Cardio Renal Syndrome

UCL Centre for Nephrology

Cardio-Renal Syndrome (CRS)

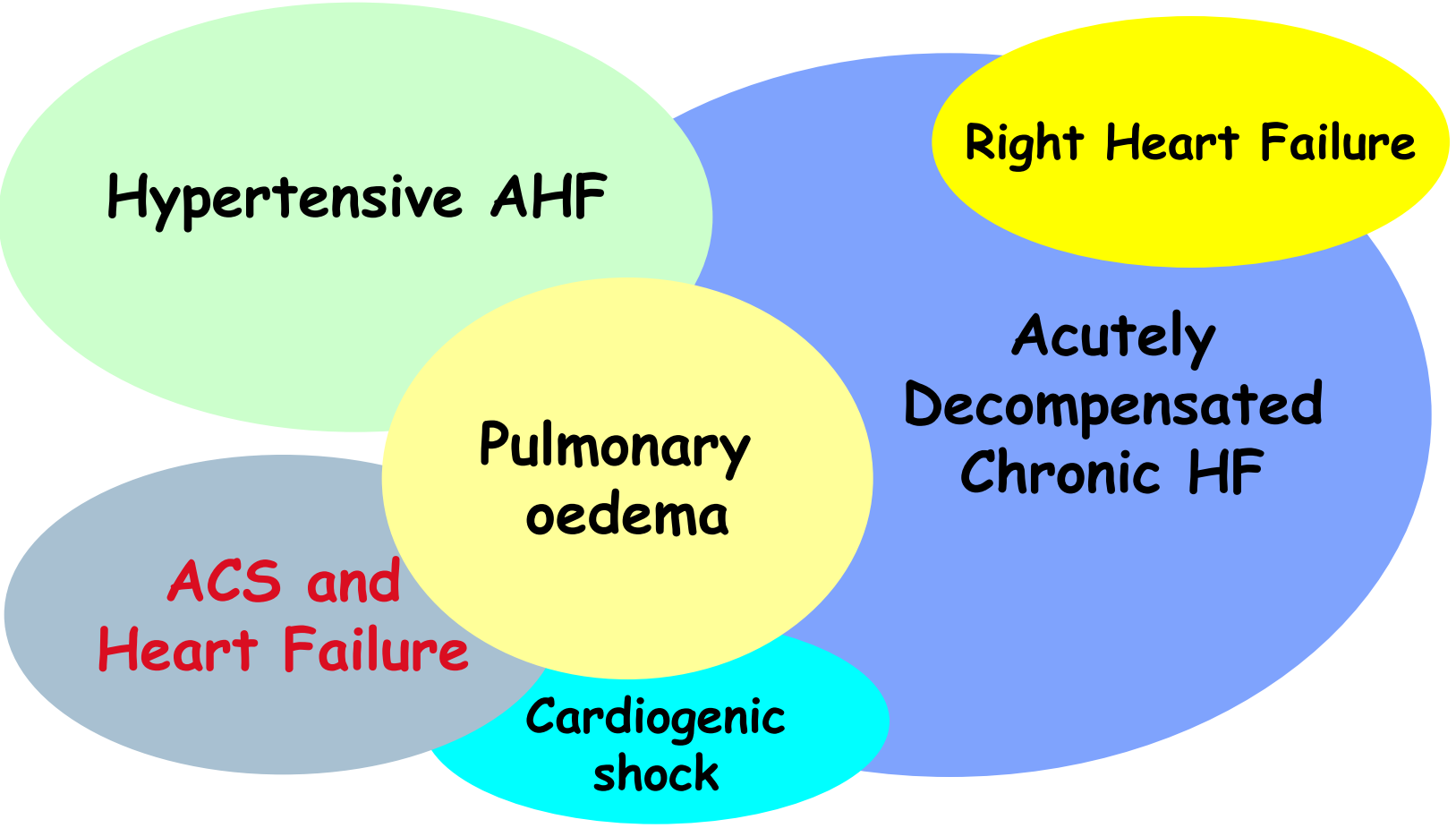
- General CRS definition:

  '*Pathophysiologic disorder of the heart and kidneys whereby acute or chronic dysfunction in one organ induces acute or chronic dysfunction in the other*'[1]

CRS Type I (Acute Cardiorenal Syndrome) *Abrupt worsening of cardiac function leading to acute kidney injury*
CRS Type II (Chronic Cardiorenal Syndrome) *Chronic abnormalities in cardiac function (e.g. chronic congestive heart failure) causing progressive and permanent chronic kidney disease*
CRS Type III (Acute Renocardiac Syndrome) *Abrupt worsening of renal function (e.g. acute kidney ischaemia or glomerulonephritis) causing acute cardiac disorders (e.g. heart failure, arrhythmia, ischemia)*
CRS Type IV (Chronic Renocardiac Syndrome) *Chronic kidney disease (e.g. chronic glomerular disease) contributing to decreased cardiac function, cardiac hypertrophy and/or increased risk of adverse cardiovascular events*
CRS Type V (Secondary Cardiorenal Syndrome) *Systemic condition (e.g. DM, sepsis) causing both cardiac and renal dysfunction*

1. Ronco C et al. *Eur Heart J* 2009;Dec 25 [epub ahead of print]

Classification of Acute Heart Failure



ESC Guidelines 2008

Euro Heart Survey Programme

ESC Quality Assurance Programme to Improve Cardiac Care in Europe

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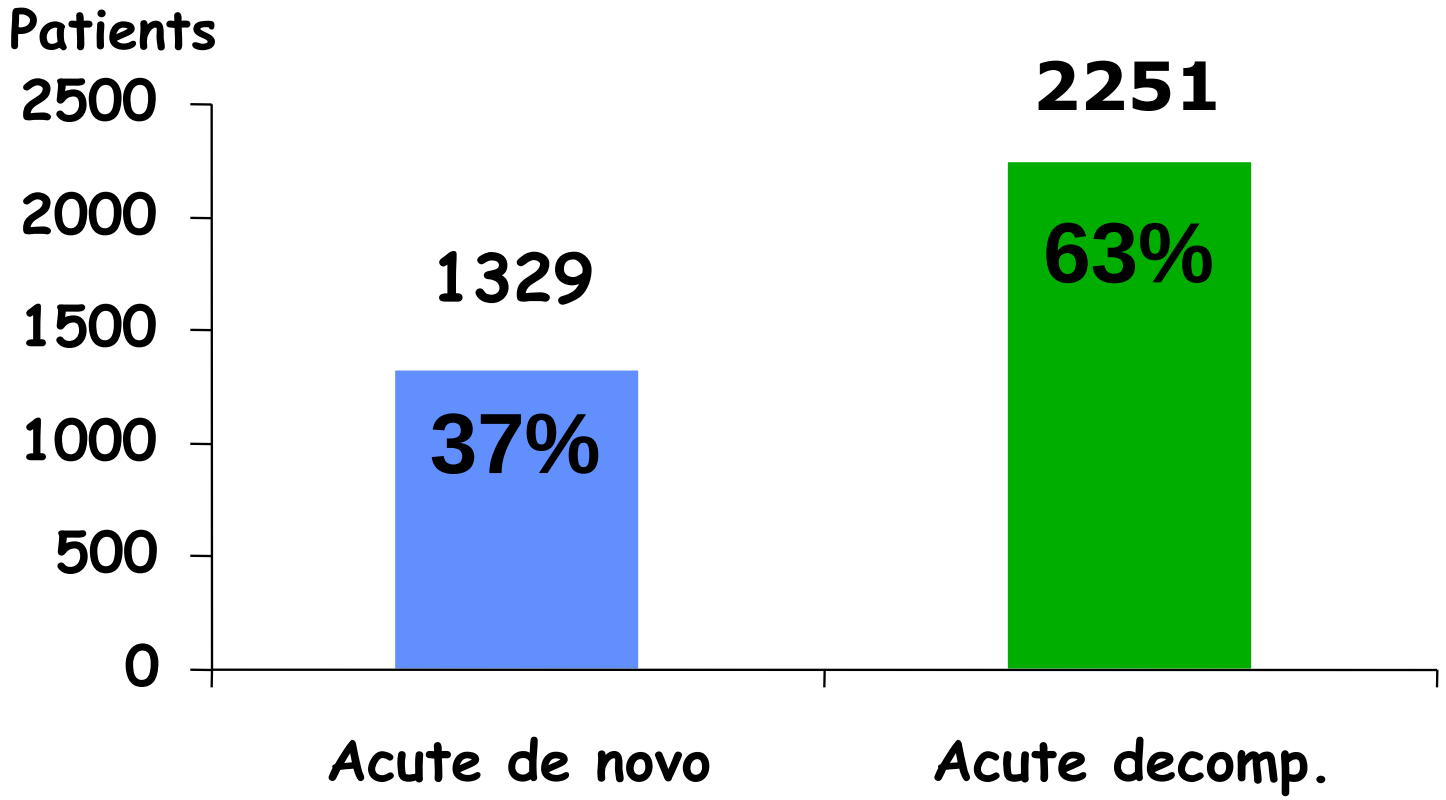
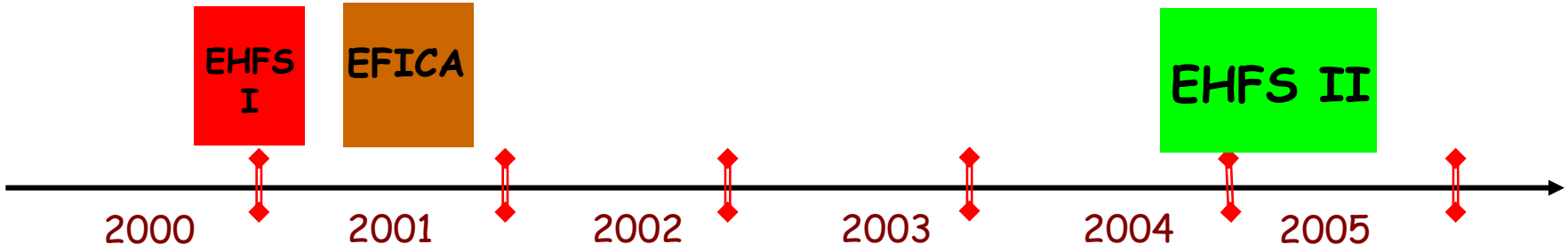
HF II - *Type of Heart Failure*

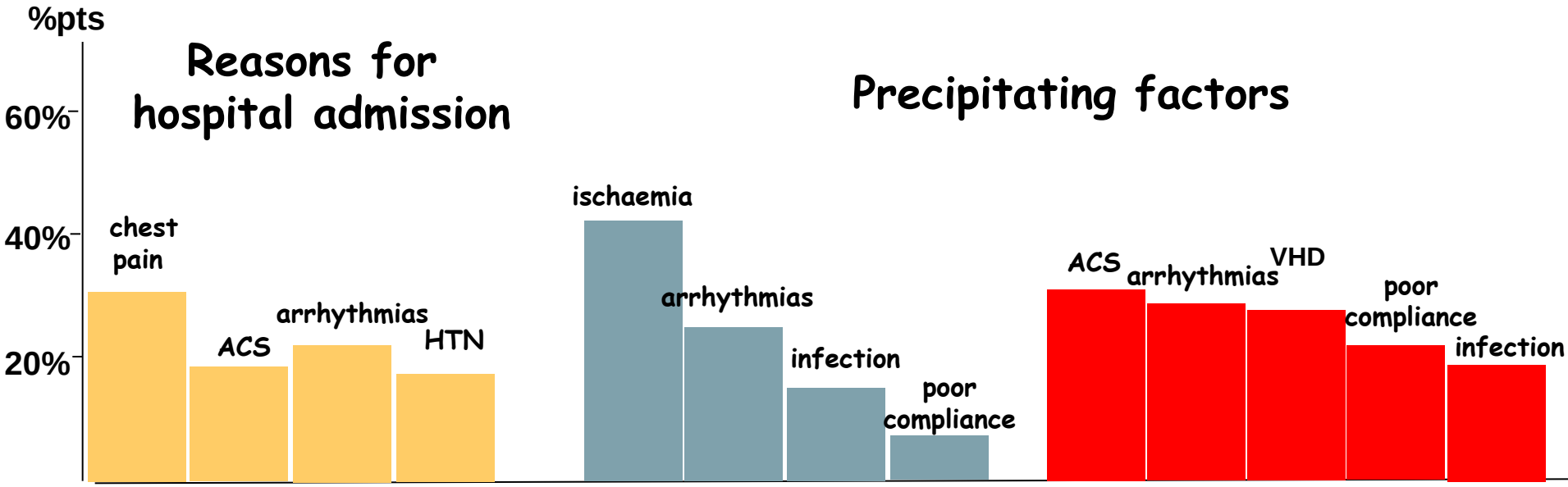
n=3580



EUROPEAN SOCIETY OF CARDIOLOGY®

Acute Heart Failure: European perspective





EHFS I

EFICA

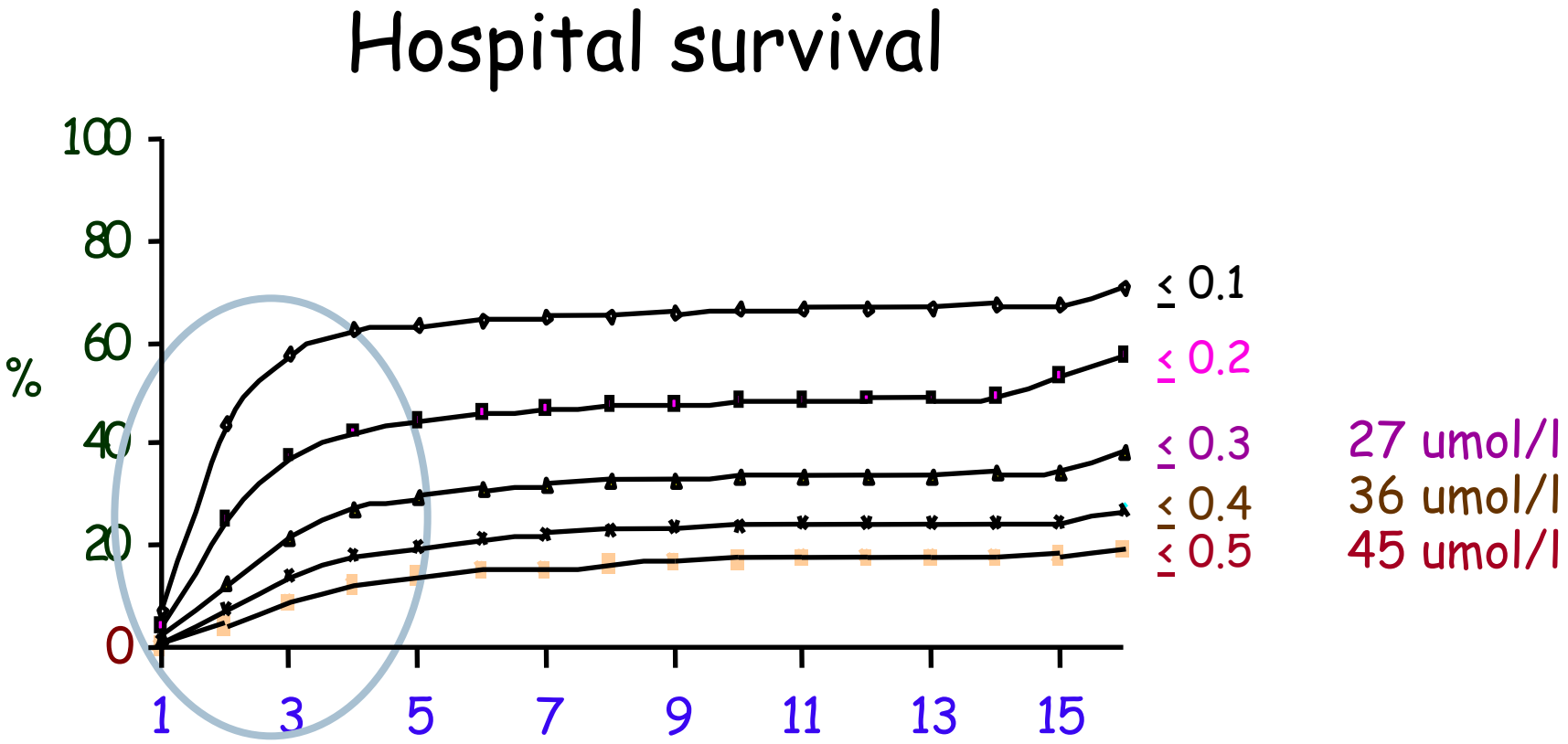
EHFS II

Cleland et al., EHJ 2002

Zannad et al., EJHF 2006

Nieminen et al., 2006

Change in Se creatinine during Rx for acute decompensated HF

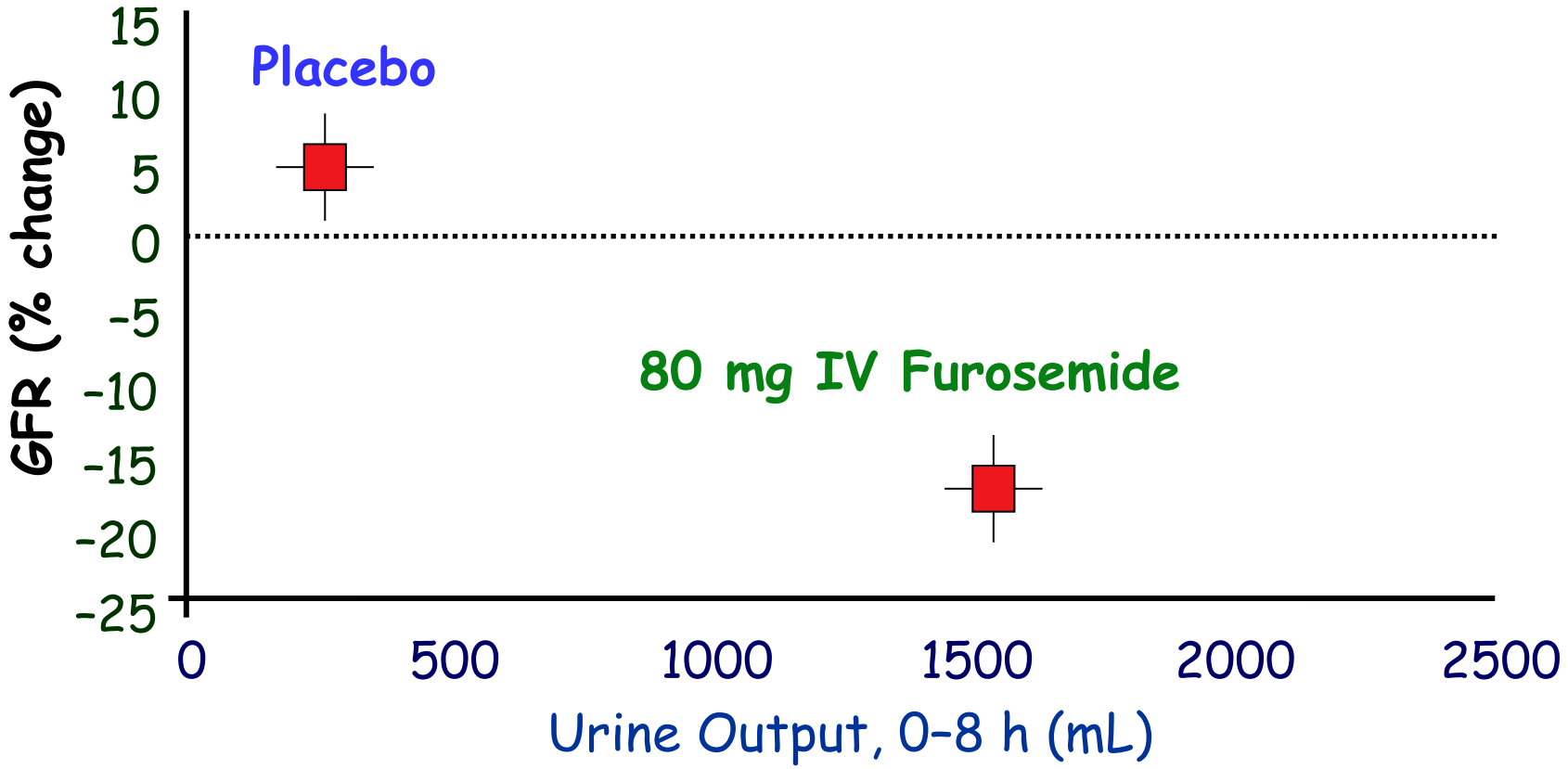


From Gottlieb et al. J Card Fail 2003.

Medical management heart failure

- diuretics
- vasodilators
- β-blockers
- ACEI/ARBs

Diuretics decrease GFR

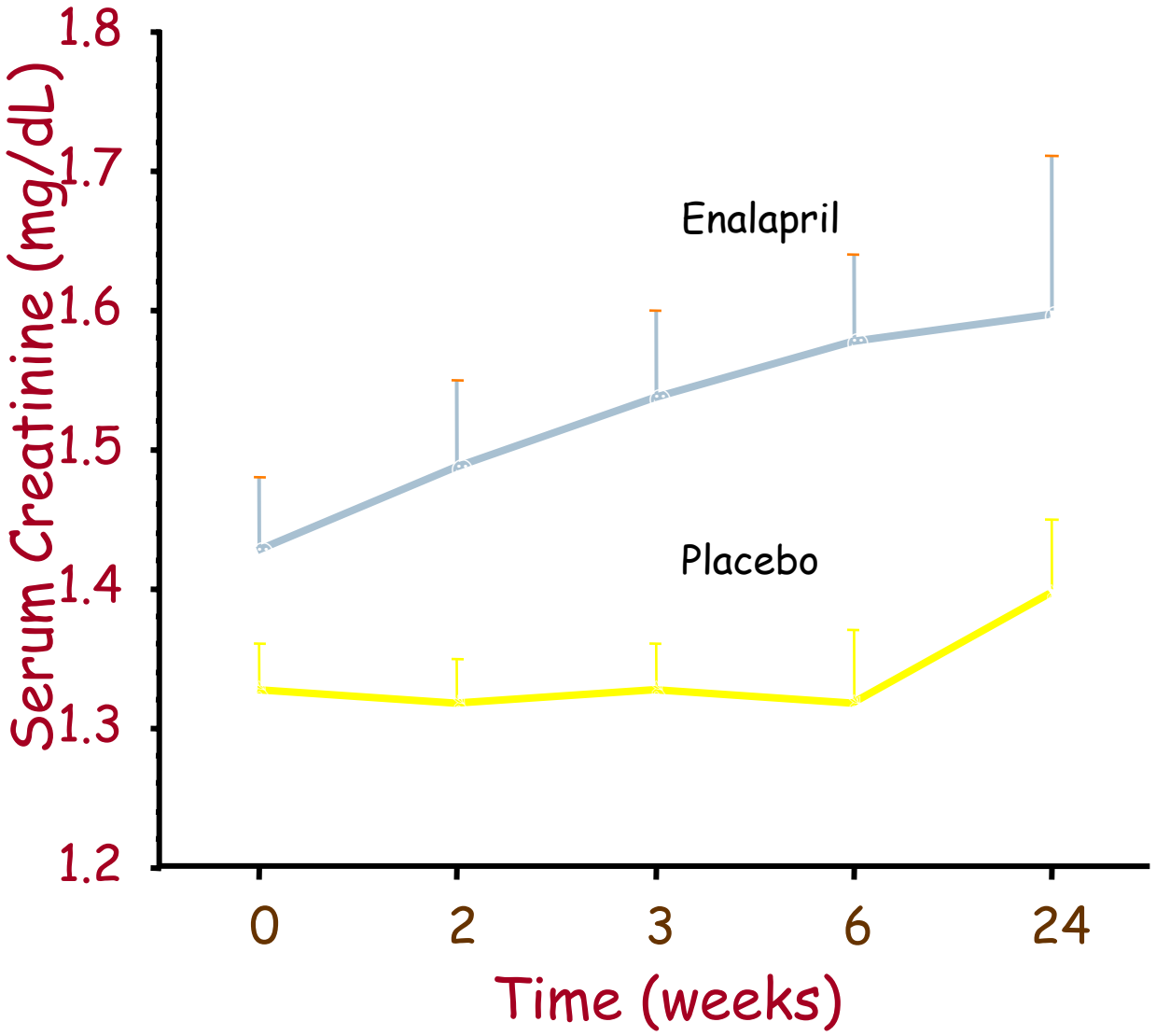


N = 16; NYHA II (19%) and III (81%);
mean baseline creatinine clearance, 108 ± 51 μg/mL.
*GFR was estimated using a 7-hour creatinine clearance.

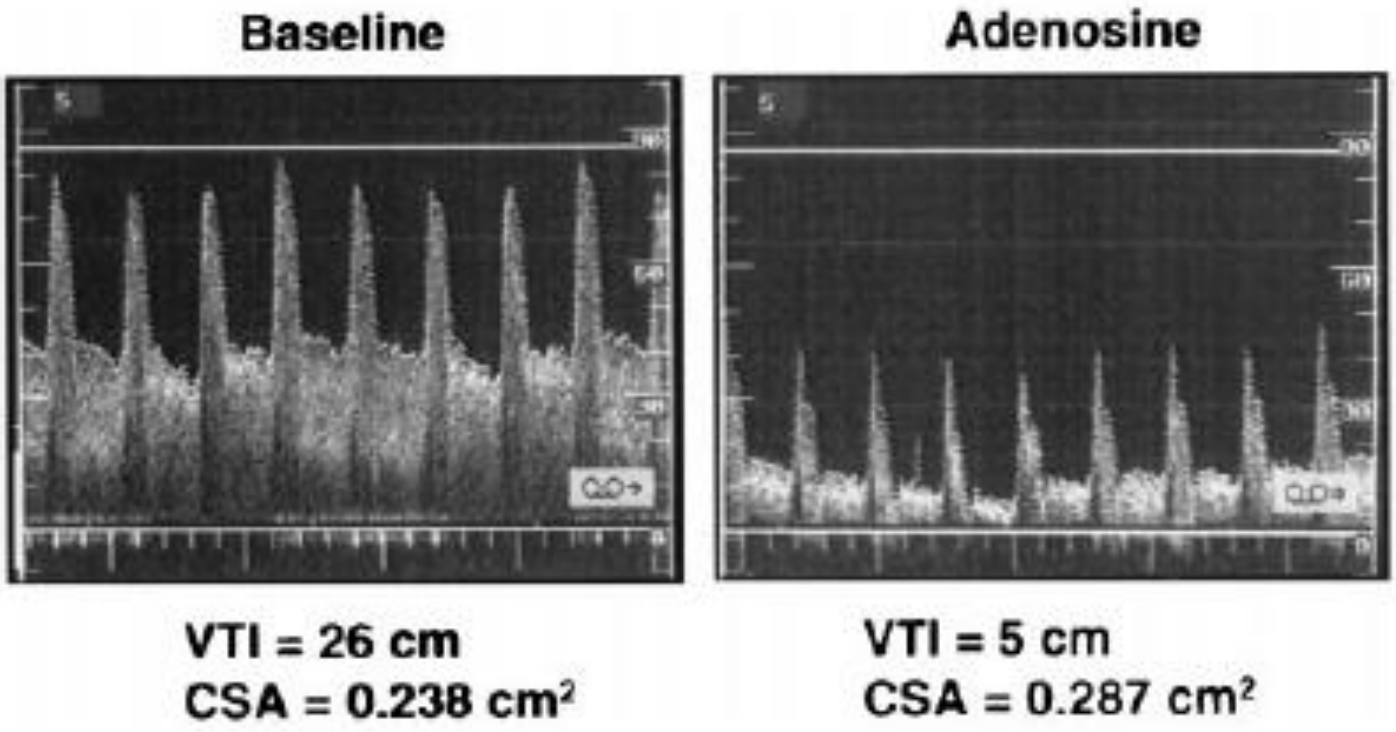
Gottlieb SS et al. *Circulation.* 2002;105:1348–1353.

Consenus trial: effect of ACEI

Ljungman et al Am J Cardiol 1992;70:479-87.



Adenosine decreases renal blood flow in patients with HF

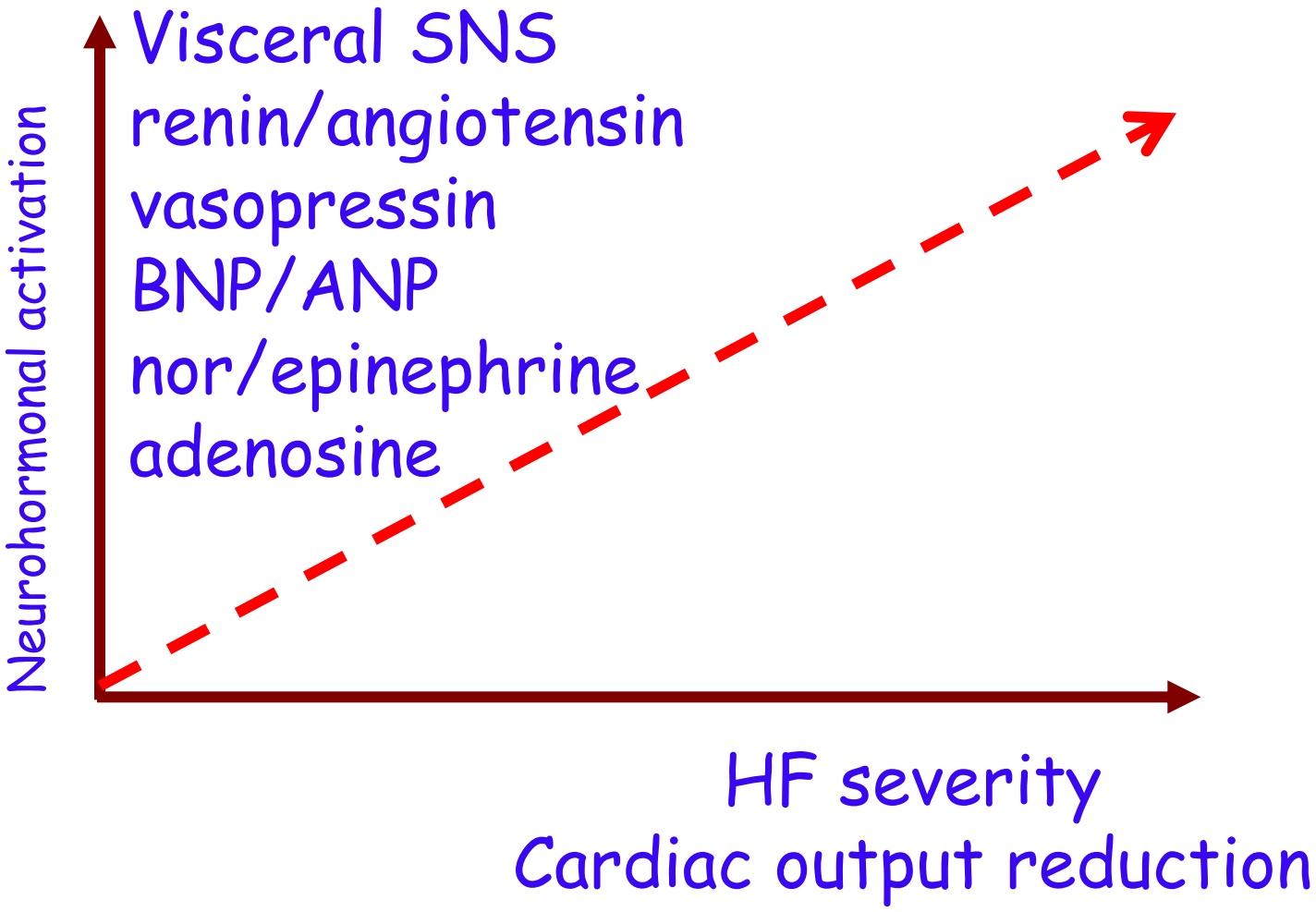


Elkayam et al., J Am Coll Cardiol 1998;32:211

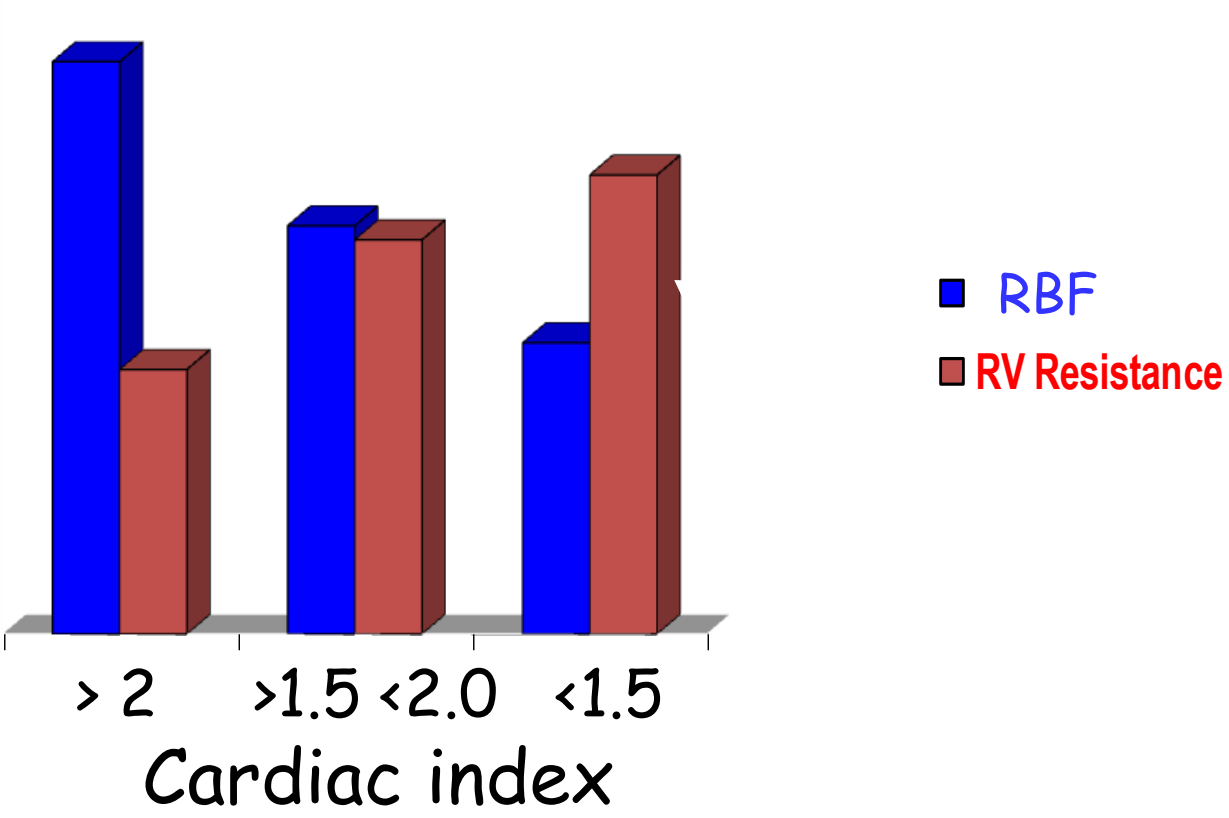
Why does heart failure affect renal function ?

- renal blood flow

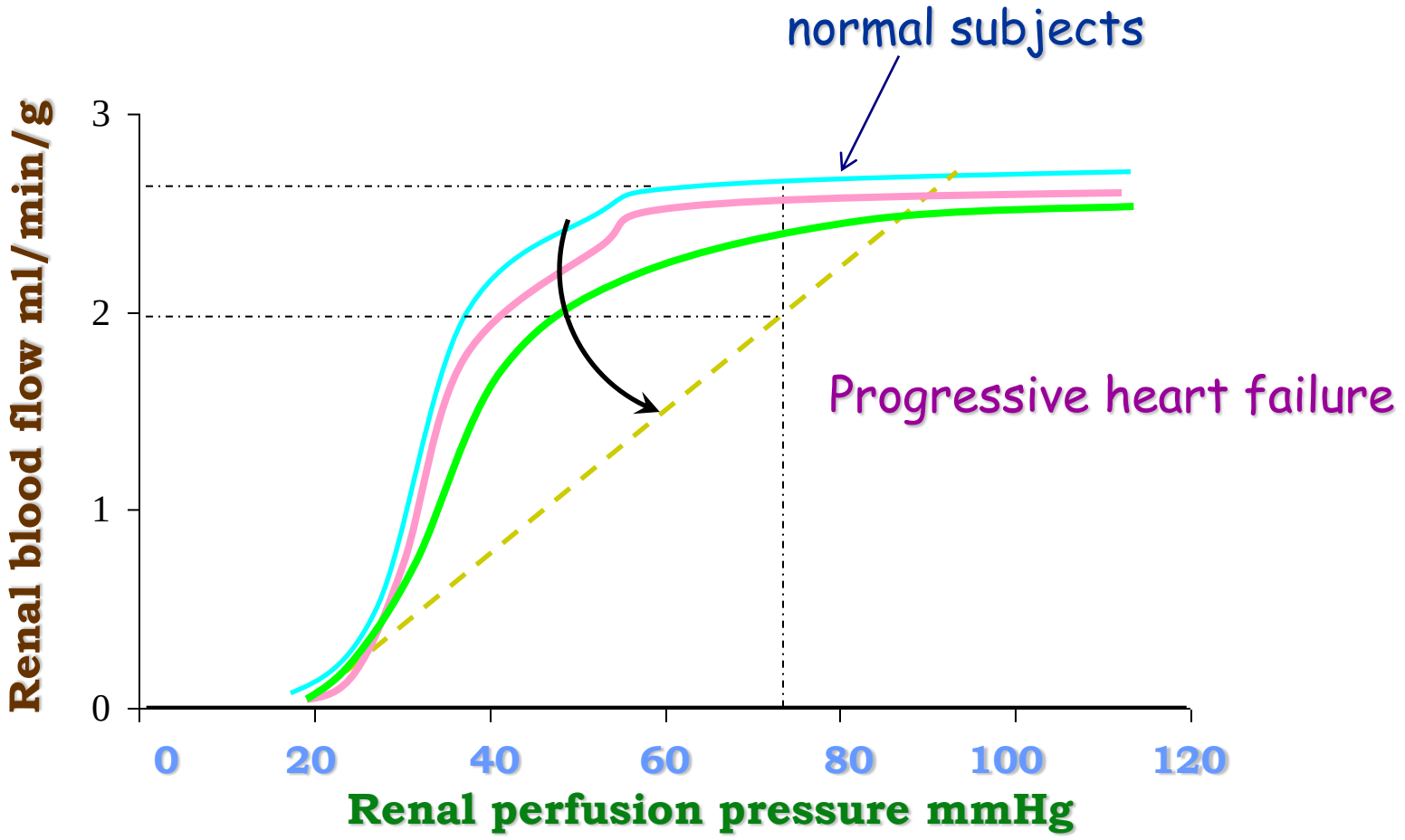
Neurohormonal activation in CHF



Change in Renal blood flow & vascular resistance

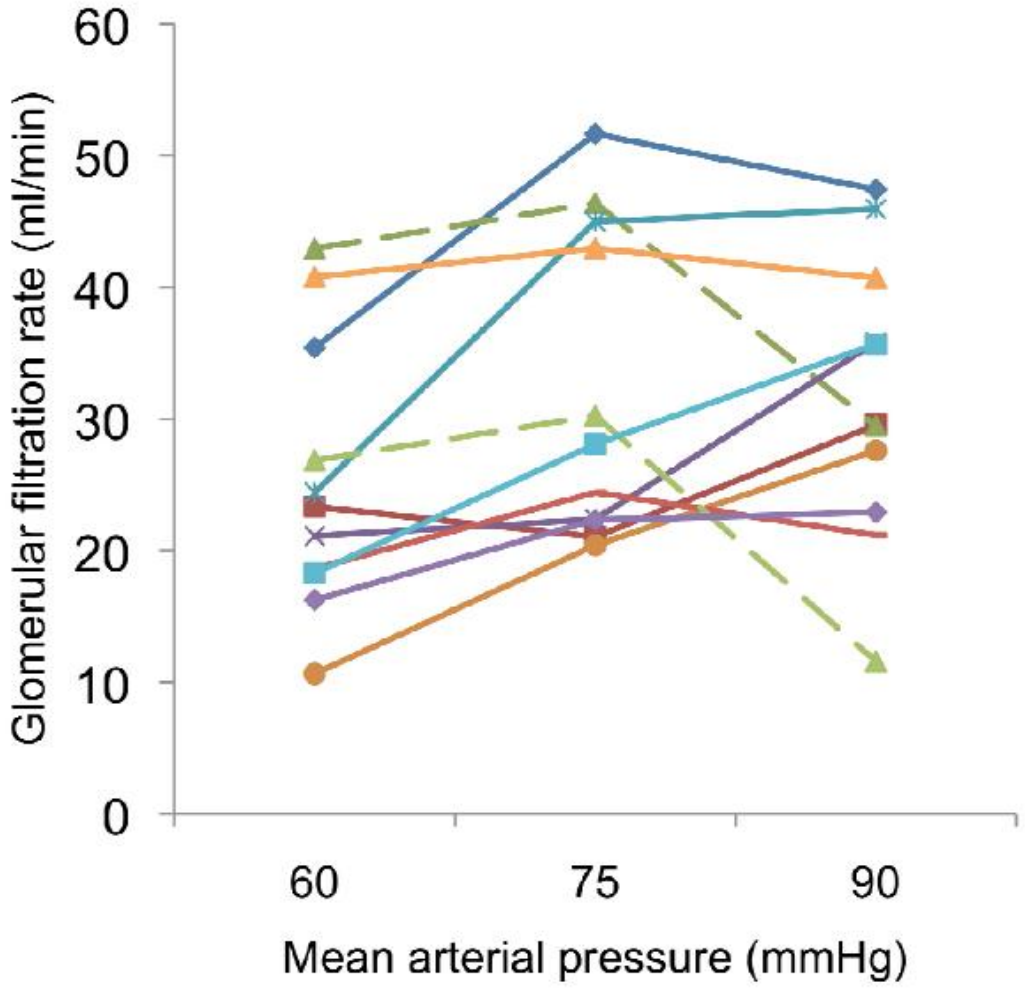


Cardio-renal syndrome



Critical renal perfusion pressure ?

Redfors et al IntensivCareMed i2011



Post cardiac surgery
renal blood flow
^{51}Cr-EDTA
NAdr

EFFECTS OF DECREASE CARDIAC OUTPUT ON RENAL VEIN PRESSURE AND GFR

DECREASED CARDIAC OUTPUT

INCREASED RIGHT ATRIAL PRESSURE

INCREASED CENTRAL VENOUS PRESSURE

INCREASED INFERIOR VENA CAVA PRESSURE

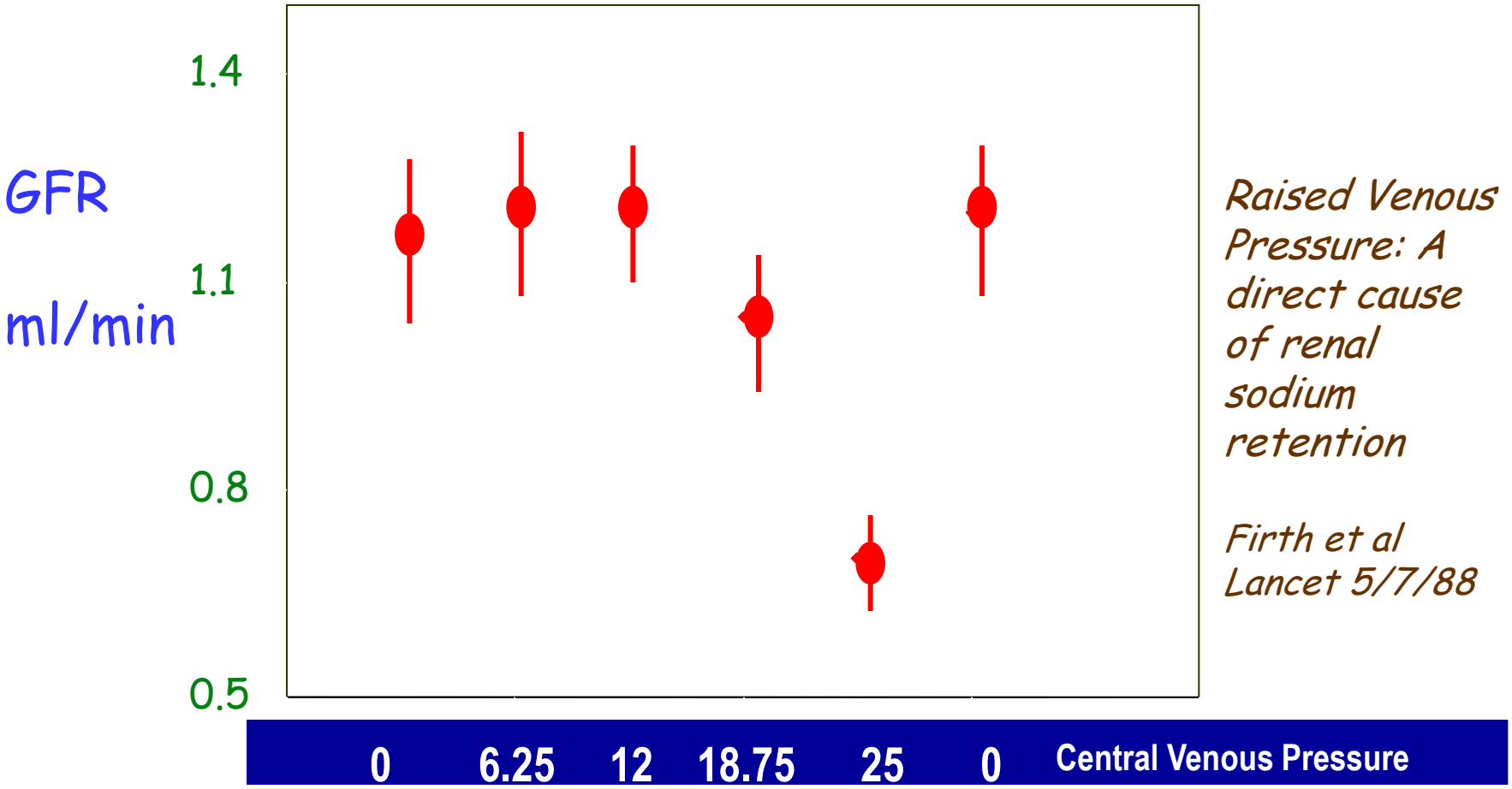
INCREASED RENAL VEIN PRESSURE

INCREASED GLOMERULAR CONGESTION

DECREASED RENAL BLOOD FLOW

DECREASED GFR

Effect of increasing central venous pressure on GFR in dogs, constant BP

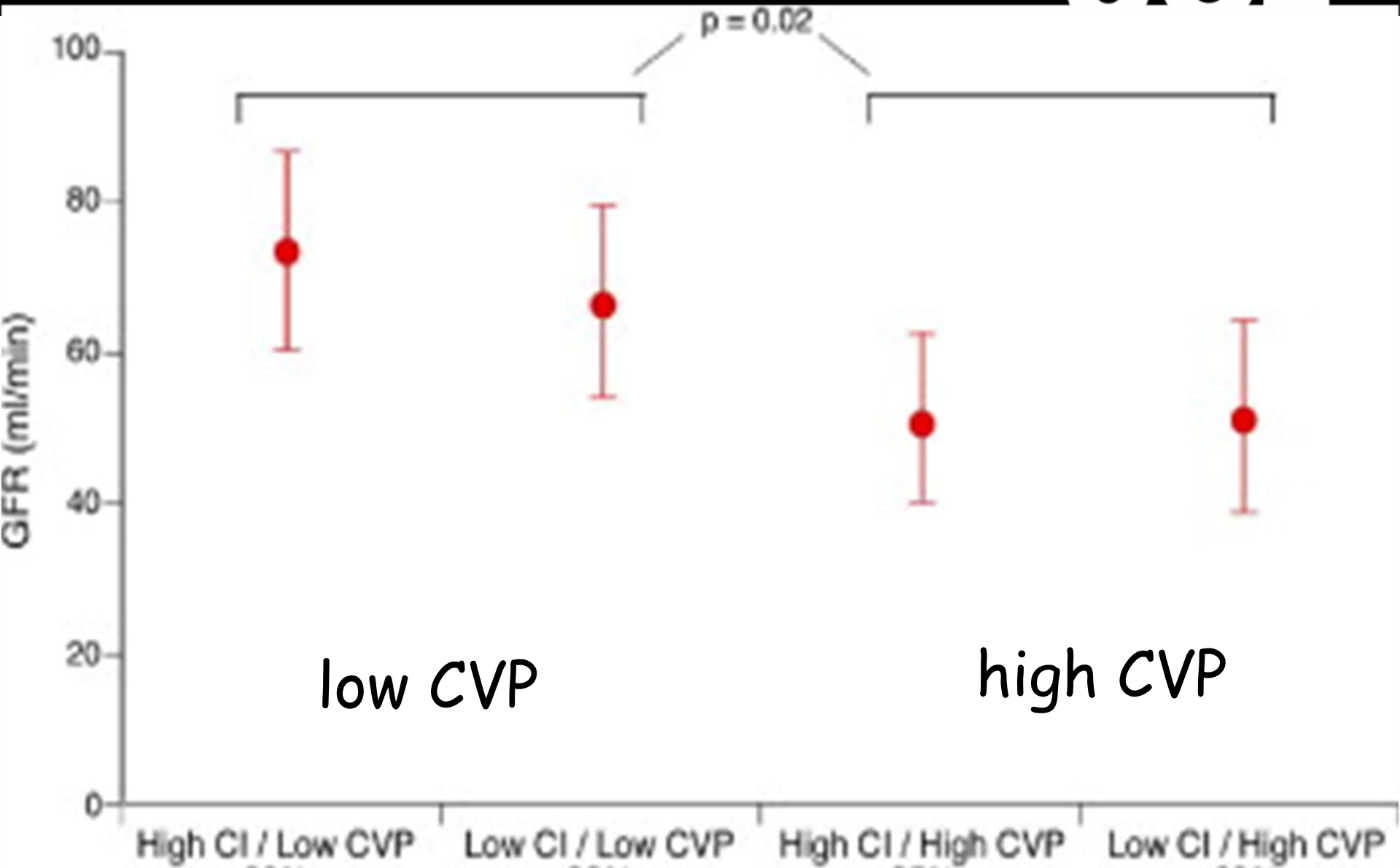


Raised Venous Pressure: A direct cause of renal sodium retention

Firth et al Lancet 5/7/88

Relative Contributions of CVP and CI to GFR

Mullens et al.JACC. 53(7) 2009



Intra-abdominal hypertension

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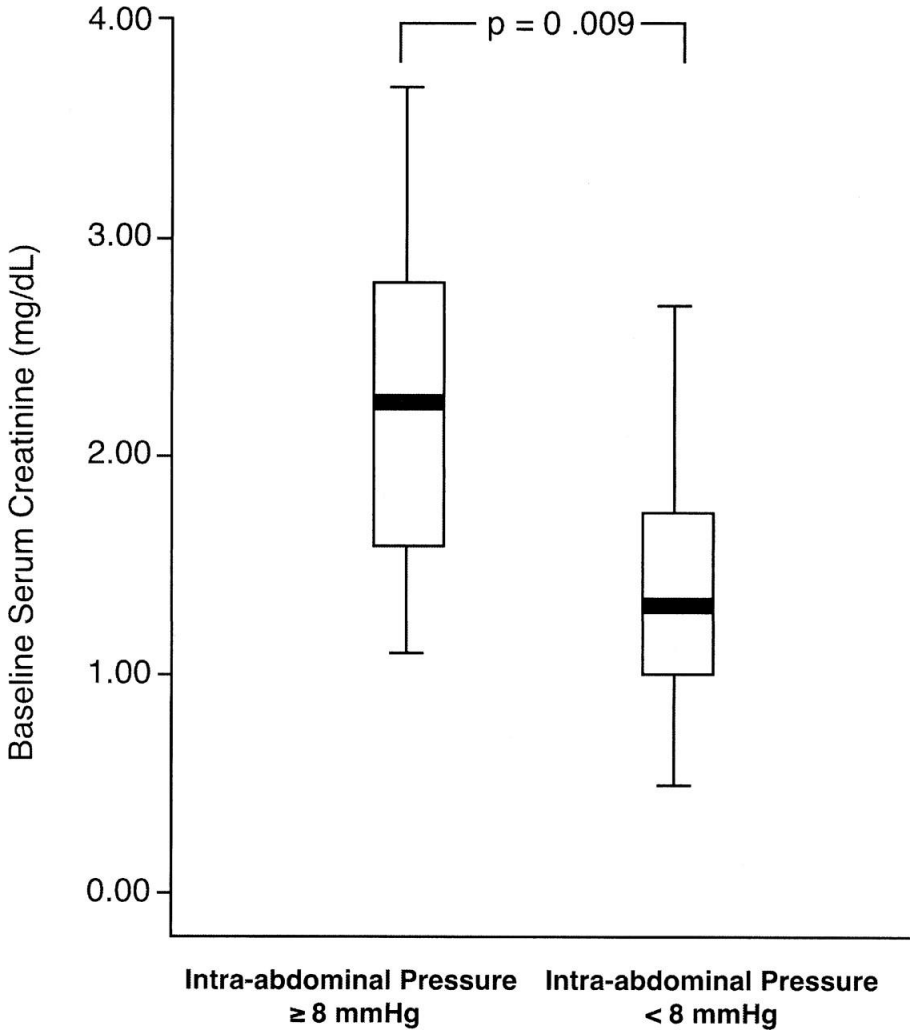
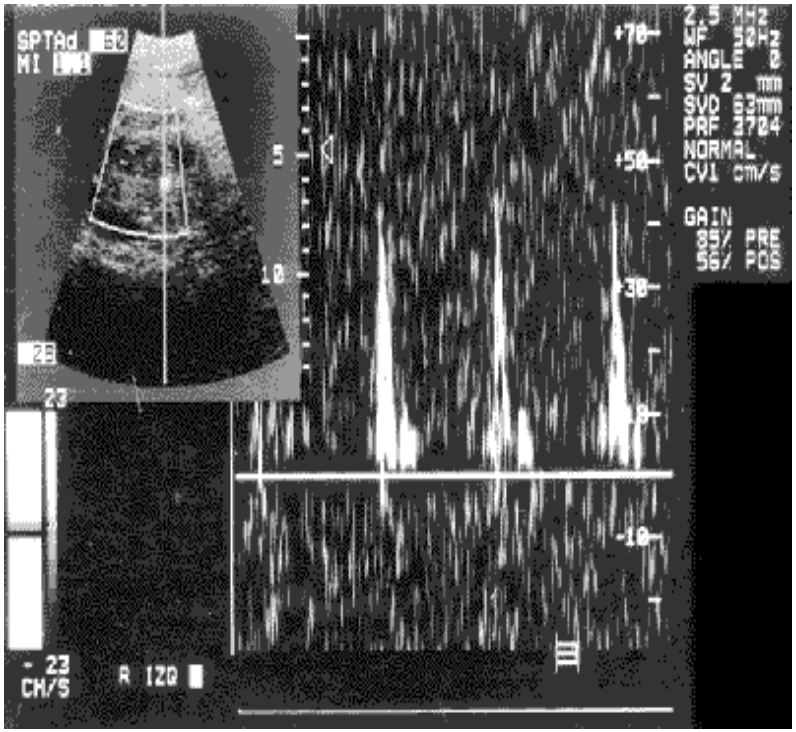
Intra-abdominal compartment syndrome

- assumptions
  - IAH > 25 mmHg
  - but AKI reported with IAP 12

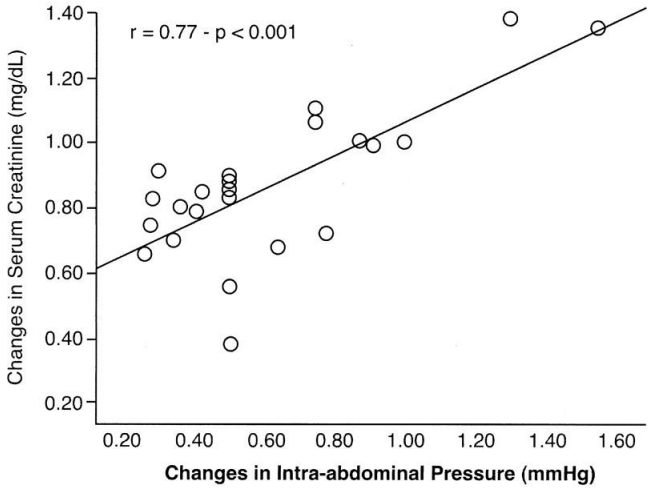
Baseline Serum Creatinine Level and IAP

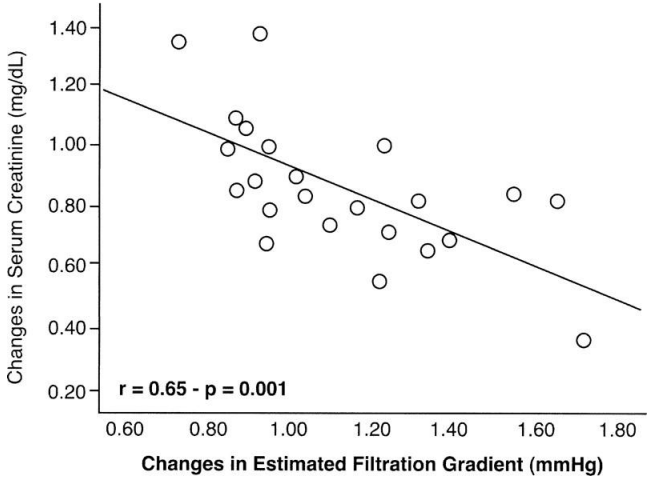
Mullens et al. J Am Coll Cardiol 2008





Changes in Renal Parameters and Changes in IAP





Filtration gdt

Bowel Wall Thickness in CHF Patients Compared With Control Subjects

Sandek et al. J Am Coll Cardiol. 2007

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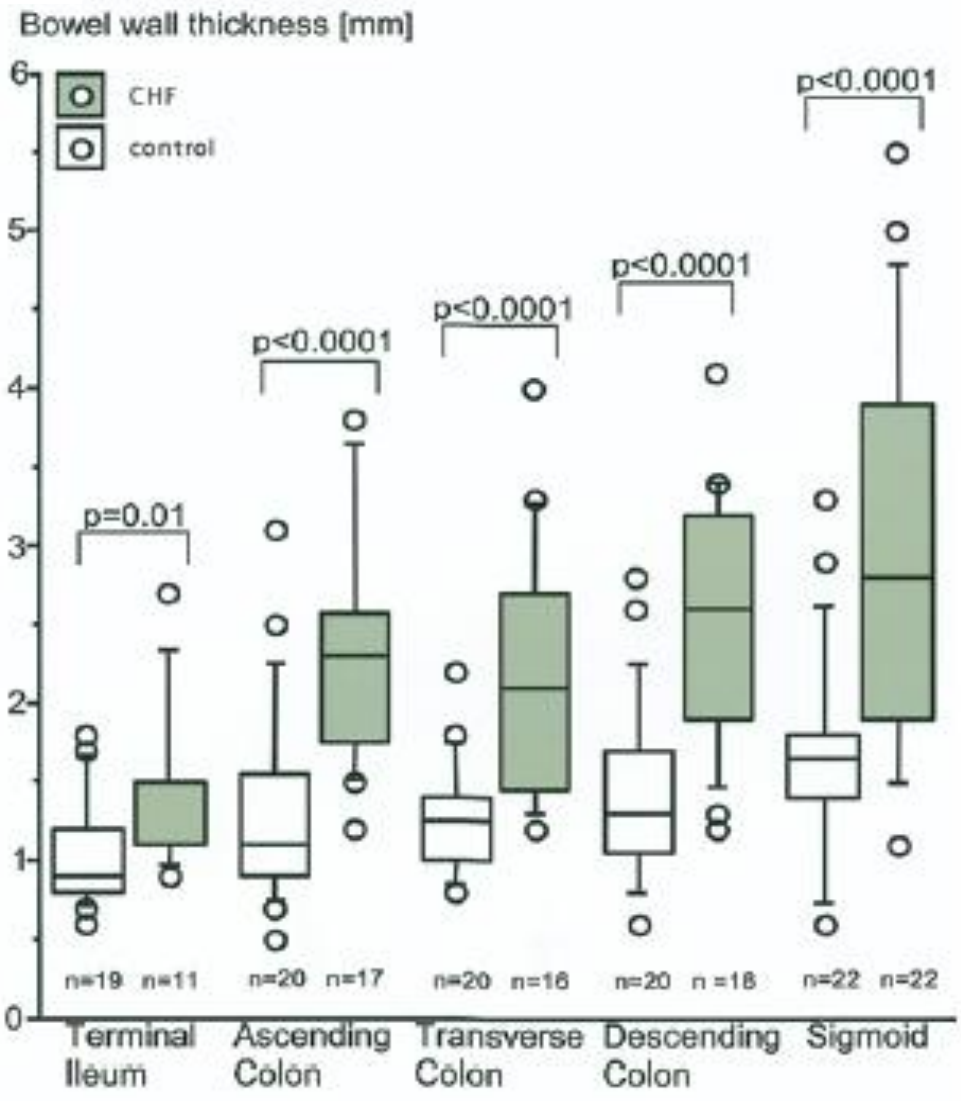
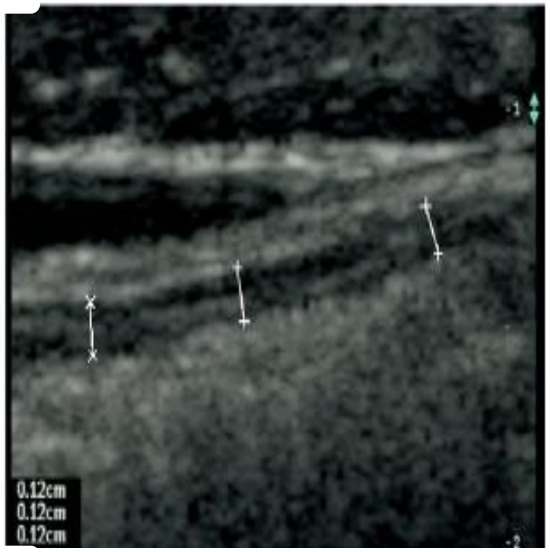
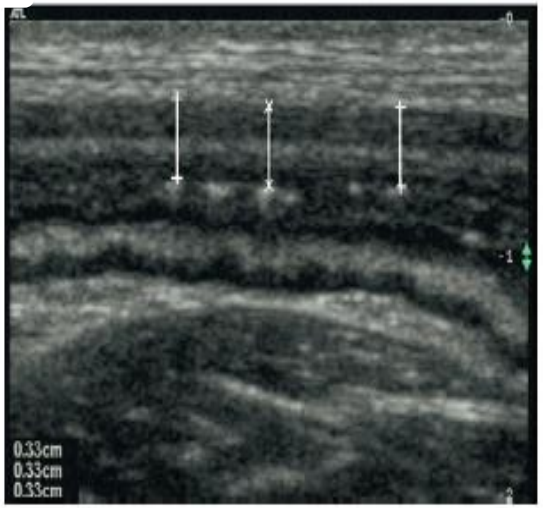




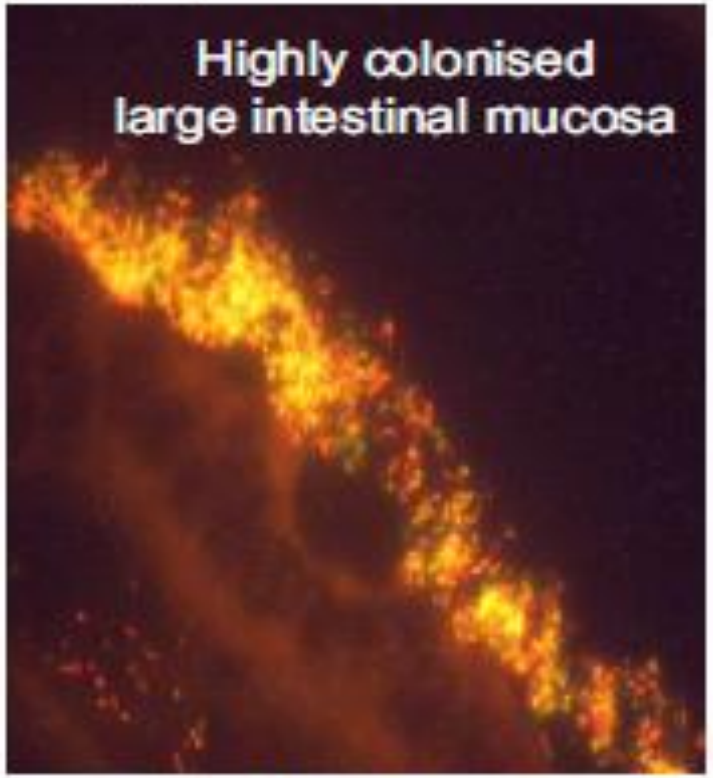


Sandek, et al. J Am Coll Cardiol. 2007

UCL

Digital fluorescence pictures showing a higher concentration of bacteria in the mucosal biofilm of the sigmoid as assessed by FISH

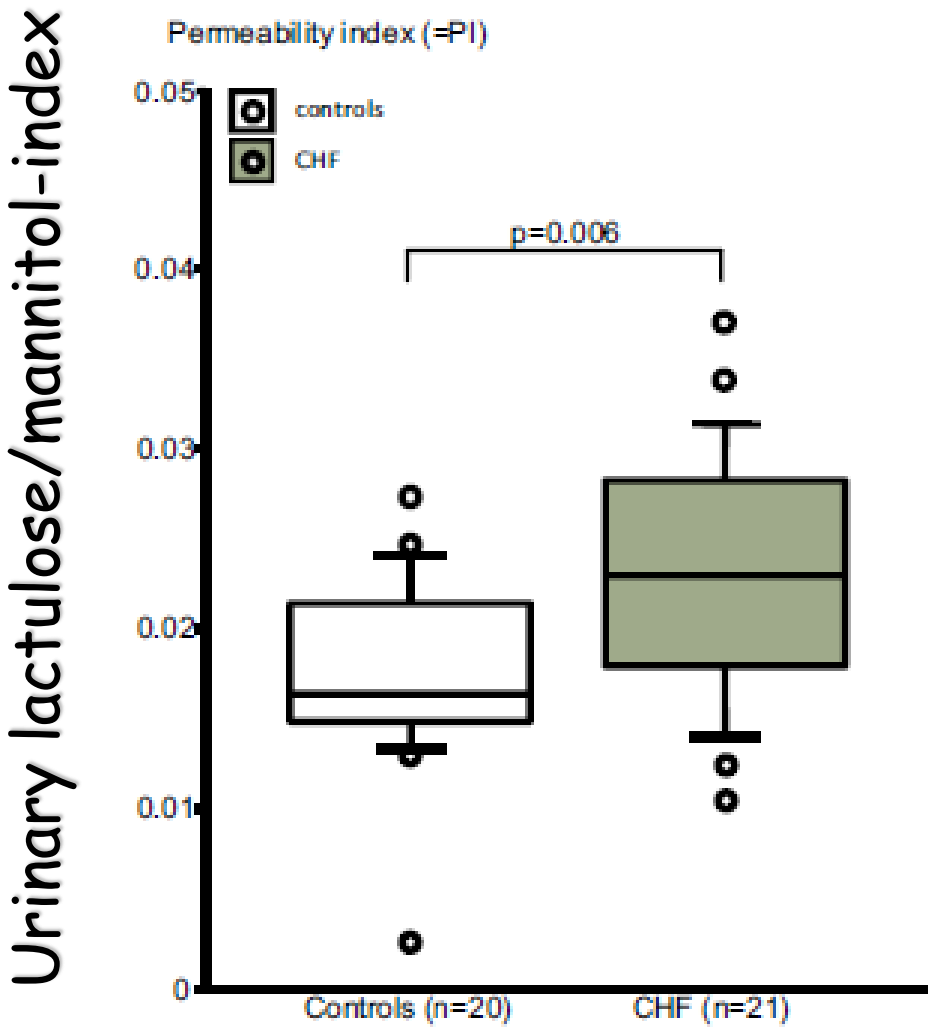
Control subject



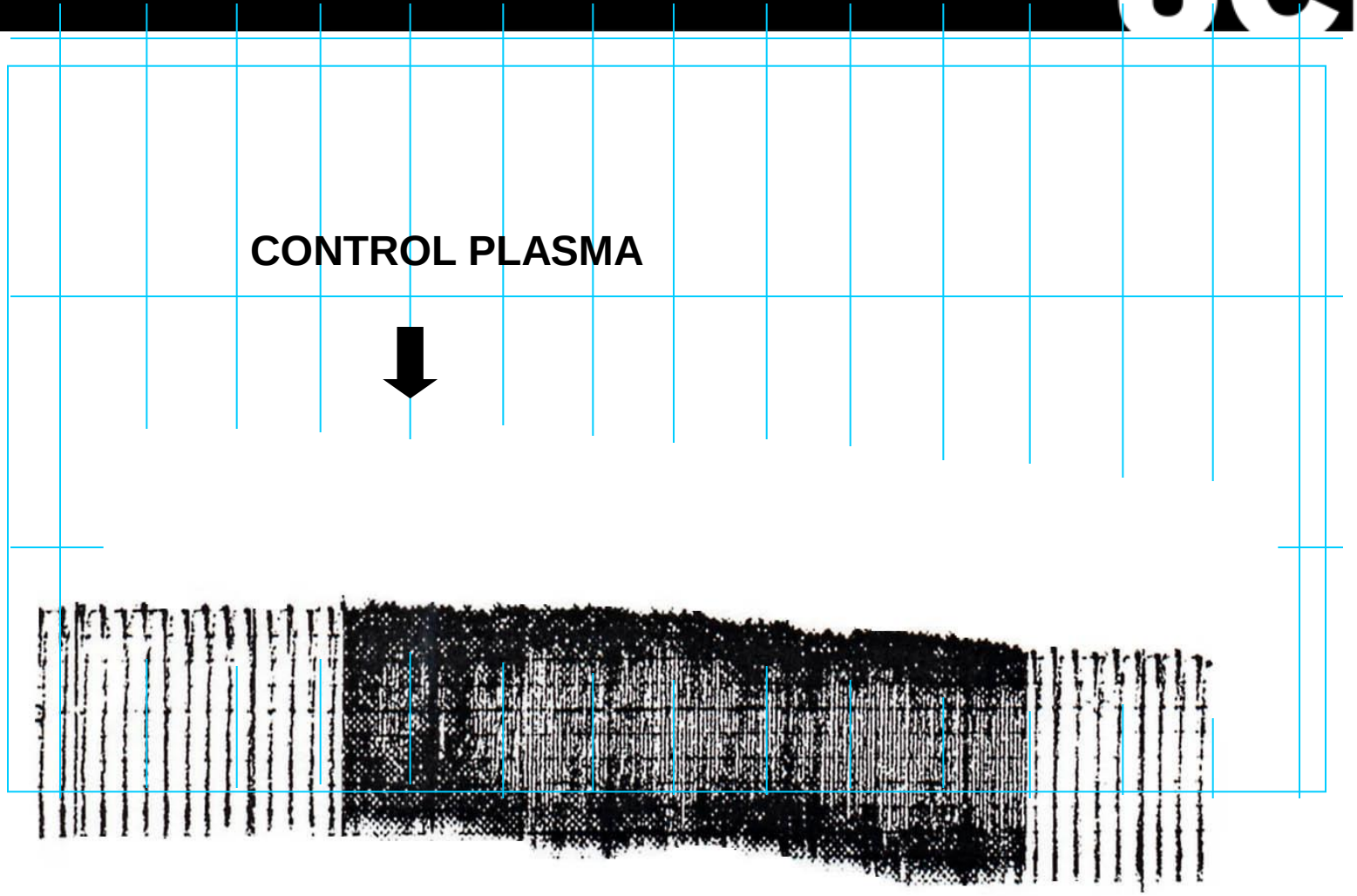
CHF patient

INCREASED PERMEABILITY OF THE GUT MUCOSA

Sandek, et al. J Am Coll Cardiol. 2007

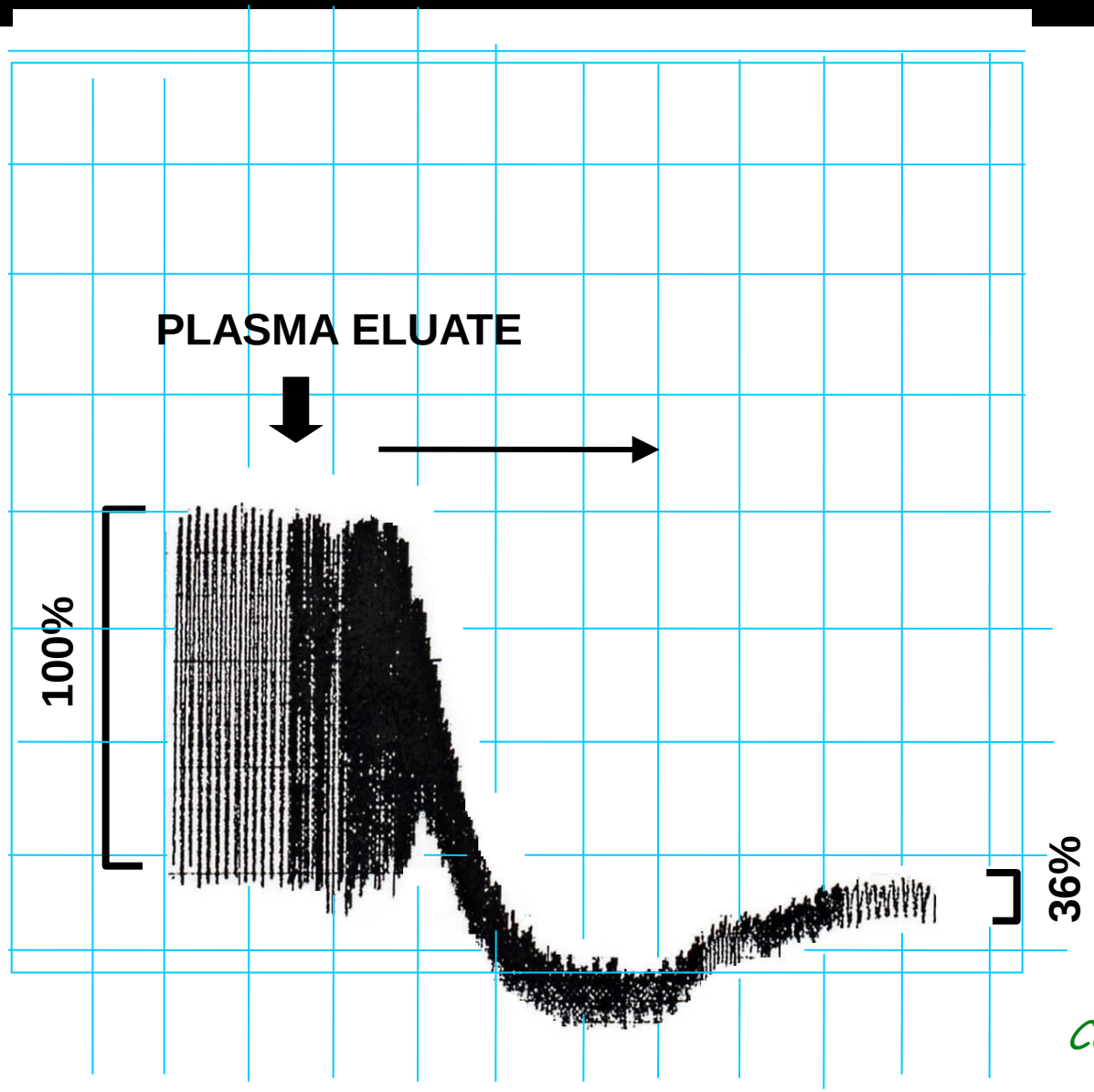


Isolated heart



Coraim et al, New Horizons 1995;3:725

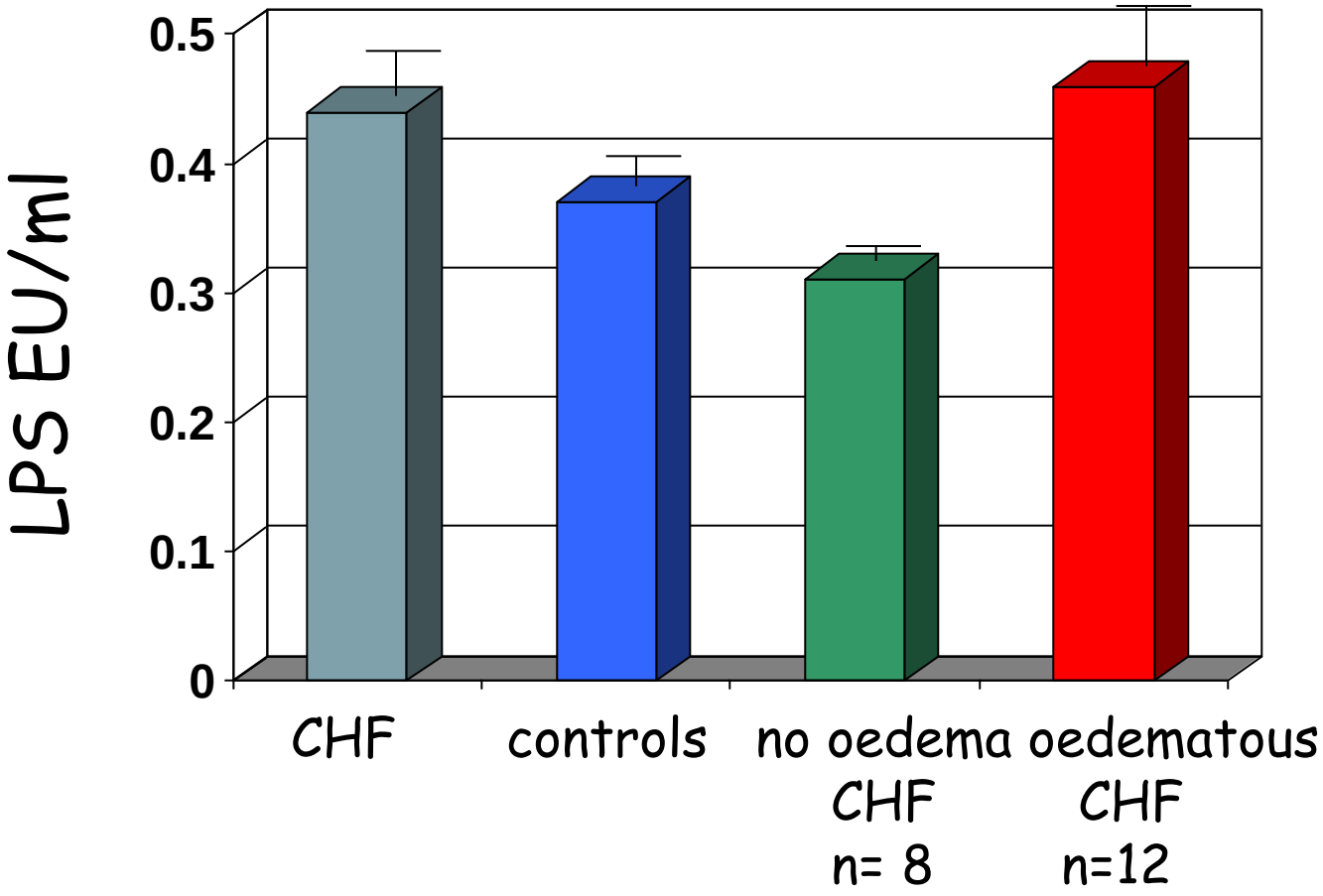
Isolated heart



circulating
cardiac
depressant factor

Coraim et al, New Horizons 1995;

Endotoxin in heart failure



What can the kidney doctor offer ?

Limitations of Diuretic Therapy in CHF

- **Diuretic therapy has been associated with worsening renal function**
  - Increase in morbidity and mortality risk
- **Electrolyte depletion**
  - predisposes to ventricular arrhythmias
- **Diuretic resistance**
  - 33% of patients with advanced CHF (*Ravnan et al. Congest Heart Fail 2002*)
- **Additional activation of the neurohormonal axis (RAAS)**
  - Systemic vasoconstriction
  - Fluid retention
  - progression of CHF?

Water and Salt Removal in Severe Heart Failure

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- ✓ Advanced CHF:
  ~ 50 mmol of Na+ for 1 liter of urine.
- ✓ Advanced CHF treated with Furosemide:
  ~ 100 mmol of Na+ for 1 liter of urine
- ✓ Advanced CHF treated with Ultrafiltration
  ~140 mmol of Na+ for 1 liter of ultrafiltrate.

Canaud et al. Am J Kidney Dis 1996

Haemodialysis ?

UCL

- **Haemodialysis**
  - Increased risk of intra-dialytic hypotension
- **Residual renal function**
  - Increased risk of loss of residual renal function

Nephrol Dial Transplant (2005) 20 [Suppl 7]: vii32–vii36
doi:10.1093/ndt/gfh1105

Nephrology
Dialysis
Transplantation

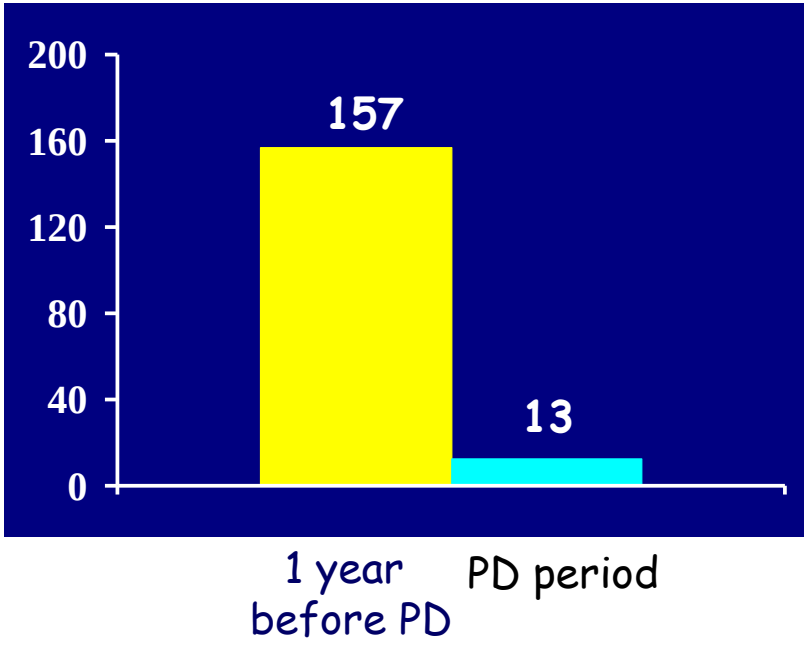
UCL

Peritoneal dialysis in refractory end-stage congestive heart failure: a challenge facing a no-win situation

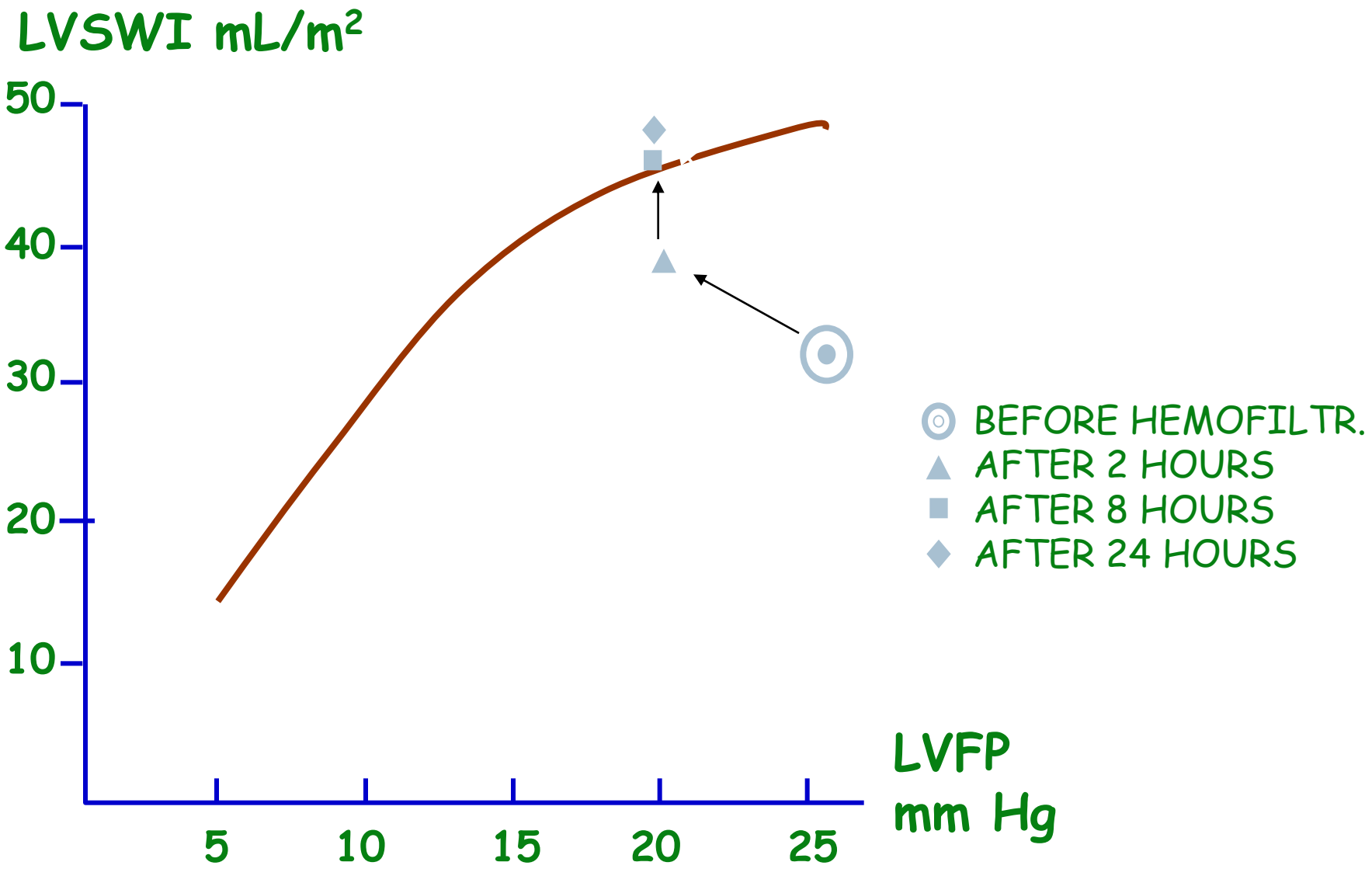
Lazaro Gotloib[1], Roberto Fudin[1], Michaela Yakubovich[2] and Joerg Vienken[2]

- 20 CHF patients (IV NYHA)
- 15 diabetics
- Cr.cl. 15±4 ml/min
- 8 hour-PD, 3 sessions/week
- mean follow-up 20 months
- 20/20 regression from NYHA class IV to I
- Patients were treated initially with CVVH

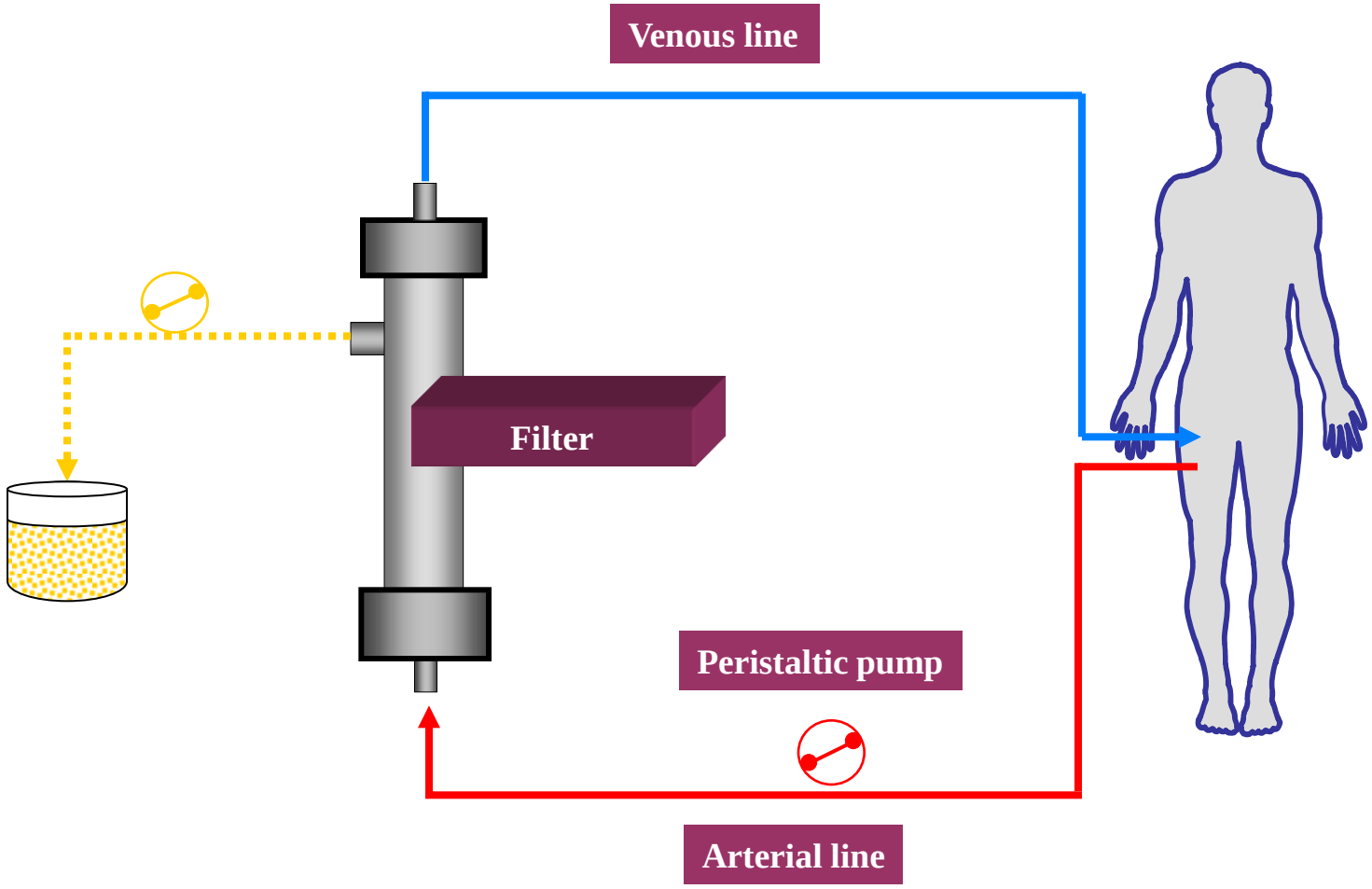
Total hospitalization days due to CHF



Coraim et al, New Horizons 1995;3:725



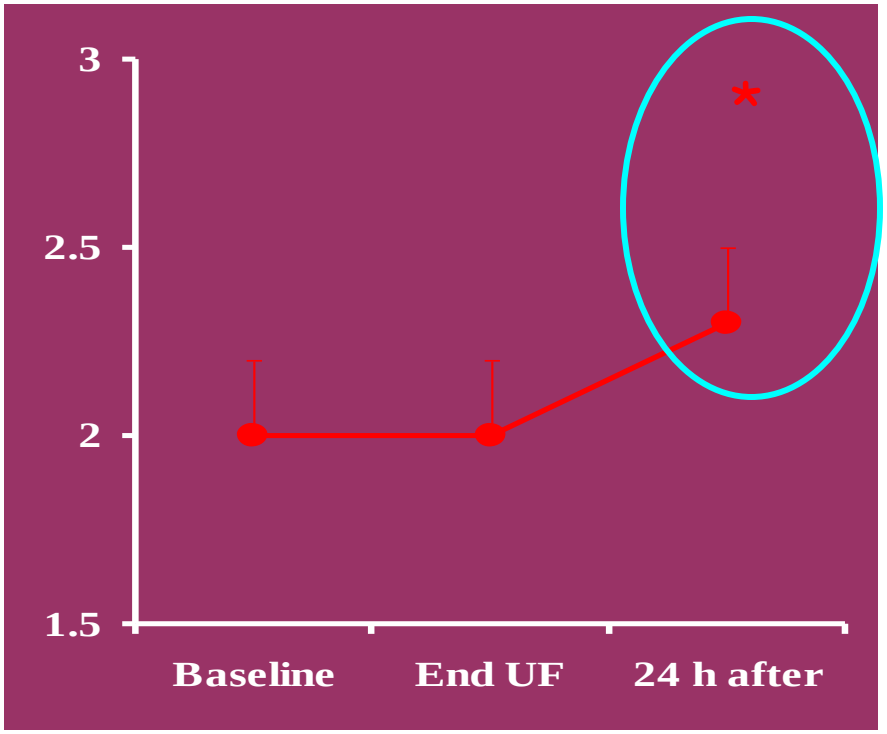
Ultrafiltration



Ultrafiltration in CHF

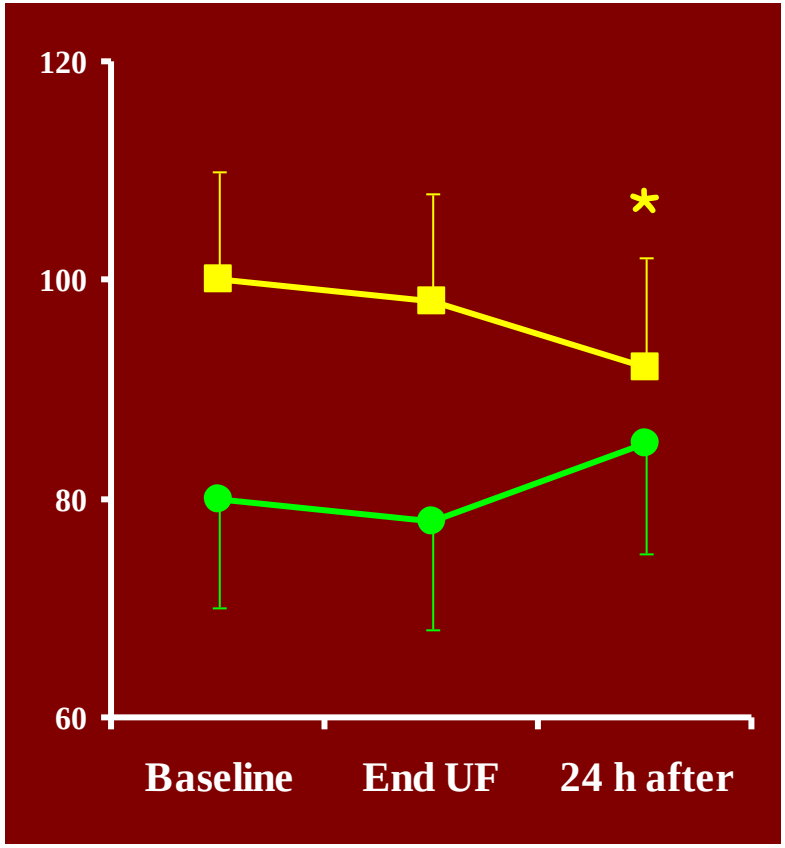
Hemodynamic Effects

L/min/m2



Cardiac Index

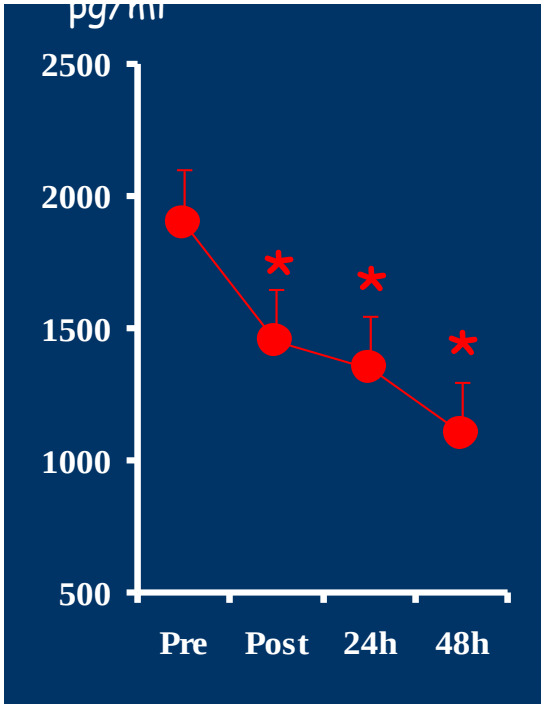
mmHg b/min



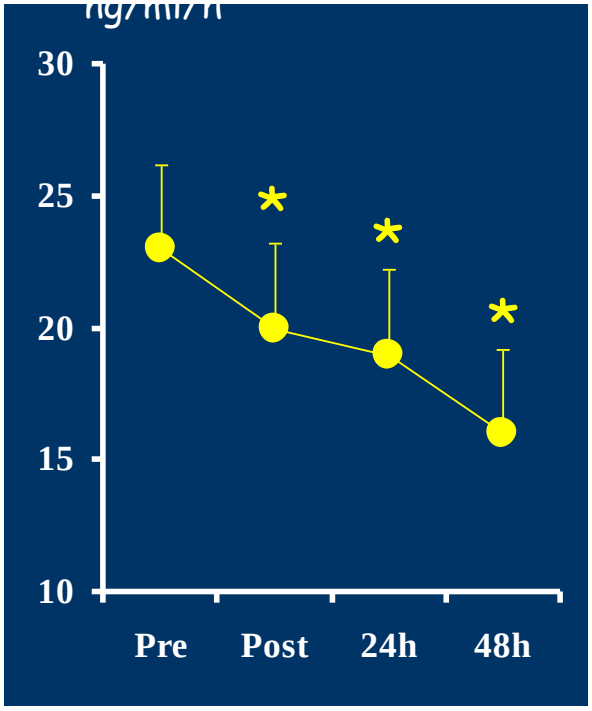
Mean arterial pressure

Heart rate

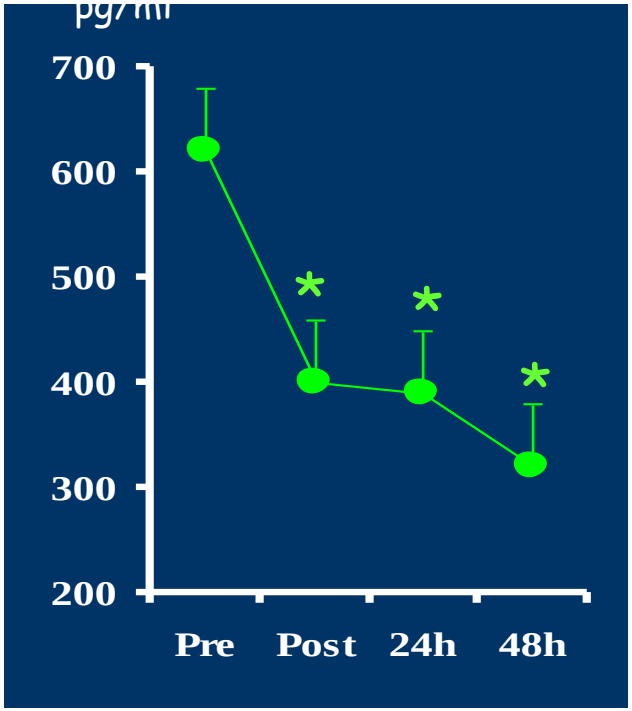
Effects of Ultrafiltration on Neurohumoral Activation in CHF



Noradrenaline



Plasma Renin Activity



Aldosterone

Guazzi et al. Br Heart J 1994

Clinical Effects of Ultrafiltration in CHF

Cipolla et al. Am J Cardiol 1990

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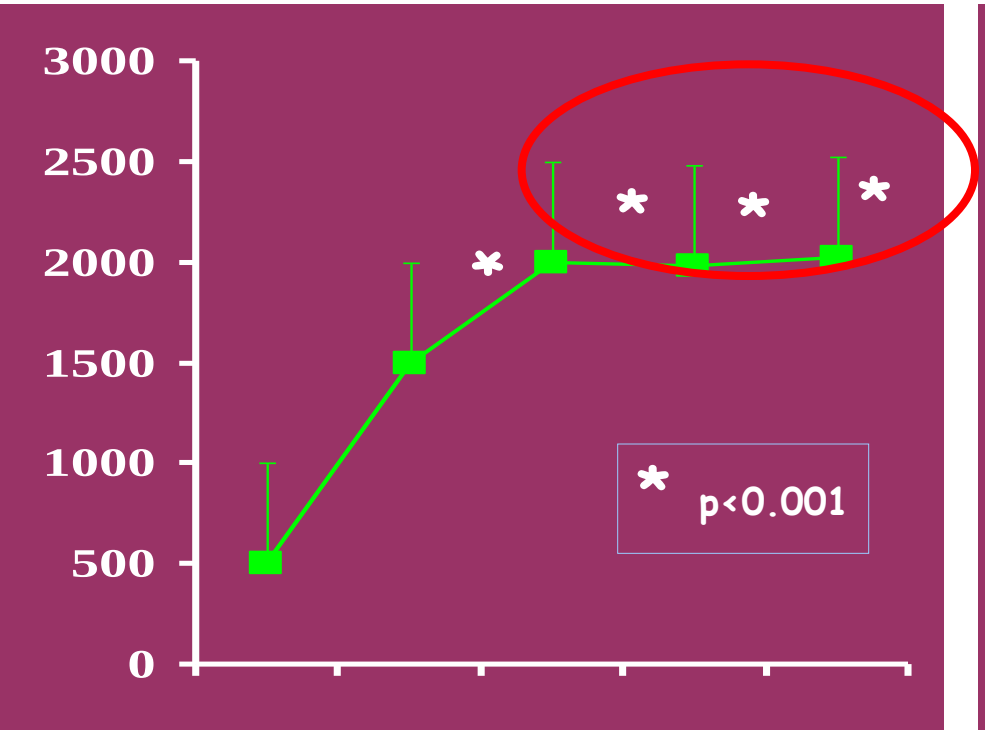
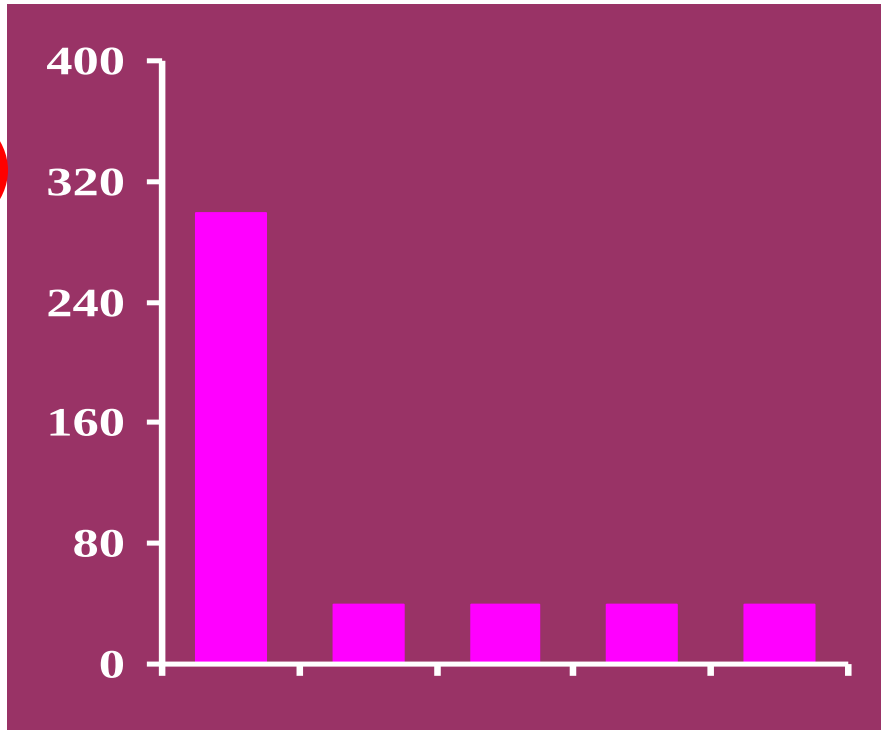
Urine output



Furosemide



Ultrafiltration vs. Loop Diuretics

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Ultrafiltration

- ✓ Lowers RAS activity
- ✓ Does not induce hypoK+
- ✓ Corrects hyponatraemia

Diuretics

- ✓ Increase RAS activity
- ✓ Induce hypoK+
- ✓ Induce hyponatraemia

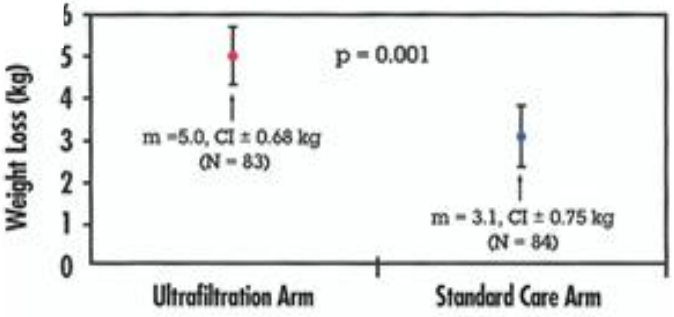
Increased RAS activity, hypokalemia, and hyponatraemia are independent predictors of mortality in CHF.

Have ultrafiltration and diuretic therapy different influence on:

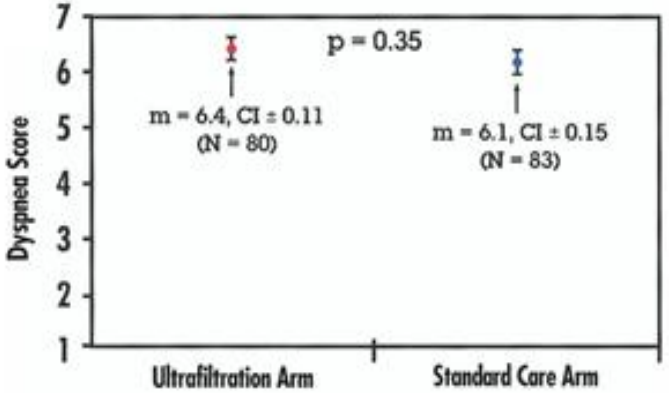
- progression of CHF?
- development of edema?
- mortality ?

UNLOAD TRIAL

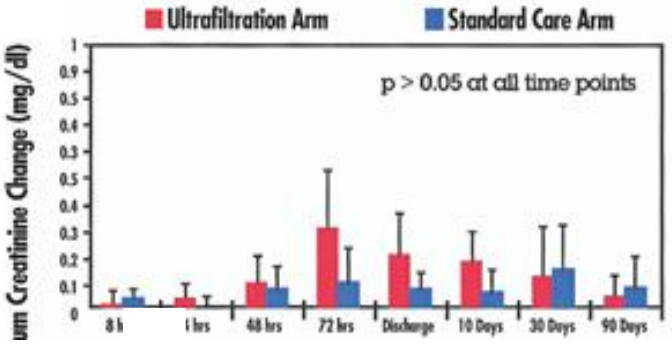
Costanzo et al JAC 2007



UF yes



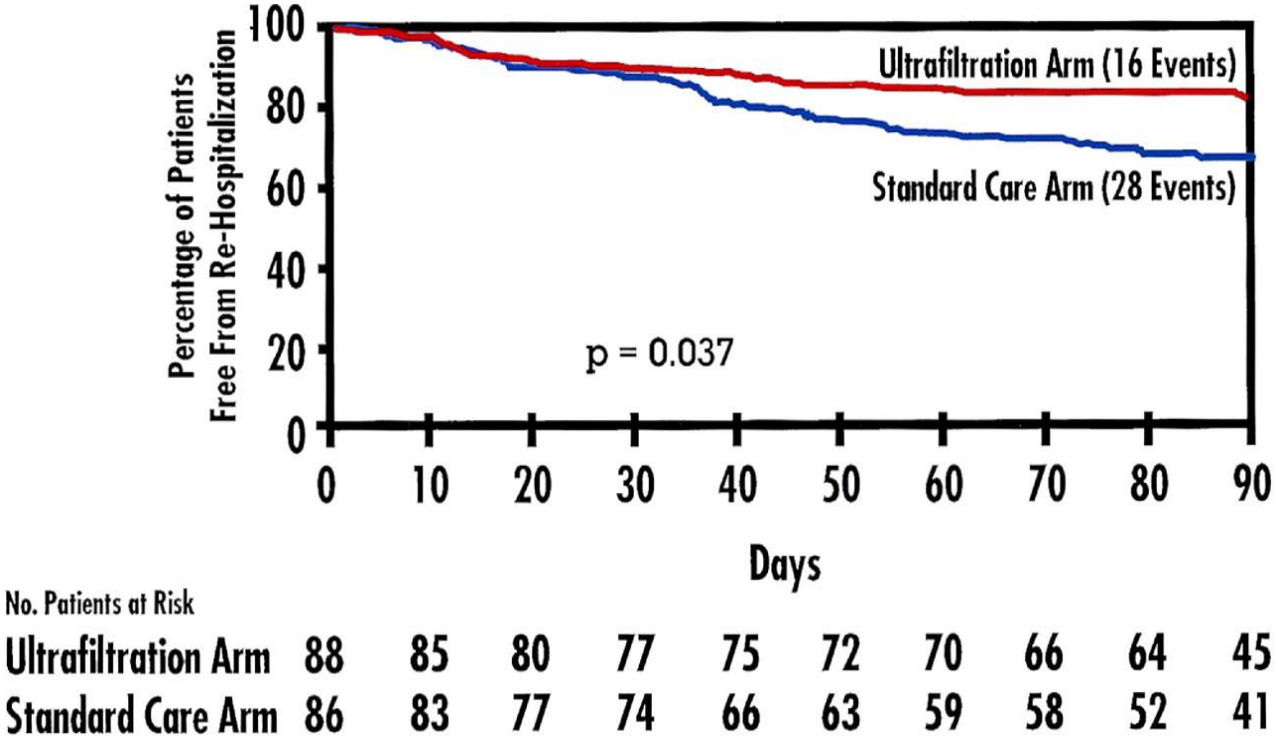
symptoms
no



creatinine
no

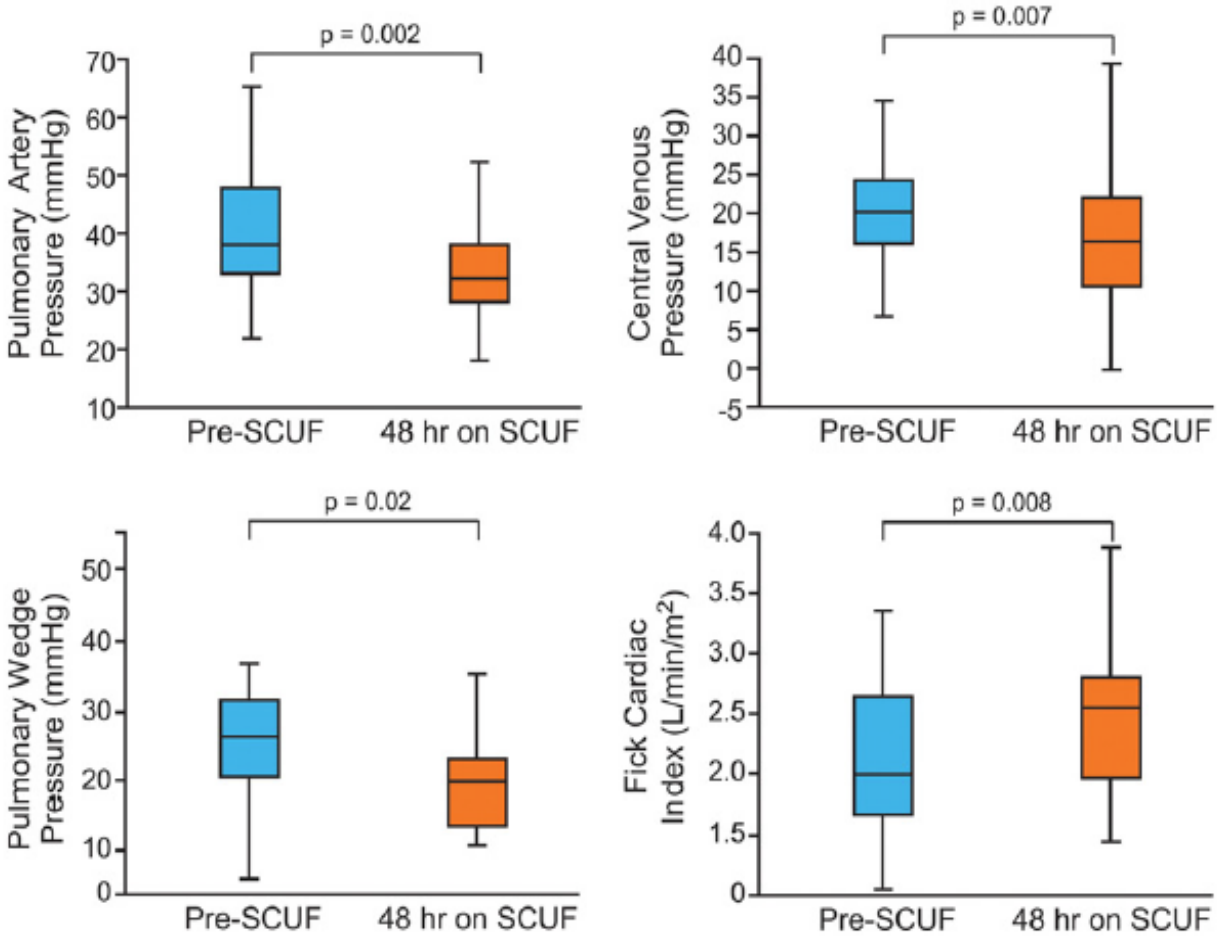
UNLOAD Trial

- 200 Patients with ADHF
- Randomized:
  - Conventional IV Diuresis
  - UF up to 500cc/hr



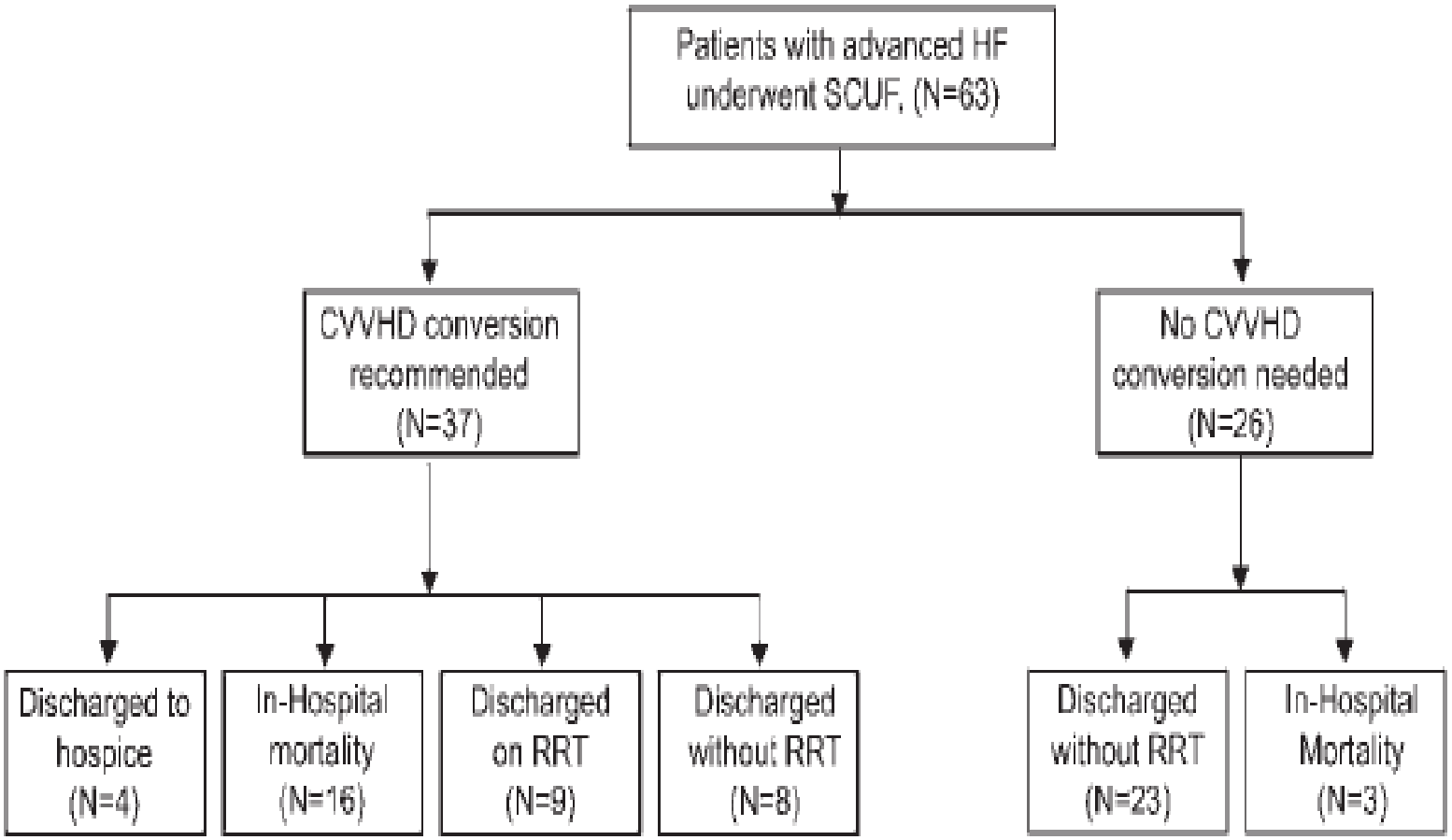
Am Coll Cardiol. 2007 Feb 13;49(6):675-83.

Mayo clinic



Patarrayo et al *JACC* 2012

Mayo clinic



Patarrayo et al *JACC* 2012

What can we say about trials ultrafiltration ?

- Results
  - increased fluid loss
  - no real clinical benefit
- Why ?
  - too fast ?

What should we do ?

- stop diuretics
- give Na+ containing fluids
- reduce (stop) ACEIs
- ? reduce intra-abdominal pressure
- slow ultrafiltration