Cirrhose Hépathique

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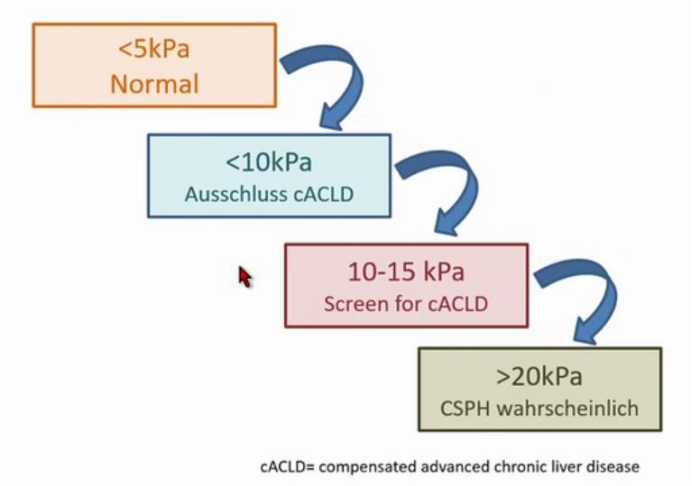
DKG
KREBSGESELLSCHAFT
Zertifiziertes Leberkrebszentrum

Diagnosis and risk stratification

Diagnosis of liver cirrhosis

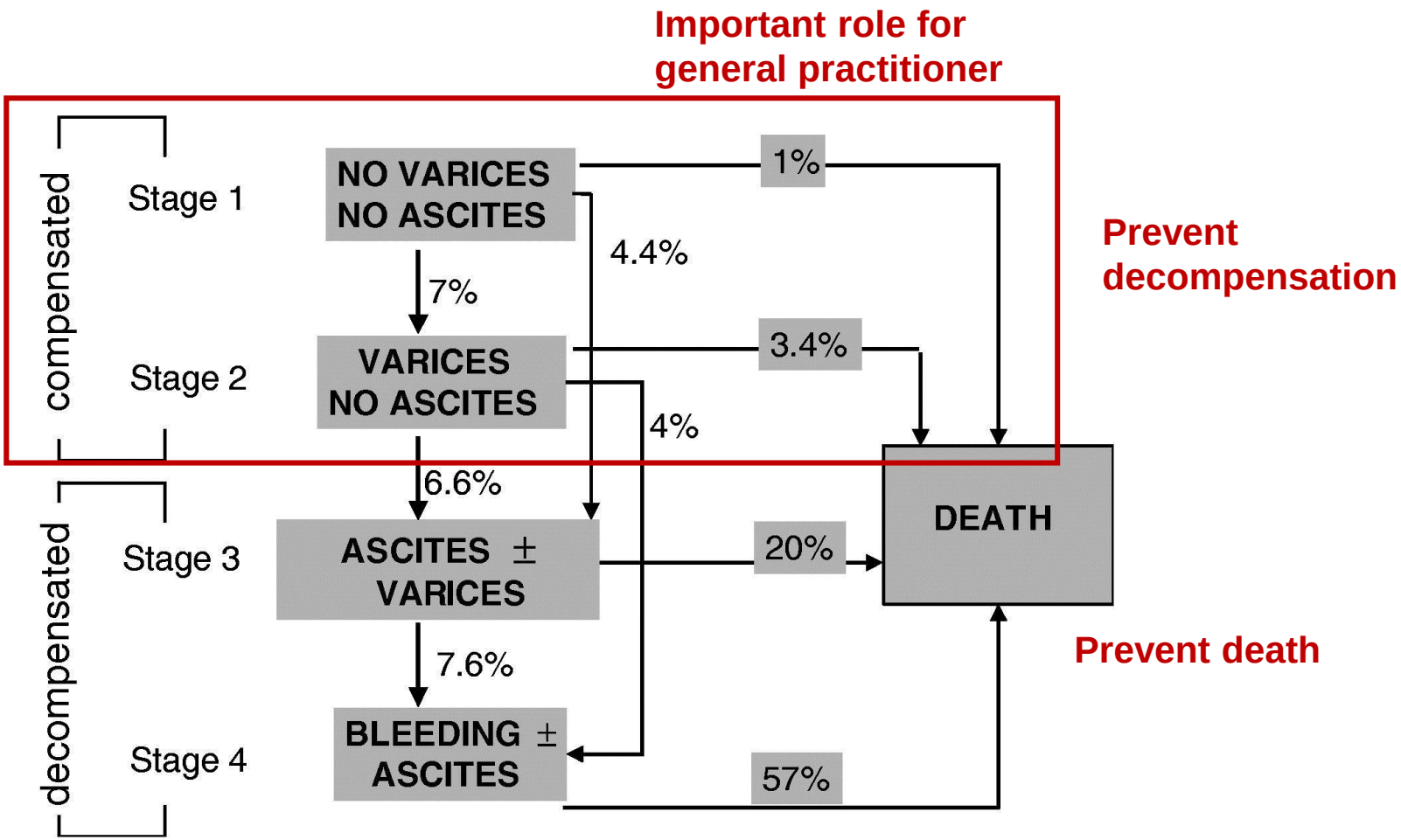
- Combination of clinical, biochemical and imaging results
  - 20-30% of cases with liver cirrhosis not detactable by ultrasound
- Liver biopsy (gold standard)
  - Risk of complications, possibility of sampling error
- Transient elastography (Fibroscan®), shear-wave elastography
  - Reliable tool to rule out liver cirrhosis and to detect significant liver fibrosis

Baveno VI consensus workshop – rule of five



Baveno VI Faculty, J Hepatol 2015

Classical prognostic stages of cirrhosis

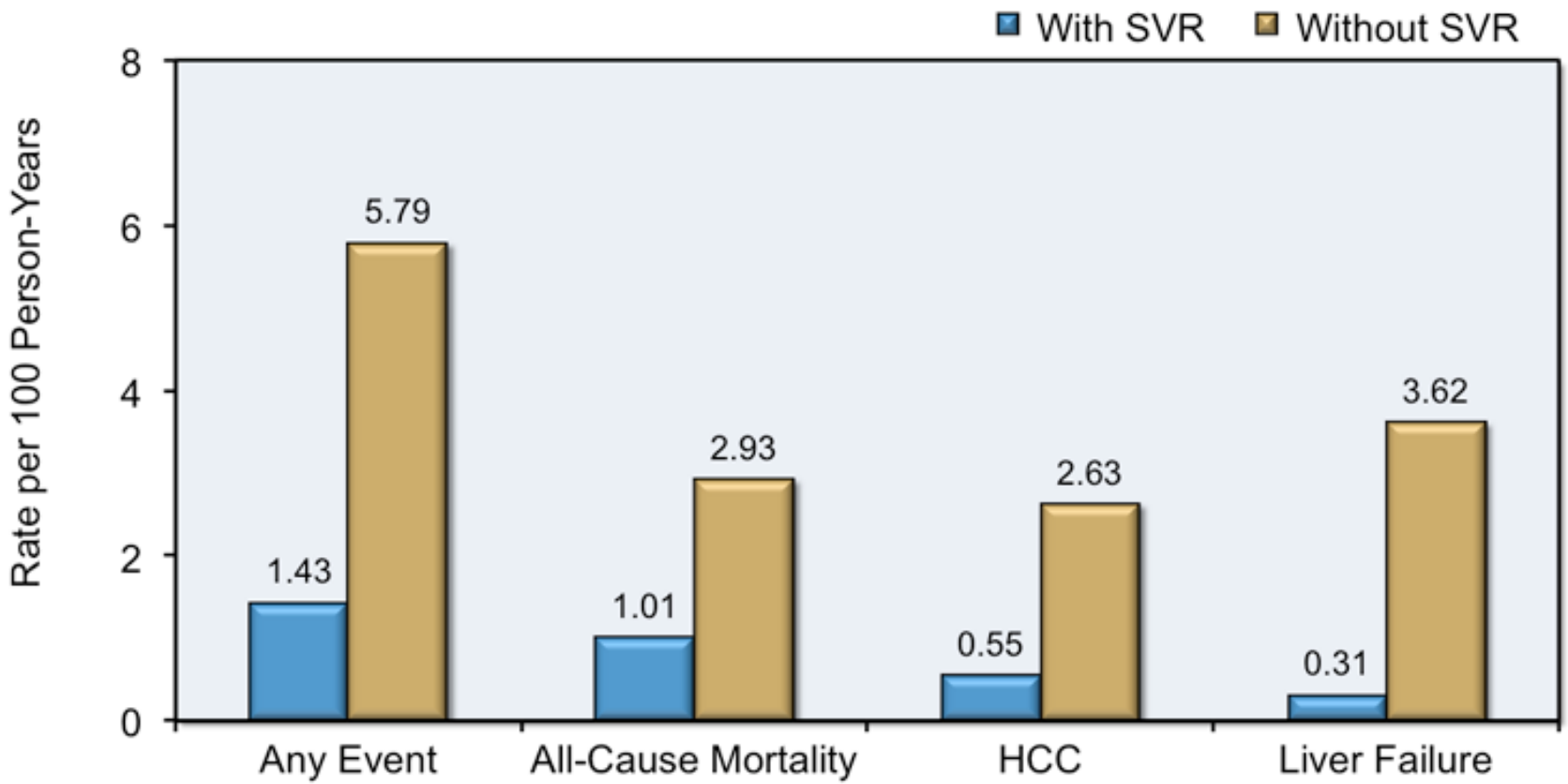


D´Amico G et al, J Hepatol 2006

Management of compensated cirrhosis

Treatment of underlying liver disease

Impact of antiviral therapy of patients with chronic hepatitis C



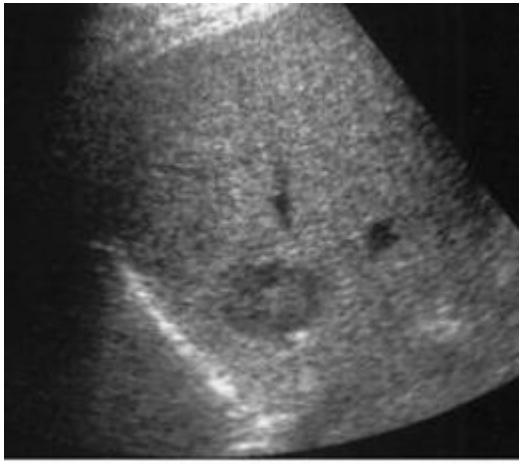
Van der Meer et al, JAMA 2012

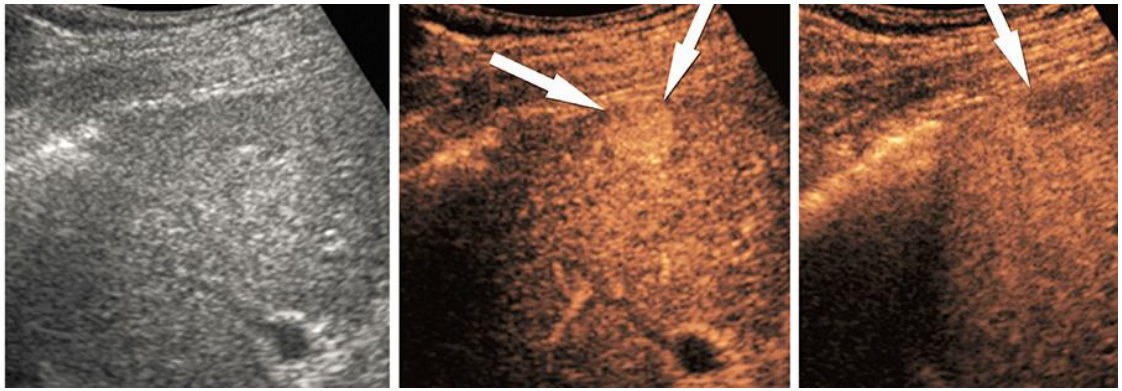
Hepatocellular carcinoma (HCC) surveillance

- Annual risk up to 5%
- Early detection crucial for curative therapy

→ High-quality ultrasound of the liver (+ AFP-quantification) every 6 months

  - Experienced operator and high-end technology (DEGUM/SGUM level II)



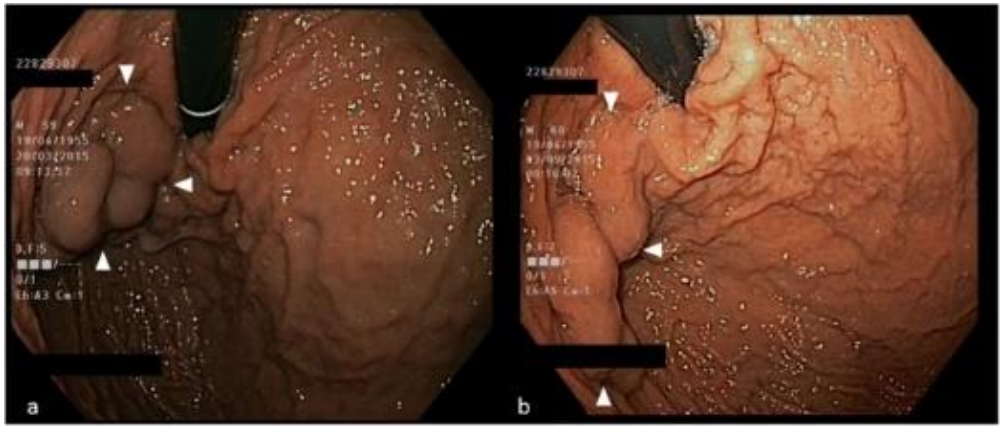


Screening for esophageal varices

Esophago-gastro-duodenoscopy every 1-2 years in patients with liver cirrhosis

Endoscopy may be omitted in case of:

- Compensated cirrhosis, liver stiffness <20 kPa, platelets >150 /nl



Prophylaxis of variceal bleeding

Primary prevention

Who?

- Small varices with red spots or Child C-cirrhosis
- Large varices

How?

- Non-selective betablockers (NSBB): carvedilol (up to 25 mg/d) or propranolol up to 160 mg twice daily
- Or endoscopic band ligation

Secondary prevention

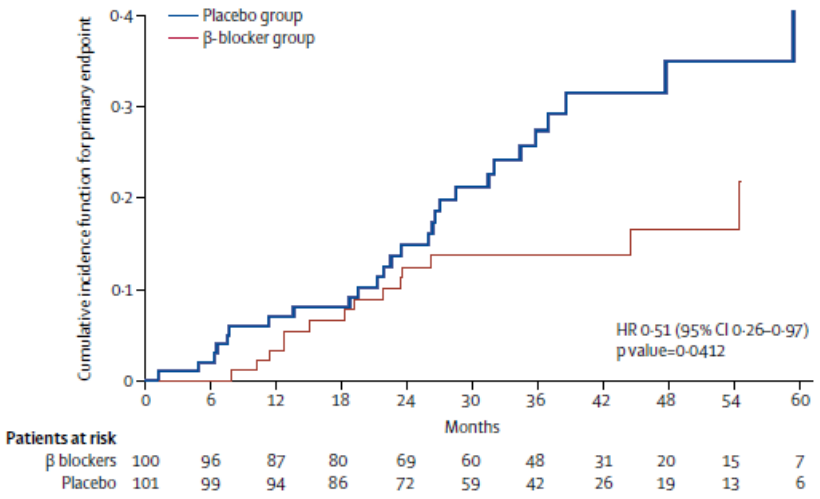
- NSBB plus EBL

NSBB in patients with clinically significant portal hypertension

- 201 patients with HVPG ≥10 mmHg without risk varices
- 57% of patients had small varices
- Propranolol or carvedilol (in non-responders) vs. placebo

Risk of decompensation or death

A



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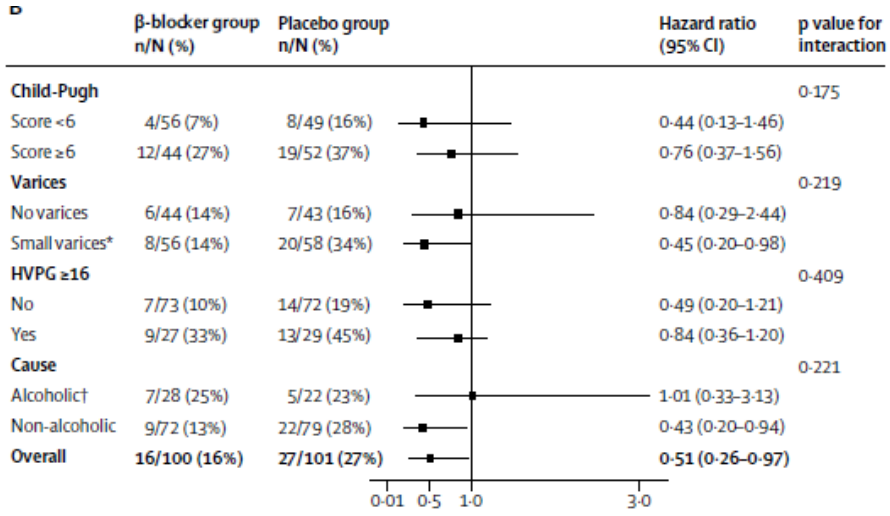
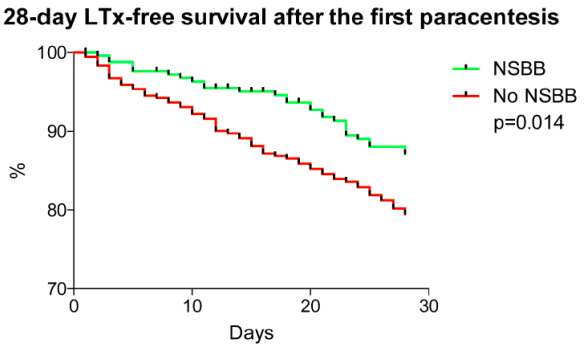
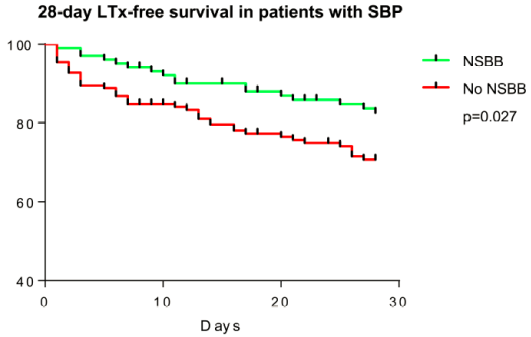


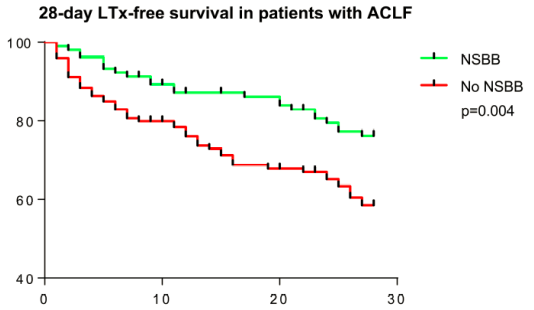
Villanueva C et al. Lancet 2019

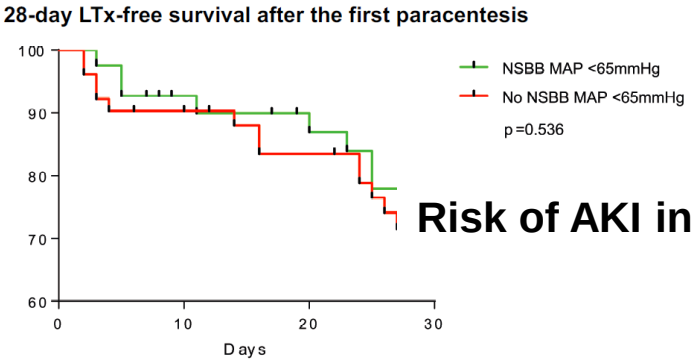
Caveats of NSBB: window hypothesis

- Careful administration of NSBB in hyponatremia, kidney failure, SBP









Risk of AKI in case of SBP

- No benefit of NSBB-therapy if MAP <65 mmHg

Tergast et al. AASLD 2019 PS-81

Drug therapy in patients with liver cirrhosis

Important agents which should be avoided

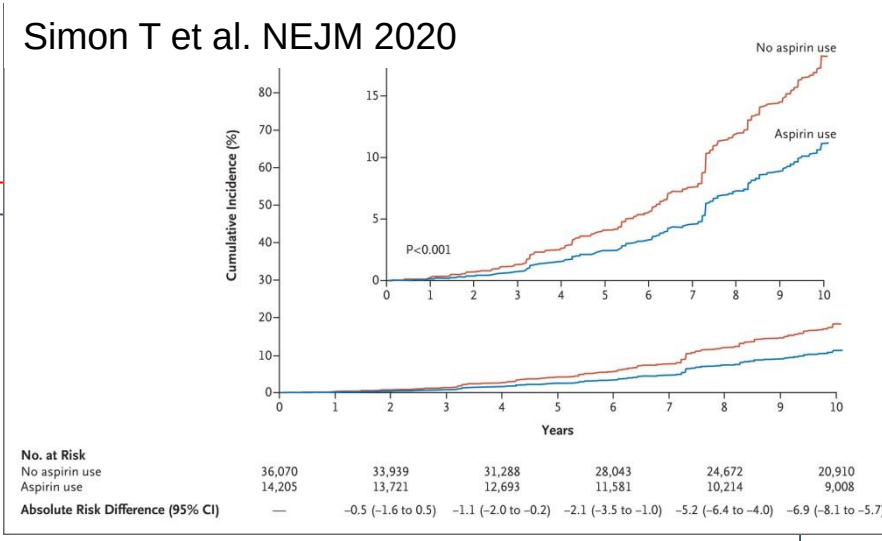
- NSAIDs
- Thiazide diuretics
- Paracetamol
- Contrast agents
- Proton pump inhibitors

Drugs which should not be avoided

- Metformin
- Statins
- Low-dose aspirin
- Antikoagulation therapy (heparin, DOACs)

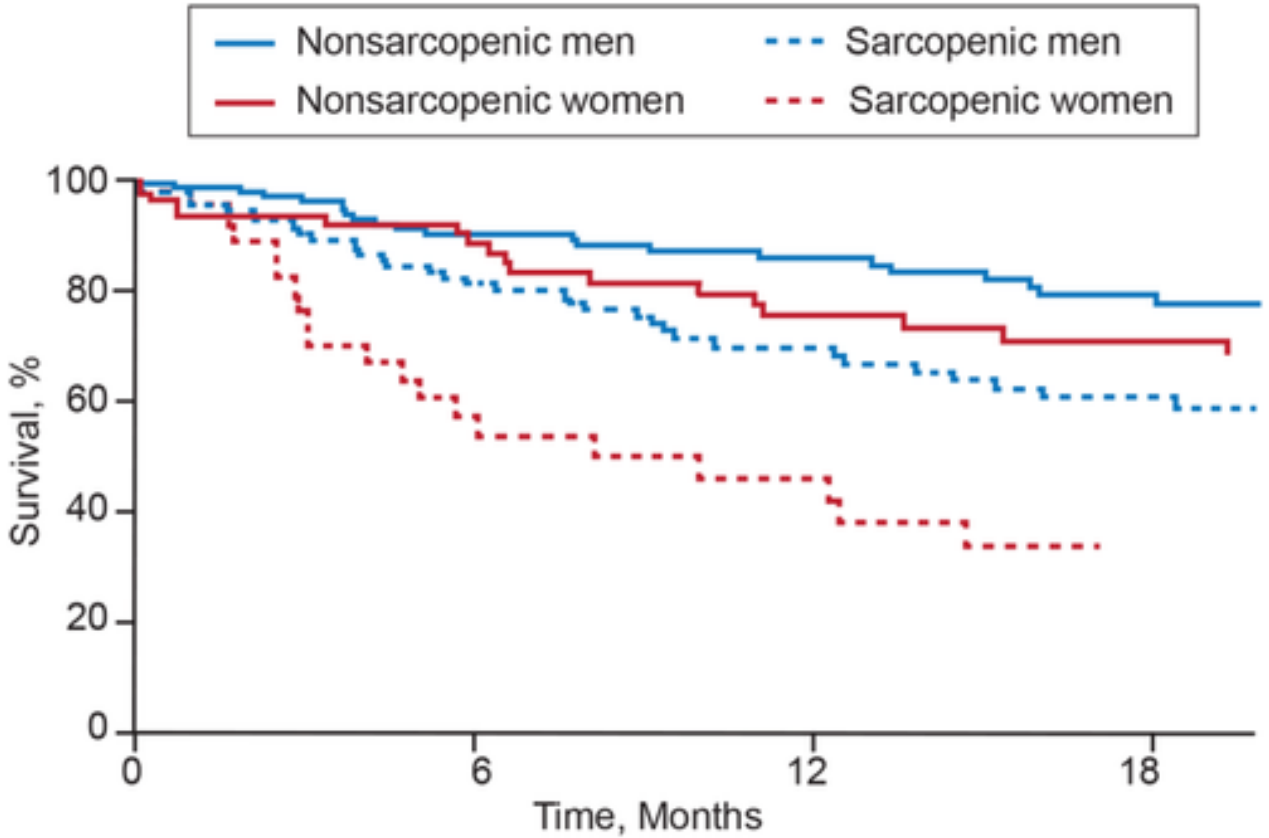
Liver-related mortality in aspirin-users

Simon T et al. NEJM 2020



Impact of sarcopenia and malnutrion

- **396 patients on the waiting list for liver transplantation (USA)**



Carey E et al. Liver Transpl 2017

Nutrition counseling

ESPEN-Guidelines:

- 35-40 kcal / kg KG
- 1,2-1,5 g protein / kg KG
- Mix of plant and animal protein
- Substitution of thiamin, zinc, folic acid
- Late-night snack
- Branched-chain amino acids

Moderate excercise

Plaut et al. Clin Nutrition 2006

Counting of protein units

20-25 g protein / 100 g

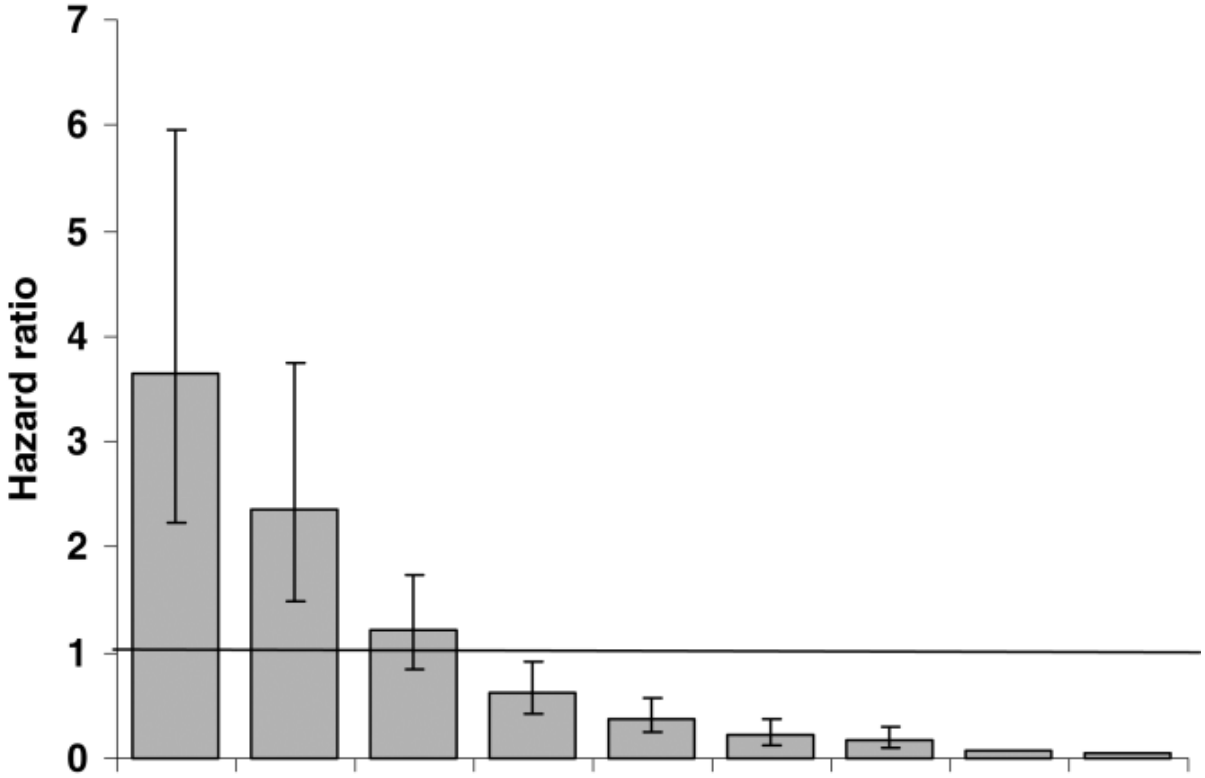
10-15 g protein / 100 g

Management of decompensated cirrhosis

- **Variceal bleeding**
- **Ascites**
- **Hepatorenal syndrome**
- **Hepatic encephalopathy**
- **Infections**
- **Acute-on-chronic liver failure**
- **…..**

Consider liver transplantation

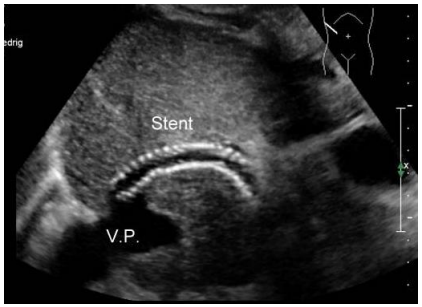
- One year survival benefit after liver transplantation

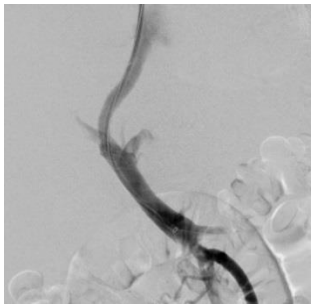


MELD	6-11	12-14	15-17	18-20	21-23	24-26	27-29	30-39	≥40
Hazard Ratio	3.64	2.35	1.21	0.62	0.38	0.22	0.18	0.07	0.04
p-values	<0.001	<0.001	0.41	<0.01	<0.001	<0.001	<0.001	<0.001	<0.001

Merion et al. Am J of Transpl 2004

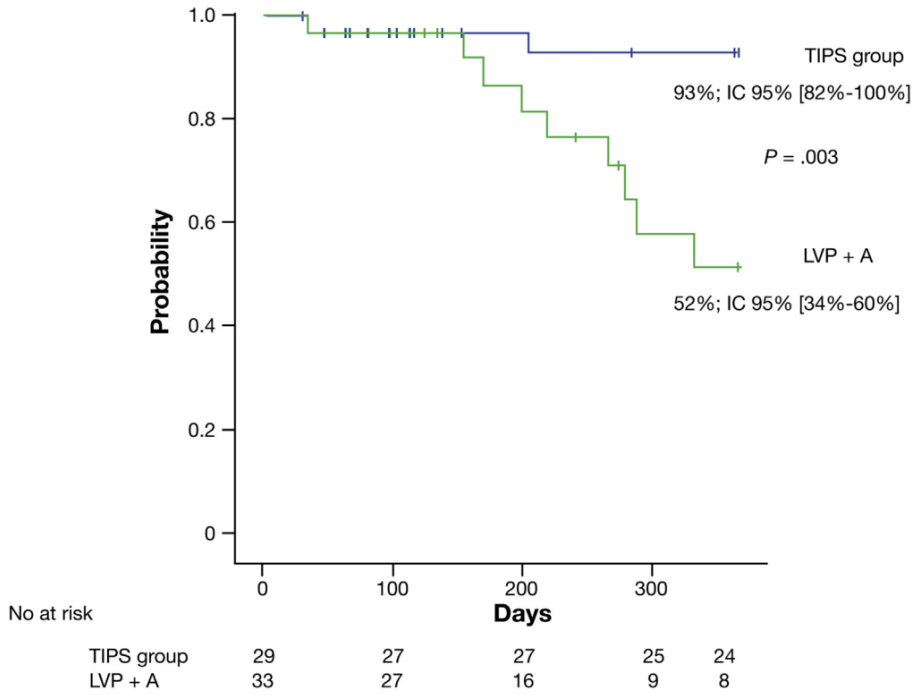
Consider TIPS (transjugular intrahepatic portosystemic shunt)





Major indications

- Variceal bleeding (early TIPS, rescue TIPS, secondary prophylaxis)
- Refractory Ascites



- TIPS after 4 paracentesis (mean)

Bureau C et al. Gastroenterology 2017

Early recognition of organ failures
New ICA-AKI criteria

	AKI definition	AKI Stage Serum Creatinine Criteria		
		Stage I	Stage 2	Stage 3
ICA (2015)	Increase Scr*≥0.3 mg/dl within 48 hours; or increase Scr*≥50% from baseline which is known, or presumed, to have occurred within the prior 7 days	Increase ≥ 0.3 mg/dl within 48 hrs or ≥1.5-2 x baseline**	Increase 2-3 x baseline	Increase 3x baseline or Scr*> 4 mg/dl with an acute rise > 0.5 mg/dl or on RRT

Already AKI stage 1 is associated with mortality

	Survivors n (%)	Nonsurvivors n (%)	OR	95% CI	*P*
Without AKI	75 (70.1%)	32 (29.9%)		Reference group	
With AKI	43 (47.3%)	48 (52.7%)	2.6	1.5-4.7	0.001
AKIN stage 1	40 (48.2%)	43 (51.8%)	2.5	1.4-4.6	0.002
AKIN stage 2	2 (40%)	3 (60%)	3.5	0.5-30.4	0.208
AKIN stage 3	1 (33.3%)	2 (66.7%)	4.6	0.34-139.9	0.253

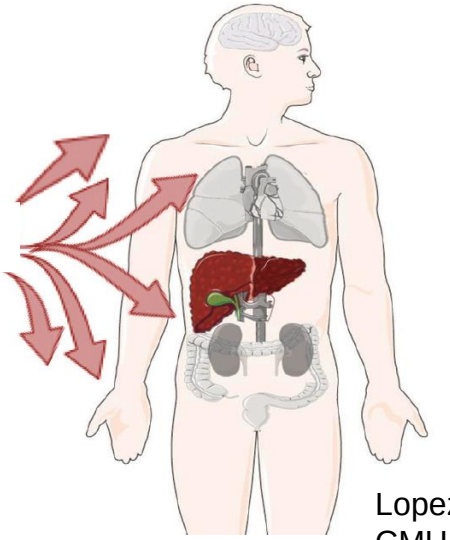
AKI indicates acute kidney injury; AKIN, Acute Kidney Injury Network; CI, confidence interval; OR, odds ratio.

Angeli P et al, GUT 2015; De Carvalho JB et al, Clin Gastro Hepatol 2012

Concept of acute-on-chronic liver failure (ACLF)

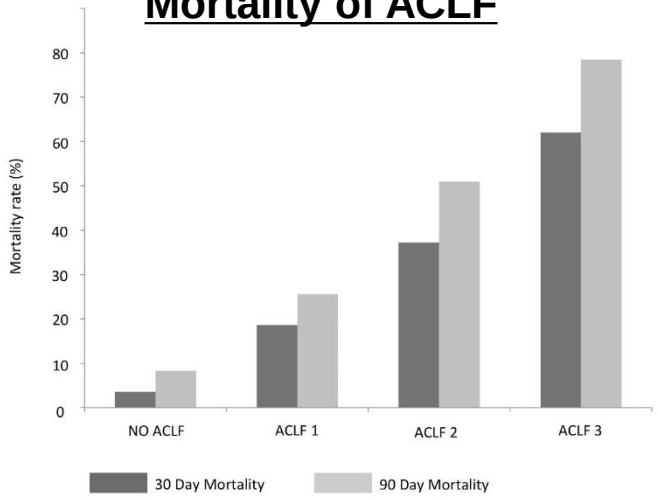
ACLF = Acute decompensation of cirrhosis + specific organ failures

- **Organ failures**:
  - Liver: Bilirubin ≥ 12 mg/dl
  - Kidney: Creatinin ≥ 1,5 mg/dl bzw. ≥ 2 mg/dL
  - Hepatic encephalopathy: HE Grade 3-4
  - Coagulation: INR ≥ 2,5
  - Circulation: Need of vasopressors
  - Lung: PaO2/FiO2 ≤ 200



Lopez et al.
CMH 2020

Mortality of ACLF



Moreau R et al, Gastroenterology 2013

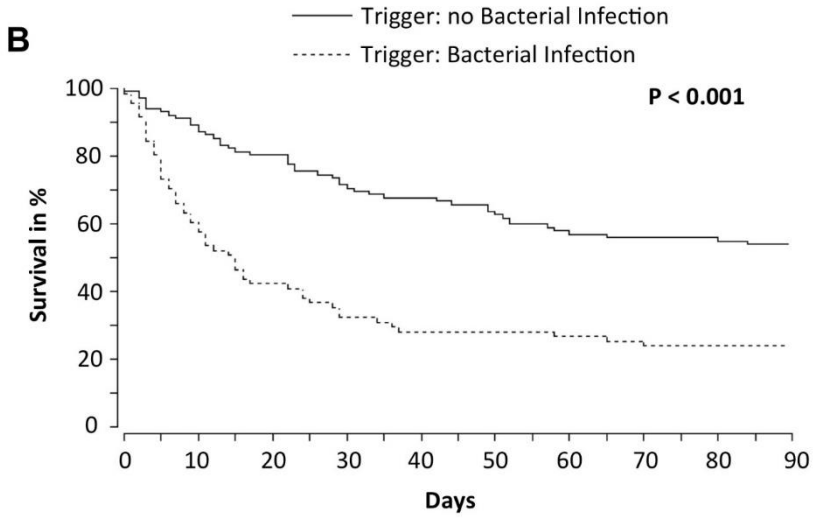
Causes of organ failures

- GI bleeding
- Elektrolyte imbalance
- Hypovolemia
- Diuretics, lactulose
- Surgery
- Portal vein thrombosis
- Alcohol
- Infections

Early diagnosis and treatment of infections

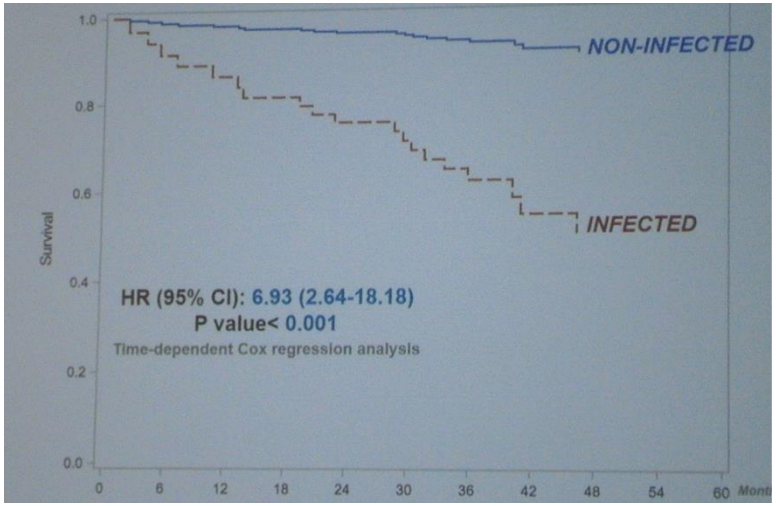
- **Frequent cause of ACLF**
  - Infections (40%)
  - Alcohol (40%)

Mortality of infection-triggered ACLF



Mücke and Lange et al. Liver Int 2018

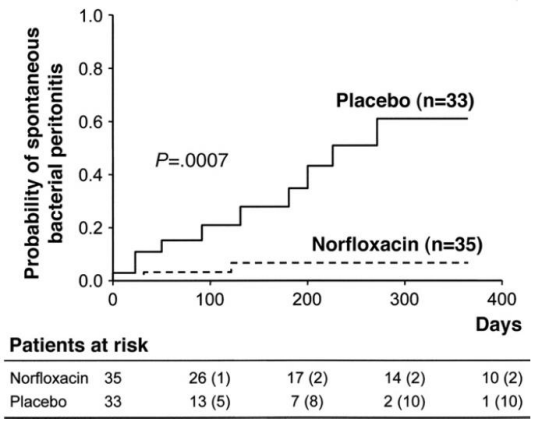
Impact of infections in compensated cirrhosis



Villanueva C et al. AASLD O-52

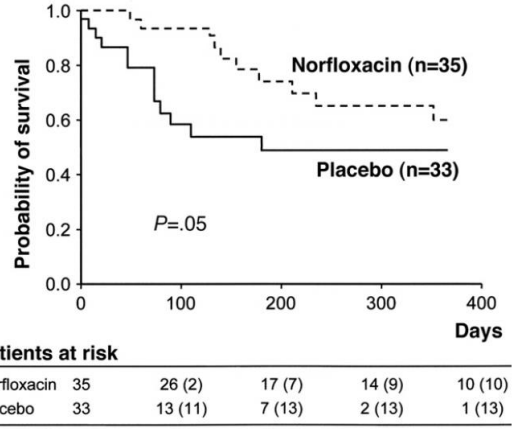
Prophylaxis of spontaneous bacterial peritonitis

Risk of SBP



Patients at risk					
Norfloxacin	35	26 (1)	17 (2)	14 (2)	10 (2)
Placebo	33	13 (5)	7 (8)	2 (10)	1 (10)

Mortality



Patients at risk					
Norfloxacin	35	26 (2)	17 (7)	14 (9)	10 (10)
Placebo	33	13 (11)	7 (13)	2 (13)	1 (13)

Fernandez et al, Gastro 2007

When?

Primary prophylaxis

- Ascites protein <1,5 g/dL and
  - Child-Pugh-Score >9 and Bilirubin > 3 mg/dL
  - Kreatinin >1,2 mg/dL or Natrium <130 mmol/l

Secondary prophylaxis

How?

Norfloxacin 400 mg/d; (Rifaximin?)

Thank you!