Renal Replacement Therapy in the ITU

Dr John Vogel

Outline

- What is AKI?
- How good is RRT compared to normal kidney function?
- Indications and timing for RRT?
- Basic principles
- Modalities
- RRT - Adverse effects
- Fluid management
- Vascular access
- Anticoagulation
- Which dose of RRT?
- Peritoneal dialysis

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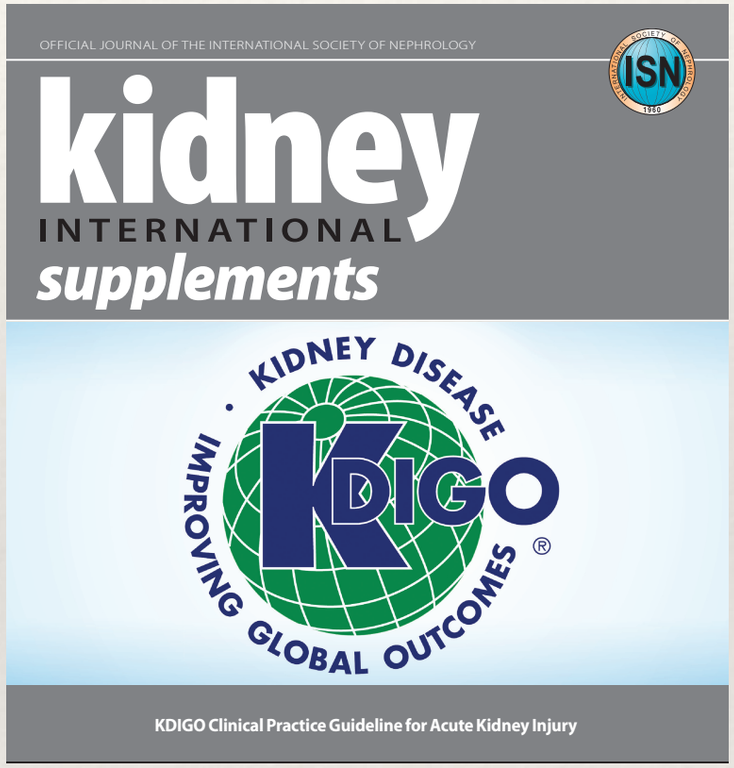
Definition of acute kidney injury

Previously **<u>35 definitions</u>** in the literature

(ex. **RIFLE, AKIN)**

Crit Care Med 2010; 38:000 – 00



"**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

But these are functional measures not of injury.

Kidney International Supplements (2012) 2, 19–36

Epidemiology of acute kidney injury in ITU

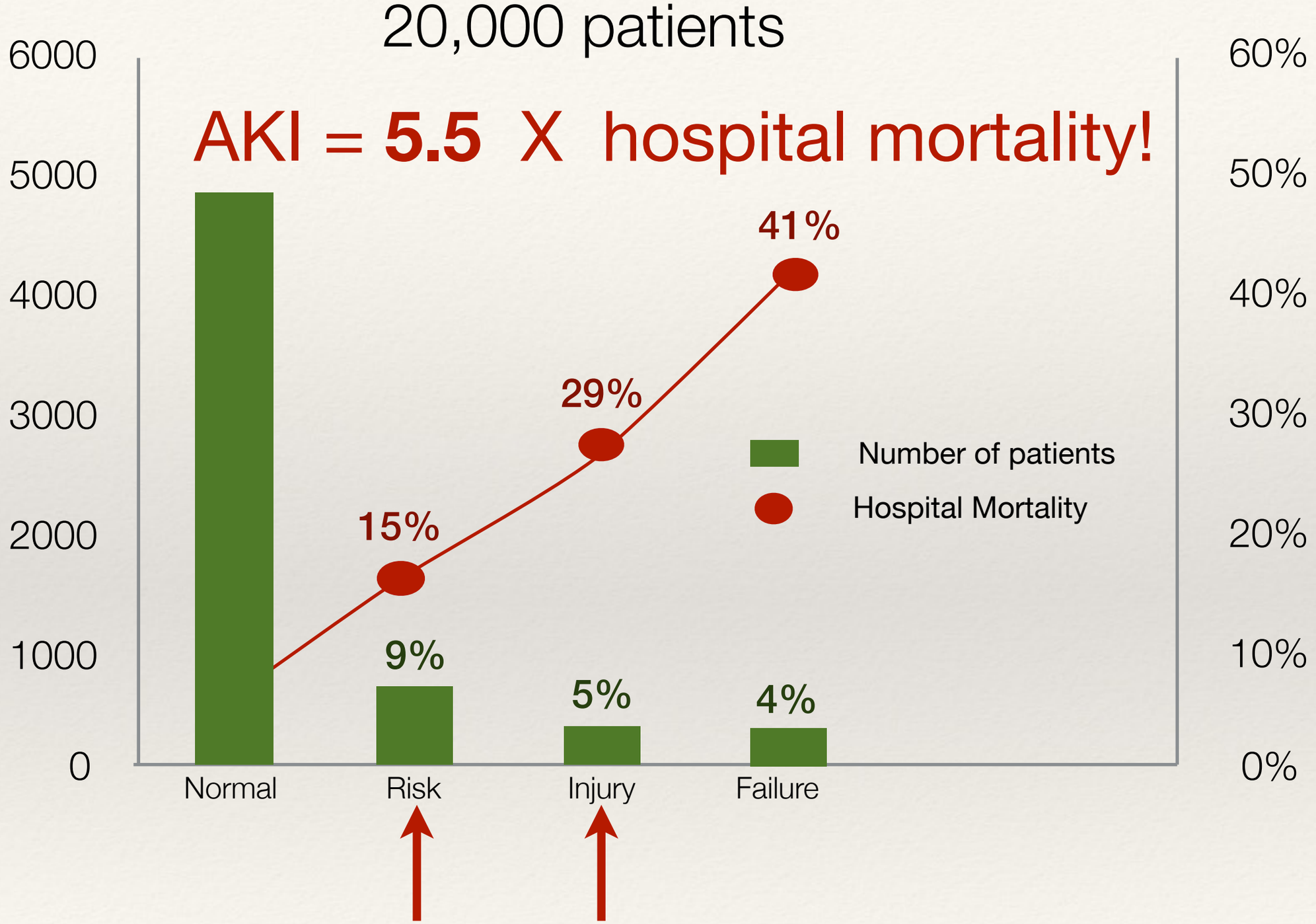
In ITU patients

- AKI develops in **36% - 67%**
- Renal Replacement Therapy (RRT) required in ~ **6%**
  - If **RRT :**

~ 6 out of 10 die!

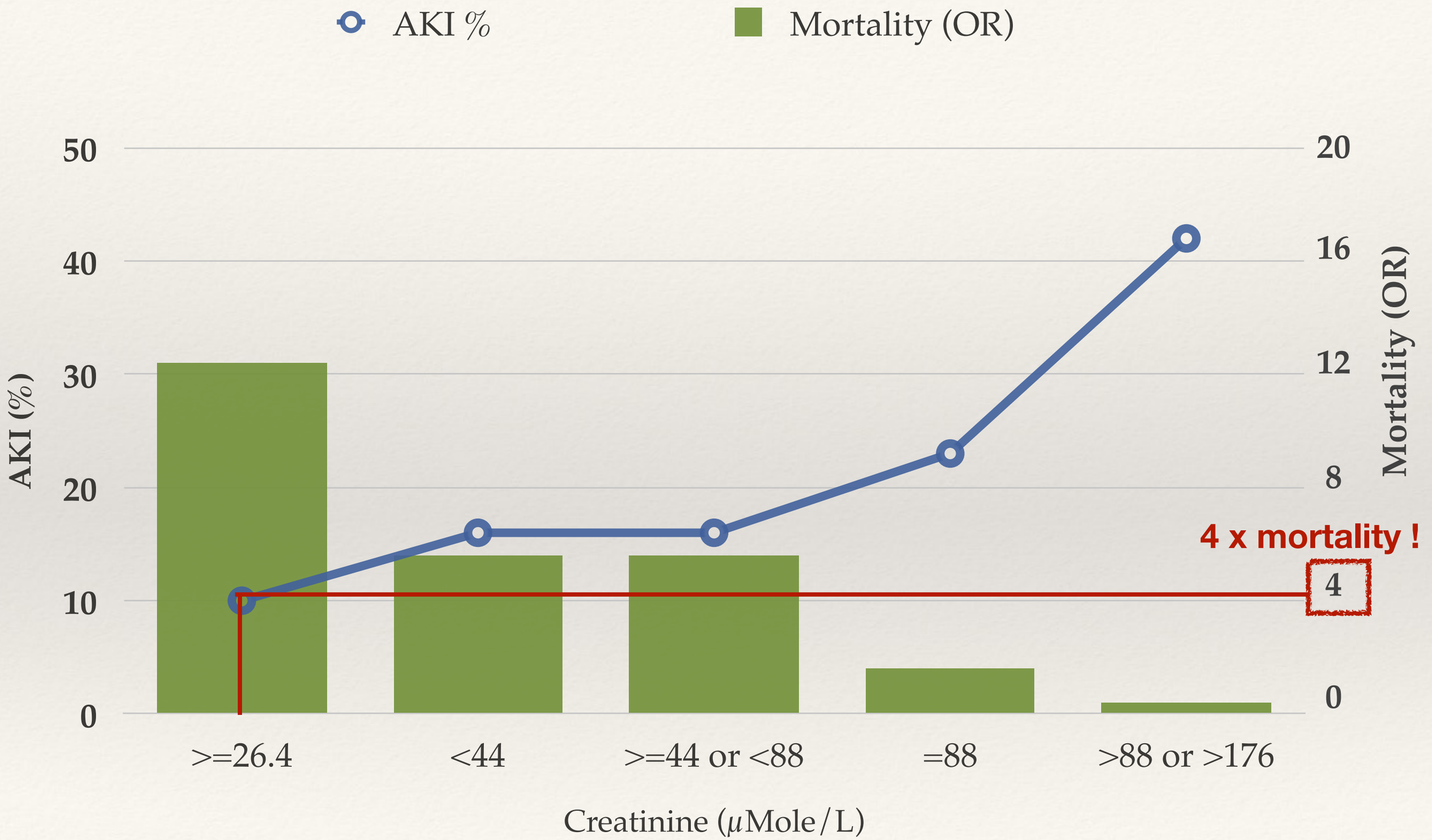
Crit Care Med 2010; 38:000 – 00

Epidemiology of AKI



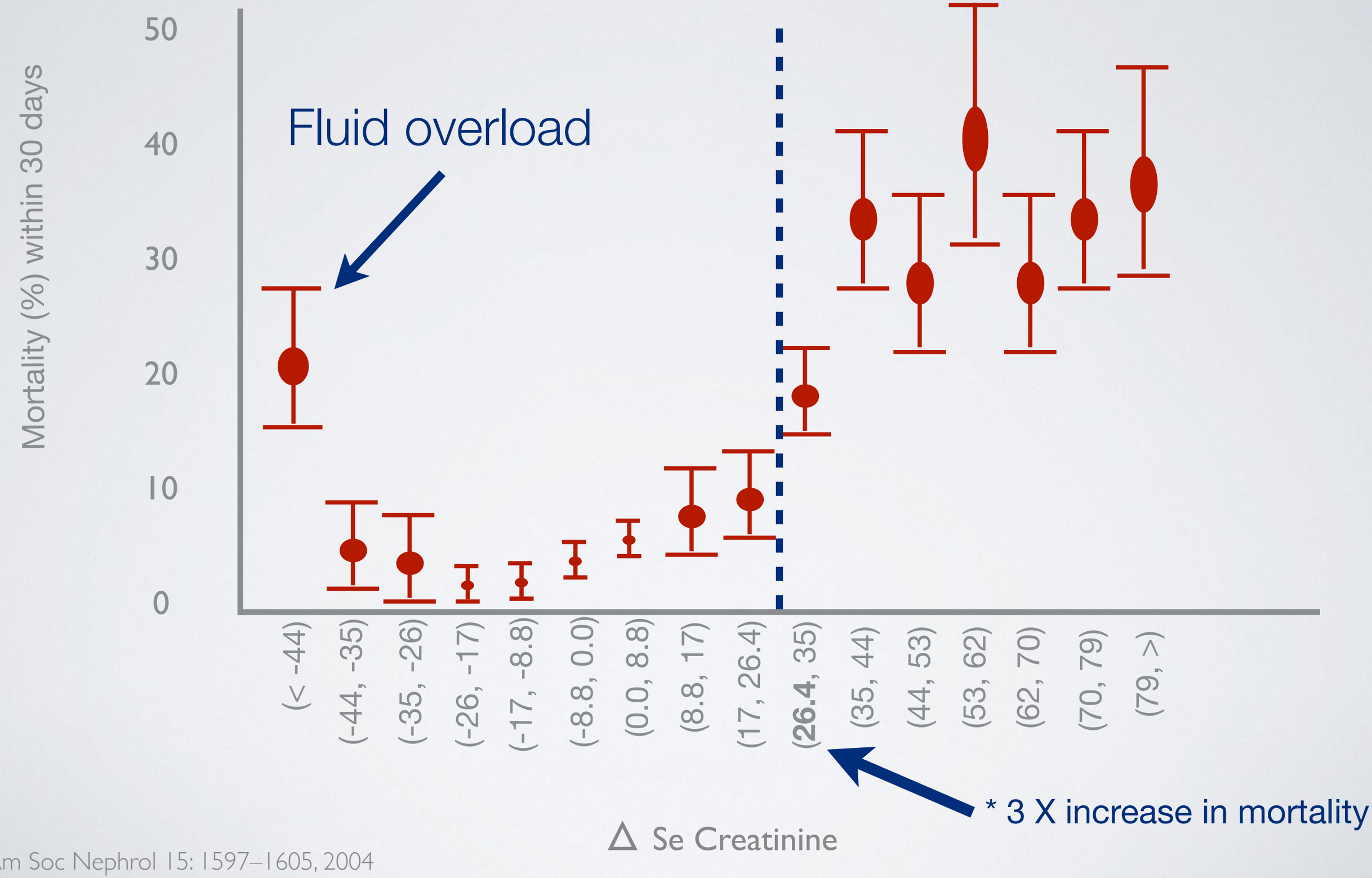
Uchino et al. Crit Care Med, 2006;34:1913-1917

Prognosis of Acute Kidney Injury



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

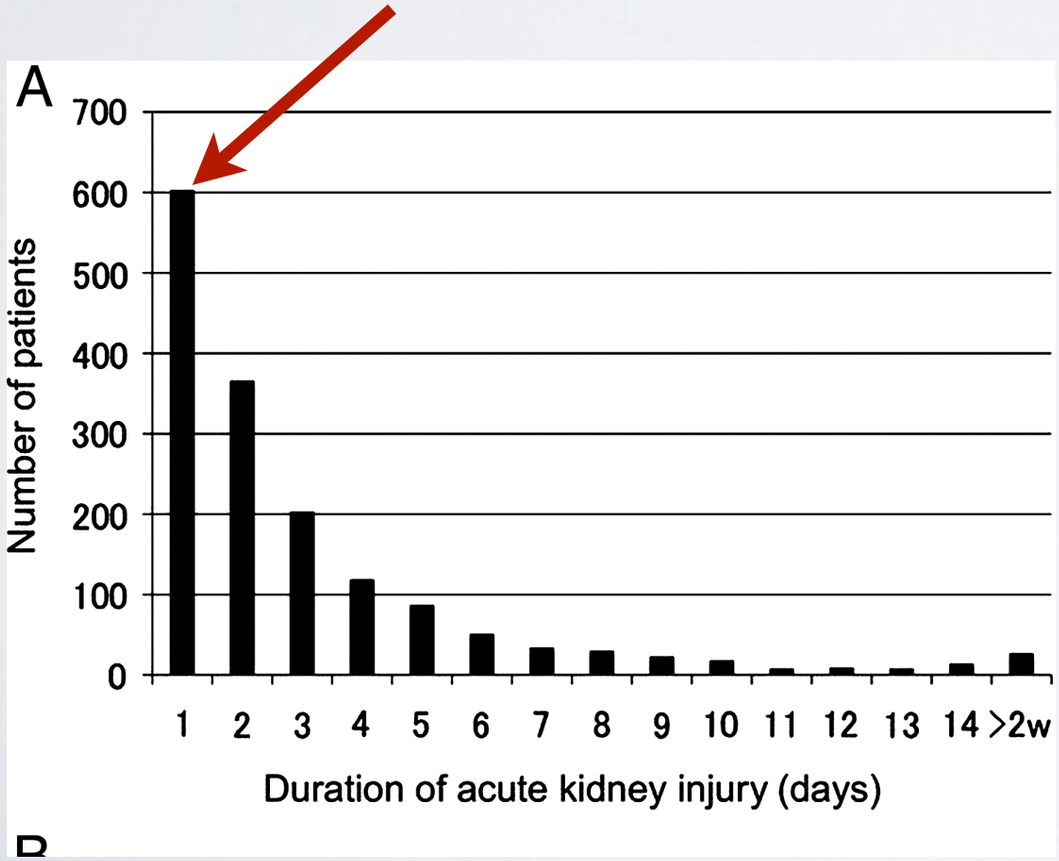
Minimal Changes of Serum Creatinine Predict Prognosis

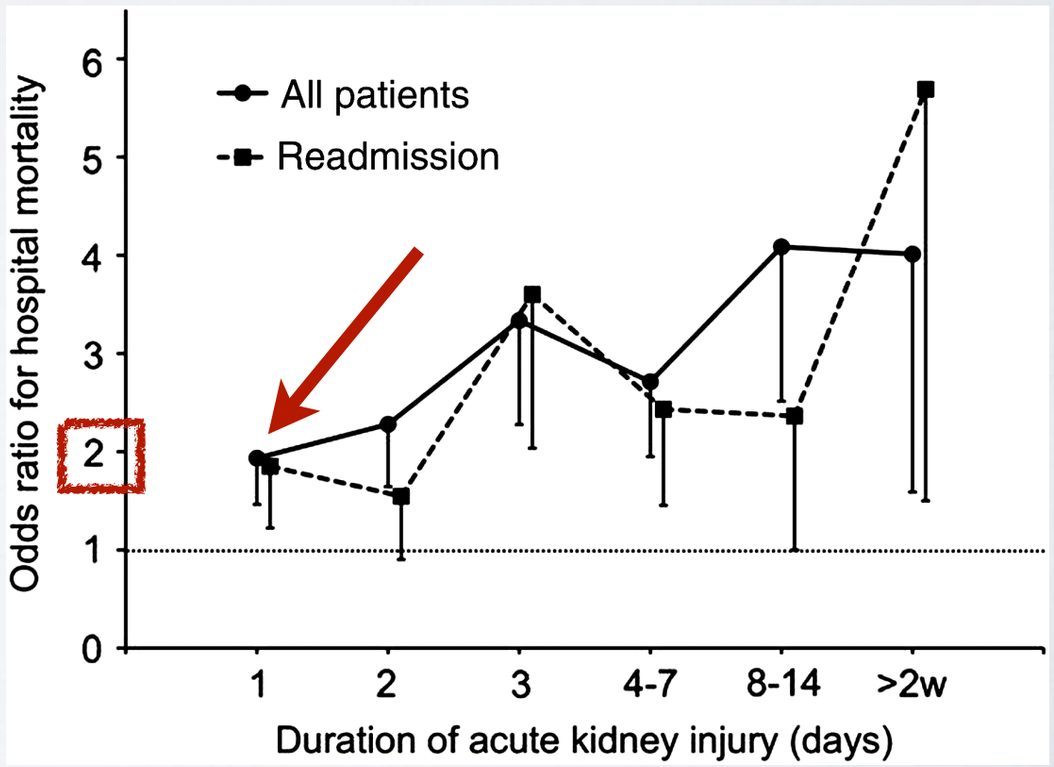


J Am Soc Nephrol 15: 1597–1605, 2004

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

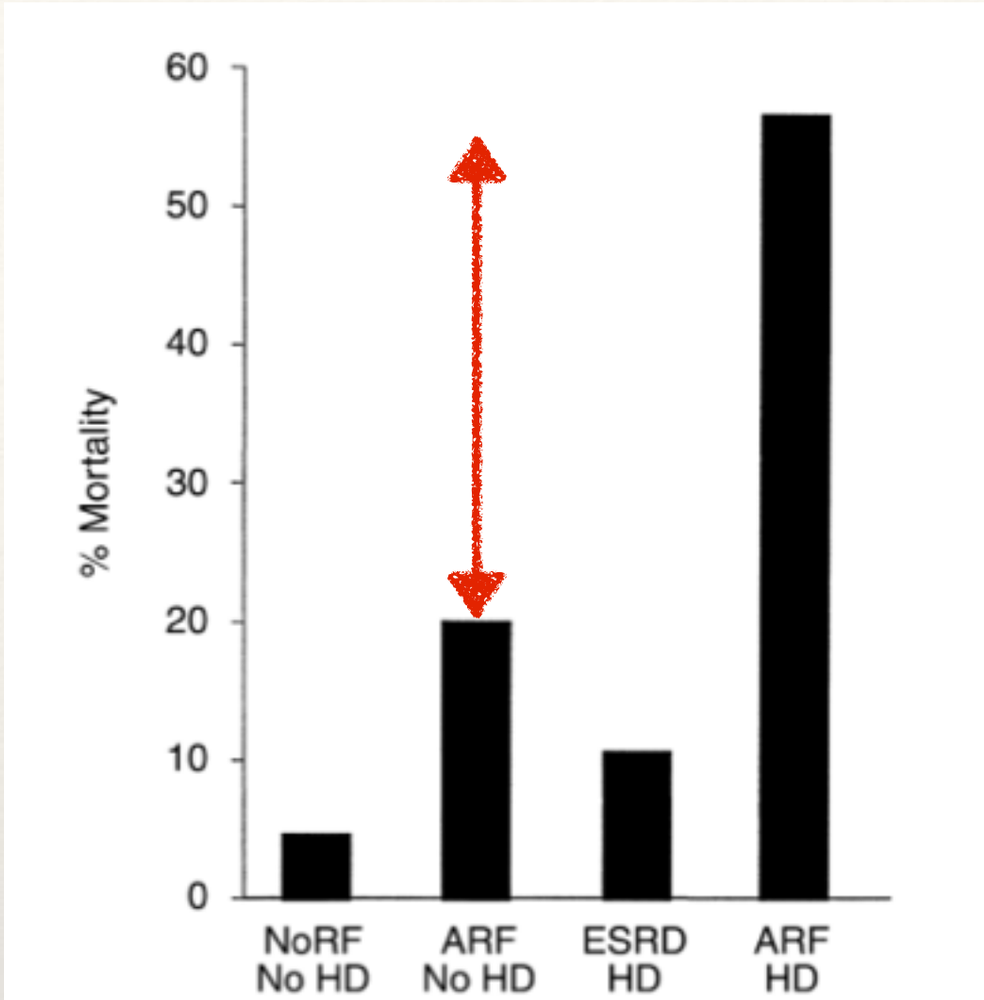
- **Transient** AKI is common in hospital patients occurring in **~6%** of admissions and accounting for almost a **third** of all cases of in-hospital AKI.
- Transient AKI had significantly higher hospital **mortality** compared to patients with no AKI
- Even 1 day of AKI had a significantly increased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



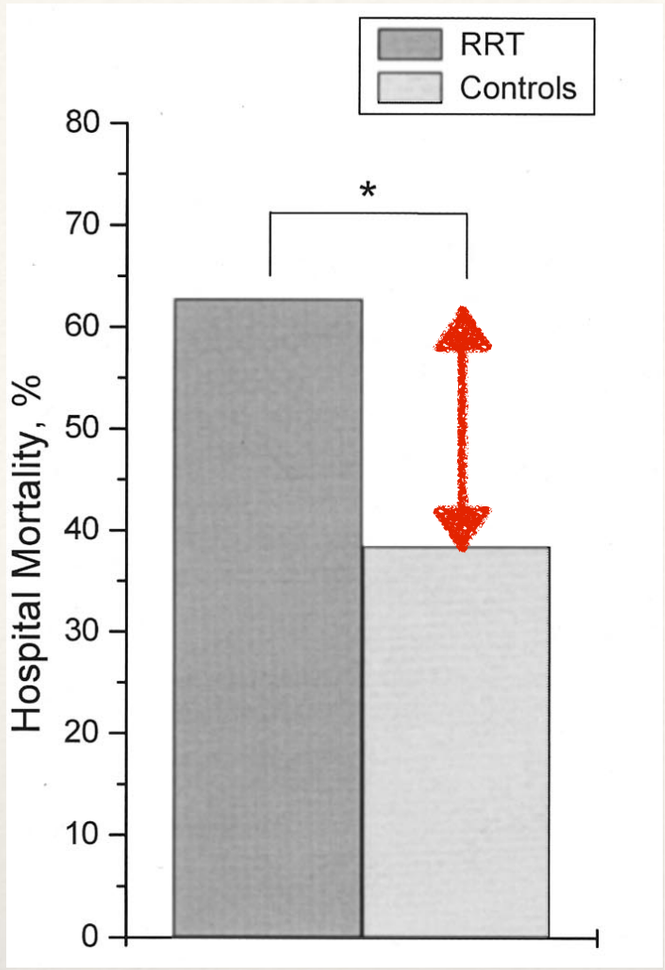


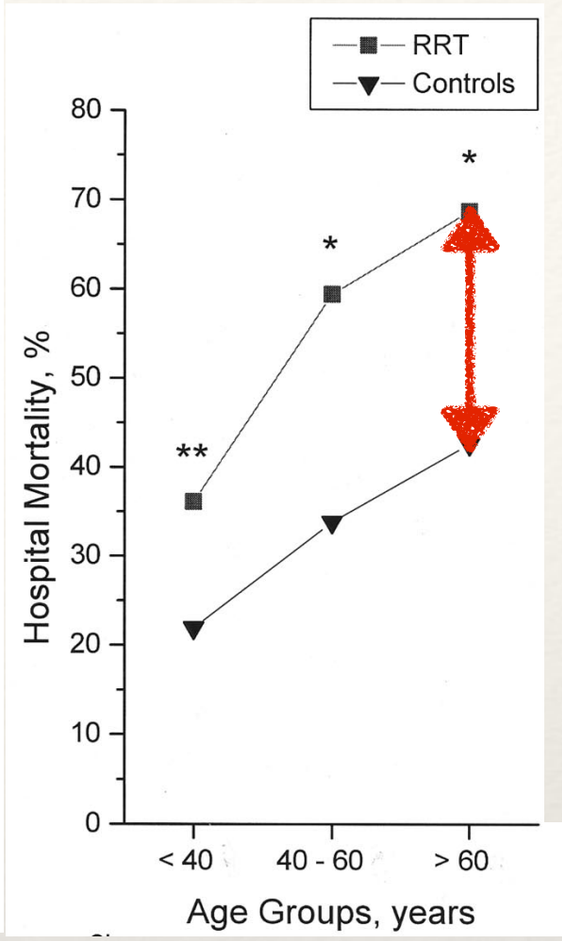
Nephrol Dial Transplant (2010) 25: 1833–1839

AKI requiring dialysis has an even higher mortality

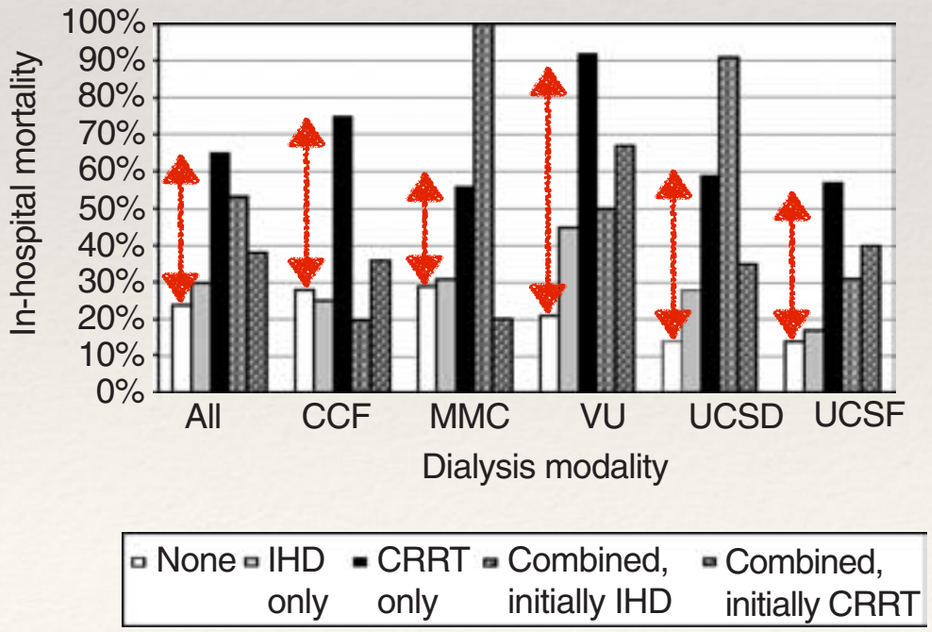


Kidney International, Vol. 62 (2002), pp. 986-996

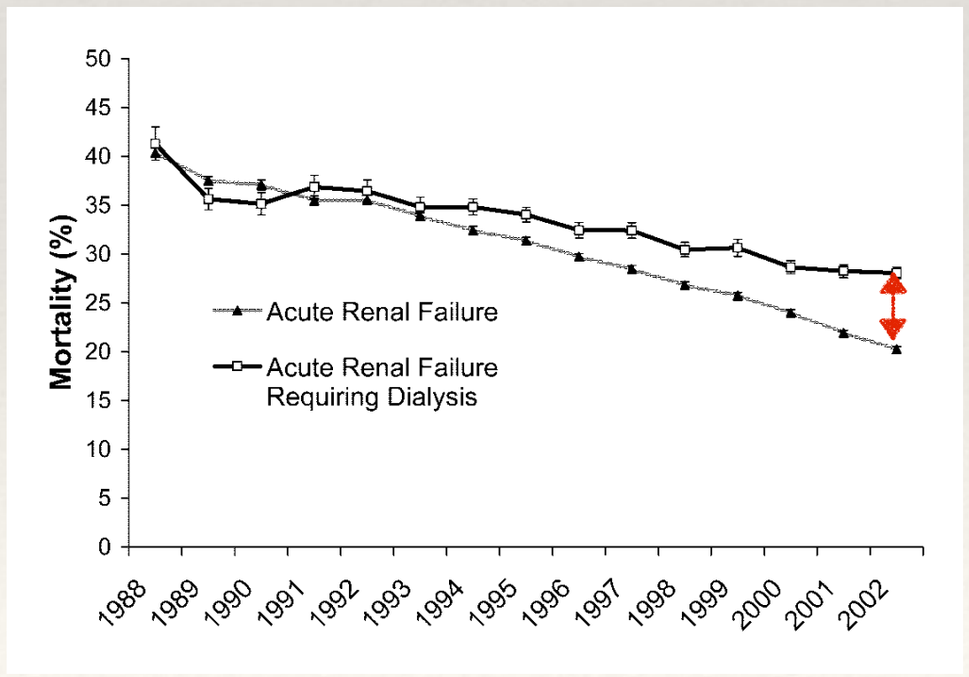




Crit Care Med 2002 Vol. 30, No. 9



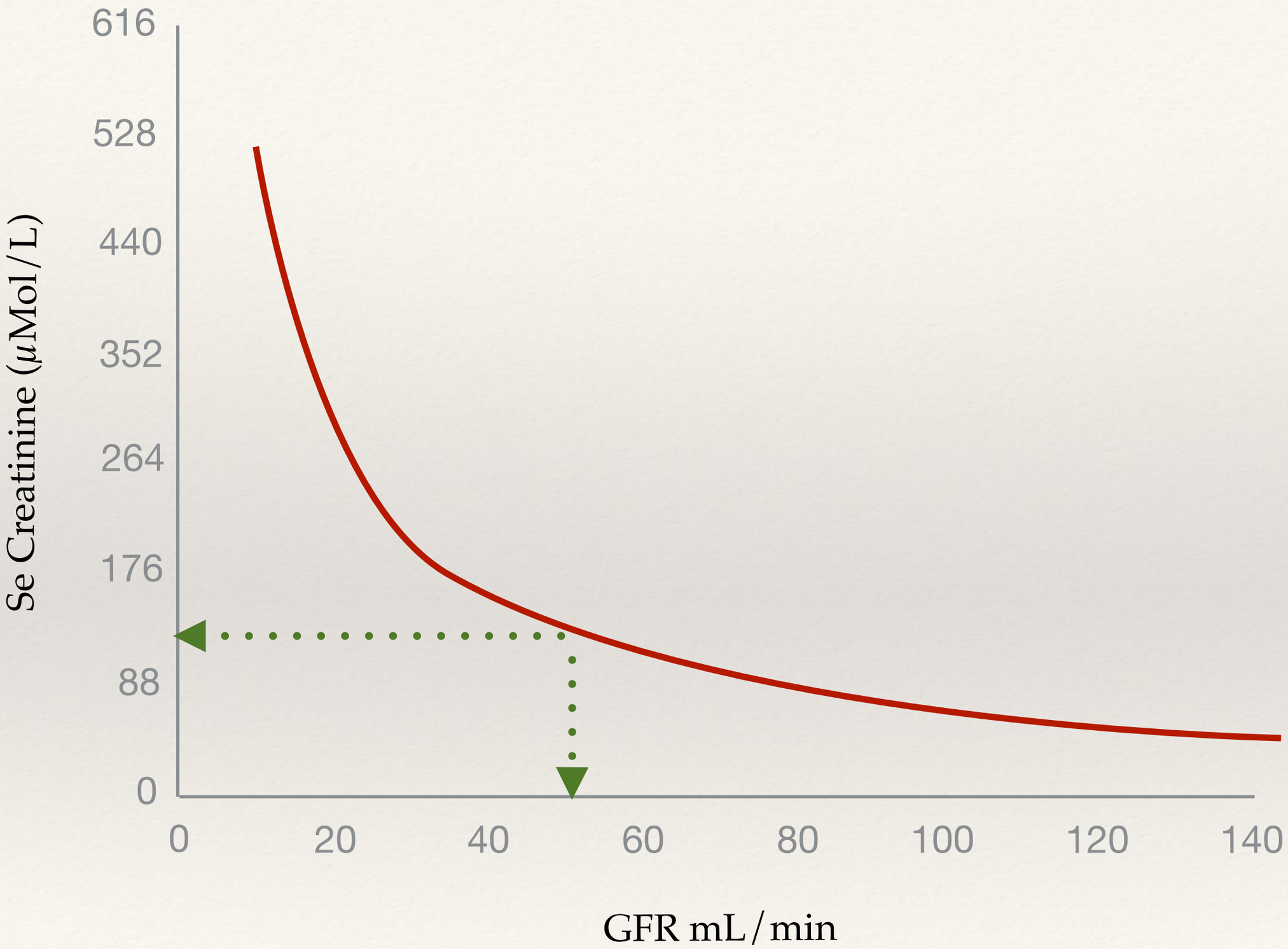
Kidney International, Vol. 66 (2004), pp. 1613–1621



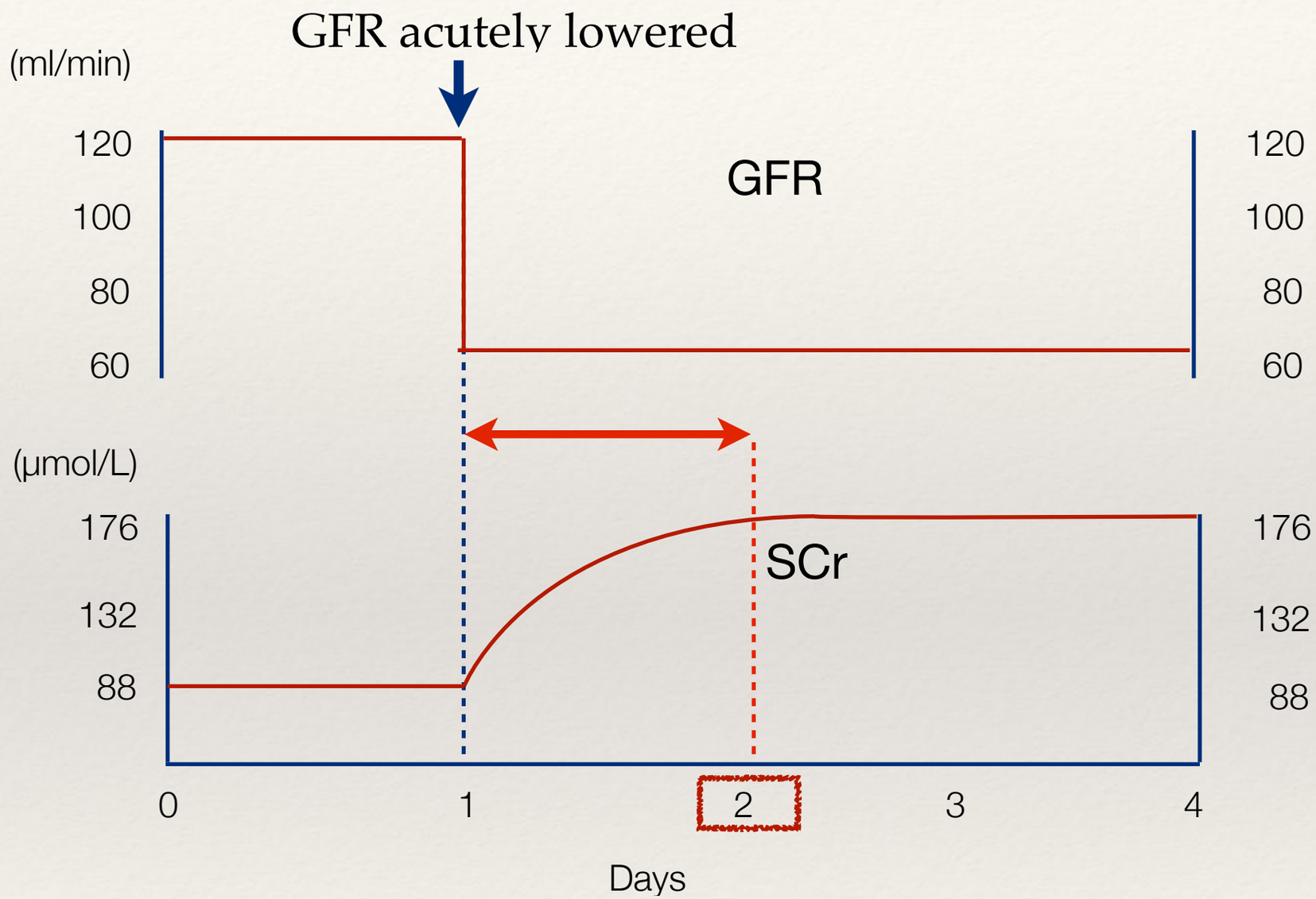
J Am Soc Nephrol 17: 1143–1150, 2006

Just a word about creatinine

Non linear relationship between Creatinine and GFR



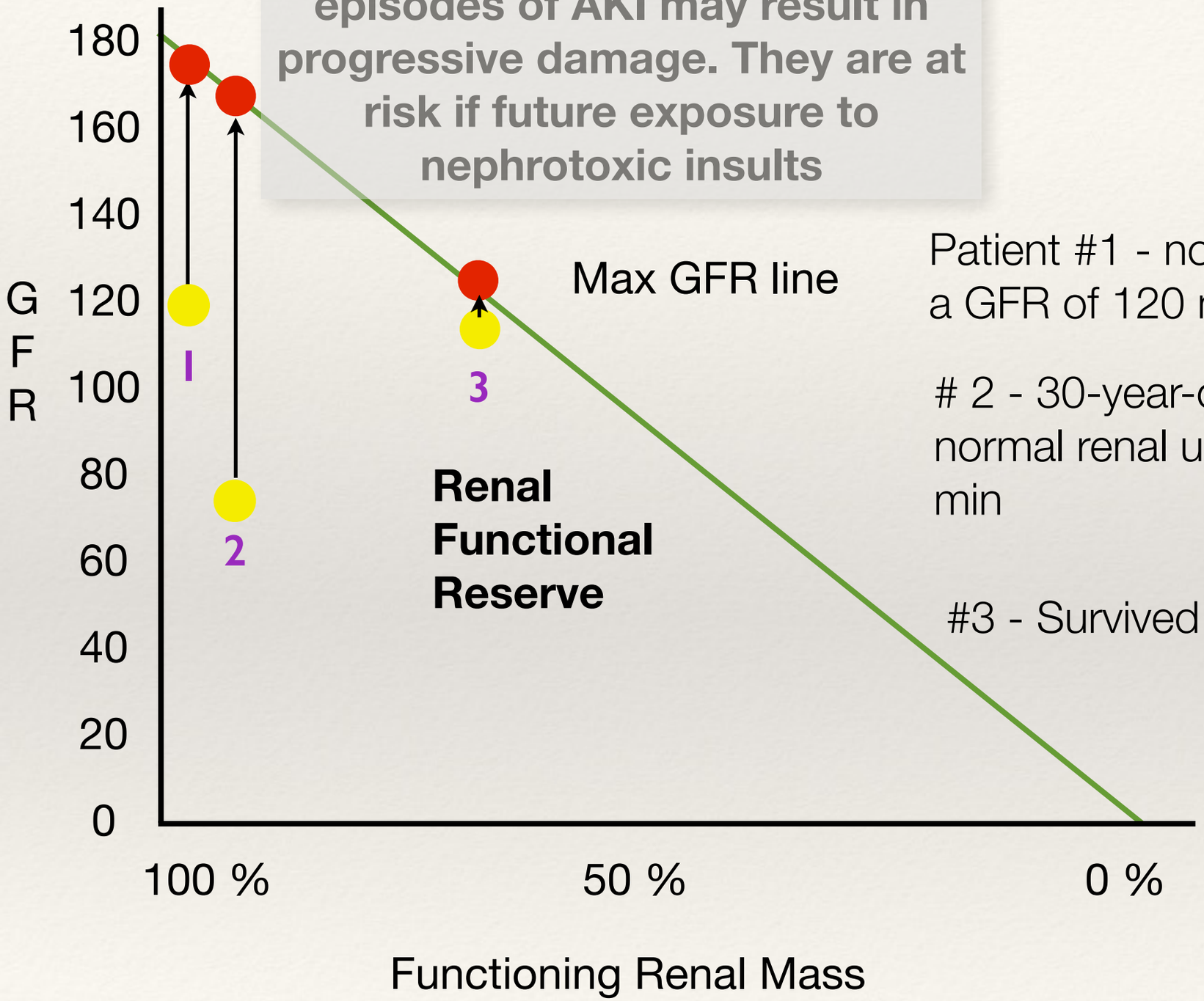
Creatinine rise lags GFR drop!



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

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/min

2 - 30-year-old female, vegetarian with a normal renal ultrasound and a GFR of 70 ml/min

#3 - Survived RRT and a GFR of 110 ml/min

Max. GFR (post protein load)

Baseline GFR

RFR = Max. GFR - Baseline GFR

Critical Care 2012, 16:144

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What the normal kidney does

- Remove toxins ✓
  - Glomerular filtration (only aspect achieved with dialysis), tubular secretion ✗?
- Volume control ✓
- Electrolyte control ✓
  - ex. phosphate (mineral bone balance), Vit D (bone, immunity), etc
- Acid-base balance ✓
- Innate immune function ✗
- Neurohumoral function ✗
  - ex. RAAS, Klotho - a hormone that has phosphaturic and anti-ageing properties, erythropoietin, calcitriol, etc

***Lancet* 2014; 383: 1831–43**

Dialysis does not replace the normal kidney

"**Dialysis cannot replace all** the different functions of the kidney, and in those that they do it is **incomplete**."

To put this in perspective, in chronic renal failure, haemodialysis and peritoneal dialysis provide a time-averaged **creatinine clearance** of around **10 mL/min**

***Lancet* 2014; 383: 1831–43**

How much is filtered by the kidneys ?

Kidneys

In 1 minute

120 mL
of filtrate
produced

99% reabsorbed
⇒ 1.5L urine / day

CRRT

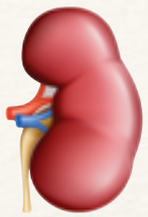
In 1 minute

~30 mL
of filtrate
produced

none reabsorbed
replace ~ 2L / hr
for neutral balance

Dialysis does not replace the normal kidney

Blood flow thru kidneys/filter



"GFR"

Normal Kidney

1 L/min

120 mL/min

99% filtrate is reabsorbed
→ 1.5 l urine

Continuous renal replacement therapy

~ 0.2 L/min

15-30 mL/min

12-25% of normal
= CKD stage 4

Chronic Haemodialysis (3X/week)

~ 0.006 L/min

6 L / week

5 mL/min

5% of normal only

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Why provide RRT

- **Solute control**
  - nitrogenous waste
  - organic acids
  - “middle molecules”
  - mediators of inflammation
- **Volume control**
  - maintain dry weight
  - avoid fluid overload

When to start RRT?

At present, there is **no consensus** regarding **when to initiate** renal-replacement therapy.

However clear indications are:

- ***hyperkalaemia***
- ***severe metabolic acidosis***
- ***volume overload***
- ***overt uraemic manifestations***
- ***drug intoxications***

Not Lactic acidosis nor Contrast

N Engl J Med 2012;367:2505-14 CCM Volume 25(1), January 1997, pp 58-62 Nephrol Dial Transplant (2008) 23: 1473–1475

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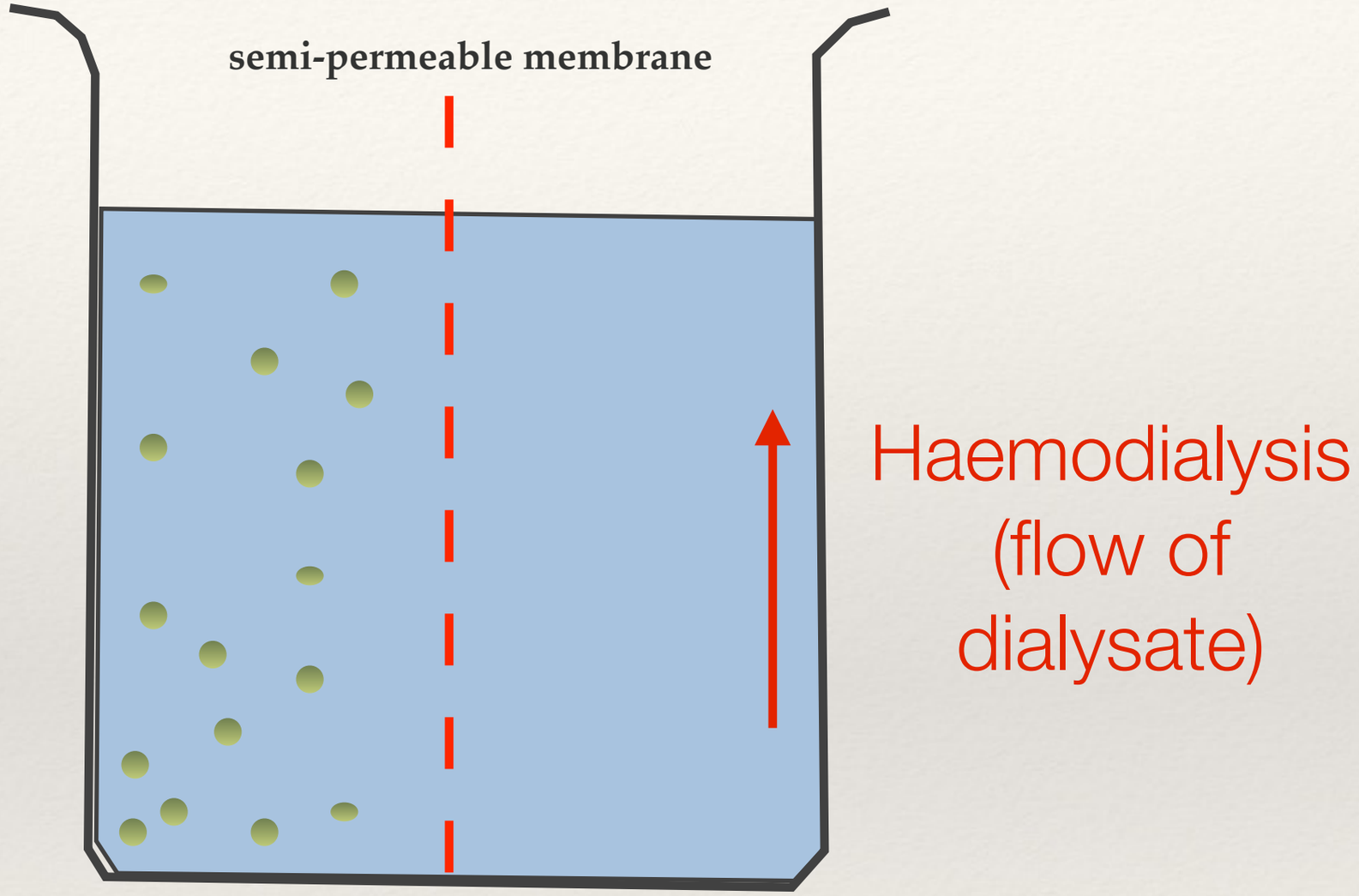
Diffusion

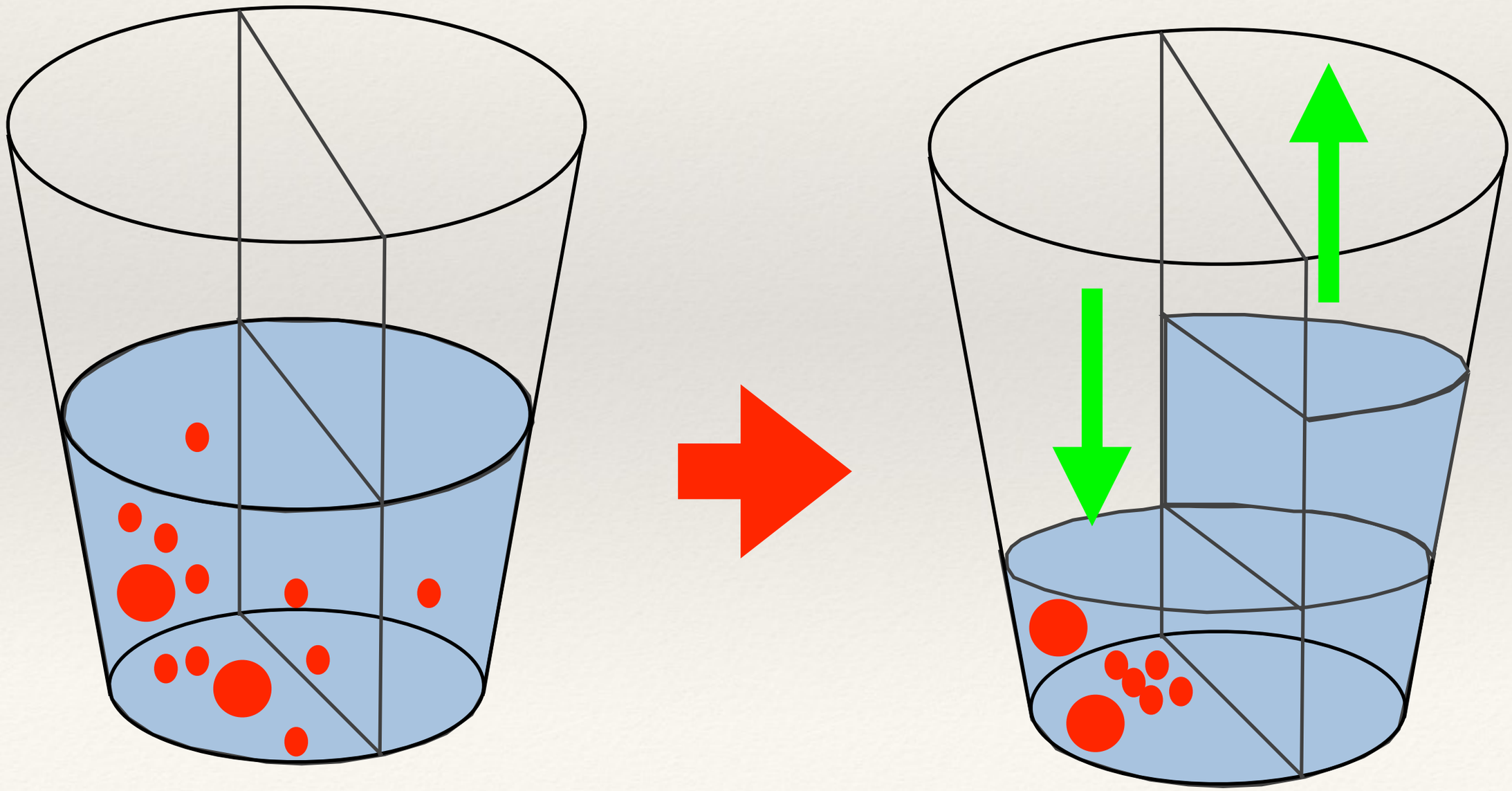


Diffusion is the movement of particles (solutes) across a semi-permeable membrane.

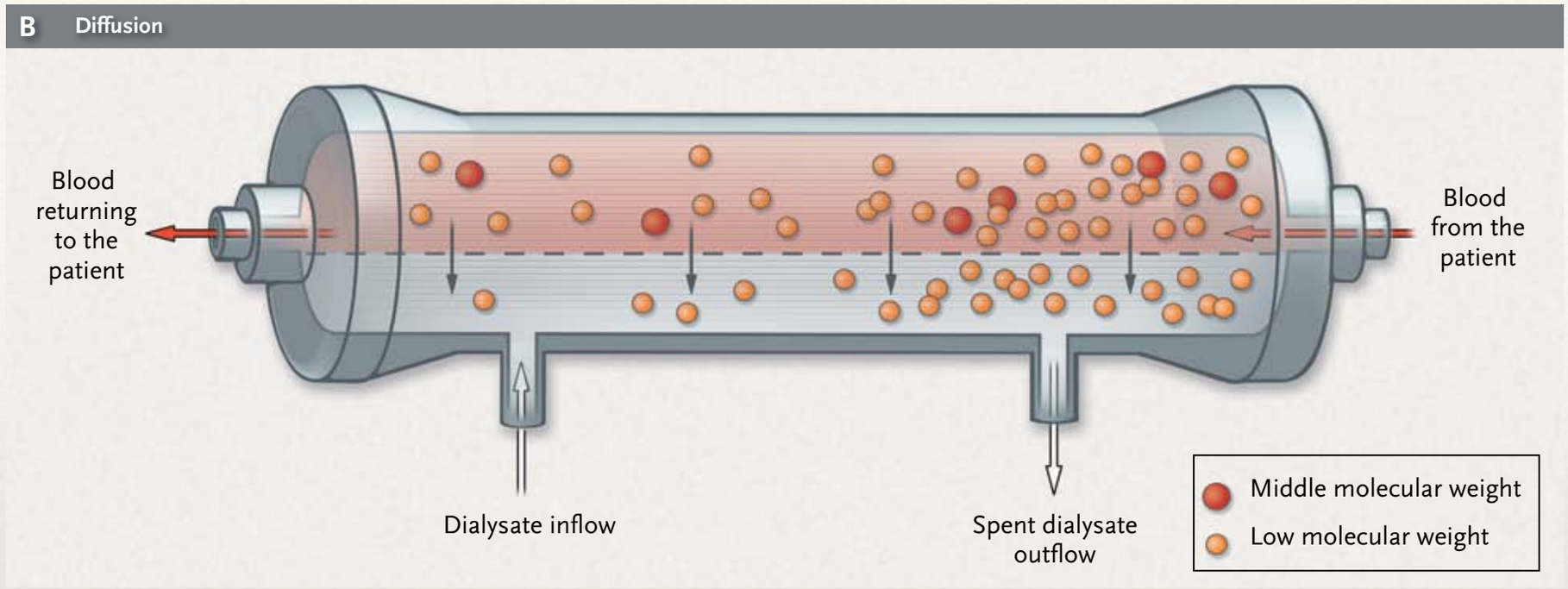
Diffusion is the movement from the side with the highest concentration of particles, to the side with the lowest concentration.

Ultrafiltration

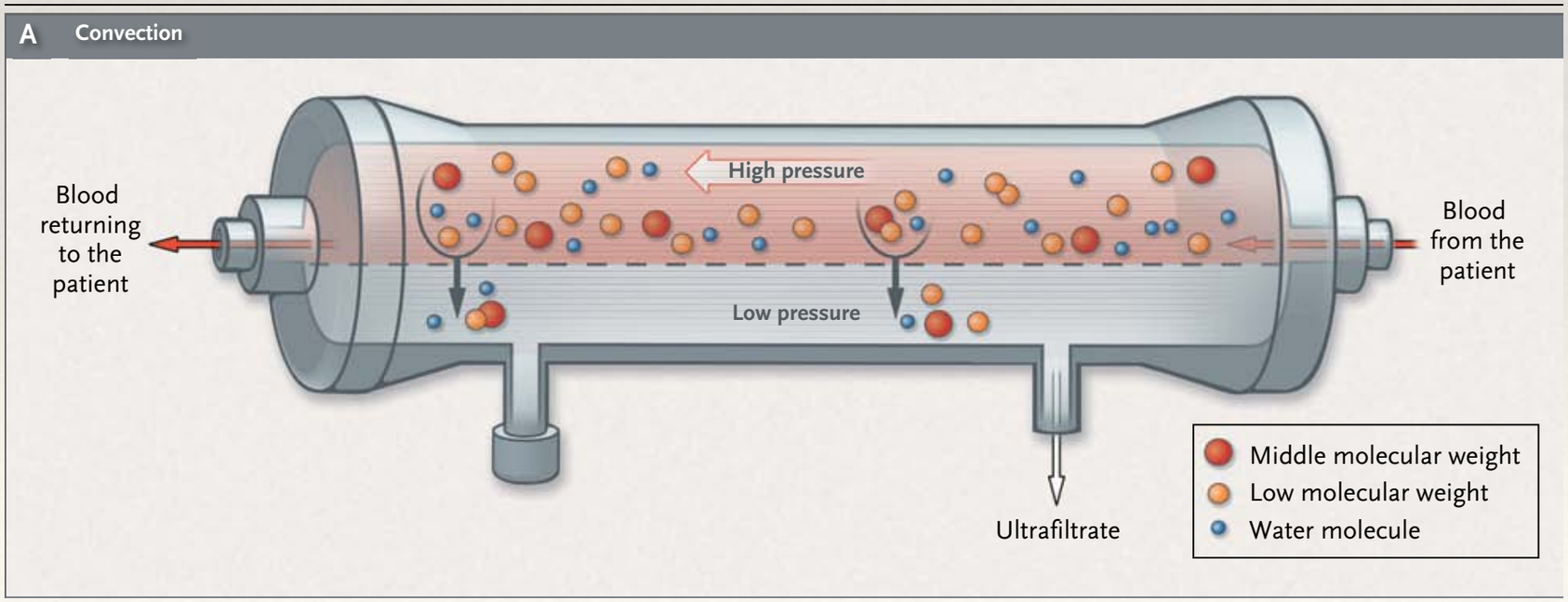
In ultrafiltration, fluids are moved across the membrane by a hydrostatic pressure gradient



Diffusion



Convection



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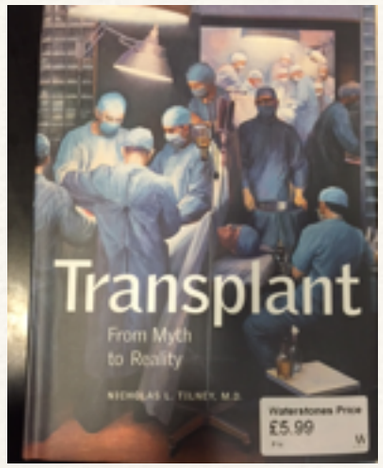


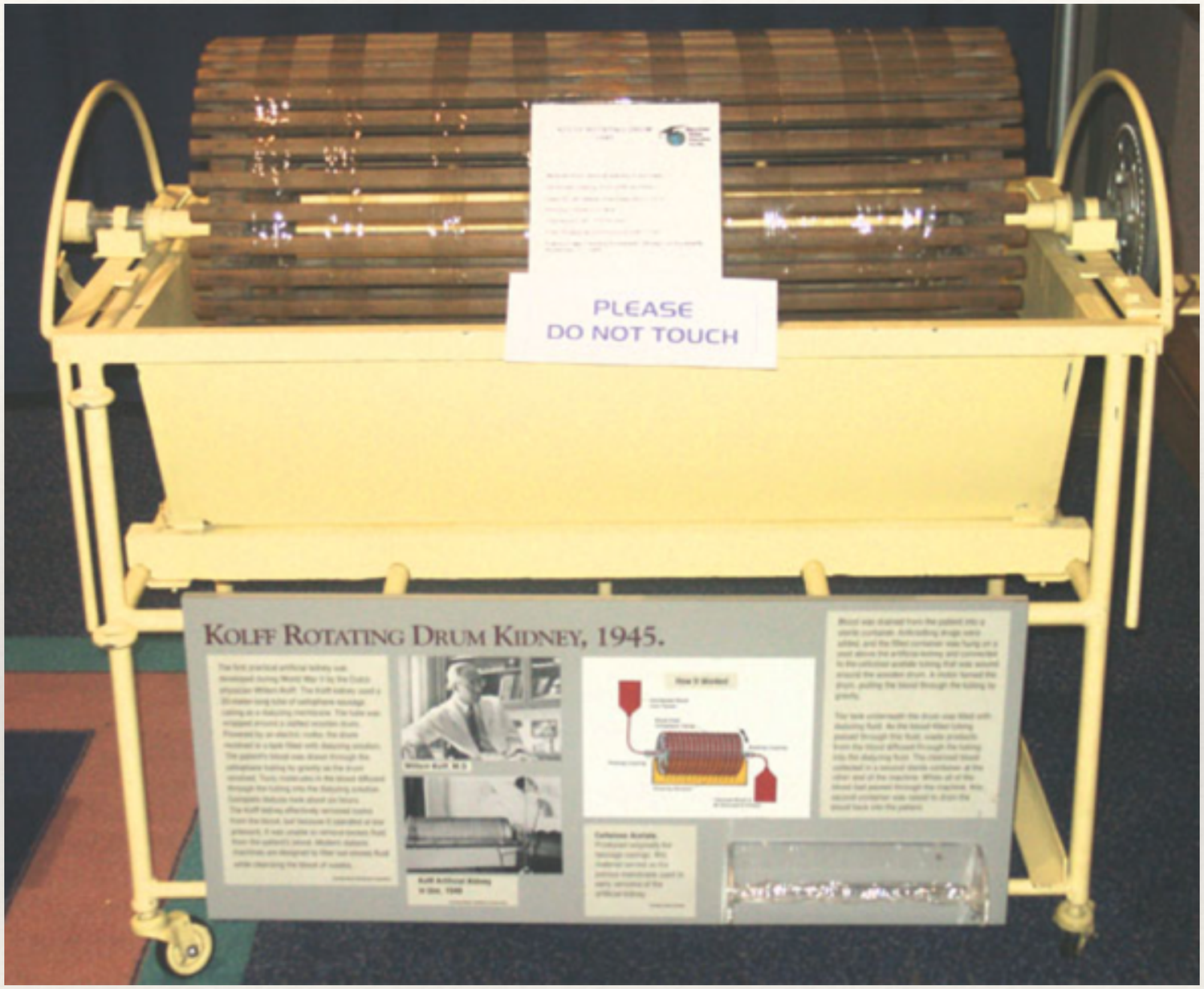
First dialysis machine

1861 - term dialysis first used by a Scottish professor of chemistry, who demonstrated that **parchment coated with albumin** (semipermeable membrane) would allow **diffusion** of crystalloid (**salts** - from high to low concentration) as well as **urea**- but **not colloids.**

1911- investigators at Johns Hopkins described a technique by which the **blood** of a living animal may be submitted to **dialysis outside the body** and returned to the normal circulation.

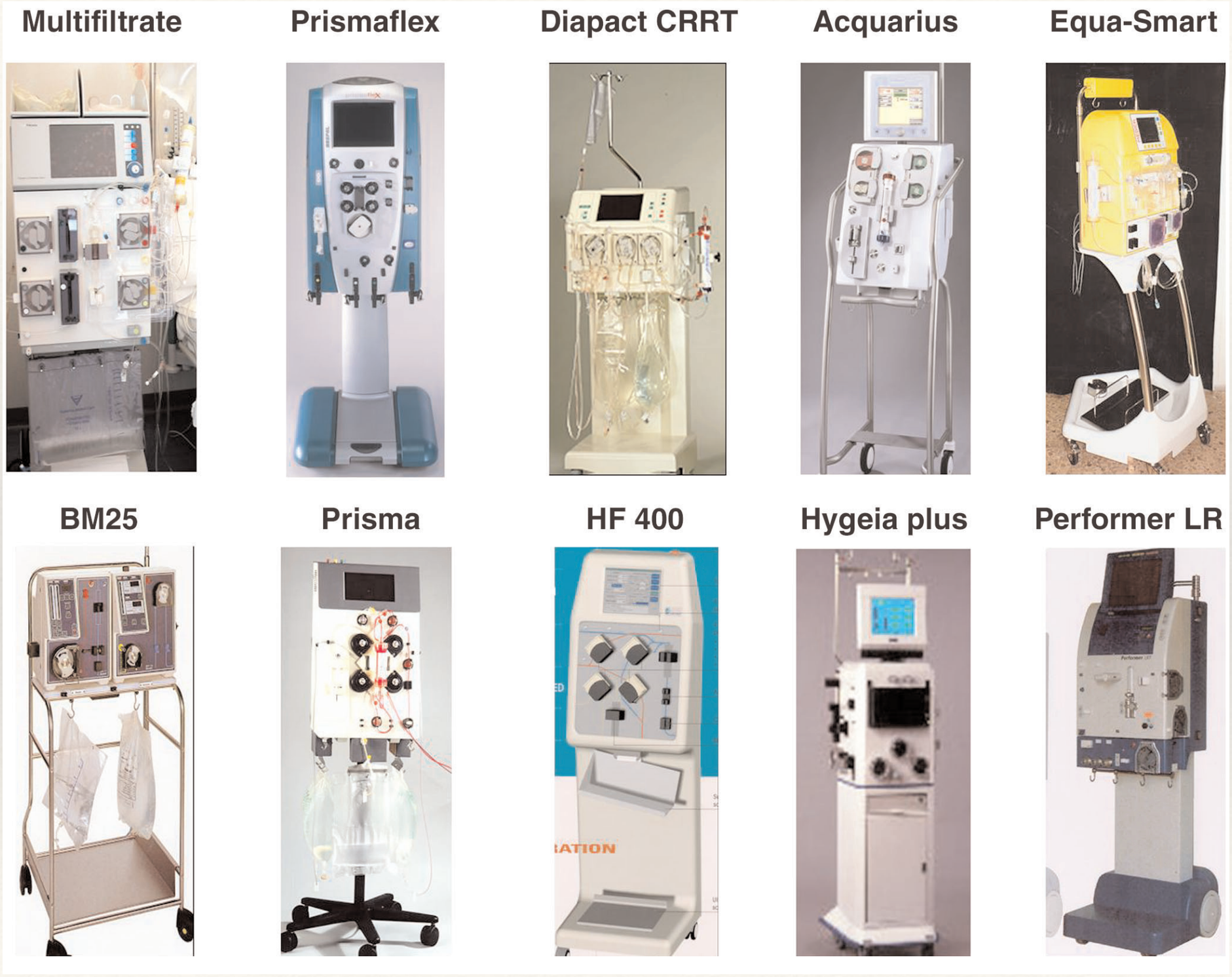
WWI - Unfortunately curtailed the experiments on humans because "when the Great War came it was no longer possible for us to get the **1500 leeches** needed from Hungary (considered by the English as of "**enemy origin**").

First dialysis machine



"Father" of dialysis Willem Kolff
Dutch physician, bioengineer and inventor during WWII

Now they look like this



Critical Care 2006, 10:123 (doi:10.1186/cc4843)

Solute clearance in RRT

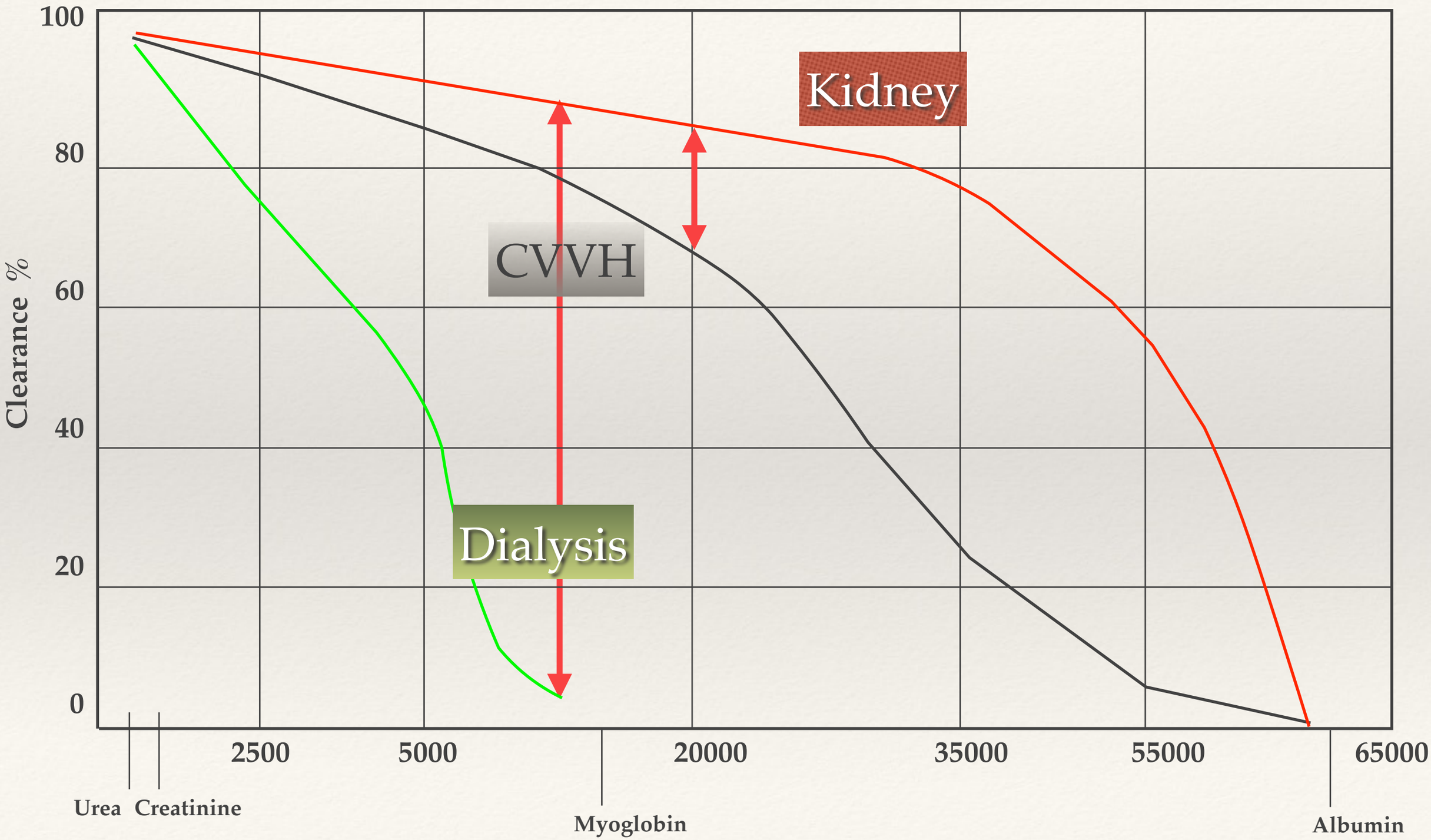
Type of therapy	Solute transport	Replacement fluid	Ultrafiltrate flow *ml/hr*
CVVH	Convection	Yes	 500-4000/hr
CVVHD	Diffusion	No	 0-350/hr
CVVHDF	Convection and diffusion	Yes	 500-4000/hr

N Engl J Med 2012;367:2505-14

Molecular weights

Daltons				Modality
100,000 -				
	Albumin (55,000-60,000)			**Minimal removal**
50,000 -				
	Cytokine		**Large**	**Convection**
	Beta 2 Microglobulin (11,800)			
10,000 -				
5,000 -	Inulin (5,200)		**Middle**	**Convection > diffusion**
	Vit B12 (1356)			
1,000 -				
500 -				
	Glucose (180)			
	Creatinine(113)			
100 -	Amino acids		**Small**	**Convection = diffusion**
	Phosphate(80)			
	Urea (60)			
50 -				
	Potassium(35)			
	Sodium(23)			
10 -				

Clearance during CVVH



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Elseviers *et al. Critical Care* 2010, **14**:R221
http://ccforum.com/content/14/6/R221

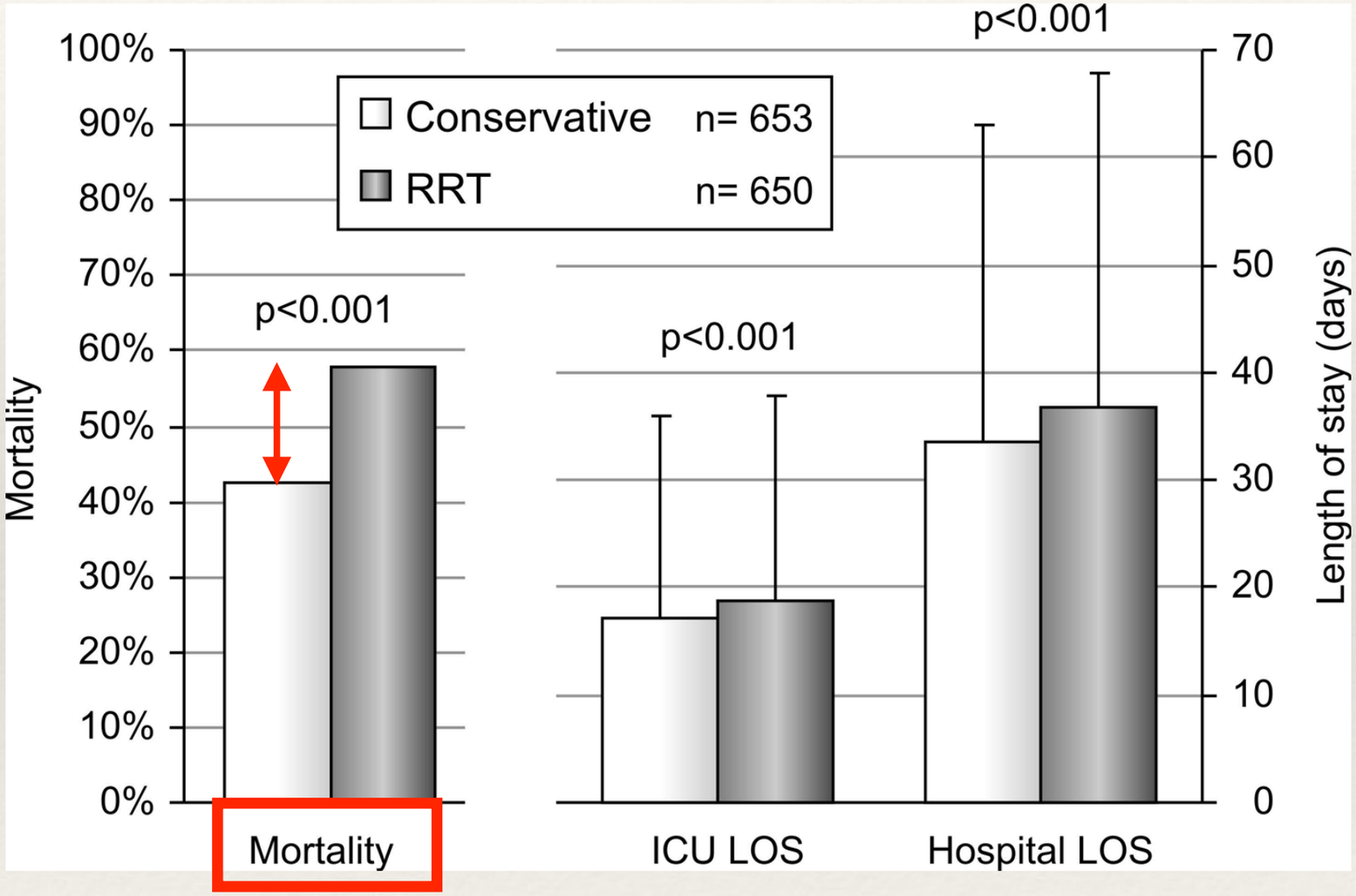
CRITICAL CARE

RESEARCH Open Access

Renal replacement therapy is an independent risk factor for mortality in critically ill patients with acute kidney injury

Monique M Elseviers[1], Robert L Lins[2*], Patricia Van der Niepen[3], Eric Hoste[4], Manu L Malbrain[5], Pierre Lamaire[6], Jacques Devriendt[7], for the SHARF investigators

? Similar to VILI?



"This study showed that the higher mortality expected in AKI patients receiving RRT versus conservative treatment **cannot** be **explained** by a **higher disease severity**…"

Consider adverse effects

- Spontaneous recovery
- Vascular access problems
- Hypotension
- Anticoagulation
- Altered drug pharmacokinetics
- Depletion of nutrients (AA) /trace elements (selenium)/vitamins
- Loss of heat
- Pro-inflammatory effects of membrane
- Cost

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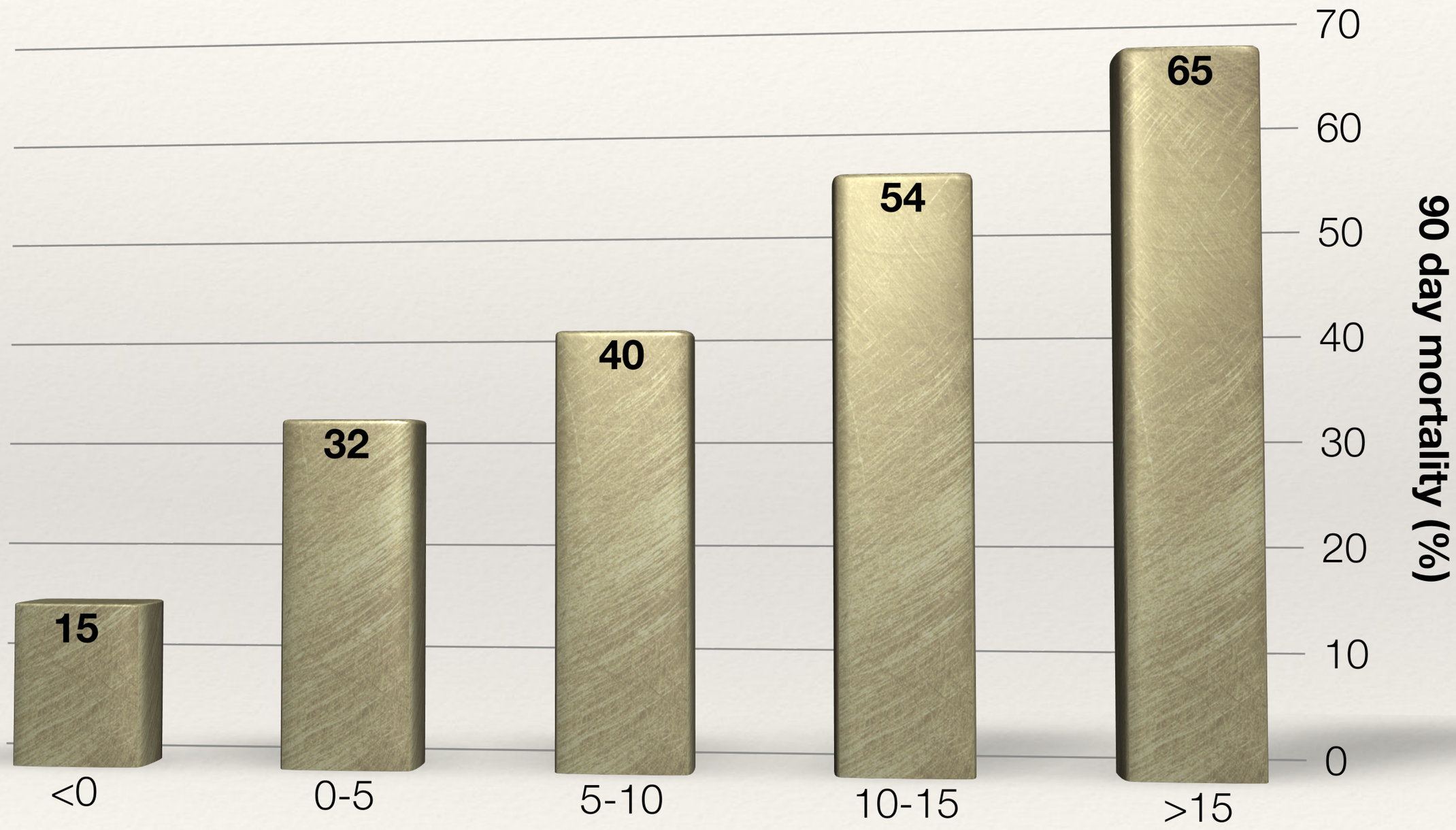
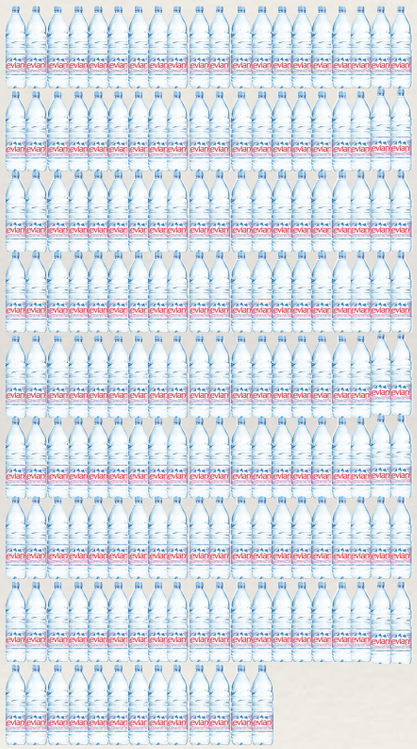
Fluid overload and mortality in ITU patients on RRT



Critical Care 2012, 16:R197

Comparison of fluid management capability

	Normal kidney	CRRT	IHD	PD
Vol. of filtrate / day (L)	 173L / day	 ~ 60 / day	 8L / day	 14L / day
Regulatory mechanism	Reabsorption (99%)	Replacement fluid	-	-

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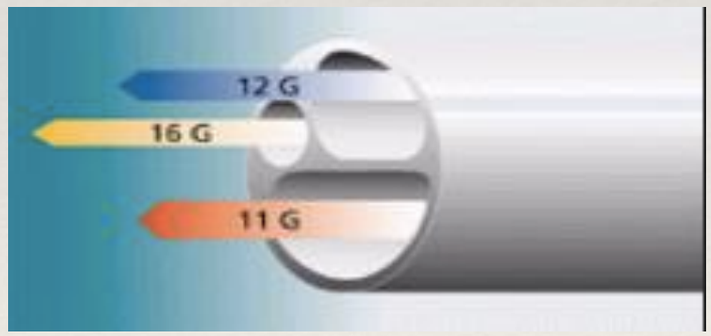
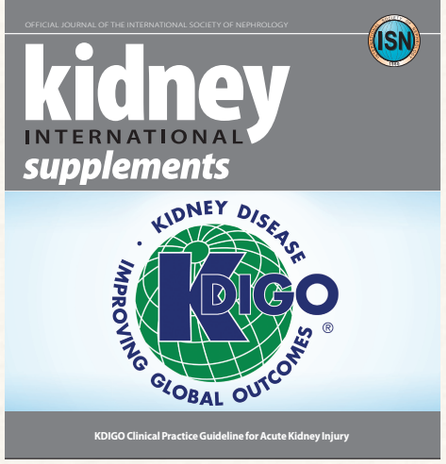
Vascular access catheters

~ 13.5 Fr

Flows of up to 400 mL/min





"When **choosing a vein** for insertion of a dialysis catheter in patients with AKI, consider these preferences:

1. right jugular vein
2. femoral vein
3. left jugular vein
4. subclavian vein with preference for the *dominant side."*

least preferred option

and please be careful !

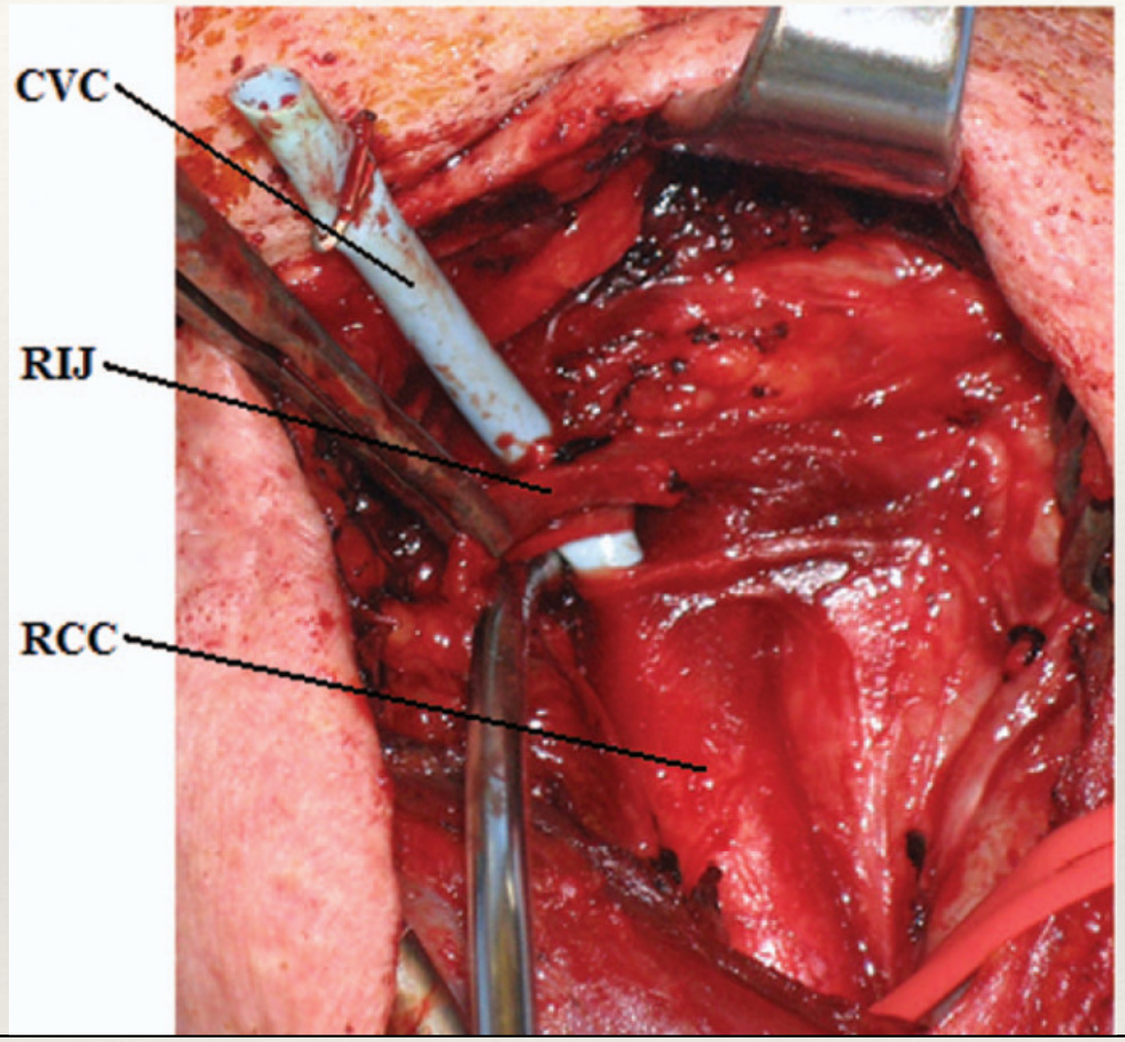


Figure 2: Open surgical repair following arterial cannulation reveals a central venous catheter traversing through the right internal jugular vein into the right common carotid artery.

From Parsons, A.J. and J. Alfa, Carotid dissection: a complication of internal jugular vein cannulation with the use of ultrasound. Anesth Analg, 2009. 109(1): p. 135-6.

J Ultrasound Med 28, 1239-44 (2009)

Be careful !

Ultrasound has **not** removed the risk of unintended arterial cannulation. And remember…a VasCath is BIG!

Age	Mechanism of injury	Outcome
67	Needle went through IJ into Carotid artery	Patient Died
75	Needle went though femoral vein into femoral artery	Vascular surgery for AV fistula
48	Needle went though IJ and entered carotid artery sitting underneath the IJ	Surgery for tear and focal dissection of carotid artery
67	Guidewire traveled through IJ and its posterior wall and into carotid artery	Hematoma with respiratory distress requiring emergent intubation.
69	Needle penetrated the carotid artery which was very close to the IJ	Emergency carotid artery repair; Patient died of complications
14	Needle penetrated rear wall of IJ and entered carotid artery	Central line removed and bleeding eventually stopped

Table 3: Analysis of six accidental arterial cannulations with dynamic ultrasound guidance

8 arterial catherisations for every 1000 cannulations prevented by using pressure monitor

J Ultrasound Med 28, 1239-44 (2009)

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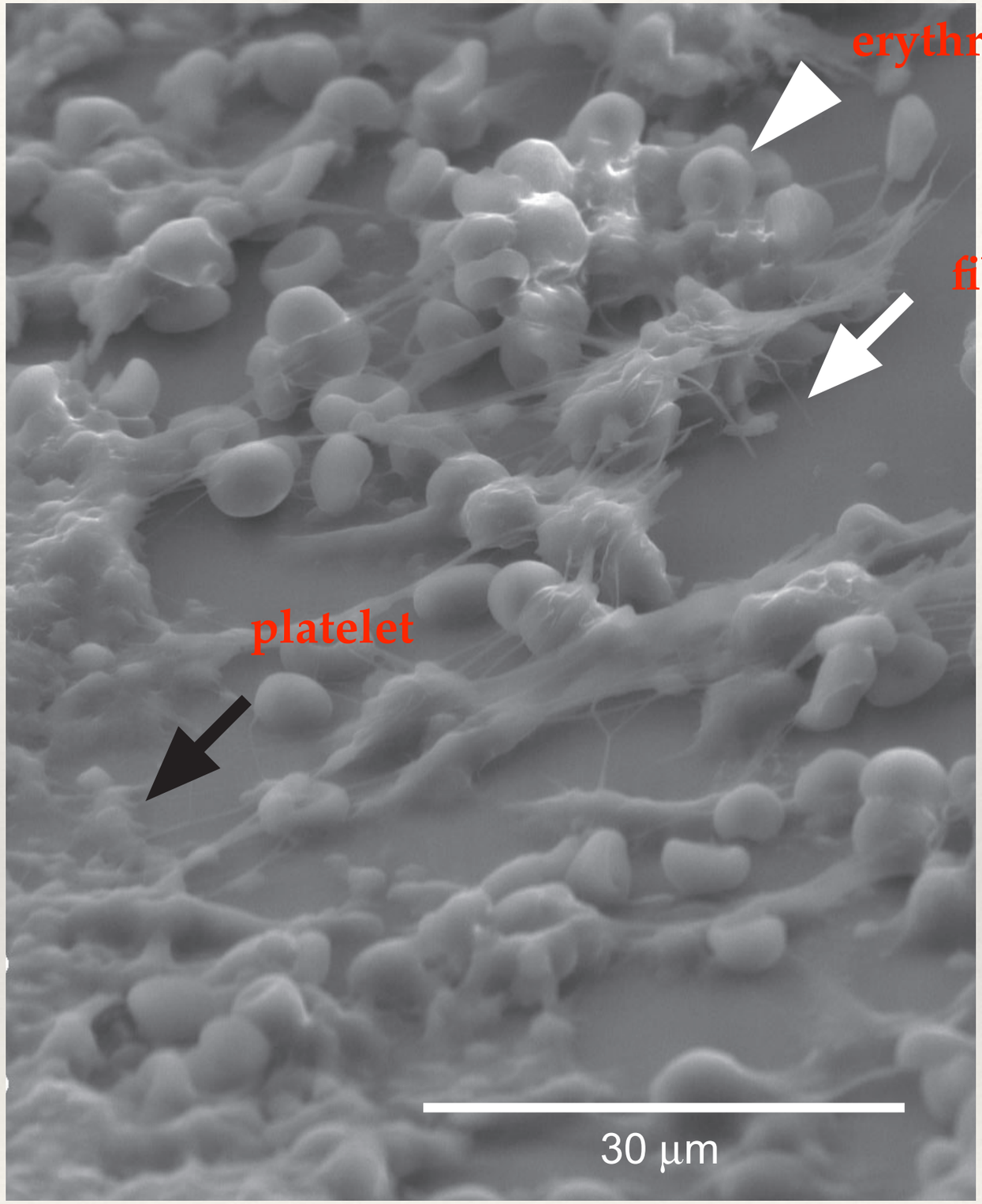
Why the need for anticoagulation?

Blood + **Extracorporeal circuit**

Activation of intrinsic pathway of coagulation and platelets

Deposition of fibrin clots and thrombotic obstruction



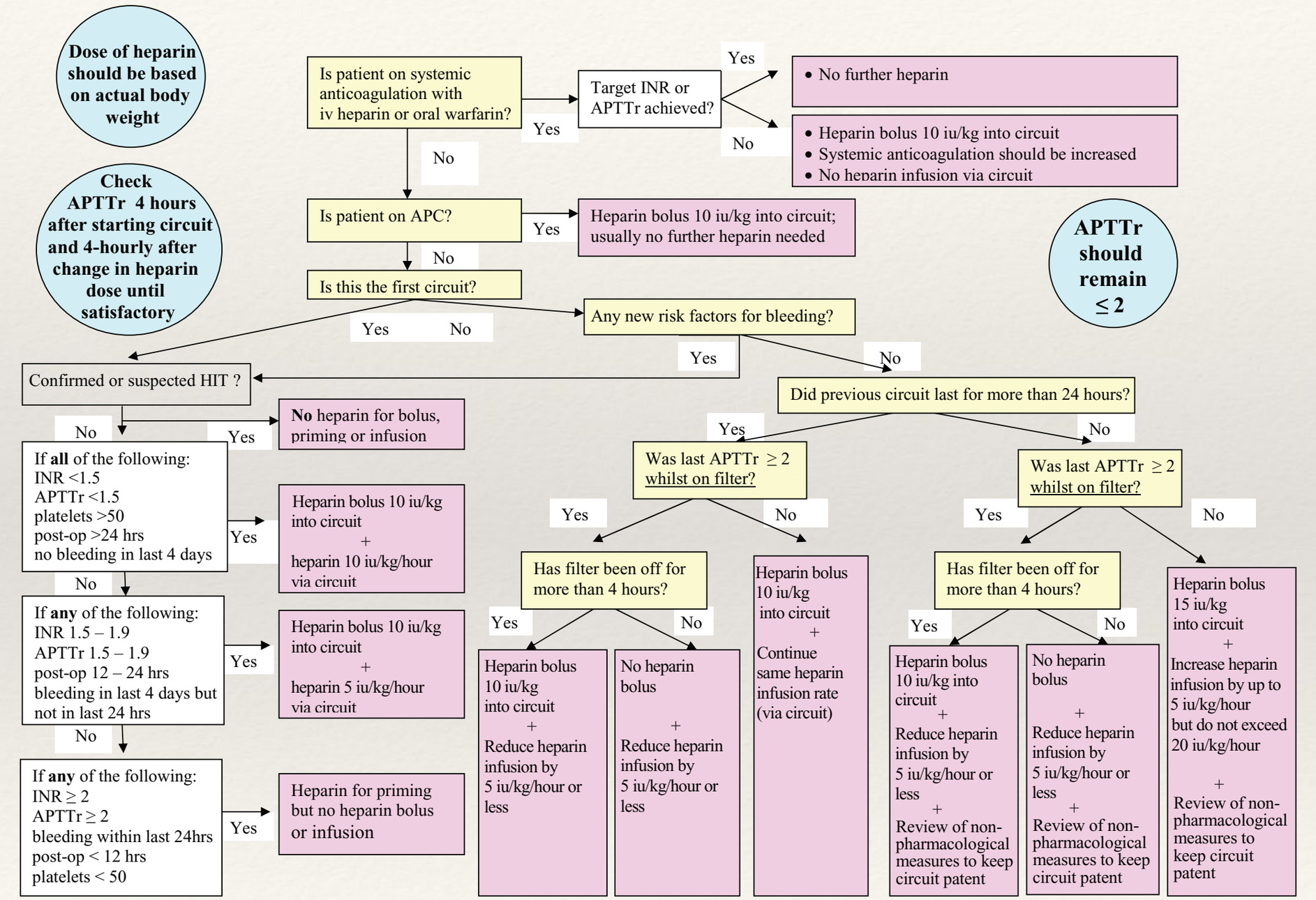
Electron micrograph of material adherent to the luminal surface of the dialysis venous tubing.

Clin J Am Soc Nephrol 3: 382-386, 2008

What type of anticoagulant

- Unfractionated heparin
- LMW heparin
- Thrombin antagonists
- Citrate
- Prostaglandins - PGI_2, PGE_1
- No anticoagulant

Heparin algorithm



Ostermann et al. Critical Care 2010, 14:419

Citrate

- **Advantages**
  - regional, avoids bleeding complications
    - doubles as buffer
    - highly effective (> heparin)
    - no thrombocytopenia
- **Disadvantages**
  - metabolic complications
  - complex protocols

And even no anticoagulant !

Intensive Care Med (2000) 26: 1652–1657
DOI 10.1007/s001340000691

ORIGINAL

H. K. Tan
I. Baldwin
R. Bellomo

Continuous veno-venous hemofiltration without anticoagulation in high-risk patients

"Critically ill patients at **high risk of bleeding** who require continuous renal replacement therapy can be safely managed **without** circuit **anticoagulation**. This strategy **minimizes bleeding risks** and is associated with an **acceptable filter life (mean of 32 hr)**.

CRRT without anticoagulation should be strongly considered in high-risk patients."

Outline

- What is AKI?
- How good is RRT compared to normal kidney function?
- Indications and timing for RRT?
- Basic principles
- Modalities
- RRT - Adverse effects
- Fluid management
- Vascular access
- Anticoagulation
- Which dose of RRT?
- Peritoneal dialysis

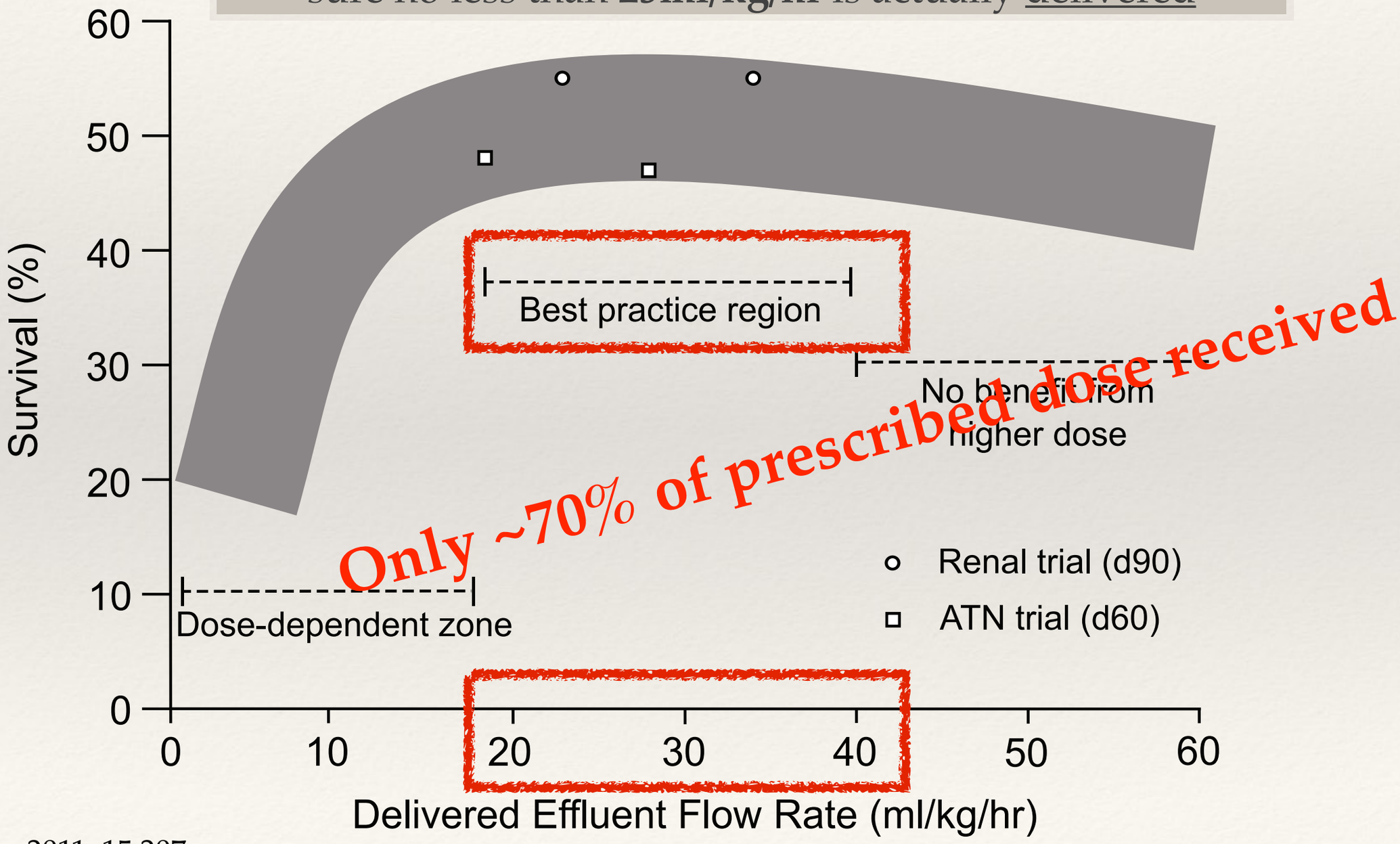
What is the “dose”?

- Urea and small molecule clearance
- Only measures one aspect of RRT
- **Effluent flow rate ~ a urea clearance**

  “quasi GFR” measure for CRRT

Optimal dose of CRRT

35 ml/kg/hr is reasonable target for prescription to make sure no less than **25ml/kg/hr** is actually delivered



Critical Care 2011, 15:207

Remember

- 35 ml/kg/hr will probably only achieve a CKD stage 4 GFR equivalent (***GFR = 15-20 ml/min***)

CRRT isn't native renal function

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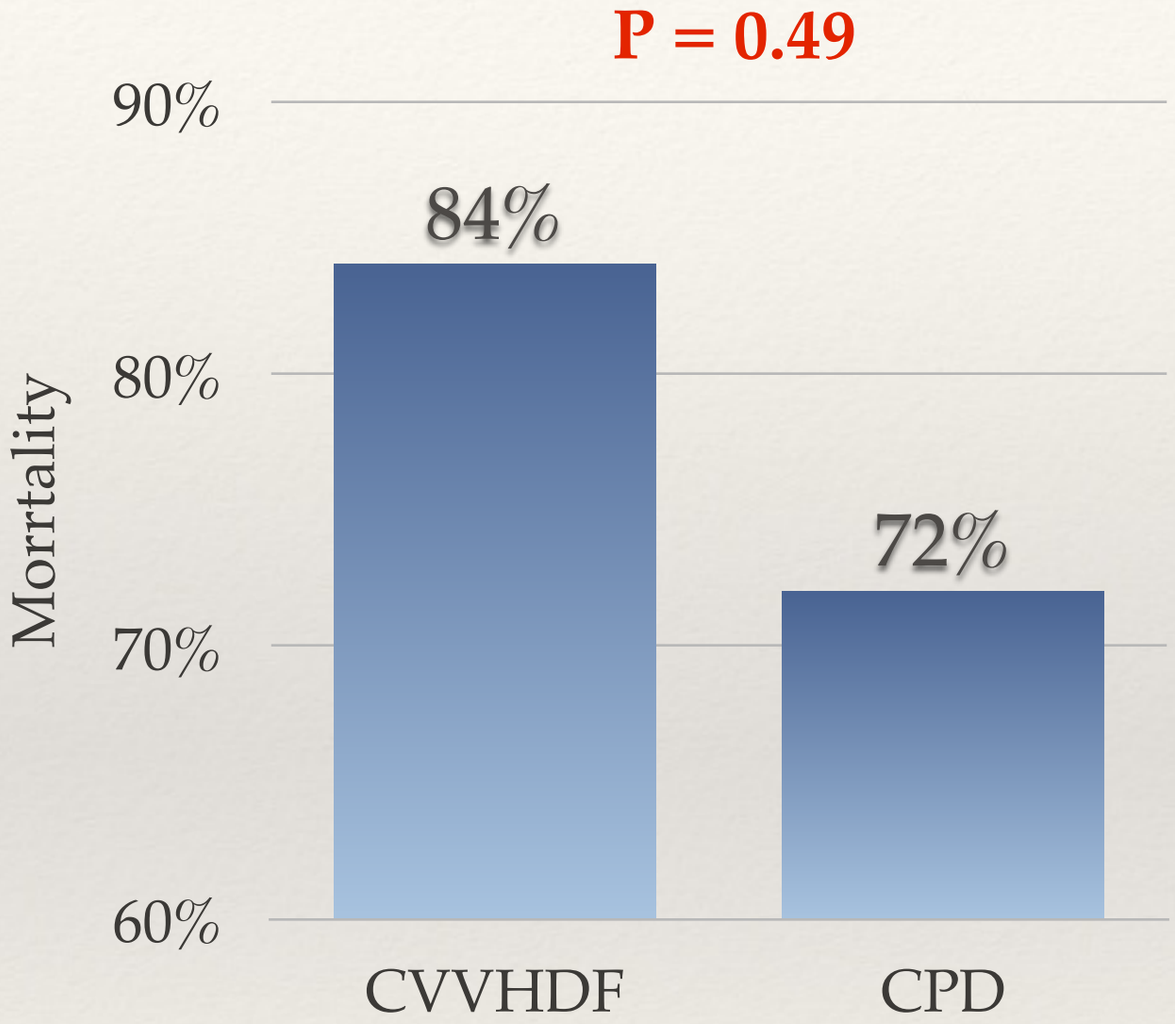
Peritoneal dialysis

Pros	Cons
Easy + available	Infection
HD tolerance	Catheter insertion
Compatibility Less inflammation? / peritoneum bio-compatible	Adequacy / dose?
No anticoagulation	Respiratory IAH / PLEURAL EFFUSION
Cheap	Exclusion abdo surgery
Simple	

Outcome with PD



Perit Dial Int 2011; 31(4):422-429

Renal transplant as a last resort

BBC NEWS

China 'kidney for iPad' trial begins in Hunan

Recap

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Thanks for listening

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