Symposium inaugural du sericve de néphrologie

Rein et foie : liaisons dangereuses !

Service de néphrologie
Centre Hospitalier du Valais Romand (CHVR)

Bruno Vogt

INSELSPITAL
UNIVERSITÄTSSPITAL BERN
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BERN UNIVERSITY HOSPITAL

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UNIVERSITÄT
BERN

Néphrologie, hypertension et pharmacologie clinique


INSEL
INSELSPITAL BERN
1354
Hauptei gang

Inselspital en 2020

A young lady with liver cirrhosis and severe ascites

Oedema formation in liver cirrhosis

RENAL FUNCTIONAL ABNORMALITIES

- Sodium retention
- Water retention
- Renal vasoconstriction (reduction RBF and GFR)

Sodium retention in liver cirrhosis

- Renin-angiotensin system
- Sympathetic nervous system
- Antidiuretic hormone
- Other mechanism(s)

Time course of renal functional abnormalities in patients with cirrhosis (HRS: hepatorenal syndrome)

Time Course

Compensated Cirrhosis

Ascites →

Degree of Liver Disease

Pre-asitic sodium retention

Sodium retention → Water retention → Renal vasoconstriction

Ginès P et al. Semin Liver Dis 1997;17:175-189

Theories of Ascites Formation in Cirrhosis

Traditional „Underfill“ Concept

Ascites Formation

↓

↓ „Effective“ Volume

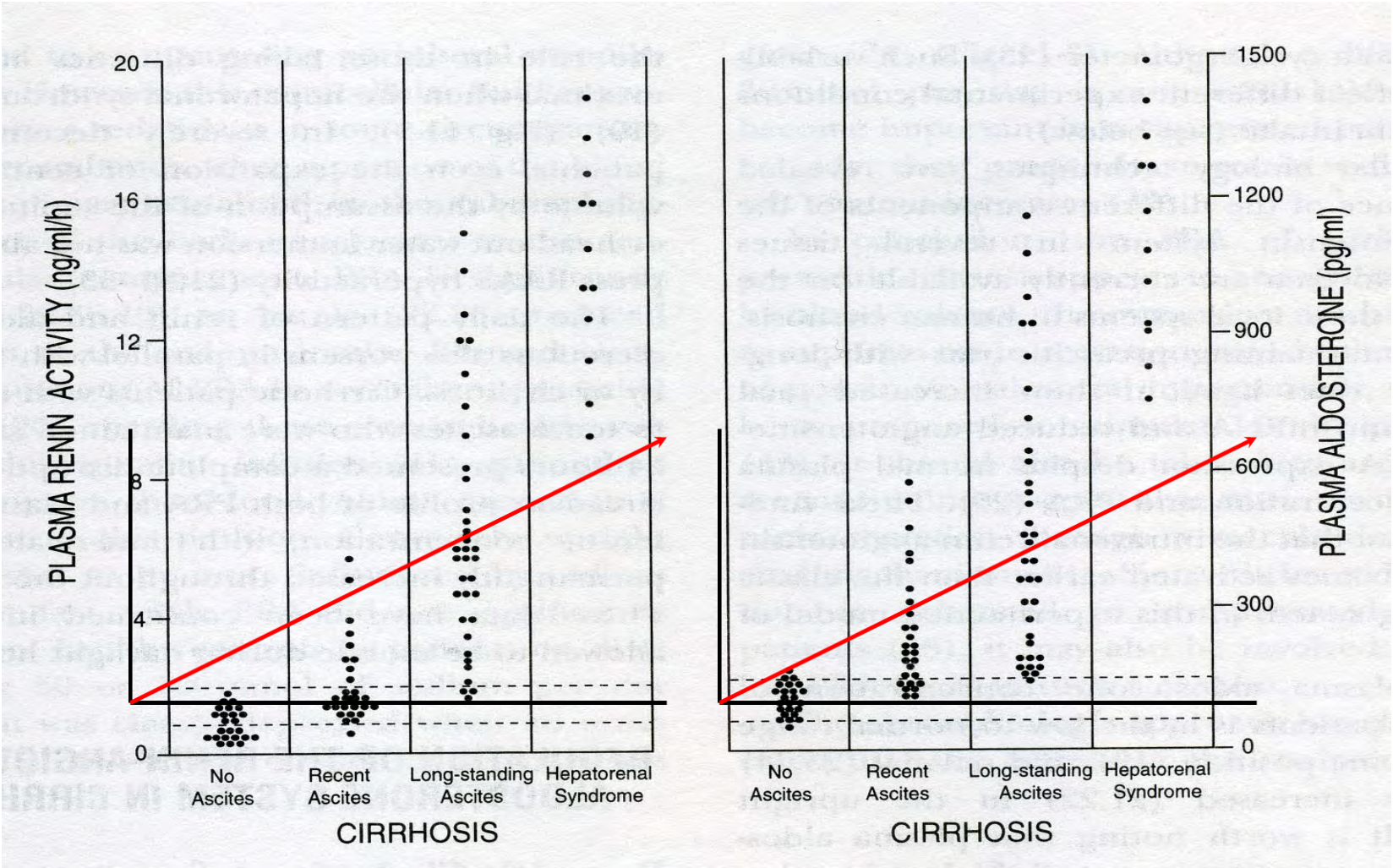
↓

Renal Sodium Retention

↓

Ascites and Edema

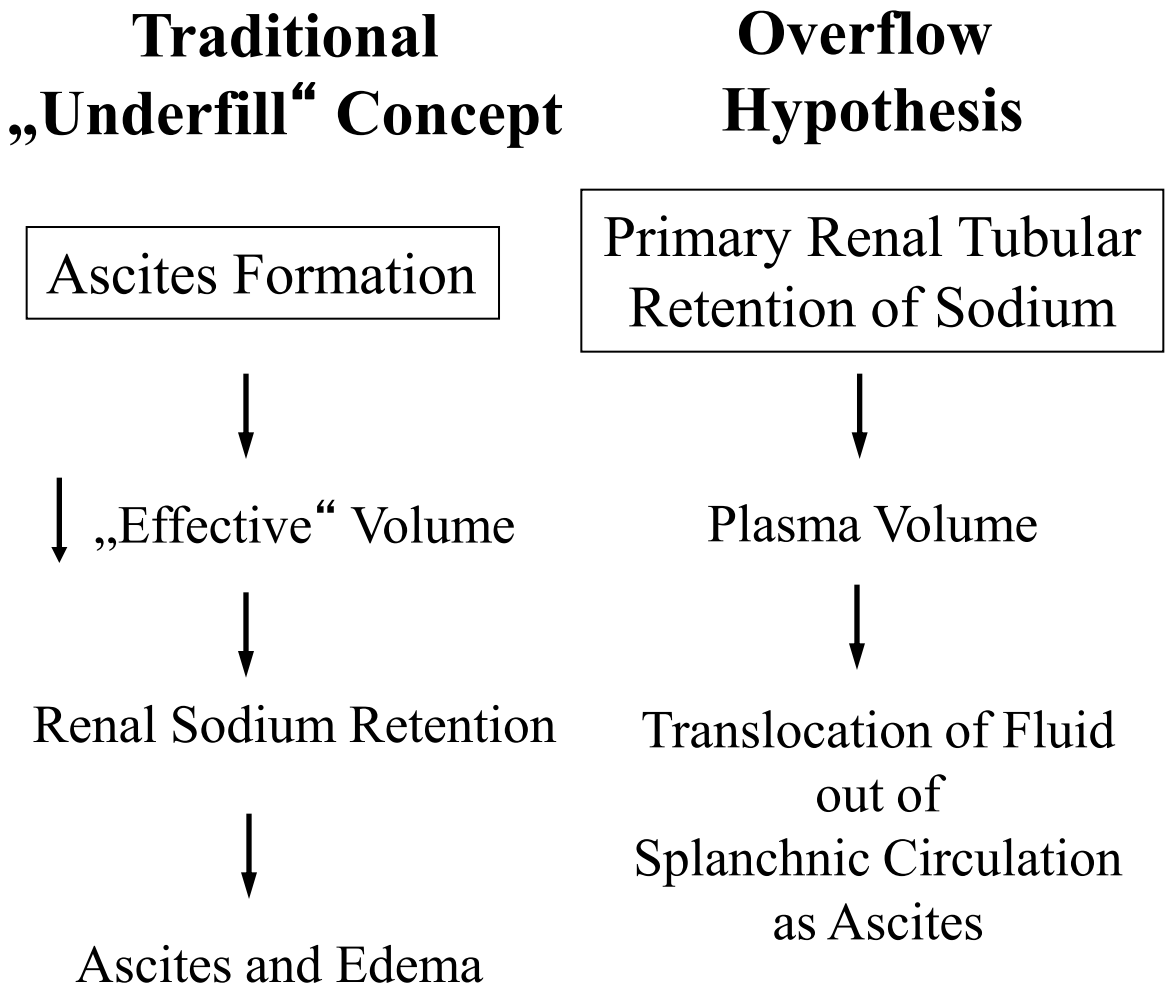
Plasma renin activity and plasma aldosterone concentration in different stages of cirrhosis



Supine position, sodium restriction 40 mmol per day

M. Bernardi, 1999

Theories of Ascites Formation in Cirrhosis



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Renal Sodium Retention

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Ascites and Edema

Overflow Hypothesis

Primary Renal Tubular Retention of Sodium

↓

Plasma Volume

↓

Translocation of Fluid out of Splanchnic Circulation as Ascites

Revised „Underfill“ Theory

Primary Peripheral Vasodilatation

↓

Imbalance of Capacitance and Volume „Relative“ Underfilling

↓

Renal Sodium Retention

Imbalance of Capacitance and Volume
„Relative“ Underfilling

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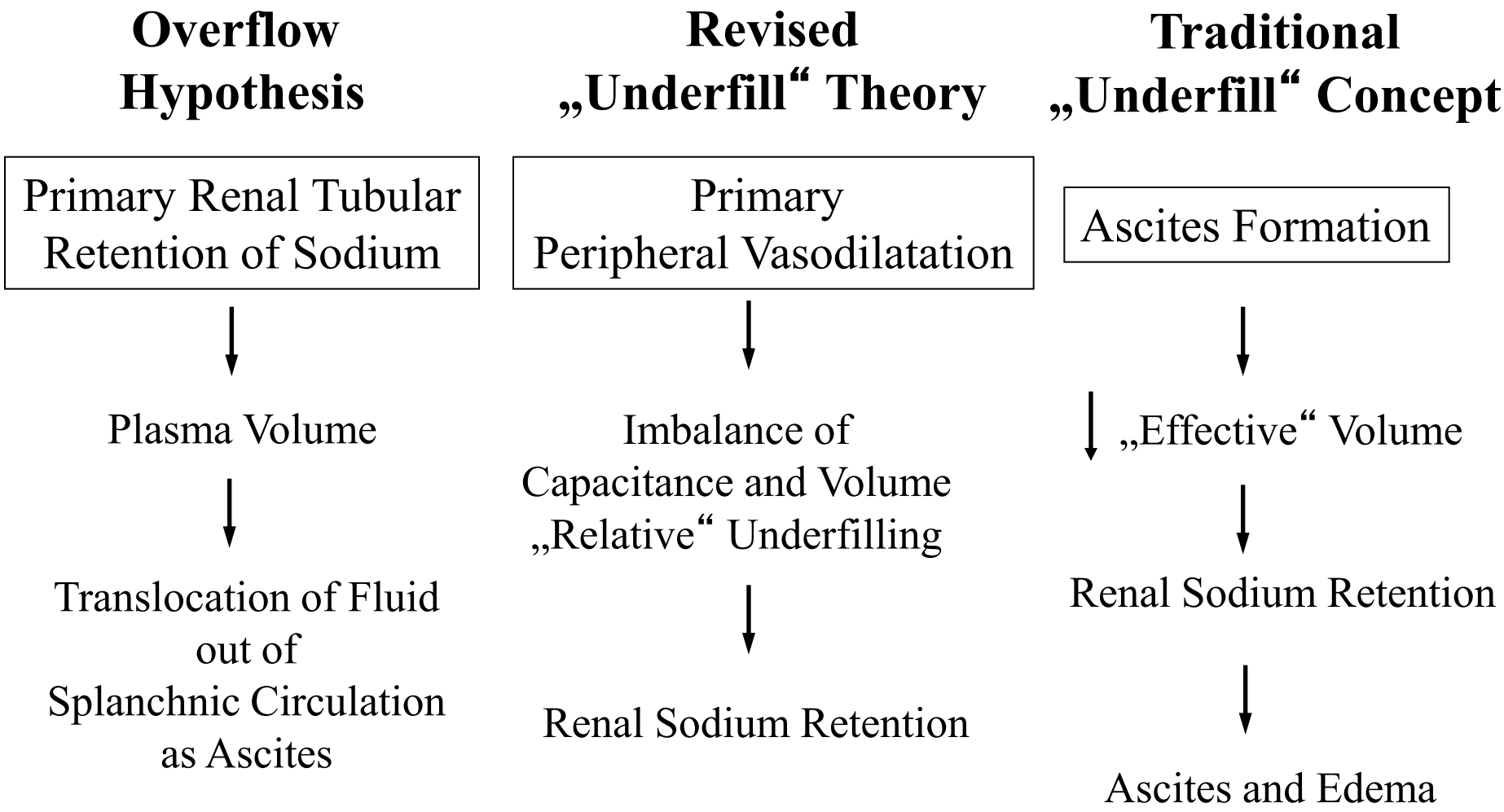
Renal Sodium Retention

Theories of Ascites Formation in Cirrhosis



Theories of Ascites Formation in Cirrhosis

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Renal Sodium Retention

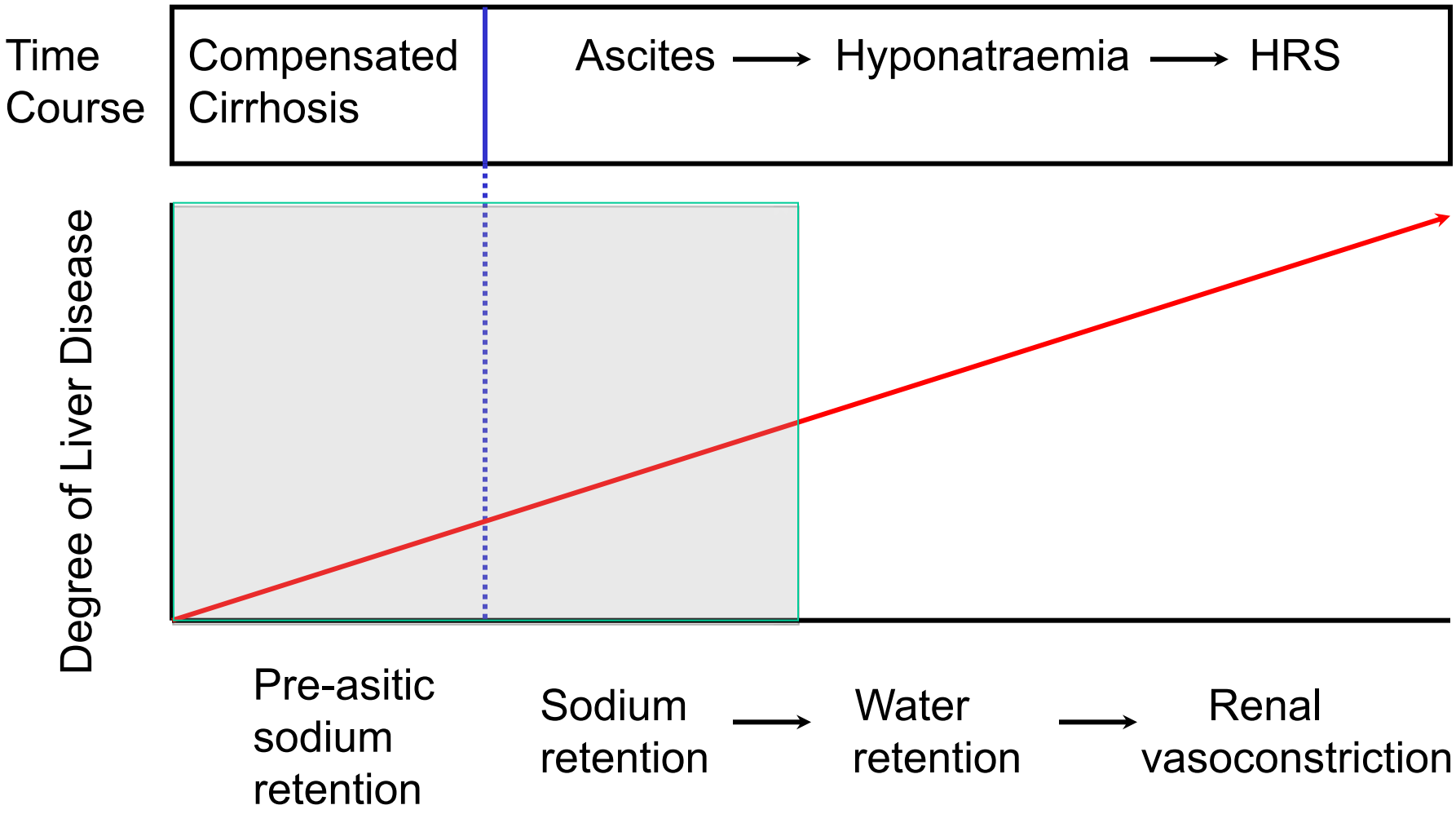
Traditional „Underfill“ Concept

Ascites Formation

Ascites and Edema

Compensated Cirrhosis — Ascites — Hyponatraemia — HRS

Time course of renal functional abnormalities in patients with cirrhosis (HRS: hepatorenal syndrome)



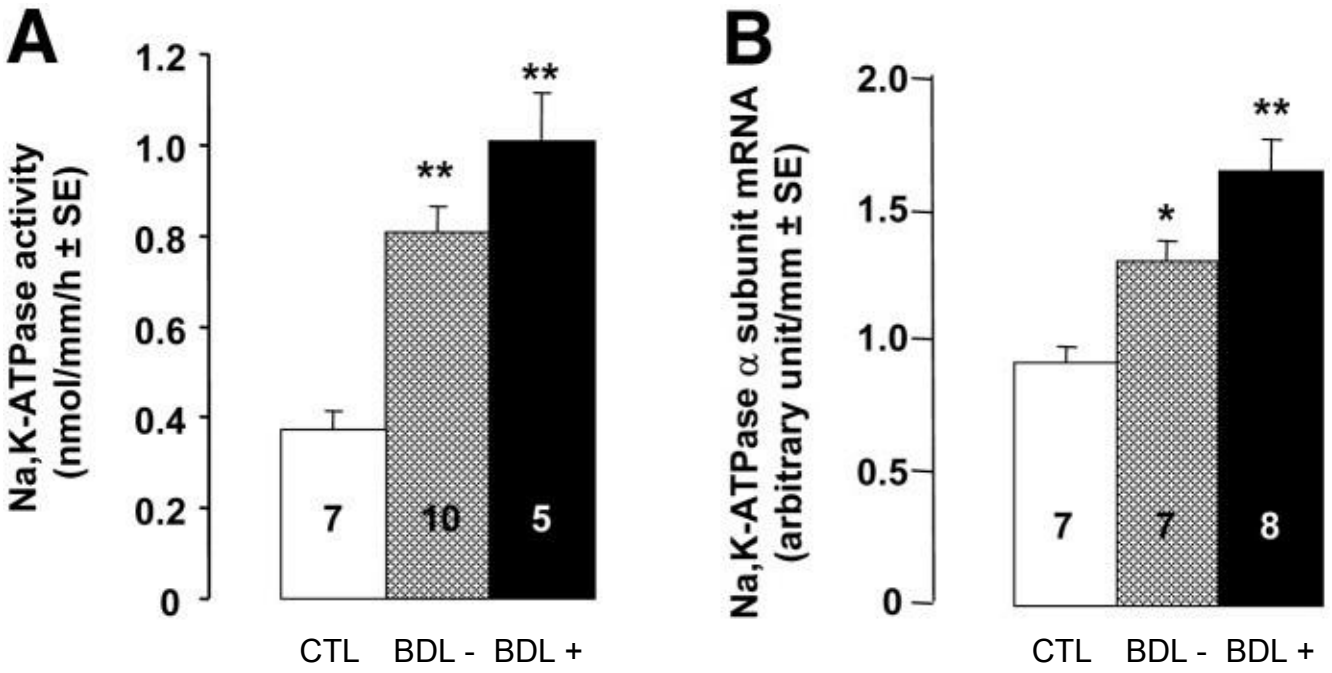
Ginès P et al. Semin Liver Dis 1997;17:175-189

Control mice (left side) and cirrhotic mice (right side)

Na^+, K^+-ATPase activity is increased in cirrhotic corticosteroid clamped BDL mice

Na,K-ATPase activity

α Na,K-ATPase mRNA



Ackermann D, et al. Hepatology 2007; 46:9-11

Sodium retention in liver cirrhosis

enal dependent

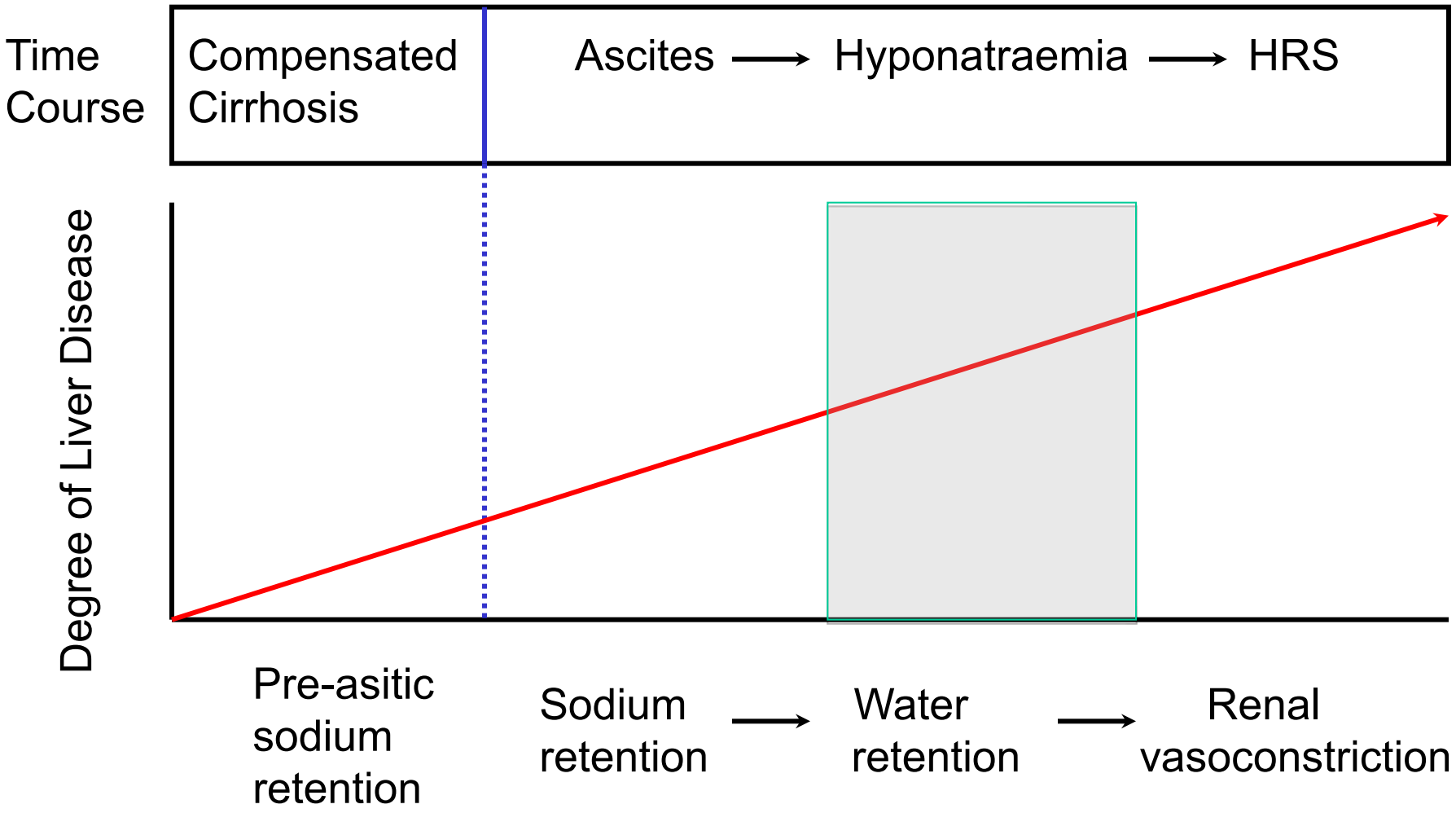
enal dependent

sterone independent

- pendrin, PAR2, ROS ? -> **adrenal independent**

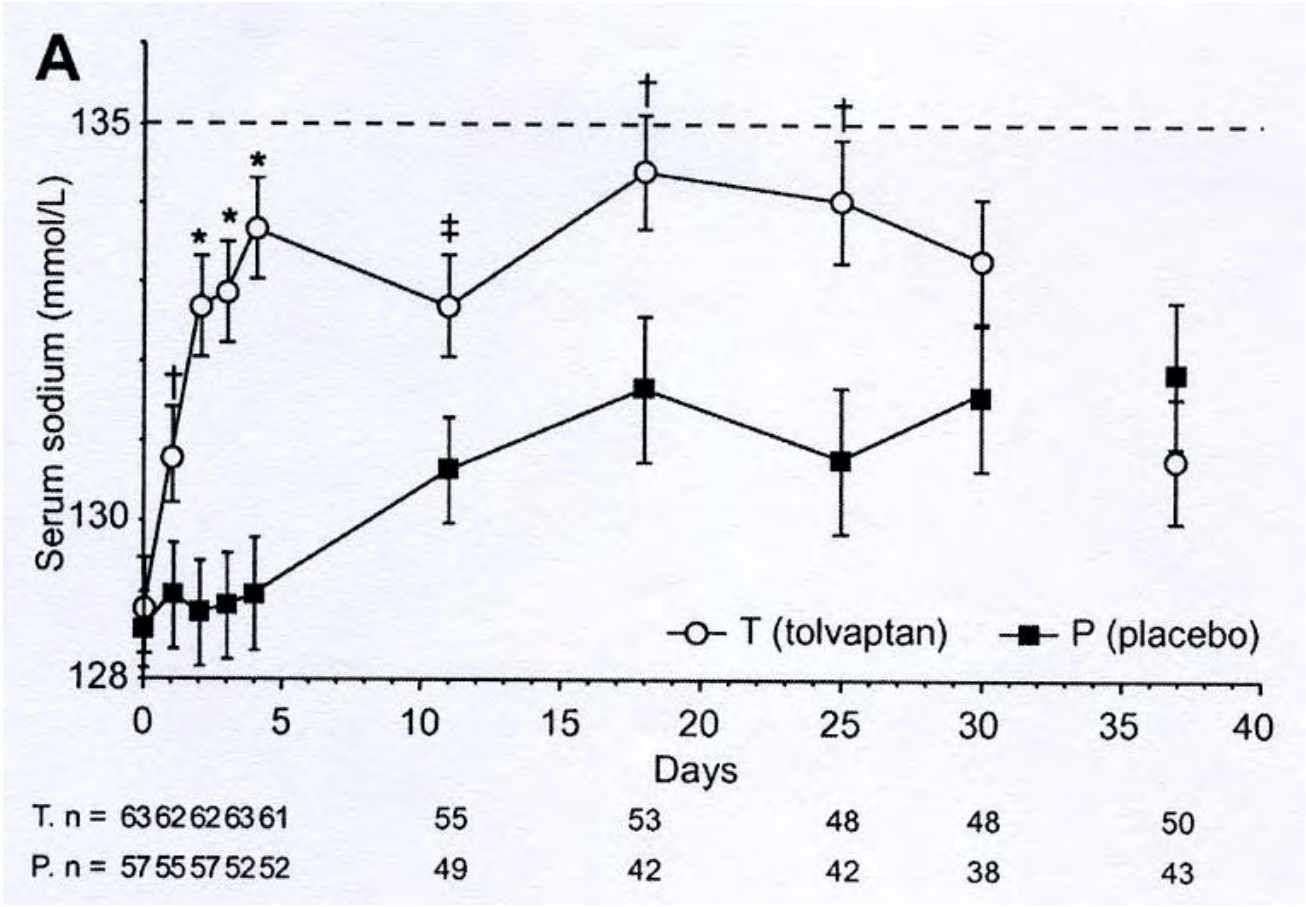
mechanism(s)

Time course of renal functional abnormalities in patients with cirrhosis (HRS: hepatorenal syndrome)



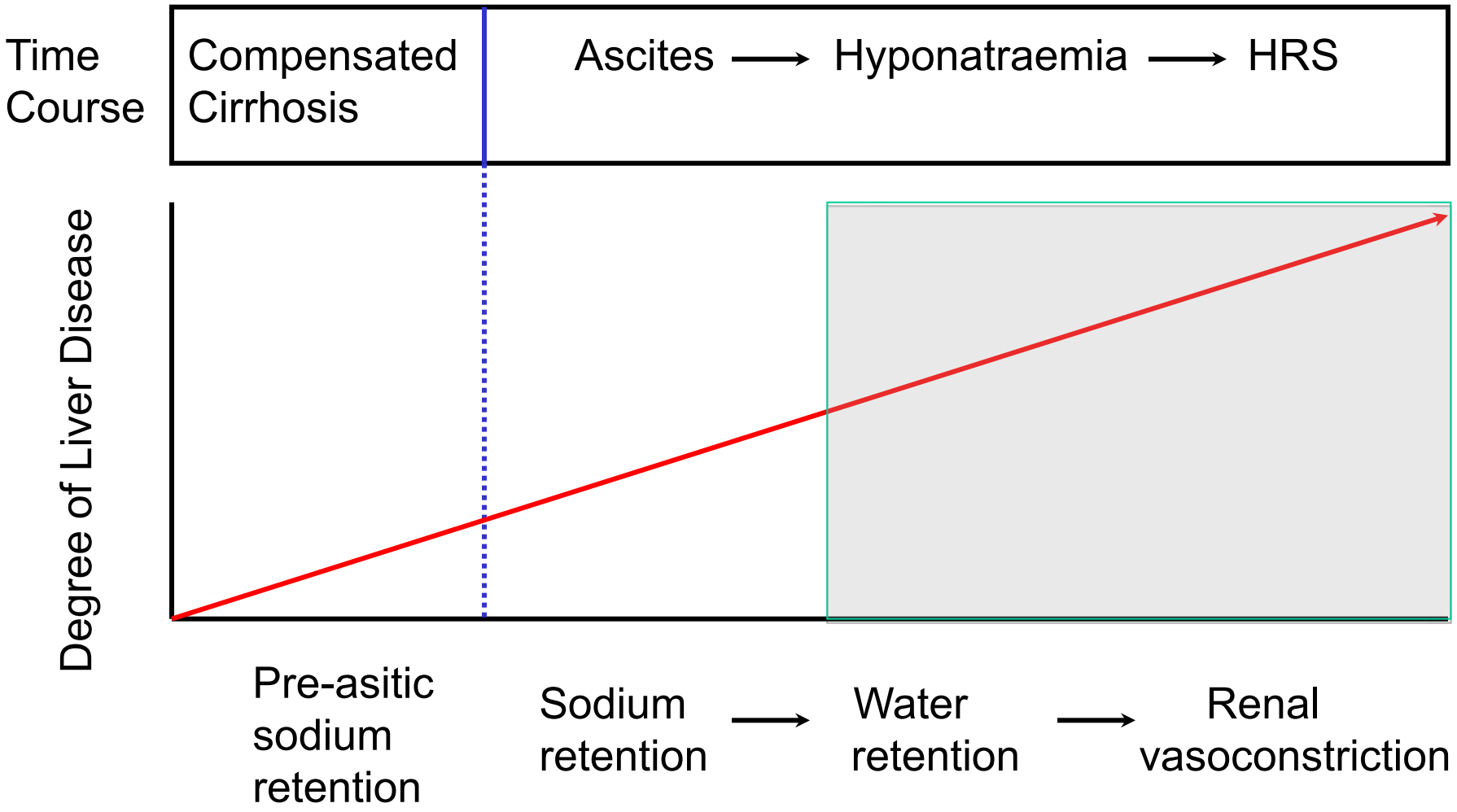
Ginès P et al. Semin Liver Dis 1997;17:175-189

Tolvaptan, an oral vasopressin antagonist, in the treatment of hyponatremia in cirrhosis



A. Cárdenas, et al. Journal of Hepatology 2012; 56:571–578

Time course of renal functional abnormalities in patients with cirrhosis (HRS: hepatorenal syndrome)



Ginès P et al. Semin Liver Dis 1997;17:175-189

Evaluation du patient avec cirrhose et insuffisance rénale aïgue

- Mesurer fonction rénale

- Evaluation fonction hépatique

- Infection bactérienne ?

N Engl J Med 2009;361:1279-90

Patient cirrhotique avec insuffisance rénale

- Syndrome hépatorénale ?

- Hypovolémie ?

- Maladie parenchymateuse – glomérulonéphrite ?

- Médicaments ?

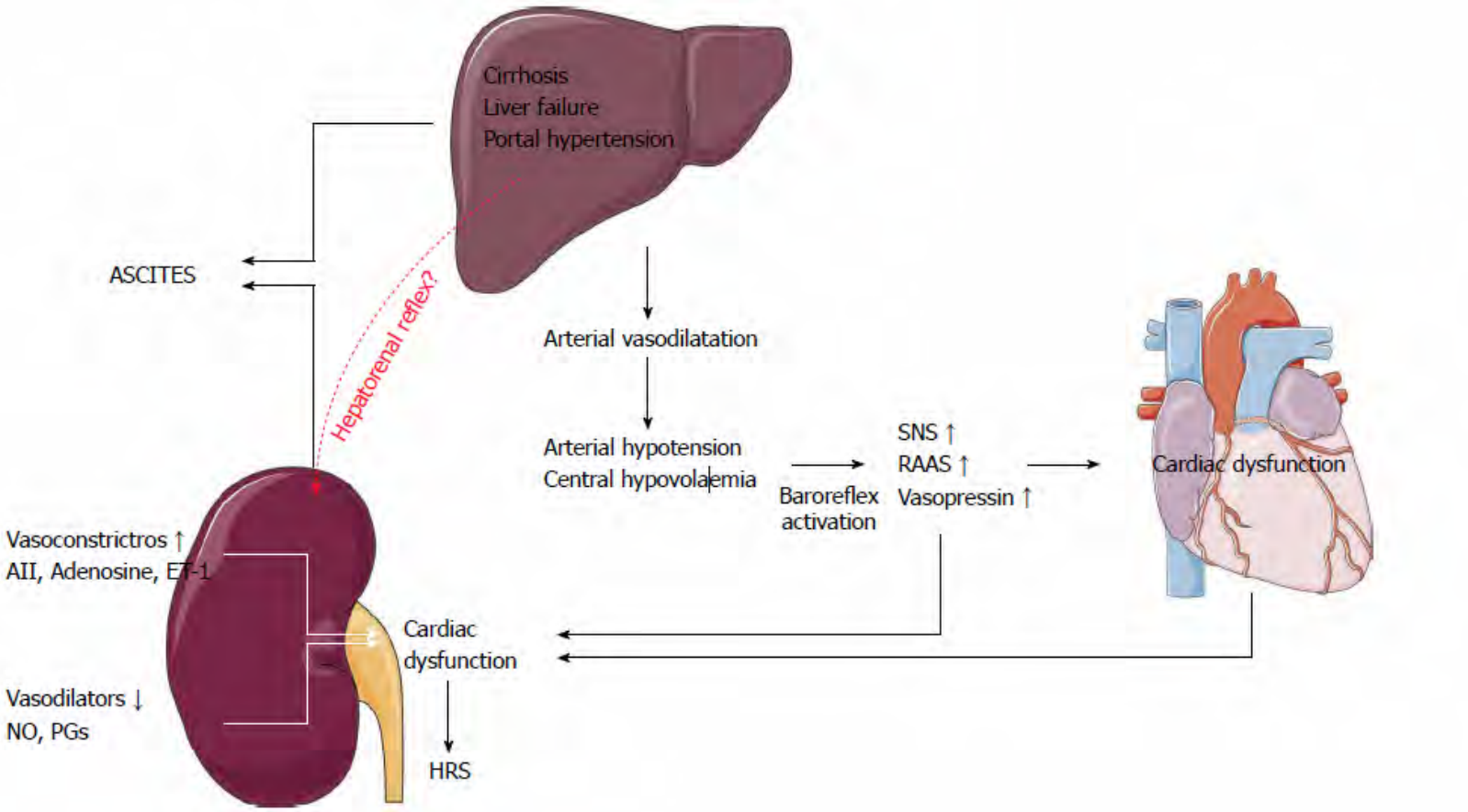
N Engl J Med 2009;361:1279-90

Syndrome hépatorénale

Maladie hépatique aigue ou chronique avec insuffisance rénale et hypertension protale.

Fonction rénale diminuée sans autre cause

Pathophysiological mechanisms in the development of ascites and the hepatorenal syndrome



SNS: Sympathetic nervous system; RAAS: The reninangiotensin-aldosterone system; AII: Angiotensin II; ET-1: Endothelin-1; NO: Nitric oxide; PGs: Prostaglandins.

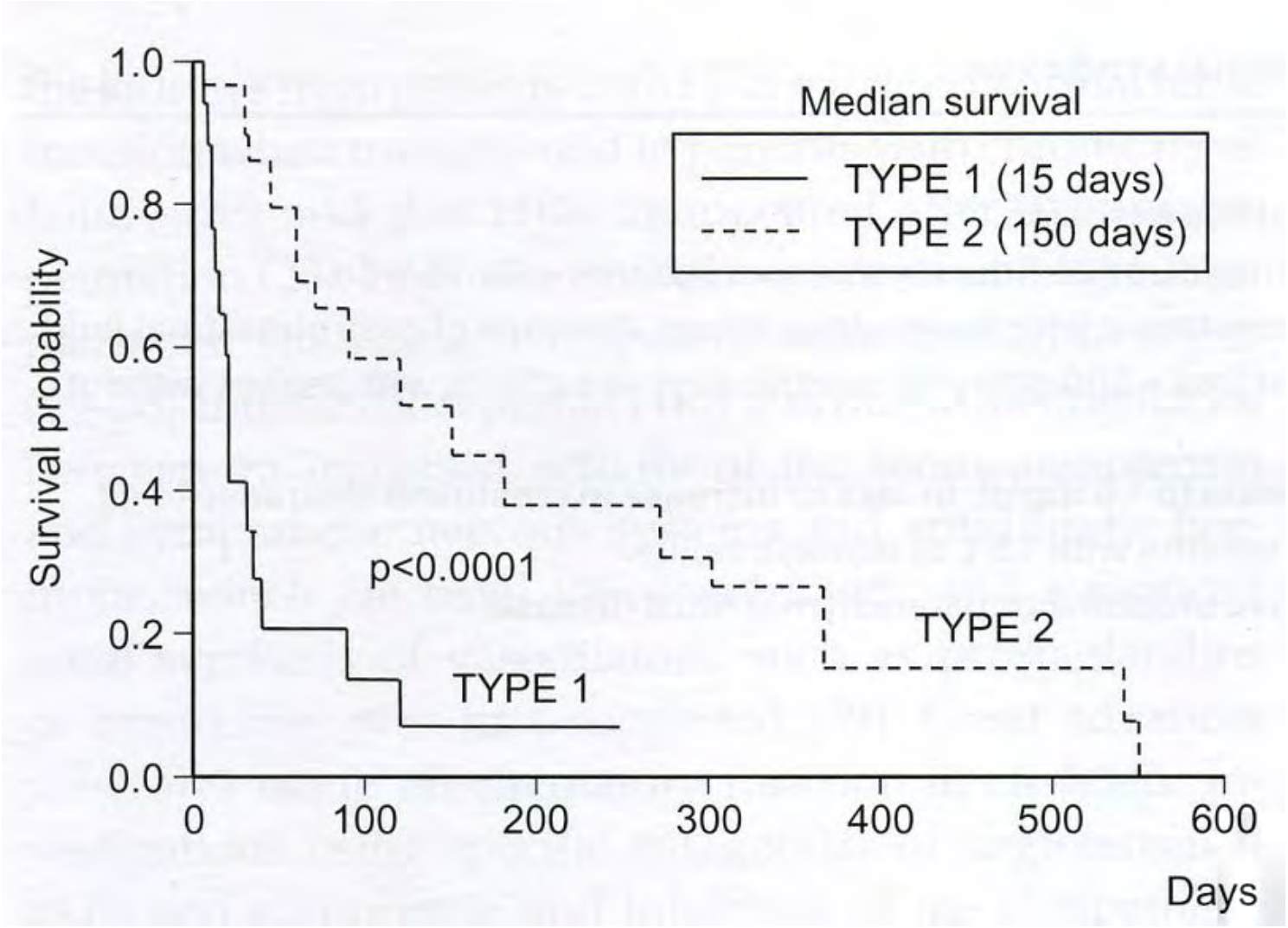
Møller S, Krag A. Cardiorenal syndrome - A new entity? In: Gerbes A, editor. Hyponatremia and hepatorenal syndrome: Progress in treatment. Basel: Karger, 2011: 102-111

The hepatorenal syndrome is classified into two types:

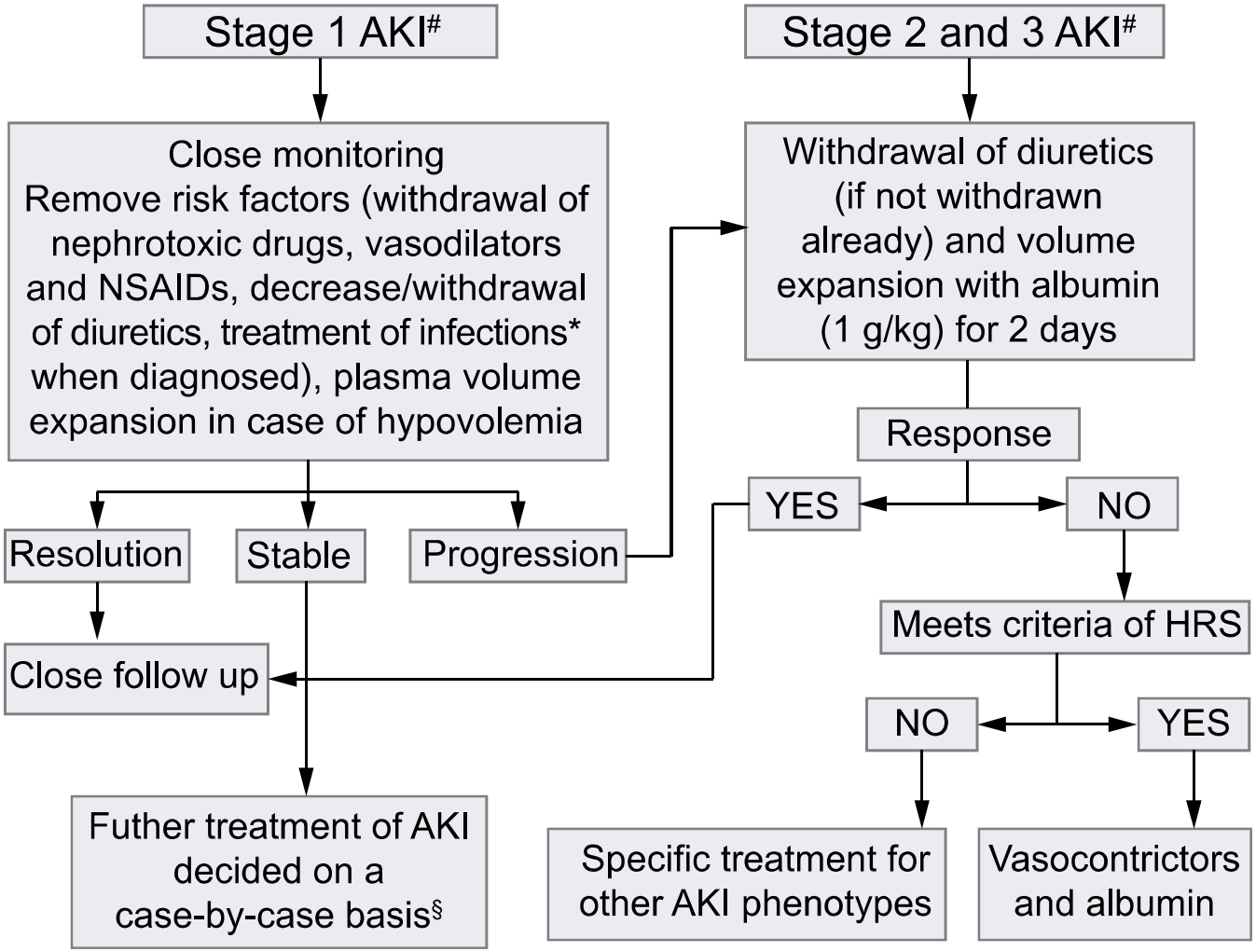
- **Type 1** is characterized by a doubling of the serum creatinine level to more than 2.5 mg/dl (221 µmol/liter) in less than 2 weeks

- **Type 2** is characterized by a stable or less rapidly progressive course than in type 1

Hepatorenal syndrome Type I and II



Proposed algorithm for the management of acute kidney injury (AKI) according to International Club of Ascites—AKI (ICA-AKI) classification



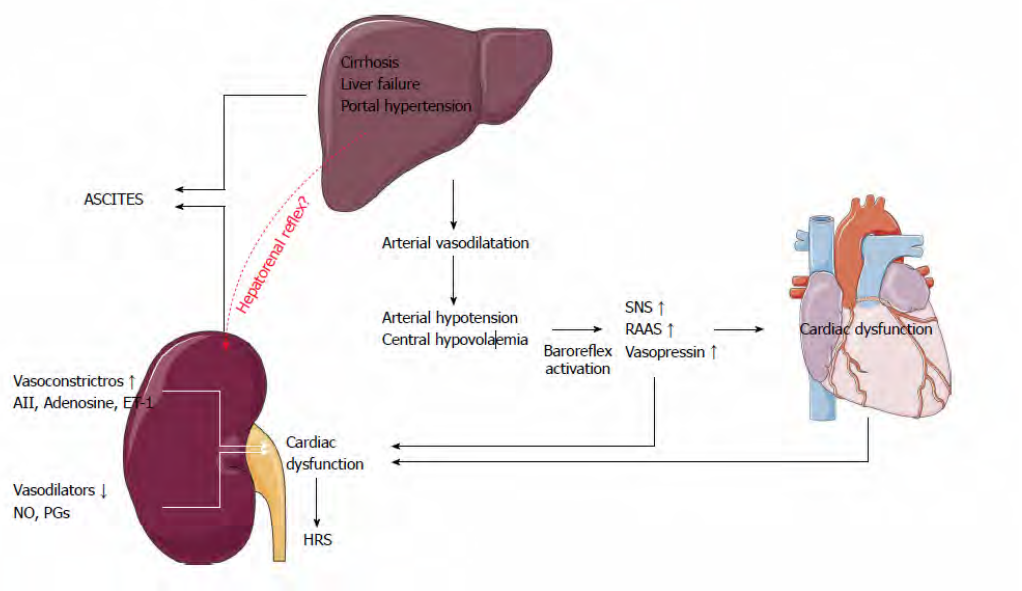
Angeli P, et al. Gut April 2015
und J Hepatology 2015

Specific Therapies for the Hepatorenal Syndrome in Patients with Cirrhosis

Vasoconstrictor drugs

- Terlipressin
- Norepinephrine
- Midodrine

Albumin

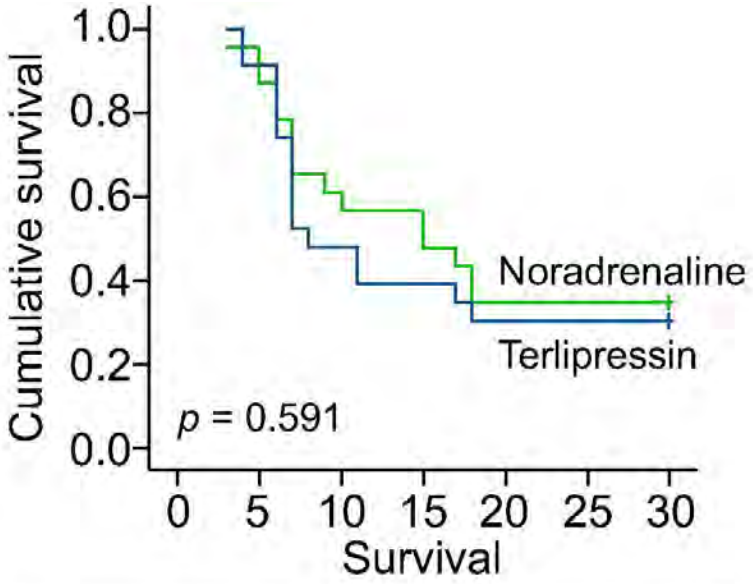


Other therapies

-Transjugular intrahepatic portosystemic shunts (TIPS)

-Liver transplantation

Noradrenaline vs. terlipressin in the treatment of hepatorenal syndrome: A randomized study

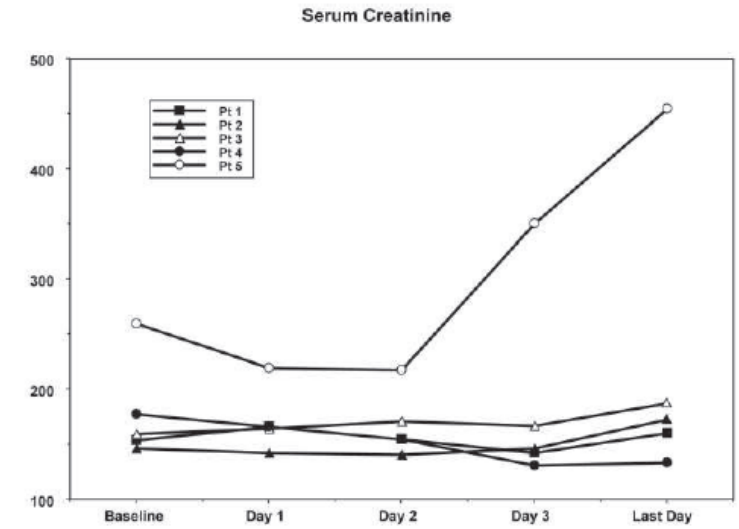


Patients at risk	Day					
	5	10	15	20	25	30
Terlipressin group (n = 23)	20	11	9	7	7	7
Noradrenaline group (n = 23)	21	13	11	8	8	8

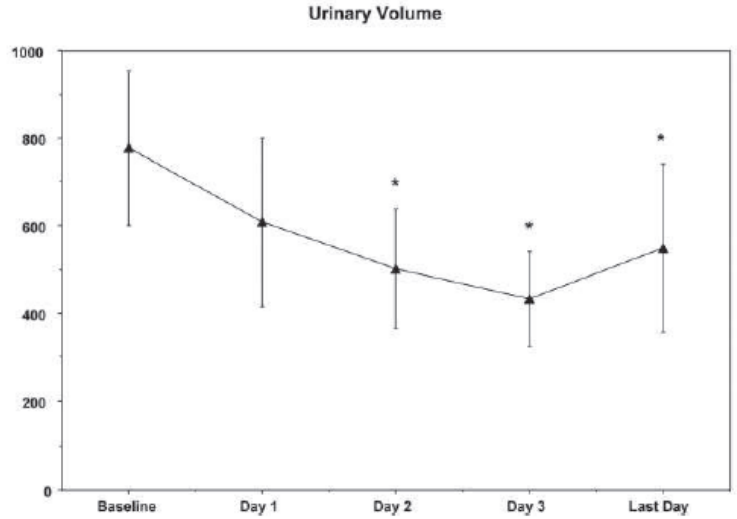
V. Singh et al. Journal of Hepatology 2012; 56:1293–1298

Lack of Renal Improvement with Nonselective Endothelin Antagonism with Tezosentan in Type 2 H

Serum creatinine



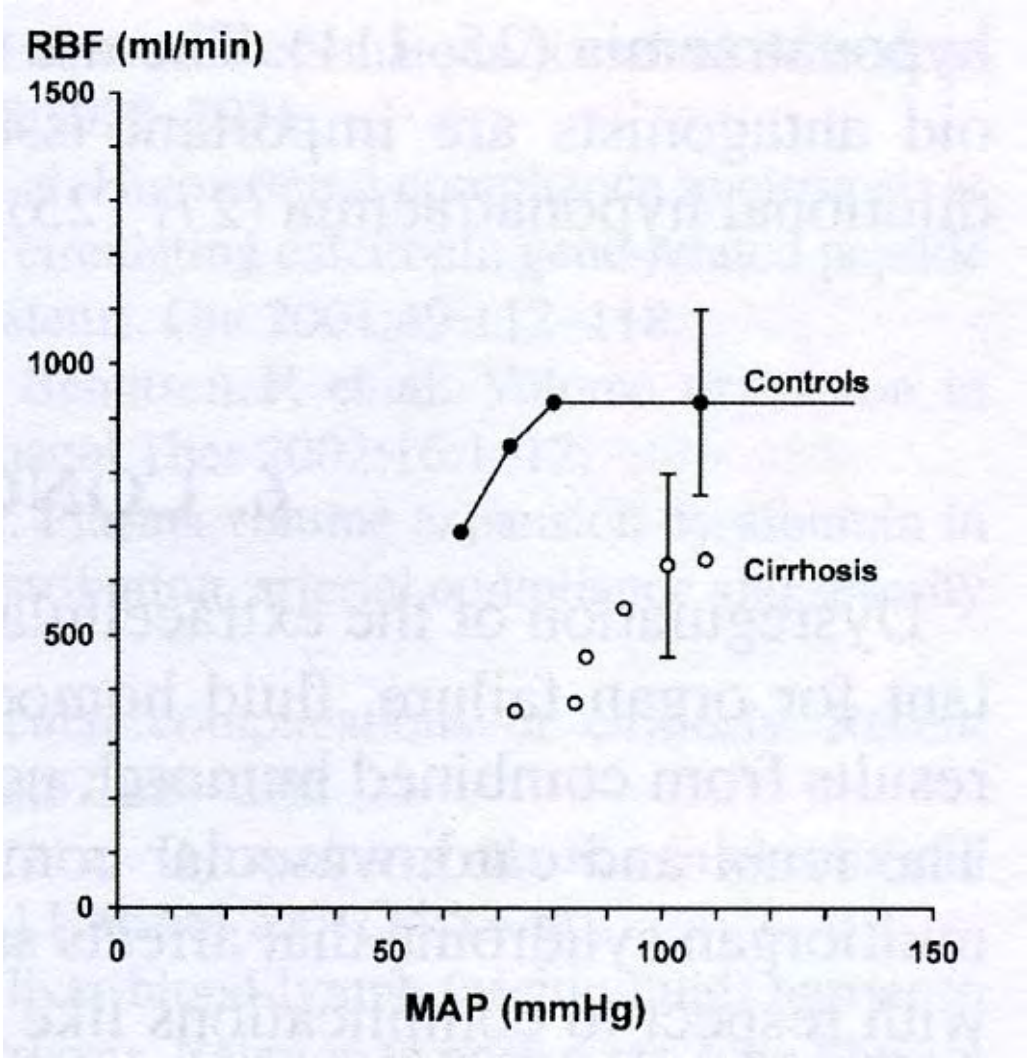
Urinary volume



Serum creatinine and 24-hour urinary volume in the 5 patients who received more than 1 day of tezosentan infusion. *P " 0.05 versus the baseline.

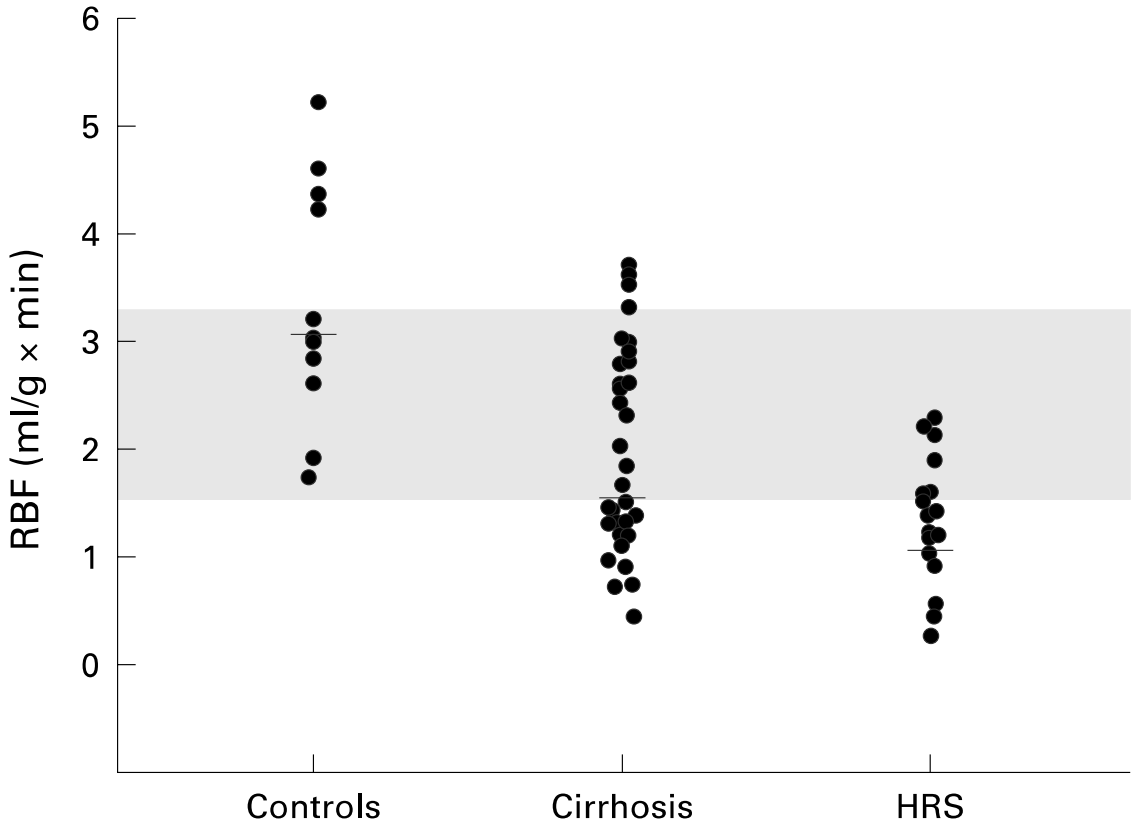
HEPATOLOGY 2008;47:160-168

Renal Blood Flow (RBF) in relation to Mean Arterial Blood Presure (MAP) in normal subjects and in patients with cirrhosis



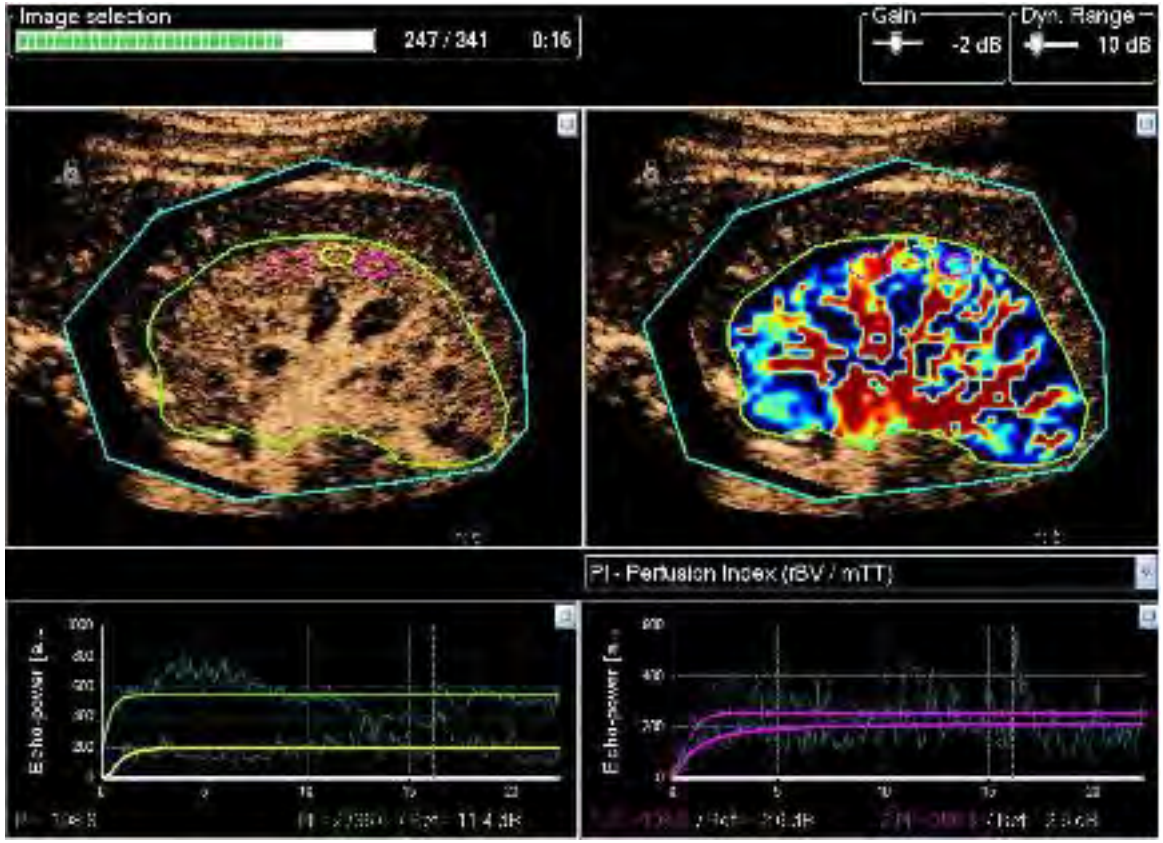
Adapted from Jens H. Henriksen

Renal blood flow in relation to systemic and portal haemodynamics and liver function



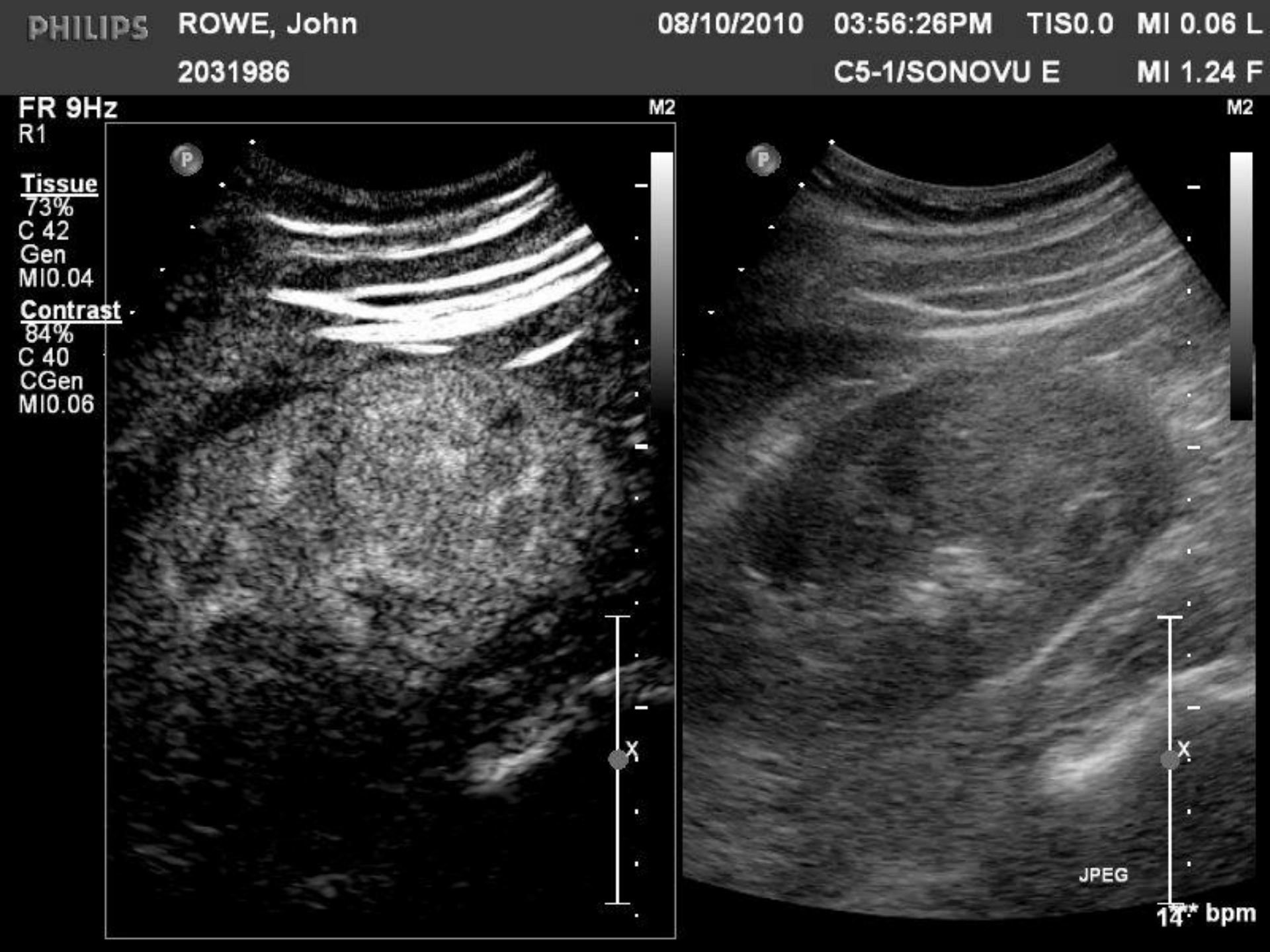
Ring-Larsen H, et. al. Scand J Clin Lab Invest 1977;37:635–42

Renal perfusion evaluation with contrast enhanced ultrasonography: A pilot study on 10 healthy subjects



Screenshot from Sonoperf® illustrating localization of region of interest and determining perfusion indices. Only PI is shown

A. Schneider, el al., NDT 2011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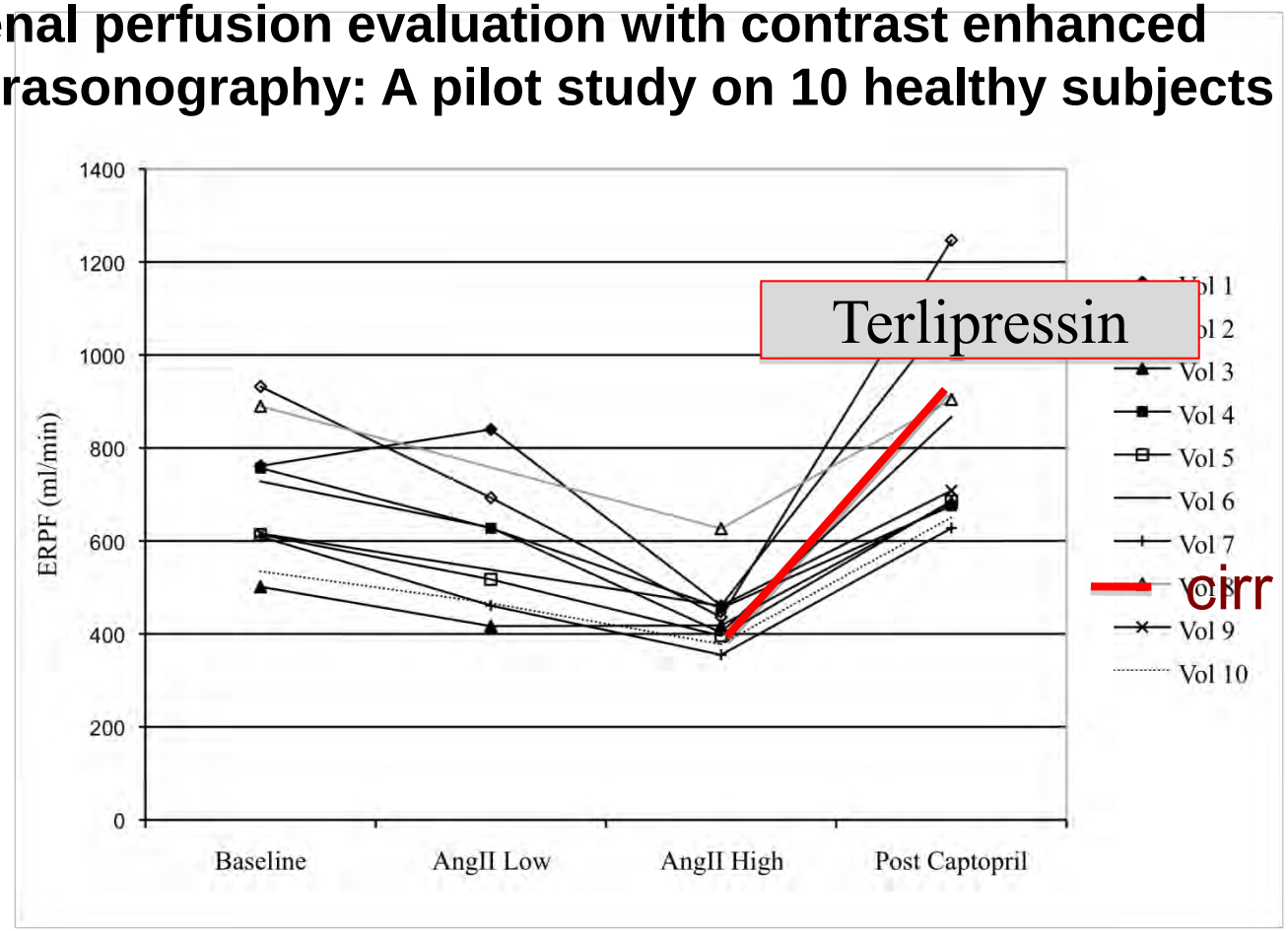
Renal perfusion evaluation with contrast enhanced ultrasonography: A pilot study on 10 healthy subjects



Effective renal plasma flow (estimated by PAH clearance)
ERPF: Effective Renal Plasma Flow (ml/min), AngII Low: Angiotensin II 1 ng/kg/min, AngII High: Angiotensin II 3 ng/kg/min, Vol: Volunteer, PAH = para-aminohippurate

BRIEF REPORT

Contrast-enhanced ultrasound evaluation of the renal microcirculation response to terlipressin in hepato-renal syndrome: a preliminary report

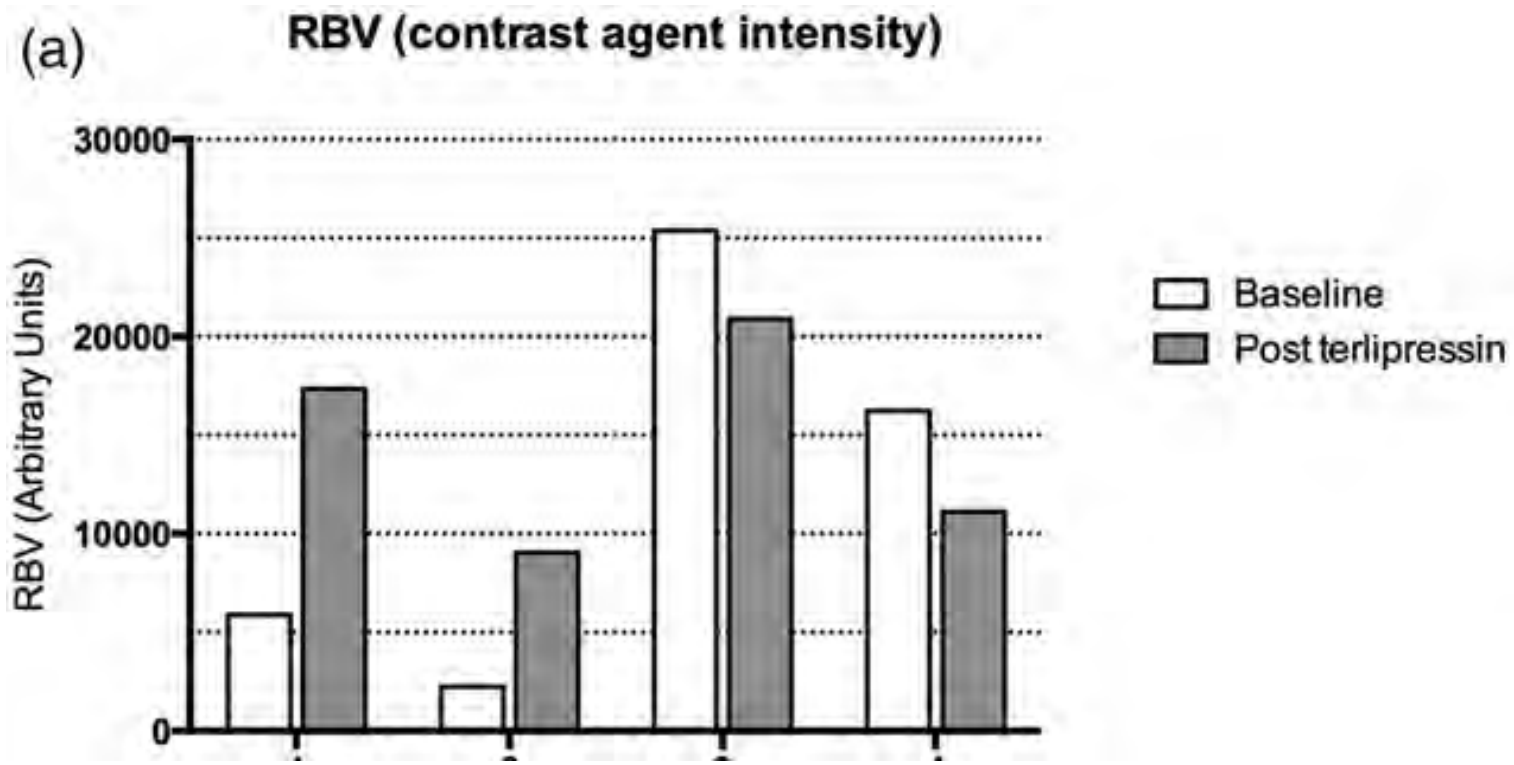


Figure 1. CEUS-derived parameters. Panel (a): RBV indicates contrast agent intensity—increases with higher perfusion. Panel (b): mTT (mean Transit Time) indicates time taken for contrast agent to travel through

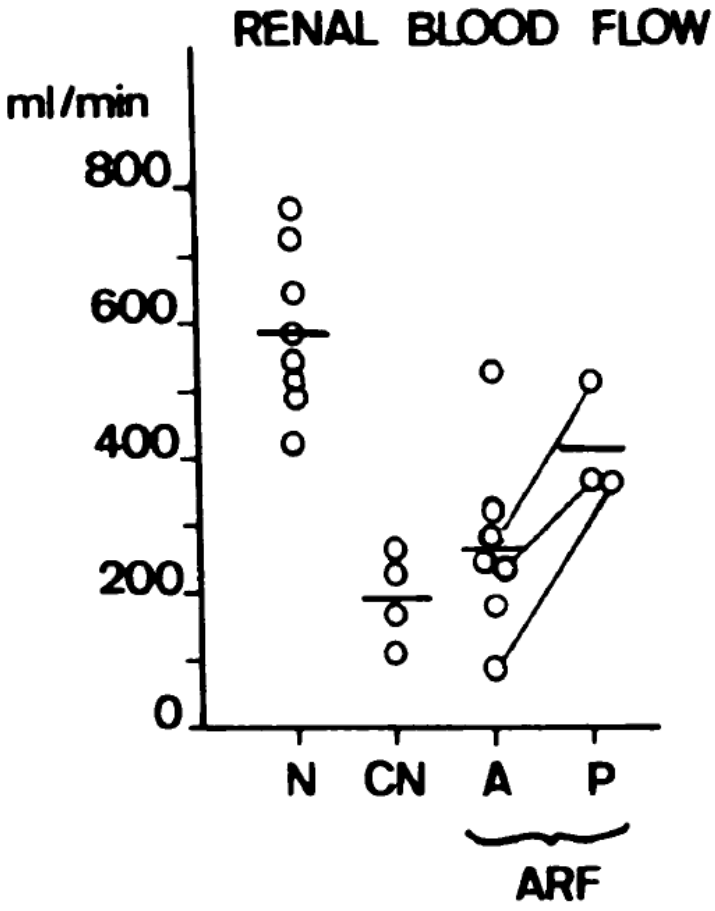
Renal Distribution Volumes of Indocyanine Green, [^{51}Cr]EDTA, and ^{24}Na in Man during Acute Renal Failure after Shock

IMPLICATIONS FOR THE PATHOGENESIS OF ANURIA

F. C. REUBI, C. VORBURGER, and J. TUCKMAN

From the Medizinische Poliklinik, University of Berne, Berne, Switzerland

The Journal of Clinical Investigation Volume 52 February 1973 223



Sans **RIFLE** et sans **AKIN**, les auteurs d'époque étaient beaucoup plus attentivs au problème de l'insuffisance rénale aïgue !

Insuffisance rénale chez le patient avec cirrhose

- Syndrome hépatorénale ?

- Hypovolémie ?

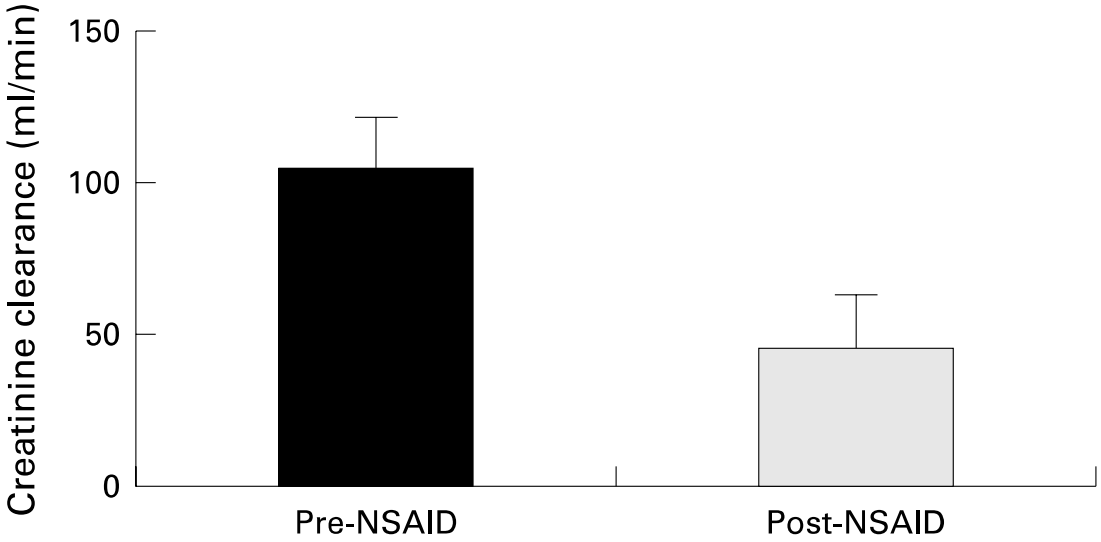
- Maladie parenchymateuse ?

- Infection – sépticémie ?

- Médicaments ?

N Engl J Med 2009;361:1279-90

Administration of indomethacin, a non-steroidal anti-inflammatory drug (NSAID), to patients with cirrhosis AND ascites, caused a significant reduction in renal plasma flow (not shown) and glomerular filtration rate, as assessed by creatinine clearance



Boyer T, Zia P, Reynold T. Effect of indomethacin and prostaglandin A, on renal function and plasma renin activity in alcoholic liver disease. *Gastroenterology* 1979;77:215–22.


Nos meilleurs Voeux pour
Daniel Teta
et son équipe de la néphrologie
de Sion !