Acute Renal Injury in ITU

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- Why worry?
- Definition
- Anatomy and physiology
- Markers of injury
- Pathophysiology
- Consequences of AKI
- Prevention
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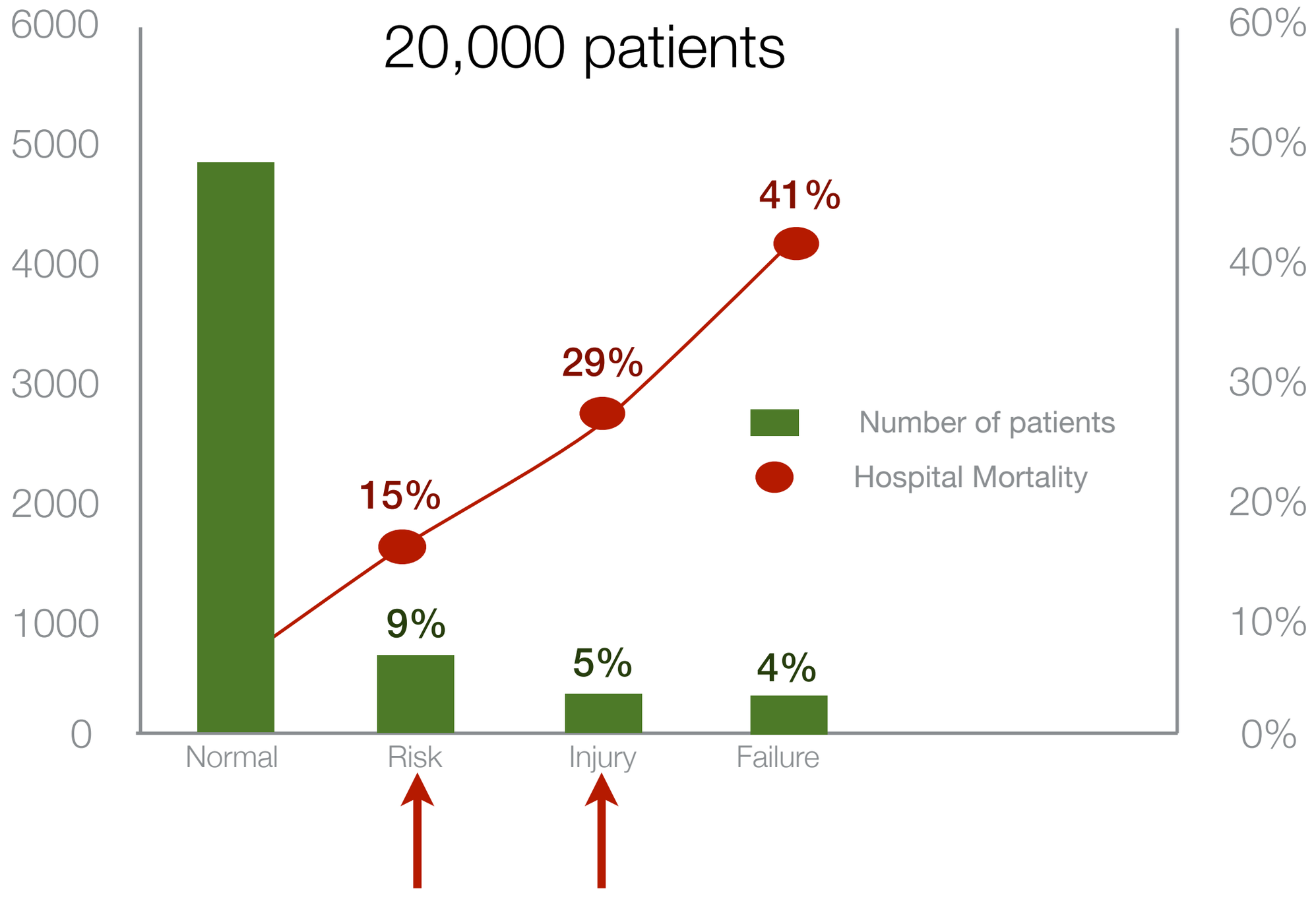
AKI = **5.5** X hospital mortality!

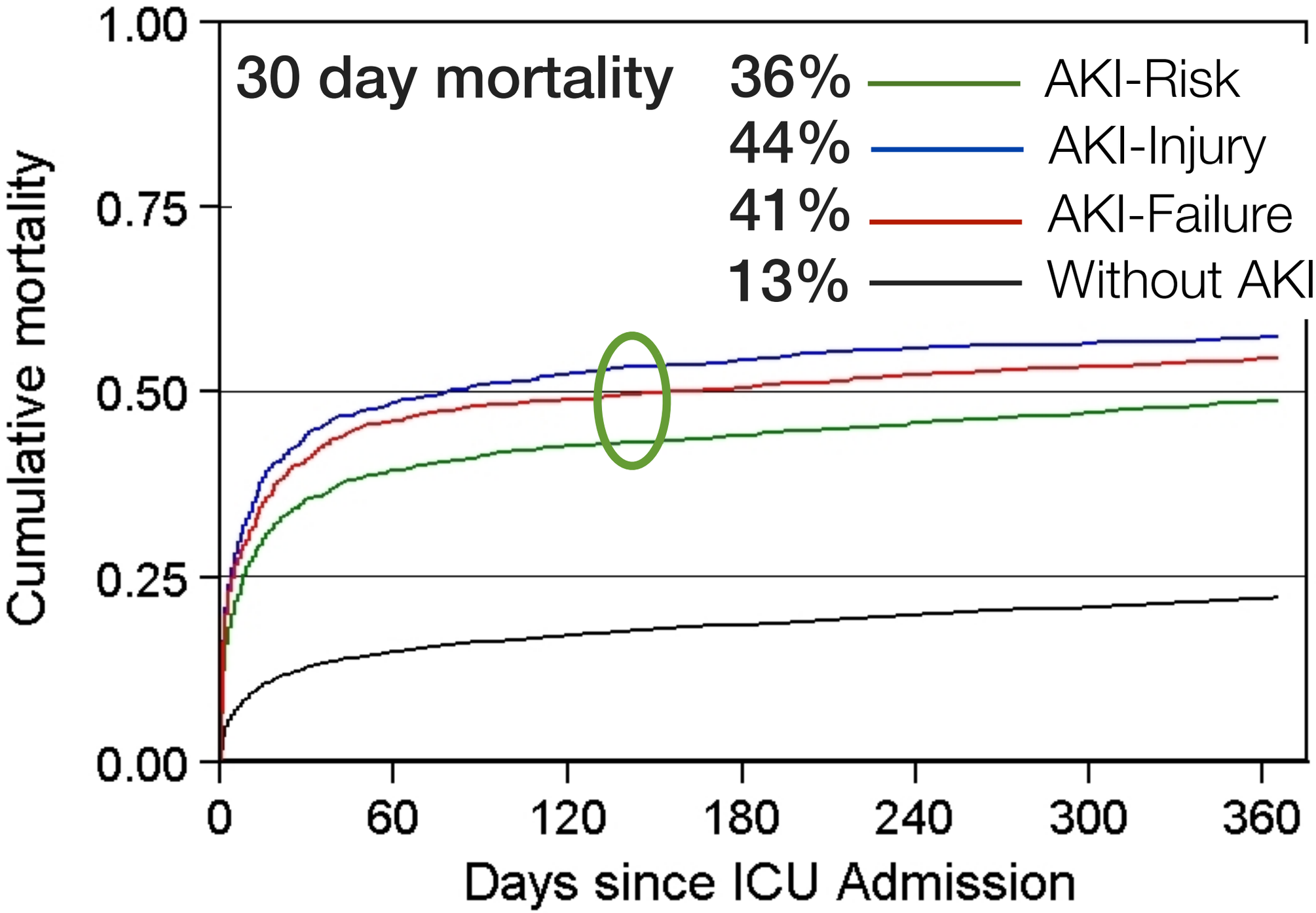
Crit Care 2006; 10:R73

Epidemiology of AKI



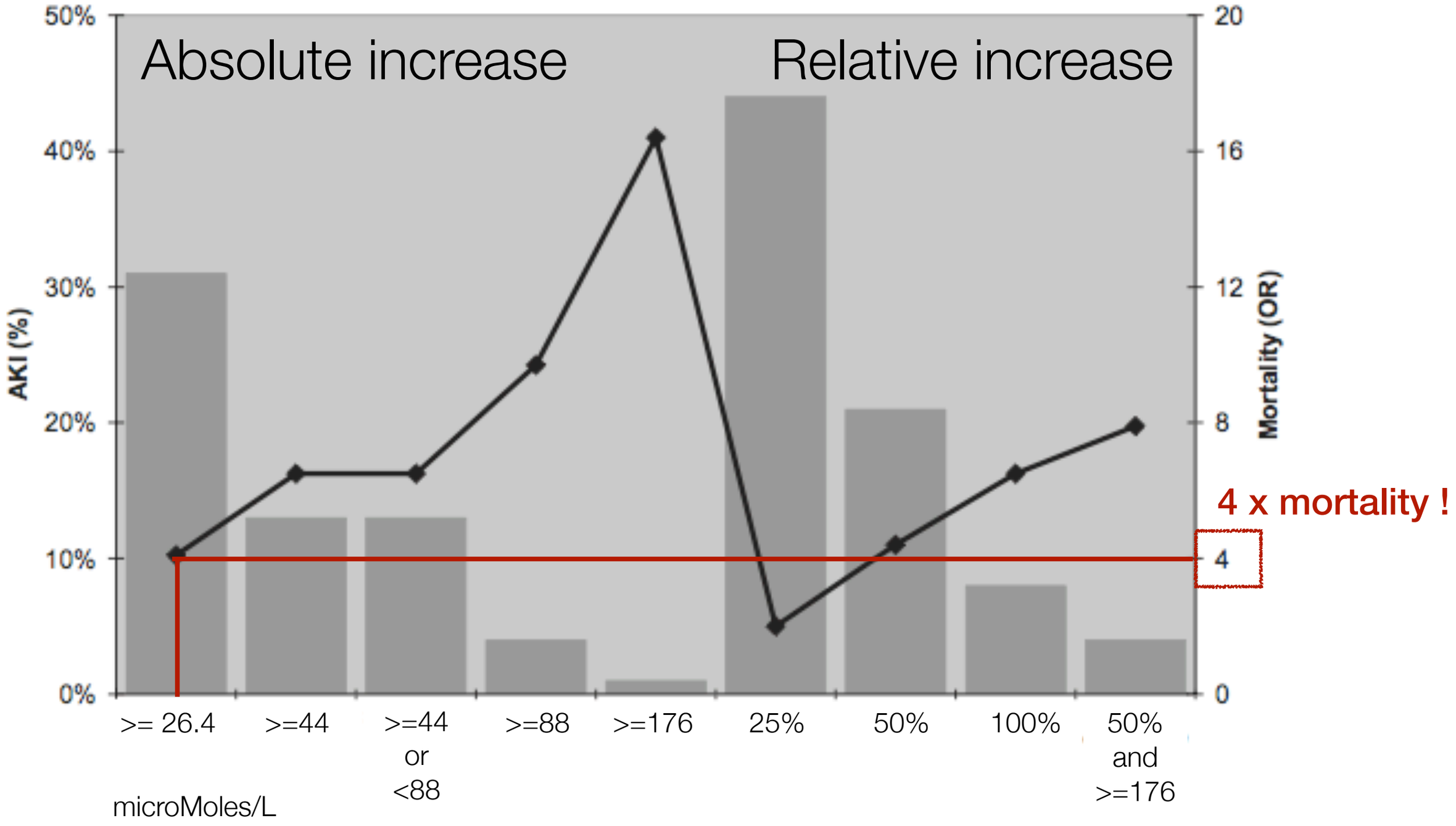
Uchino et al. Crit Care Med, 2006;34:1913-1917

Prognosis of Acute Kidney Injury



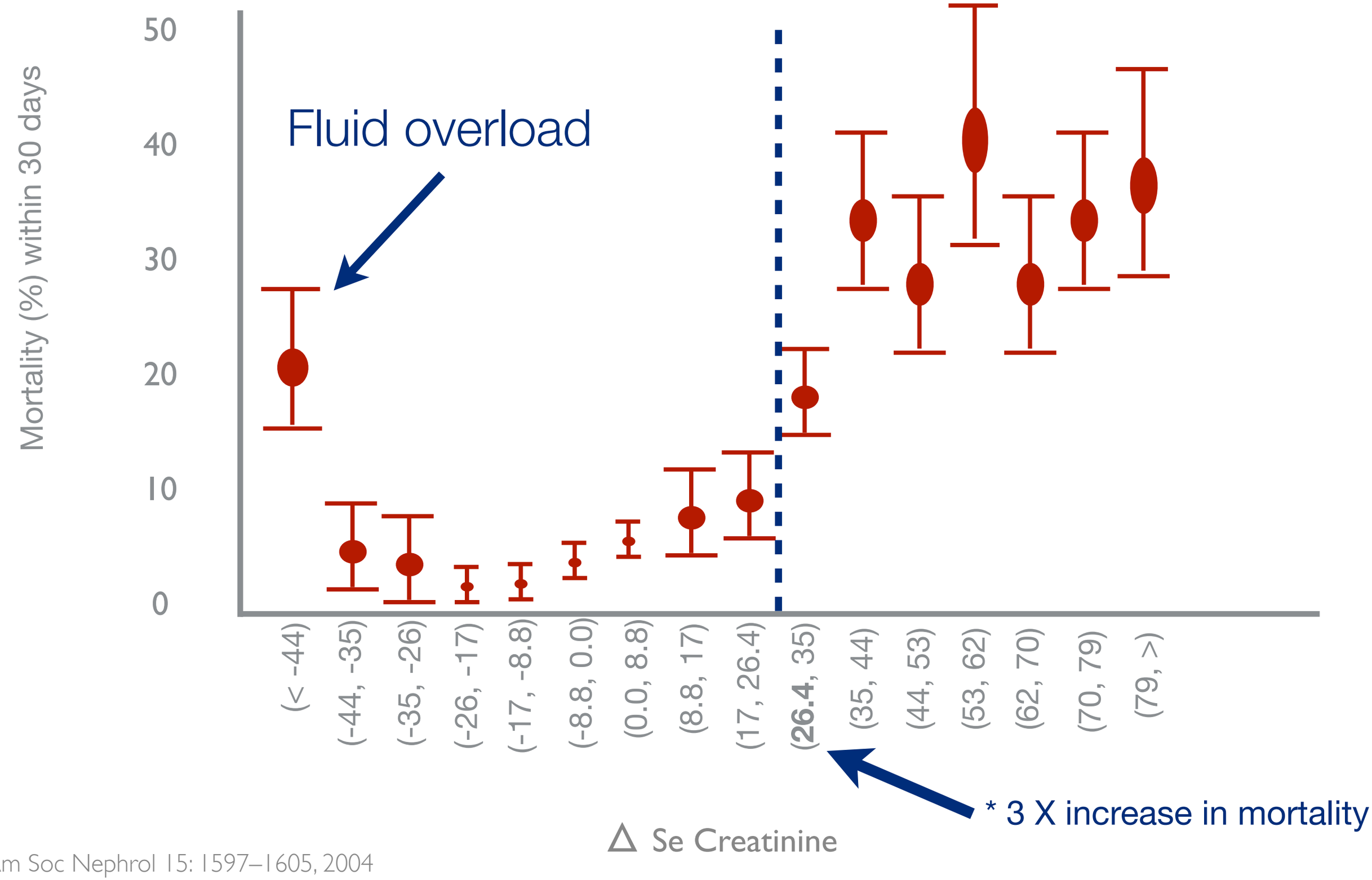
Critical Care 2012, **16**:R124

Prognosis of Acute Kidney Injury



CCM 2008,Vol 36, No 4, pg S146 (Suppl)

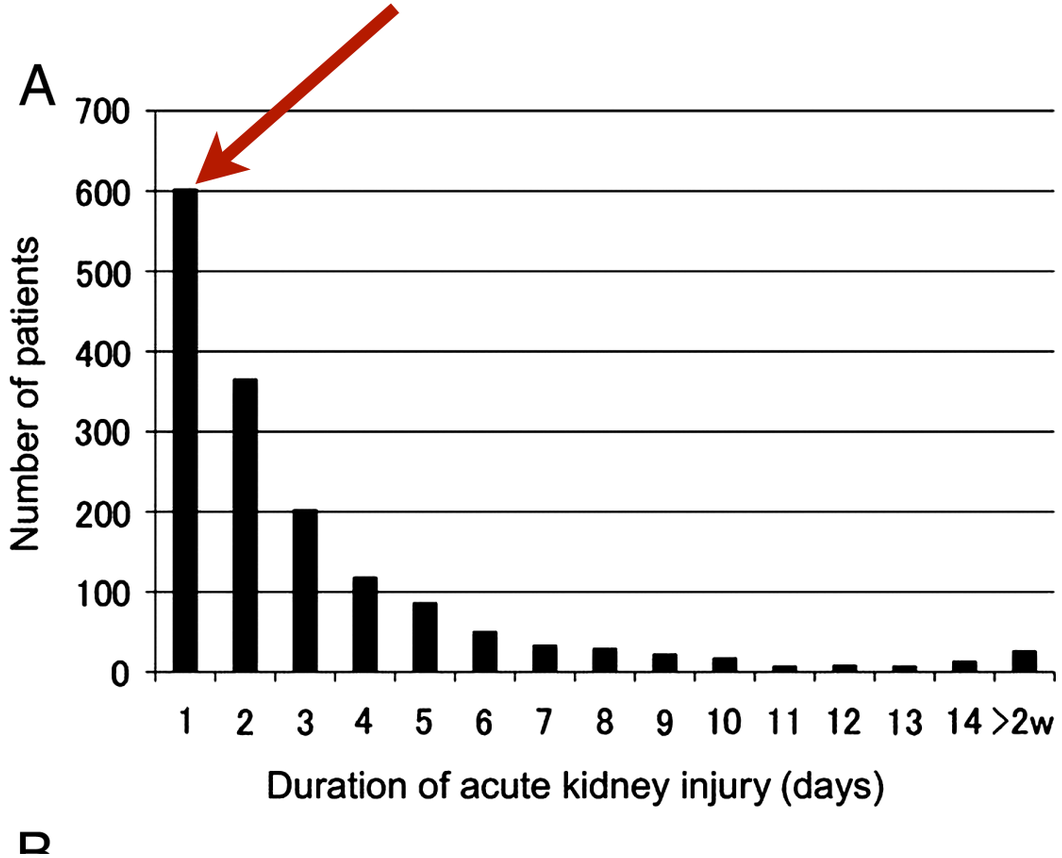
Minimal Changes of Serum Creatinine Predict Prognosis

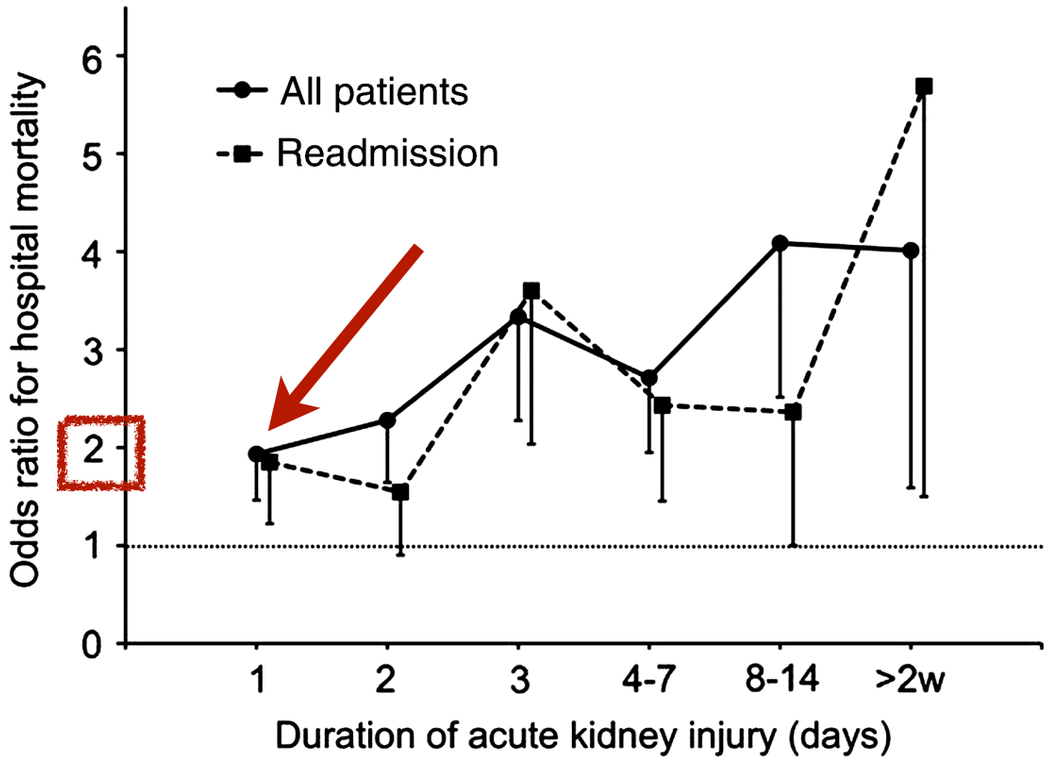


J Am Soc Nephrol 15: 1597–1605, 2004

Even **transient** AKI associated with increased hospital mortality

- **Transient** AKI is common in hospital patients occurring in **~6%** of admissions and accounting for almost a **third** of all cases of in-hospital AKI.
- Transient AKI had significantly higher hospital **mortality** compared to patients with no AKI
- Even 1 day of AKI had a significantly increased odds ratio for hospital mortality.





Nephrol Dial Transplant (2010) 25: 1833–1839

Epidemiology of Acute Kidney Injury

- AKI covers a spectrum
  - from subclinical to organ failure
- AKI in **36% - 67%** of ITU patients
- AKI needs Renal Replacement Therapy (RRT) in **~ 6%**
- Mortality increases with increasing severity
  - If **RRT** - mortality 60% - **70%**
  - AKI increases risk of death despite adjusting for co-morbidities and severity of illness

Crit Care Med 2010; 38:000 – 00

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Acute Renal **Failure**

Harrison’s Textbook of Medicine - 1991

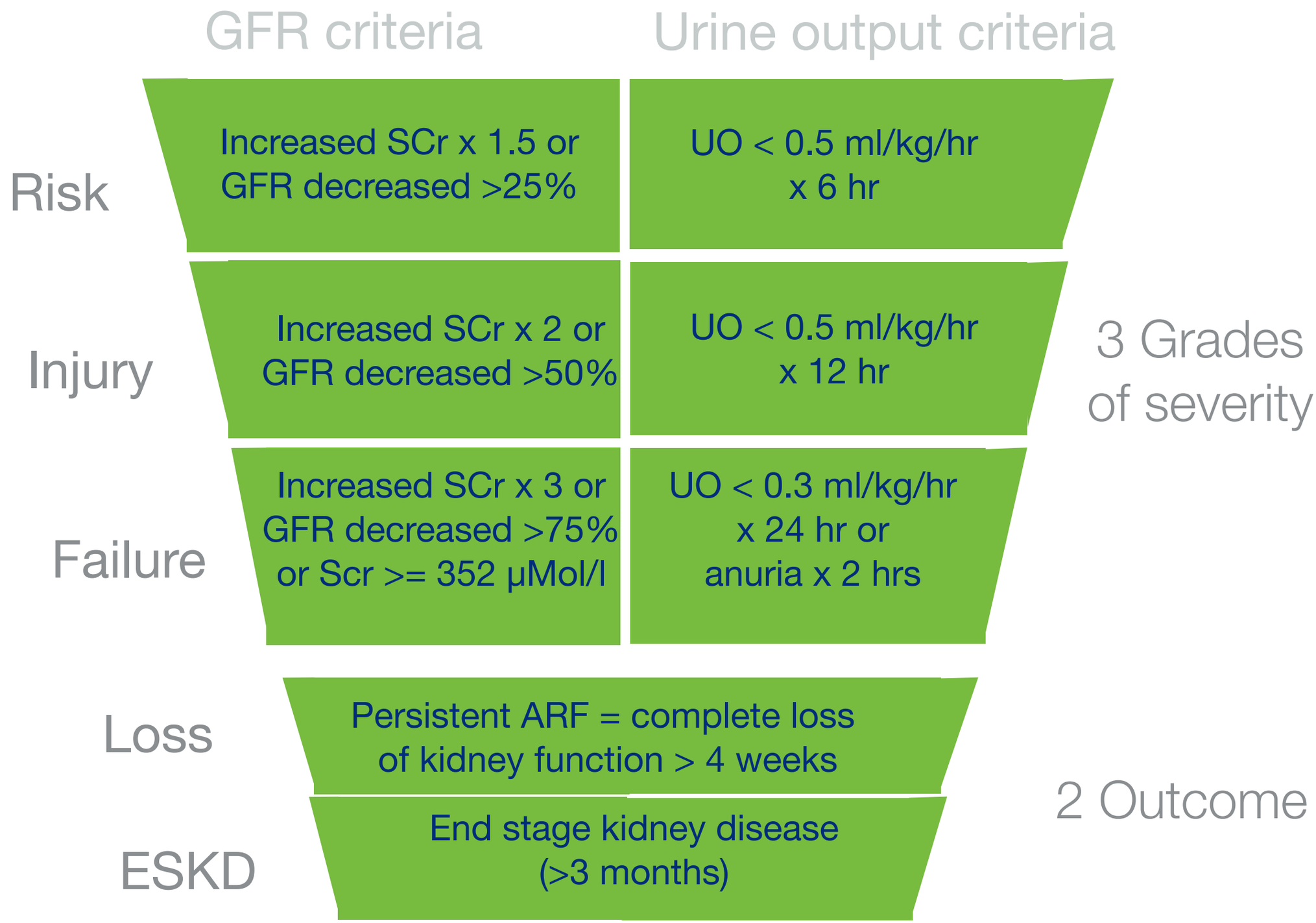
“Acute Renal Failure
defined as a rapid deterioration in renal **function** sufficient
to result in accumulation of nitrogenous wastes.....in
intensive care units, it occurs in up to 20%.....mortality rates
range from 20 to 90%.”

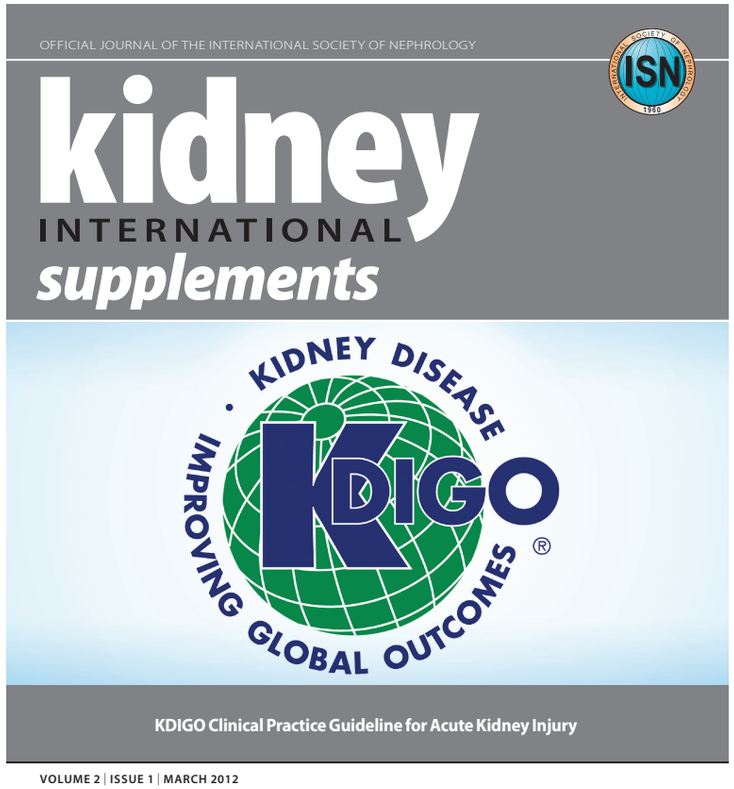
Definition of Acute Kidney **Injury**

- Previously 35 definitions in the literature
- **RIFLE -** Acute Dialysis Quality Initiative definition
  - simple, depends on **creatinine** and **urine output**
  - **spectrum** of injury
- **AKIN -** Acute Kidney Injury Network further modified RIFLE
  - stresses importance of **small**, **abrupt** increase in creatinine
- **KDIGO -** Kidney Disease: Improving Global Outcomes
  - **final**, single definition

Crit Care Med 2010; 38:000 – 00

RIFLE - Proposed staging for AKI





"**K**idney **D**isease, **I**mproving **G**lobal **O**utcomes"

www.KDIGO.org

KDIGO- Proposed staging for AKI

Stage	Se Creatinine	Urine output
1	1.5 - 1.9 times baseline (in 7 days) or >= 26.5 µmol/L increase (in 48 hrs)	< 0.5 mL/kg/h for 6 - 12 hours
2	2.0 - 2.9 times baseline	< 0.5 mL/kg/h for 12 hours
3	3.0 times baseline or increase in se Creatinine to >=353.6 µmol/L or initiation of RRT	< 0.3 mL/kg/hr for 24 hrs or Anuria for >= 12 hrs

Creatinine - Urine output - Time

Kidney International Supplements (2012) 2, 19–36

Diagnosis of AKI - Beware variations

Fluid balance and urine volume are independent predictors of mortality in acute kidney injury

Critical Care 2013, **17**:R14

Comparison of RIFLE with and without urine output criteria for acute kidney injury in critically ill patients

Critical Care 2013, 17:408

"RIFLE using Creatinine only significantly **underestimated** the presence and severity of AKI and significantly **delayed** AKI diagnosis."

"The authors also found that RIFLESCr was associated with higher **mortality** than RIFLESCr+UO."

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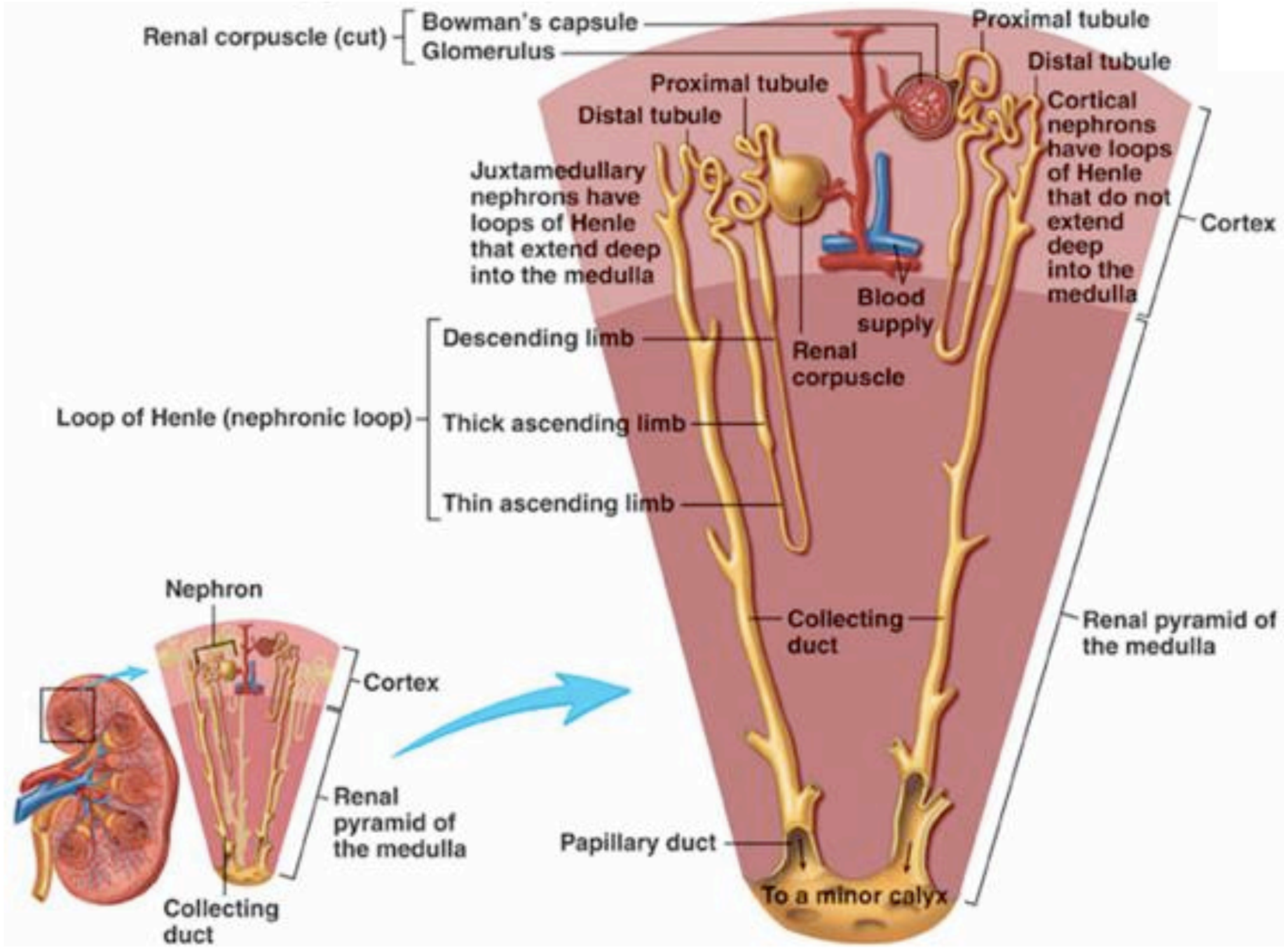
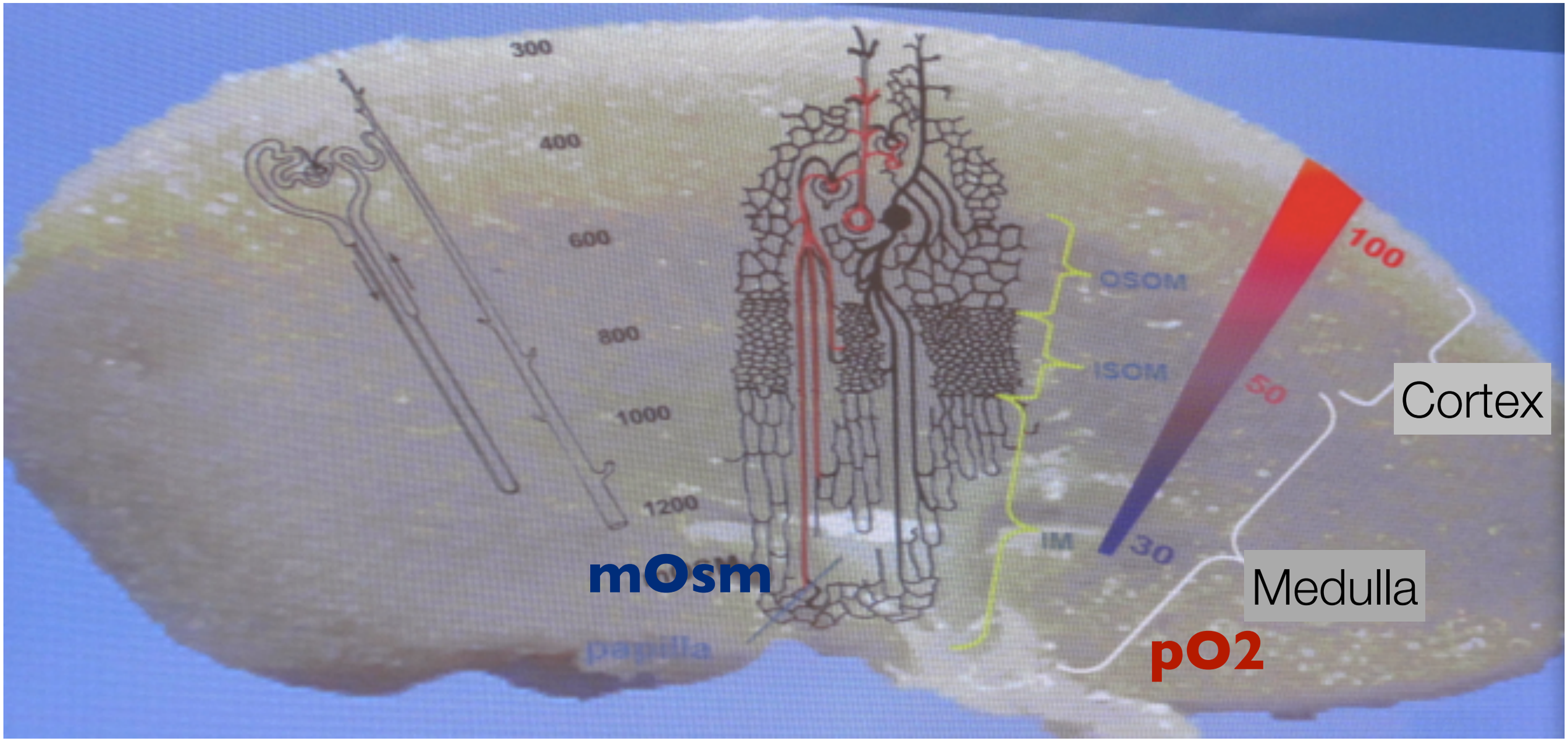
Anatomy of the nephron



Physiology of the nephron



Kidneys have a high blood flow but little O2 uptake

SvO2

SaO2

69%

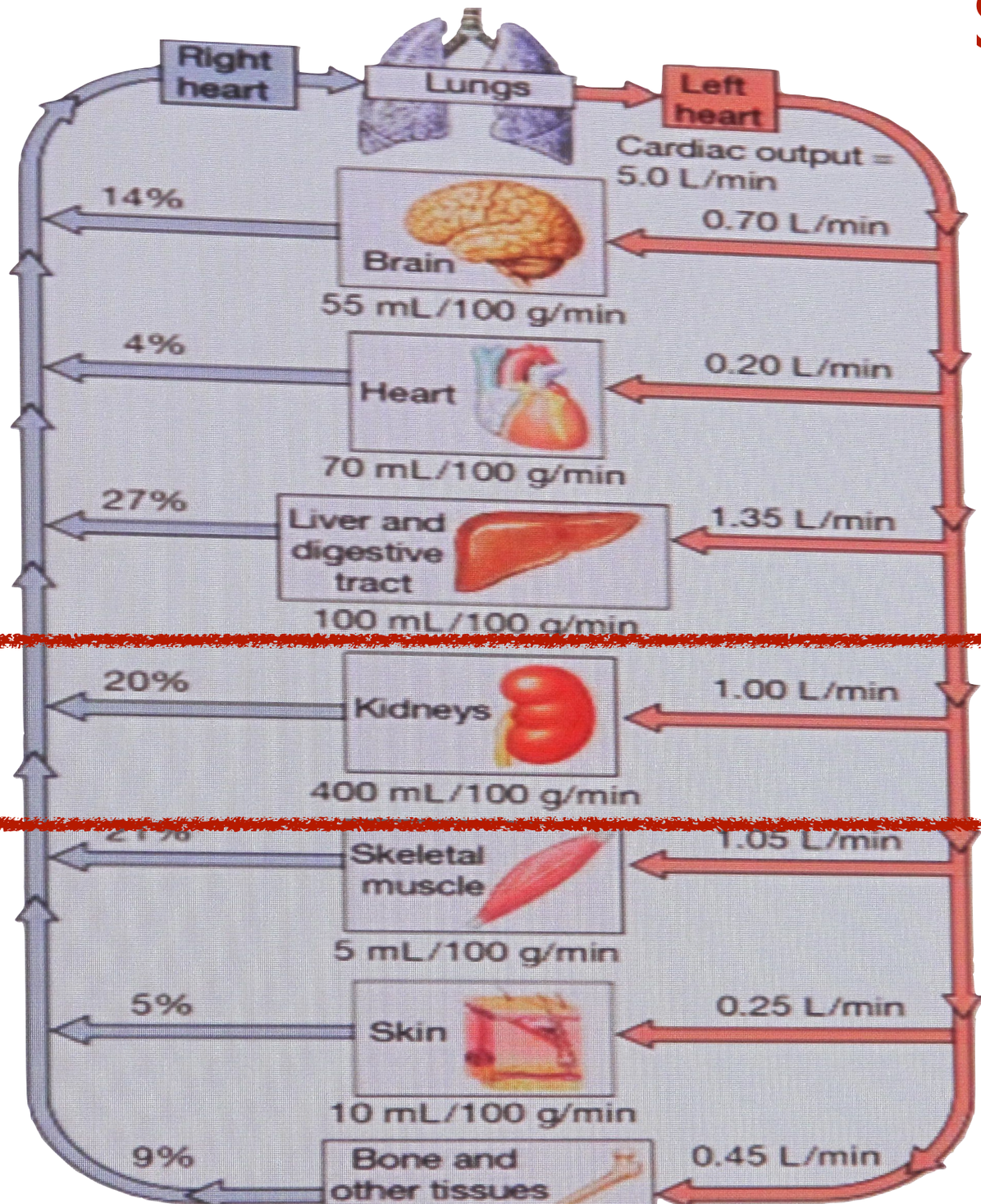
75%

66%

92%

71%

88%



20% of C.O.

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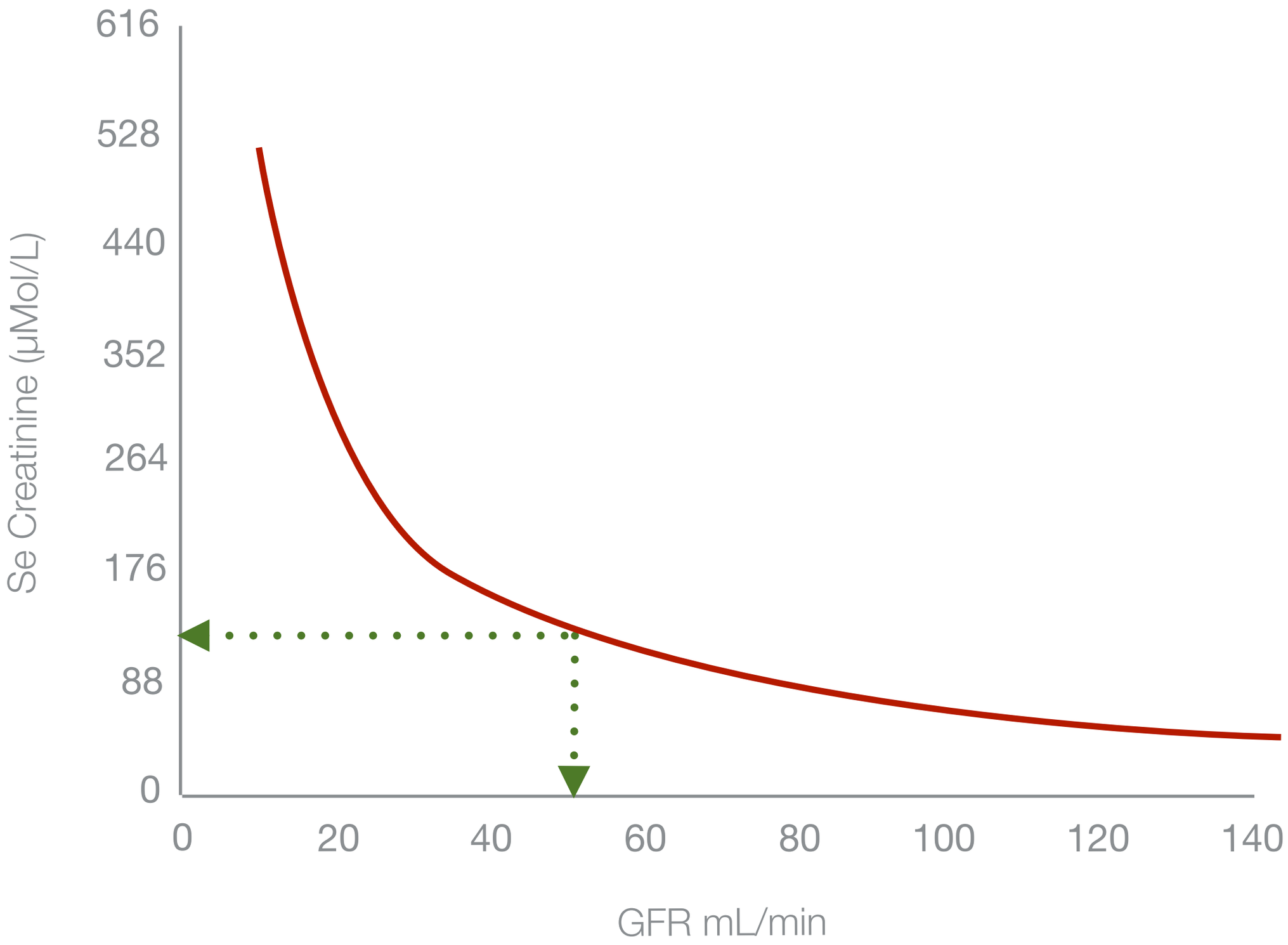
Creatinine in Acute Kidney Injury

Se. Creatinine key element in definition but:

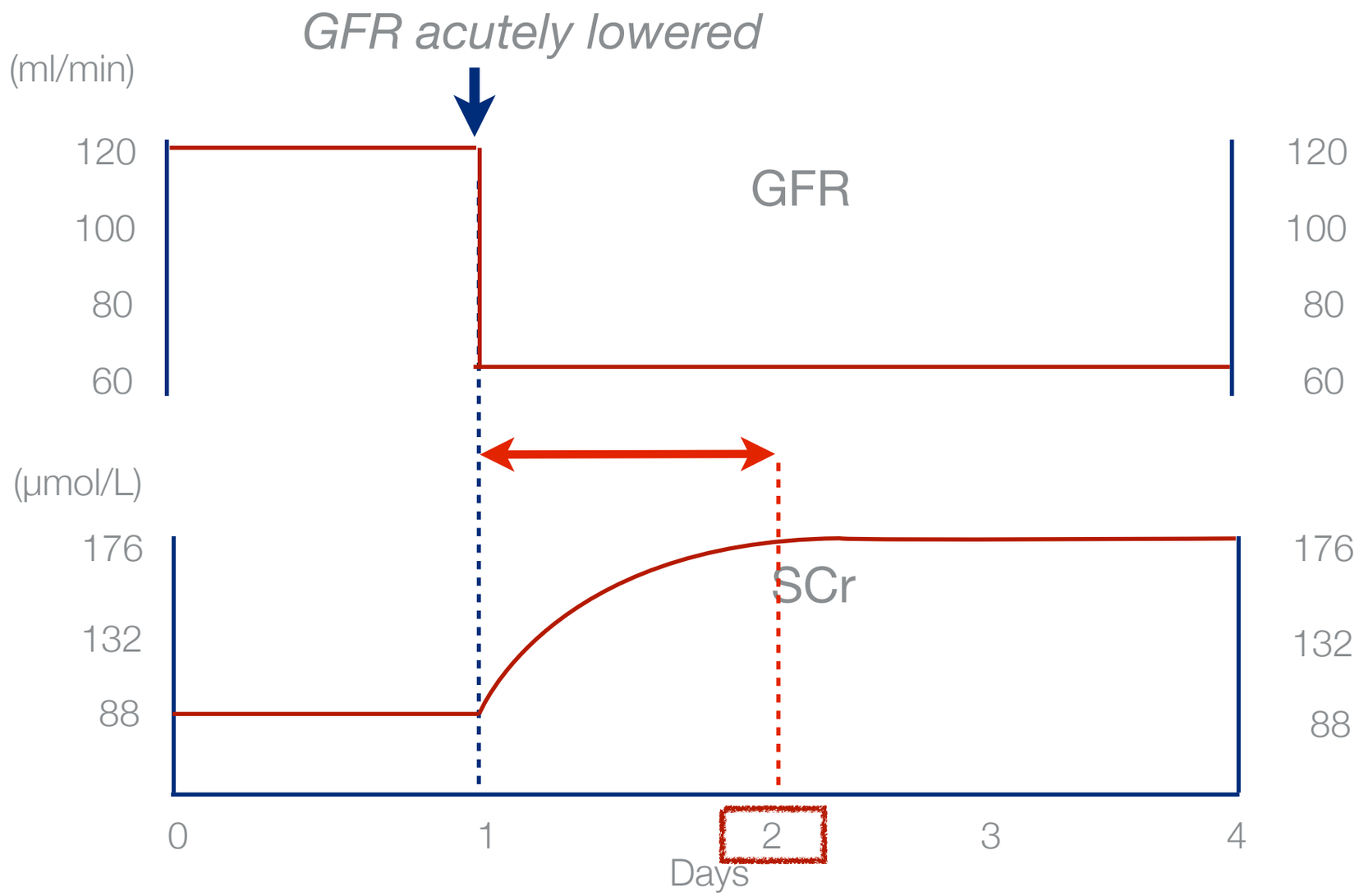
- Tests **function** not **injury**
- **Non linear** relationship
- Not steady state - **lag** behind decrease in GFR
- Depends on :
  - age
  - ethnicity
  - gender
  - muscle mass
  - volume of distribution
  - protein intake
  - medication

Crit Care Med 2010; 38:000 – 00

Non linear relationship between Creatinine and GFR

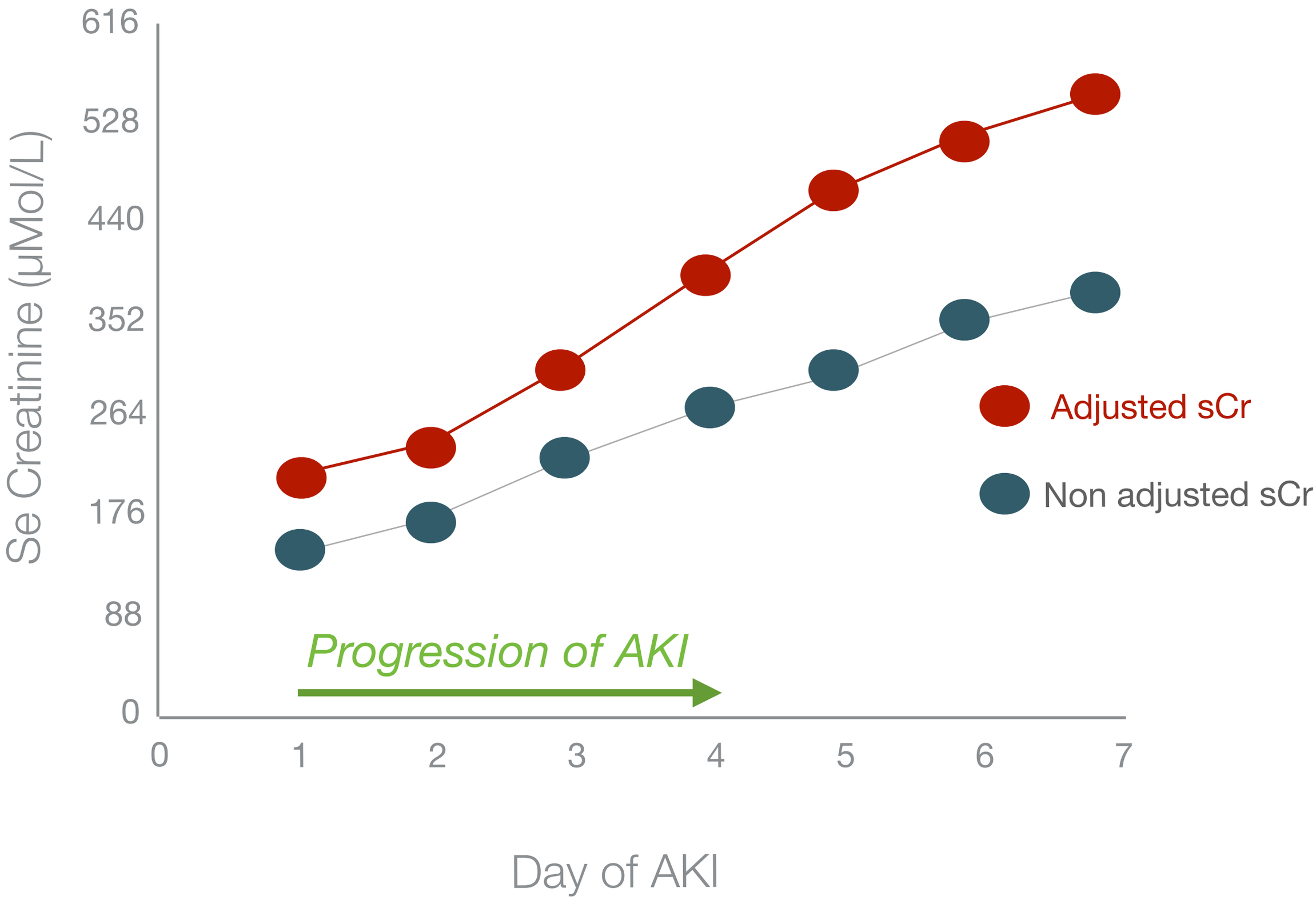


Creatinine rise lags GFR drop!



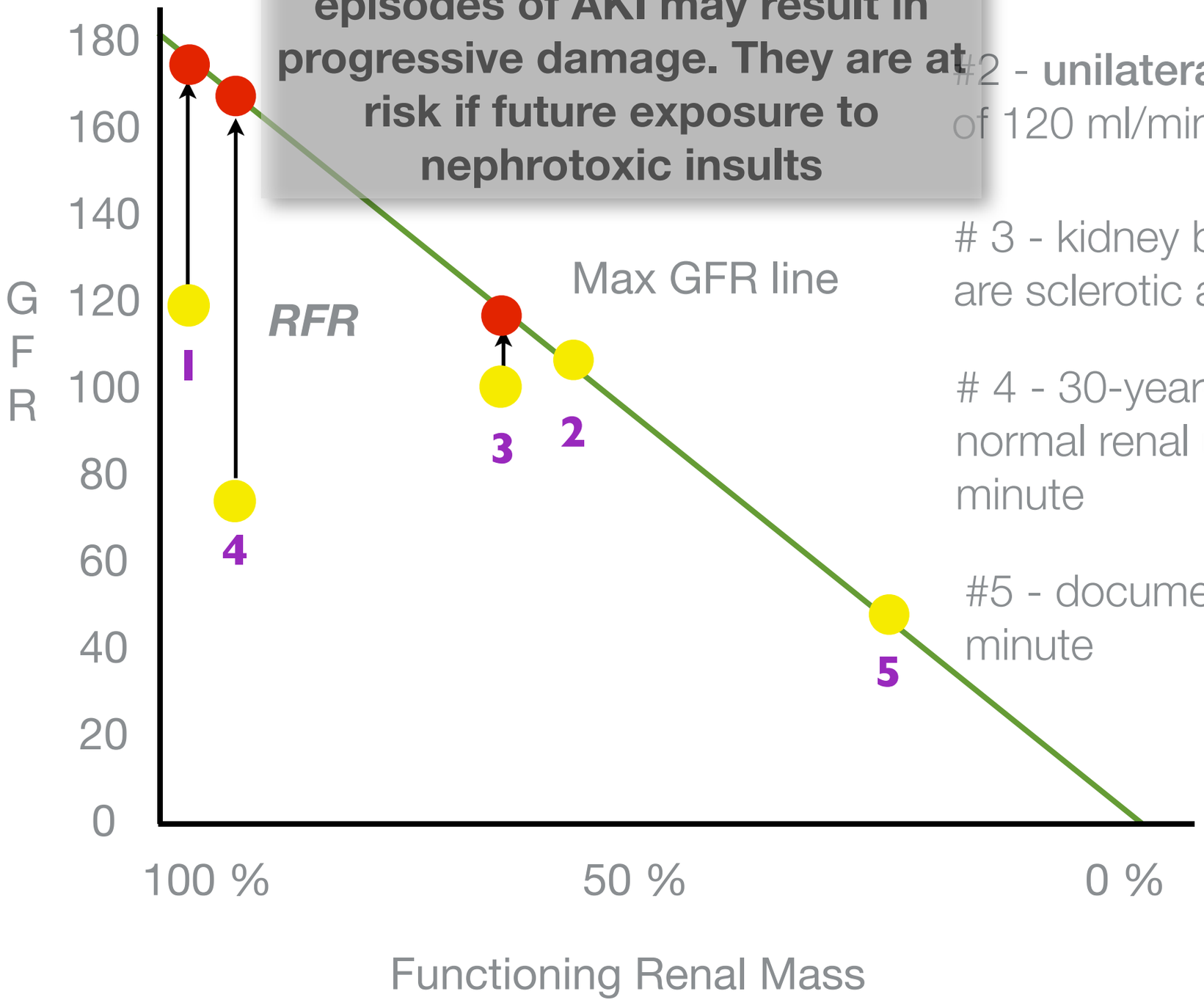
Kassirer JP, Clinical Evaluation of Kidney Function-Glomerular Function NEJM 1971

Fluid accumulation underestimates severity of AKI in ITU patients



Acute kidney injury and renal reserve

In survivors of ICU, repeated episodes of AKI may result in progressive damage. They are at risk if future exposure to nephrotoxic insults



Patient #1 - normal renal ultrasound and a GFR of 120 ml/minute

#2 - **unilateral** nephrectomy and a GFR of 120 ml/minute

3 - kidney biopsy -> 30% of his glomeruli are sclerotic and a GFR of 97 ml/minute

4 - 30-year-old female, vegetarian with a normal renal ultrasound and a GFR of 70 ml/minute

#5 - documented CKD and a GFR of 42 ml/minute

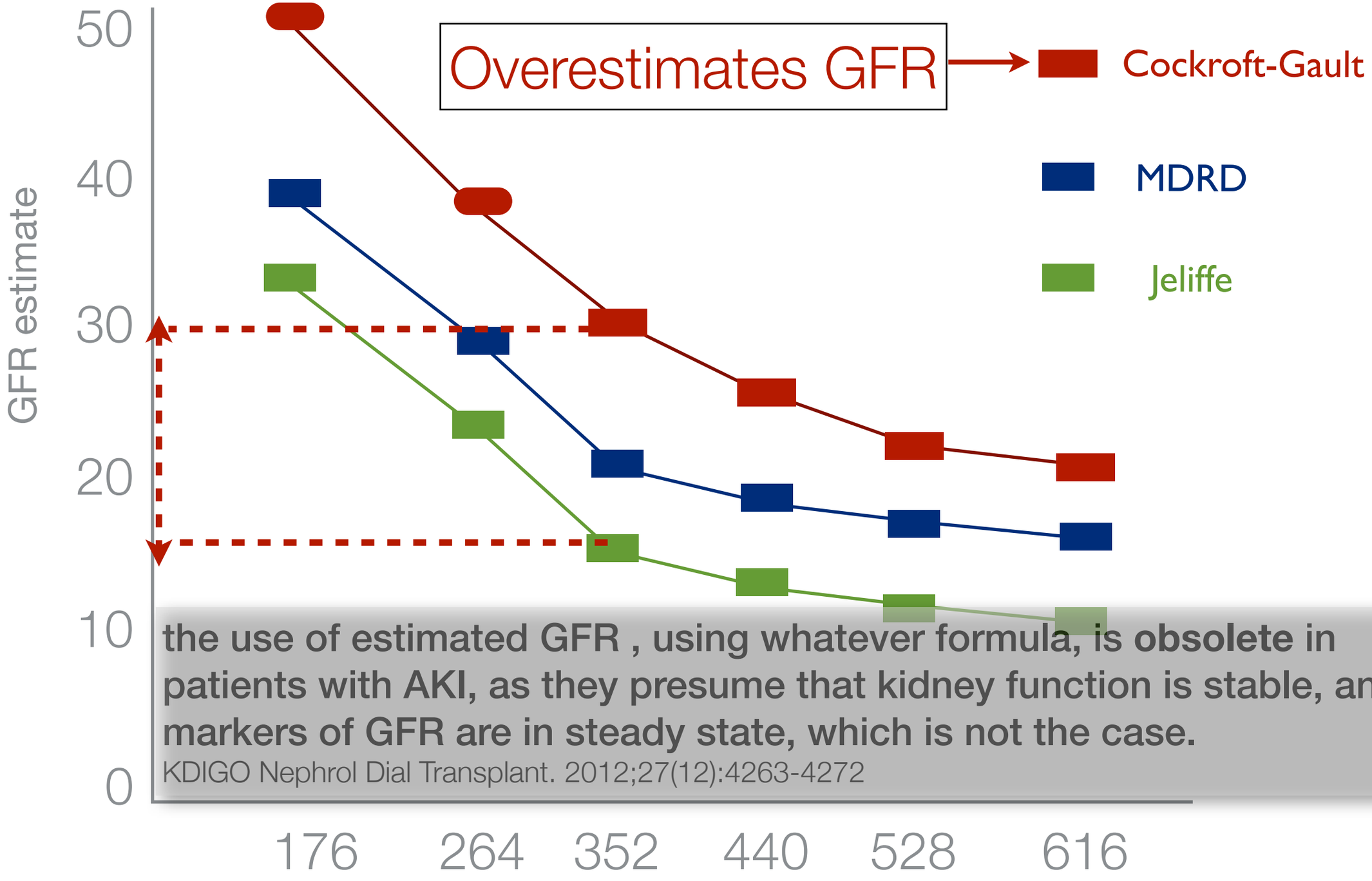
Max. GFR (post protein load)

Baseline GFR

RFR = Max. GFR - Baseline GFR

Critical Care 2012, 16:144

Different techniques for **estimating** GFR in ITU patients with AKI



the use of estimated GFR , using whatever formula, is obsolete in patients with AKI, as they presume that kidney function is stable, and markers of GFR are in steady state, which is not the case.

KDIGO Nephrol Dial Transplant. 2012;27(12):4263-4272

Nephrol Dial Transplant. 2010 Jan;25(1):102-107

Other Bio markers

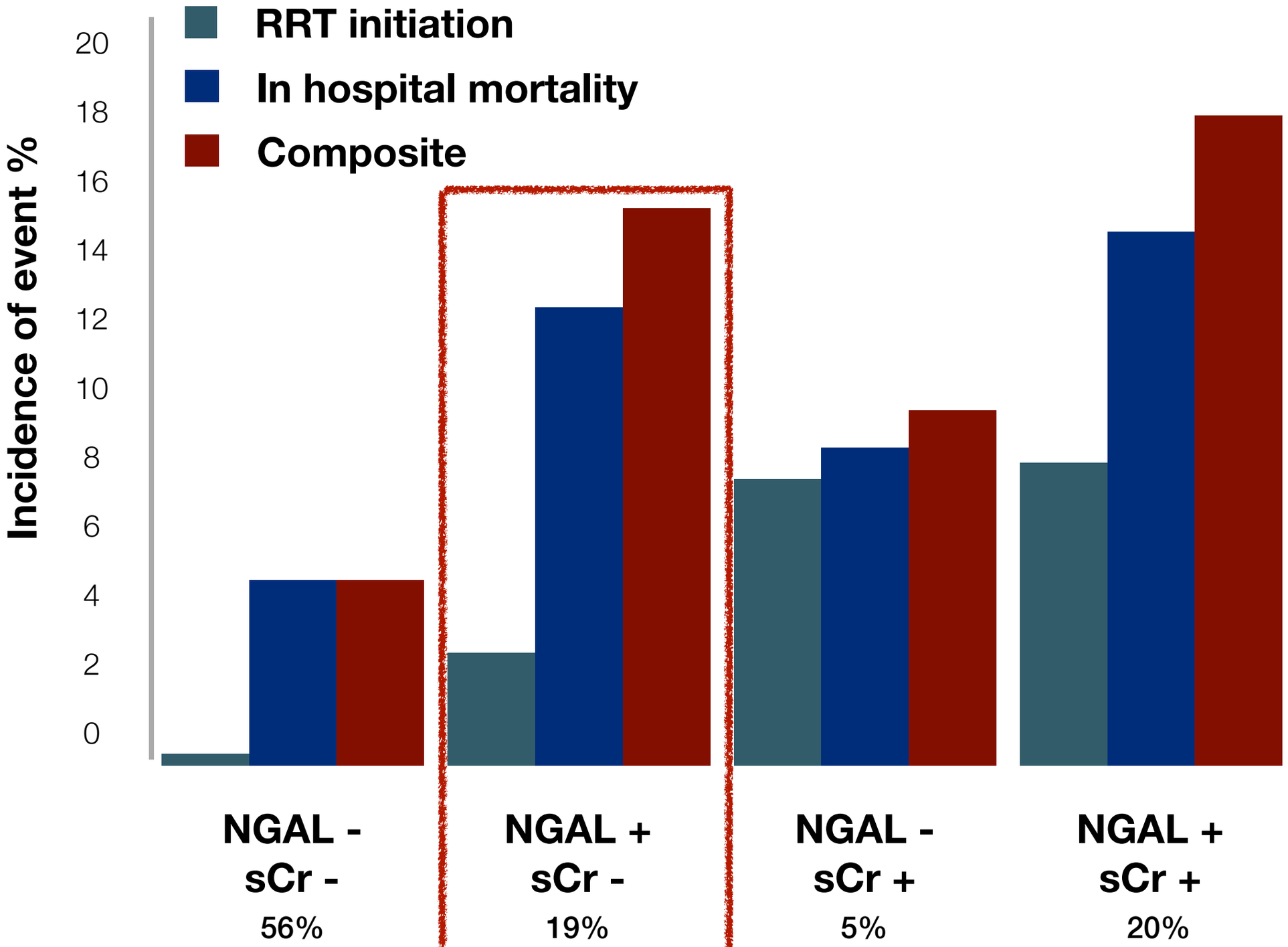
Creatinine negative AKI

- AKI implies **damage** but not necessarily **dysfunction**.
- The human kidney has an important reserve, dysfunction seen when >**50% of the renal mass is compromised**.
- Even slight changes in serum creatinine still represents a **functional** criterion for AKI, this is a **late** phenomenon
- An **early** diagnosis of AKI by using tubular **damage** biomarkers **preceding** filtration **function** loss even in the absence of subsequent dysfunction.
- Tubular damage **without** glomerular function loss leads to worse renal and overall outcomes
- This challenges the traditional view that a kidney problem is a loss of filtration function.
- A new domain of AKI diagnosis could then include **functional** criteria and **damage** criteria.

The kidney's answer to troponin

Ronco et al. Critical Care 2012, 16:313

Prognosis of creatinine negative AKI



JACC Vol. 57, No. 17, April 26, 2011:1752–61

Acute kidney injury biomarkers

Biomarkers

Potential urinary biomarkers for **early** diagnosis of AKI

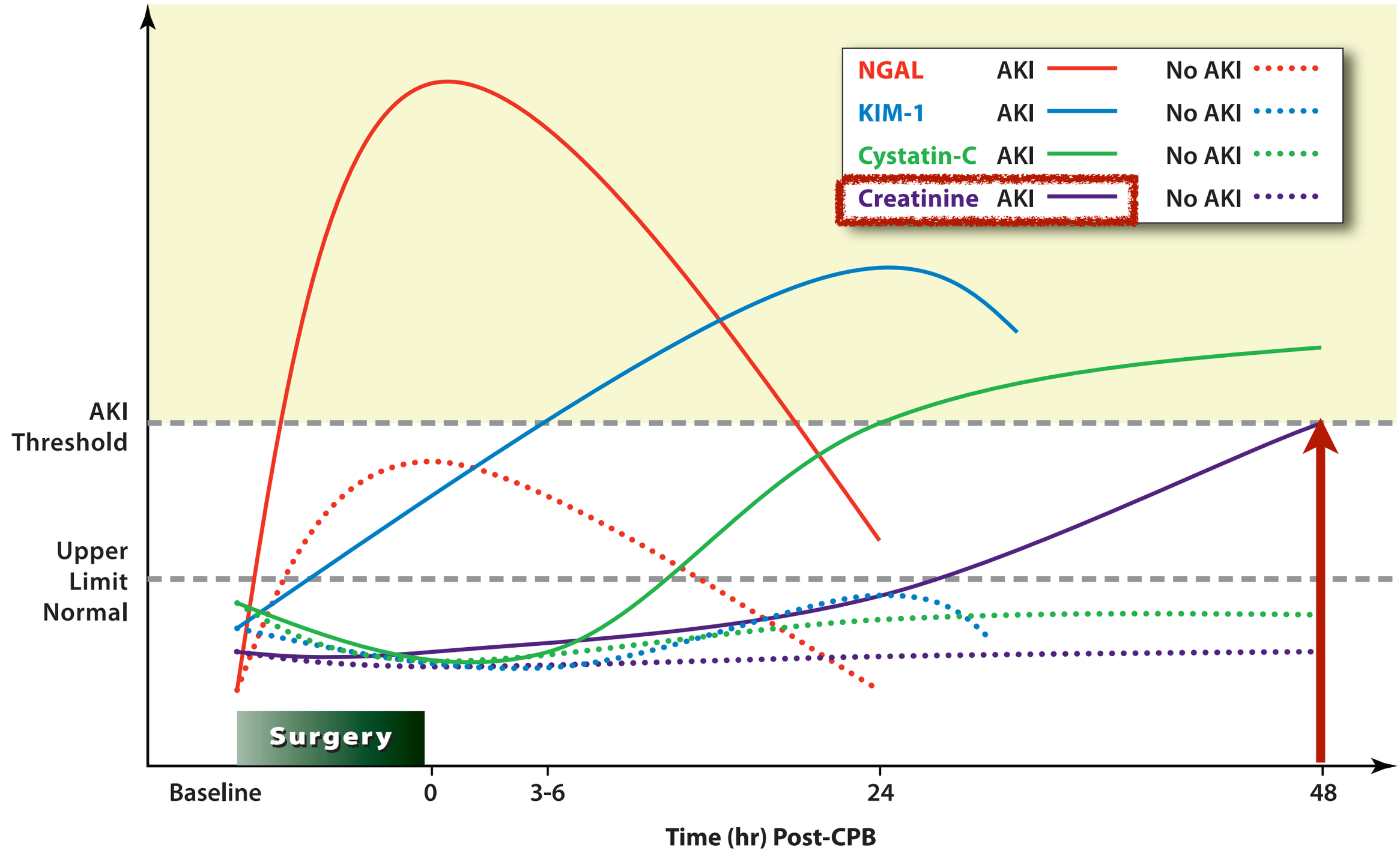
NGAL
Cystatin C
KIM-1
Microalbumin
NAG
IL-18
etc, etc

Decreased GFR

Delayed biomarkers for diagnosis of AKI

Increase S Creatinine
Increase Urea

Acute kidney injury biomarkers



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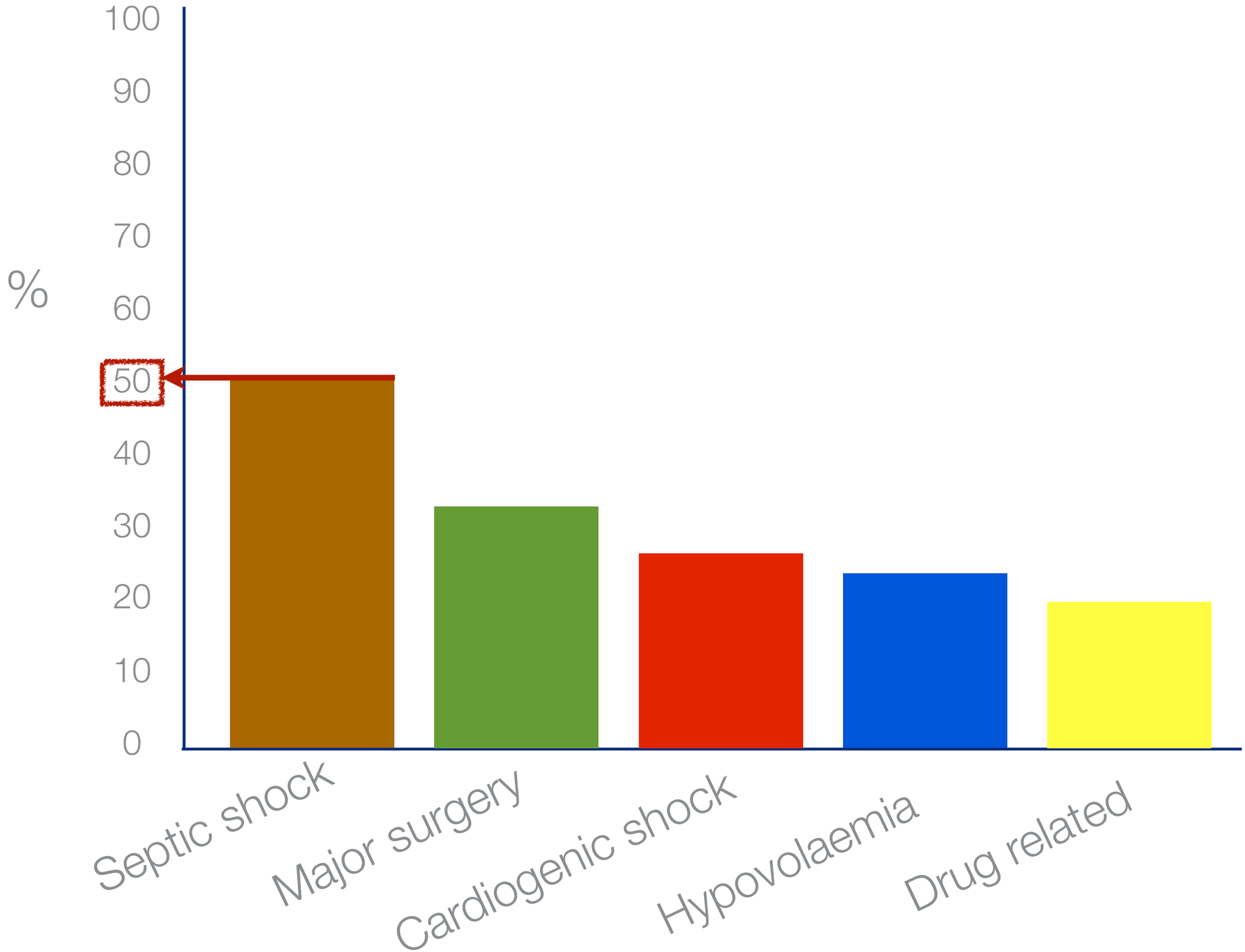
Aetiology of AKI in the ITU - “BEST KIDNEY Study”



JAMA. 2005;294(7):813-818.

Other causes of ARI in the ICU

- Hepatorenal syndrome
- Trauma
- Cardiopulmonary bypass
- Abdominal compartment syndrome
- Rhabdomyolysis/Hemolysis
- Obstruction
- Intrinsic renal disease

Crit Care Med 2010; 38:000 – 00

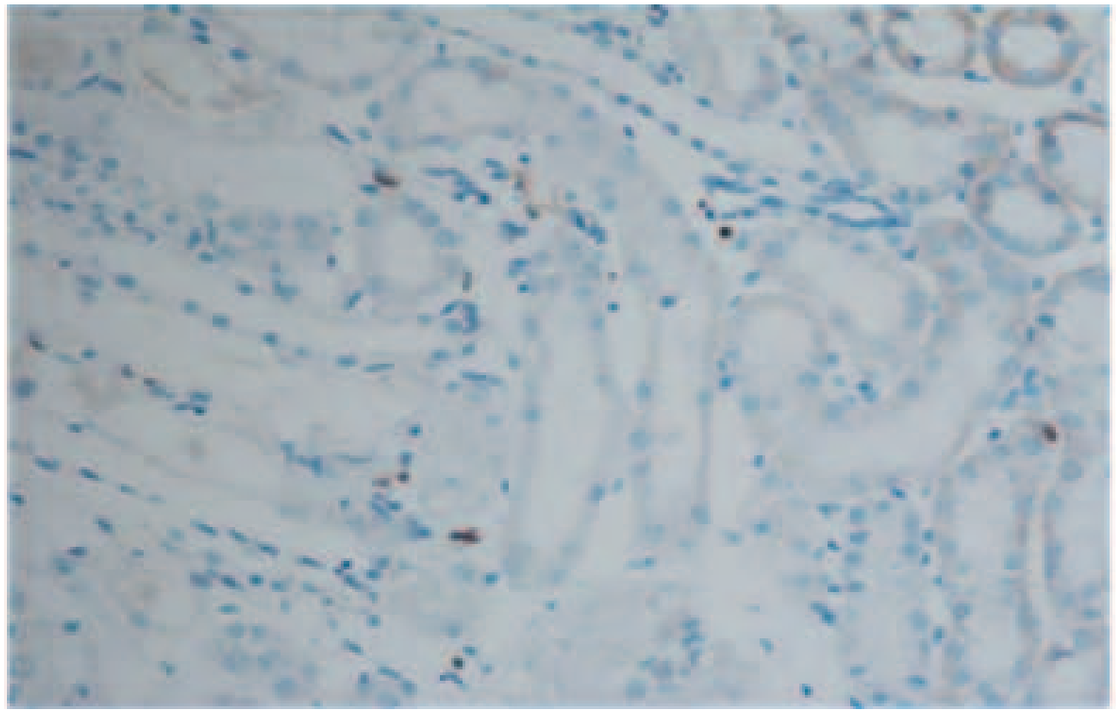
Pathophysiology- Septic AKI

- Pathogenesis of septic acute kidney injury is **different** from that of ischemia/reperfusion
- Systemic arterial dilatation and intense renal vasoconstriction were considered the cause of septic AKI. This “haemodynamically mediated ischaemic paradigm” is probably **wrong**!
- Several studies have shown the loss of glomerular filtration rate was accompanied by **increased** renal blood flow
- Post-mortem studies of septic kidneys show **apoptosis,** rarely overt acute tubular necrosis
- Data showed a link between apoptosis, immune **suppression**, and the development of acute kidney injury during sepsis
- Tissue inflammation was **not** evident in septic acute kidney injury. Unlike I/R injury, neutrophil or macrophage infiltration was **minimal** in septic kidney

“The pathophysiology of septic AKI is completely different and does not result from a classical “ischaemic paradigm.”

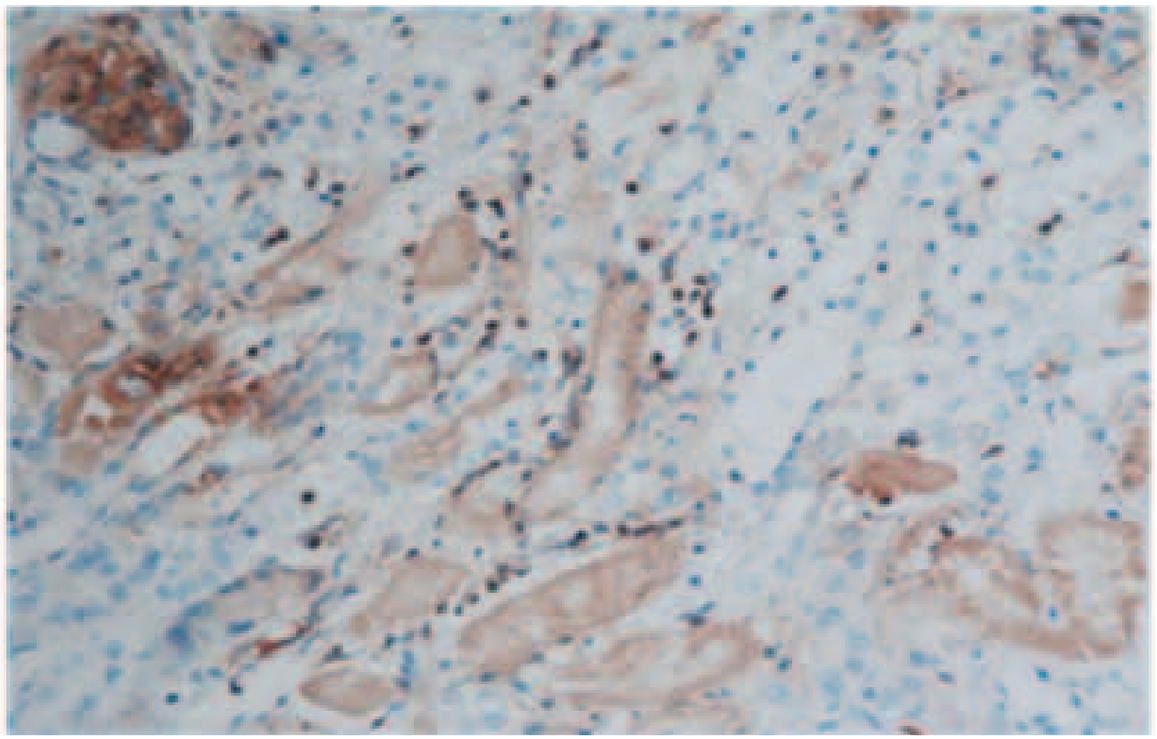
Crit Care Med 2012; 40:2997–3006 Curr Opin Crit Care 9:496–502. © 2003 Intensive Care Med (2010) 36:385–388

Pathophysiology- Septic AKI



septic kidneys

were characterised by **lack** of neutrophil or macrophages infiltration



ischaemic kidneys

infiltration of neutrophil or macrophages infiltration

Crit Care Med 2012; 40:2997–3006

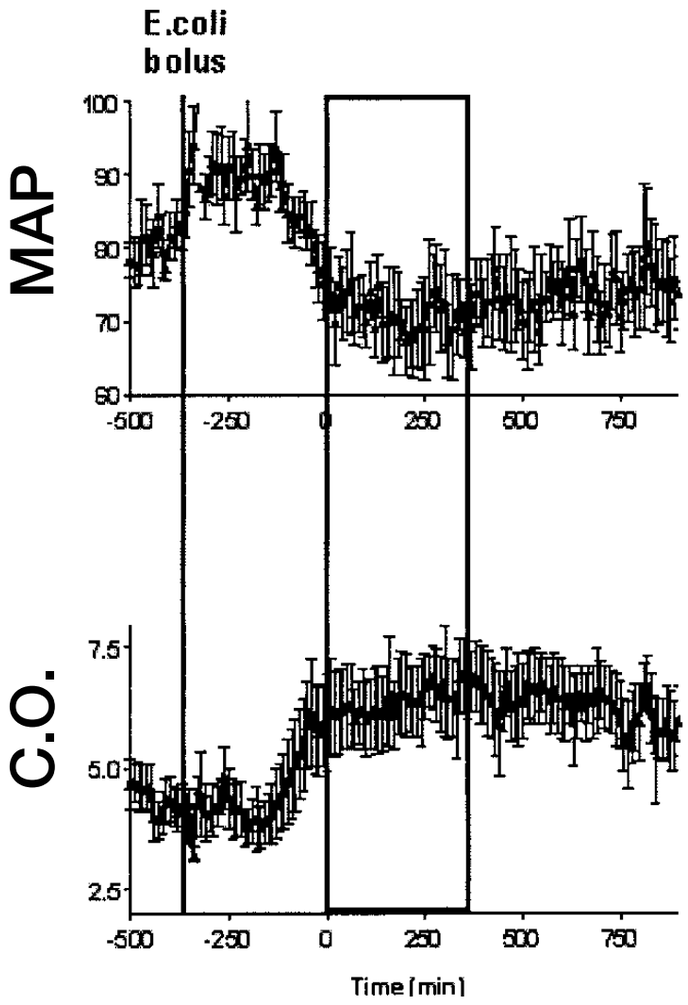
Pathophysiology- Septic AKI

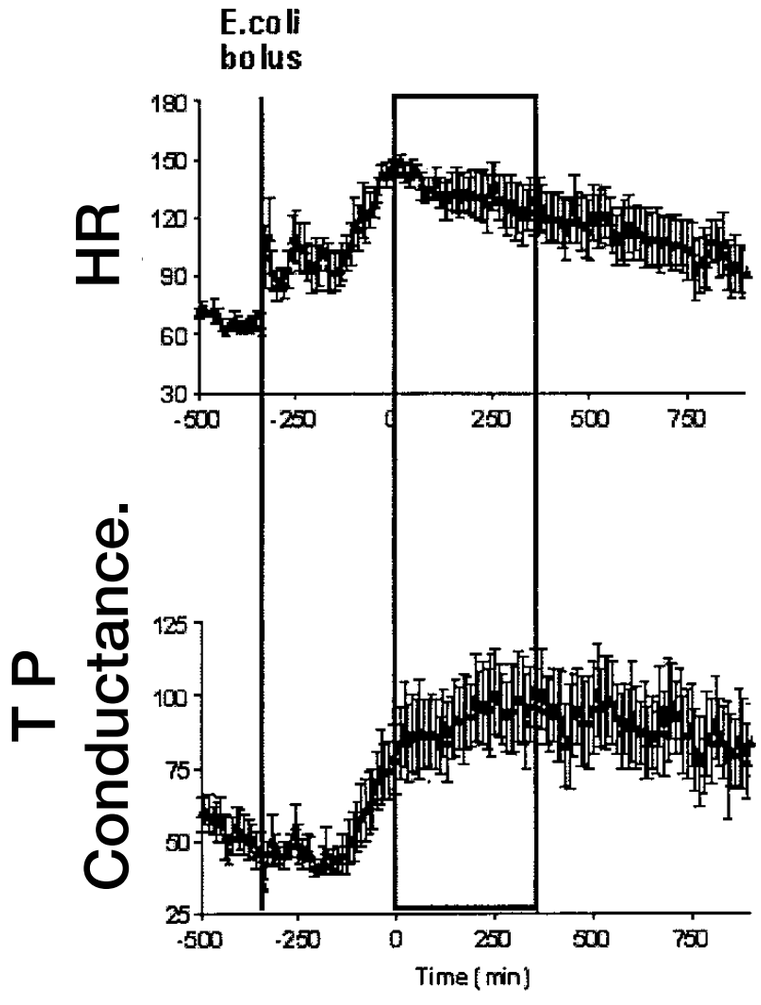
- Tubular cells require large supply of energy for electrolyte and fluid reabsorption
- Tubular injury should thus cause **polyuria**, but:
  - Oliguria more common
  - Necrosis rare
  - <10% AKI survivors require long term dialysis
- Renal **dysfunction** during sepsis/inflammation, rarely structural damage
- Bioenergetic dysfunction leads to decrease of GFR (altered NO and tubulo-glomerular feedback)
- AKI seems to be a disease of the **micro-circulation**
  - Massive therapeutic implications
    - Efforts were concentrated on increasing renal flow by **increasing cardiac flow** and perfusion **pressure**
  - If so, large amounts of fluids might do more **harm** than good

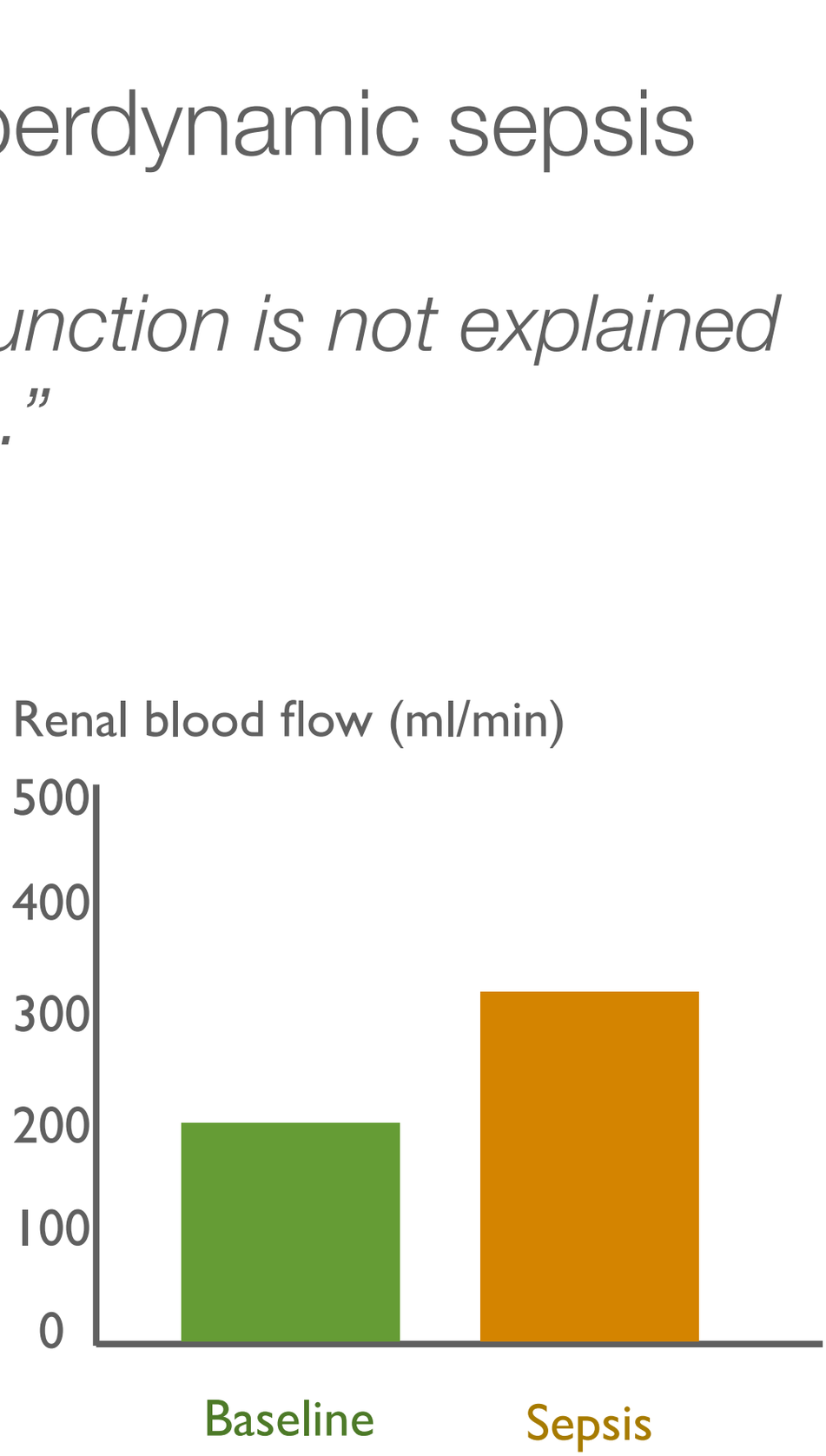
Lancet Vol 380 Dec 1,2012; pg 1904

Vital organ blood flow during hyperdynamic sepsis

*"During hyperdynamic sepsis, renal dysfunction is not explained by **global** ischemia."*







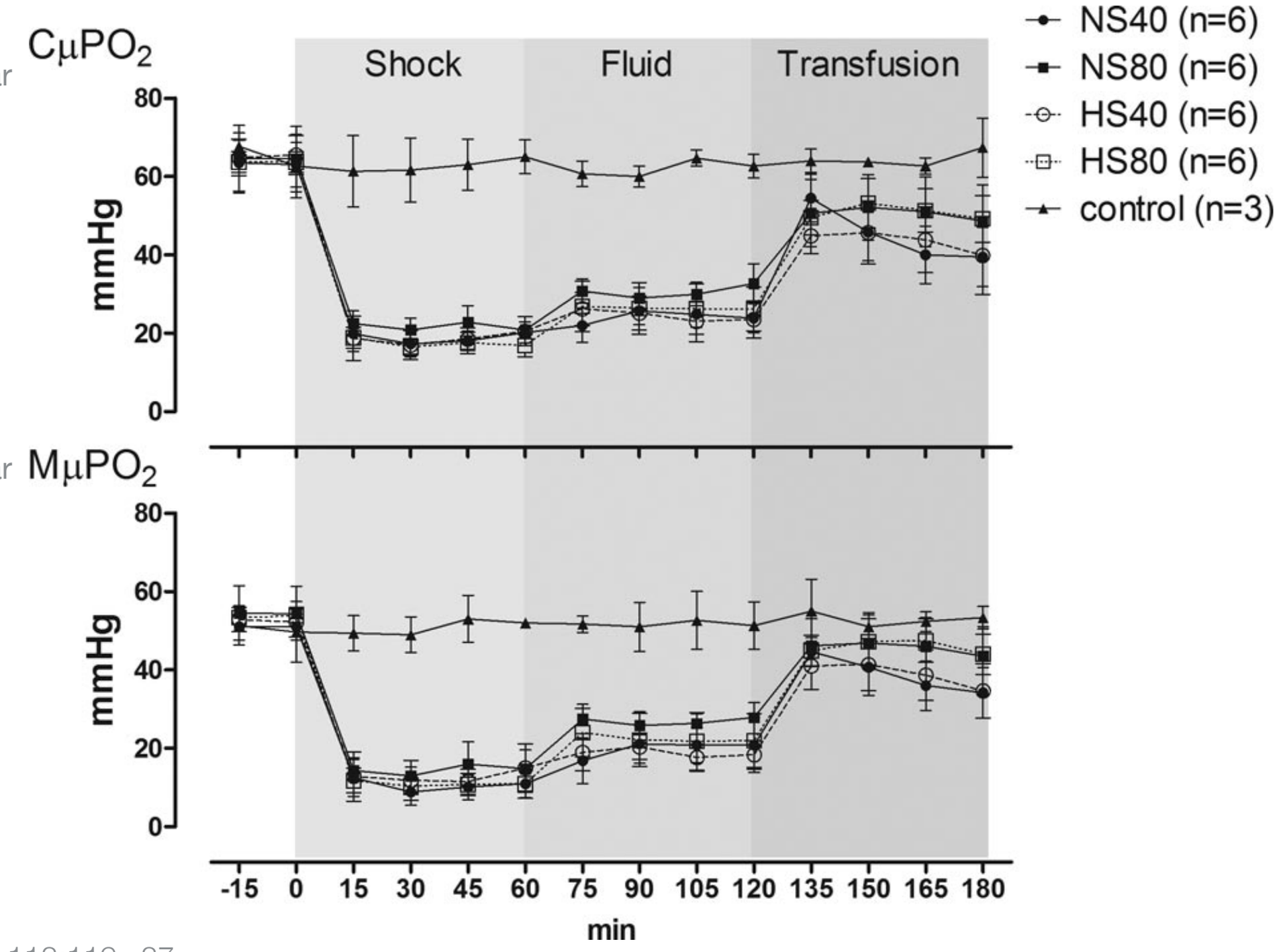
Chest 2003;124;1053-1059

Pathophysiology- ischaemic AKI

Resuscitation to normal BP does not guarantee normal renal perfusion

Cortical microvascular PO_2

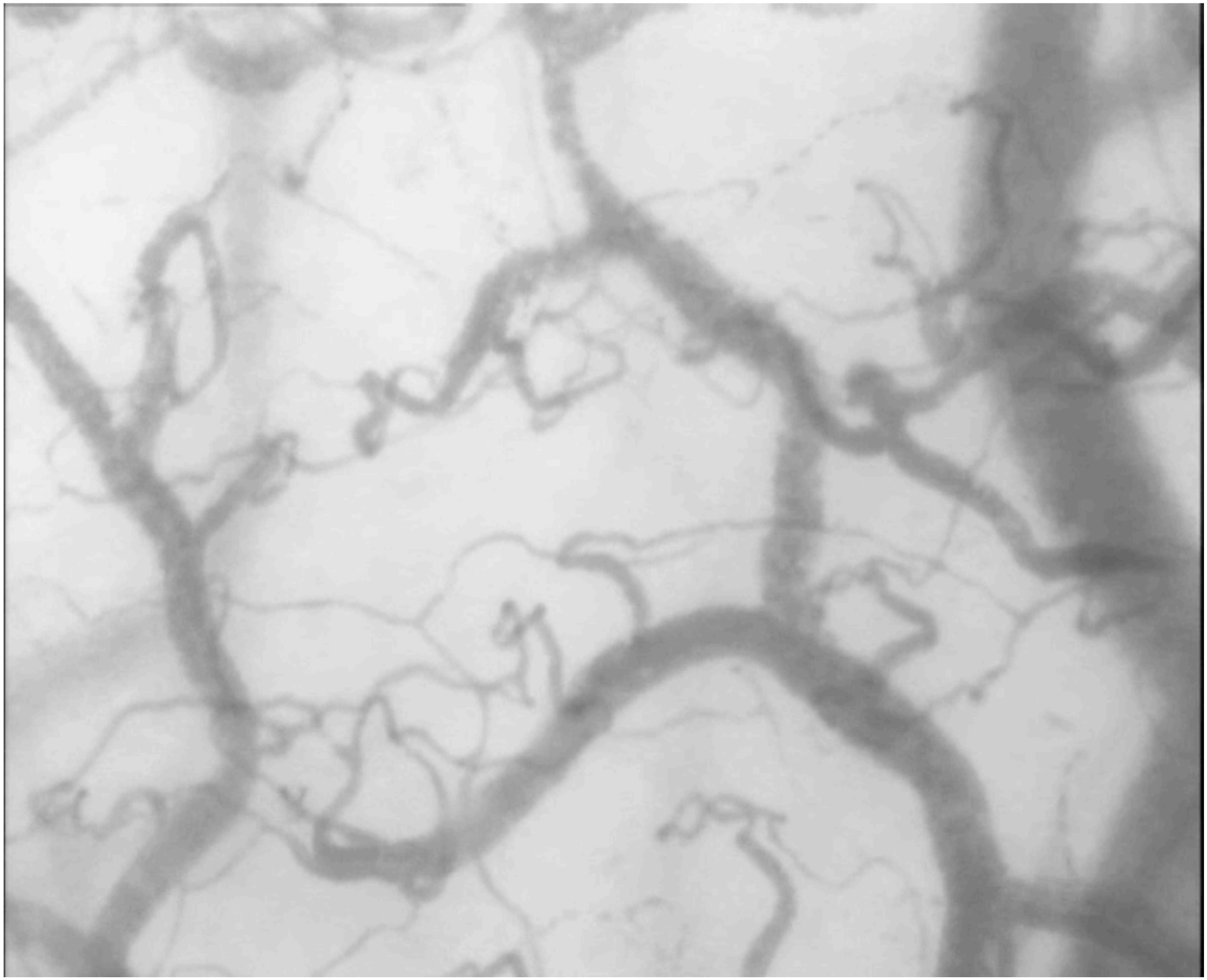
Medullary microvascular PO_2



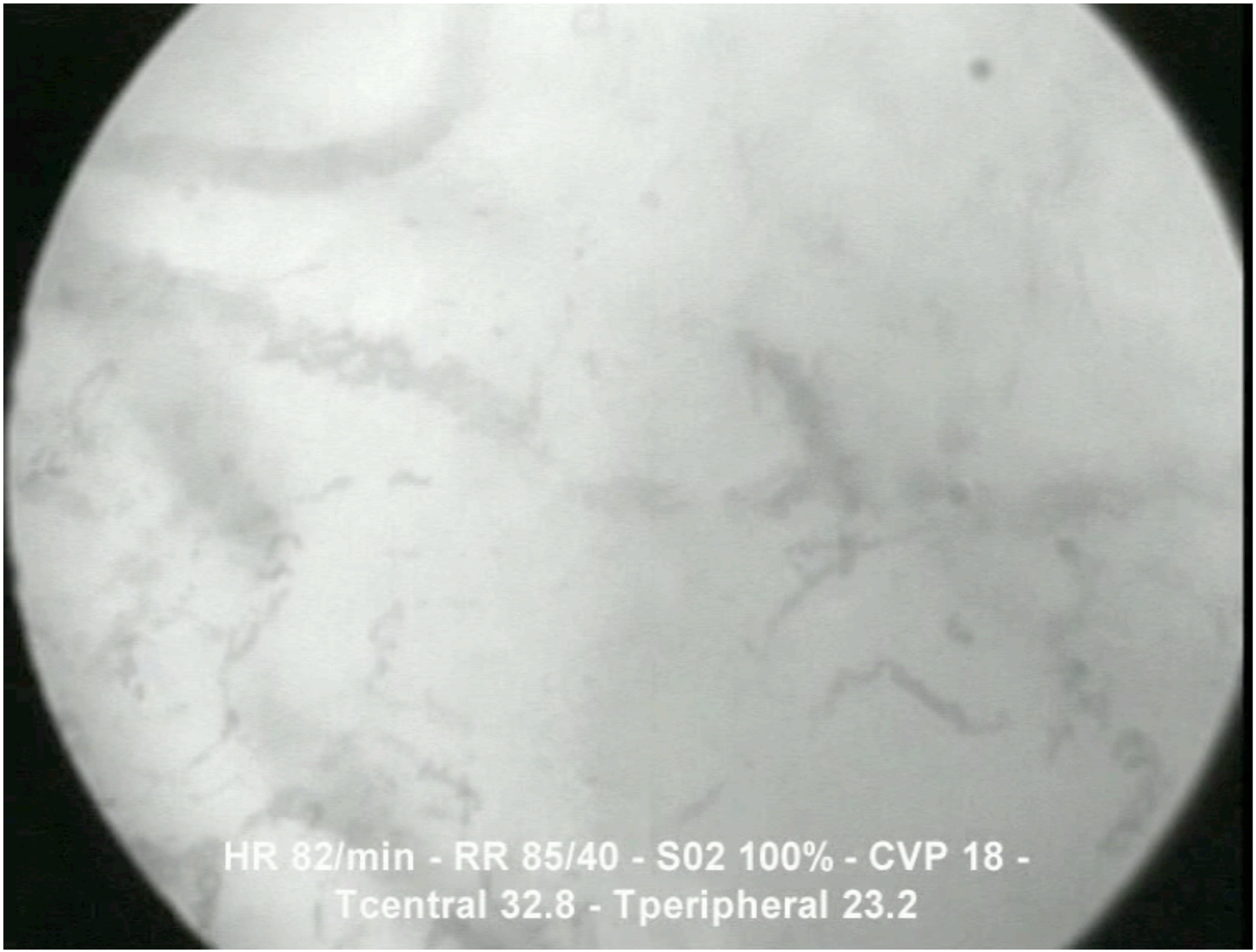
Anesthesiology 2010; 112:119 –27

Microcirculation and ARI

Microcirculation - Normal



Microcirculation - Sepsis



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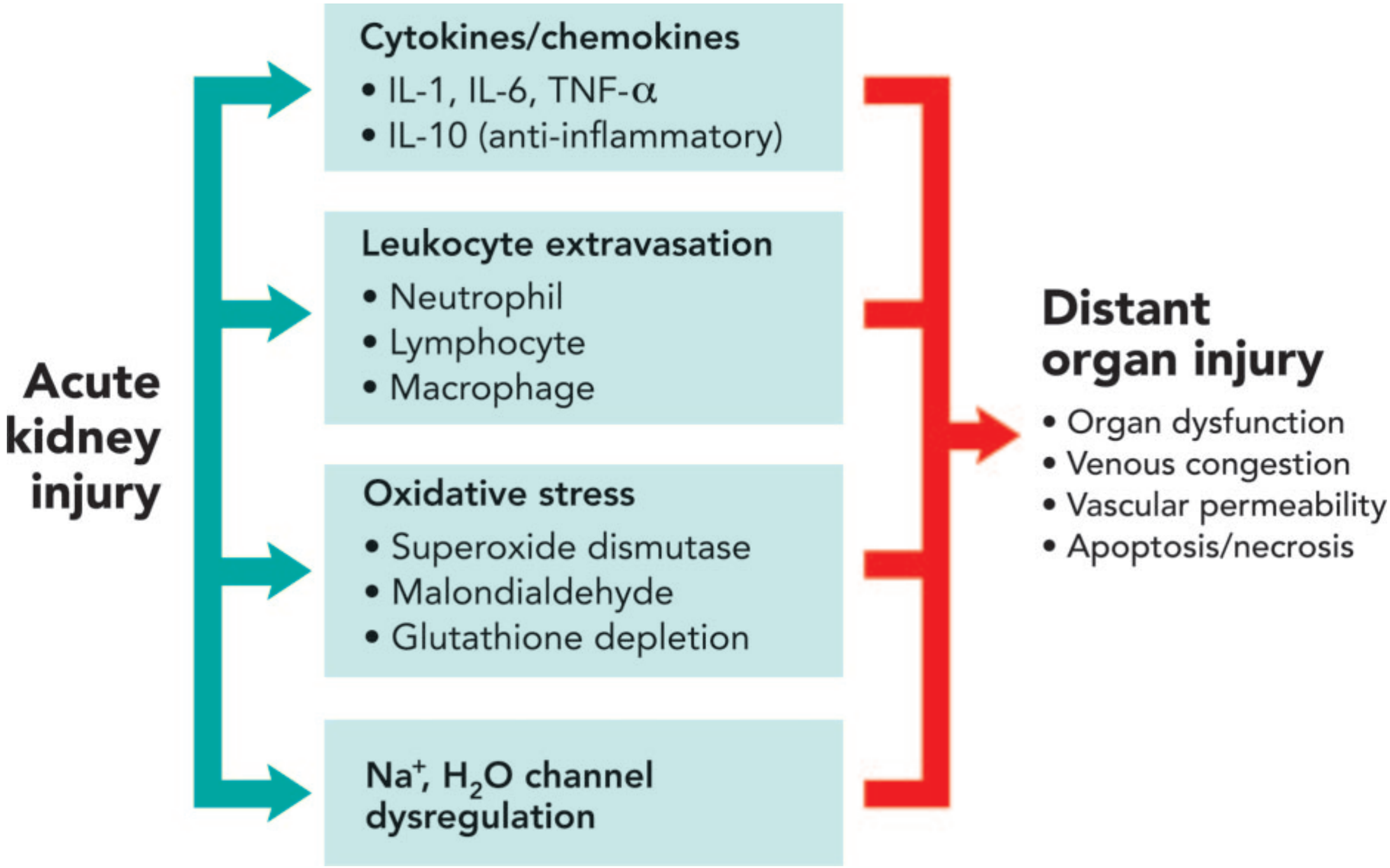
Acute renal injury and organ cross talk

AKI is a systemic disorder



Anesthesiology 2012; 116:1139–48

Scheel et al; Kid Int

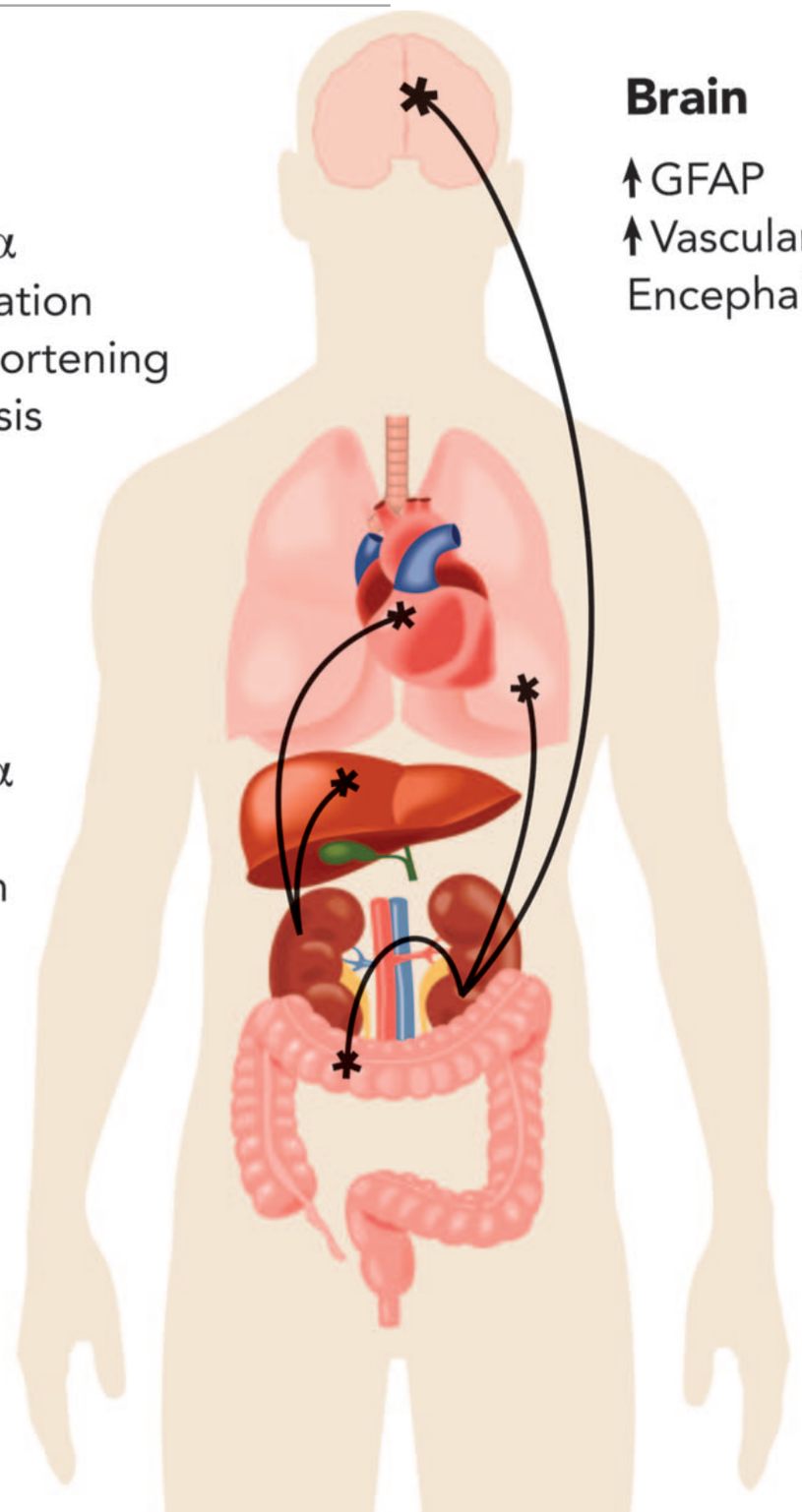
AKI is a systemic disorder

Heart

↑IL-1, IL-6, TNF-α
Neutrophil infiltration
↓LV Fractional shortening
Myocyte apoptosis

Brain

↑GFAP
↑Vascular permeability
Encephalopathy



Lungs

↑Vascular permeability
Na^+ channels downregulated
Pulmonary edema
Alveolar hemorrhage
Endothelial cell apoptosis

Liver

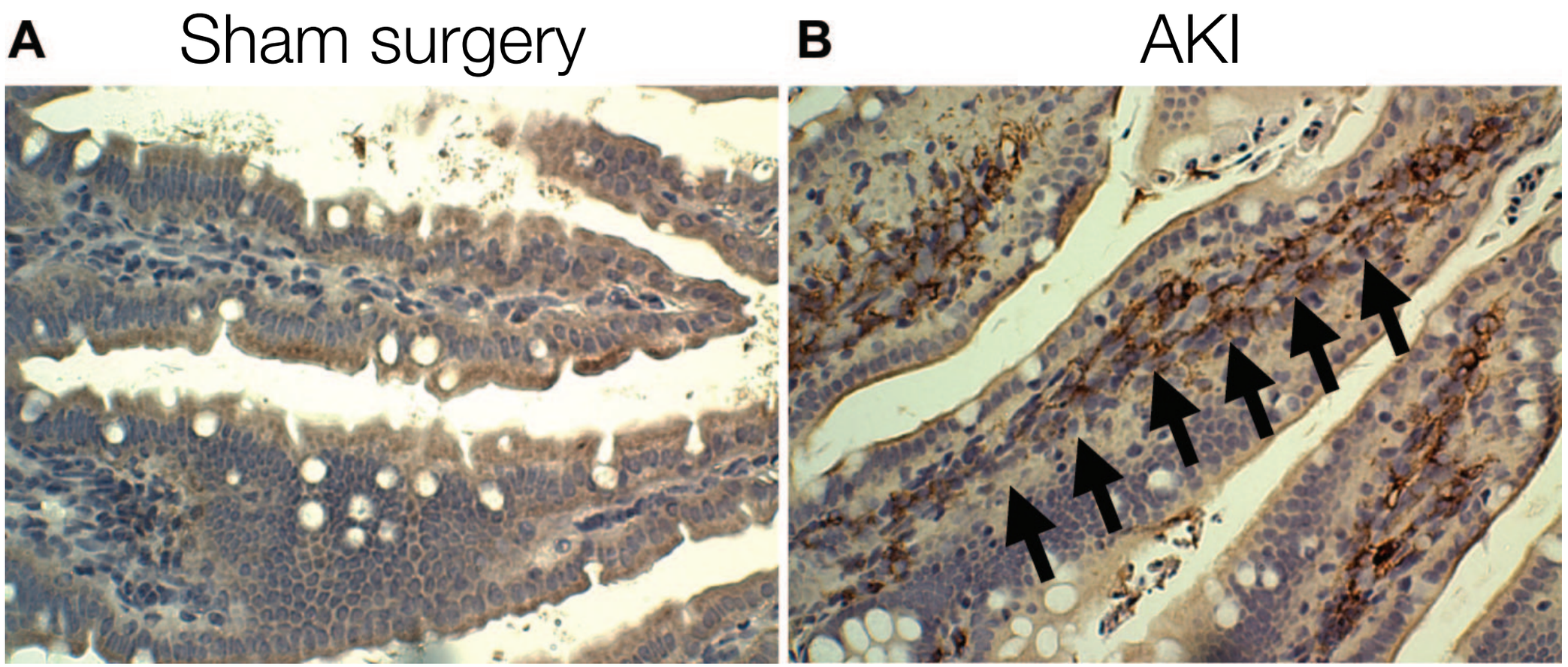
↑ICAM-1, IL-6, TNF-α
Transaminitis
Neutrophil infiltration
Oxidative stress
Periportal necrosis

Intestines

↑IL-17A
↑Vascular permeability
Neutrophil infiltration
Villous endothelial cell apoptosis
Villous epithelial cell necrosis

Anesthesiology 2012; 116:1139–48

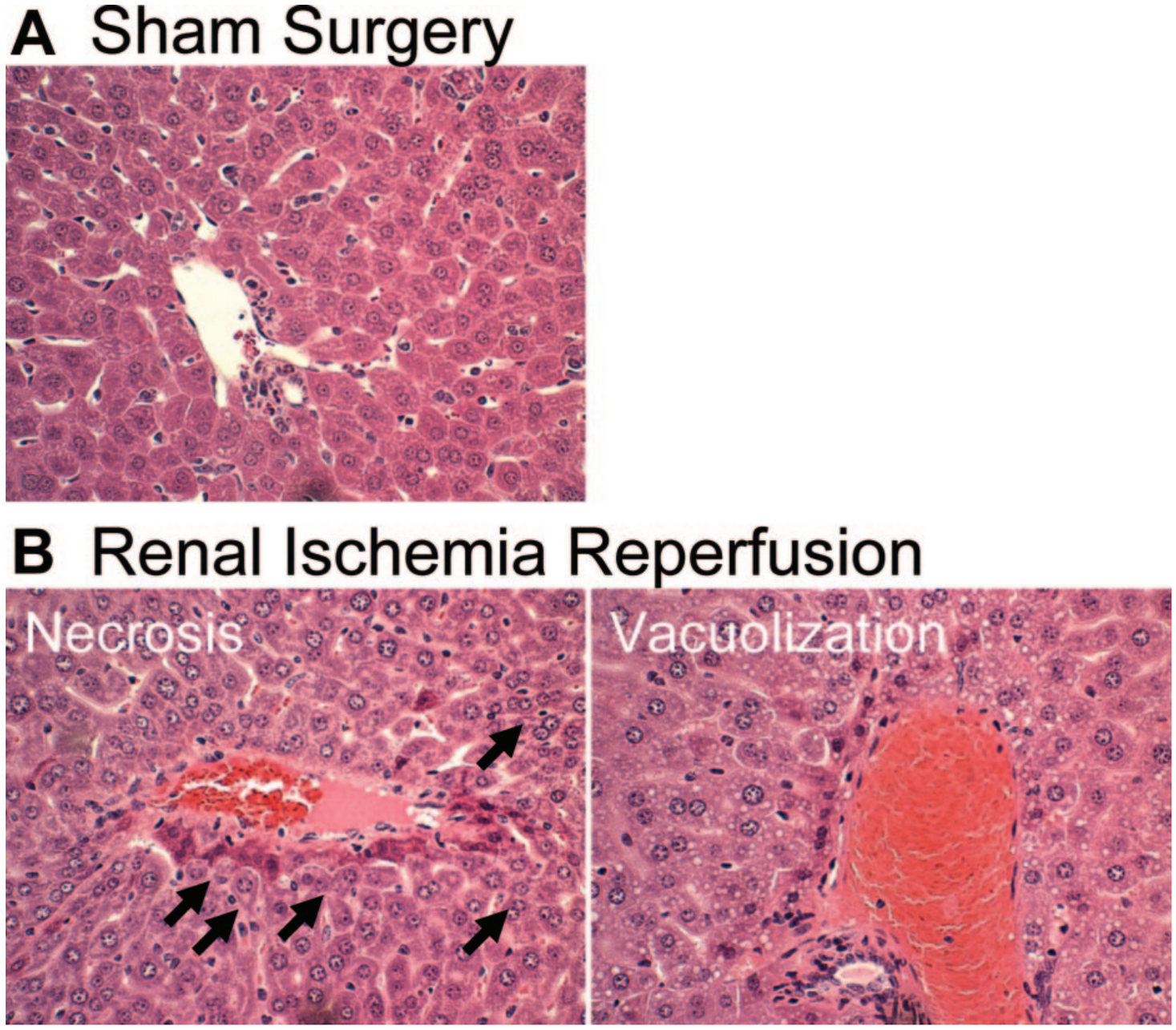
AKI is a systemic disorder



Increased **small intestinal** macrophage infiltration after acute kidney injury (AKI).

Anesthesiology 2012; 116:1139–48

AKI is a systemic disorder

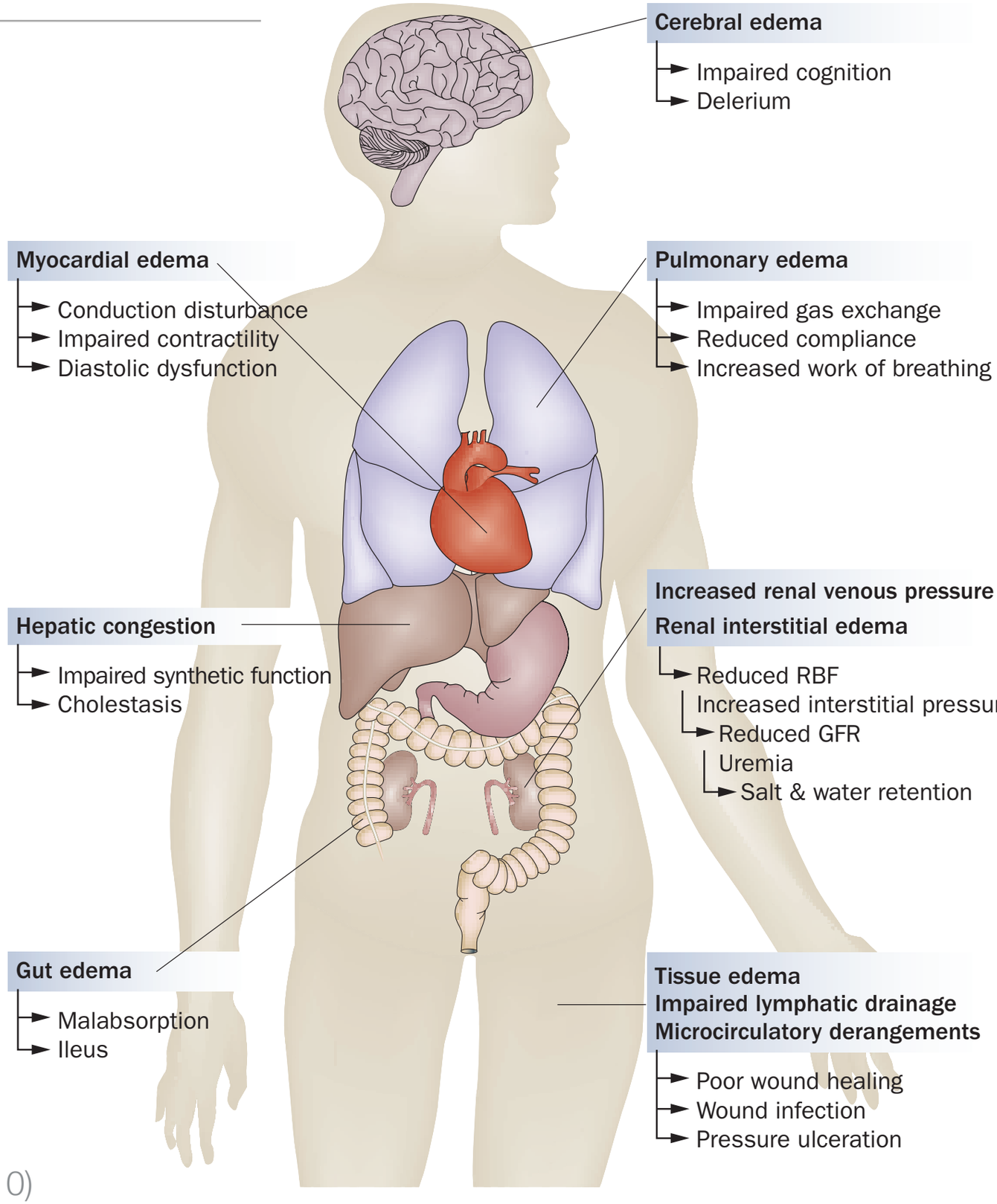


Hepatic injury after acute kidney injury
(30 min ischaemia - 24 hr reperfusion)

Anesthesiology 2012; 116:1139–48

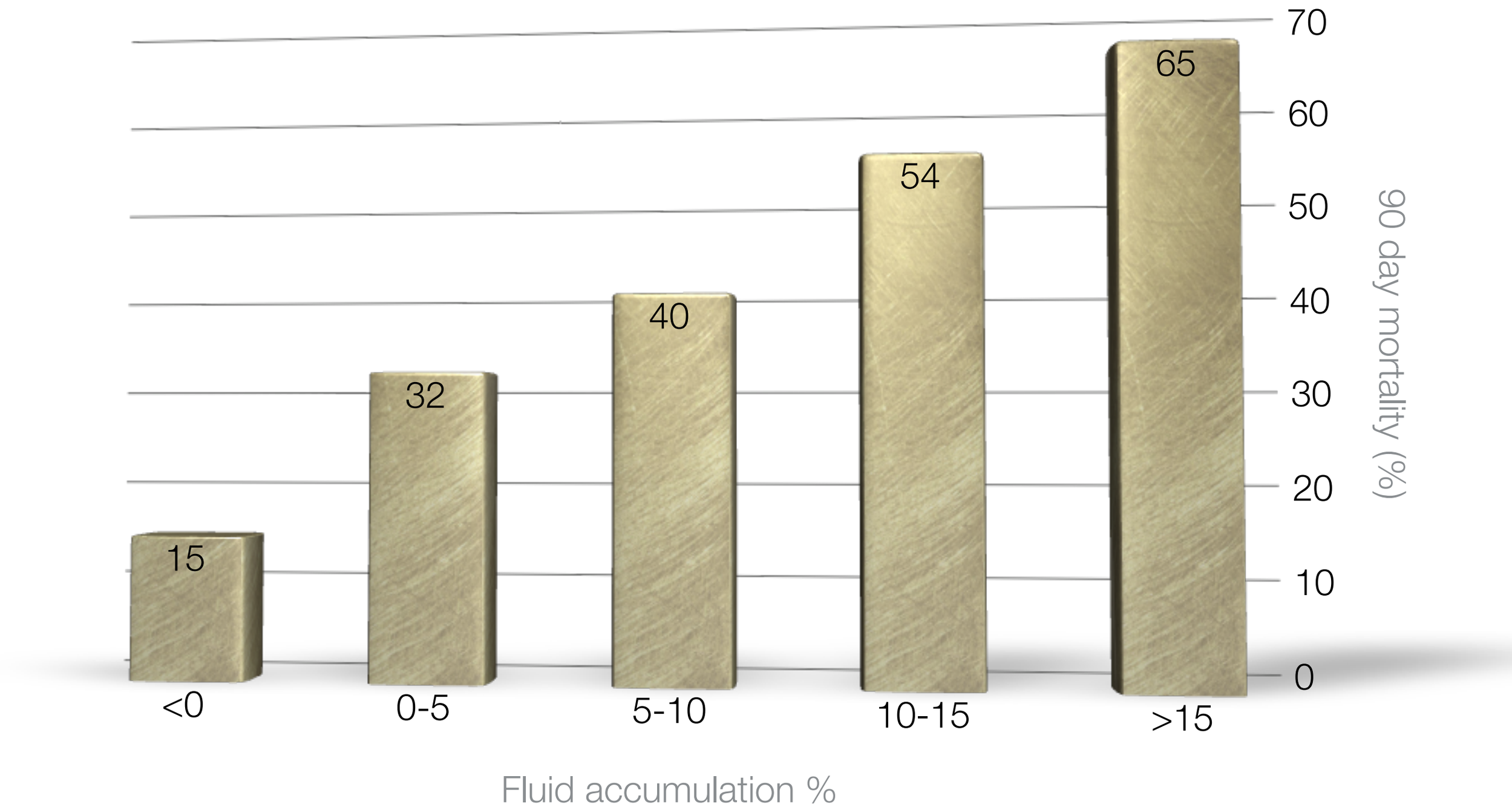
Other effects - Fluid overload

Effect of Fluid Overload



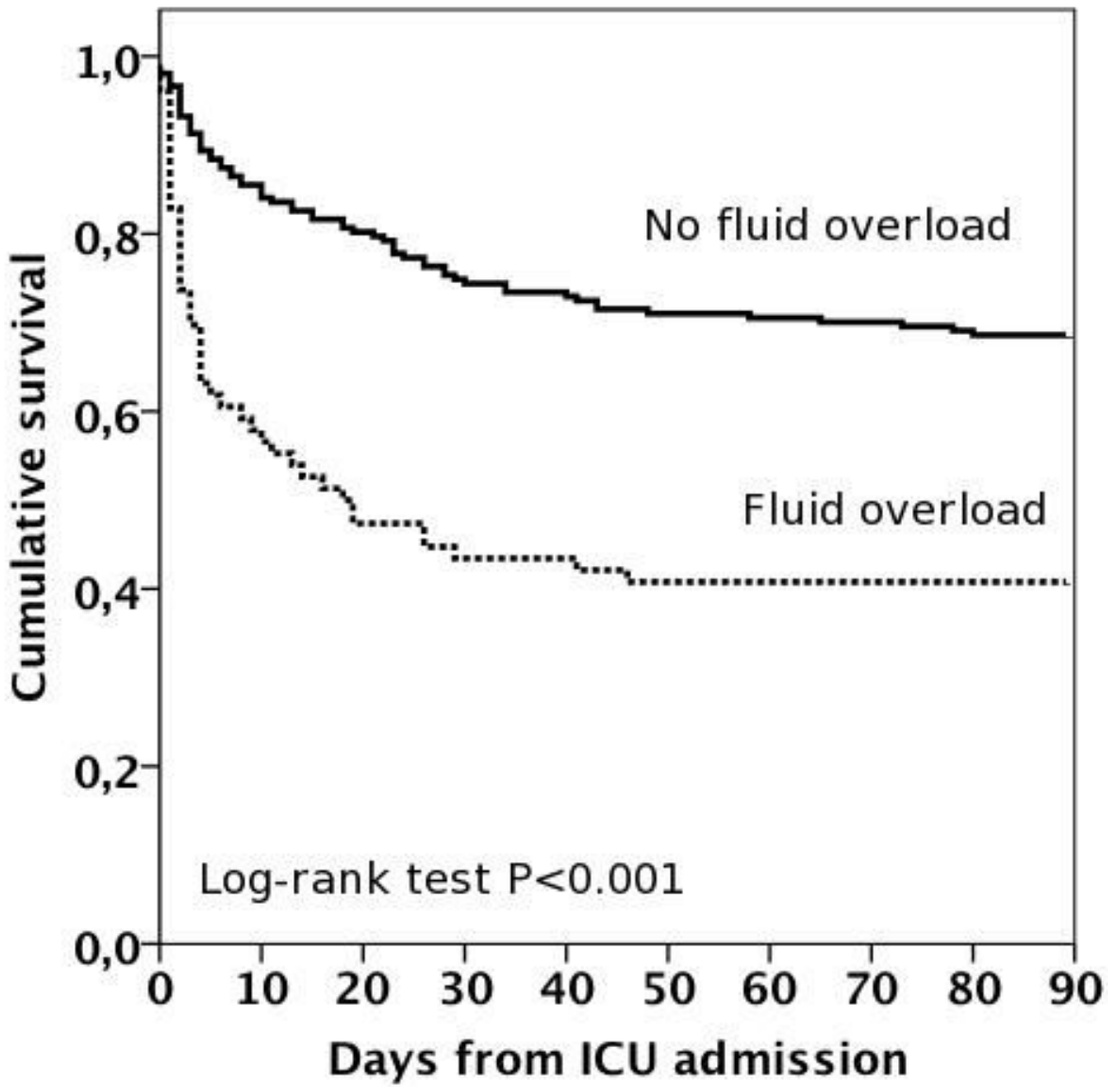
Nat. Rev. Nephrol. 6, 107–115 (2010)

Fluid overload and mortality in ITU patients on RRT



Critical Care 2012, 16:R197

Fluid overload and mortality in ITU patients on RRT



"Patients with fluid overload at RRT initiation had **twice** as high crude 90-day **mortality** compared to those without.
Fluid overload was associated with increased risk for 90-day mortality even after adjustments for other factors."

Critical Care 2012, 16:R197

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Management of AKI

Risk stratify

- 50% of ARI occur in the **wards**, not ITU
- Watch for: **pre-existing proteinuria** , DM, CCF, Liver disease and **CKD**
- Exclude a.s.a.p. **reversible** causes: hypovolaemia, post-renal causes and nephrotoxic drugs

- Monitor urinary output (ex. per shift) and creatinine in hospitalised patients outside the ICU, in at risk for AKI.

- Although rare, a minimal work-up for the presence of underlying rapidly progressive forms of glomerular disease should also be performed, especially in the absence of other potential explanations.

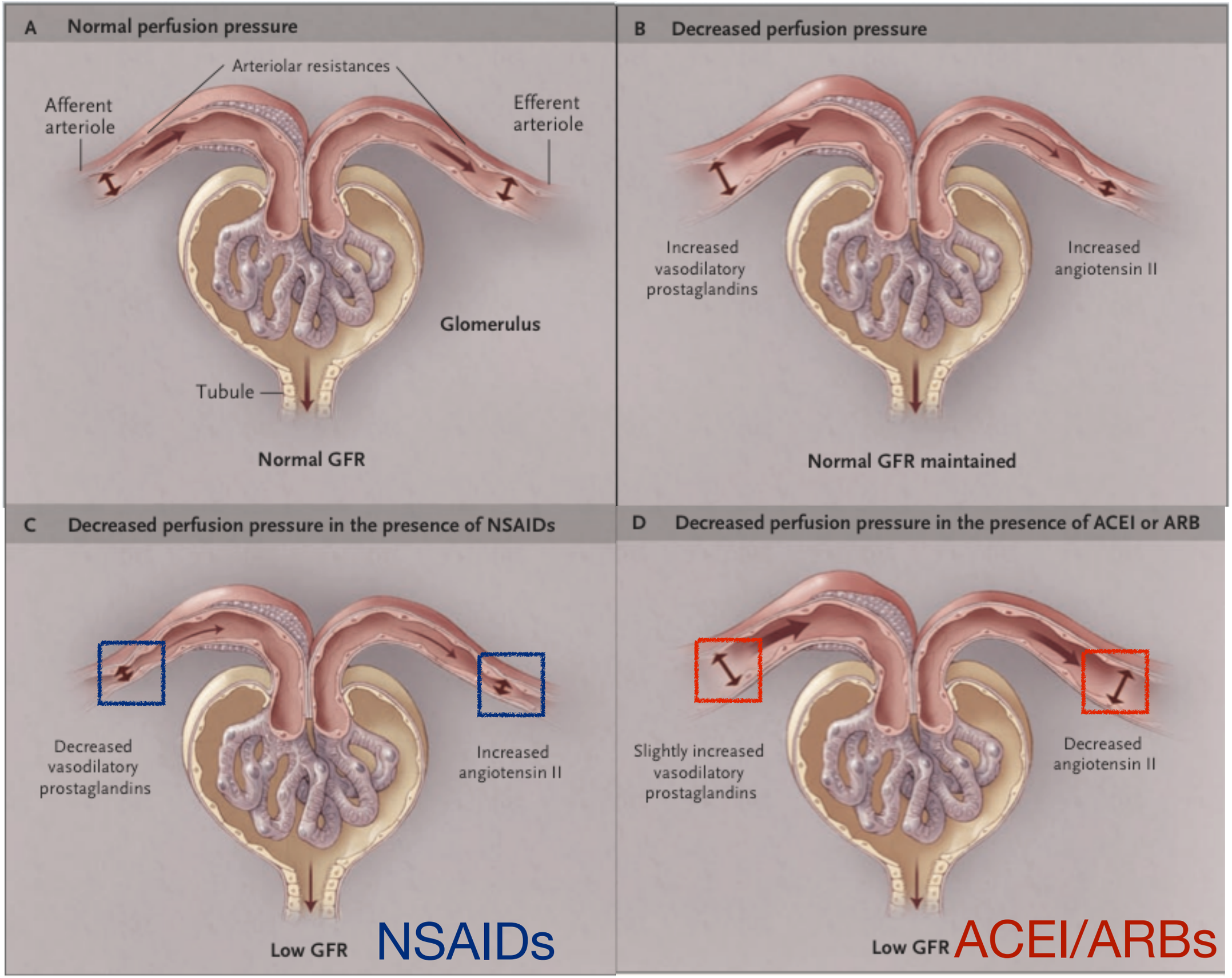
Nephrol Dial Transplant. 2012;27(12):4263-4272.

Avoid nephrotoxic agents

Common Nephrotoxins in the ICU

- NSAIDS
- ACEI
- Antimicrobials
  - Aminoglycosides
  - Amphotericin
  - Acyclovir
- Chemotherapeutic agents
- Radiocontrast dye

Crit Care Med 2010; 38:000 – 00 Antimicrobial agents and Chemotherapy, May 1999, p. 1003–1012



Abuelo NEJM 2007

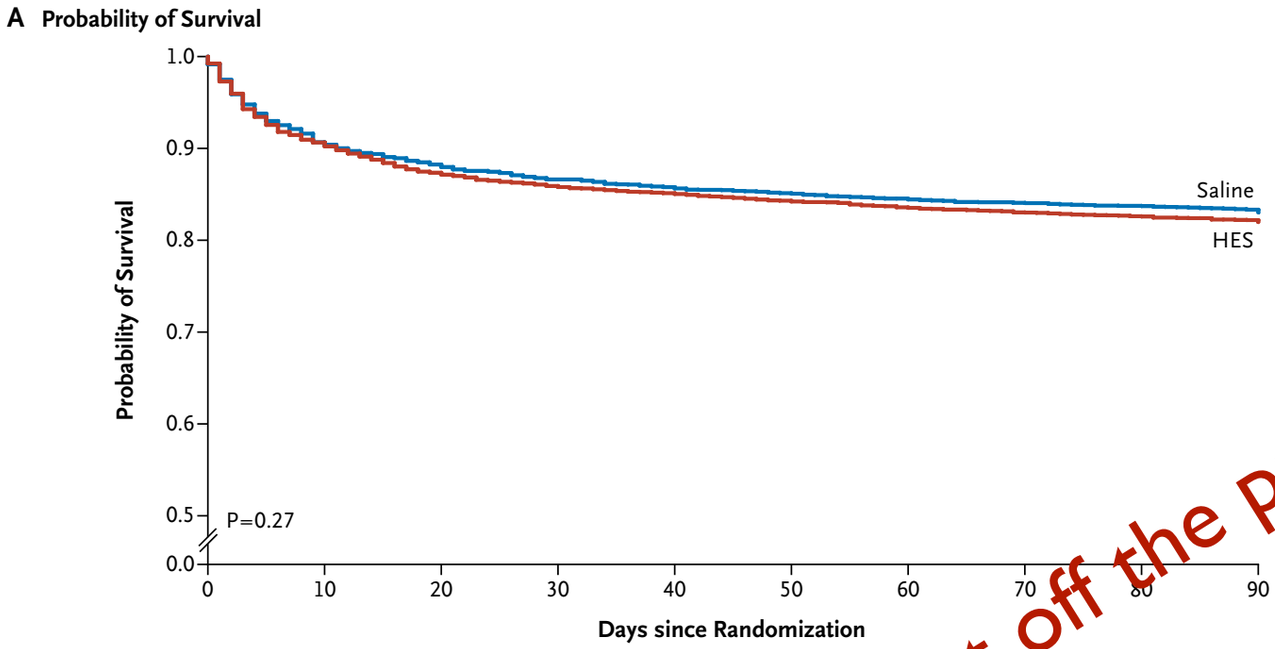
Aminoglycosides

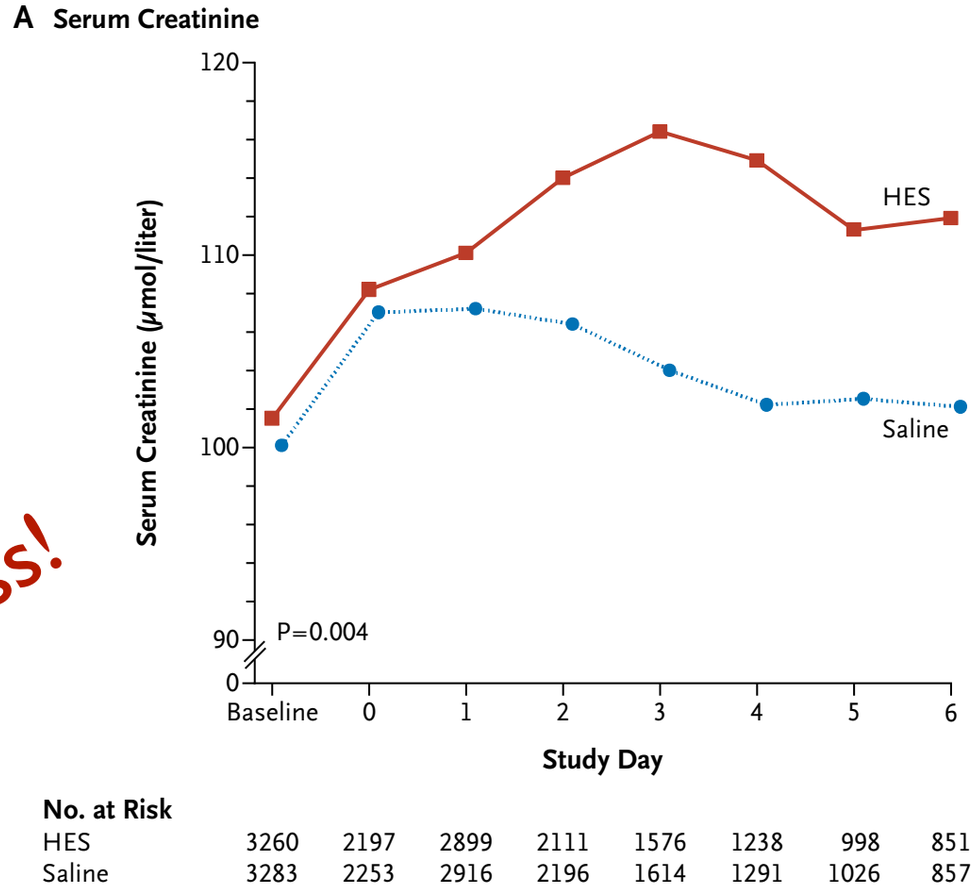
- tubular damage
- non oliguric renal failure
- hypo-osmolar urine
- rare after 1 dose
- recovery upon drug discontinuation usual

Antimicrobial agents and Chemotherapy, May 1999, p. 1003–1012

The NEW ENGLAND JOURNAL of MEDICINE

Hydroxyethyl Starch or Saline for Fluid Resuscitation in Intensive Care





Hot off the Press!

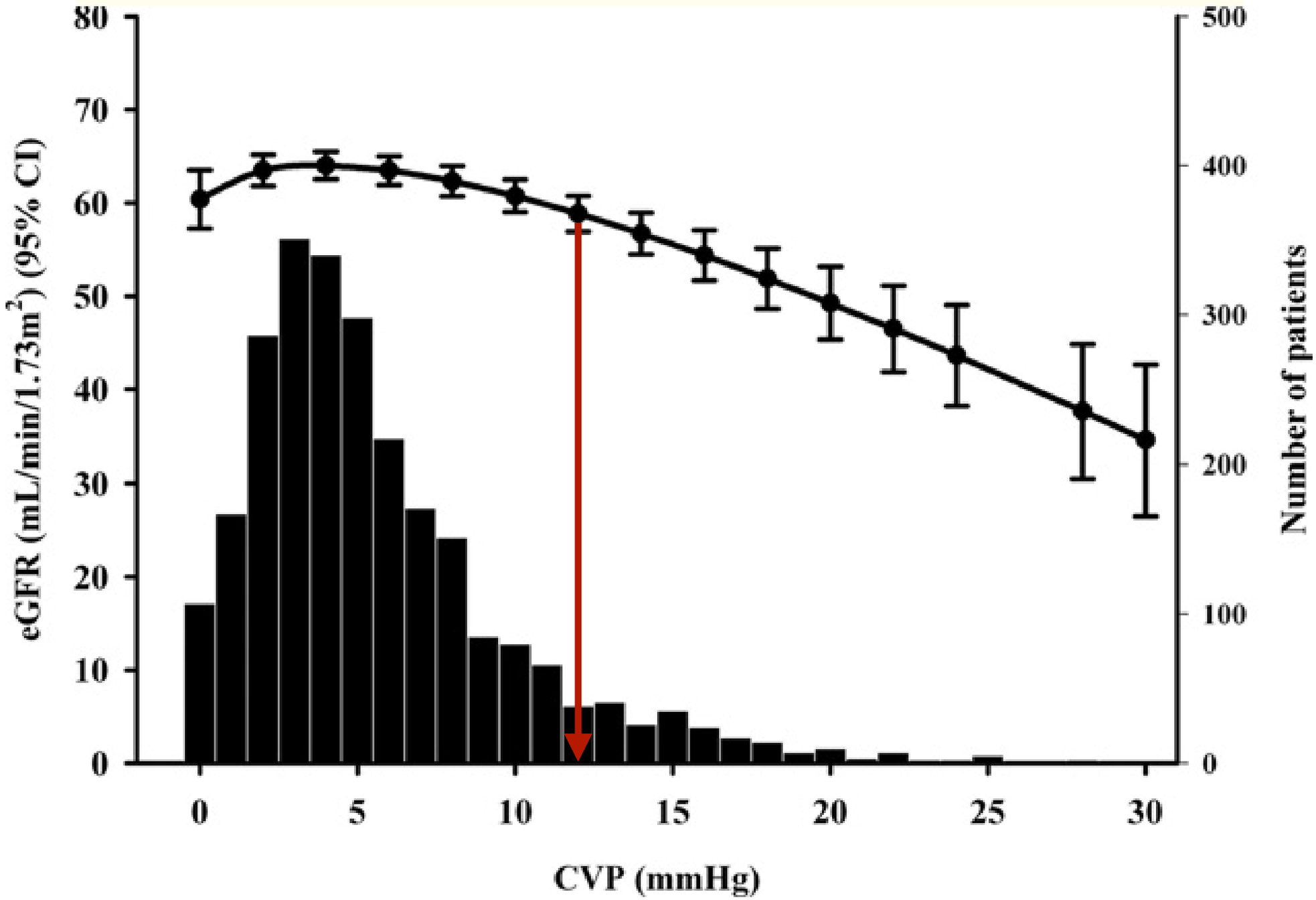
"no significant difference in 90-day mortality between patients resuscitated with 6% HES (130/0.4) or saline."

"..more patients who received resuscitation with HES were treated with renal-replacement therapy."

NEJM Oct 17, 2012

Care if high CVP

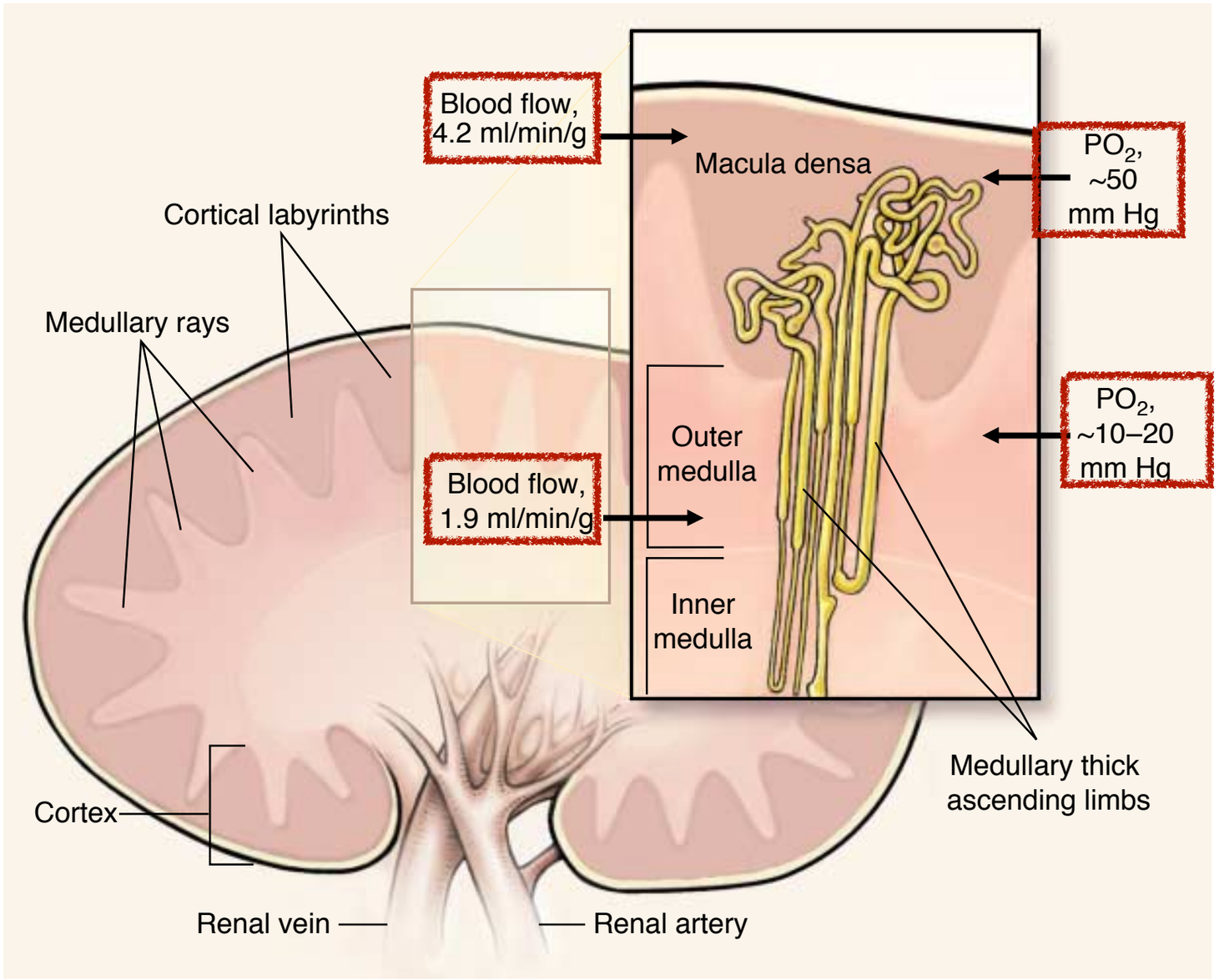
Increased Central Venous Pressure Is Associated With Impaired Renal Function and Mortality in a Broad Spectrum of Patients With Cardiovascular Disease



J Am Coll Cardiol 2009;53 582-6

Prevention - Diuretics?

WHY DIURETICS?



The medulla, whose meagre blood supply optimises the concentration of urine, is poorly oxygenated. Medullary hypoxia results both from countercurrent exchange of oxygen within the vasa recta and from the consumption of oxygen by the medullary thick ascending limbs. Renal medullary hypoxia is an obligatory part of the process of urinary concentration.

NEJM 1995: Vol 332: No 10

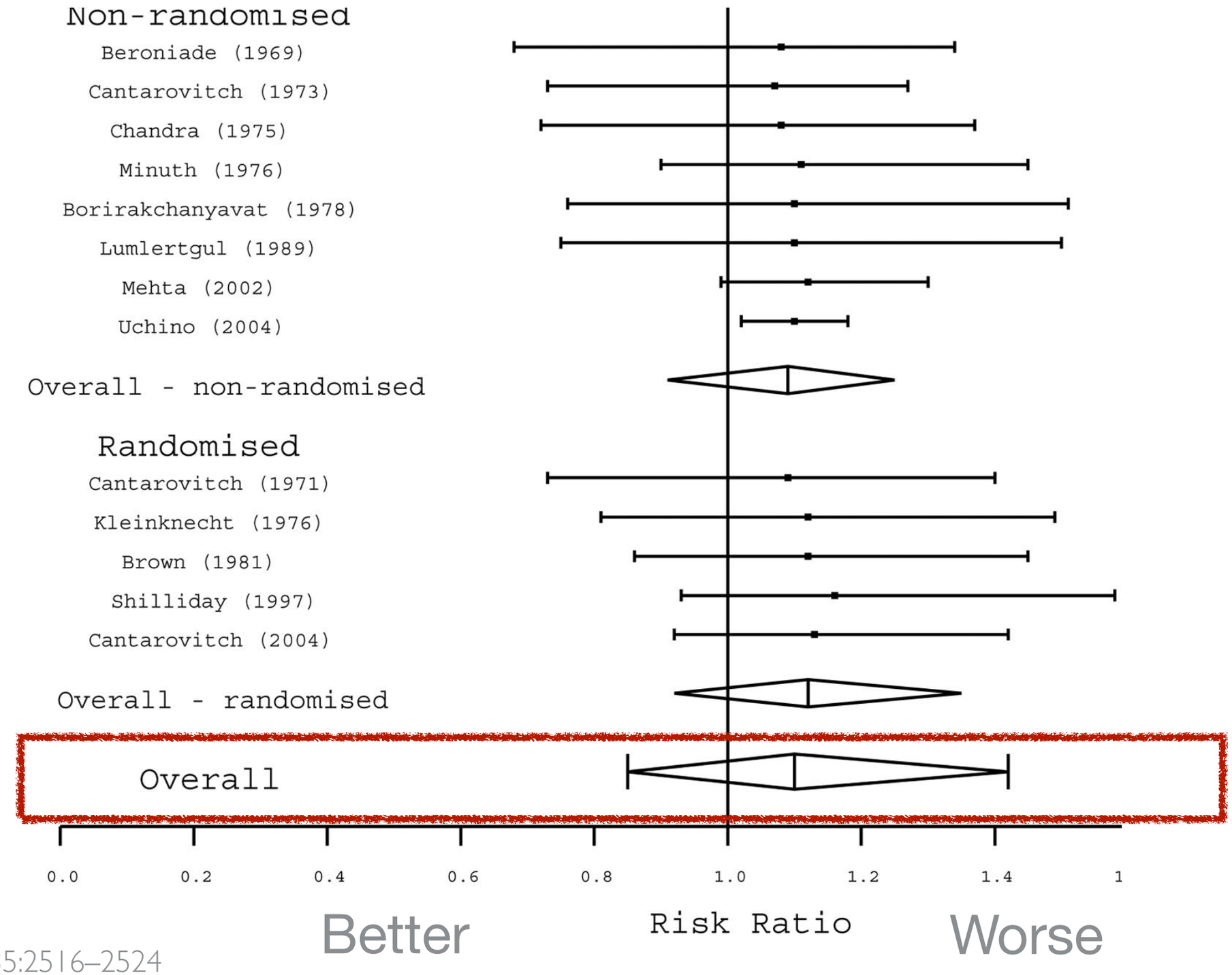
WHY DIURETICS?

"The work of concentrating the urine predisposes a person to medullary hypoxic damage, reducing this work may prevent medullary injury."

"Furosemide, which inhibits reabsorptive transport in the medullary thick ascending limb, increased medullary PO2 from 16 to 35 mmHg without altering cortical PO2. This effect was directly due to decreased tubular O2 consumption."

NEJM 1995: Vol 332: No 10 Am J Physiol Renal Physiol 267: F1059-F1062, 1994

So do loop diuretics protect in acute renal failure?



Crit Care Med 2007; 35:2516–2524

JAMA®

Online article and related content
current as of March 30, 2009.

Diuretics, Mortality, and Nonrecovery of Renal Function in Acute Renal Failure

Ravindra L. Mehta; Maria T. Pascual; Sharon Soroko; et al.

JAMA. 2002;288(20):2547-2553 (doi:10.1001/jama.288.20.2547)

"the Devil's drug" ....Dr Paul Marik

Conclusions

"The use of diuretics in critically ill patients with acute renal failure was associated with an **increased risk of death** and nonrecovery of renal function.....

....the widespread use of diuretics in critically ill patients with acute renal failure should be **discouraged**."

So diuretics or not ?

- We recommend **not** using diuretics to prevent AKI. (1B)
- We suggest **not** using diuretics to treat AKI, except in the management of volume overload. (2C)

Acute Renal Injury in ITU

- Why worry?
- Definition
- Anatomy and physiology
- Markers of injury
- Pathophysiology
- Consequences of AKI
- Prevention
- Special Circumstances

Renal Injury-Special Circumstances

- Contrast induced nephropathy
- Hepatorenal syndrome
- Rhabdomyolysis

Contrast Induced Nephropathy - Definition

3 components

- Diagnosis of AKI using KDIGO criteria
- Within 48-72 hours
- Exclude
  - Cholesterol embolism, hypotension, sepsis, etc

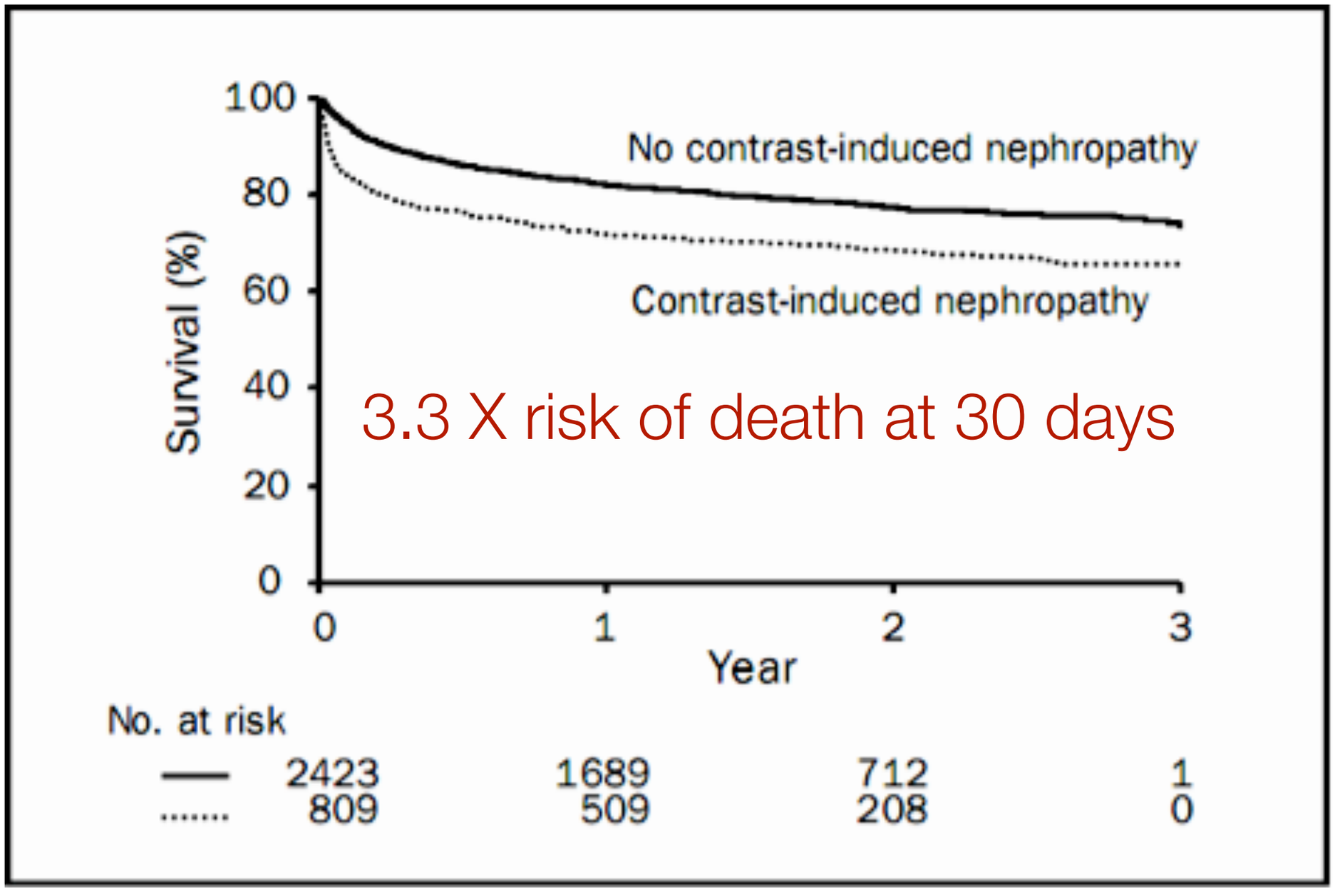
Contrast Induced Nephropathy - Who's at risk

Risk factors

- Hypotension (5)
- CCF (5)
- >75 years (4)
- Diabetes (3)
- Anaemia (3)
- Contrast volume (1 for each 100 mL)
- Se Creatinine > 132 (4)

J Am Coll Cardiol 2004, 44, 1393-99

Contrast Induced Nephropathy - Mortality



Mayo Clin Proc. 2008;83(10):1095-1100

Contrast Induced Nephropathy - N-acetyl cysteine

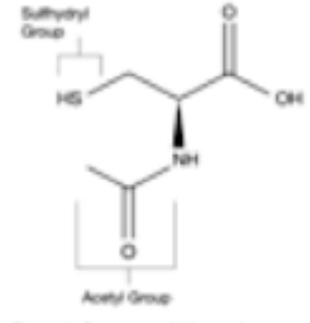
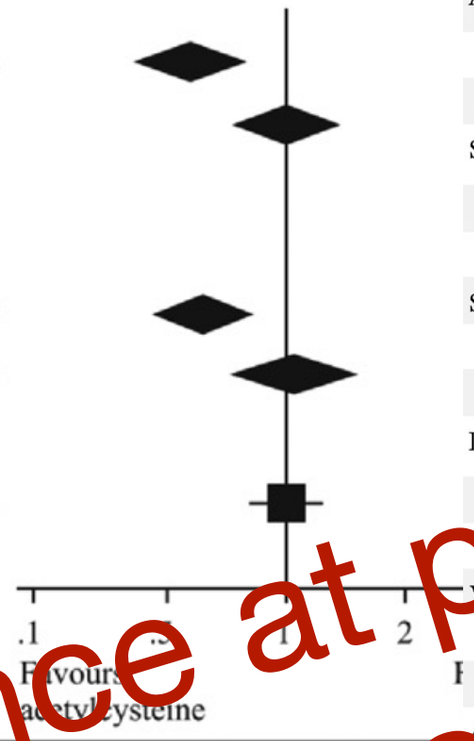
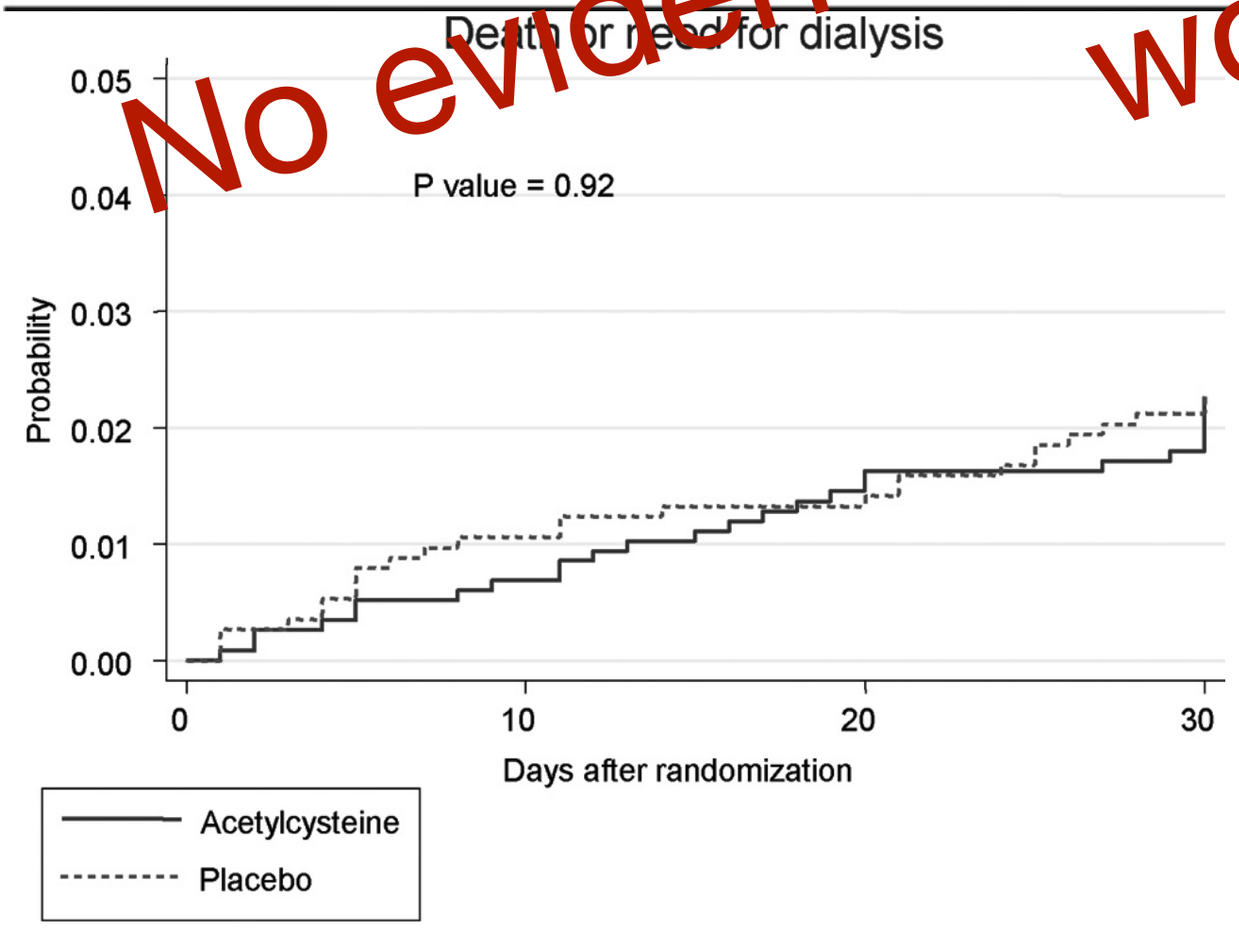


Figure 1. Structure of N-acetylcysteine.

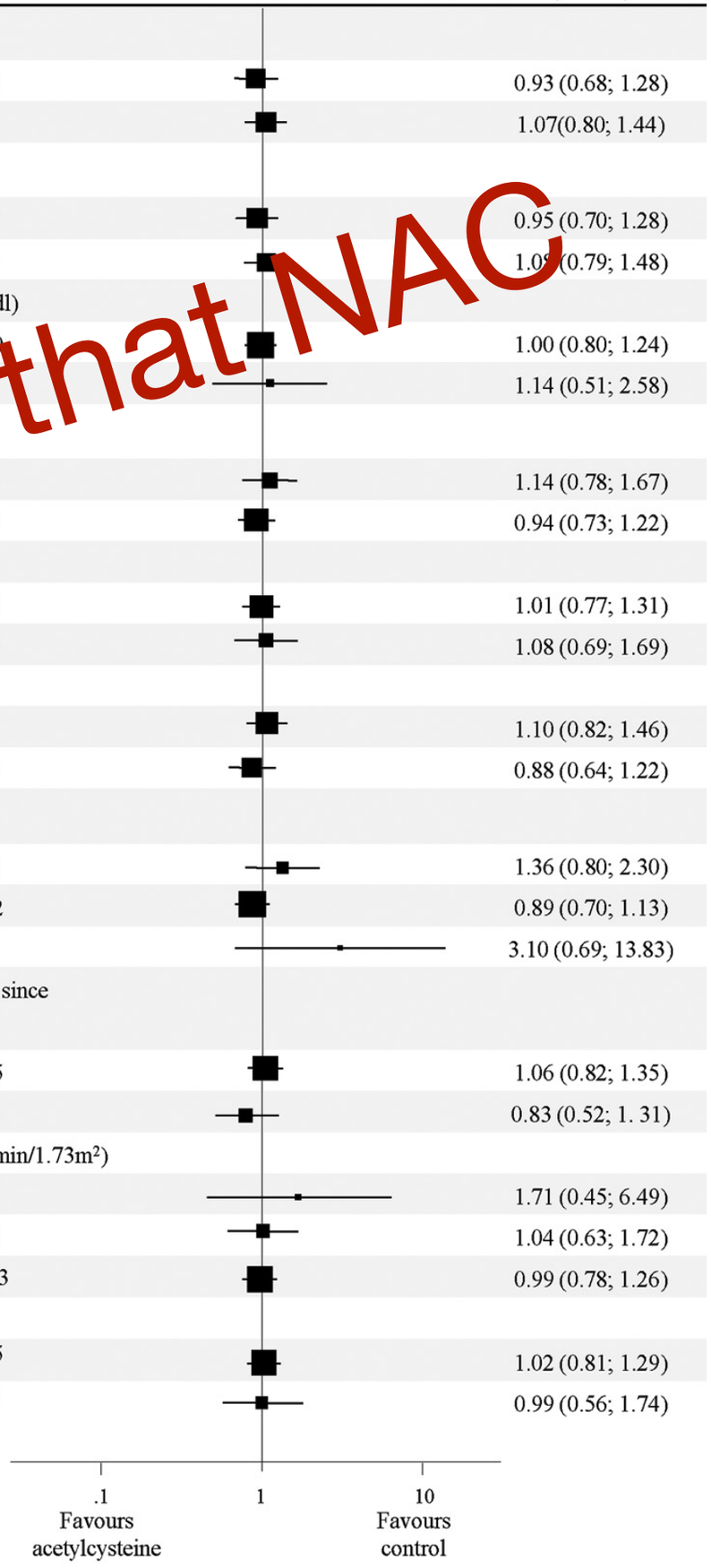
- Potent anti-oxidant
- Scavenger of oxygen derived free radicals
- Prevent direct oxidative tissue damage

Subgroup	Trials, n	N	Relative Risk (95%CI)	I^2
Allocation concealment				
No or unclear	34	3,778		
Yes	11	1,581		
All methodological criteria adequate				
No or unclear	40	4,359		
Yes	5	1,000		
ACT Trial	1	2,308		





Age			
≤ 70 years	67/558	68/528	0.93 (0.68; 1.28)
> 70 years	80/595	74/591	1.07(0.80; 1.44)
Sex			
Male	77/716	77/680	0.95 (0.70; 1.28)
Female	70/437	65/439	1.09 (0.79; 1.48)
Serum creatinine > 132.6 µmol per liter (1.5mg/dl)			
No	135/965	132/940	1.00 (0.80; 1.24)
Yes	12/188	10/179	1.14 (0.51; 2.58)
Diabetes			
No	50/451	44/452	1.14 (0.78; 1.67)
Yes	97/702	98/667	0.94 (0.73; 1.22)
Volume of contrast agent			
<140ml	100/837	96/810	1.01 (0.77; 1.31)
≥140ml	35/262	32/259	1.08 (0.69; 1.69)
Acute coronary syndrome			
No	88/738	79/726	1.10 (0.82; 1.46)
Yes	59/413	63/389	0.88 (0.64; 1.22)
Type of contrast			
High osmolar	29/247	22/255	1.36 (0.80; 2.30)
Low osmolar	108/854	117/822	0.89 (0.70; 1.13)
Iso-osmolar	7/35	2/31	3.10 (0.69; 13.83)
Timing for serum creatinine sampling since angiography			
48 to 72 hours	114/869	105/845	1.06 (0.82; 1.35)
>72 to ≤96 hours	30/266	35/257	0.83 (0.52; 1. 31)
Estimated glomerular filtration rate - eGFR (ml/min/1.73m²)			
<30	6/56	3/48	1.71 (0.45; 6.49)
30 - 60	30/425	27/398	1.04 (0.63; 1.72)
>60	111/672	112 /673	0.99 (0.78; 1.26)
eGFR<60 ml/min/1.73m² and diabetes			
No	122/889	122/905	1.02 (0.81; 1.29)
Yes	24/260	20/214	0.99 (0.56; 1.74)



Circulation. 2011;124:1210-1211

Before “tossing out” NAC, consider:

- All forms of intravascular iodinated contrast are taken up by renal tubular cells, and retained for **>7 days**

  -> direct oxidative cellular damage and acute tubular dysfunction.

“Researchers have always used **short**-term N-aceytlcysteine .... stimulate researchers to study **longer** durations of therapy to match the time iodinated contrast is present in the renal tubular cells…”

Circulation. 2011;124:1210-1211

Before “tossing out” NAC, consider:

- Oral NAC is poorly absorbed with a bioavailability of 3-20%

  (but glutathione values higher after oral)

- Most trials did not use NAC with adequate fluid loading
  - Contrast agents themselves may decrease creatinine secretion thereby increasing se creatinine

- Conversely, NAC in the absence of contrast has been shown to decrease serum creatinine levels through increased tubular secretion in volunteers
  - NAC-induced decreases in serum creatinine not associated with changes in Cystatin C which may be a more accurate indicator of GFR

BMC Medicine 2007, 5:32

Before “tossing out” NAC, consider:

ORIGINAL ARTICLE

Glucocorticoids plus *N*-Acetylcysteine in Severe Alcoholic Hepatitis

so giving more for longer may work ???

The prednisolone–N-acetylcysteine group received intravenous N-acetylcysteine on day 1 (at a dose of 150, 50, and 100 mg per kilogram of body weight ... on days 2 through **5** (100 mg per kilogram per day in 1000 ml of 5% glucose solution).

Death due to the hepatorenal syndrome was less frequent in the prednisolone + N-acetylcysteine group than in the prednisolone-only group at 6 months (**9% vs. 22%**)

The dose, duration, and administration route used were the same as those used for the treatment of drug intoxication.

N Engl J Med 2011;365:1781-9. Lancet 1999;353:294-5.

Hemofiltration and prevention of contrast induced nephropathy

"We wonder why hemofiltration, with its low clearance of radiocontrast material, should have prevented nephropathy, since many believe that renal injury occurs on initial exposure to radiocontrast material."

"We have reported that prophylactic hemodialysis had **no benefit** in preventing radiocontrast-agent–induced nephropathy and associated morbidity."

n engl j med 350;8, february 19, 2004

Haemofiltration to prevent CIN

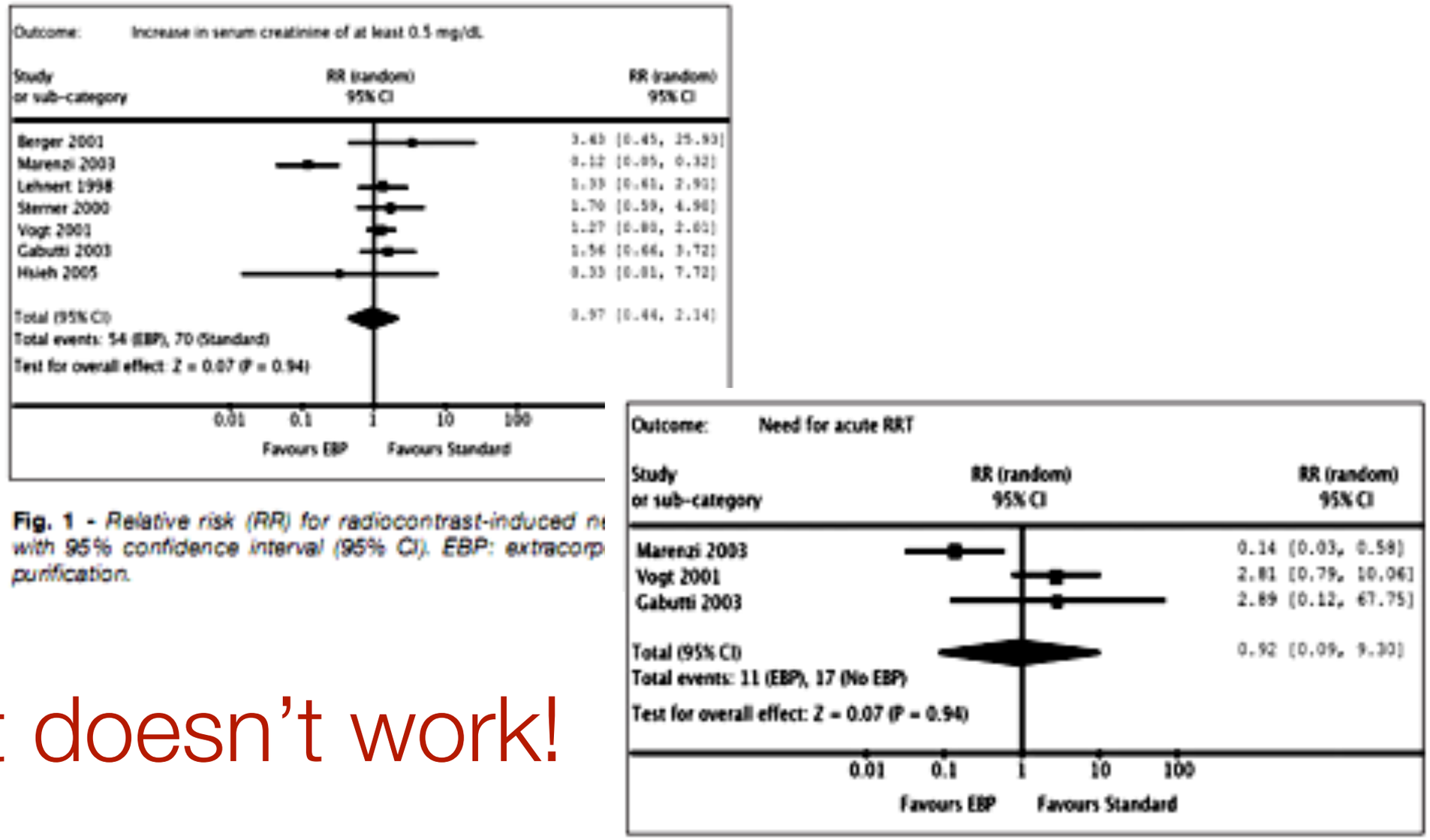


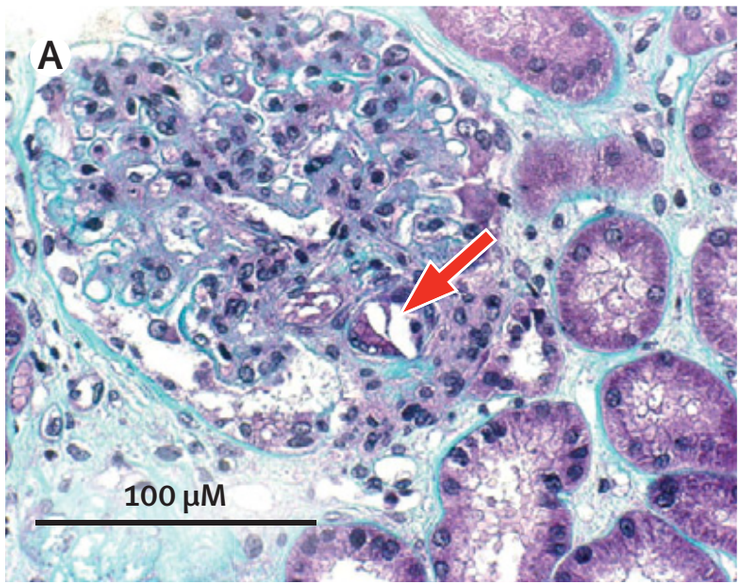
Fig. 1 - *Relative risk (RR) for radiocontrast-induced n with 95% confidence interval (95% CI). EBP: extracorp purification.*

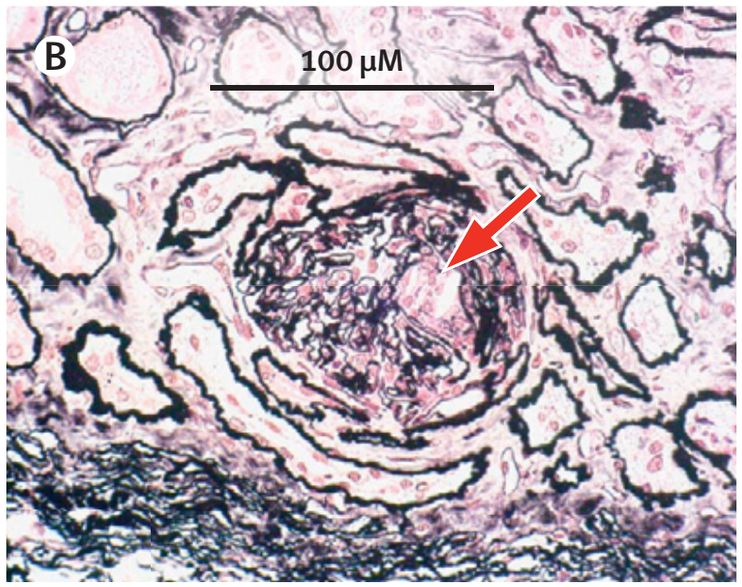
It doesn't work!

Fig. 2 - *Relative risk (RR) for need for acute temporary renal replacement therapy (RRT), with 95% confidence interval (95% CI). EBP: extracorporeal blood purification.*

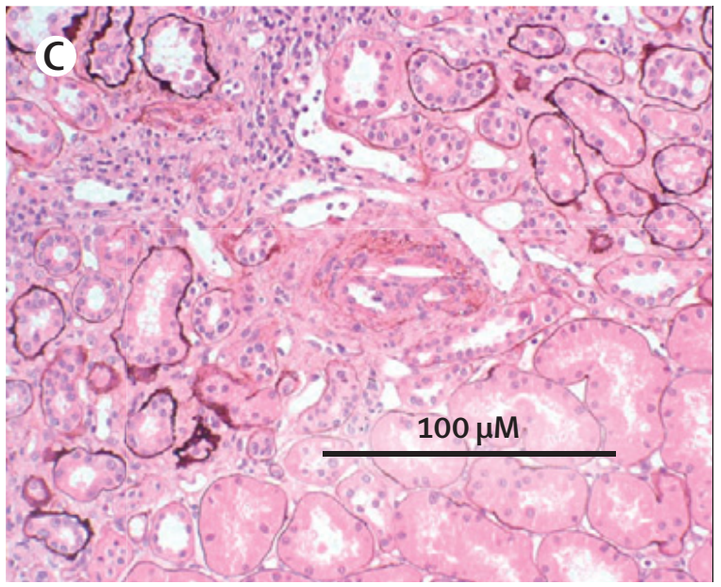
Not all ARI post-angio is from contrast - Atheroembolic renal disease

...”estimated that 5–10% of all cases of acute renal failure could be due to atheroembolism”





Intraglomerular cholesterol crystals



cholesterol crystals in renal arteriole

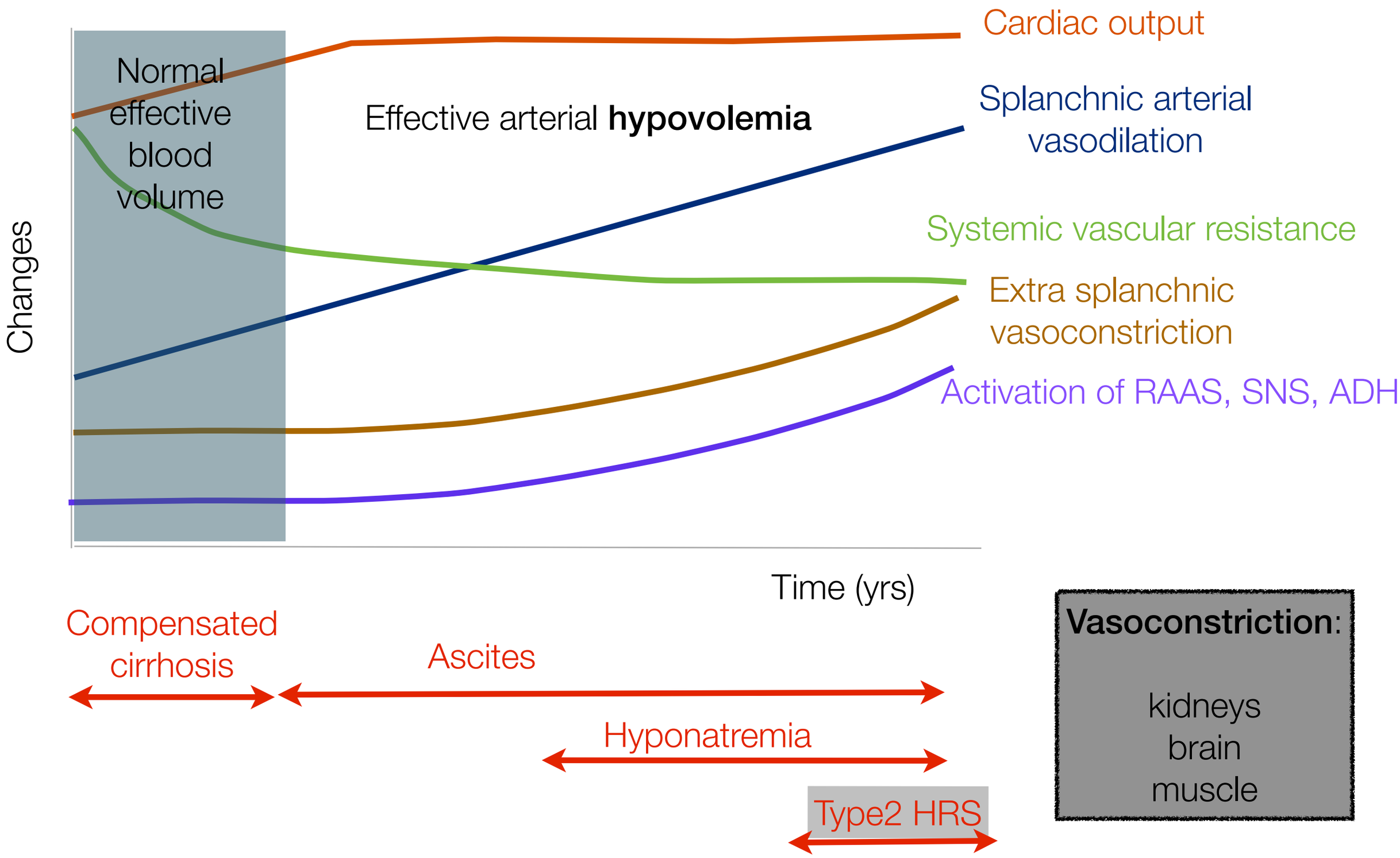
Scolari et al; The Lancet; April 9, 2010

Contrast Induced Nephropathy - reducing the risk

- Alternative imaging methods
- Lowest possible dose of contrast
- Either iso-osmolar (iodixanol) or low-osmolar iodinated contrast (Grade 1B)
- Intravenous volume expansion with isotonic fluids
  - either NaCl or Na bicarbonate (Grade 1A)
- Do not use prophylactic hemofiltration for contrast removal (Grade 2C)
- oral NAC- evidence of benefit not overwhelming, but low risk and cheap (Grade 2D)

Hepato-Renal Syndrome

Peripheral arterial vasodilation hypothesis



Vasoconstriction:

kidneys
brain
muscle

Hepatorenal syndrome -

- Profound renal vasoconstriction
- Low RBF and GFR
- Marked Na and water retention
- “Pre-renal” chemistries

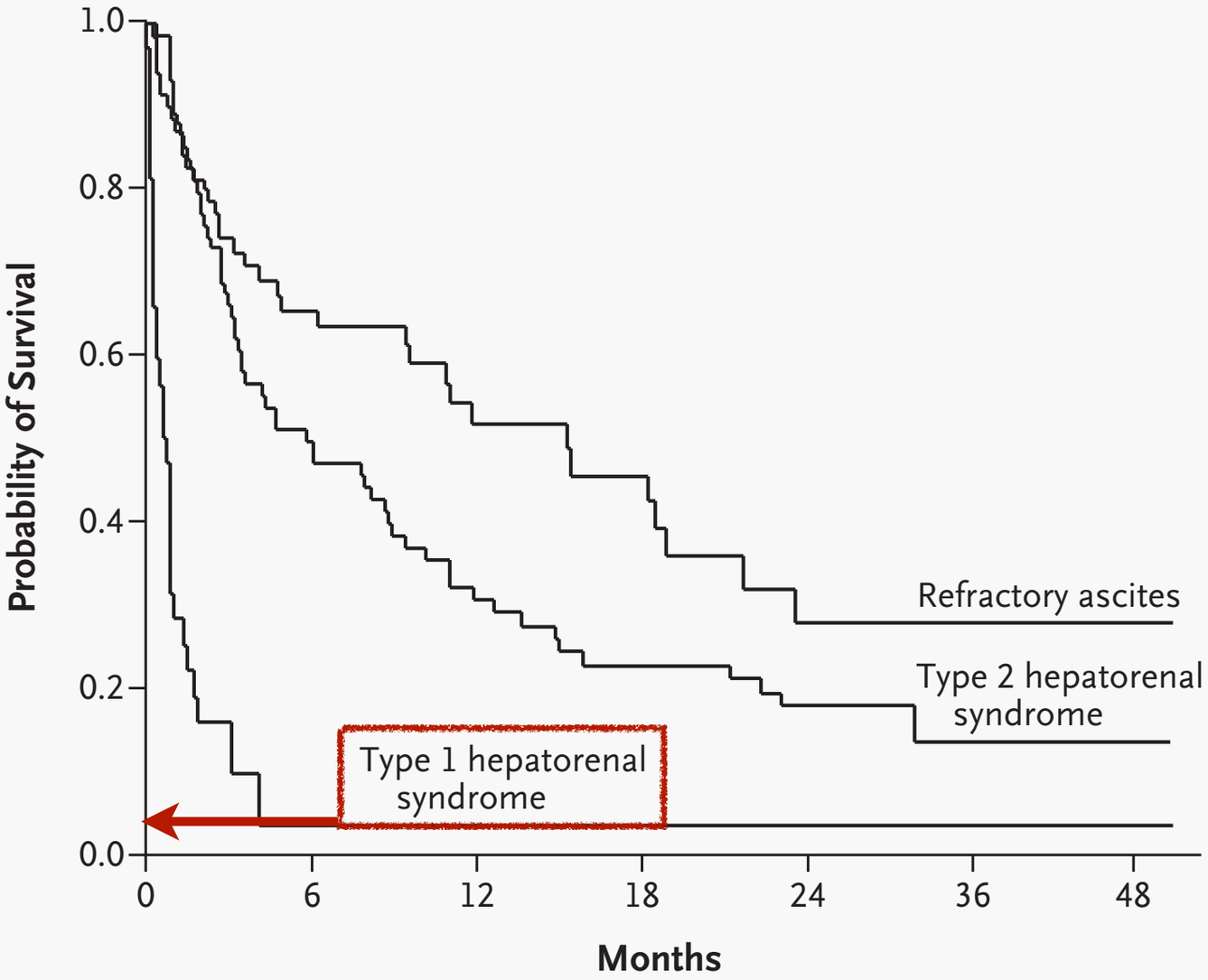
N Engl J Med 2004;350:1646-54

Types of the Hepatorenal syndrome

- Type 1 HRS
  - **Rapid** impairment in renal function - < 2 weeks
  - **Deadly**- untransplanted-median survival time of approximately 3 months
- Type 2 HRS
  - **Slowly** progressive impairment of renal function - better prognosis
- Diagnosis of **exclusion**
  - Remember, **most** patient with cirrhosis and acute renal failure do **not** have HRS
    - Acute Tubular Necrosis - 42%
    - Pre-renal failure - 38%
    - HRS - 20%

N Engl J Med 2004;350:1646-54

Hepatorenal syndrome - Prognosis + Treatment

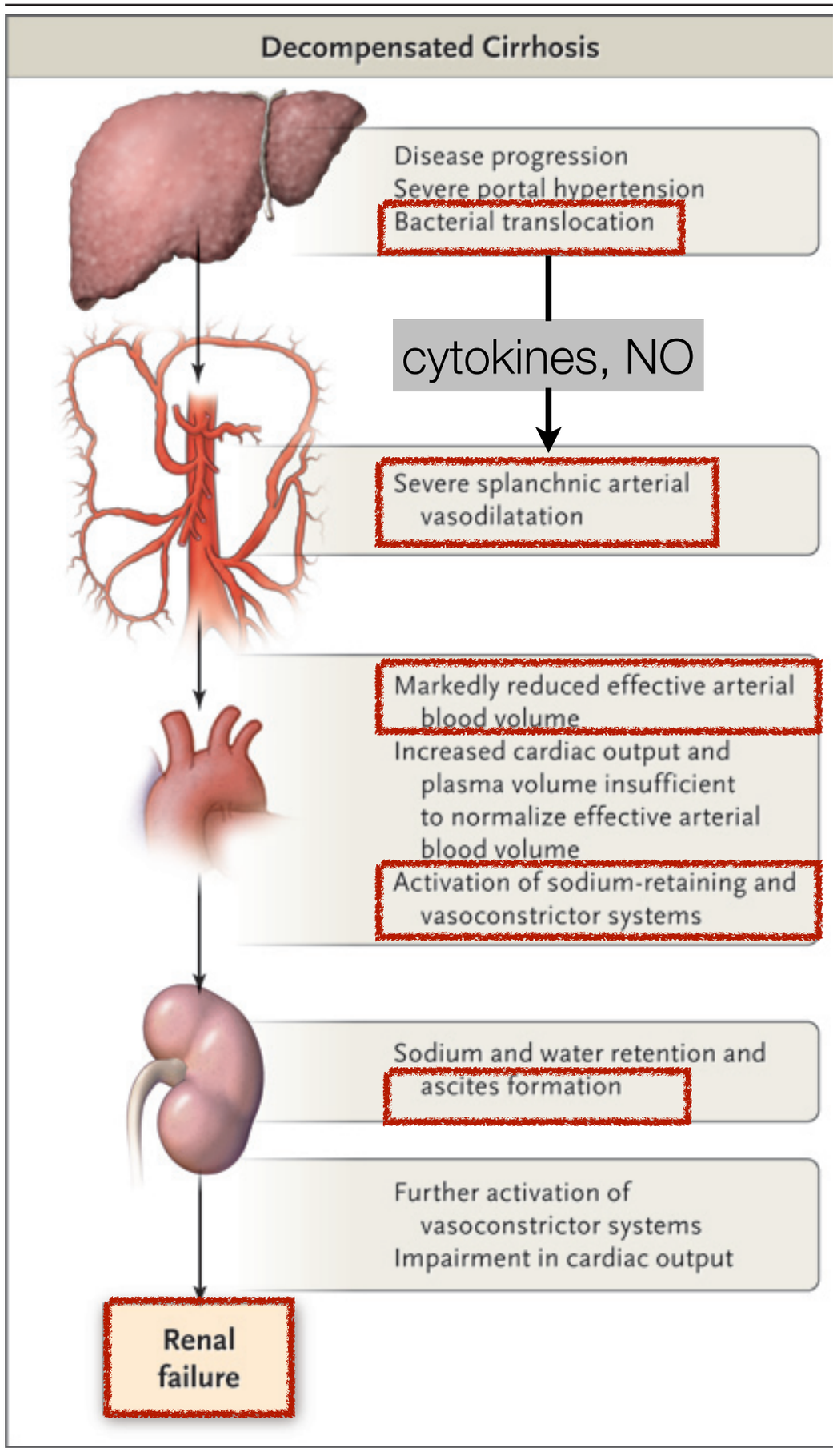


Treatment

- **Albumin**
  - 1g/kg day 1
  - 20-40g/day thereafter
- **Vasoconstrictor**
  - Terlipressin/Noradrenaline
- **Paracentesis**
  - Replace albumin (8 gm /Litre removed)
- **Liver transplant**
  - Definitive treatment

NB. transplanted kidneys still work!

N Engl J Med 2004;350:1646-54

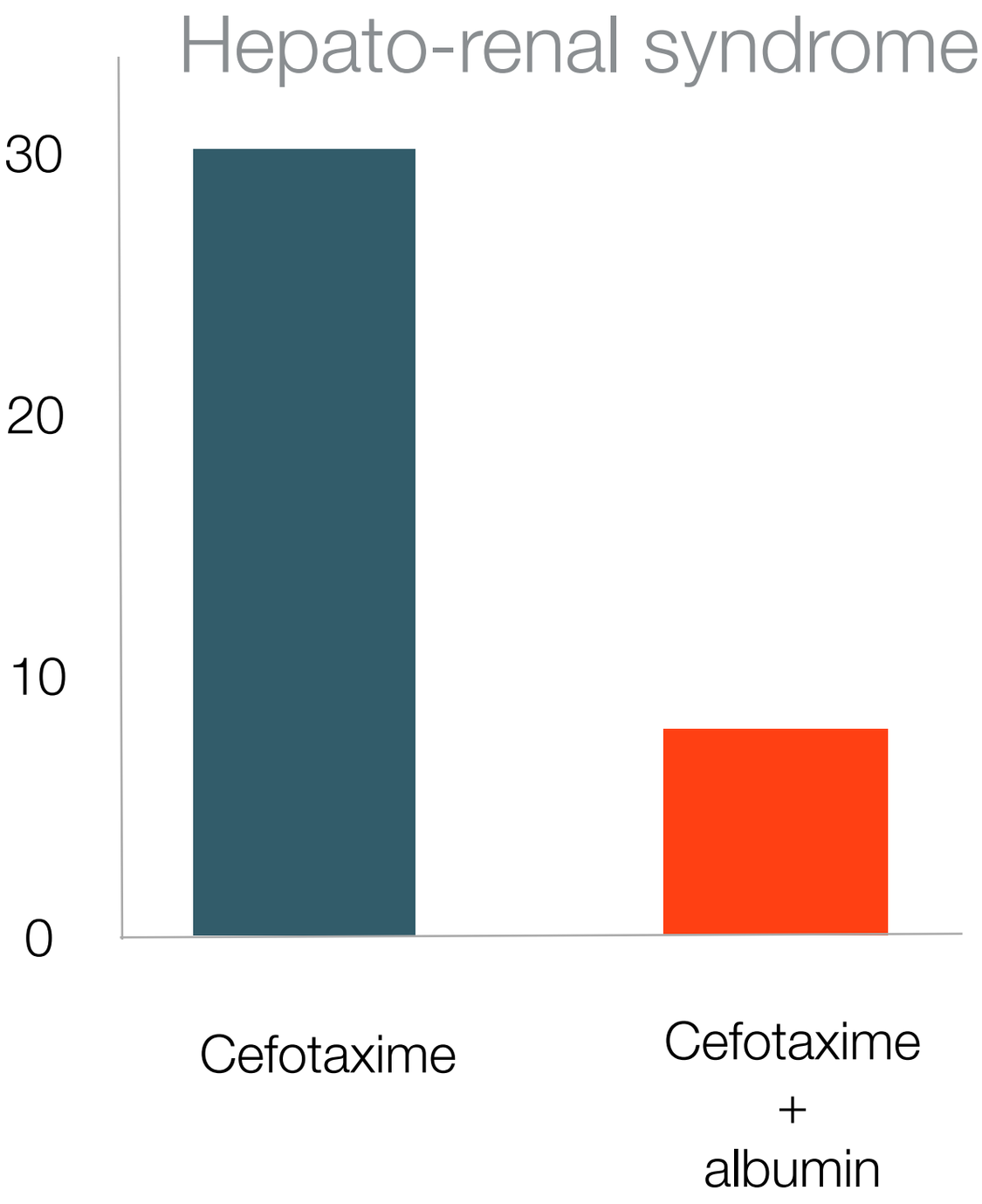


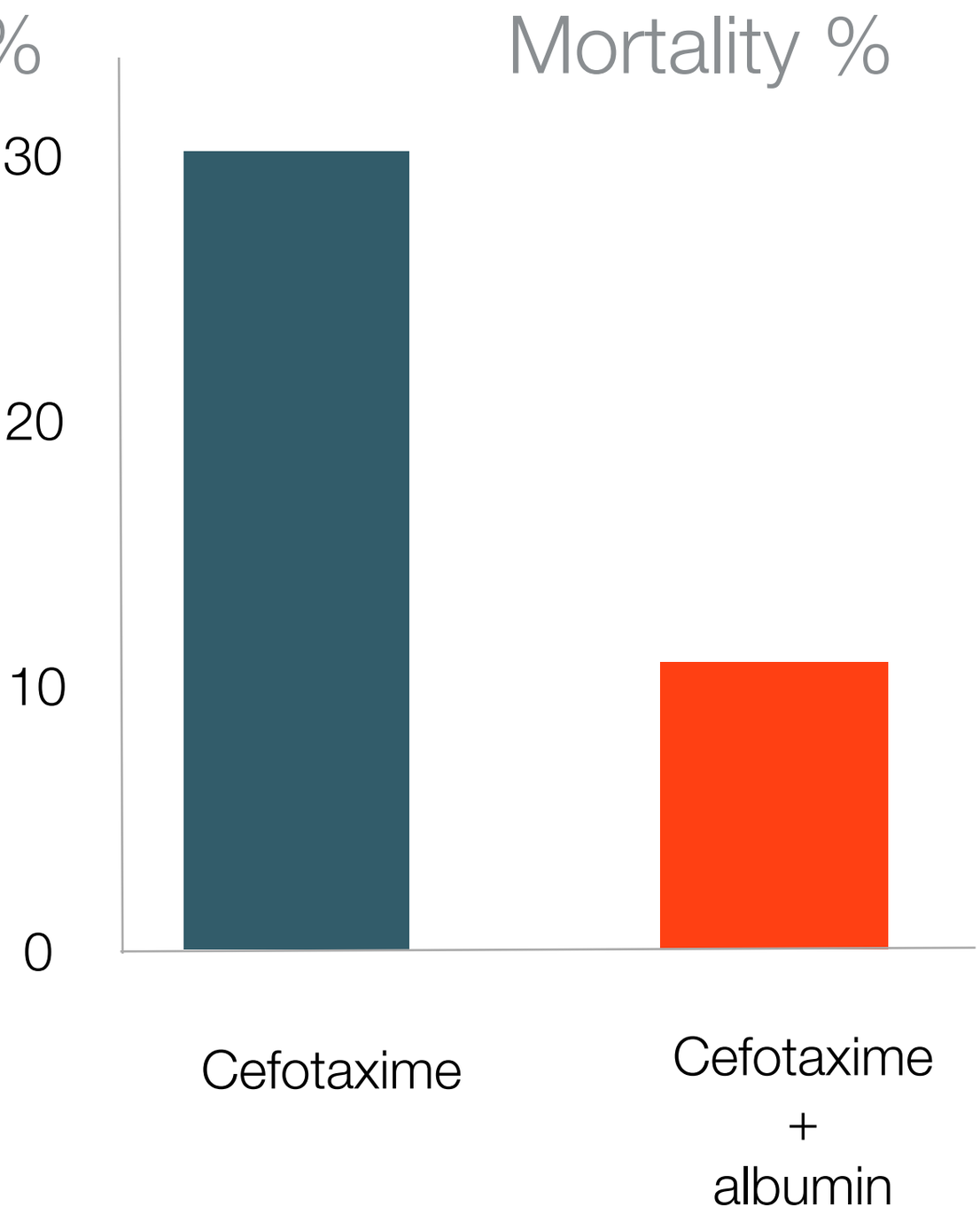
N Engl J Med 2009;361:1279-90.

Beware of:

- **Infection**
  - ex. SBP
- **Blood loss**
  - ex. GI bleed
- **Large volume paracentesis**
- **Drug toxicity**

Effects of volume expansion with albumin in **SBP**

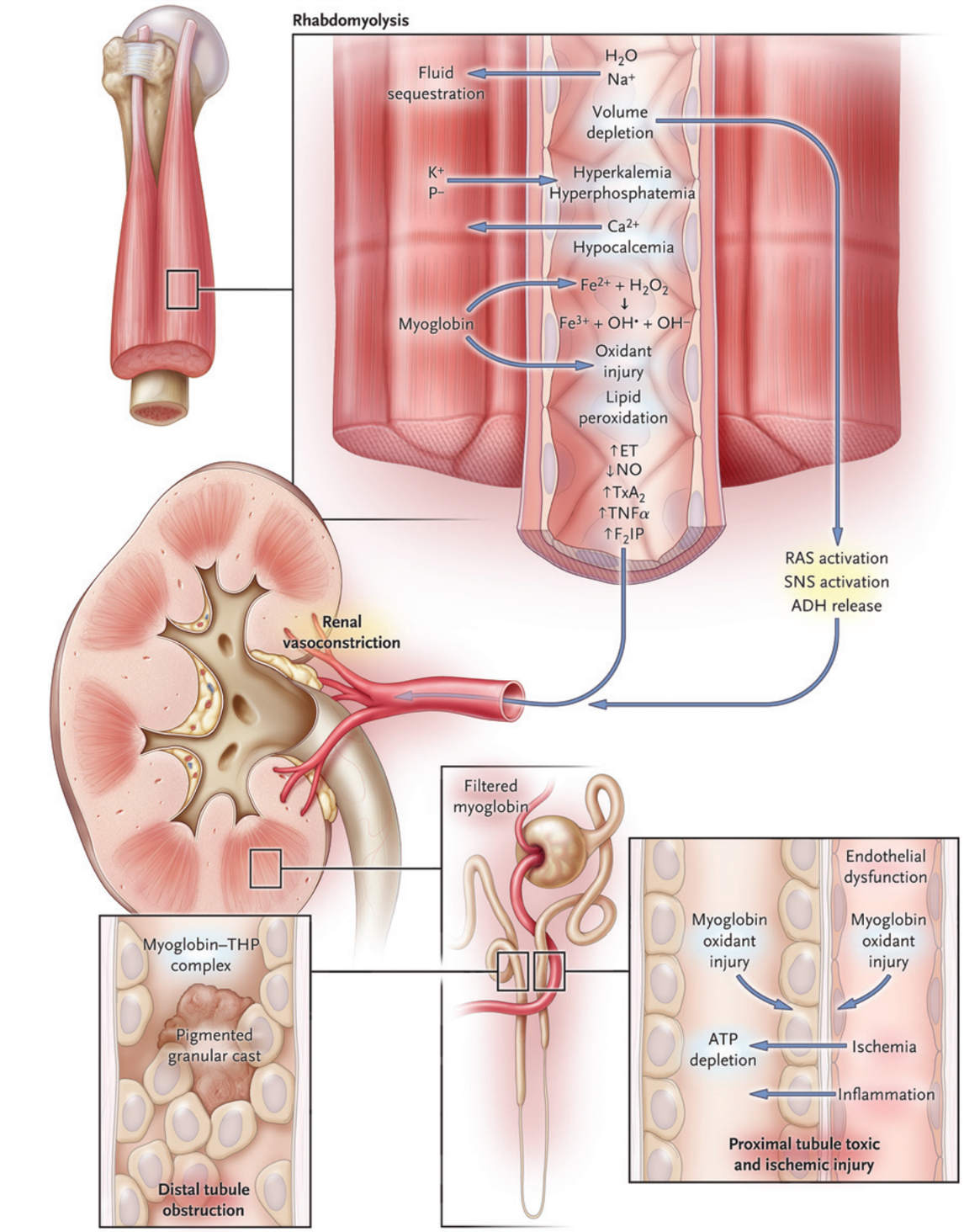




Sort et al. NEJM 1999

ARI and Rhabdomyolysis

Pathophysiology of ARI and Rhabdomyolysis



N Engl J Med 2009;361:62-72.

- Fluid sequestration in injured muscle induces volume depletion
- -> Activation of the SNS, ADH, and RAS
- -> **Vasoconstriction**
- -> **Tubular injury**
  - Ischaemia due to renal vasoconstriction
  - **Direct toxicity**
    - Myoglobin-associated oxidative injury
    - Tubule obstruction due to
      - protein–myoglobin complex
      - sloughed tubular cells forming cellular casts.

Treatment of ARI and Rhabdomyolysis

- Check volume status (often need ~10 L/ day)
- Measure creatine kinase (risk of ARI low if < 15,000 U/L)
- Measure plasma and urine creatinine, K+, Na+, Ca++, Mg, PO4 and albumin
- Urine dipstick and urine sediment (+ for blood in myoglobinuria and haemoglobinuria)
- Initiate volume repletion with normal saline at ~400 mL/hr
- Target urine output >200 mL/hr
- Check K+ frequently
- Only correct Ca++ if symptomatic (beware malignant precipitation of CaPO4)
- Treat cause of rhabdomyolysis
- If urine pH <6.5, alternate each liter of saline with Na bicarbonate
- Maintain diuresis until myoglobin is cleared (clear urine, urine dipstick negative for blood
- Consider RRT if resistant hyperkalaemia, anuria, volume overload resistant acidosis

N Engl J Med 2009;361:62-72.

Renal transplant as a last resort

BBC NEWS

China 'kidney for iPad' trial begins in Hunan

Acute kidney injury-Recap

- Acute kidney injury is **common and deadly**
- Experimental models have defined pathophysiology of AKI
- AKI leads to **distant** organ dysfunction
- Risk stratify and watch for **reversible** causes as soon as possible -
  - hypovolaemia
  - nephrotoxic drugs
  - post-renal causes
- Diuretics - “the Devil’s drug”

???

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