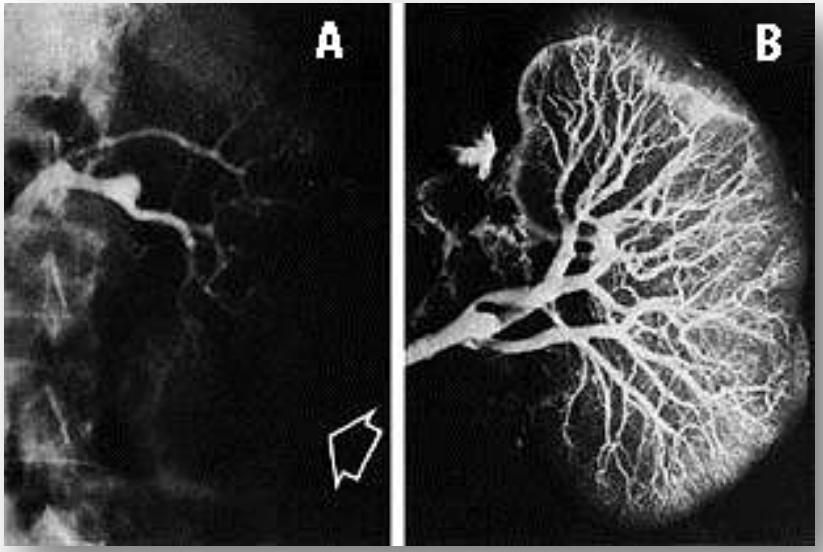
Hepatorenal syndrome



Jan T. Kielstein
Departent of Nephrology
Medical School Hannover

Hepatorenal Syndrome

1) History of HRS
2) Pathophysiology of HRS
3) Definition of HRS
4) Clinical presentation of HRS
5) Treatment of HRS
   -conservative (albumine, vasopressin analogues)
   -artificial and bioartificial liver support systems
6) Prevention of HRS

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History of the hepatorenal syndrome

- **coincidence of hepatic and renal failure** (FRERICHS 1861)
- **renal function ↓, RR ↓, CO ↑, HR ↑, venousO_2-saturation ↑ → *peripheral arterial vasodilation*** (HECKER and SHERLOCK, Electrolyte and circulatory changes in terminal liver failure. Lancet; 2: 1121-5, 1956)
- **„terminal functional renal failure“** (VESIN et al. Línsufissance rénale circulatoire spontané du cirrhotique. Son évolution. Sem Hôp Paris; 38: 3598-602, 1962)
- **reversebility of the hepatorenal syndrome** (KOPPEL et al. Transplantation of cadaveric kidneys from patients with hepatorenal syndrome. Evidence for the functional nature of renal failure in advanced liver disease. N Engl J Med 1969; 280:1367-71, 1969)

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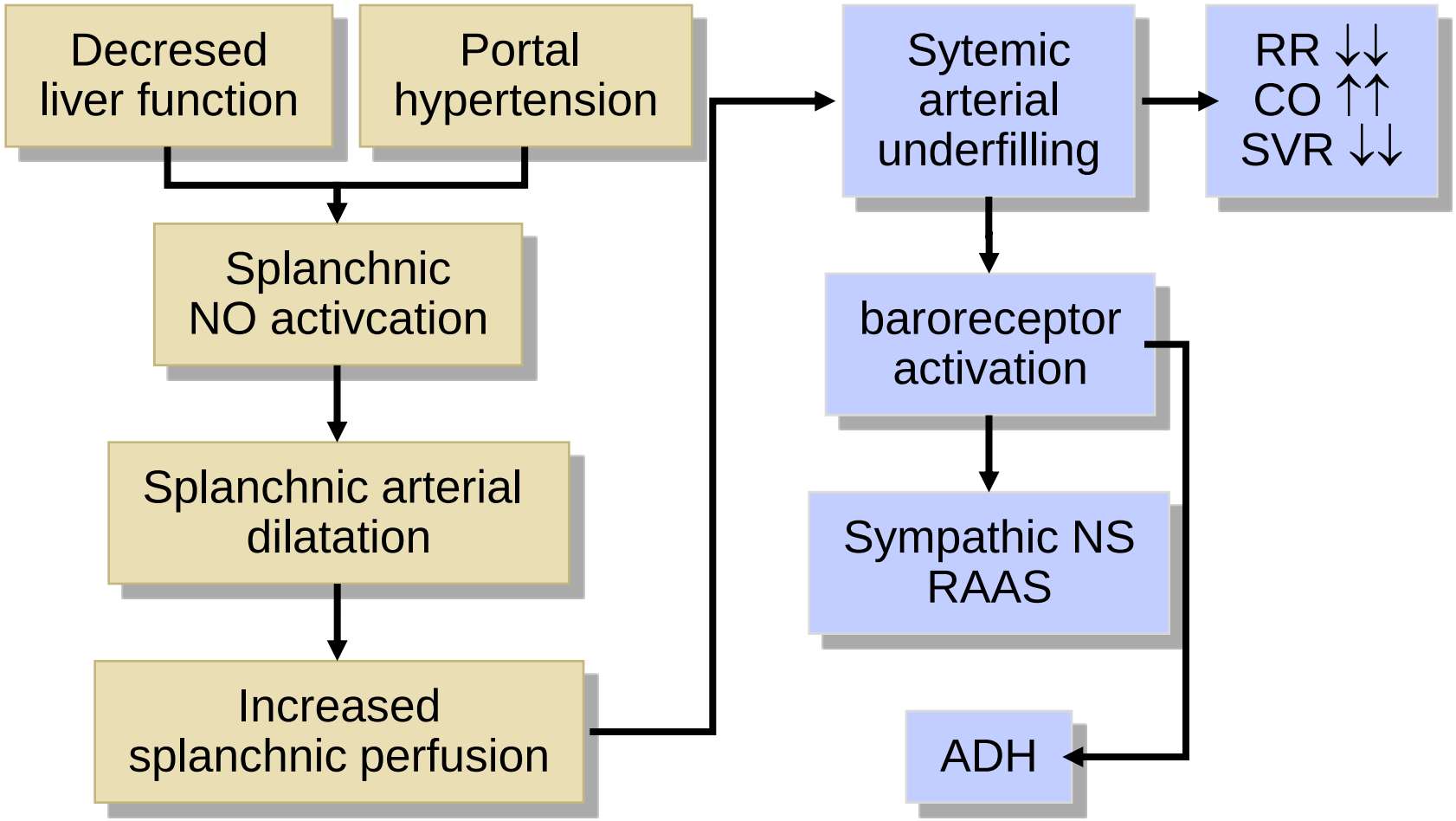
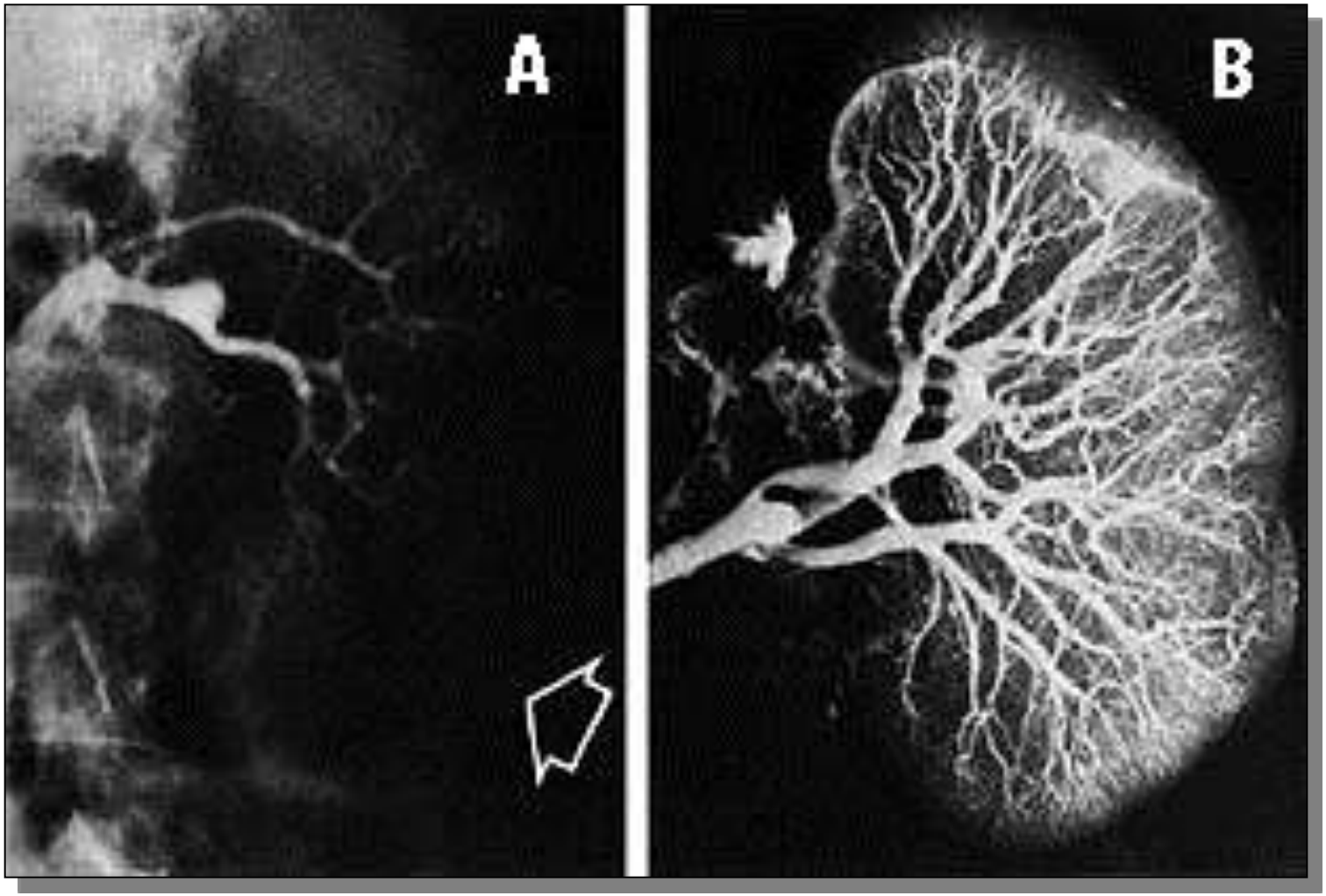
Understanding the pathophysiology of the hepatorenal syndrome „Arterial underfilling“

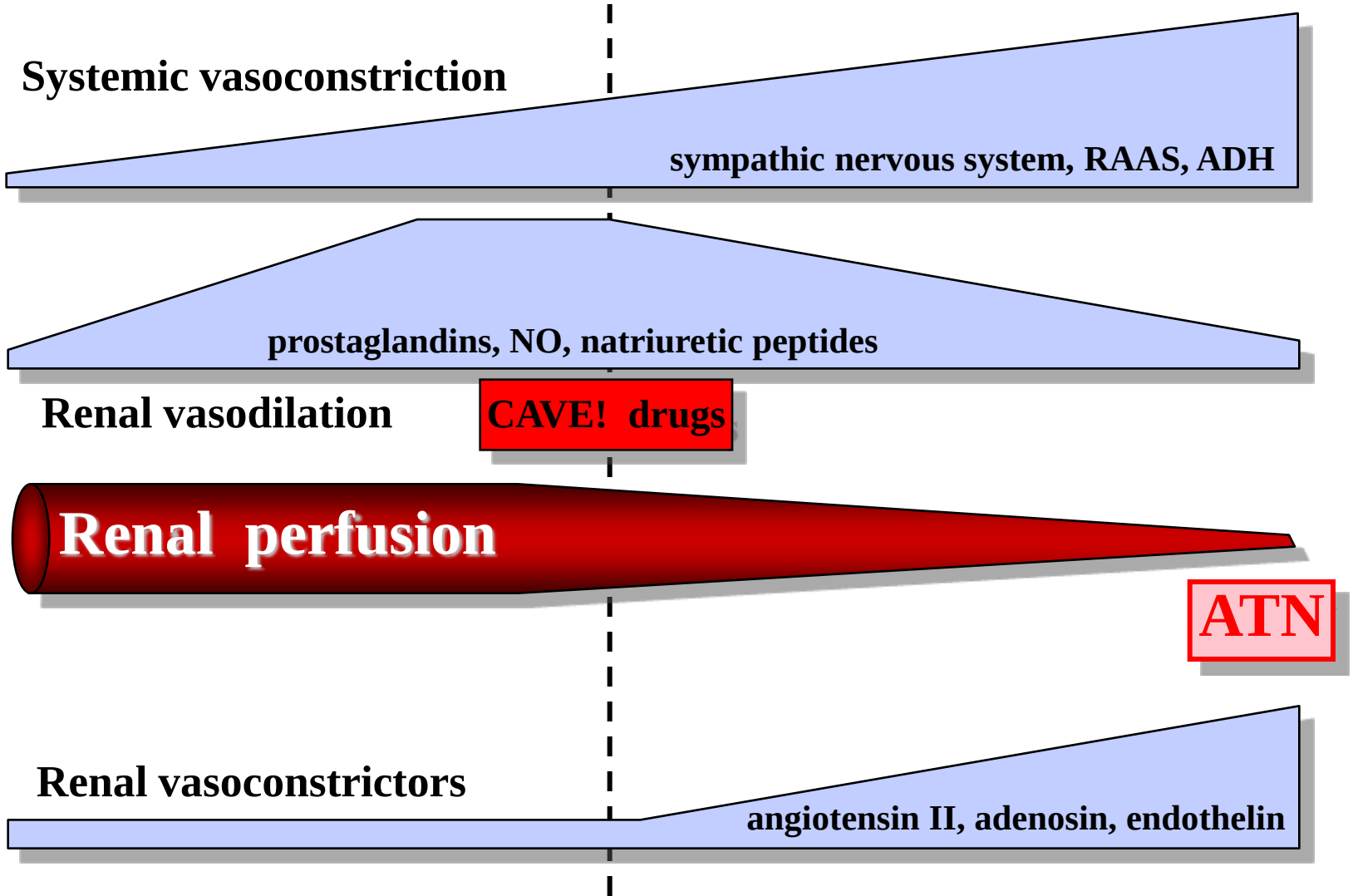


Plasma renin activity and urinary sodium excretion as prognostic indicators in cirrhosis with ascites.

ARROYO et al. *Ann Intern Med* 94(2):198-201. 1981



Renal perfusion in HRS



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Acute Renal Failure in critically ill patients (n=29,260)
A multinational, multicenter study

UCHINO et al. *JAMA* 294:813-818, 2005

Contributing factors (n = 1726)	
Septic shock	820 (47.5)
Major surgery	592 (34.3)
Cardiogenic shock	465 (26.9)
Hypovolemia	442 (25.6)
Drug-induced	328 (19.0)
Hepatorenal syndrome	99 (5.7)
Obstructive uropathy	45 (2.6)
Other	211 (12.2)

Diagnosis, prevention and treatment of hepatorenal syndrome in cirrhosis.

SALERNO et al. *Gut* 56:1310, 2007

1. Presence of cirrhosis and ascites

2. Serum creatinine >1.5 mg/dL (or 133 micromoles/L)

3. No improvement of serum creatinine (decrease equal to or less than 1.5 mg/dL) after at least 48 hours of diuretic withdrawal and volume expansion with albumin (recommended dose: 1 g/kg b.w. per day up to a maximum of 100 grams of albumin/day)

4. Absence of (septic) shock

5. No current or recent treatment with nephrotoxic drugs

6. Absence of parenchymal kidney disease as indicated by proteinuria >500 mg/day, microhematuria (>50 RBCs/high power field, and/or abnormal renal ultrasound scanning

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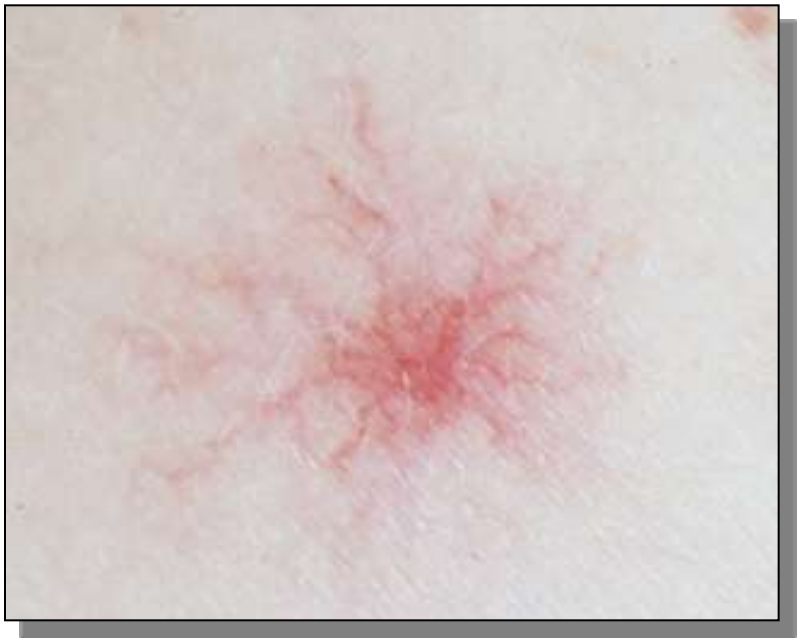
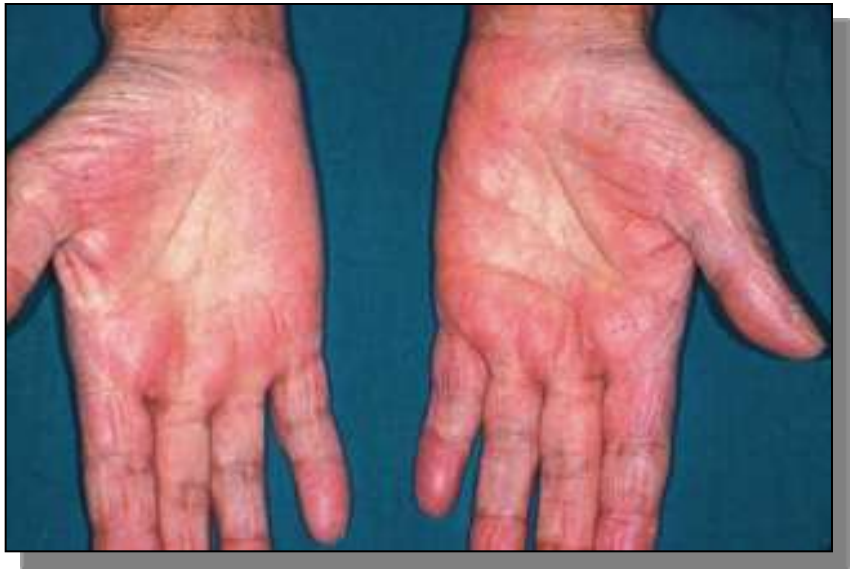
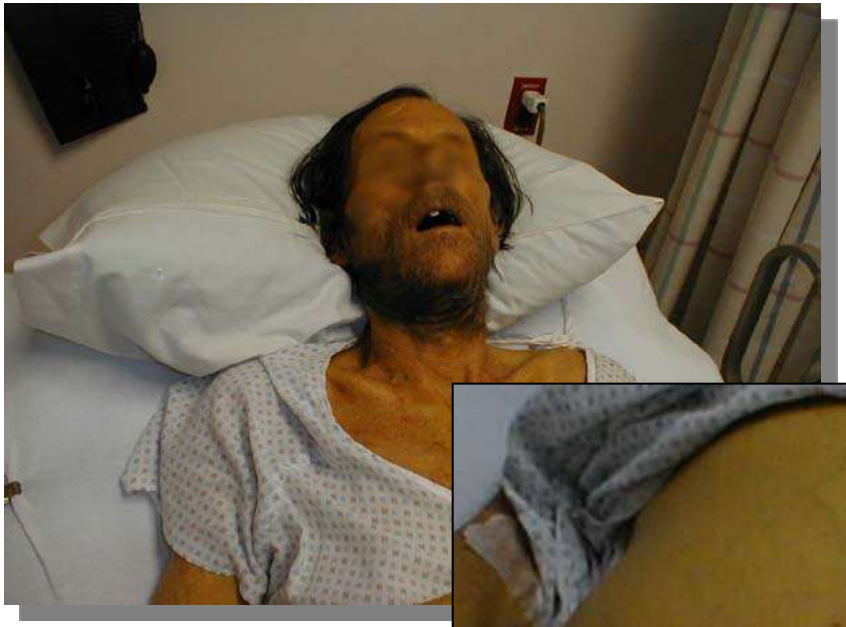
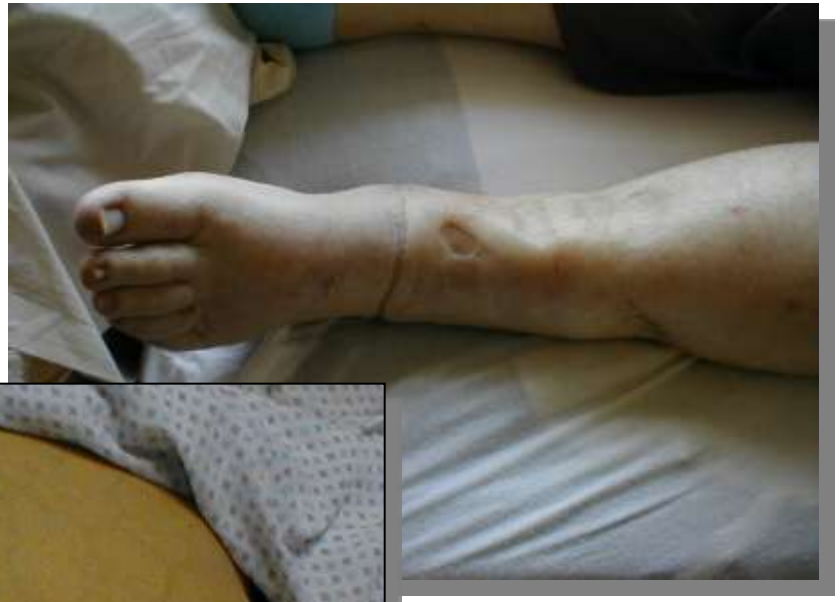
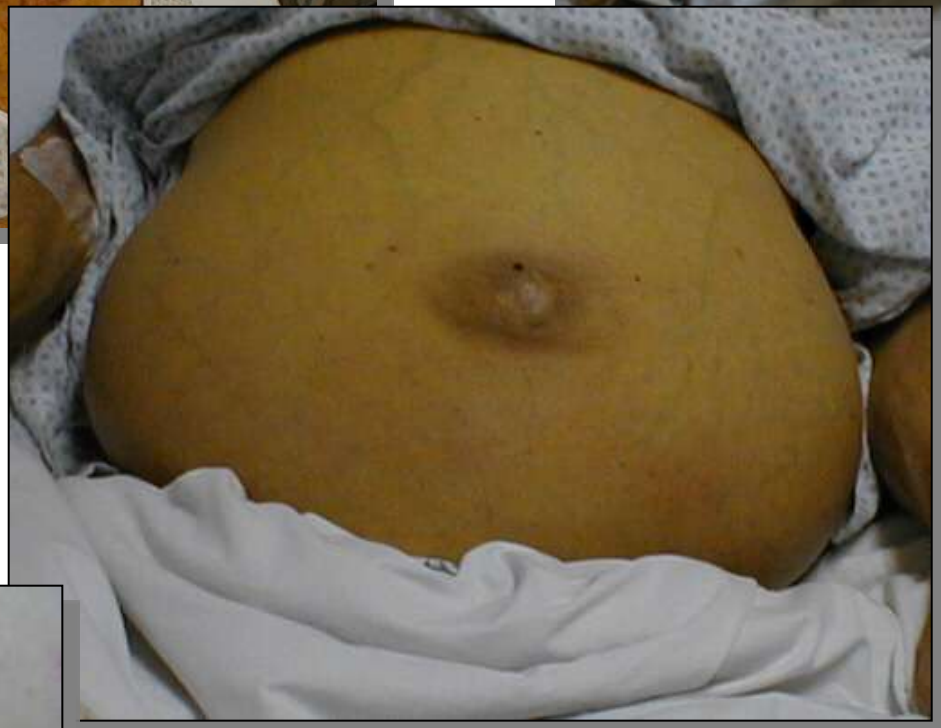
Understanding the pathophysiology of the hepatorenal syndrome

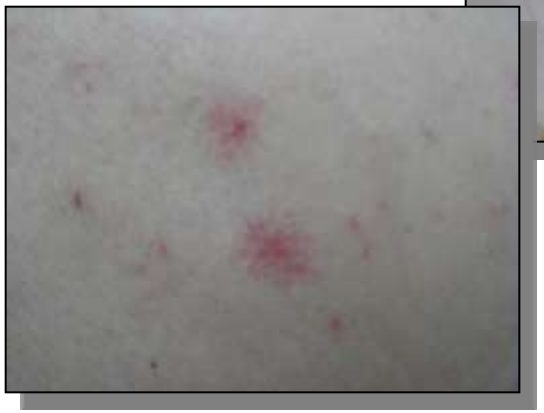


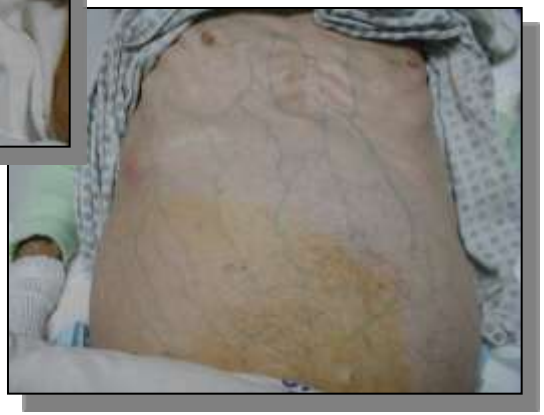






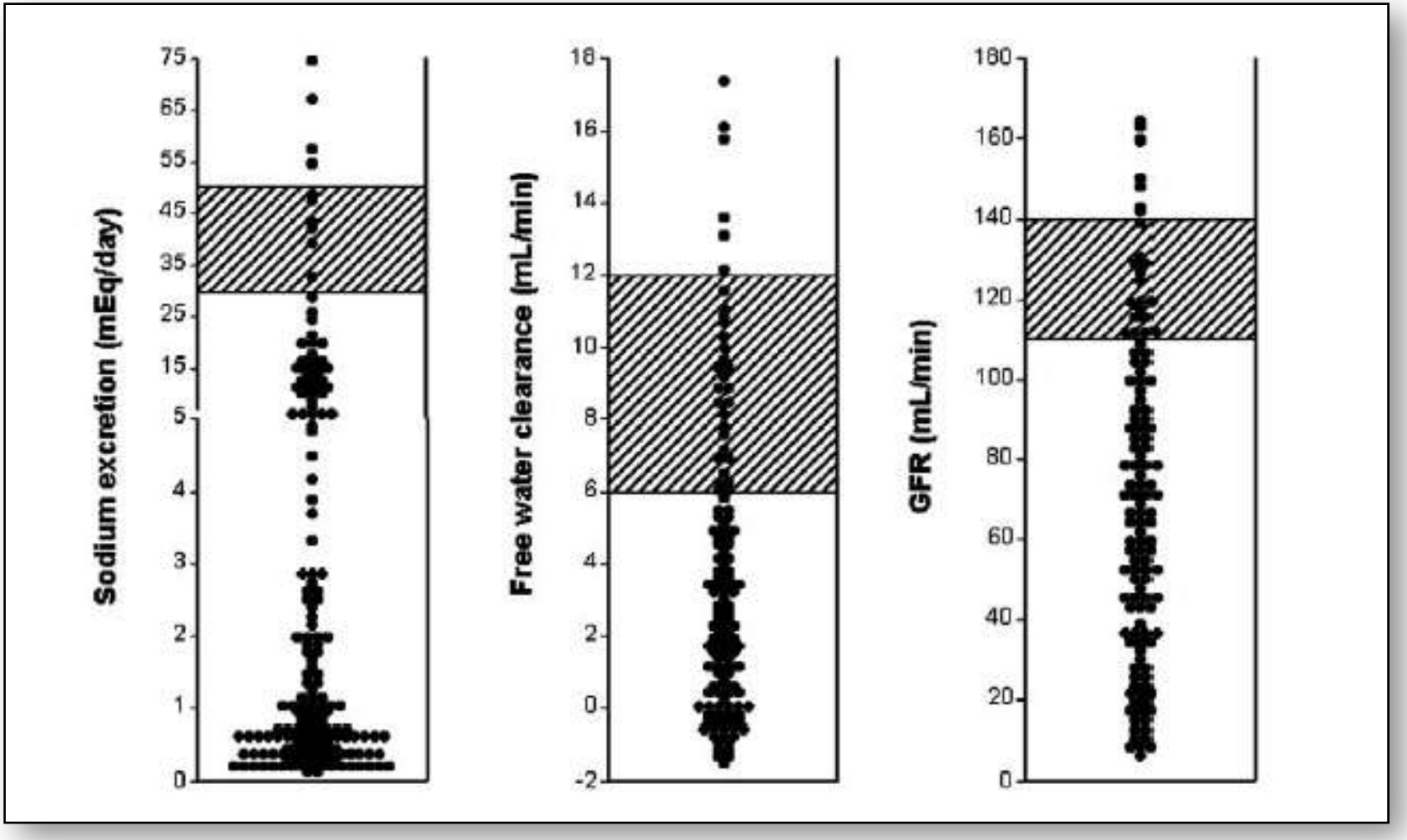






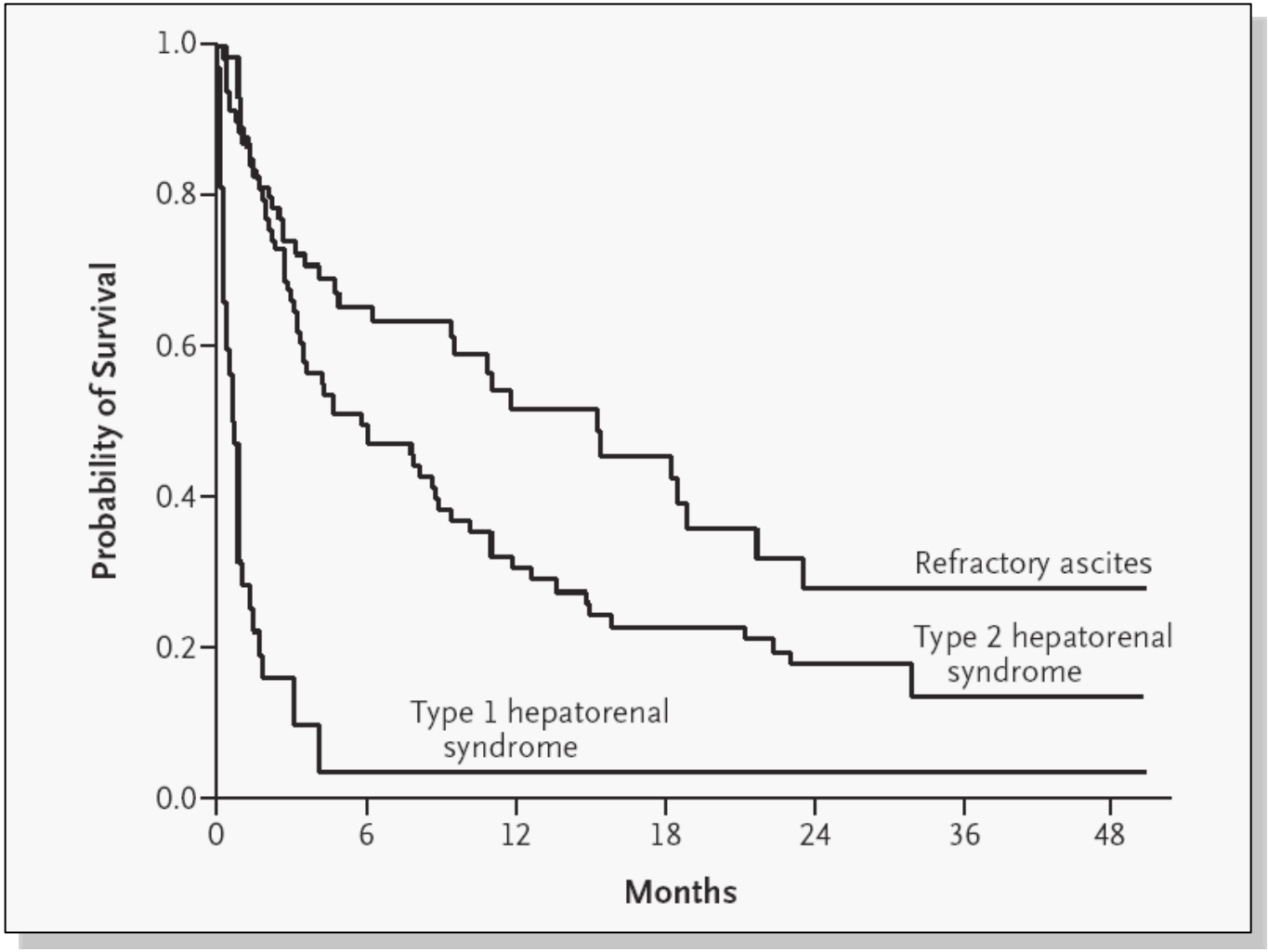
Renal function in patients with ascites

GINES et al. in ZAKIM Hepatology, a textbook of liver diseases. 1996



Management of Cirrhosis and Ascites

GINES et al. *NEJM* 350: 1646-56, 2004



Types of hepatorenal syndrome

- **Type I**
  - **rapidly progressive**
  - **serum creatinine doubles to >2.5mg/dL or creatinine clearance <20mL/min in <2weeks**
  - **prognosis horrible - 80% die in 2 weeks**
  - **frequently precipitating events (SBP)**

Types of hepatorenal syndrome

- **Type II**
  - **slower deterioration**
  - **serum creatinine >1.5mg/dL or cretinine clearance <40mL/min but decline is slow**
  - **most patients will die within several weeks**
  - **most frequent cause of therapy resistant ascites**

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Reversibility of HRS by prolonged administration of ornipressin and plasma volume expansion (n=16)

GUEVARA et al. *Hepatology* 27:35-41, 1998

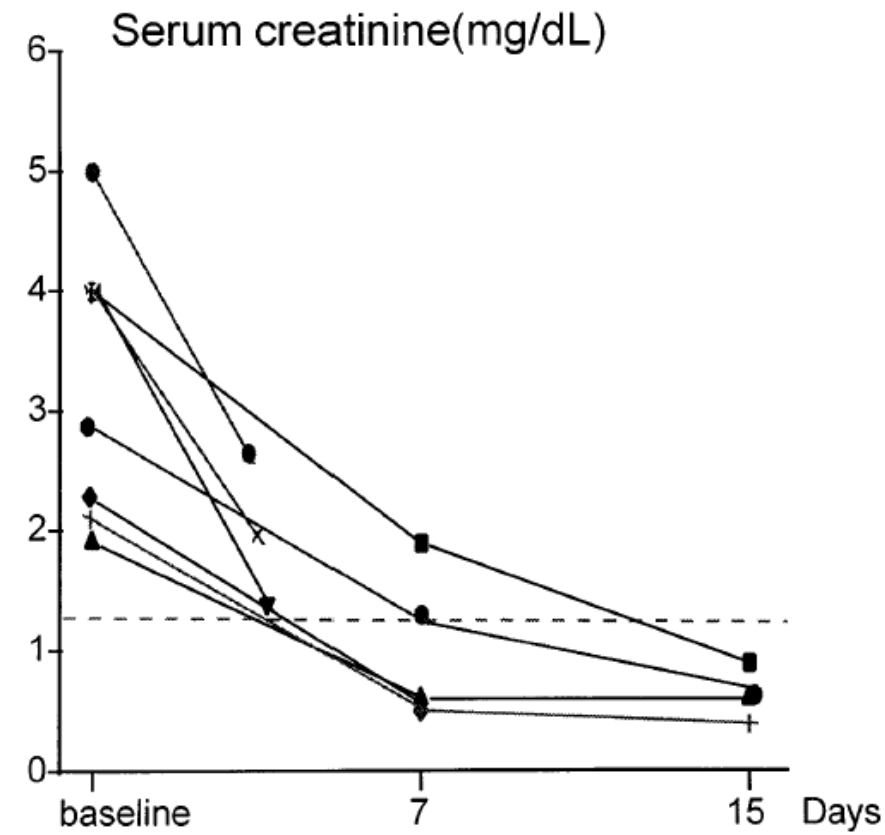


FIG. 2. Individual values of serum creatinine in the eight patients treated with ornipressin and albumin for 15 days included in the second protocol. In four patients, treatment was stopped before the end of therapy (see text for detailed explanation).

Reversibility of HRS by prolonged administration of ornipressin and plasma volume expansion (n=16)

GUEVARA et al. *Hepatology* 27:35-41, 1998

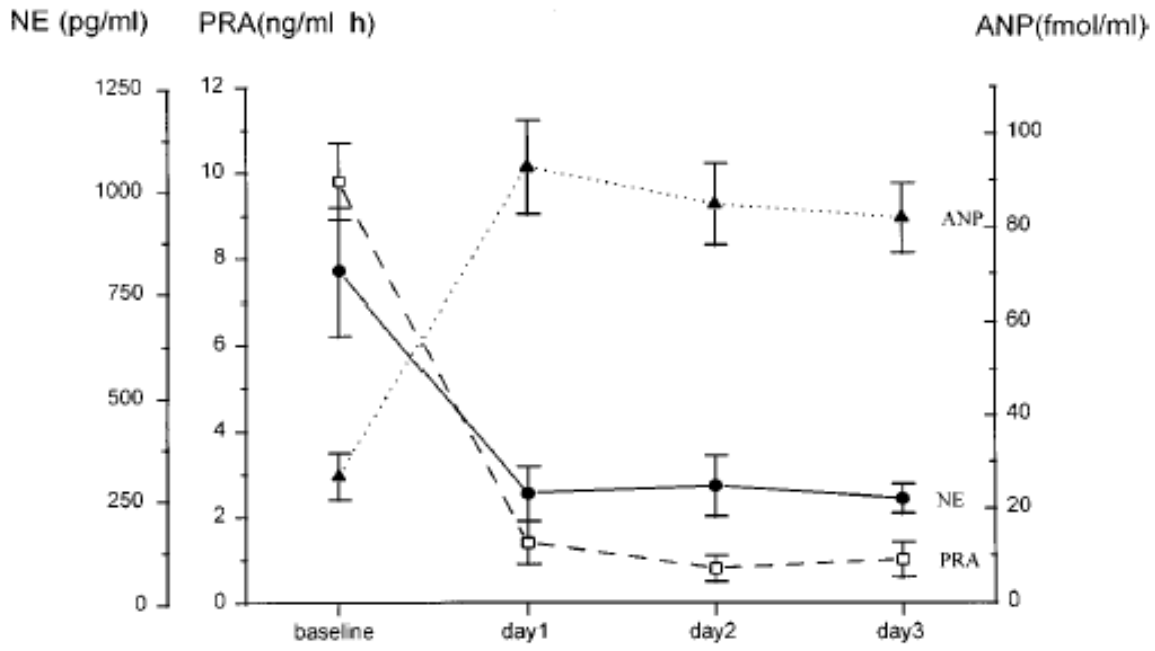
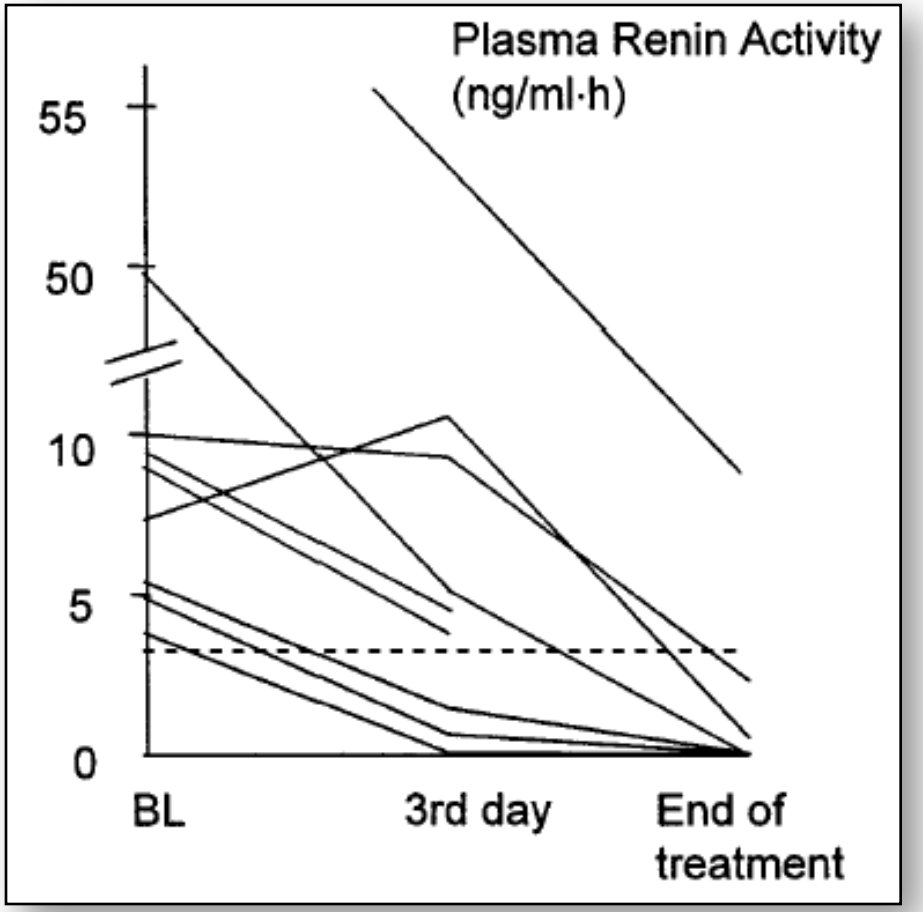
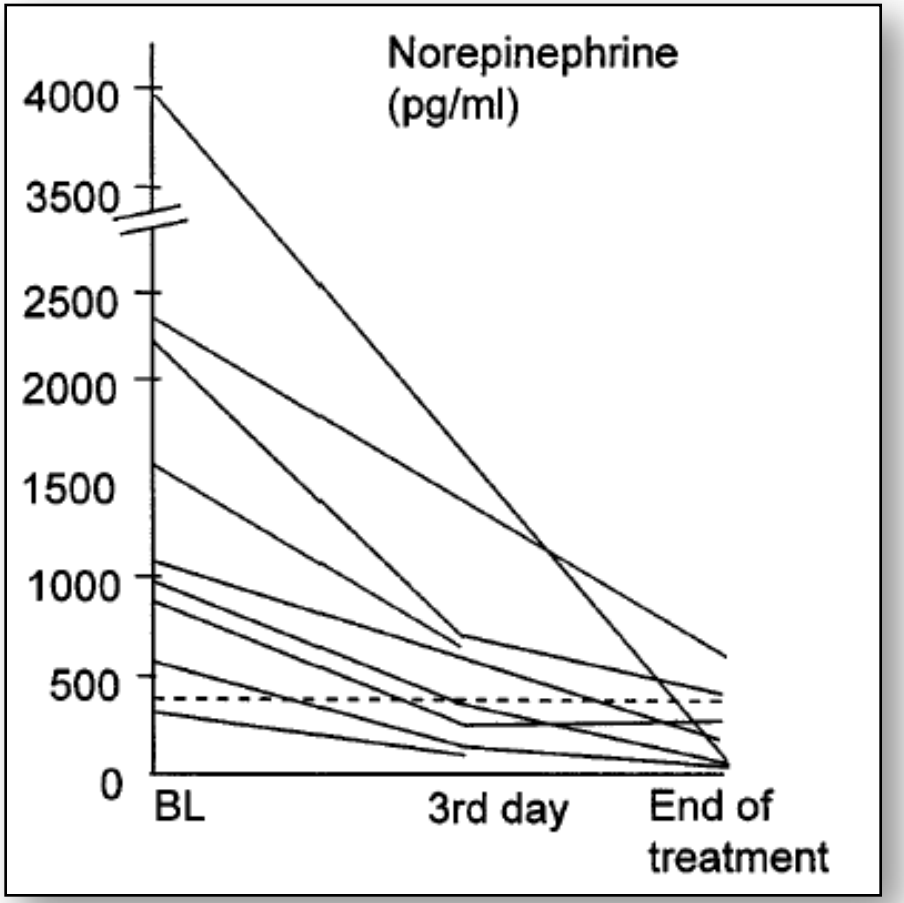


FIG. 1. PRA (– – – –), and plasma concentration of norepinephrine (NE) (———), and ANP (·····), in the eight patients included in the first protocol, in baseline conditions, and during the three days of therapy. Normal values of PRA, NE, and ANP are: 1.2 ± 0.1 ng/mL per hour, 233 ± 17 pg/mL, and 6 ± 0.5 fmol/mL. Values at day 1, day 2, and day 3 are significantly different ($P < .01$) with respect to baseline.

Terlipressin plus albumin infusion: an effective and safe therapy of hepatorenal syndrome (n=9)

URIZ et al. *Journal of Hepatology* 33:43–48, 2000





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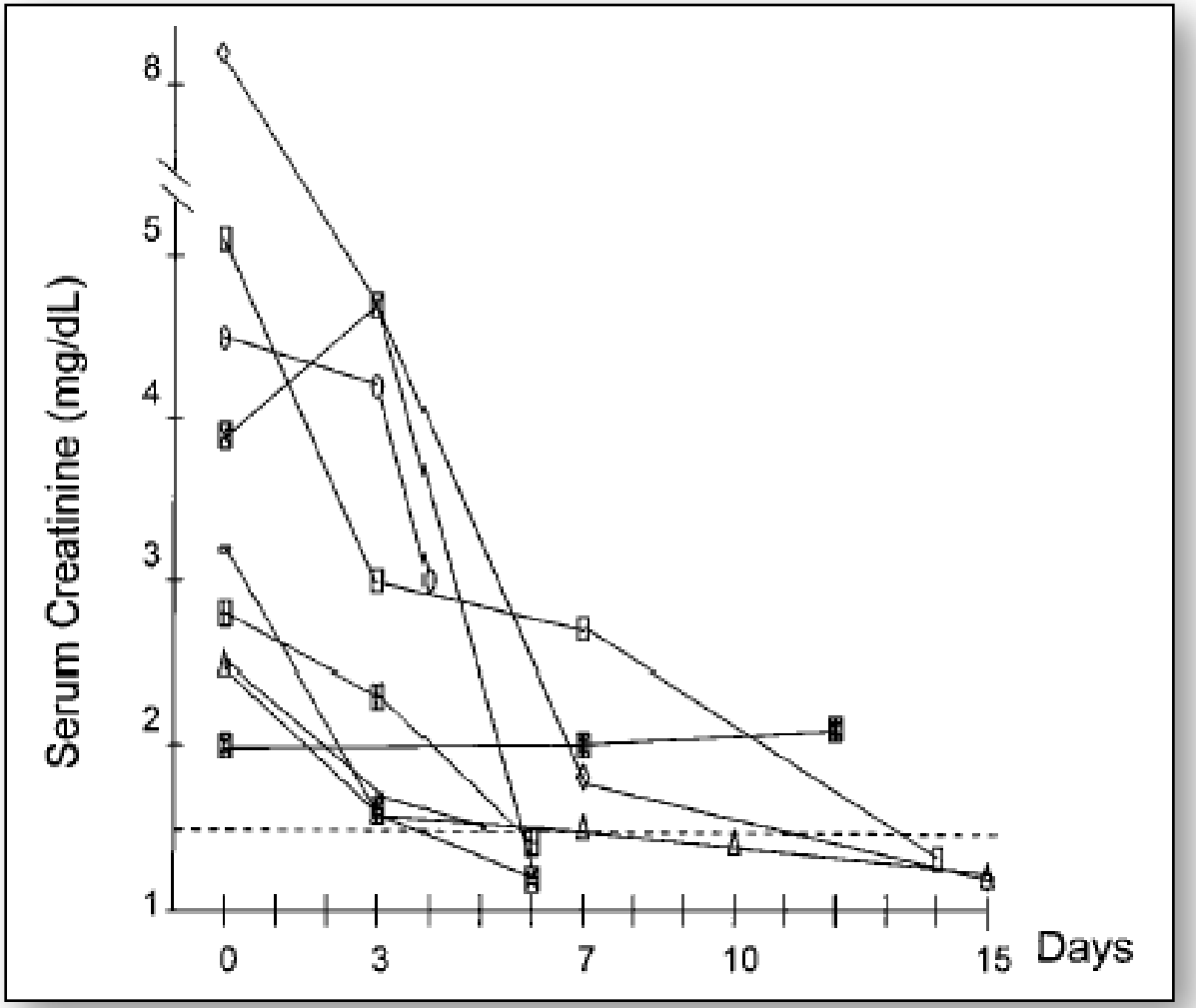
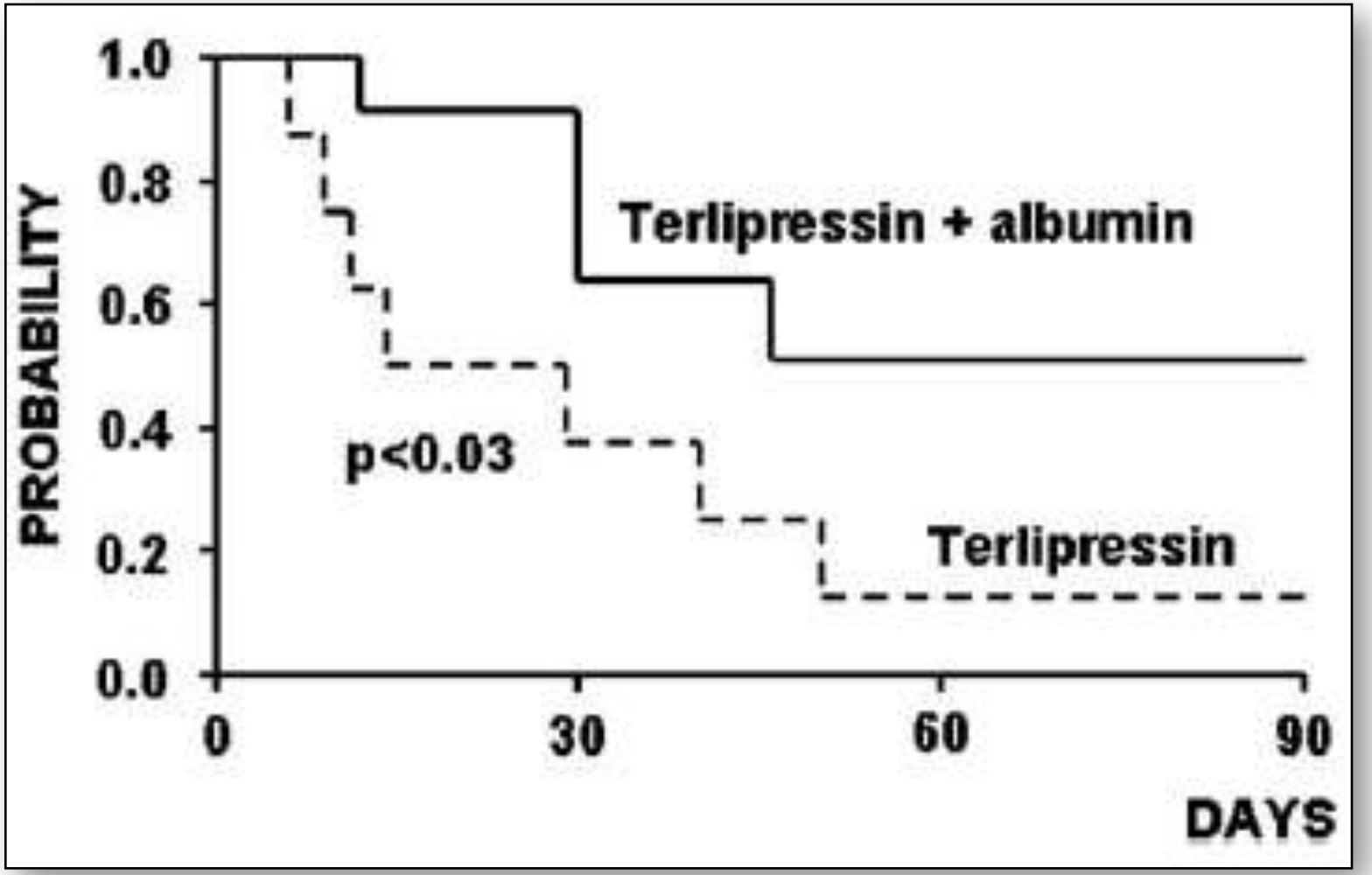


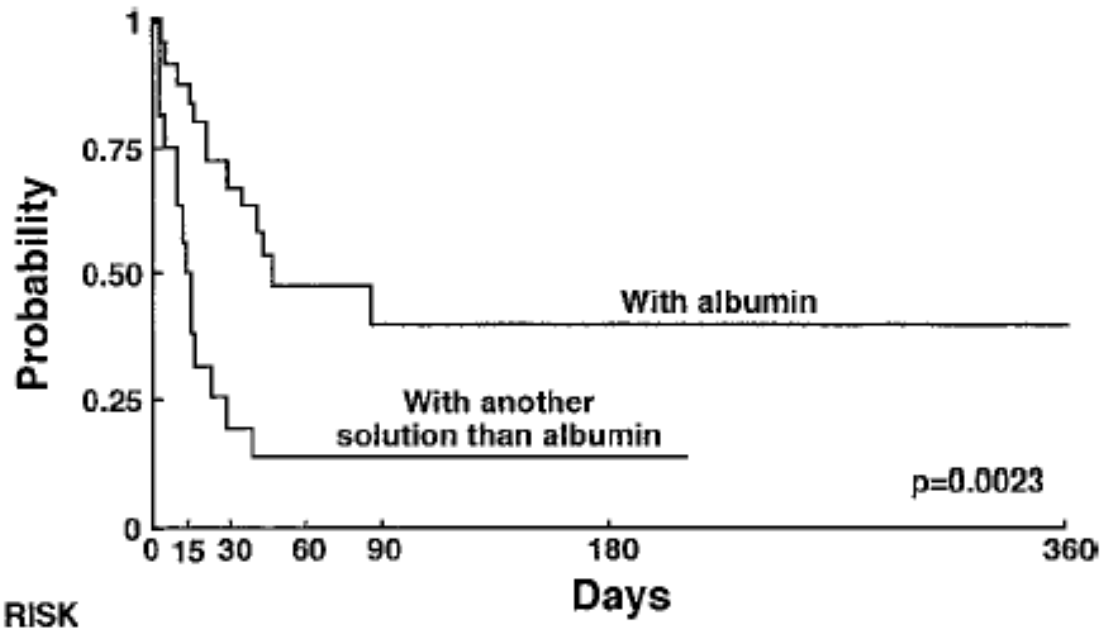
Terlipressin therapy with and without albumin for patients with hepatorenal syndrome: results of a prospective nonrandomized study (n=21)

ORTEGA et al. *Hepatology* 36: 941–948, 2002



Terlipressin in Patients With Cirrhosis and Type 1 Hepatorenal Syndrome: A Retrospective Multicenter Study (n=99)

MOREAU et al. *Hepatology* 122:923–930, 2002



No. AT RISK Paracentesis compensated							
with albumin	25	21	15	8	5	3	1
with another solution than albumin	16	5	3	2	2	1	0

A Randomized Unblinded Pilot Study Comparing Albumin Versus Hydroxyethyl Starch in Spontaneous Bacterial Peritonitis

FERNANDEZ et al. *Gastroenterology* 42:627-634, 2005

	Group 1 (Albumin)			Group 2 (Hydroxyethyl Starch)		
	At Diagnosis	At Resolution	*P*	At Diagnosis	At Resolution	*P*
Systemic hemodynamics						
Mean arterial pressure (mmHg)	76 ± 9	85 ± 13	.01	80 ± 15	81 ± 8	.36
Cardiac index (L/min/m^2)	4.9 ± 0.7	4.6 ± 0.9	.21	4.8 ± 1.0	4.9 ± 1.4	.44
Systemic vascular resistance (dyn·sec/cm^5)	668 ± 134	803 ± 197	.03	777 ± 239	778 ± 290	.96
Systolic volume (mL)	97 ± 20	104 ± 17	.05	83 ± 15	92 ± 23	.12
Heart rate (beats/min)	91 ± 14	80 ± 13	.01	90 ± 10	84 ± 9	.01
Stroke work index (g·m/m^2)	51 ± 17	59 ± 17	.01	48 ± 13	53 ± 13	.24
Right atrial pressure (mmHg)	8 ± 2	9 ± 2	.03	7 ± 3	7 ± 3	1.0
Pulmonary artery pressure (mmHg)	17 ± 4	21 ± 5	.01	18 ± 6	18 ± 7	.88
Pulmonary capillary pressure (mmHg)	11 ± 3	14 ± 4	.03	10 ± 4	11 ± 5	.51

Effects of noradrenalin and albumin in patients with type I HRS: a pilot study (n=12)

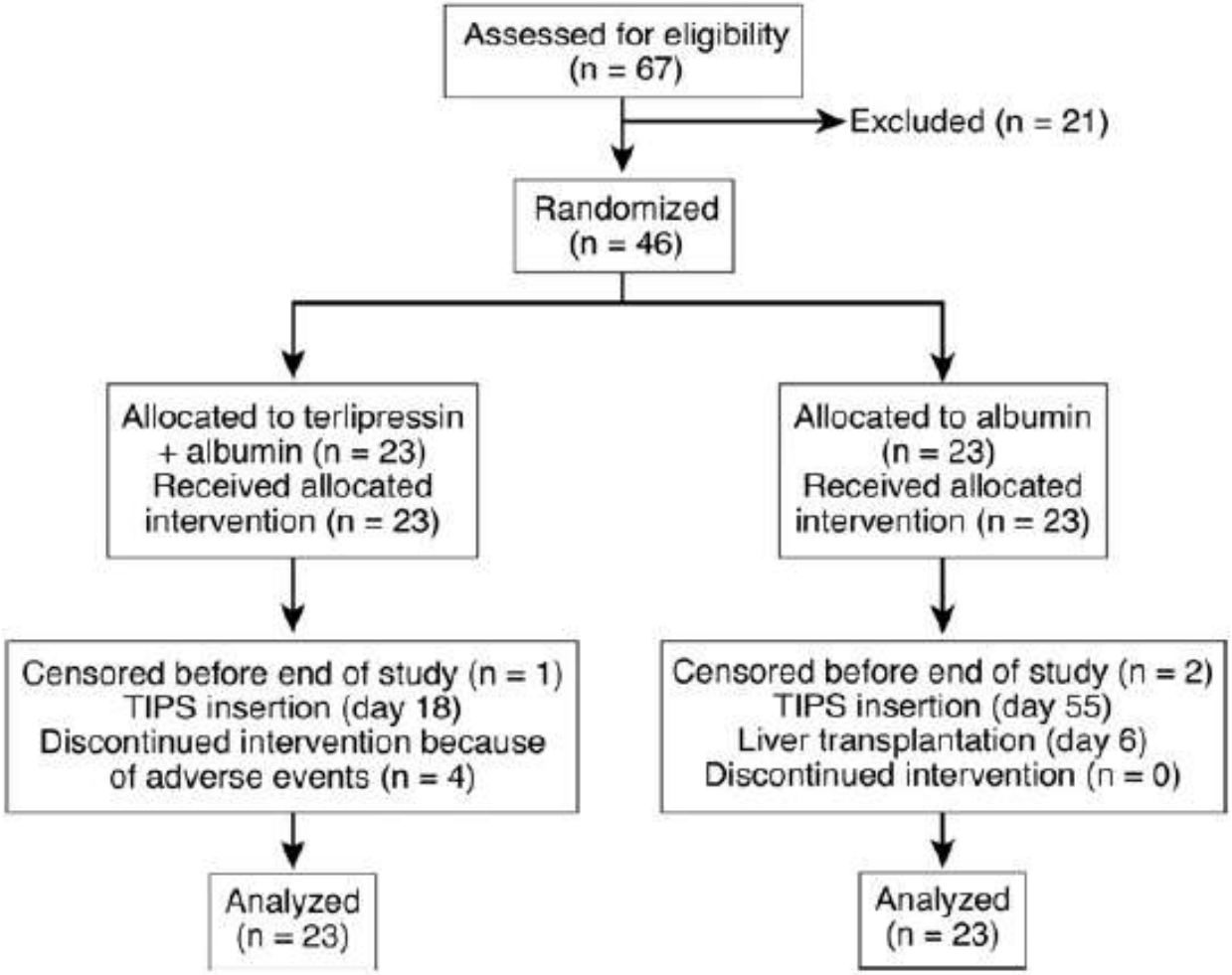
DUVOUX et al. *Hepatology* 36: 374-80, 2002

Table 2. Effects of NA on Renal and Liver Function in the 12 Cirrhotic Patients With Type 1 HRS

	Day −2 n = 12	Day 0 n = 12	Day 1 n = 12	Day 3 n = 12	Day 5 n = 12	Day 10 n = 11*	P†
Serum creatinine							
(μmol/L)	240 ± 99‡	358 ± 161	351 ± 177	254 ± 145‡	188 ± 77‡	145 ± 78‡	<.0001
(mg/dL)	2.6 ± 1.1	3.9 ± 1.8	3.8 ± 1.9	2.8 ± 1.6	2.1 ± 0.8	1.6 ± 0.8	
Creatinine clearance	16.1 ± 14.0	13.2 ± 8.7	22.5 ± 13.5	30.6 ± 17.0	39.6 ± 22.0	40.1 ± 15.2	.003
Urine output (mL/d)	697 ± 555	638 ± 690	2,047 ± 129	2,300 ± 840	2,453 ± 926	1,982 ± 917	.0003
Urinary sodium excretion							
(mEq/24 h)	10 ± 16	8 ± 14	44 ± 70‡	47 ± 57‡	40 ± 35‡	52 ± 72‡	.002
Serum sodium concentration							
(Meq/L)	123.0 ± 6.0	125.3 ± 5.6	126.6 ± 5.0	130.0 ± 6.4	130.7 ± 4.6	131.2 ± 4.1	.01
Prothrombin time (%)	29 ± 15	26 ± 12	26 ± 10	26 ± 11	27 ± 14	27 ± 13	NS
Serum bilirubin (μmol/L)	283 ± 176	287 ± 206	303 ± 219	287 ± 121	312 ± 250	337 ± 279	.06
Alanine transaminase (IU/L)	46 ± 37	38 ± 27	–	–	34 ± 25	30 ± 21‡	.01

Terlipressin and Albumin vs Albumin in Patients With Cirrhosis and HRS: A Randomized Study (n=46)

MARTÍN–LLAHÍ et al. *Gastroenterology* 134:1352–1359, 2008



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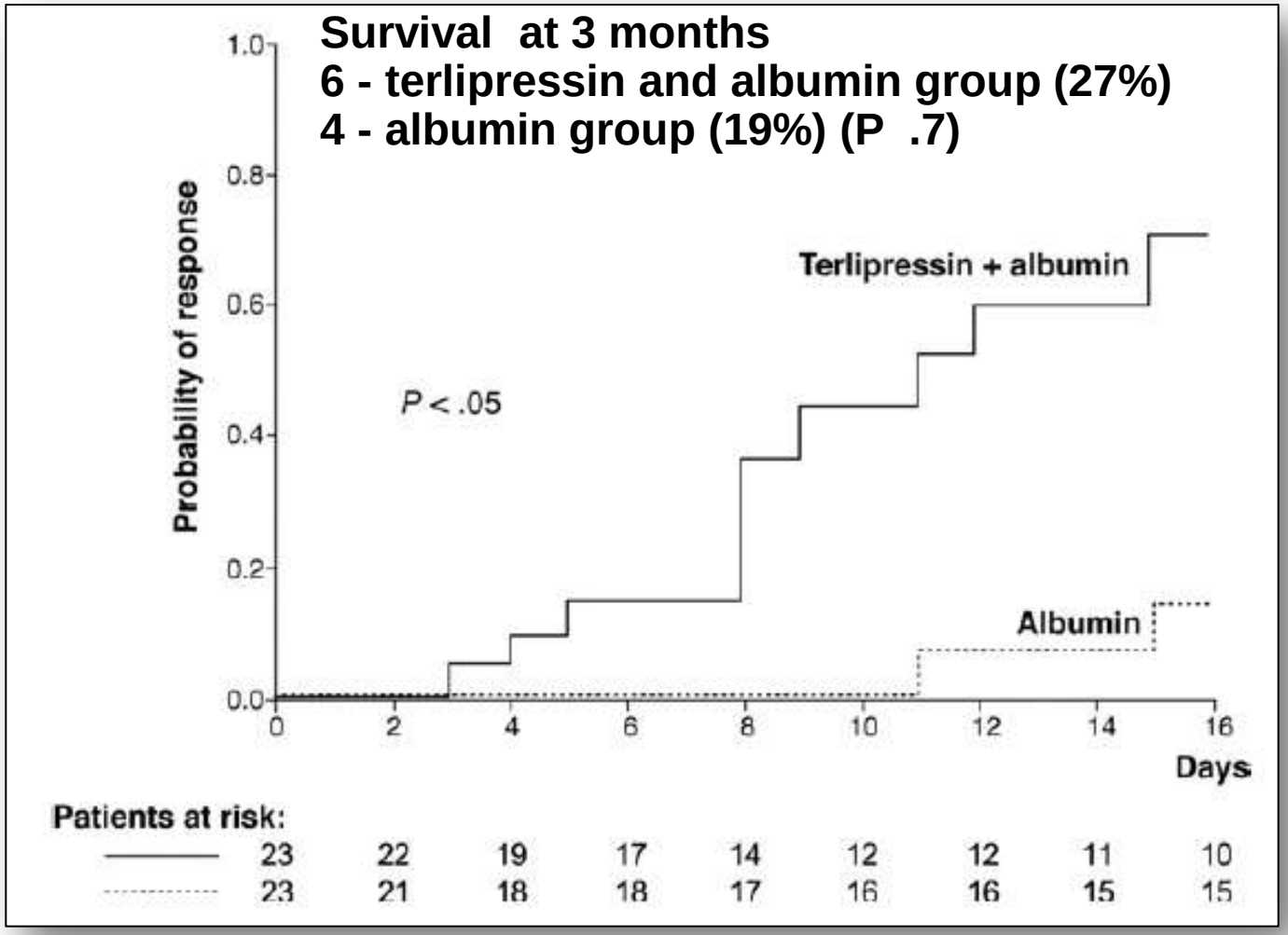

Vaptans: a promising therapy in the management of advanced cirrhosis

GINES *J Hepatol* 46:1150-2, 2007

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GINES *J Hepatol* 46:1150-2, 2007

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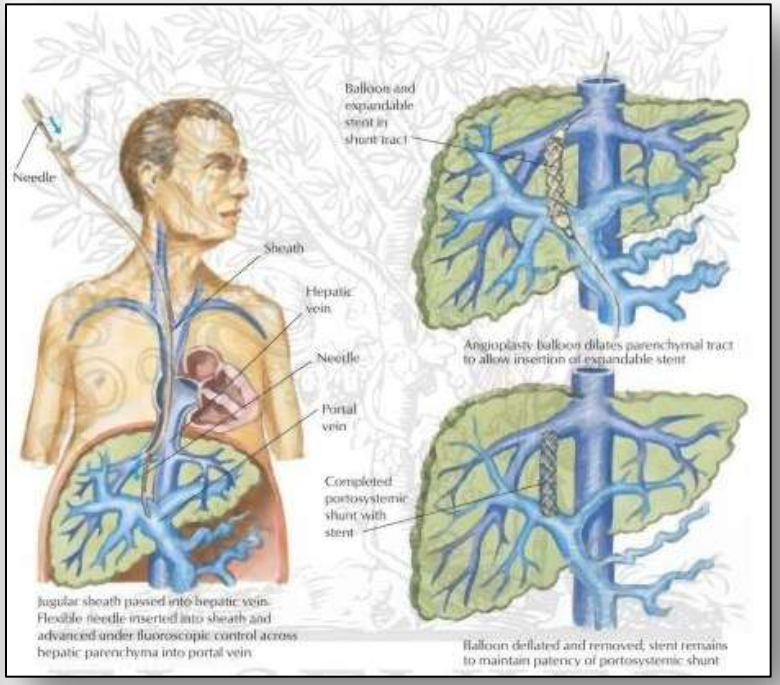
Transjugular intrahepatic portosystemic shunt in hepatorenal syndrome: effects on renal function and vasoactive systems (n=7)

GUEVARA et al. *Hepatology* 28(2):416-22, 1998

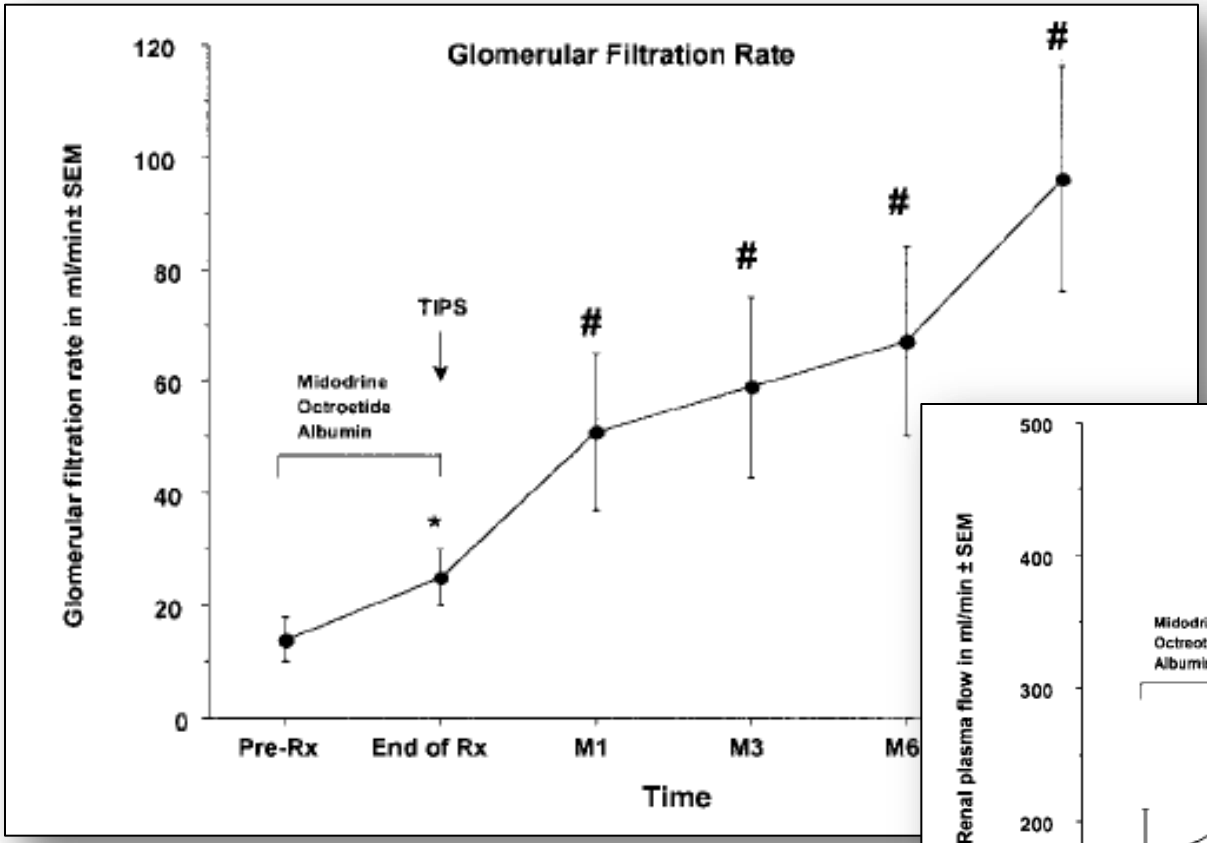
TABLE 3. Effects of TIPS on Renal Function, Mean Arterial Pressure and Vasoactive Systems

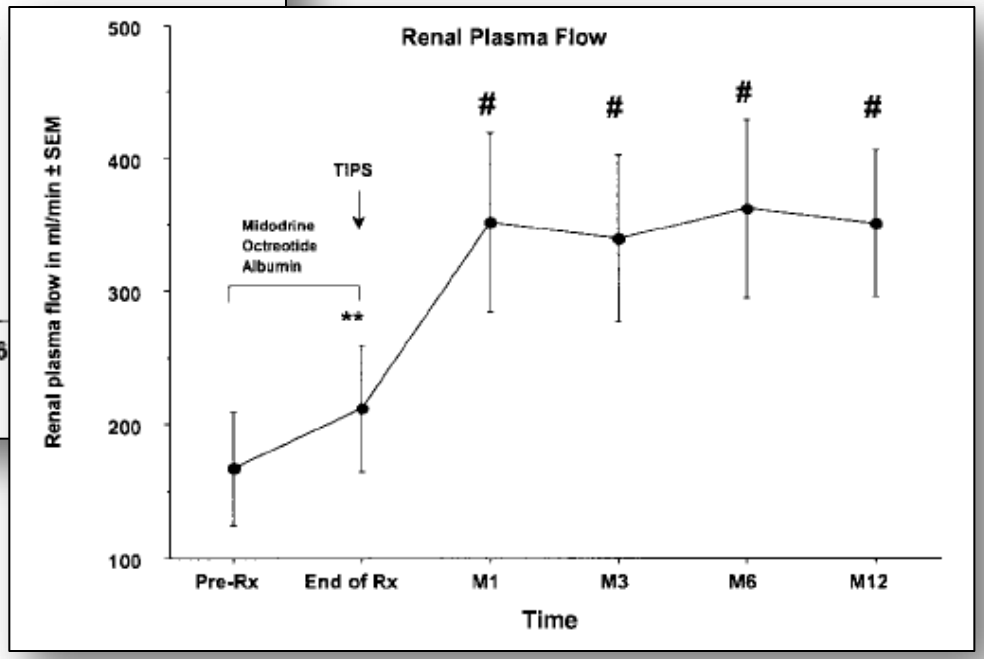
	Baseline	7 Days	30 Days	*P*
Serum creatinine (mg/dL)	5.0 ± 0.8	3.7 ± 1.0	1.8 ± 0.4*‡	.04
BUN (mg/dL)	109 ± 7	120 ± 12	56 ± 11*†‡§	.007
RPF (mL/min)	103 ± 33	138 ± 54	233 ± 40*‡	.07
GFR (mL/min)	9 ± 4	11 ± 5	27 ± 7*‡	.04
Serum sodium (mEq/L)	126 ± 3	129 ± 2	134 ± 2	NS
Free water clearance (mL/min)	−0.1 ± 0.06	0.3 ± 0.2	0.1 ± 0.2	NS
Urine volume (mL/d)	253 ± 43	898 ± 155*‡	1,080 ± 205*‡	.003
Urine sodium (mEq/d)	2.4 ± 0.4	6.7 ± 3.0	9.4 ± 4.2	NS
Mean arterial pressure (mm Hg)	72 ± 4	75 ± 5	73 ± 3	NS
PRA (ng/mL · h)	18 ± 5	6 ± 2	3 ± 1*‡	.015
ALDO (ng/dL)	279 ± 58	214 ± 92	99 ± 56*‡	.09
NE (pg/mL)	1,257 ± 187	853 ± 102	612 ± 197	.047
ET (pg/mL)	28 ± 7	33 ± 9	27 ± 11	NS



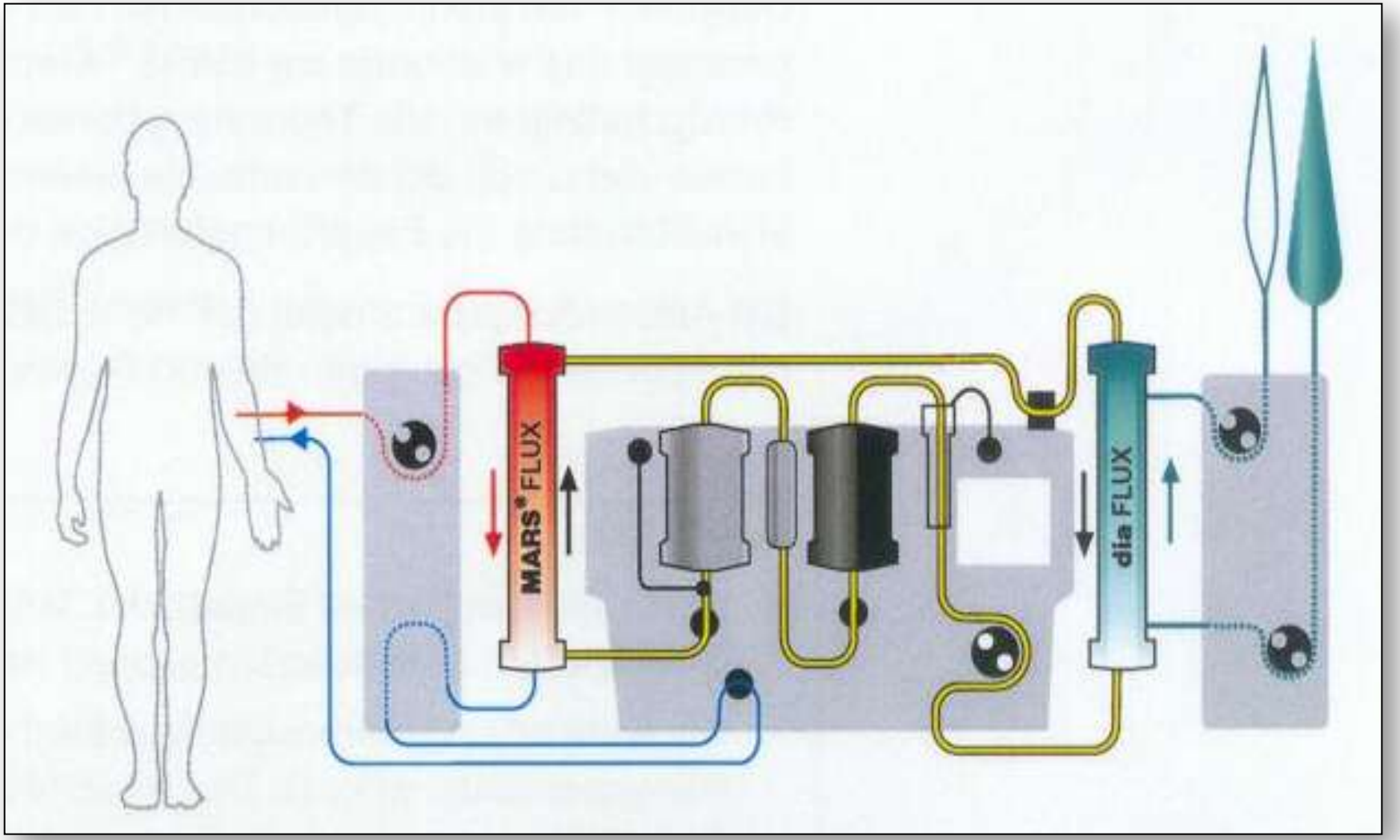
Midodrine, Octreotide, Albumin and TIPS in selected patients with type I HRS (n=14)

WONG et al. *Hepatology* 40: 55-65, 2004



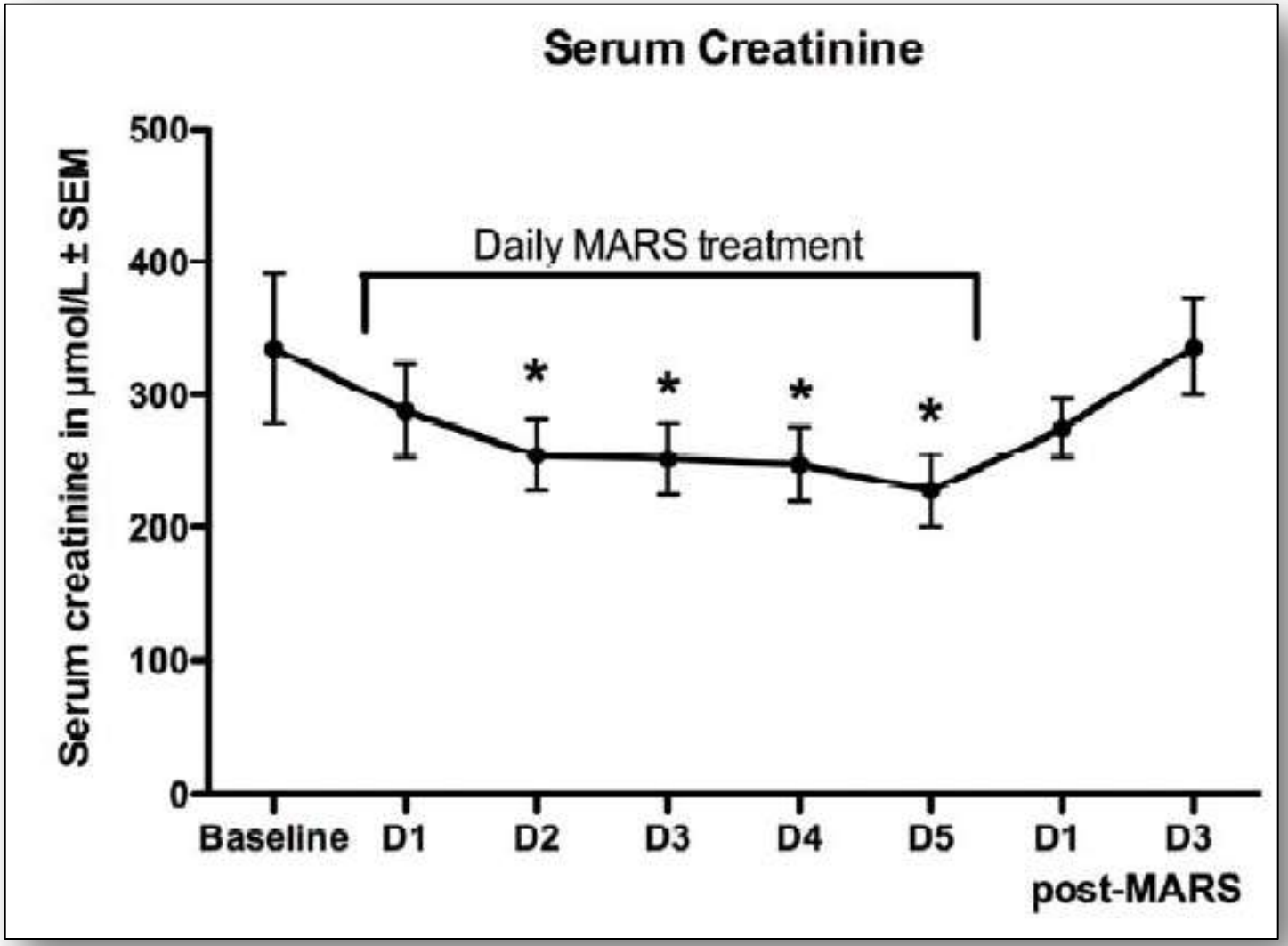


MARS
= Molecular Adsorbents Recycling System



MARS is ineffective in the management of type 1 HRS in cirrhotic patients (n=6) with ascites who have failed vasoconstrictor therapy

WING et al. *Gut* published on August 25, 2009



Artificial and bioartificial support systems for acute and acute-on-chronic liver failure

KJAERGARD et al. *JAMA* 289(2):217-22, 2003

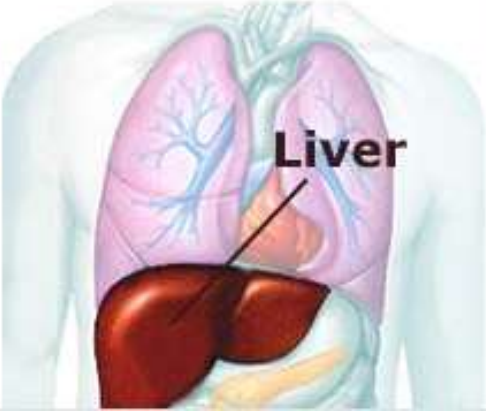
Table 2. Effect of Artificial and Bioartificial Support Systems on Mortality in Acute and Acute-on-Chronic Liver Failure*

Source	No. of Events/ No. of Patients: Intervention	No. of Events/ No. of Patients: Control	Weight, %	Risk Ratio (95% Confidence Interval)
Acute Liver Failure				
Redeker and Yamahori,[22] 1973	14/15	9/13	24.6	1.35 (0.92-1.98)
O'Grady et al,[31] 1988	19/29	20/33	24.9	1.08 (0.74-1.58)
Hughes et al,[32] 1994	4/5	2/5	5.8	2.00 (0.63-6.38)
Ellis et al,[11] 1996	4/12	5/12	7.0	0.80 (0.28-2.27)
Mazariegos et al,[33] 1997	1/5	1/5	1.4	1.00 (0.08-11.93)
Wilkinson et al,[9] 1998	0/1	1/2	1.3	0.50 (0.04-7.10)
He et al,[37] 2000	10/37	15/33	14.2	0.59 (0.31-1.14)
Stevens et al,[12] 2001	20/73	30/74	20.9	0.68 (0.42-1.08)
Total	**72/177**	**83/177**	**100**	0.95 (0.71-1.29)
Acute-on-Chronic Liver Failure				
Kramer et al,[34] 1998	4/10	4/10	7.0	1.00 (0.34-2.93)
Wilkinson et al,[9] 1998	3/5	3/3	15.7	0.60 (0.39-1.23)
Ellis et al,[35] 1999	5/5	5/5	0	NA
Mitzner et al,[36] 2001	6/8	5/5	50.4	0.75 (0.50-1.12)
He et al,[37] 2000	10/27	17/27	24.8	0.59 (0.33-1.04)
Heemann et al,[38] 2002	1/12	6/12	2.1	0.17 (0.02-1.18)
Total	**29/67**	**40/62**	**100**	0.67 (0.51-0.90)

MARS and Prometheus Artificial Liver Devices Offer Some Benefits for Patients with Liver Failure, but Did Not Improve Survival

SUMMARY: An out-of-body liver dialysis device known as the Molecular Adsorbents Recirculating System (MARS) -- which takes over some lost filtering function in people with liver failure -- reduced levels of toxic substances in the blood and improved symptoms of hepatic encephalopathy in patients with acute-on-chronic liver failure, though it did not significantly extend survival, according to a late-breaker presentation at the 45th Annual Meeting of the European Association for the Study of the Liver (EASL 2010) this month in Vienna. Another study found that the Prometheus extracorporeal liver support system also did not improve survival overall, though it did help specific groups of patients.

By Liz Highleyman



One of the key functions of the liver is to filter out toxic substances, including ammonia produced by bacteria in the gut. When the liver is heavily damaged -- due to chronic hepatitis B or C, long-term heavy alcohol use, or other causes -- toxins can build up in the body leading to hepatic encephalopathy (brain impairment), coma, and death.

Liver transplantation is the definitive treatment for liver failure, but donor organs are in short supply, and in some cases the existing liver can recover. Researchers have therefore explored various methods for taking over the

MARS in patients with acute on chronic liver failure (AOCLF) – the RELIEF trial

BANARES et al.

Methods:

-189 patients with AOCLF (bili> 5mg/dl & HE grade II-IV; HRS or bili > 20

-randomized to MARS (n=95) or to standard therapy (ST) (n=94).

-MARS was scheduled at low doses (up to ten 6-8 hours sessions during 21 d)

- main endpoint was 28-day survival

Results:

-greater decrease from baseline in serum creatinine and bilirubin in MARS

-age and MELD were independent predictors of mortality.

-SBP was also associated to higher mortality (15.9% vs. 8.6%; p=0.1).

-a significant beneficial effect of MARS on survival was not observed

Conclusions: MARS at low dosage is a safe procedure, has significant dialysis effect and improves severe HE in AoCLF. A significant beneficial effect on survival could not be demonstrated

PROMETHEUS in patients with acute on chronic liver failure (AOCLF) – the HELIOS study

RIFAI et al.

Methods:

-145 patients with AOC recruited in 10 centers from 7 European countries randomized to standard medical therapy (n=68) or PROMETHEUS (n=77)

-FPSA therapy was intended for 8-11 treatments (minimum duration 4 hours each) during the first 3 weeks of study. Primary endpoints were survival at days 28 and 90 irrespective of liver transplantation.

Conclusions:

Prometheus was not associated with an improved survival in all patients with AOC compared to standard medical therapy alone.

Treatment of hepatorenal syndrome

GINES Lancet 362: 1819-27, 2003

Panel 1: **Recommendations for the management of type 1 HRS**

Consider the patient for liver transplantation.
Set up high priority for transplantation in suitable patients.
Start vasoconstrictors plus intravenous albumin.
Consider TIPS in patients without severe liver failure in whom vasoconstrictors have failed.
Consider renal replacement therapy if there is pulmonary oedema, severe hypokalaemia, or metabolic acidosis not responding to medical therapy.
If high priority for cadaveric liver transplantation is not possible, consider liver transplantation from a living relative in patients with moderate liver failure in whom renal function has improved after therapy.

Treatment of hepatorenal syndrome

GINES Lancet 362: 1819-27, 2003

Panel 2: **Recommendations for management of type 2 HRS**

Consider the patient for liver transplantation.
Use diuretics for management of ascites only if they cause significant natriuresis (>30 mmoles per day). Restrict dietary sodium intake to 40–80 mmoles per day.
Use repeated paracentesis plus intravenous albumin to treat recurrent large/tense ascites.
Restrict fluid intake if hyponatraemia is present.
Consider vasoconstrictors or TIPS before liver transplantation.

Treatment of hepatorenal syndrome

GINES et al. NEJM 350: 1646-56, 2006

Table 4. Recommendations for Treatment with Vasoconstrictors in Patients with the Hepatorenal Syndrome.

Recommendation	Reference
Administration of one of the following drugs or drug combinations	
Norepinephrine (0.5–3.0 mg/hr intravenously)	Duvoux et al.[48]
Midodrine (7.5 mg orally three times daily, increased to 12.5 mg three times daily if needed) in combination with octreotide (100 μg subcutaneously three times daily, increased to 200 μg three times daily if needed)	Angeli et al.[49]
Terlipressin (0.5–2.0 mg intravenously every 4–12 hr)*	Uriz et al.,[50] Moreau et al.,[51] Mulkay et al.,[52] Ortega et al.[53]
Concomitant administration of albumin (1 g/kg intravenously on day 1, followed by 20–40 g daily)	Duvoux et al.,[48] Angeli et al.,[49] Uriz et al.,[50] Ortega et al.[53]
Duration of therapy: 5–15 days	
End point: reduction of serum creatinine concentration to <1.5 mg/dl†	

Albumin

100 ml 20 %

43,10 €

Glycilpressin

5 mg

411,70 €

Gutron

100 Tbl a 2,5 mg

50,05

Hepatorenal Syndrome

1) History of HRS
2) Pathophysiology of HRS
3) Definition of HRS
4) Clinical presentation of HRS
5) Treatment of HRS
   -conservative (albumine, vasopressin analogues)
   -artificial and bioartificial liver support systems
6) Prevention of HRS

Therapeutic suggestions

Phase 1: Sodium restriction 2 -5g/d

Phase 2: Spironolactone and Furosemide

Phase 3: refractory ascitis, paracentesis (and albumin)

Phase 4: (HRS Type 2) paracentesis of TIPS, LTx

Phase 5: (HRS Type 1) vasoconstroctor plus albumin, LTx

Effect of intravenous albumin on renal impairment and mortality in patients with cirrhosis and peritonitis.

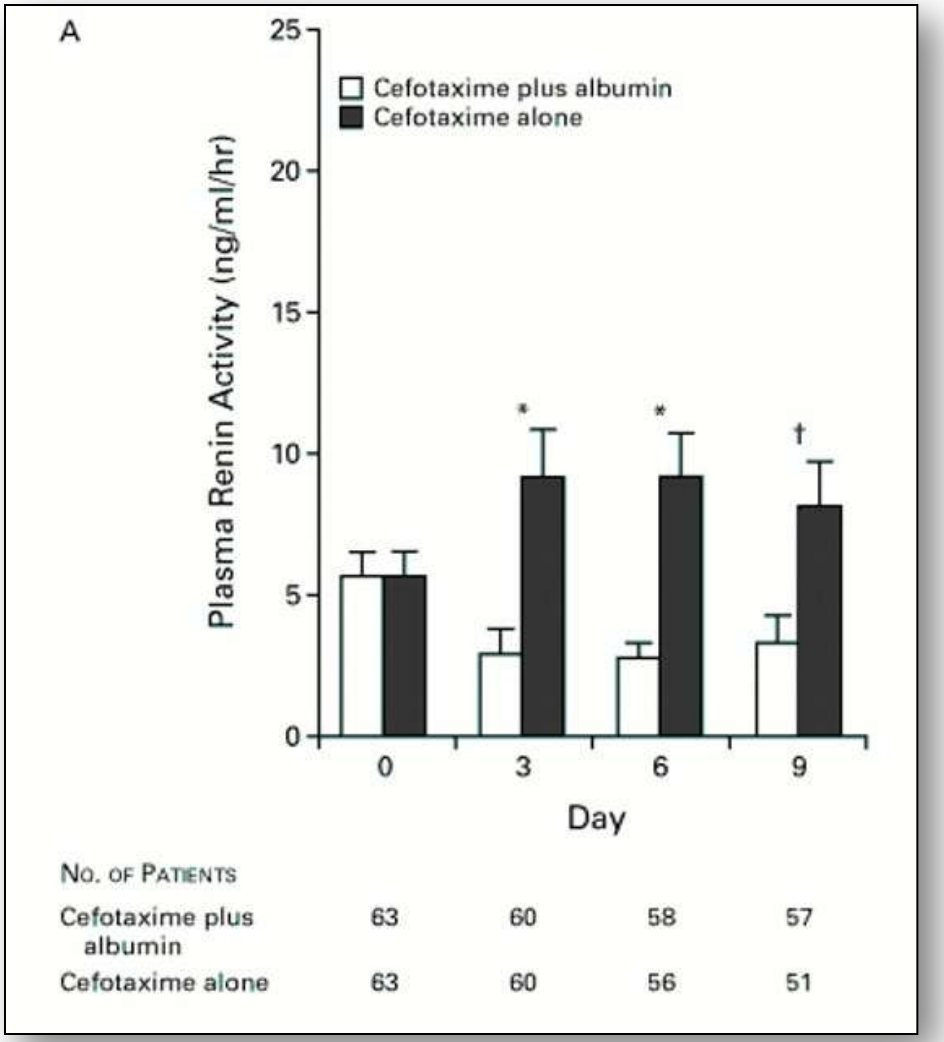
SORT et al. NEJM 341:403-409, 1999

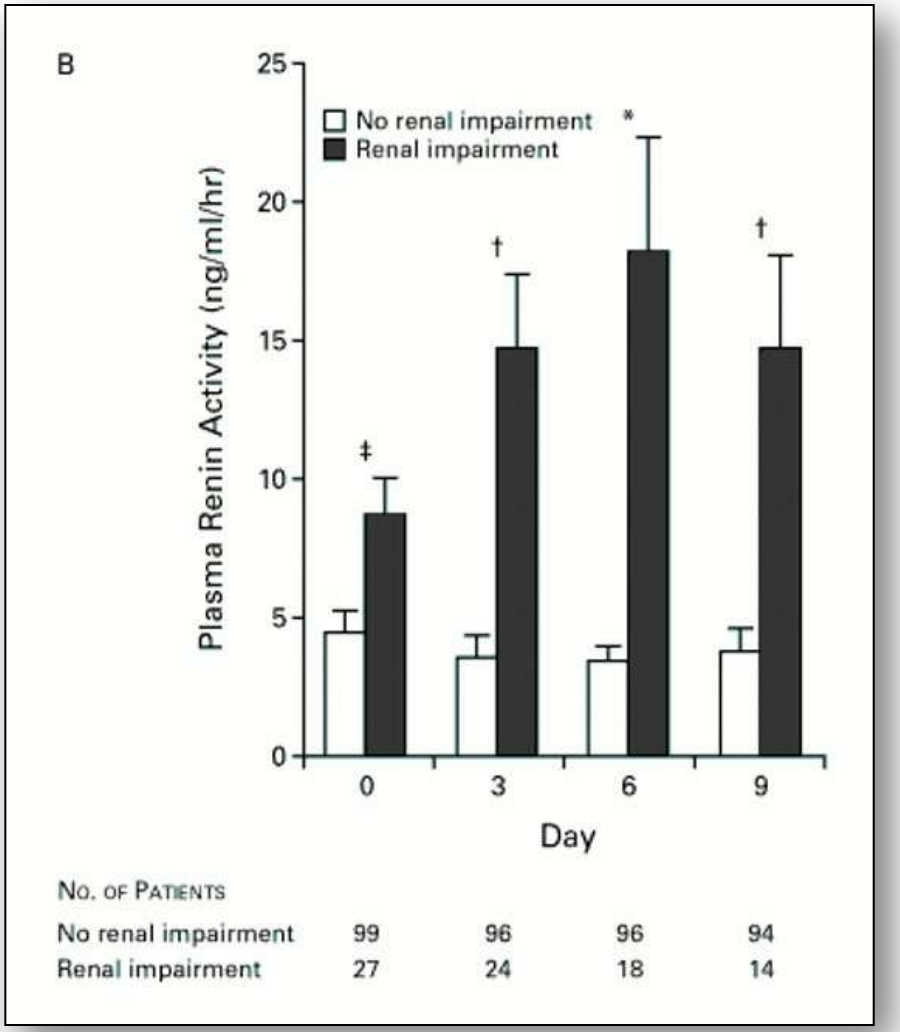
TABLE 2. CLINICAL OUTCOME ACCORDING TO THE ASSIGNED TREATMENT.*

OUTCOME VARIABLE	CEFOTAXIME (N=63)	CEFOTAXIME PLUS ALBUMIN (N=63)	P VALUE
Resolution of infection — no. (%)†	59 (94)	62 (98)	0.36
Duration of antibiotic therapy — days	6±1	5±1	0.48
Paracentesis for ascites after resolution of infection — no. (%)‡	16 (25)	14 (22)	0.83
Hospital stay — days	13±1	14±1	0.48
Renal impairment — no. (%)	21 (33)	6 (10)	0.002
Death — no. (%)			
In hospital§	18 (29)	6 (10)	0.01
At three months¶	26 (41)	14 (22)	0.03

Effect of intravenous albumin on renal impairment and mortality in patients with cirrhosis and peritonitis.

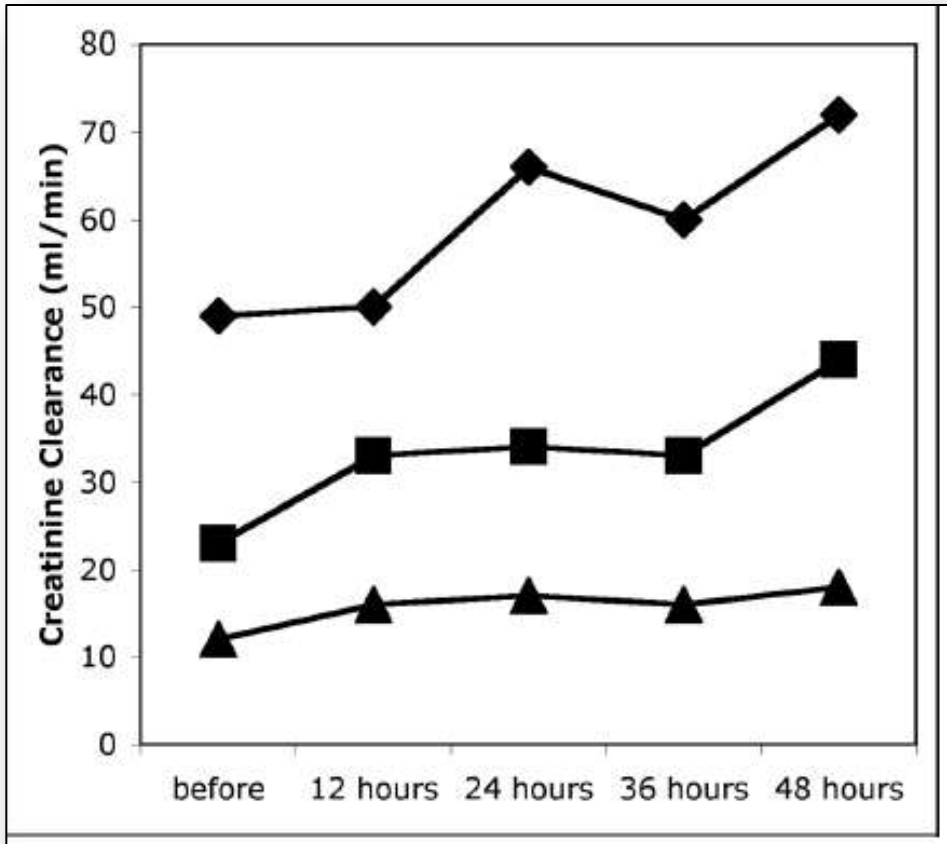
SORT et al. *NEJM* 341:403-409, 1999



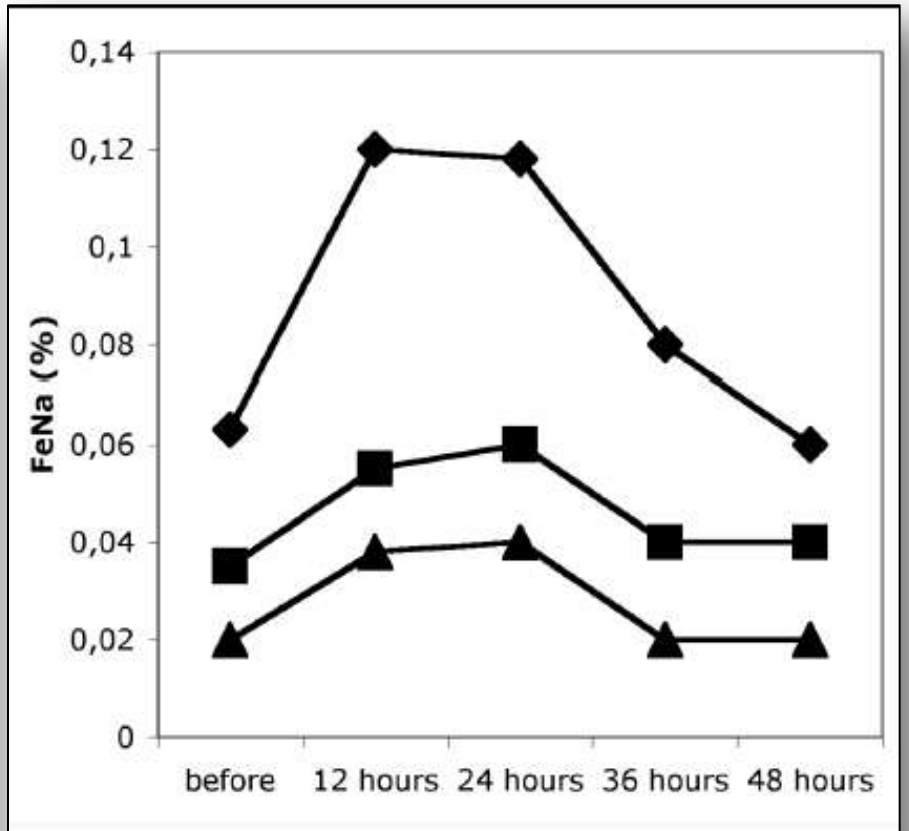


Effects of plasma expansion with albumin and paracentesis on haemodynamics and kidney function in critically ill cirrhotic patients with ascites and HRS: a prospective uncontrolled trial

UMGELTER et al. *Critical Care* 12:R4, 2008



Creatinine clearance before and after paracentesis. The 25th, 50th and 75th centiles are given.



ractional excretion of sodium before and after paracentesis. FeNa, ractional excretion of sodium. The 25th, 50th and 75th centiles are iven.

Renal resistive index and renal function before and after paracentesis in patients with HRS and tense ascites

UMGELTER et al. *Intensive Care Med* 35:152–156, 2009

Table 2 Hemodynamic, clinical and Doppler parameters before and after paracentesis

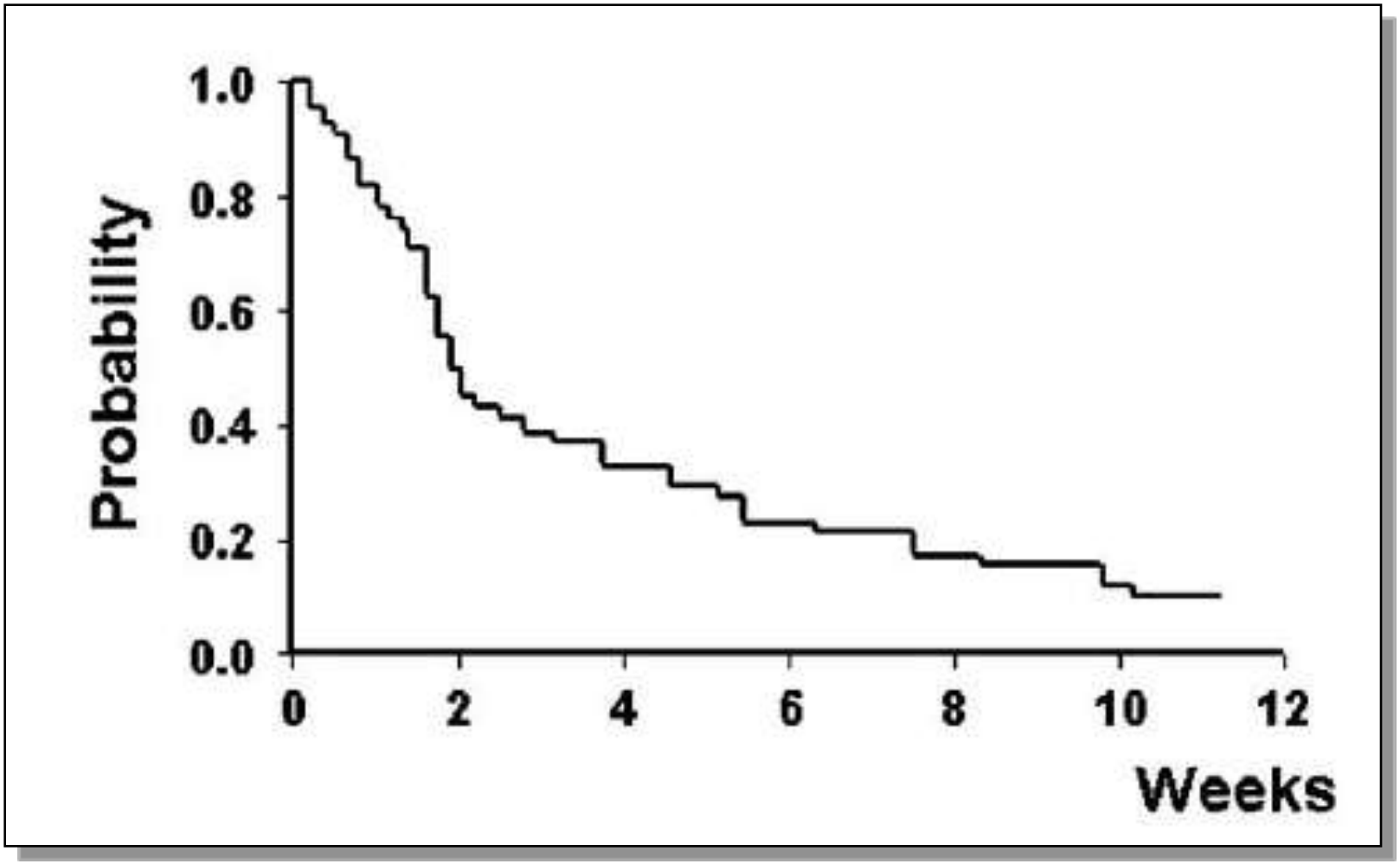
	Before paracentesis	After paracentesis	*p*
IAP (mmHg)	20 (19–22)	12 (10–13)	0.002
RPP (mmHg)	57 (52–71)	63 (59–72)	0.025
FG (mmHg)	38 (31–46)	51 (47–62)	0.002
CVP (mmHg)	14 (11–16)	11 (9–14)	0.041
GEDVI (mL/m^2) (*n* 680–800)	660 (540–748)	700 (565–725)	0.814
CI (L/min/m^2) (*n* 3–5)	4.12 (3.13–5.03)	4.49 (3.40–5.26)	0.041
SVI (mL/m^2) (*n* = 40–60)	48 (41–54)	55 (43–63)	0.016
HR (bpm)	101 (85–116)	91 (80–101)	0.026
SVRI (dyn s/cm^5/m^2) (*n* 1,700–2,400)	1,243 (1,095–1,745)	1,058 (987–1,337)	0.131
comp$_a$ (mL/mmHg)	1.33 (0.89–1.74)	1.49 (1.05–1.81)	0.071
MAP (mmHg)	77 (72–96)	77(69–85)	0.023
PPI	0.53 (0.47–0.57)	0.53 (0.51–0.58)	0.032
RI	0.848 (0.810–0.884)	0.807 (0.770–0.844)	0.002

Data presented as median (25th–75th percentile)
IAP intra-abdominal pressure; *RPP* renal perfusion pressure; *FG* filtration gradient; *CVP* central venous pressure; *GEDVI* global end-diastolic volume index; *CI* cardiac index; *SVI* stroke volume index; *HR* heart rate; *SVRI* systemic vascular resistance index; *comp$_a$* arterial compliance; *MAP* mean arterial pressure; *PPI* pulse pressure index; *RI* renal resistive index

Prevention of hepatorenal syndrome…

Incidence, predictive factors, and prognosis of hepatorenal syndrome in cirrhosis with ascites.

GINES et al. *Gastroenterology* 105: 229229-36, 1993



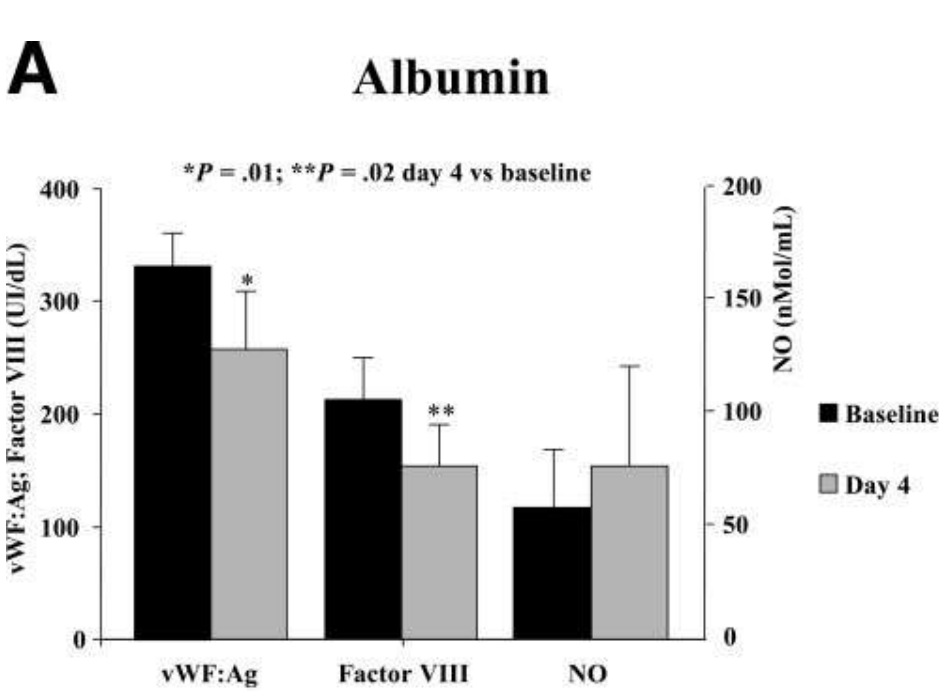
Definition and diagnostic criteria of refractory ascites and hepatorenal syndrome in cirrhosis. International Ascites Club.

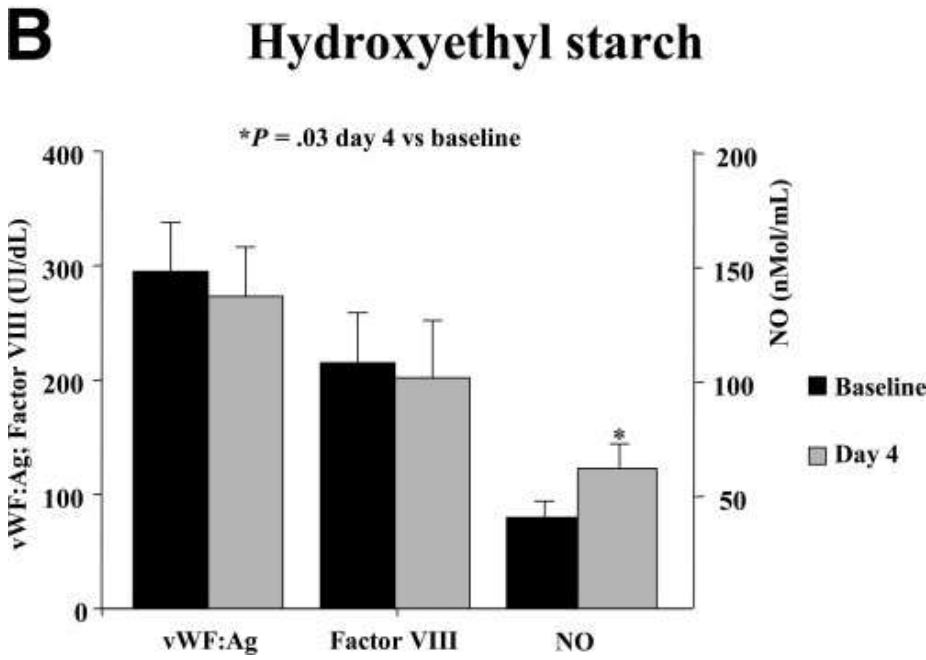
ARROYO et al. *Hepatology* 23: 164-76, 1996

- **Major criteria**
  - **low GFR (SCr>1.5 mg/dl or CrCl < 40 ml/min)**
  - **absence of shock, ongoing bacterial infection, treatment with nephrotoxins, or fluid losses**
  - **no sustained improvement in renal function following diuretic withdrawal and expansion of plasma volume with 1.5 L isotonic saline**
  - **proteinuria < 500 mg/dL and no ultrasonographic evidence of obstructive uropathy or paranchymal renal disease**

A Randomized Unblinded Pilot Study Comparing Albumin Versus Hydroxyethyl Starch in Spontaneous Bacterial Peritonitis

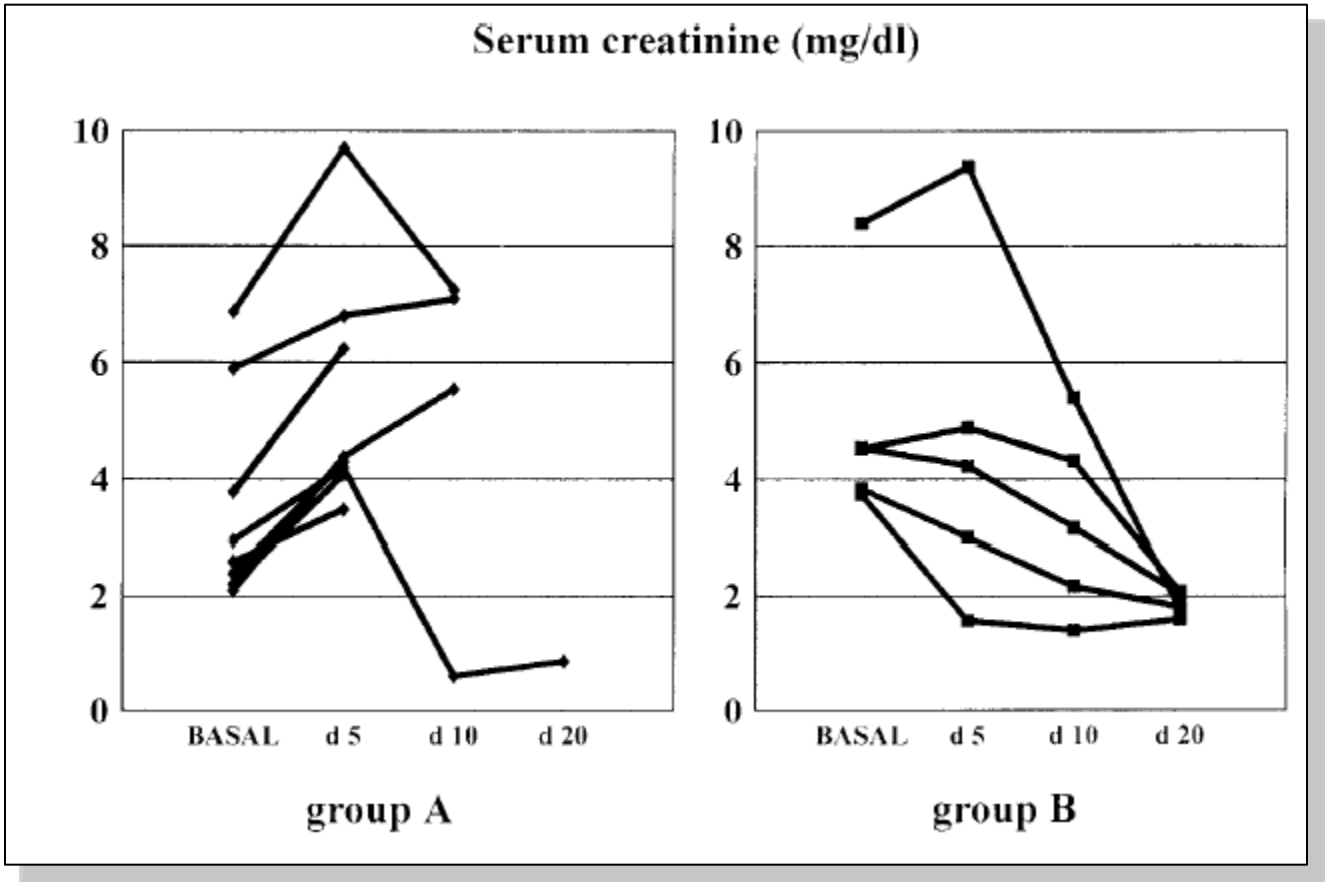
FERNANDEZ et al. *Hepatology* 42:627-634, 2005





Reversal of type I hepatorenal syndrome with the administration of midodrine and octreotide (n=13)

ANGELI et al. *Hepatology* 26: 1690-1697, 1999



Ascites and HRS in cirrhosis: pathophysiological basis of therapy and current management

ARROYO et al. *Journal of Hepatology* 38: S69–S89, 2003

Results of several studies with vasoconstrictor agents in type-1 HRS: response to treatment and outcome

Study	Treatment	Number of patients	Reversal of HRS	Patients surviving >1 month	Patients undergoing OLT
Guevara et al.[115]	Ornipressin plus albumin	8	4	5	–
Uriz et al. [a] [117]	Terlipressin plus albumin	9	7	5	3
Gülberg et al.[241]	Ornipressin plus dopamine plus albumin	7	4	4	2
Mulkay et al. [242]	Terlipressin plus albumin	12	7	4	2
Ortega et al. [b] [244]	Terlipressin with or without albumin	13	10	9	5
Angeli et al. [245]	Midodrine plus octreotide plus albumin	5	4	4	2
Duvoux et al. [116]	Noradrenaline plus albumin	12	10	6	3
Moreau et al. [c] [243]	Terlipressin with or without albumin	99	58	36	13
Total		165	104 (63%)	73 (44%)	30 (18%)

[a] This study included three patients with type-2 HRS.
[b] This study included four patients with type-2 HRS. Results include only patients treated with terlipressin plus albumin.
[c] This study was retrospective and not all patients received volume expansion (only 68 out of 99 were treated with albumin infusion as a concomitant treatment).

. Captopril in the hepatorenal syndrome.

COBDEN et al., *J Clin Gastroenterol* 7(4):354-60, 1985

1: J Clin Gastroenterol. 1985 Aug;7(4):354-60.

Captopril in the hepatorenal syndrome.

Cobden I, Shore A, Wilkinson R, Record CO.

Five patients with hepatorenal syndrome were treated with the orally active angiotensin-converting enzyme inhibitor captopril (25 or 50 mg 6 hourly) for up to 48 hours. Only one patient showed a significant increase in urinary sodium concentration (from less than 10 to 70 mmol/liter), but without associated diuresis; renal function continued to deteriorate in all patients with persistent oliguria and rising serum creatinine. The outcome was uniformly fatal. These results suggest that in the hepatorenal syndrome, captopril in standard dosage is without benefit, and provide further evidence that the changes in the renin-angiotensin system are probably secondary to reduced renal perfusion from some other cause.

PMID: 2995480 [PubMed - indexed for MEDLINE]