

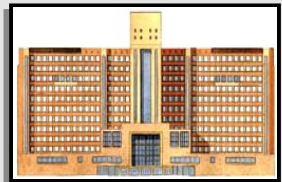
Management of decompensated cirrhosis

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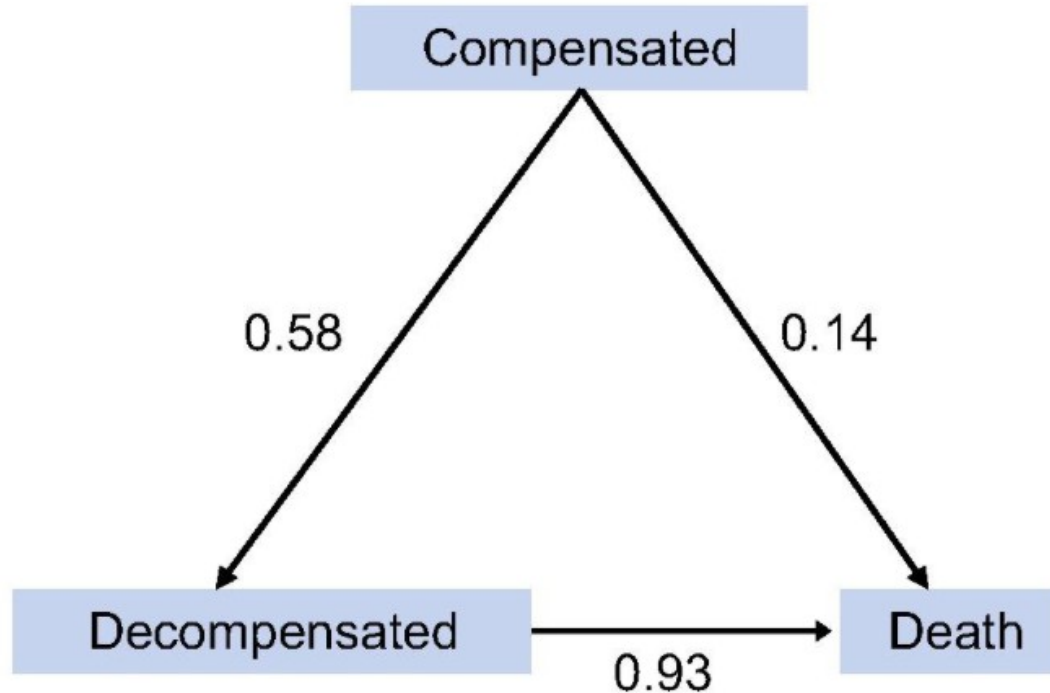


Disclosures

- Gilead
- Astellas
- BMS
- Novartis

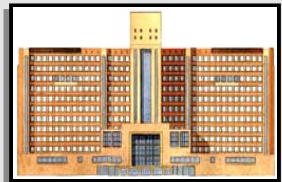
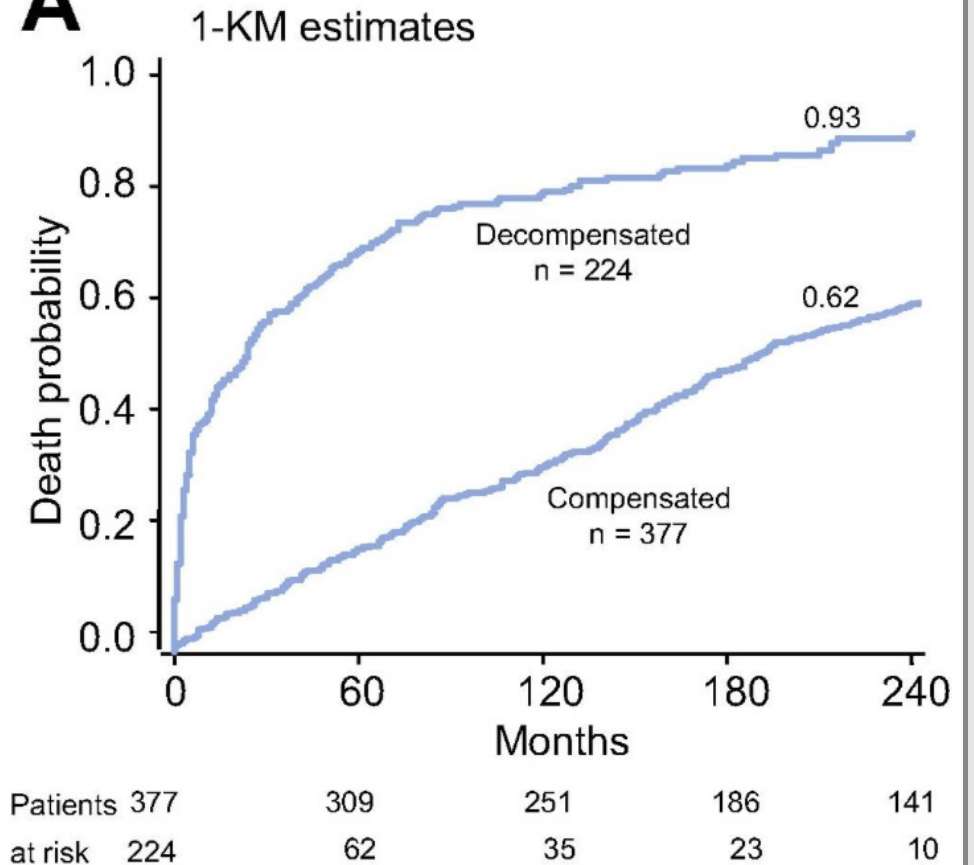
Natural history of cirrhosis

C



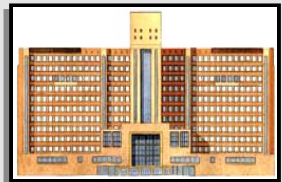
20-year transition probabilities from compensated cirrhosis towards decompensation and death and from decompensation to death

A

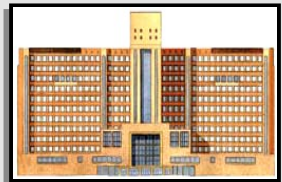
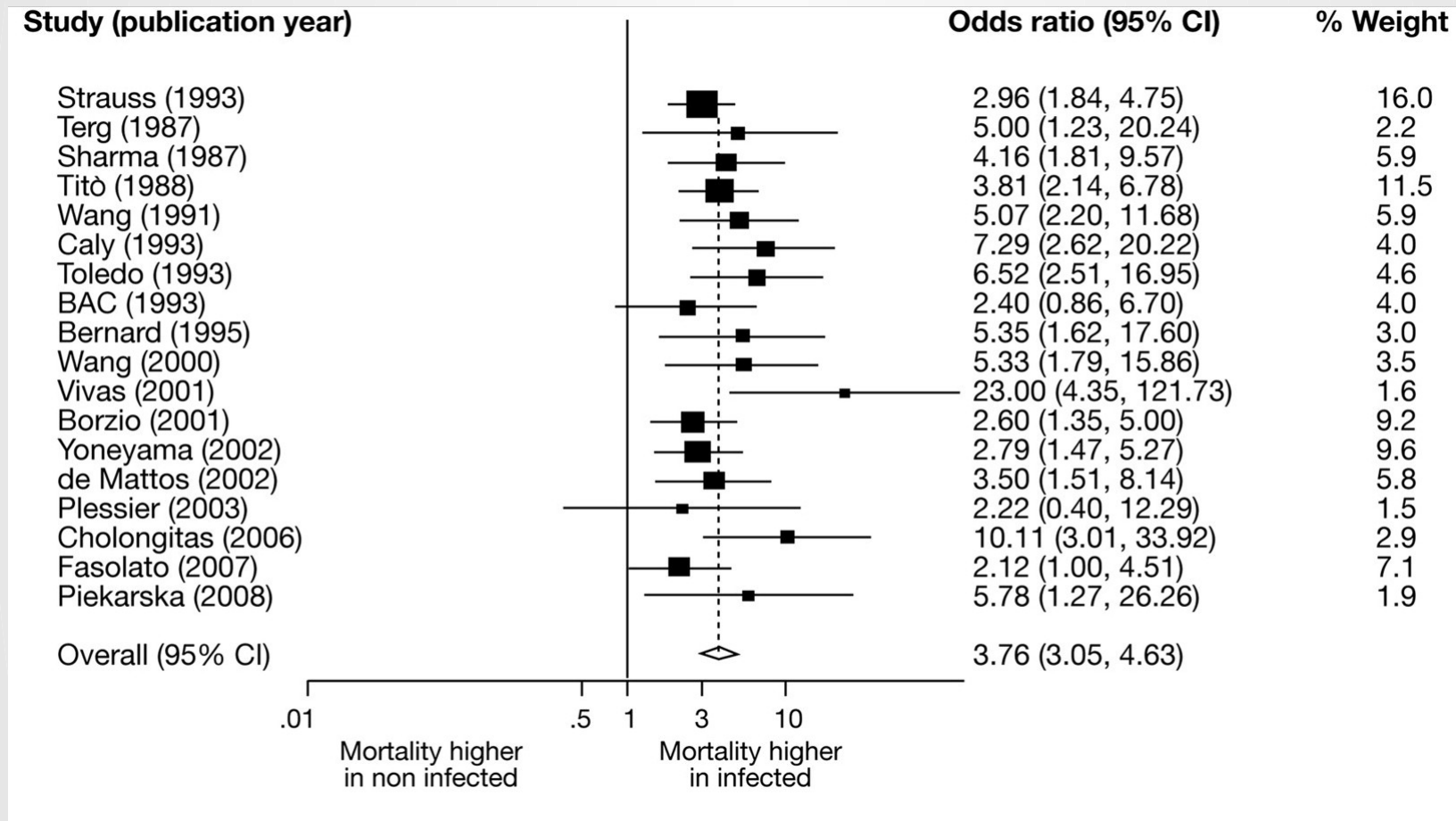


New aspects in the management of decompensated cirrhosis

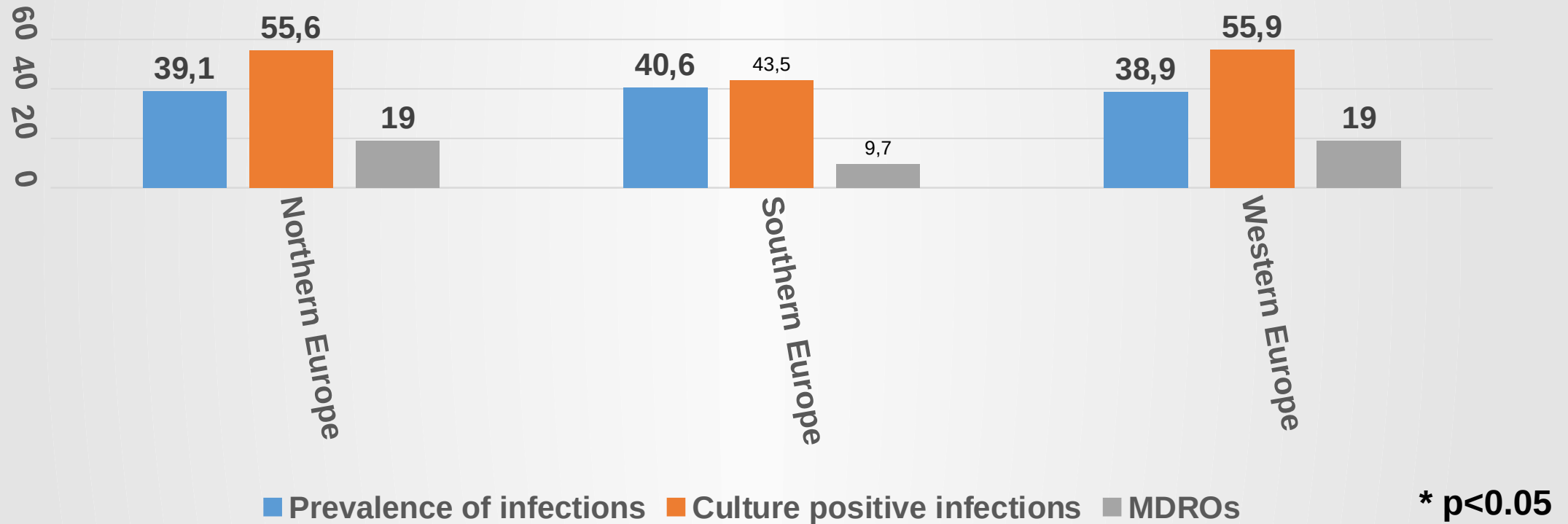
- **Bacterial infections and resistance to antibiotics in cirrhosis**
- **Albumin and bacterial infections in cirrhosis**
- **Acute kidney injury in cirrhosis**
- **Management of refractory ascites**



Bacterial infection in cirrhosis and mortality: meta analysis



Multidrug resistance in European patients with cirrhosis



Fernandez J et al. J Hepatol 2018.

Multidrug resistance associated with a worse prognosis

Bacterial infections in cirrhosis

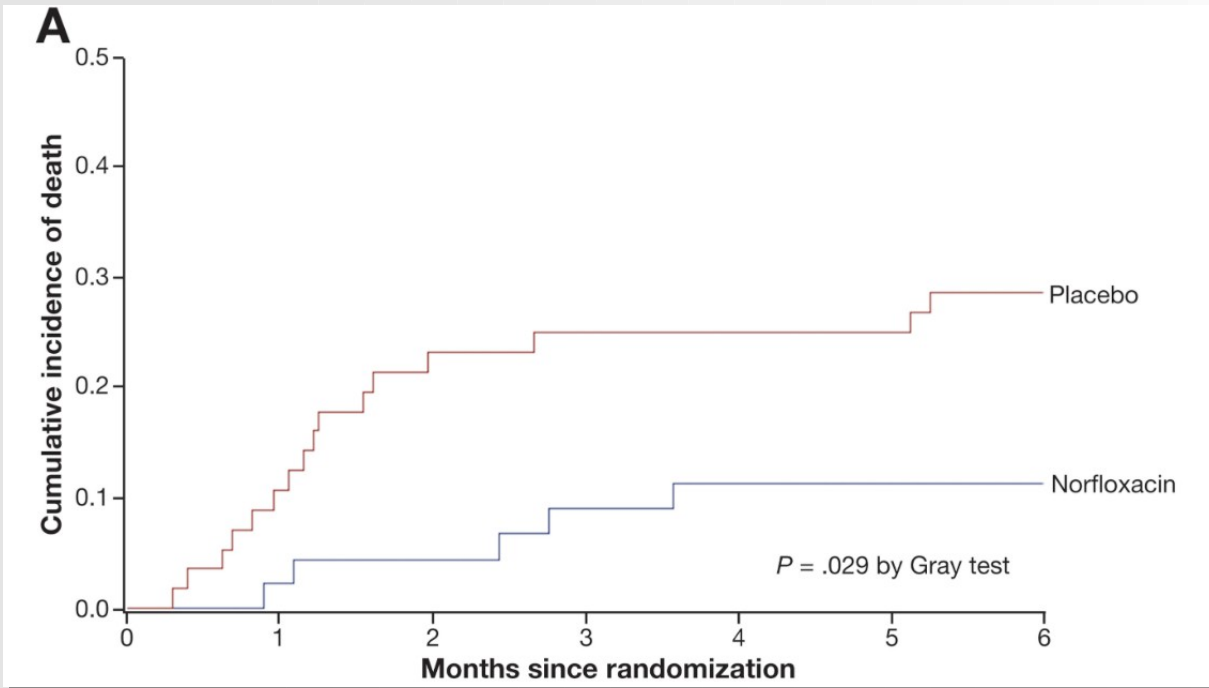
worldwide

	America	Asia	Europe	P value
Patients with infections	321	416	565	
Sites of infection				
UTI	27%	14%	25%	
SBP	31%	35%	20%	<0.001
Gram - infections	56%	70%	54%	<0.001
MDROs	27%	50%	28%	<0.001
XDROs	4%	16%	5%	<0.001

Multidrug resistance associated with a worse prognosis

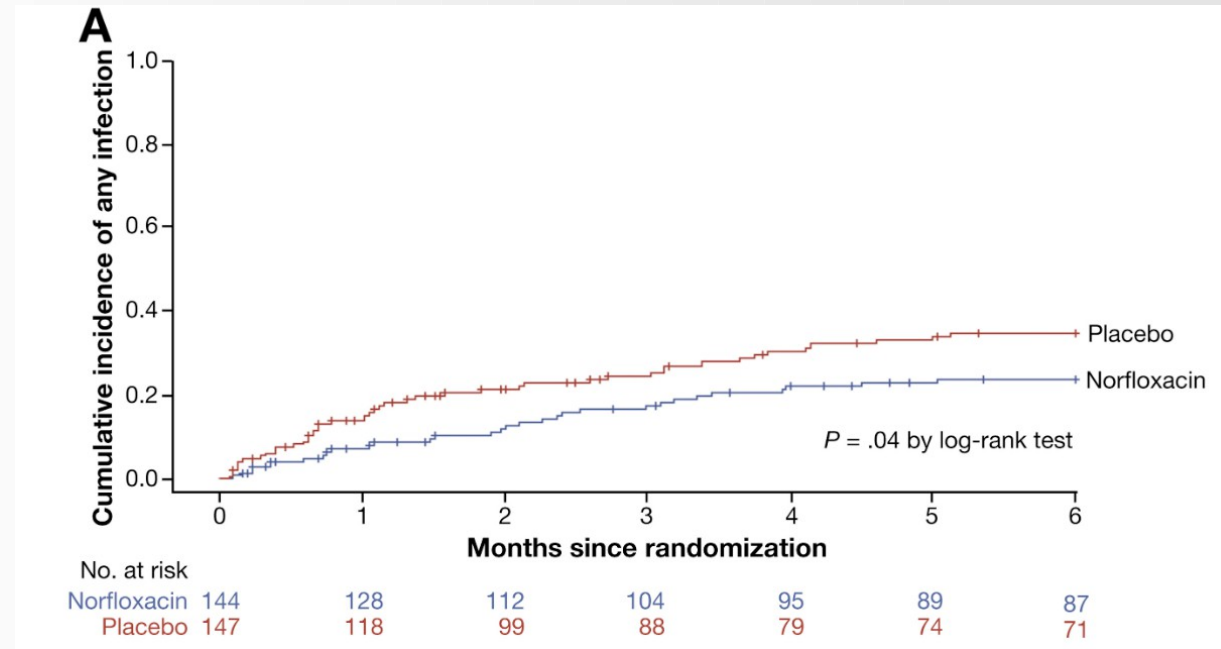
Long term norfloxacin to prevent complications in decompensated cirrhosis

291 Child-Pugh C patients randomized to receive Norfloxacin or placebo



Survival in patients with ascites protein concentration < 15g/L

Moreau R et al. Gastroenterology 2018; 155: 1816.

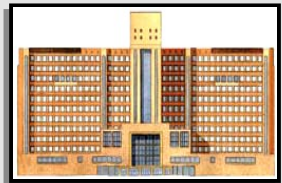


Cumulative incidence of any infection

No increase in the incidence of multidrug resistant bacteria

New aspects in the management of decompensated cirrhosis

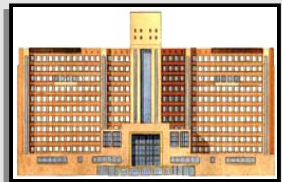
- Bacterial infections and resistance to antibiotics in cirrhosis
- **Albumin and bacterial infections in cirrhosis**
- Acute kidney injury in cirrhosis
- Management of refractory ascites



Albumin in the treatment of spontaneous bacterial peritonitis

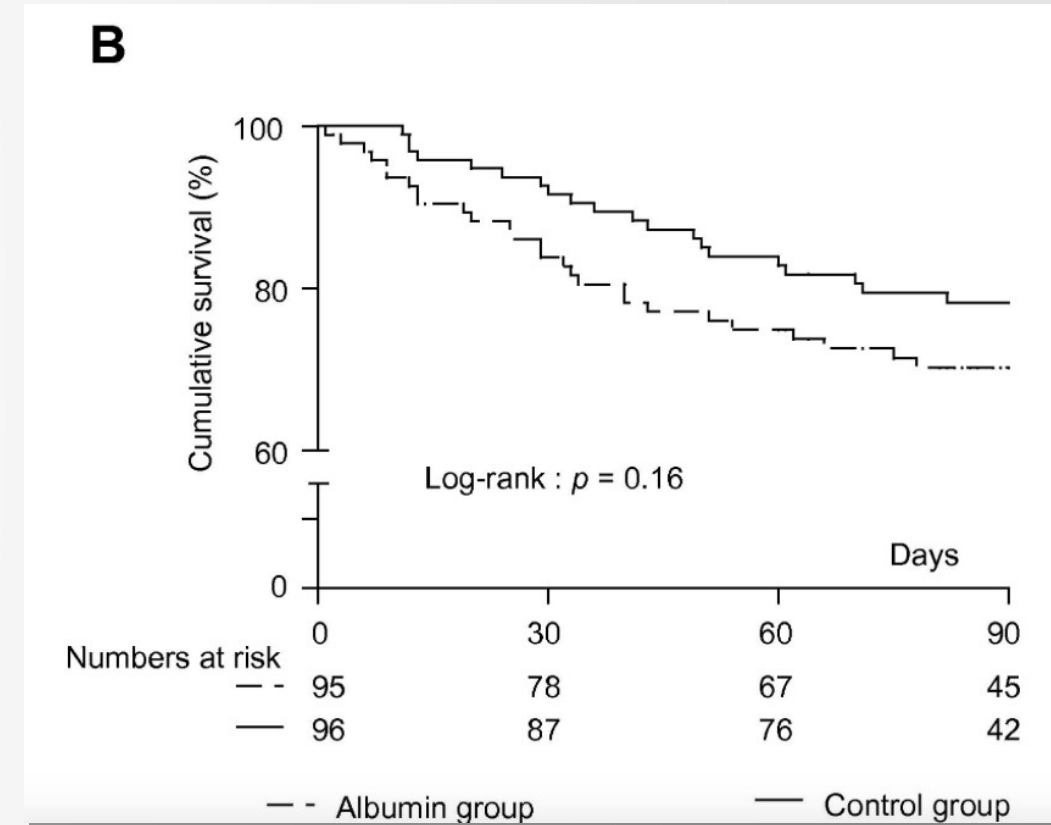
	Cefotaxime	Cefotaxime + albumin	P value
Patients	63	63	
Resolution of infection	94%	98%	ns
Duration of antibiotics	6 days	5 days	ns
Renal impairment	33%	10%	0.002
In hospital mortality	29%	10%	<0.05
3-month mortality	41%	22%	<0.05

Sort P et al. N Engl J Med 1999; 341: 403.



Antibiotics + albumin vs antibiotics alone in infections other than SBP

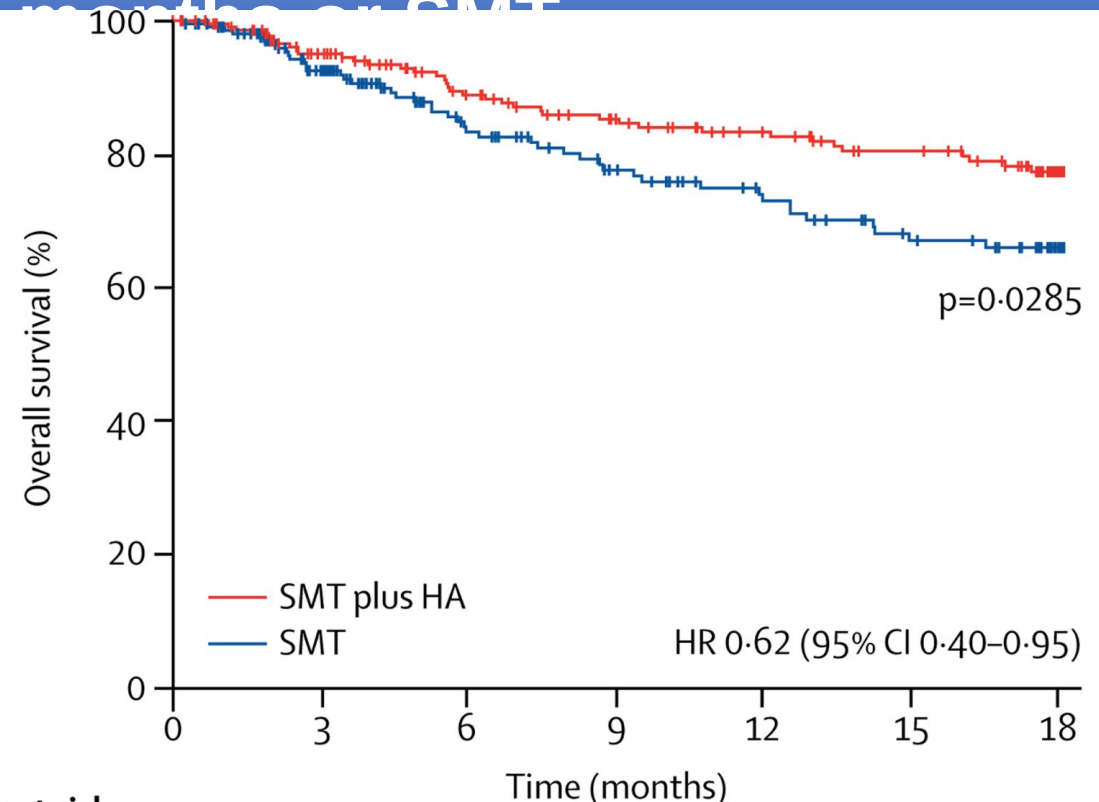
	193 patients with cirrhosis and sepsis other than SBP	
	Antibiotics + albumin	Antibiotics alone
Patients	96	97
Age	55	55
Alcoholic cirrhosis	94%	90%
MELD	21	20
Pneumonia	30%	36%
UTI	34%	28%



Long term administration of albumin in patients with decompensated cirrhosis

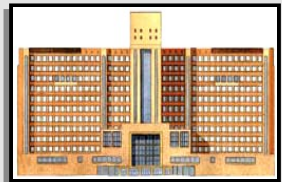
440 patients randomly assigned to albumin for up to 18

months or SMT



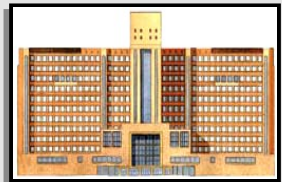
Lower incidence in the albumin group

SBP	$p<0.001$
Non SBP infection	$P= 0.005$
Impaired renal function	$P<0.001$
Type-1 HRS	$P=0.004$



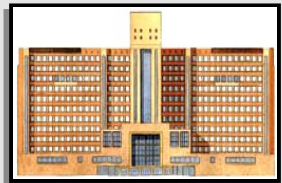
Cirrhosis, sepsis and albumin: still controversies

- **“Old” evidence that albumin + antibiotics > antibiotics alone in SBP**
- **No evidence that albumin + antibiotics > antibiotics alone in bacterial infections other than SBP**
- **“Recent” evidence that albumin improves survival in patients with decompensated cirrhosis**
 - **At least in part by decreasing bacterial infections other than SBP**



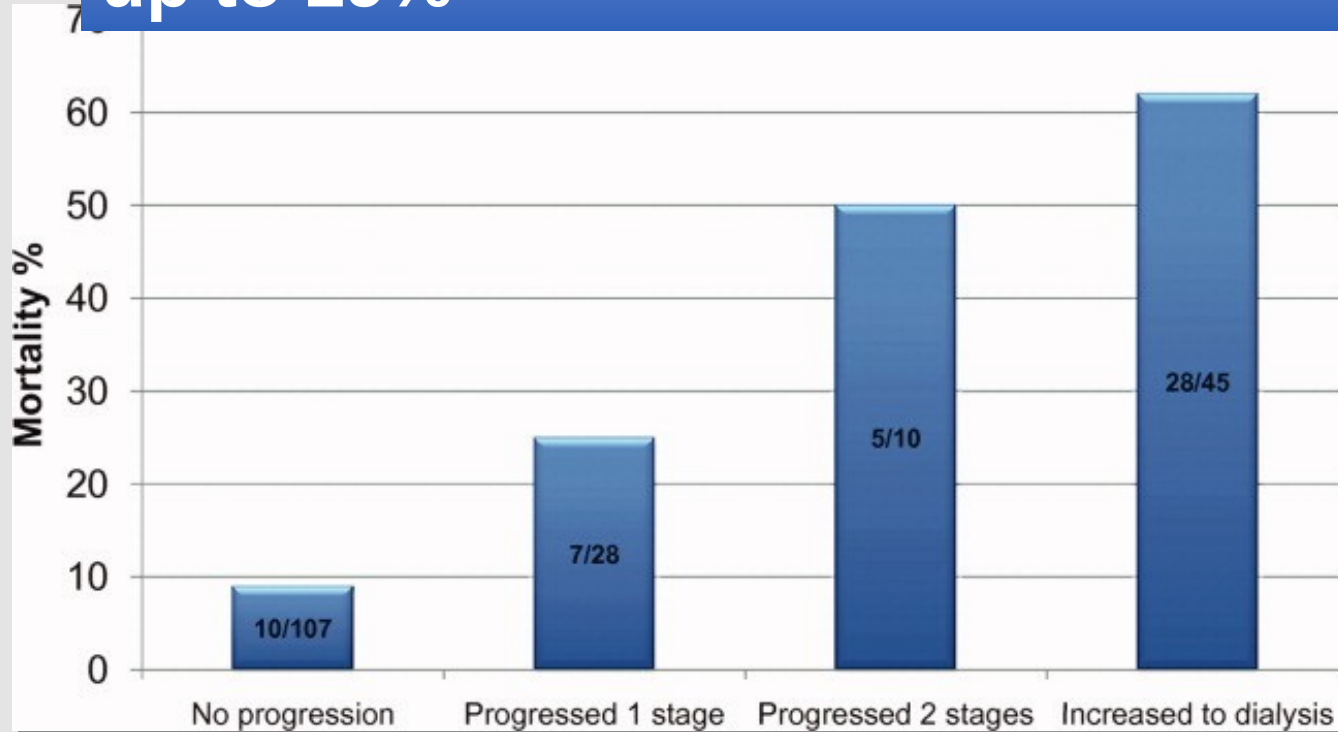
New aspects in the management of decompensated cirrhosis

- Bacterial infections and resistance to antibiotics in cirrhosis
- Albumin and bacterial infections in cirrhosis
- **Acute kidney injury in cirrhosis**
- Management of refractory ascites



The burden of acute kidney injury in cirrhosis

Acute kidney injury in hospitalized patients with cirrhosis:
up to 19%

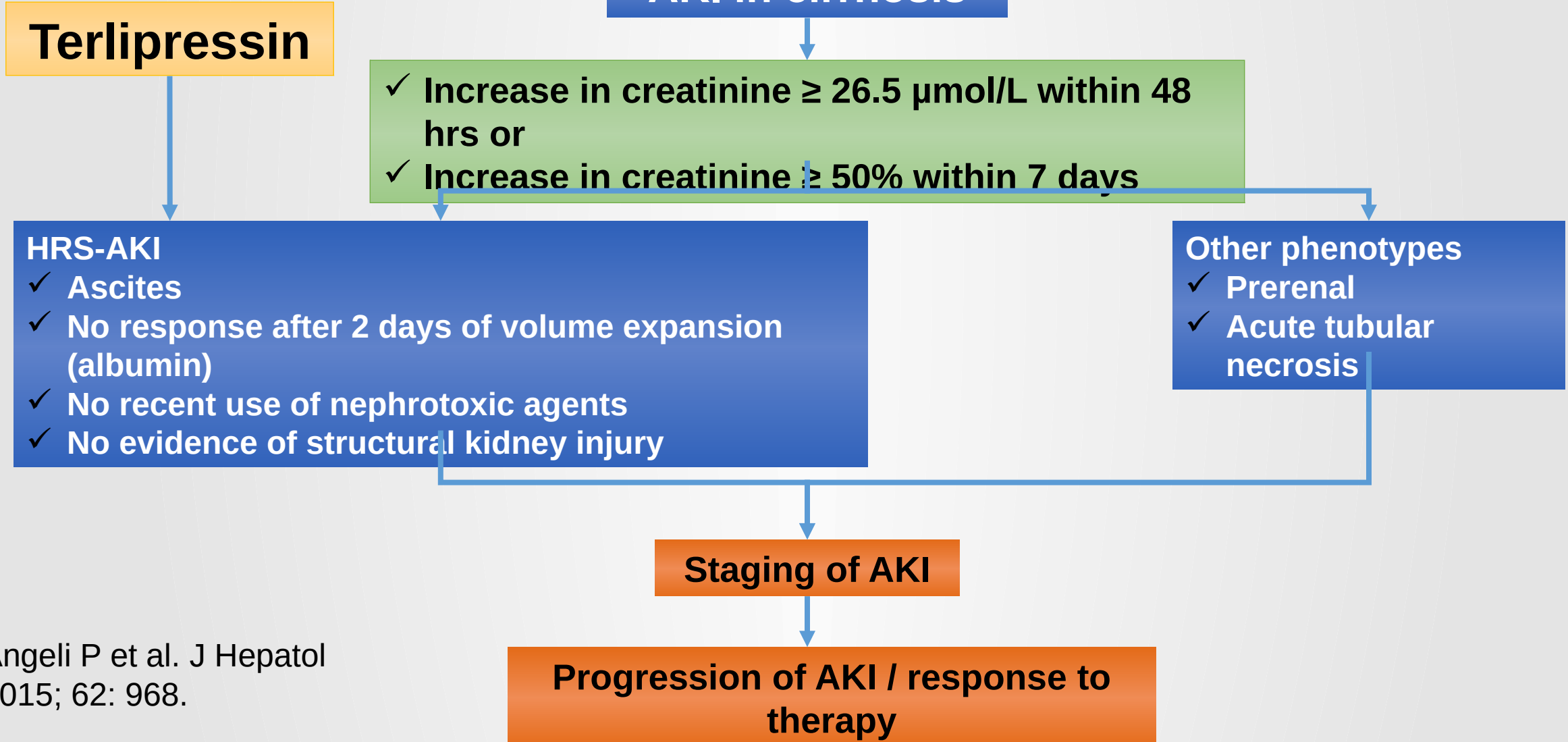


Mortality according to progression of AKI

Belcher JM et al. Hepatology 2013; 57: 753-62.

- ✓ Serum creatinine overestimates GFR in cirrhosis
- ✓ Urine output poorly informative
- ✓ Different phenotypes of AKI with different prognosis
- ✓ Need for early initiation of specific therapy in specific

Re definition of AKI in cirrhosis



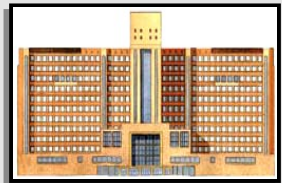
Management of hepatorenal syndrome

- Terlipressin + albumin is the first line option
- IV boluses or continuous infusion ?

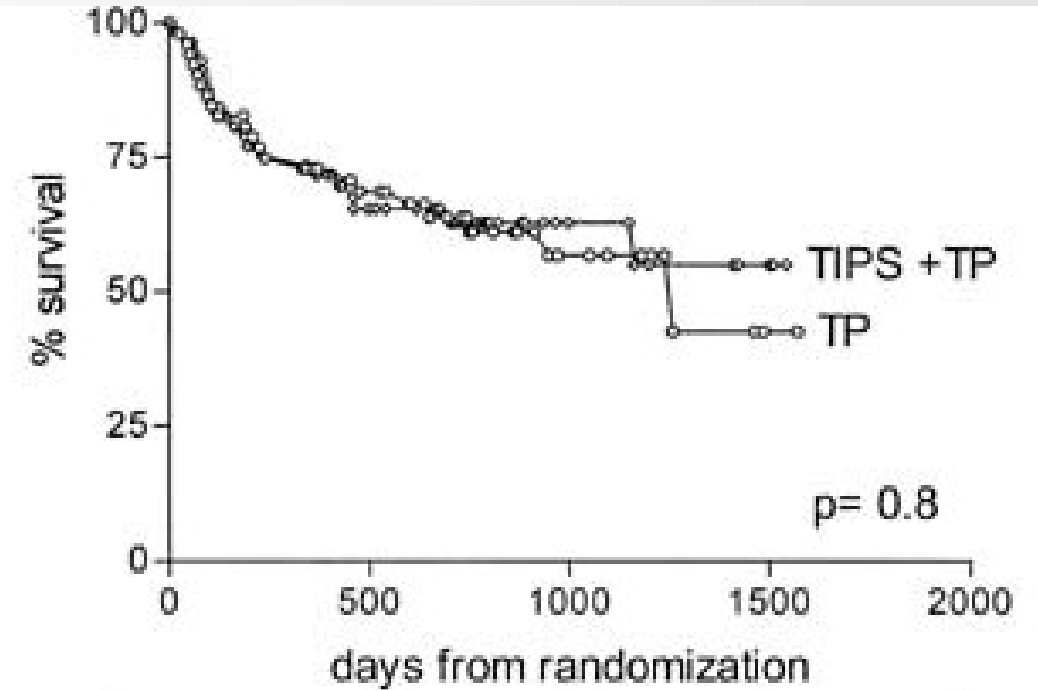
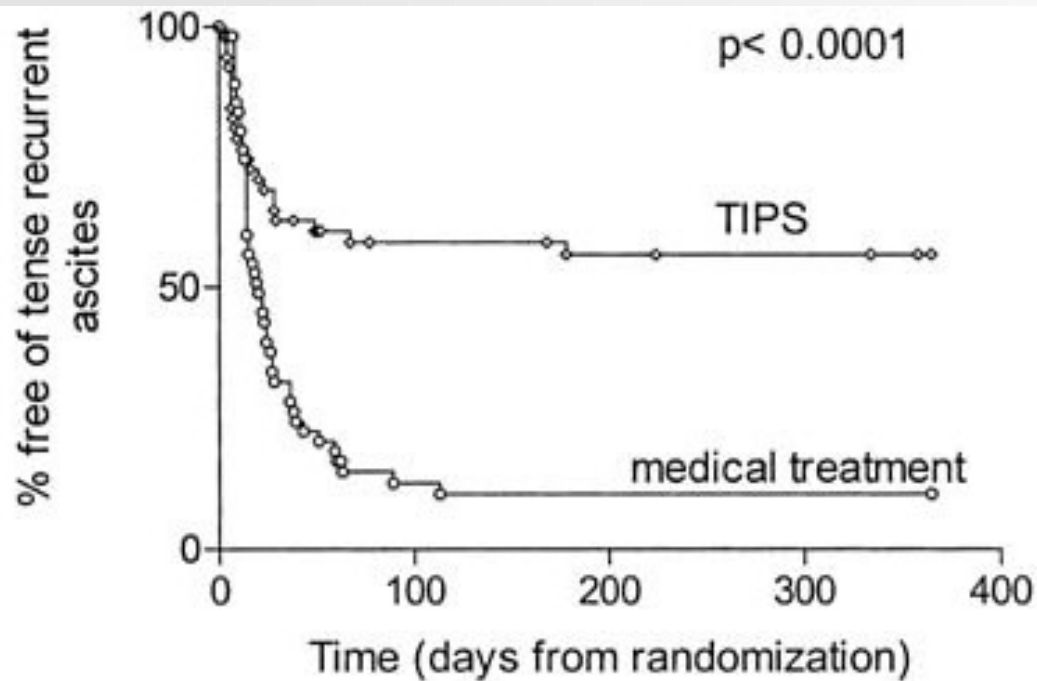
	Terlipressin administration		p value
	Continuous infusion	IV boluses	
Patients	34	37	
Baseline MELD	29	29	ns
Baseline sCR ($\mu\text{mol/L}$)	296	275	ns
End of treatment sCr ($\mu\text{mol/L}$)	120	121	ns
90-day transplant-free survival	53%	69%	ns
Serious adverse events	21%	43%	<0.05

New aspects in the management of decompensated cirrhosis

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TIPS and medical treatment in refractory ascites in the past



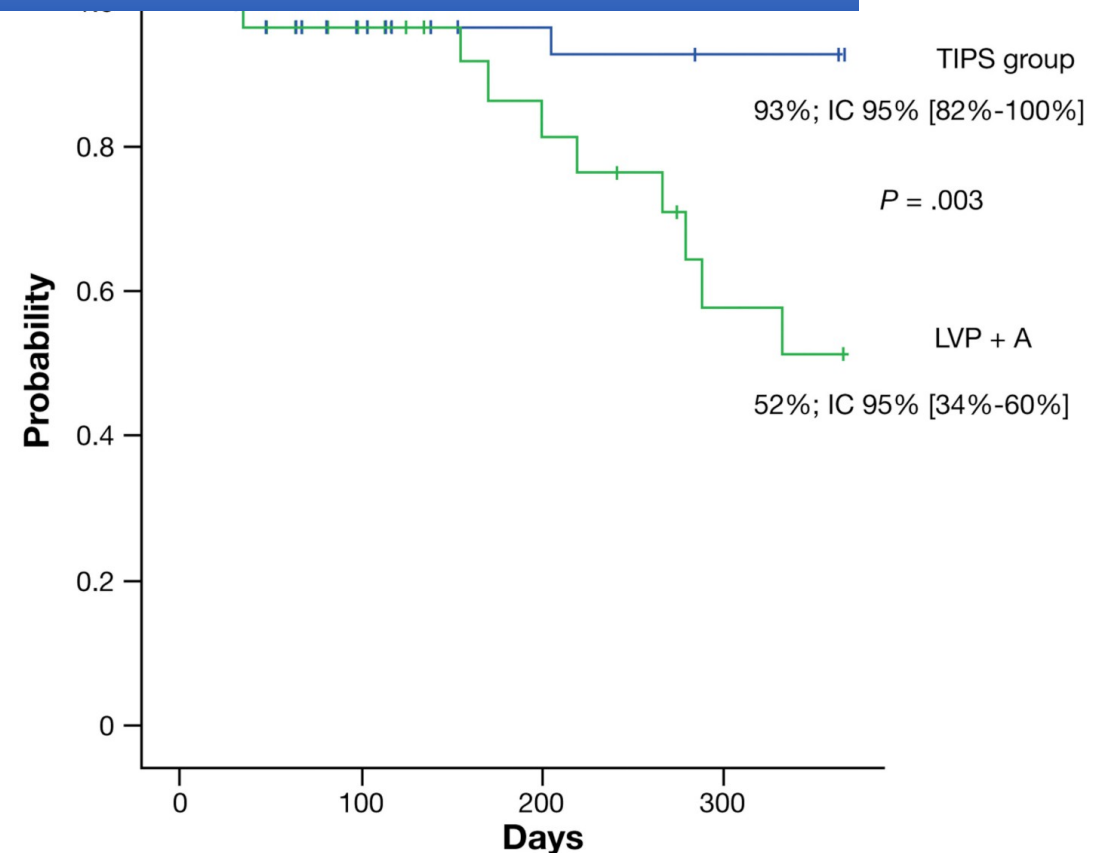
TIPS vs paracentesis in ascites: recent data

62 patients with at least 2 large volume paracentesis within ≥ 3 weeks

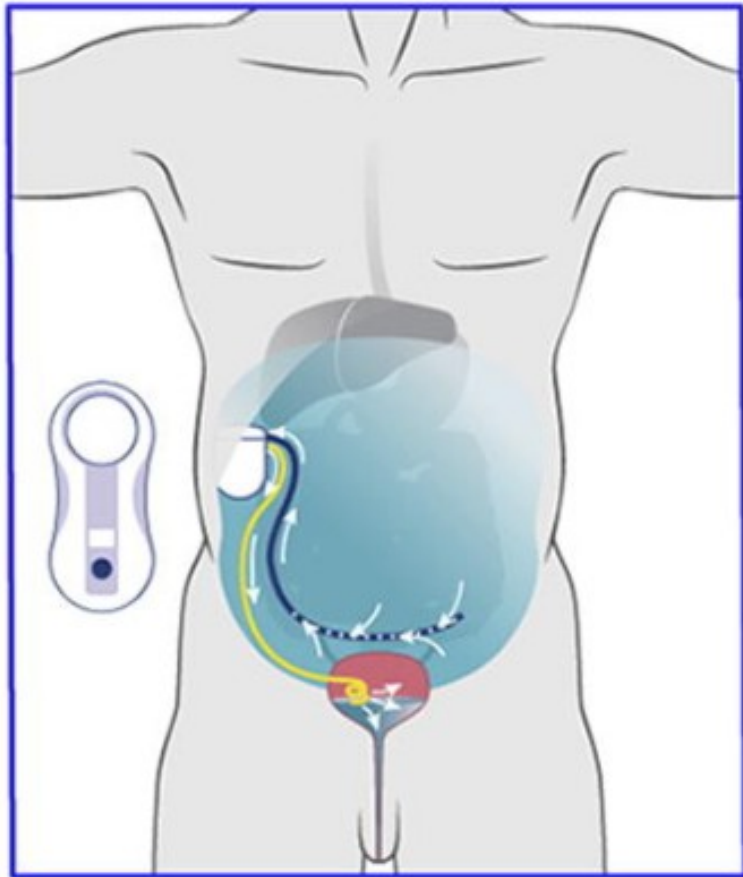
	TIPS	paracentesis	p
Patients	29	33	
Age	57	56	
Alcoholic cirrhosis	90%	85%	ns
Nb paracentesis	4.5	4.2	ns
MELD score	12	13	ns

\neq refractory ascites

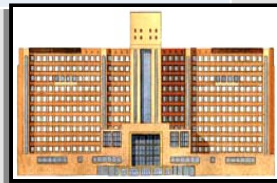
Bureau C et al. Gastroenterology 2017; 152: 157.



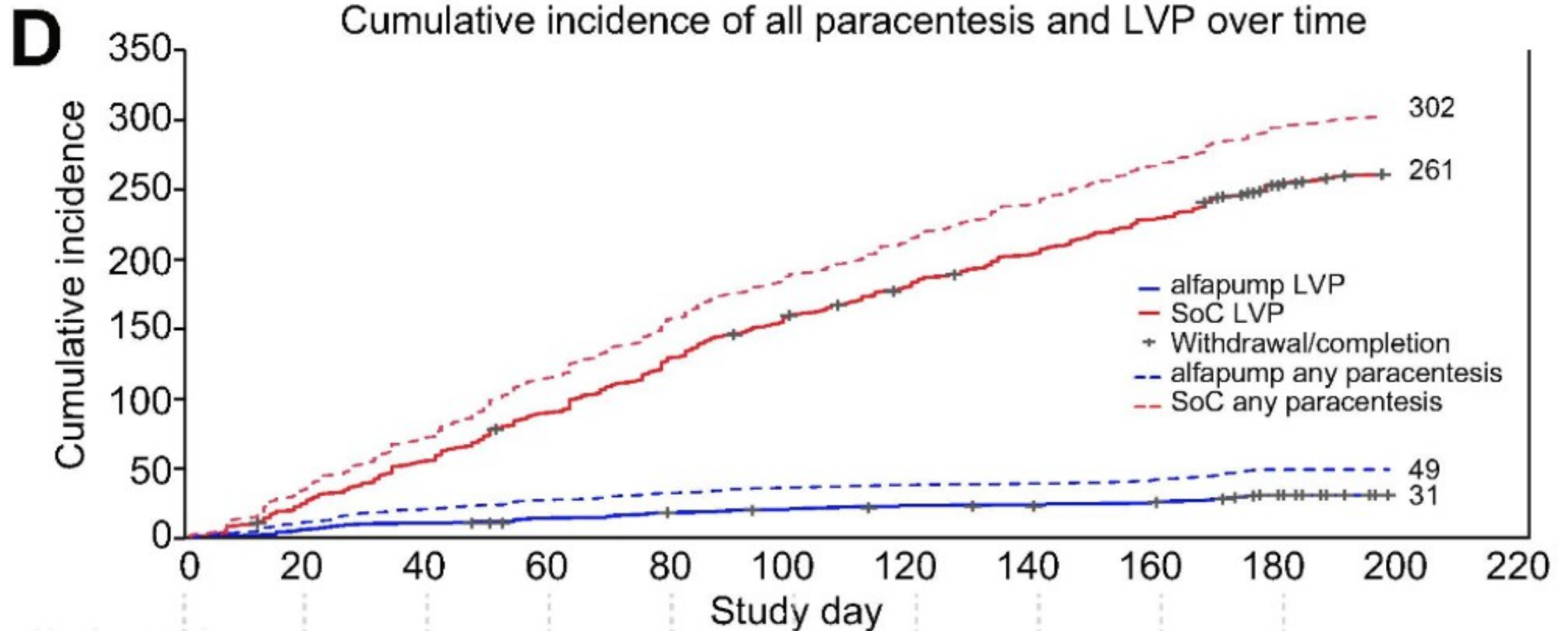
Alfapump vs paracentesis in refractory ascites



	Alfapump	paracentesis	P value
Patients	27	31	
Age	61	62	ns
Alcoholic cirrhosis	74%	67%	ns
MELD	12	11	ns
Infections	25%	30%	ns
Δ creatinine /baselines (d 21)	12.4	4.9	ns

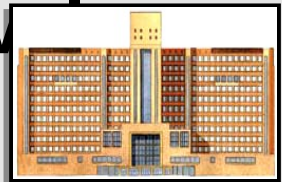


Alfapump vs paracentesis in refractory ascites



Take home messages # 1

- **Decompensated cirrhosis is still associated with high mortality rates in the absence of transplantation**
- **Bacterial infections are a major source of mortality**
 - Multidrug resistance is common in Europe and even more in Asia
- **Long term administration of norfloxacin may improve survival in patients with ascites protein concentration < 15 g/L**
 - Without increasing the incidence of multidrug resistant bacteria
- **Long term administration of albumin may improve survival in patients with decompensated cirrhosis**
 - The role of albumin in non SBP infections needs to be clarified



Take home messages # 2

- **Could norfloxacin + albumin do better?**
- **TIPS may improve survival in patients with “persistent” ascites**
 - Needs to be confirmed in refractory ascites
 - Use of TIPS limited by encephalopathy and disease severity (high MELD)
- **Alfapump could be an alternative to paracentesis or TIPS in patients awaiting transplantation**

