Management of Hepatorenal Syndrome

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Fundación ICALMA

Disclosures:

- None

Management of Hepatorenal Syndrome (HRS)

Agenda:

1. Case

2. HRS as a phenotype of Acute Kidney Injury (AKI)

3. Current management
   - SoC (Terlipressin plus albumin)
   - Biomarkers…do we have them?
   - Priority to HRS treated patients and decresed MELD

Case

- 61 year old man
- Comorbidities:
  - Obesity, DM-T2
  - Decompensated cirrhosis, secondary to NASH
  - Grade II ascites
  - Hepatic encephalopathy
  - Large esophageal varices on primary prophylaxis
- Spironolactone 100 mg/d; Furosemide 40 mg/d; Lactulose; Rifaximin 1100 mg/d; Propranolol 20 mg/twice a day.
- Admitted for drowsiness and increased abdominal circunference

Case

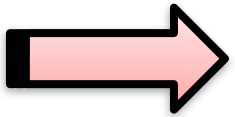
Laboratory	Admission
White blood cells	13.000/mm3
Cells in ascitic fluid	1800/mm3
Neutrophils in ascitic liquid	80% (>1000…)
Creatinine	1.7 mg/dL (previous 1.1 mg/dL one month before)
Total bilirrubin	5.0 mg/dL
INR	2.6
Albumin	3,20 g/dL
Sodium	129 mEq/L
Urinary sodium	3 mEq/L
Child Pugh	C 10
MELD Score	28

Case

Diagnosis:

- Decompensated cirrhosis

  - Grade II ascites
  - Grade II hepatic encephalopathy
  - Spontaneous bacterial peritonitis
  - Hyponatremia
  - Acute Kidney Injury ? HRS ???



LT

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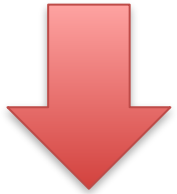
Definition of Acute Kidney Injury in Cirrhosis

Conventional criteria: Rapid reduction in kidney function defined as an increase in creatinine ≥ to 50 % (1,5 times from baseline) with a final value equal or greater than 1.5 mg/dl.



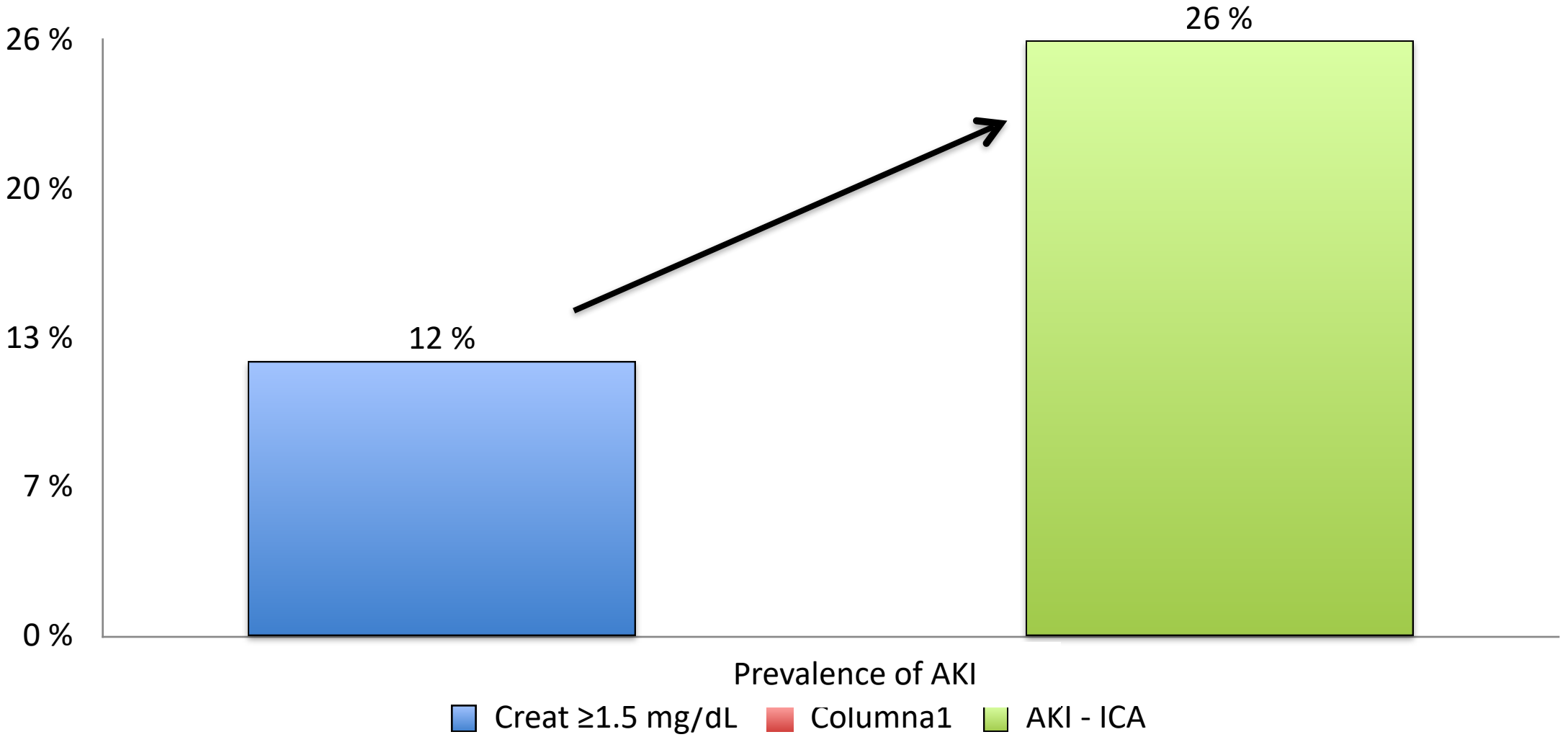
KDIGO criteria (Acute Kidney Injury, AKI): Abrupt reduction of the kidney function which is evidenced by an increase in creatinine of 0.3 mg/dL or more (48 hours), or an increase in creatinine of 50% or more, from basal creatinine known or presumed to have ocurred within the prior 3 months

Basal Creatinine: Creatinine obtained in the last 3 months. Closest value to hospital admission time should be used. In patients without a previous creatinine value, the creatinine at admission.

P. Gines et al NEJM 2009

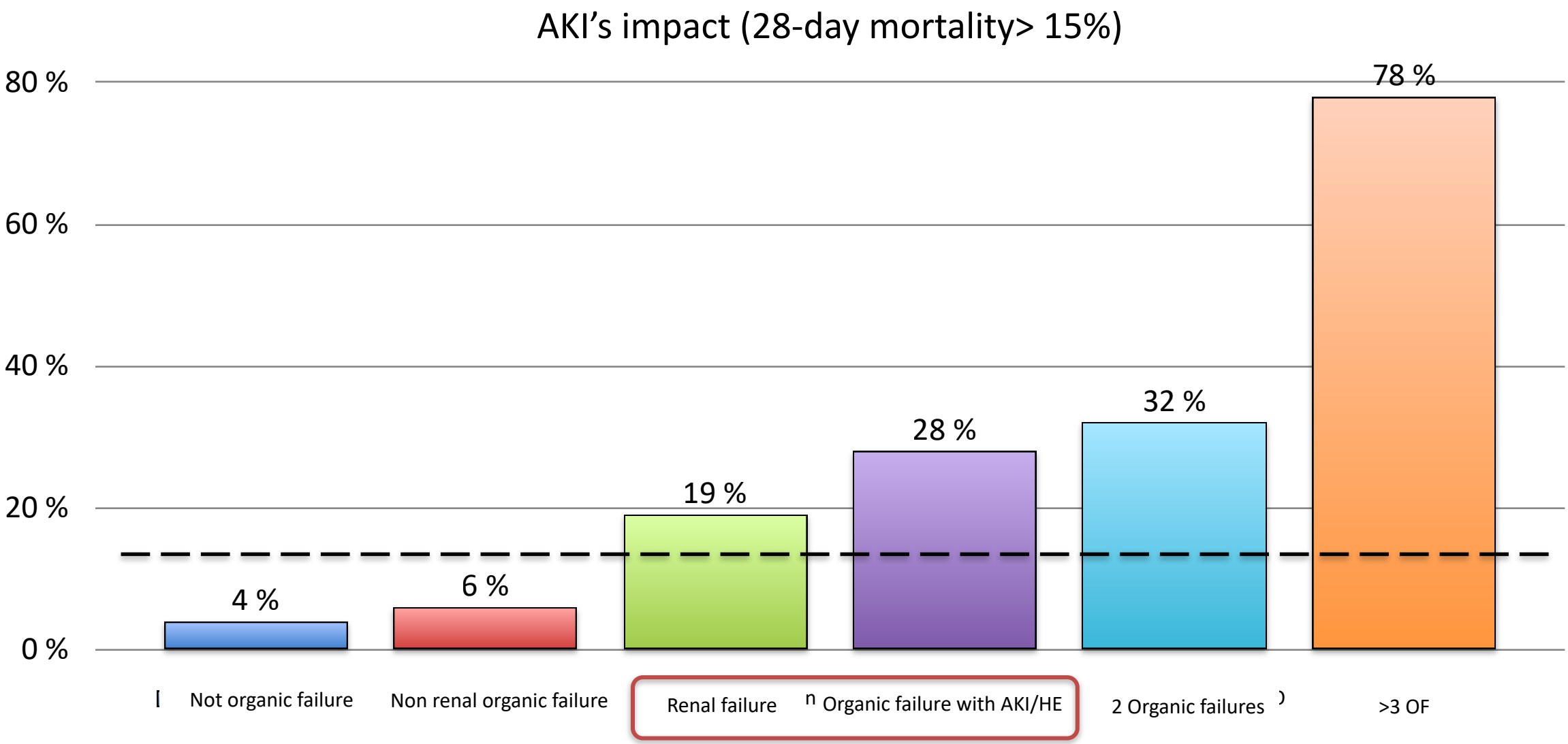
P. Angeli et al J Hepatol 2015

Prevalence of AKI in hospitalized patients



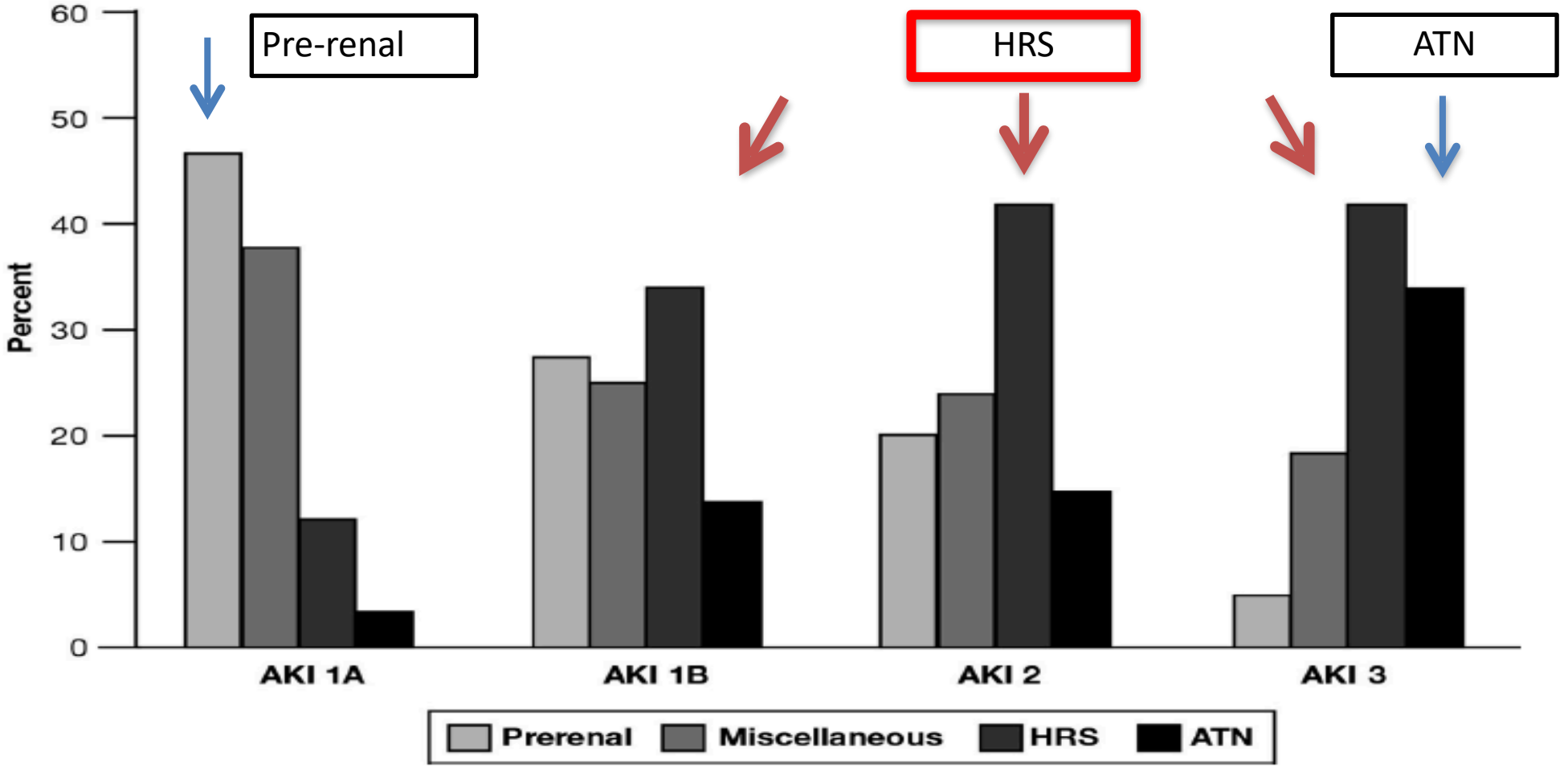
S Piano et al J Hepatol 2013

Prognosis of AKI in hospitalized patients



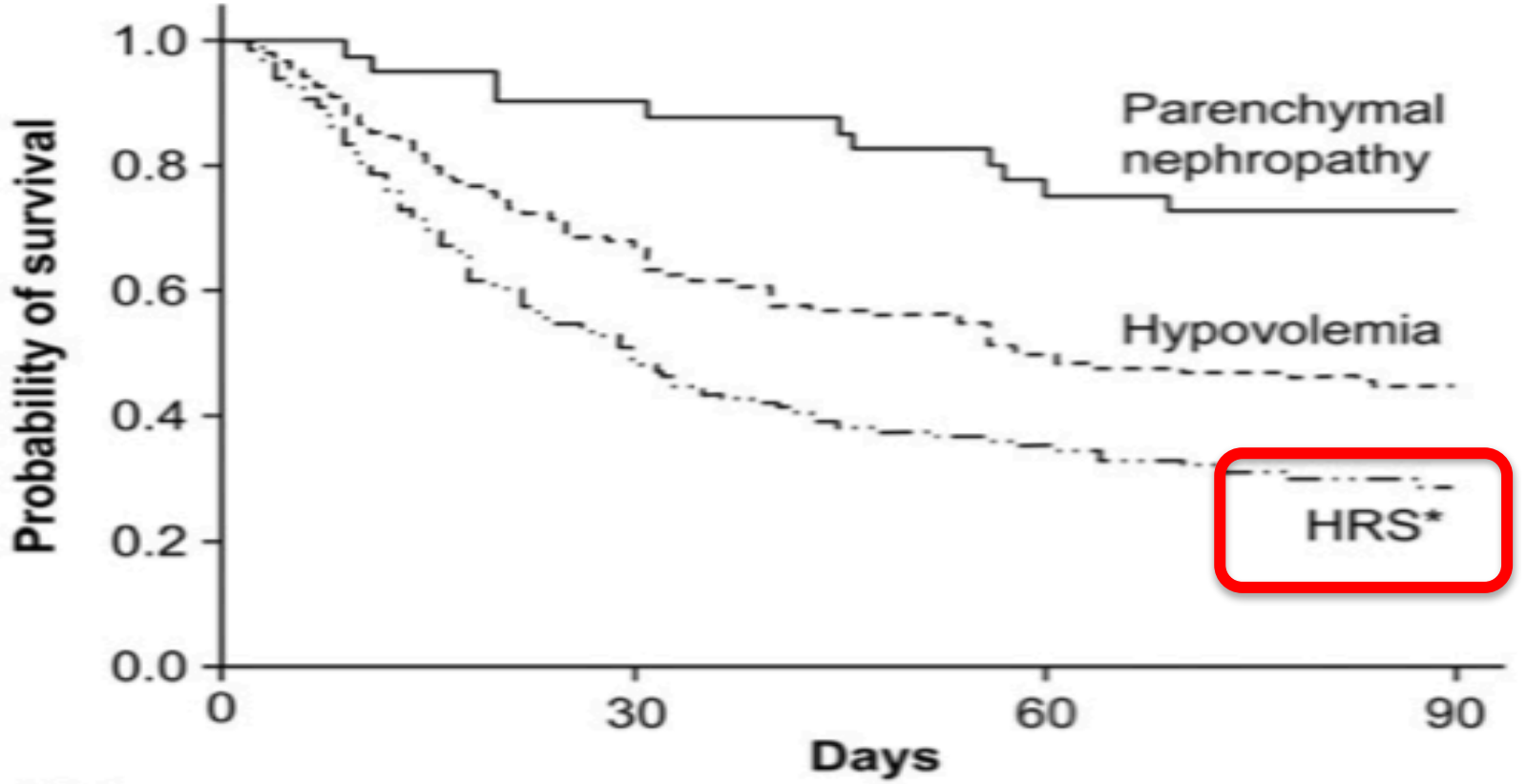
Moreau R et al Gastroenterology 2013

Phenotypic distribution of AKI



Huelin et al, Clinical Gastroenterol Hepatol 2017

Impact of the phenotype of AKI



Patients at risk				
- Parenchymal nephropathy	41	36	31	29
- Hypovolemia	149	98	70	62
- HRS*	201	85	62	47

Marti-Llahi M et al Gastroenterology Hepatol 2011

ICA diagnostic criteria for HRS-AKI (previous type 1 HRS)

- Cirrhosis and ascites
- Diagnosis of AKI according to ICA-AKI criteria
- No response after 2 consecutive days of diuretic withdrawal and plasma volume expansion with albumin 1 g per kg of body weight
- Absence of shock
- No current or recent use of nephrotoxic drugs (NSAIDs, aminoglycosides, iodinated contrast media, etc.)
- No macroscopic signs of structural kidney injury,* defined as:
  - Absence of proteinuria (>500 mg/day)
  - Absence of microhaematuria (>50 RBCs per high power field)
  - Normal findings on renal ultrasonography

*Patients who fulfil these criteria may still have structural damage such as tubular damage

Angeli et al. J. Hepatol 2015;62:968–74;
EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024

Clinical case

Laboratory	Admission		
White blood cells	13.000/mm3		
Cells in ascitic fluid	1800/mm3		
Neutrophil count in ascitic fluid	80 %		
Creatinine	1.7 mg/dL (previous 1.1 mg/dL)		
TB	5 mg/dL		
RIN	2.6		
Albumin	32 g/L		
Na	129 mEq/L		
Urinary Na	5 mEq/L		
Child Pugh	C10		
MELD Score	28		

→ Albumin and ATB

1. Diagnosis:
- Decompensated cirrhosis.

- Ascites +++
- Encephalopathy
- SBP
- Hyponatremia
- AKI ? → YES

Clinical case

Laboratory	Admission	Day 3	
White blood cells	13.000/mm3	11.000/mm3	
Cells in ascitic fluid	1800/mm3	560/mm3	
Neutrophil count in ascitic fluid	80 %	30 %	
Creatinine	1.7 mg/dL (previous 1.1 mg/dL)	2.1 mg/dL	
TB	5 mg/dL	4.5 mg/dL	
RIN	2.6	2.3	
Albumin	32 g/L	36 g/L	
Na	129 mEq/L	128 mEq/L	
Urinary Na	5 mEq/L	5 mEq/L	
Child Pugh	C10	C10	
MELD Score	28	28	

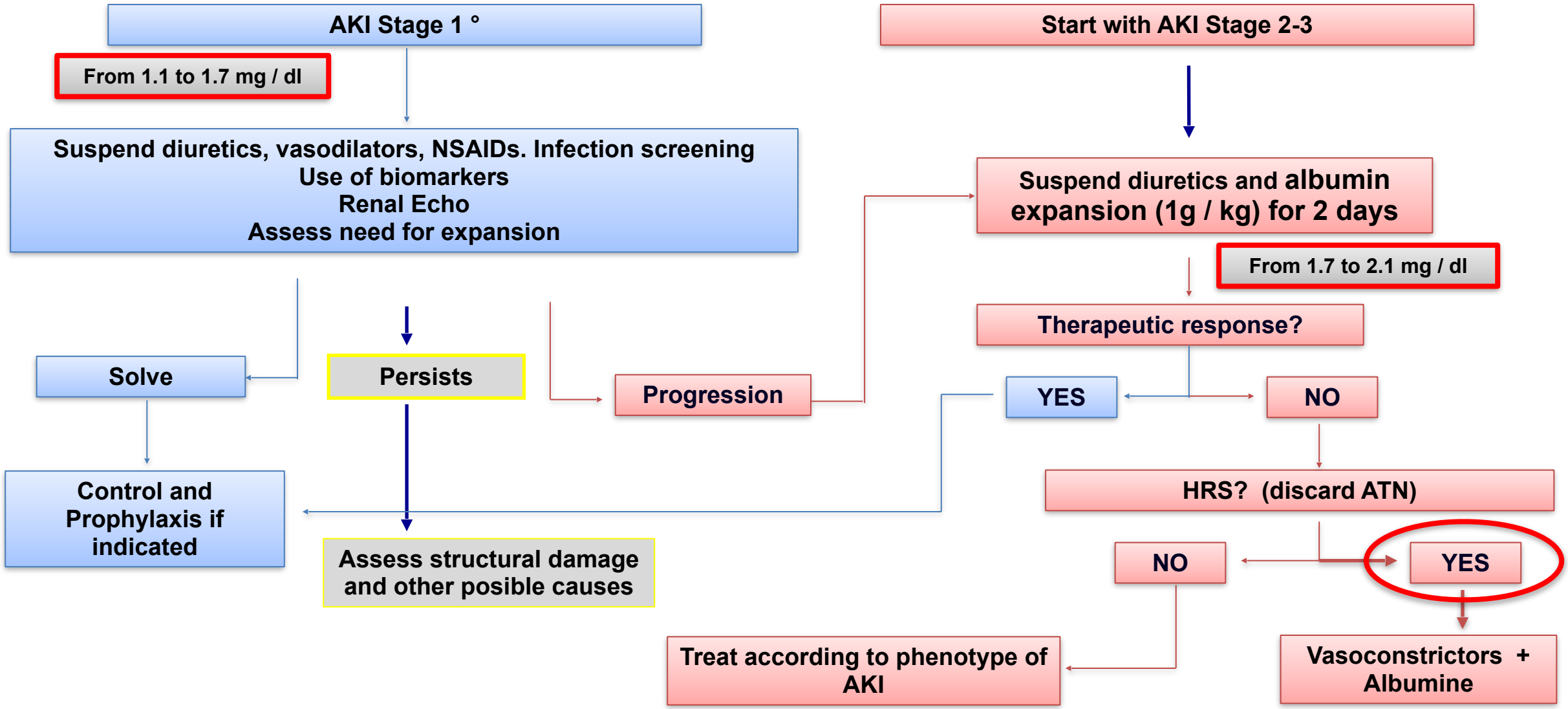
→ Albumin and ATB

1. Diagnosis:

- Decompensated cirrhosis.

- Ascites +++
- Encephalopathy
- SBP
- Hyponatremia
- AKI → YES
- HRS ?

AKI Management Algorithm in Cirrhosis



Wong & Angeli et al. J Hepatol 2017

Clinical case

Laboratory	Admission	Day 3	
White blood cells	13.000/mm3	11.000/mm3	
Cells in ascitic fluid	1800/mm3	560/mm3	
Neutrophil count in ascitic fluid	80 %	30 %	
Creatinine	1.7 mg/dL (previous 1.1 mg/dL)	2.1 mg/dL	
TB	5 mg/dL	4.5 mg/dL	
RIN	2.6	2.3	
Albumin	32 g/L	36 g/L	
Na	129 mEq/L	128 mEq/L	
Urinary Na	5 mEq/L	5 mEq/L	
Child Pugh	C10	C10	
MELD Score	28	28	

→ Albumin and ATB → + Terlipressin

1. Diagnosis:

- Decompensated cirrhosis.

- Ascites +++
- Encephalopathy
- SBP
- Hyponatremia
- AKI ? → YES
- HRS ? → YES

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Management of HRS-AKI: treatment

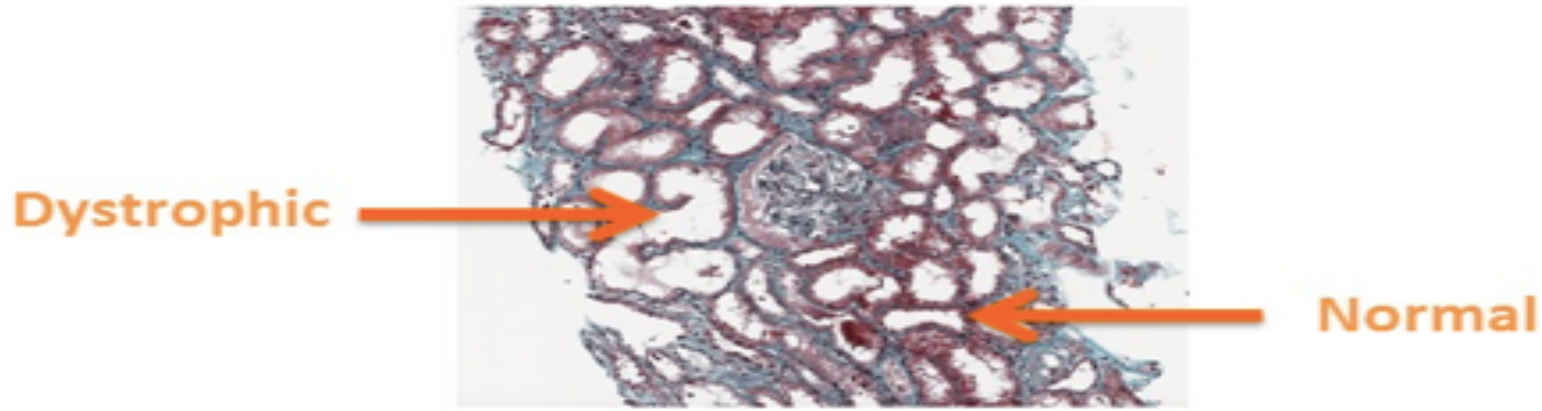
- First-line therapy is terlipressin plus albumin*

Recommendation	Grade of evidence	Grade of recommendation
All patients meeting the current definition of HRS-AKI stage >1A should be expeditiously treated with vasoconstrictors and albumin	III	1
Terlipressin can be administered by IV boluses (1 mg every 4–6 hours) or by continuous IV infusion (2 mg/day)† • In case of non-response (decrease in SCr <25% from the peak value) after 2 days, the dose of terlipressin should be increased in a stepwise manner to a maximum of 12 mg/day	I	1
Albumin solution (20%) should be used at 20–40 g/day • Serial measures assessing central blood volume can help to titrate the dose of albumin to prevent circulatory overload	II-2	1
Noradrenaline can be an alternative to terlipressin‡ • Requires a central venous line often in an ICU Midodrine + octreotide can be an option when terlipressin or noradrenaline are unavailable (but efficacy is much lower)	I I I	2 1 1

*Grade of evidence I, grade of recommendation 1;
†Continuous IV infusion allows for dose reduction to reduced adverse effects; ‡ Limited data are available
EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024

Phenotype of AKI: HRS vs ATN or both ?

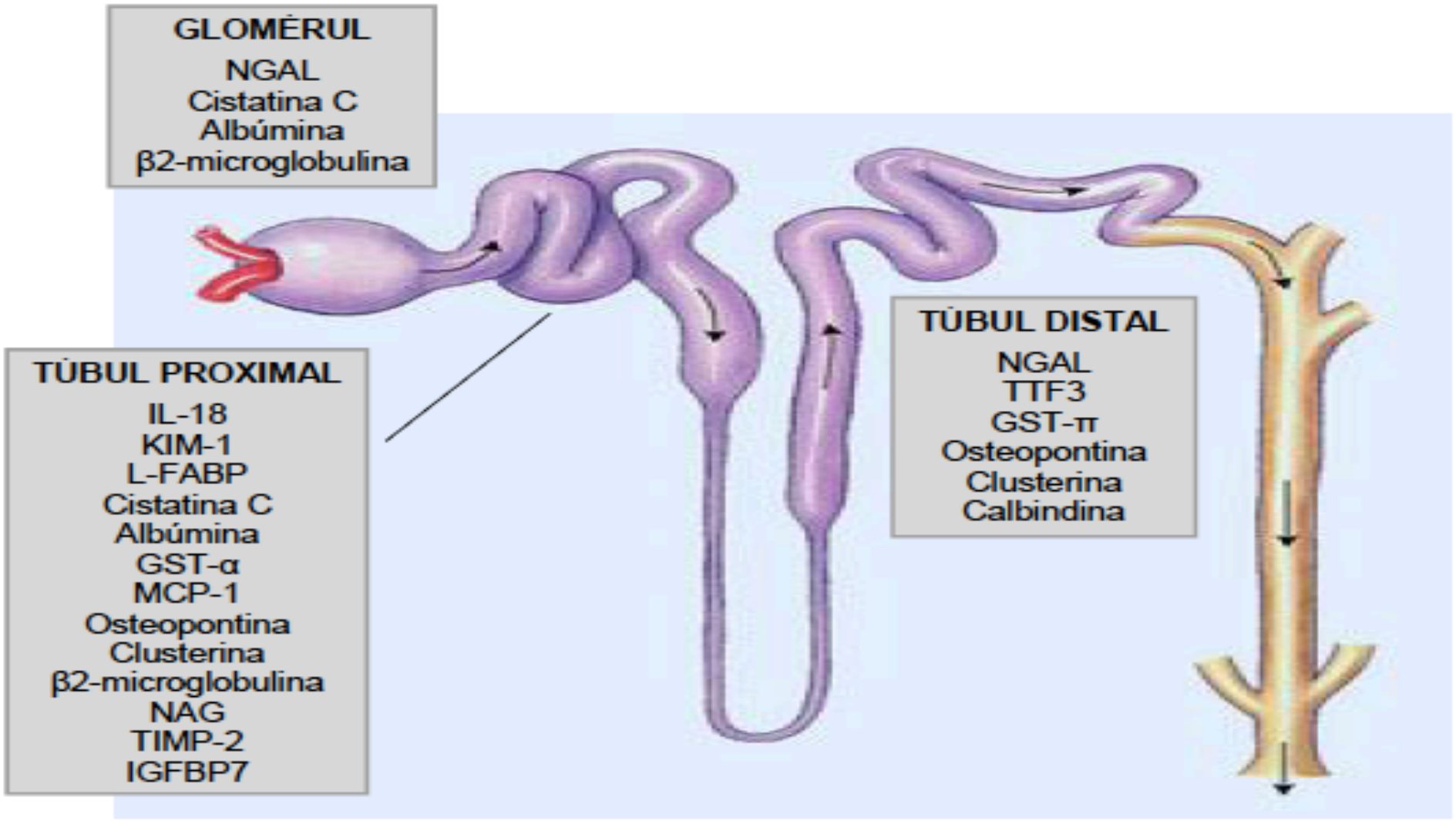
- HRS can be the prelude to an ATN, and even coexist.



- 40-60 % of the HRS do not respond to therapy: Terlipressin plus albumin.
- Many patients with HRS fail to recover after Liver Tx, suggesting the possibility of co-existing kidney damage.
- The differential diagnosis between HRS and ATN is not easy, being therapy very different between both syndromes.

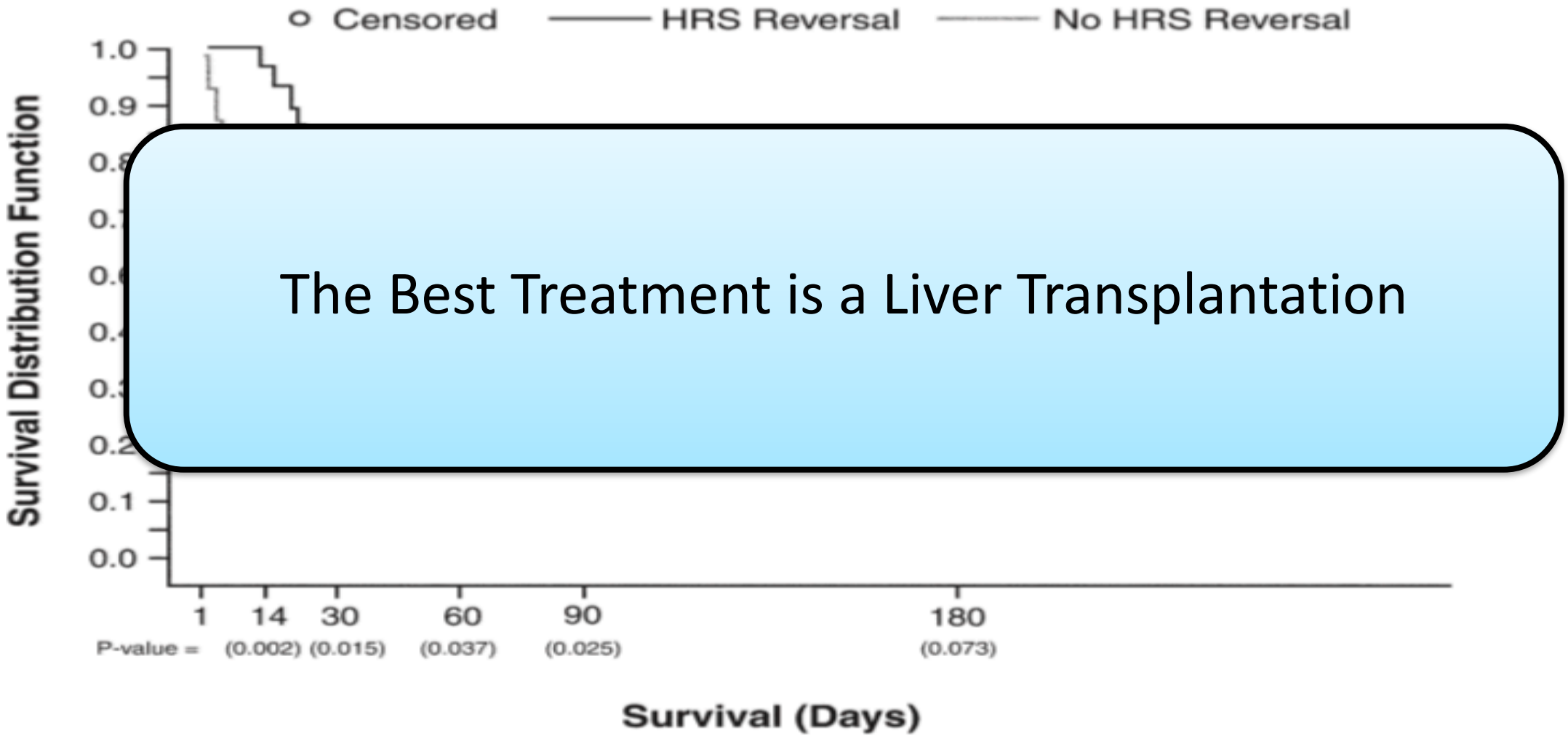
C Francoz et al EASL 2017

Biomarkers…



X. Ariza et al Clinical Gastroenterol Hepatol 2017

HRS-AKI: Treatment



The Best Treatment is a Liver Transplantation

Sanyal A et al Gastroenterology 2008

Clinical case

Laboratory	Admission	Day 3	Day 7
White blood cells	13.000/mm3	11.000/mm3	10.000/mm3
Cells in ascitic fluid	1800/mm3	560/mm3	
Neutrophil count in ascitic fluid	80 %	30 %	
Creatinine	1.7 mg/dL (previous 1.1 mg/dL)	2.1 mg/dL	1.3 mg/dL
TB	5 mg/dL	4.5 mg/dL	2.8 mg/dL
RIN	2.6	2.3	2.0
Albumin	32 g/L	36 g/L	35 g/L
Na	129 mEq/L	128 mEq/L	130 mEq/L
Urinary Na	5 mEq/L	5 mEq/L (FENa < 0.1)	5 mEq/L
Child Pugh	C10	C10	C9
MELD Score	28	28	24

→ Albumin (ATB)

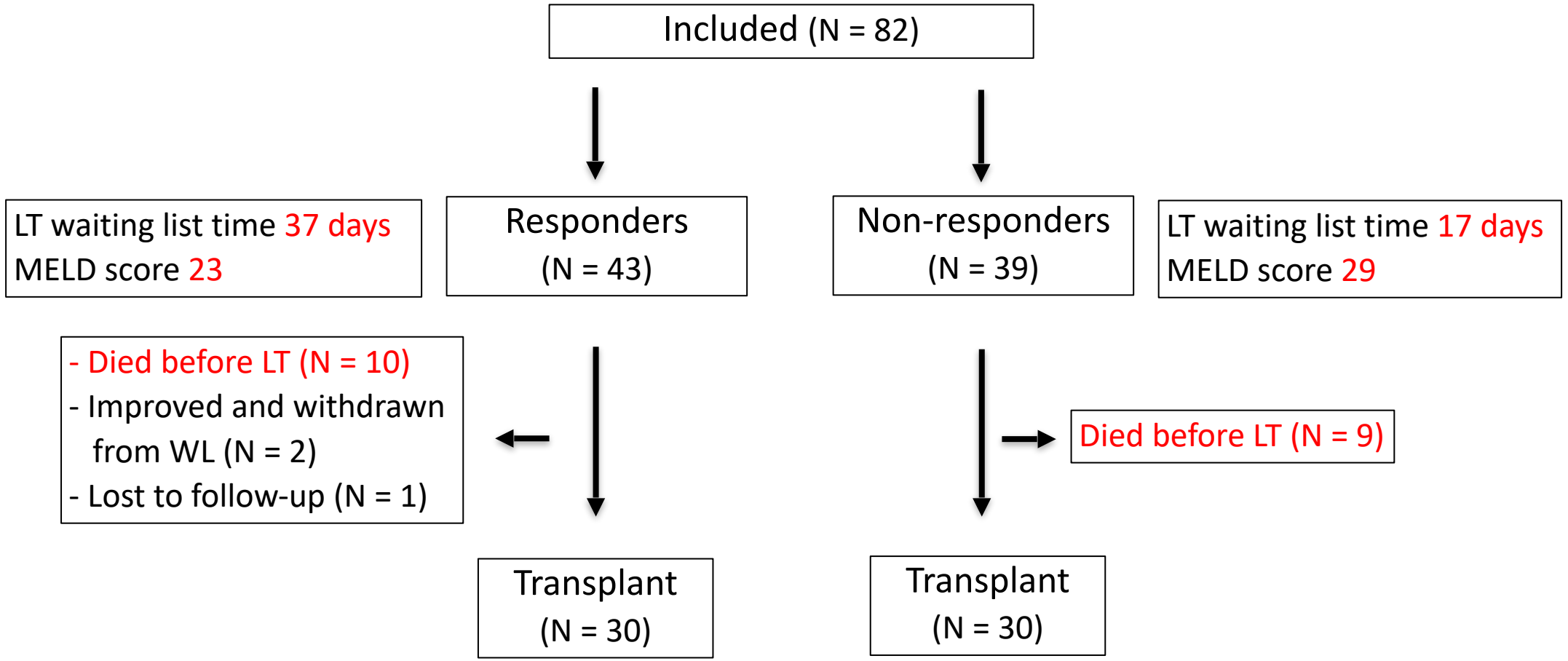
→ + Terlipressin

1. Diagnosis:

- Decompensated cirrhosis.

- Ascites +++
- Encephalopathy
- SBP
- Hyponatremia
- AKI
- HRS

Penalization of HRS patients responders to Terlipressin



Experts in the field suggested using baseline MELD/MELD-Na score (pretreatment value) for giving priority on the LT waiting list…

Piano S et al. Hepatology 2020

Summary

- HRS-AKI in the patient with cirrhosis is a severe complication associated with decrease survival.
- The current definition of HRS-AKI allows an early diagnosis and therefore, an early onset of therapy.
- Phenotypic diagnosis is essential for proper treatment but often difficult to establish. Biomarkers may help in the future…

Summary

- Terlipressin + albumin is currently the best therapy available to achieve improvement or reversal of HRS-AKI.

- LT is the only curative strategy. Therefore, policies should be adopted in order to transplant these patients as soon as possible.

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- Juan Carlos Bandi
- Alejandra Villamil
- Paola Casciato
- Ezequiel Mauro
- Leila Haddad
- Carla Bermúdez
- Adrian Narváez
- Natalia Sobenko
- Fabiola Moreno
- Agustina Martinez Garmendia
- Lucrecia Garcia Oliveira

Thank you !!!!