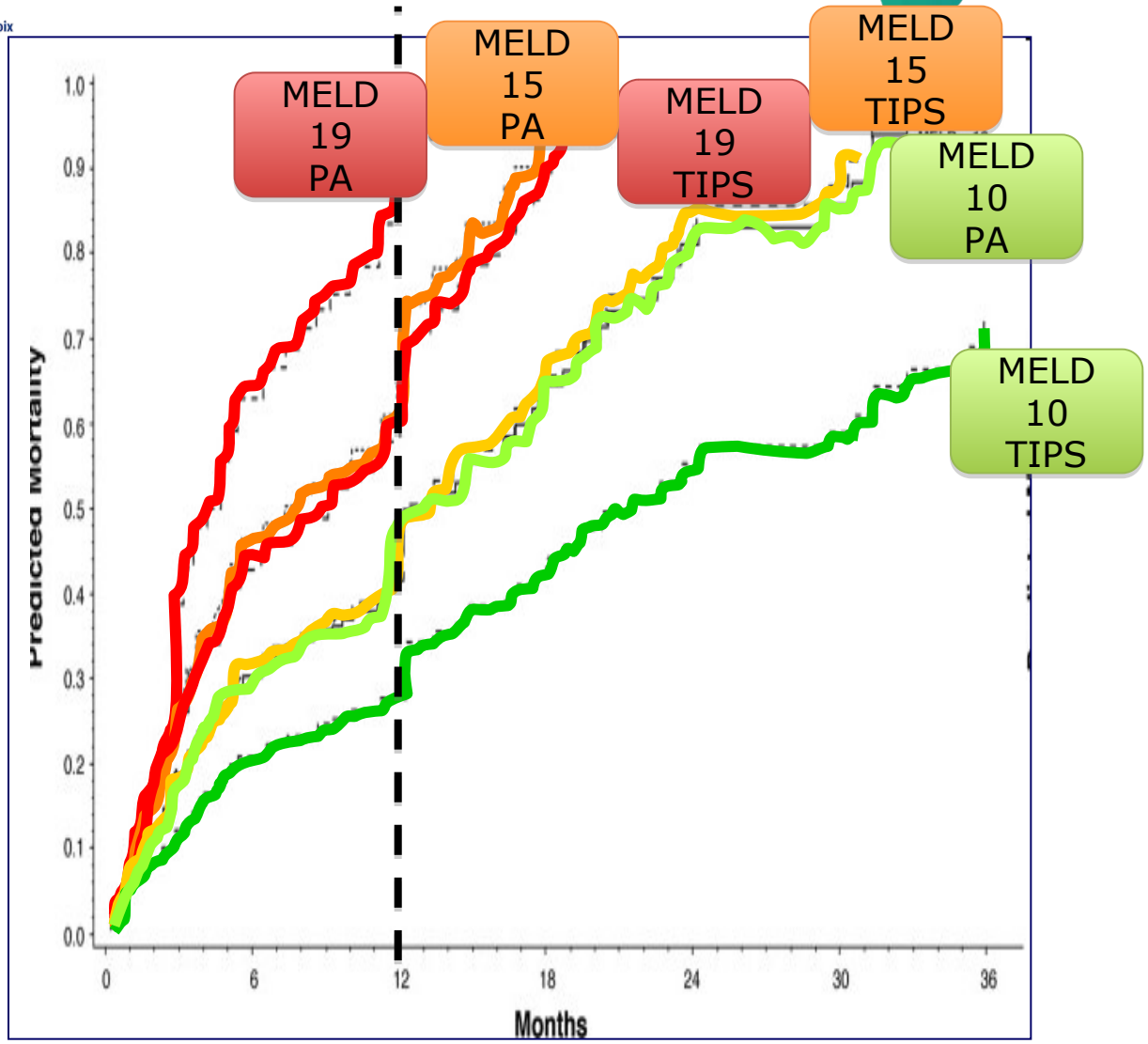
(non covered TIPS, n=305)



- More HE in TIPS group (not statistically significant)

Salerno F et al., Gastroenterology 2007

TIPS and refractory ascites: meta-analyse



Salerno F et al., Gastroenterology 2007

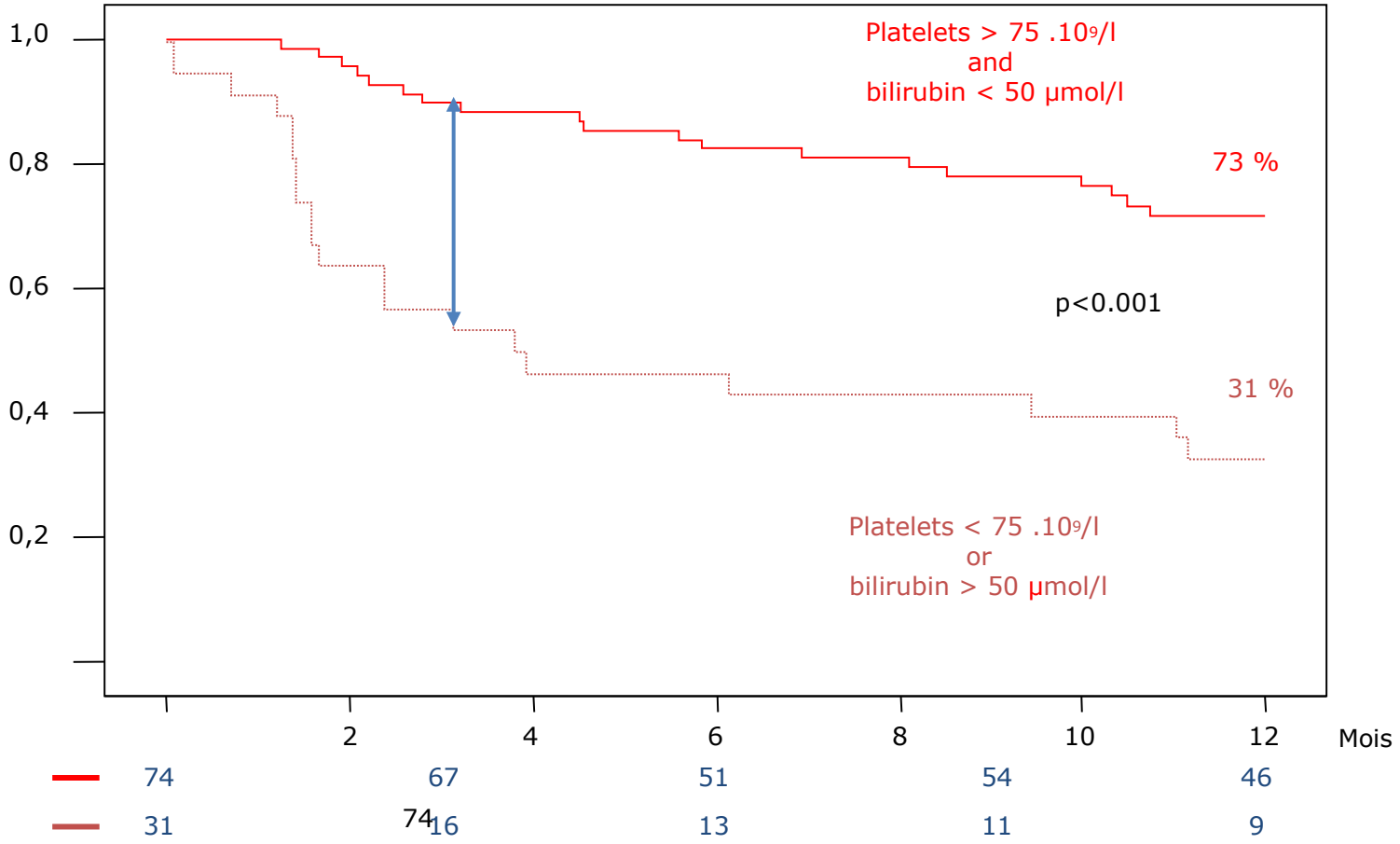
TIPS in refractory ascites:
It's all about patients' selection

3 main issues after TIPS placement:

- Liver failure and death
- Cardiac decompensation≈20%
- HE≈35% (refractory HE ≈5%)

Discuss TIPS placement AND liver transplantation at the same time (no TIPS/ TIPS failure/ complication after TIPS)

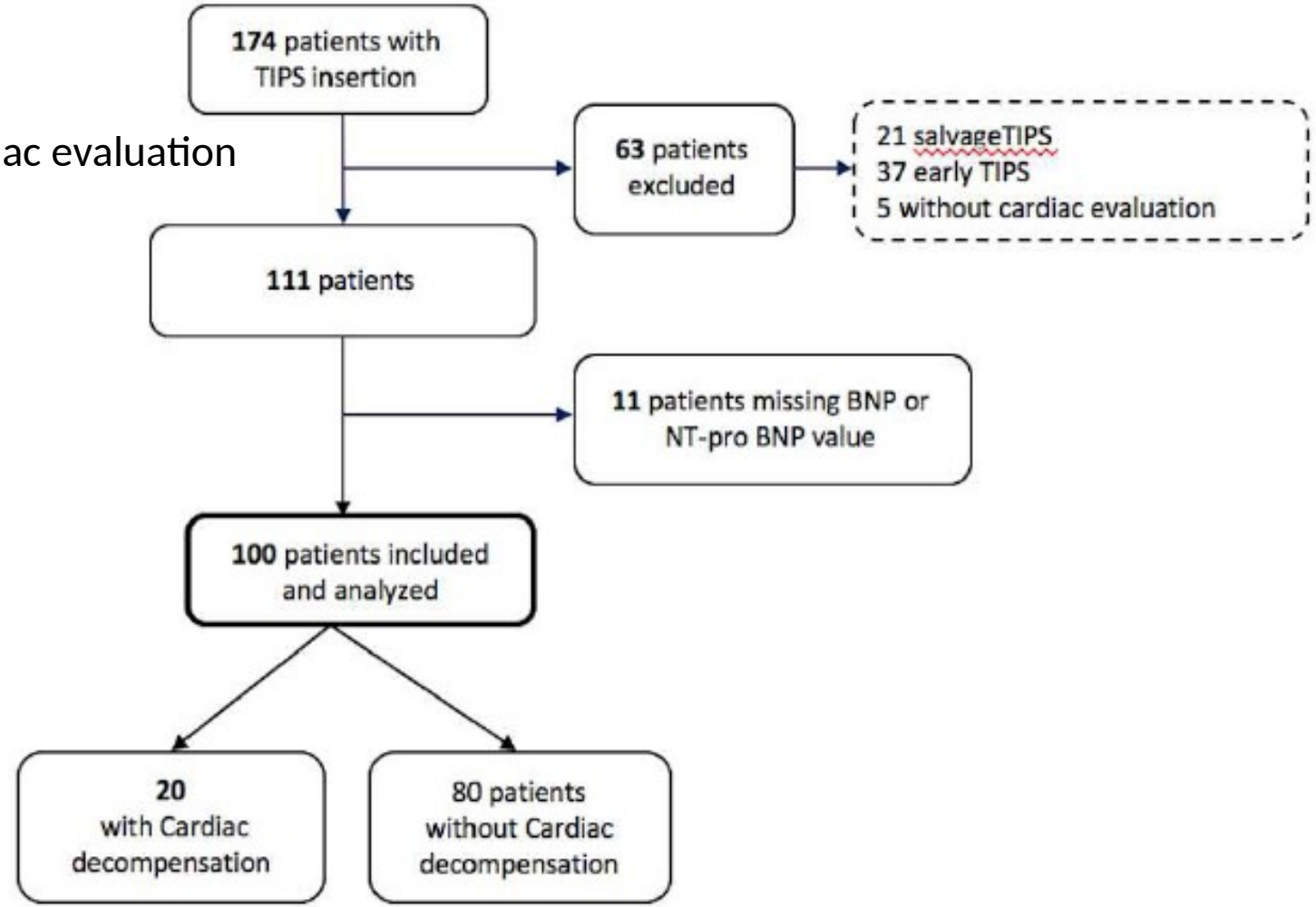
TIPS in refractory ascites:
Patients' selection



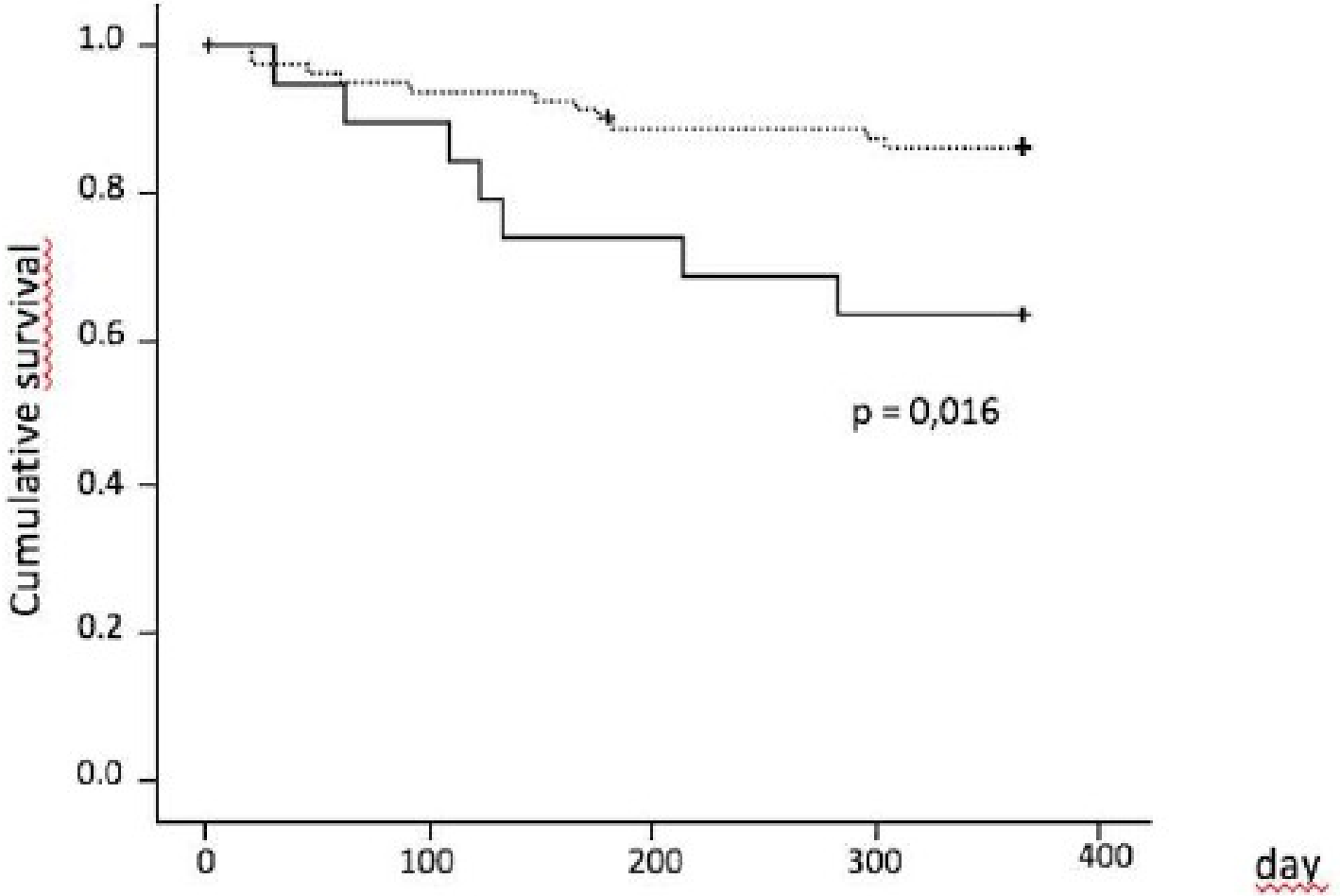
Bureau et al. J Hepatol 2011

Covered TIPS in refractory ascites:
Patients' selection

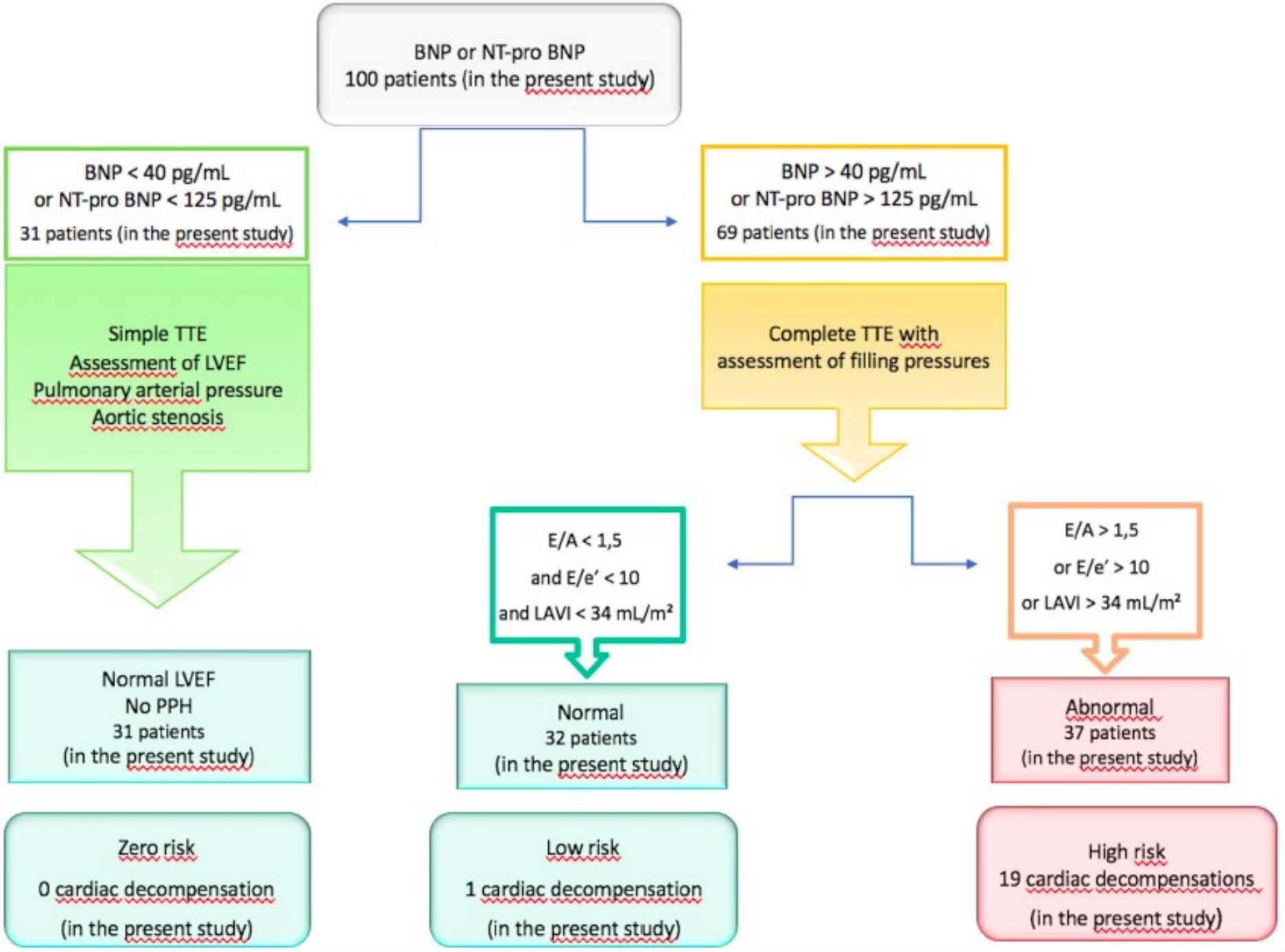
Careful cardiac evaluation
Biological
TTE



Billey et al. Hepatology 2019



·····	No cardiac decompensation	80	75	69	67	66
———	Cardiac decompensation	20	17	14	12	11


BNP or NT-pro BNP
100 patients (in the present study)
BNP < 40 pg/mL
or NT-pro BNP < 125 pg/mL
31 patients (in the present study)
BNP > 40 pg/mL
or NT-pro BNP > 125 pg/mL
69 patients (in the present study)
Simple TTE
Assessment of LVEF
Pulmonary arterial pressure
Aortic stenosis
Complete TTE with
assessment of filling pressures
E/A < 1,5
and E/e' < 10
and LAVI < 34 mL/m²
E/A > 1,5
or E/e' > 10
or LAVI > 34 mL/m²
Normal LVEF
No PPH
31 patients
(in the present study)
Normal
32 patients
(in the present study)
Abnormal
37 patients
(in the present study)
Zero risk
0 cardiac decompensation
(in the present study)
Low risk
1 cardiac decompensation
(in the present study)
High risk
19 cardiac decompensations
(in the present study)

Risk factors of HE after TIPS:
Patients' selection

Age

MELD score and Child-Pugh score

Previous history of HE

Minimale HE (PHES/CFF)

PPG <5 mmHg

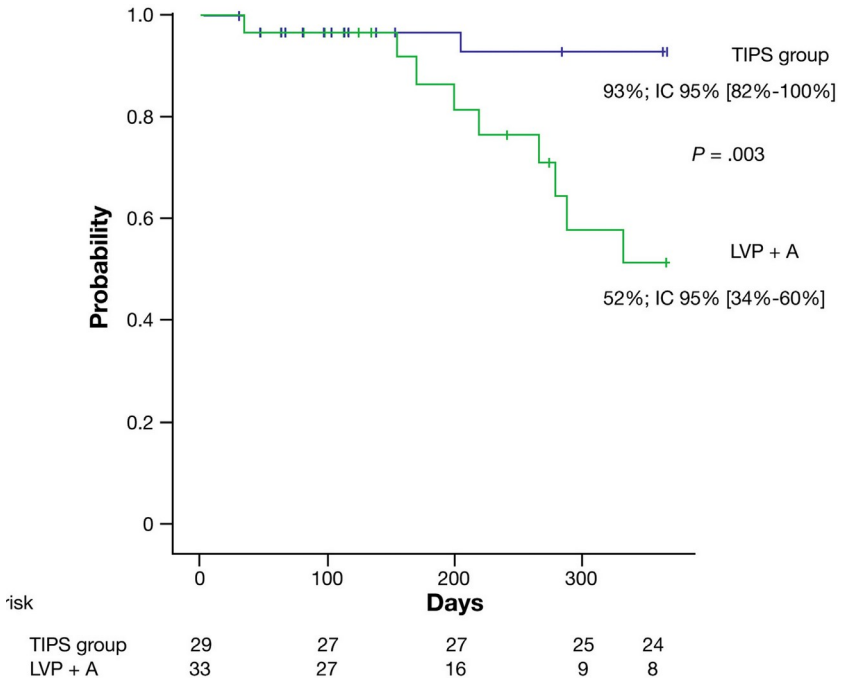
Sarcopenia

→ Not too late?

Saad et al., Annals of Hepatology 2016
Nardelli et al.,Clinical Gastro 2017

Covered TIPS in recurrent ascites:
Transplant-free survival

- 62 patients with recurrent ascites:
  - 2 LVP with a minimal interval of 3 weeks
  - less than 6 within 3 months
- 10 mm TIPS dilated to 8 or 10 (PPG<12 mmHg)



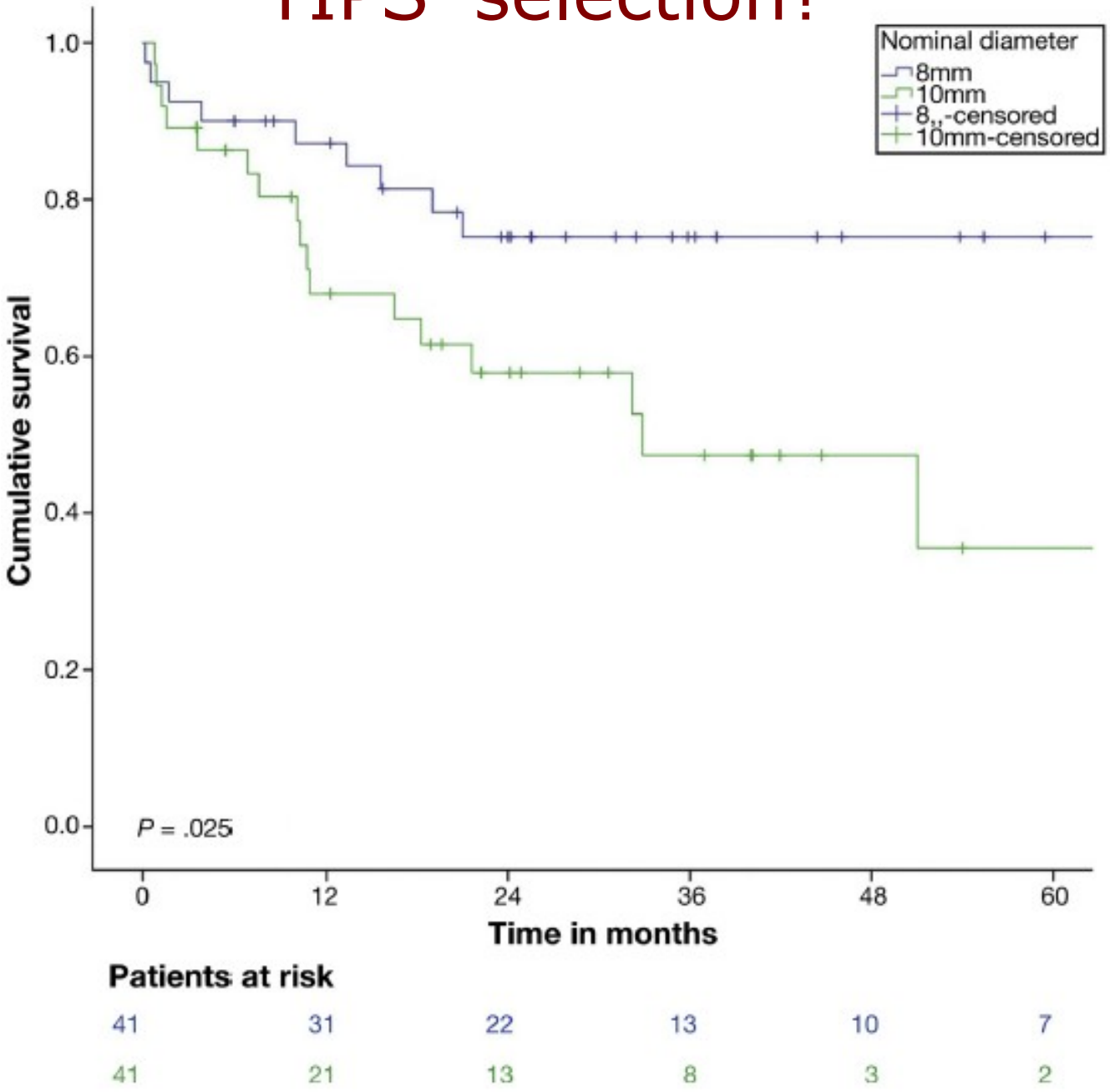
Bureau et al., Gastroenterology 2017

Parameters associated with survival

	Alive n = 51	Dead or transplanted n = 11	Univariate	Multivariate
INR	1,4 ± 0,3	1,5± 0,2	p=0,009	0,8 [0,3-2,3] NS
Serum sodium (mmo/l)	134 ± 4	129 ± 3	p=0,001	0,9 [0,9-1,0] NS
Bilirubin (mmol/l)	15 ± 12	27 ± 21	p=0,05	1,0 [1,0-1,0] NS
TIPS / LVP+A	93 % / 73 %	7 % / 27 %	p=0,048	2,0 [1,1-4,0] p=0,03

Bureau et al., Gastroenterology 2017

TIPS' selection?



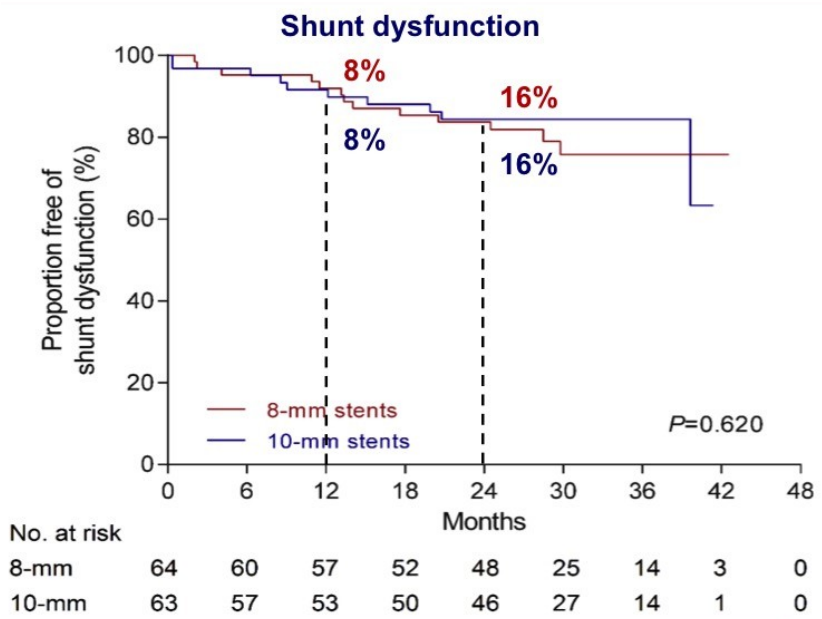
185 pts included
107 for refractory ascites

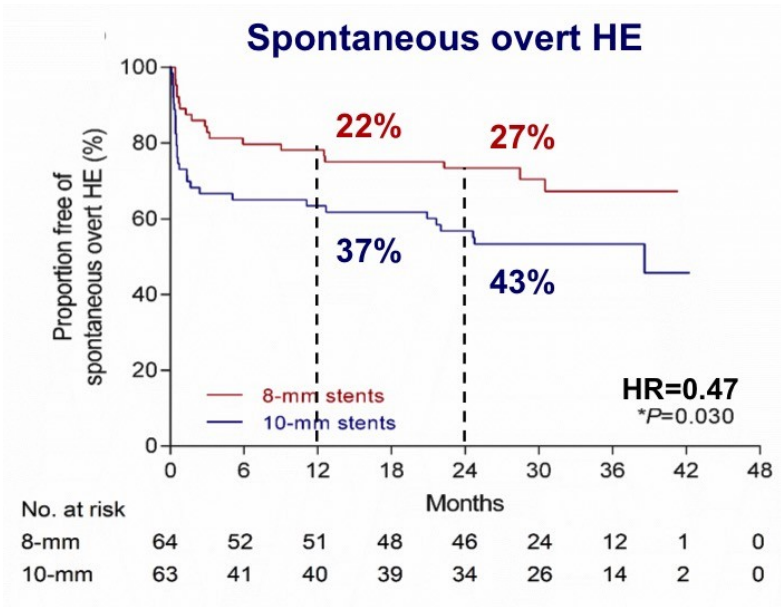
Kaplan–Meier analysis comparing 1:1 propensity-matched patients with 8-mm or 10-mm stent diameters adjusted for age, MELD, and bilirubin concentration.

Trebicka et al. Clinical Gastro 2019

BLIPS

Hepatic Encephalopathy (HE) rate is reduced after 8mm TIPS for Prophylaxis of Re-Bleeding: TIPS‘ selection?





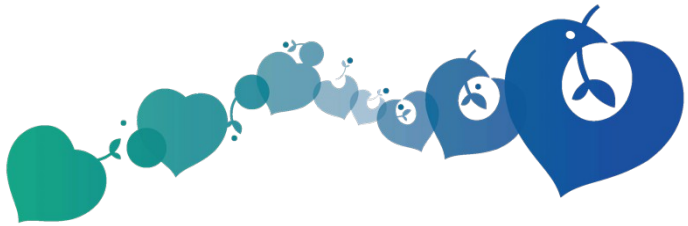
Wang et al. J Hepatol 2017

TIPS & ascites: how to select the patients ?

- Careful selection
- **NOT too late**
- age<65; case by case >65
- BiliT < 50 µmol/L
- Plt > 75 G/L
- No chronic HE, < 2 episodes of HE
- No infection (delay)
- No pulmonary hypertension
- Normal BNP and NT-proBNP; normal echocardiography
- 8 mm stents?

J Hepatol 2018

Clinical Vignette 1: Mr FC, 51 years old



*Ascites, **one paracentesis/week of 8 liters since one year***
Last EOGD: grade 1 EV (Sept 2017)
US exam: dysmorphia, no nodule, ascites (Sept 2017)
Treatment: spironolactone 75 mg/d, furosemide 40 mg/j
No history of HE
*Plt 65000, BiliT 55 micromol/l, PT 65%, INR 1,4, Creat 127 micromol/l, Na+ 134 mmol/l, Albumin 32 g/l, Child B8, **MELD 18***

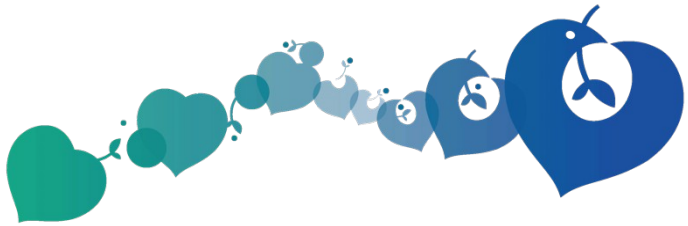
- Large volume paracentesis is the best option
- **The patient should be referred to a liver transplant unit ASAP**
- Increase of diuretics is the best option
- TIPS should be indicated
- **It is probably too late for TIPS ???**

Clinical Vignette 1: Mr FC, 51 years old Outcome …

- TIPS placed
- 2 weeks after TIPS: increase of Bili 250 micromol/l, PT 20%, AST 750, ALT 652, creat 176
- Tense ascites
- Hepatic encephalopathy stade 3

- Liver transplant after 5 weeks

Clinical Vignette 2: Mr MA, 62 years old



Cirrhosis with active OH consumption
Persistence of tense ascites, Na+ 128, creat 89, decrease diuretics
3 paracentesis within 2 months
No HE
Plt 123000, BiliT 16 micromol/l, PT 73%, INR 1,0, Creat 78 micromol/l, Na+ 134 mmol/l, Albumin 33 g/l, Child B8, ***MELD 6***

- Large volume paracentesis is the best option
- The patient should be referred to a liver transplant unit ASAP
- Alcohol withdrawal is the best option
- **TIPS should be indicated**
- It is probably too late for TIPS

Clinical Vignette 2: Mr MA, 62 years old

TIPS placed (8 mm dilated 8 mm)

HVPG 12 mmHg, PPG 9 mmHg

No ascites

Stopped drinking

Child A

Followed up regularly /6 months

TIPS and refractory ascites
Conclusions

- TIPS should be the first-line option
- In carefully selected patients (liver failure/HE/cardiac decompensation)
- 8 mm stents probably associated with a better prognosis
- The best bet is to consider TIPS early … (recurrent ascites)
- Discuss TIPS placement AND liver transplantation at the same time

Hôpitaux Universitaires
Pitié Salpêtrière - Charles Foix

Merci

BLIPS