



MÁSTER EN HEPATOLOGÍA

UAM
Universidad Autónoma
de Madrid

 Universidad
de Alcalá

Asignatura: Cirrosis III

“Síndrome hepatorenal: forma clásica y en ACLF. Insuficiencia renal en el paciente en UCI. Diálisis en el paciente con cirrosis”

Pere Ginés

Hospital Clínic de Barcelona. Universitat de Barcelona. Institut d'Investigacions Biomèdiques August Pi-Sunyer (IDIBAPS), CIBERehd, Barcelona

Disclosure of interests

PERE GINÈS

I disclose the following financial relationship(s) with a commercial interest:

Mallinckrodt, Novartis, Sequana Medical, Gilead,

Grifols, Martin Pharmaceuticals, Intercept, Echosens

DEFINITION OF HEPATORENAL SYNDROME

Syndrome characterized by marked impairment of kidney function with the following main characteristics:

- 1.No significant alterations in kidney histology
- 2.No specific markers for diagnosis, which is therefore dependent on ruling out other types of kidney failure
- 3.Potential of reversibility, by liver transplantation or pharmacological therapy
- 4.Frequently associated with extra-renal organ dysfunction (circulation, liver,..)
- 5.Prognosis generally poor, but dependent on reversibility of kidney function and associated organ failures

“One of the most interesting syndromes in medicine”

CASE PRESENTATION (1)

83-yr old female with decompensated cirrhosis admitted to the Liver Unit on April 2020 for skin infection, increased ascites/edema, and worsening kidney function.

Main health issues:

- Obesity for 20+ years (BMI approx 32 Kg/m²)
- Type-2 DM for 15+ years
- Arterial Hypertension
- Other: dyslipidemia, hypothyroidism, depression
- **NASH cirrhosis** diagnosed in December 2019 because of ascites
- Current treatment: lactitol, glicazide, aspirin, atorvastatin, citalopram, levothyroxin
- Spironolactone stopped because of hyperkalemia.

CASE PRESENTATION (2)

Main issues related to cirrhosis in the 4 months after diagnosis:

- Clinical manifestations:
 - First admission: Ascites/edema and Hepatic Encephalopathy
 - Second admission: Skin infection in left lower extremity associated with transient AKI stage 1B, likely due to HRS
 - Iron-deficiency anemia due to portal hypertensive enteropathy
- Last labs: bili 1.4 mg/dL, albumin 33 g/L, PT 49%, AST 36 IU/mL, creatinine 1.1 mg/dL, Child B 7 and MELD 14
- Ultrasound: cirrhotic liver, patent portal vein, splenomegaly, ascites
- Upper GI endoscopy: small esophageal varices
- Patient was admitted to the Unit for new skin infection associated with ascites and worsening kidney function. Diagnosis: criteria of AKI-HRS (no response to iv albumin)

CASE PRESENTATION (3)

Evolution of kidney function

	Admission	D3	D7	D10	D14	D21	D28	D32
SCr(mg/dL)	3.0	3.8	3.5	2.3	2.1	1.5	1.1	3.6
NGAL(ug/gCr)	62							
Treatment								
Albumin	Yes	Yes	Yes	Yes	Yes	Yes	STOP	No
Terlipressin	No	2mg/d	4mg/d	4mg/d	5mg/d	5mg/d	STOP	No
Furosemide		Intermittently during terli and alb treatment						
Antibiotics	Yes	Yes	Yes	-	-	-	-	-
Albumin(g/L)	31	31	31	32	38	34	34	36

MANAGEMENT OF HRS

Current Guidelines

- Terlipressin in combination with albumin should be considered the first line therapeutic agent for AKI-HRS, continuous iv infusion starting at 2 mg/day.

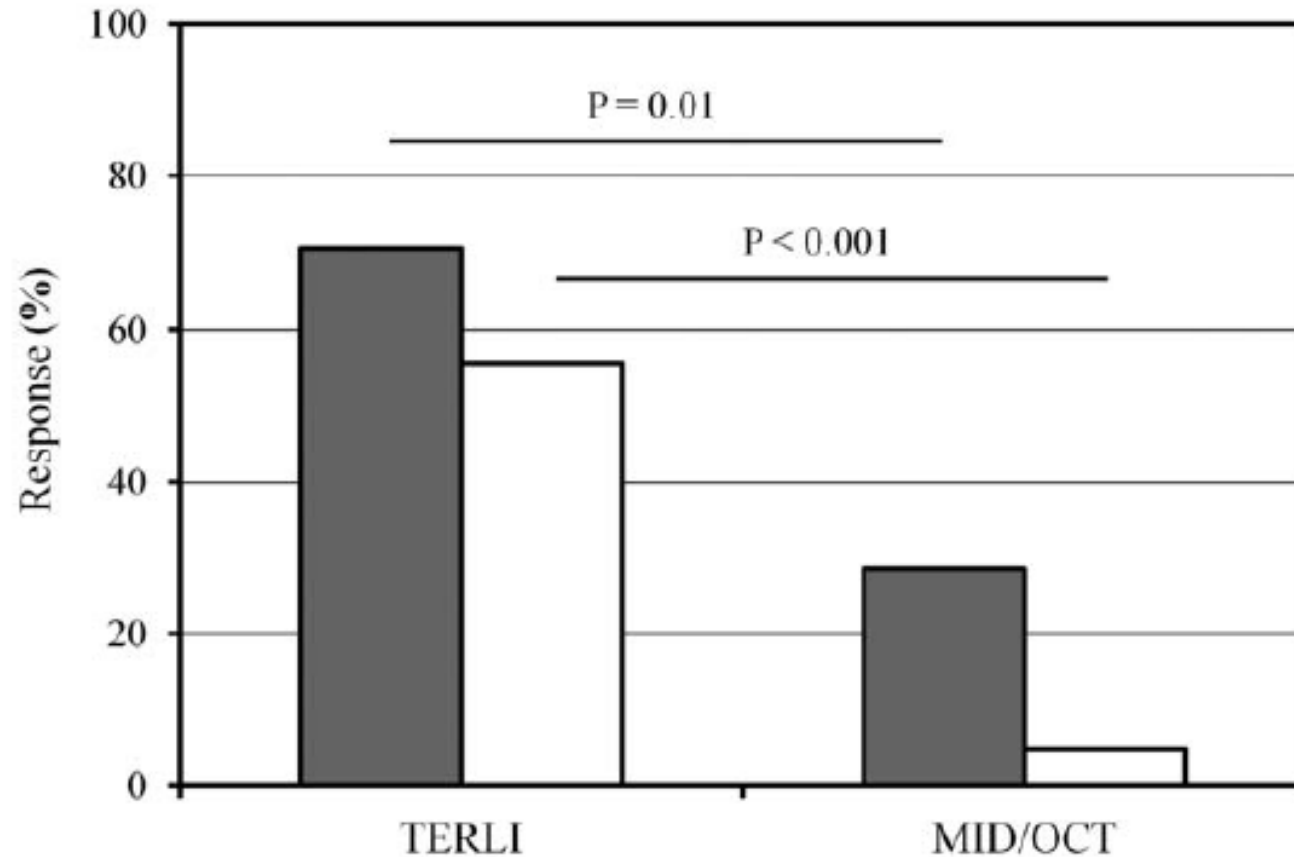
EASL Clinical Practice Guidelines, J Hepatol, 2018

- Terlipressin and albumin first line therapy for AKI-HRS, preferably as continuous iv infusion starting 2 mg/day. Use other vasoconstrictors if terlipressin is not available

AASLD Clinical Practice Guidance Hepatology 2022

TREATMENT OF HEPATORENAL SYNDROME

Comparison between Terlipressin and Midodrine plus Octreotide



Cavallin M et al., Hepatology, 2015

MANAGEMENT OF HEPATORENAL SYNDROME

Pros and cons of vasoconstrictor therapy

PROS

- . Pathophysiologically-oriented
- . Administration simple
- . Low cost
- . Allows transplant without RRT
in responders
- . Survival improved in responders

CONS

- . Terlipressin not available in all countries
- . ICU required in some countries for
norepinephrine treatment
- . Ischemic side effects possible (up to 10%)
- . MELD score decreases in responders
- Risk of pulmonary edema if excessive
albumin is given

HEPATORENAL SYNDROME AND ACLF

Independent predictors of response
to terlipressin and albumin

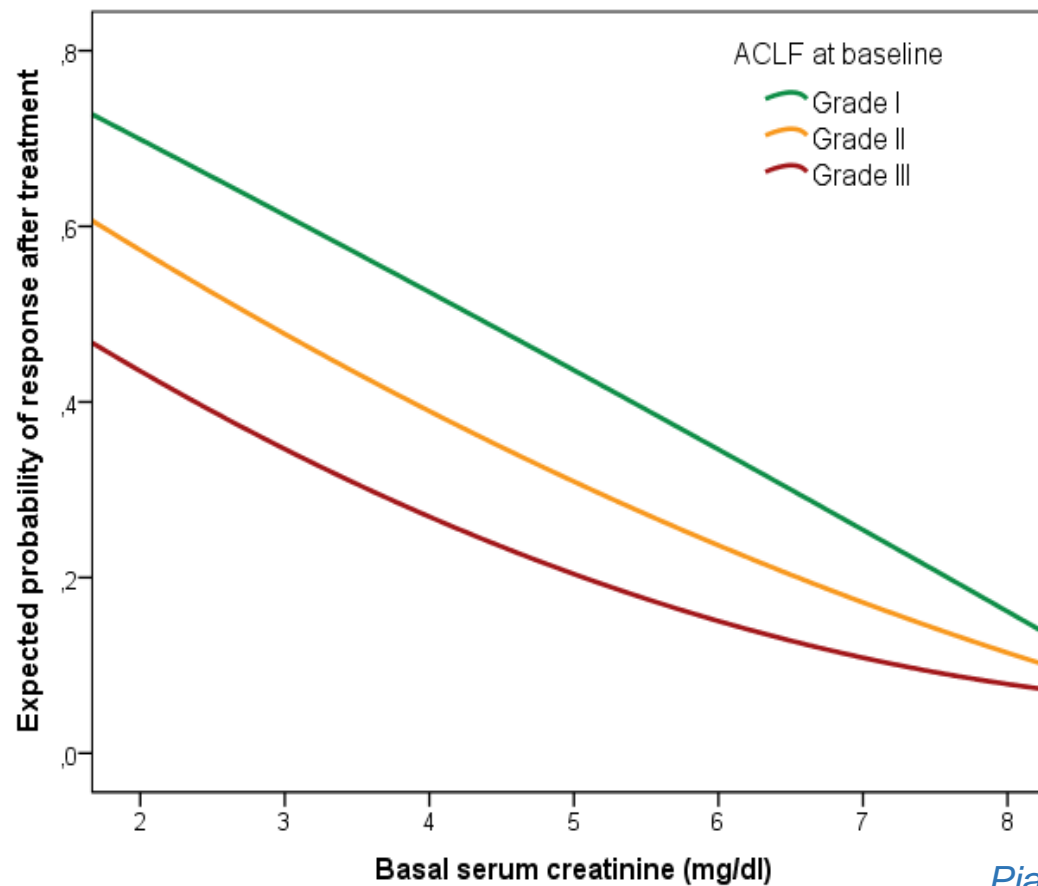
Response rate 30 – 70%

Variable	OR	P
Precipitating event	2.08 (1.21 – 3.07)	0.008
Baseline serum creatinine	0.21 (0.09 – 0.53)	0.001
ACLF grade	0.62 (0.42 – 0.90)	0.005

Piano et al., Clin Gastroenterol Hepatol 2018

HEPATORENAL SYNDROME AND ACLF

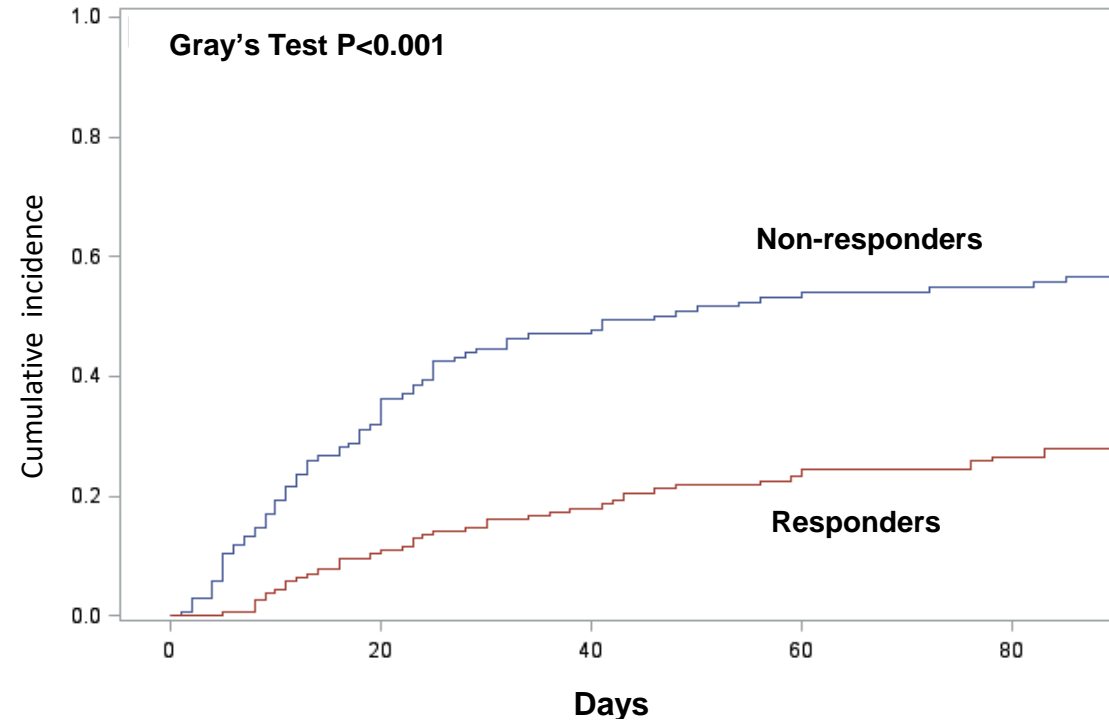
Reversal of type 1 HRS according to ACLF grade and baseline creatinine



Piano et al., Clin Gastroenterol Hepatol 2018

HEPATORENAL SYNDROME AND ACLF

Cumulative incidence of mortality according to response to treatment with terlipressin and albumin



Piano et al., Clin Gastroenterol Hepatol 2018

HEPATORENAL SYNDROME AND ACLF

Independent predictors of 90-day mortality in patients with type-1 hepatorenal syndrome

	HR	95% CI	P
Age (years)	1.05	1.03 – 1.07	<0.001
Leukocytes (cells/mm ³)	1.03	1.12 – 2.02	0.006
ACLF grade	2.06	1.54 – 2.75	<0.001
Response to treatment	0.41	0.29 – 0.60	<0.001

Piano et al., Clin Gastroenterol Hepatol 2018

RRT in liver disease

- Main indications
 - Bridge to LT in both ALD and ESLD
 - Reversible causes of AKI
 - ATN, (differential diagnosis with HRS)
 - Glomerulonephritis, Tubulointerstitial nephropaties
- Peculiarities
 - No published evidence to guide RRT (dose, timing)
 - Better hemodynamic stability with CRRT
 - Probably shorter lifespan circuits in CRRT
 - Increased bleeding risk with heparin
 - Citrate anticoagulation likely safe



CLÍNIC
BARCELONA
Hospital Universitari

ciberehd
Centro de Investigación Biomédica en Red
Enfermedades Hepáticas y Digestivas

ID BAPS
Institut
D'Investigacions
Biomèdiques
August Pi i Sunyer

 **UNIVERSITAT DE
BARCELONA**

 **Agència
de Gestió
d'Ajuts
Universitaris
i de Recerca**

***iCrea**
INSTITUCIÓ CATALANA DE
RECERCA I ESTUDIS AVANÇATS

 **European
Commission**

Horizon 2020
European Union funding
for Research & Innovation

 **Fondo de
Investigación en Salud
Instituto de Salud Carlos III**

 **Generalitat de Catalunya
gencat.cat**



MÁSTER EN HEPATOLOGÍA



UAM
Universidad Autónoma
de Madrid



Universidad
de Alcalá