

Acute Kidney injury in PICU: Management Challenges

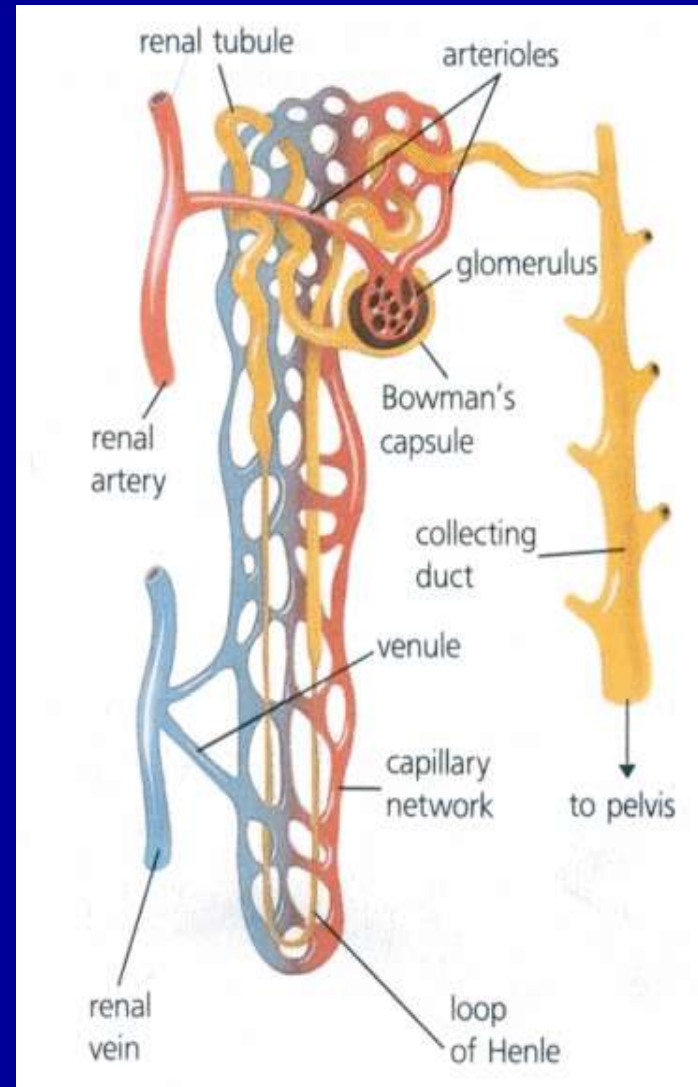
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OBJECTIVES

- **The Problematic Definition of ARF / AKI**
- **The spectrum of AKI and pRIFLE**
- **Epidemiology**
- **Biomarkers of AKI**
- **Management and Renal replacement therapy**
- **(RRT) Treatment Modalities of choice?**

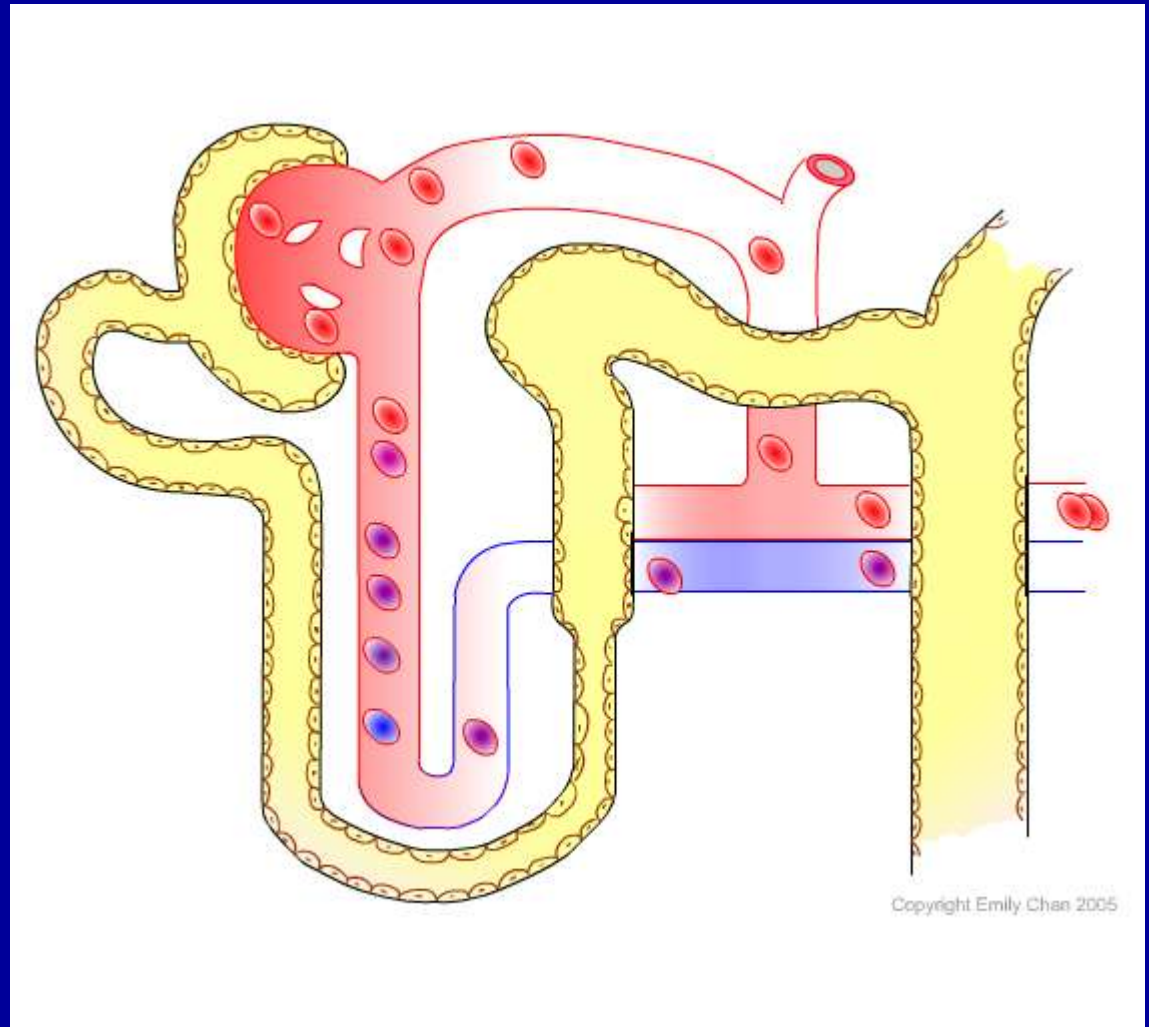
Renal blood flow

- Aorta → Renal artery → interlobar arteries → interlobular arteries → afferent arterioles → glomerulus → efferent arterioles
- In the cortex → peritubular capillaries
- In the juxtamedullary region → vasa recta
- Back to the heart through the interlobular → intralobar → renal veins

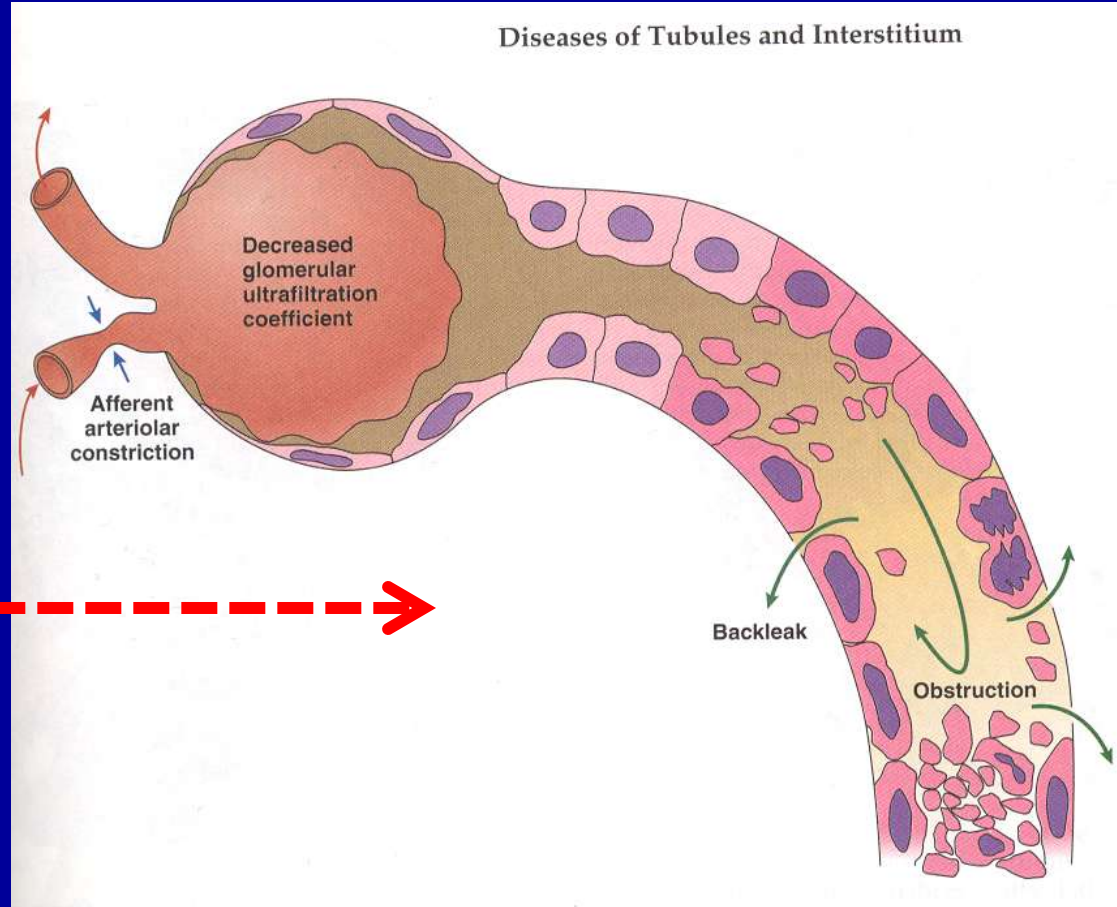
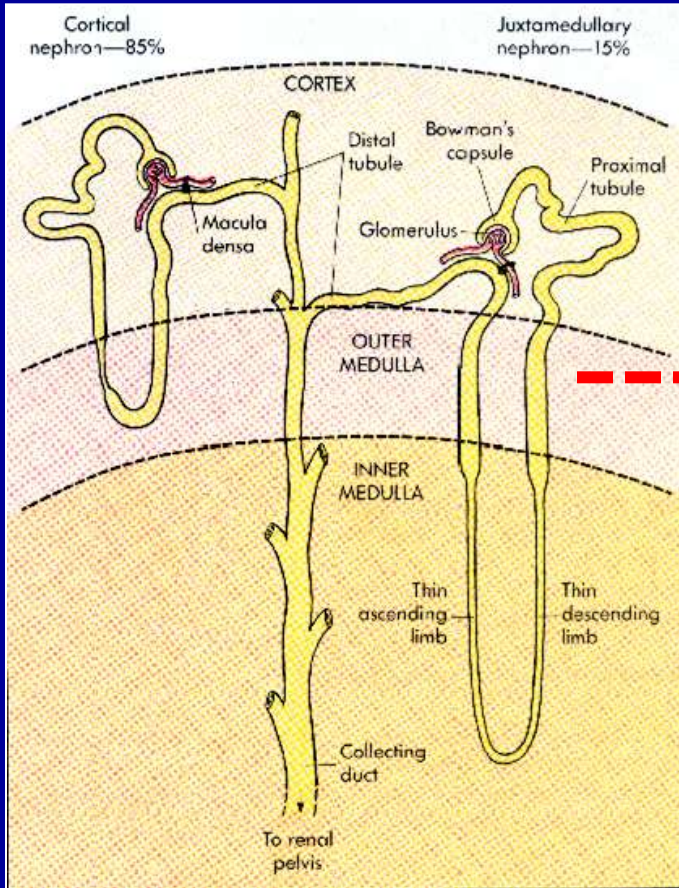


Pathophysiology

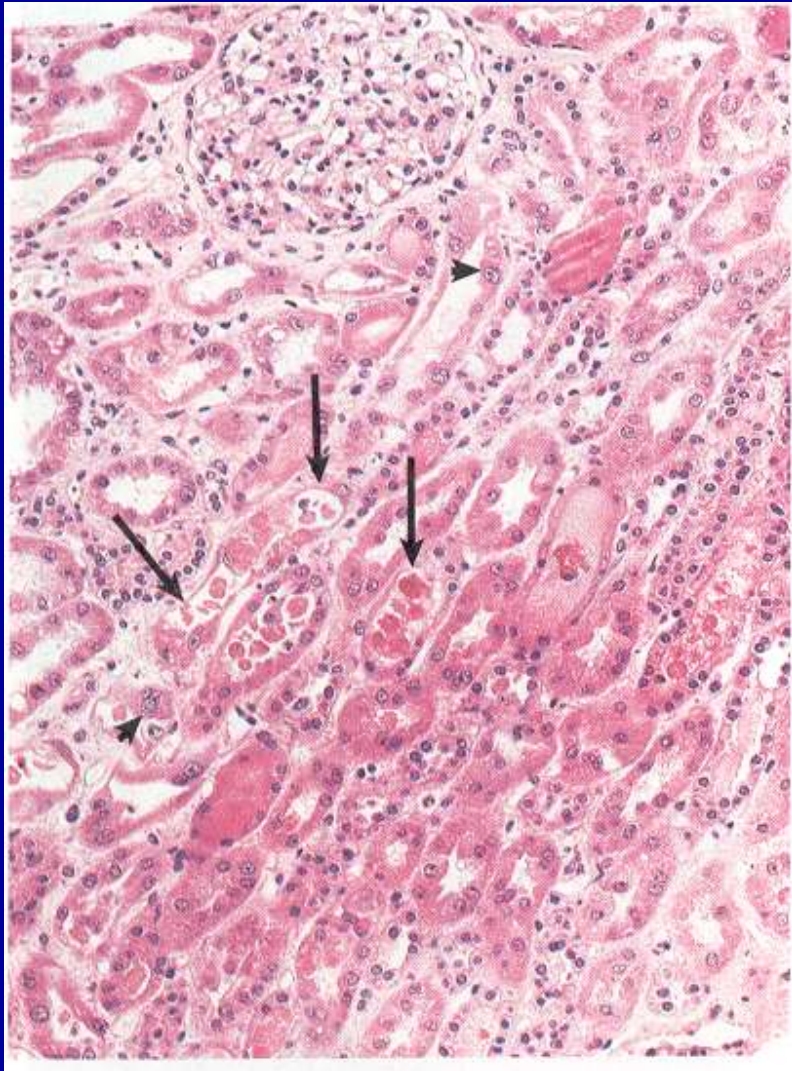
- outer renal medulla prone to ischaemia
- reduced renal blood flow worsens medullary ischaemia
- ischaemia causes structural changes and ultimately acute tubular necrosis



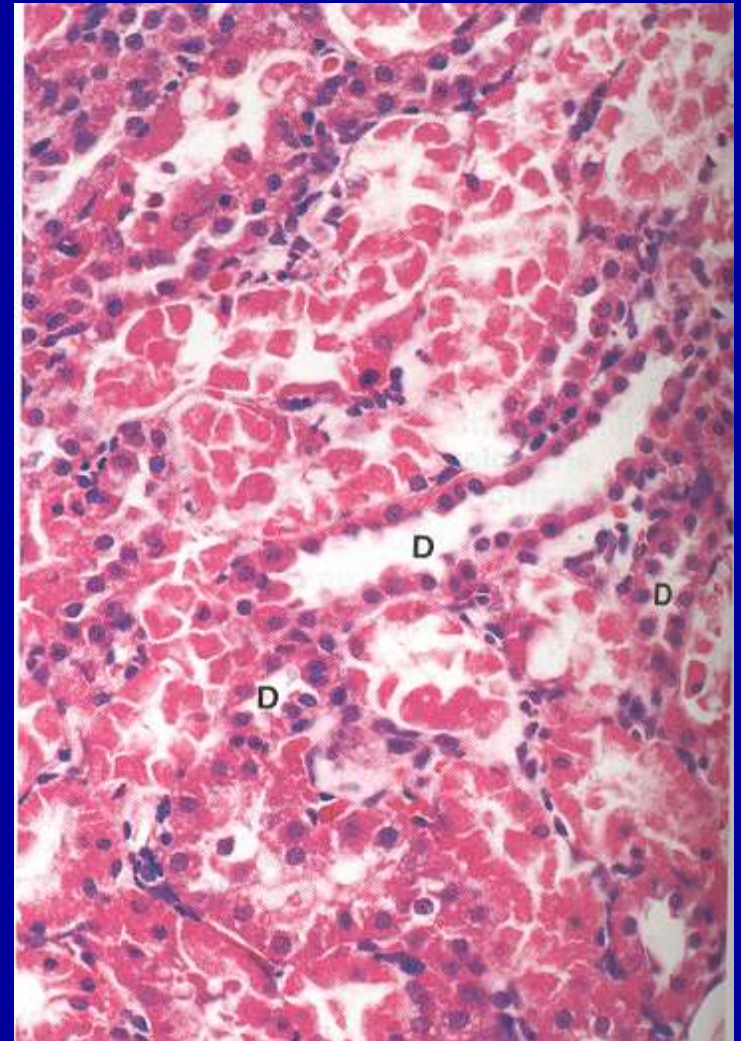
ATN



Ischemic ATN



Nephrotoxic ATN



Traditional Definition of ARF

- Acute Renal Failure:

- “Sudden loss of renal function resulting in the loss of the kidneys’ ability to regulate electrolyte and fluid homeostasis”
- Failure of the kidneys to excrete nitrogenous waste products
- A rise in serum BUN or creatinine concentration, with or without decrease in urine output
- ARF is often transient and completely reversible.

The Problematic Definition of ARF

- Pediatric AKI definition: a moving target
 - Infants
 - ◆ Creatinine in the first few weeks of life may reflect maternal values
 - Children
 - ◆ Low baseline Cr makes 0.2-0.3 changes in Cr significant
 - ◆ Varying muscle mass
 - Adolescents
 - ◆ Creatinine rise may be a late sign of AKI

The Problematic Definition of ARF

- The lack of a uniform ARF definition has prevented optimal ARF outcome research
 - One study's ARF is another study's lab error
 - (or maybe not)
- Inherent problems with SCr as ARF marker
 - Does not differentiate
 - ▲ the nature and type of renal insult
 - ▲ site of renal insult
 - ▲ Prognosis of AKI
- Changes in SCr may lag changes in GFR and may be a very late indicator of renal injury

Consensus Definition: RIFLE

Acute Dialysis Quality Initiative (ADQI) 2002

Stratification system intended to establish the presence or absence of AKI and describe the severity of the AKI syndrome

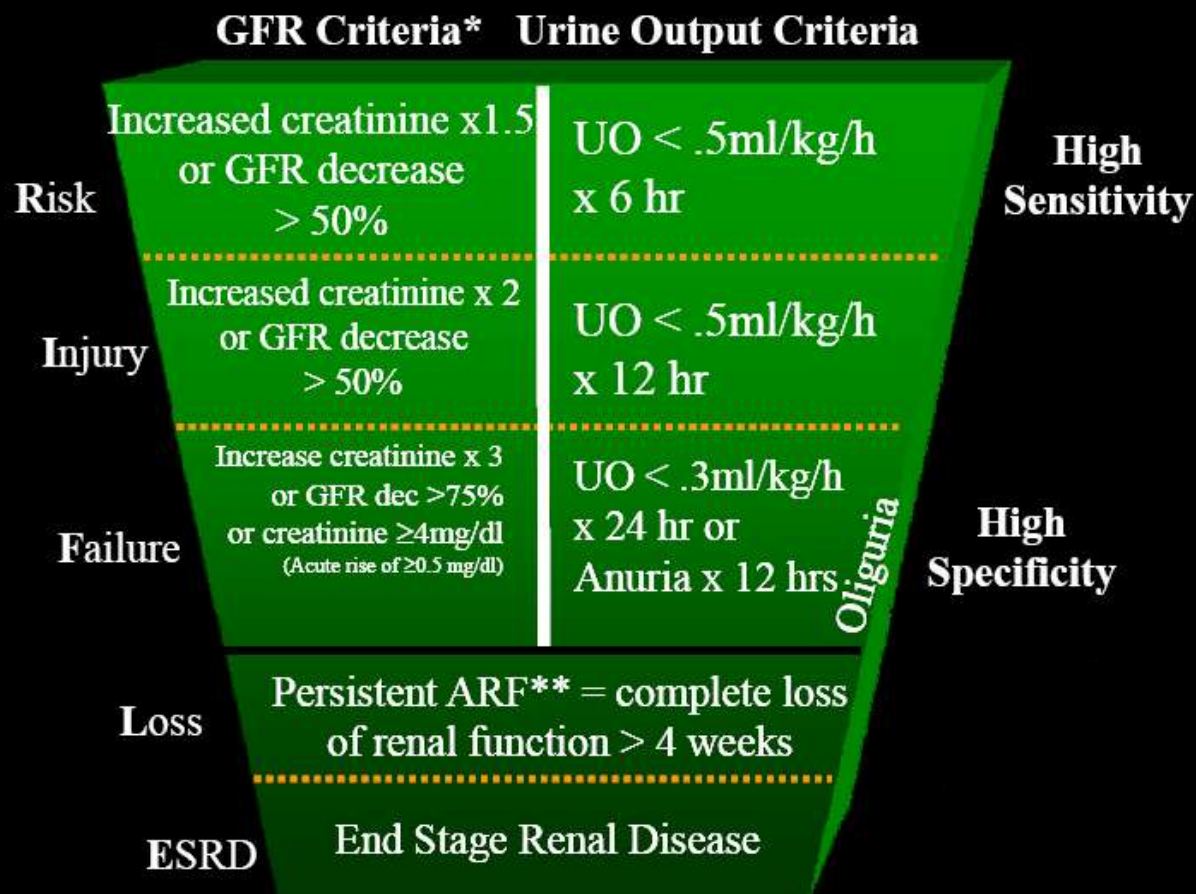


Table 6 | Pediatric-modified RIFLE (pRIFLE) criteria

	Estimated CCI	Urine output
Risk	eCCI decrease by 25%	<0.5 ml/kg/h for 8 h
Injury	eCCI decrease by 50%	<0.5 ml/kg/h for 16 h
Failure	eCCI decrease by 75% or eCCI <35 ml/min/1.73 m ²	<0.3 ml/kg/h for 24 h or anuric for 12 h
Loss	Persistent failure >4 weeks	
End stage	End-stage renal disease (persistent failure >3 months)	

eCCI, estimated creatinine clearance; pRIFLE, pediatric risk, injury, failure, loss and end-stage renal disease.

**Early sign of AKI: Oliguria
(UO < 0.5 CC/KG/Hour x 8 hours)**

- warning sign of impaired tissue perfusion
- leads to acute renal failure if not corrected
- 2 hours' oliguria **MUST** be treated urgently

Normal

AKI

ATN

Oliguria, worsening ischemia



Predict....Prevent..... Treat

Causes - multi-factorial

- **Pre-renal: hypoperfusion**
 - dehydration
 - hypovolemia
 - hemodynamic factors that can compromise renal perfusion (CHF, shock)
- **Renal:**
 - nephrotoxins
 - aminoglycosides, glycopeptides, NSAIDs, ACEIs, contrast media, loop diuretics
 - rhabdomyolysis, hypercalcaemia, hyperphosphatemia, tumor lysis syndrome
 - intrinsic renal disease
 - interstitial nephritis, glomerulonephritis
- **Post-renal: Obstruction**
 - stones, papillary necrosis

Epidemiology of AKI in Children

AKI incidence

- ❑ Paediatric incidences of AKI in PICU 8-30%
- ❑ Neonates have higher rates of AKI, especially following cardiac surgery, severe asphyxia, VLBE, low Apgar score, PDA, maternal receipt of antibiotics or NSAID
- ❑ The incidence of AKI in newborns in a developing country was 3.9 /1000 (0.4%) live births

Pediatric AKI: Recent Epidemiology

Patient Selection

- Reviewed all admissions to Texas Children's Hospital from January 1998 through June 2001
- Selected patients ≤ 20 years of age with ARF listed as diagnosis on discharge or death summary
- Reviewed list and defined AKI as GFR by Schwartz < 75 ml/min/1.73m² (n=254)

Pediatric AKI: Recent Epidemiology

Most Common ARF Causes

- ATN-Dehydration (21%)
- Nephrotoxic drugs (16%)
- Sepsis (11%)
- Unknown (14%)

Pediatric AKI: Recent Epidemiology

Renal Function at Hospital Discharge

- (66%) completely recovered
- (29%) had improved renal function or chronic renal insufficiency
- (5%) required renal replacement therapy

BIOMARKERS

Biomarkers: AMI versus AKI

Period	Acute Myocardial Infarction	Acute Kidney Injury
1960s	LDH	
1970s	CPK, myoglobin	
1980s	CK-MB	
1990s	Troponin T	
2000s	Troponin I	



Multiple Therapies
50% ↓ Mortality

Biomarkers: AMI versus AKI

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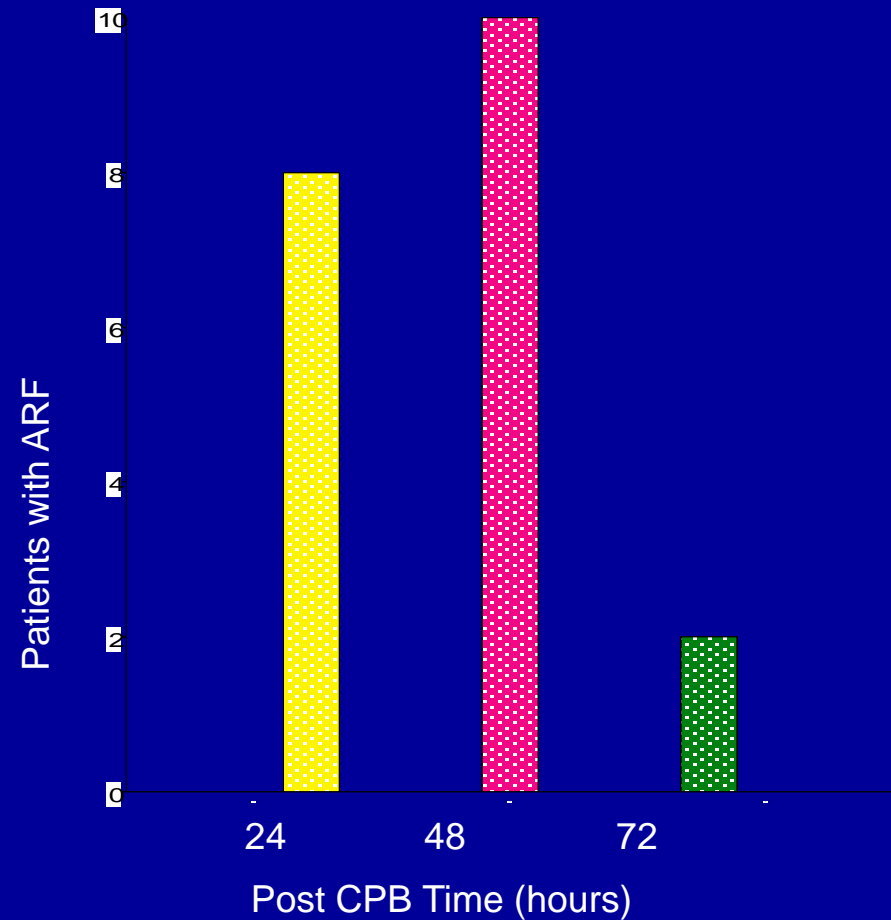
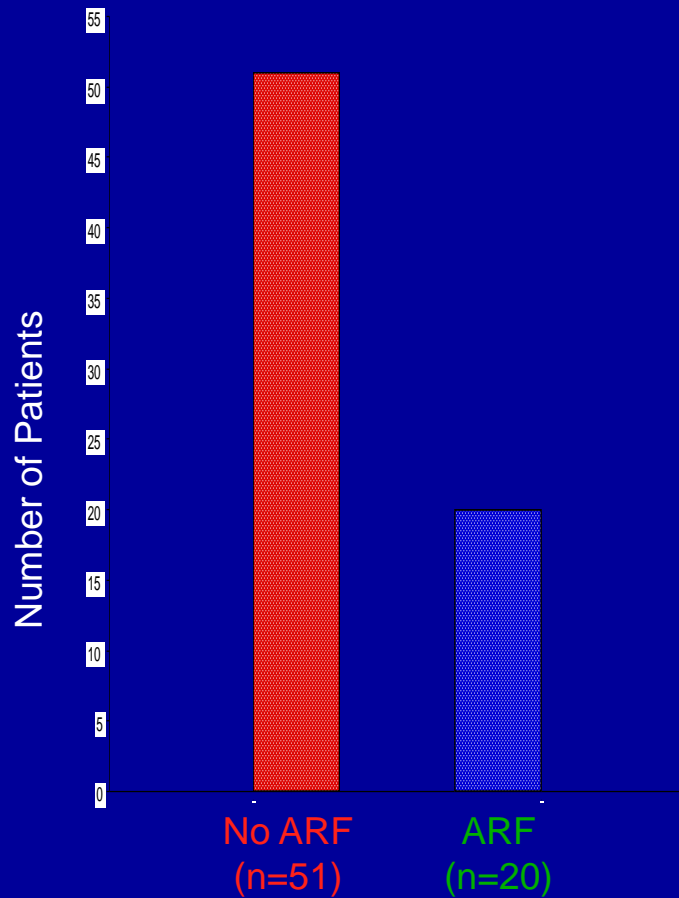
Supportive Care
High Mortality

Need early biomarkers of AKI for improved understanding, early treatment and better outcomes

Biomarkers for Acute Kidney Injury

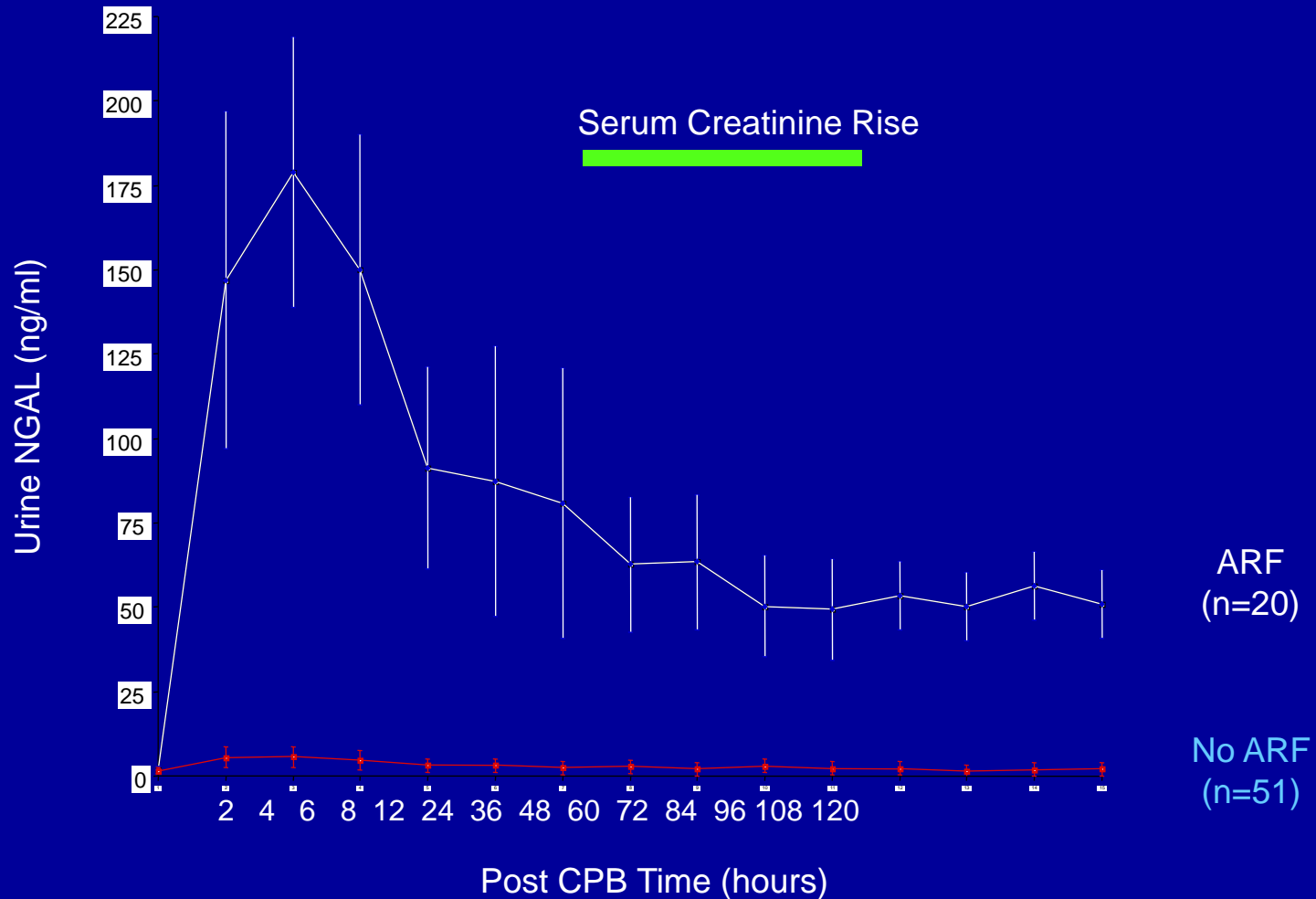
- Ideally AKI would have a biomarkers like myocardial infarction
 - (i.e. troponin-1)
- Currently no Troponin-I like marker to identify the site or severity of injury, although various markers are being evaluated
 - Kidney Injury Molecule (**KIM-1**)
 - Neutrophil gelatinase-associated lipocalcin (**NGAL**)
 - **IL-18**
 - **Cystatin C**

Incidence and Timing of AKI



Using serum creatinine, the diagnosis of ARF can be made only after 24-72 hours post CPB

Detection of Urinary NGAL by ELISA



Urine NGAL is upregulated 15-fold within 2 hours after CPB in patients who later develop ARF

Mishra J et al: Lancet 2005

Management

Management

- Avoid volume overload
- Treat complications
- Adjust drug doses
- Renal replacement therapy

Management

Treatable factors

- ❑ hypovolaemia and shock - resuscitate
- ❑ infection - antibiotics and source control
- ❑ nephrotoxic drugs - discontinue where possible
- ❑ abdominal compartment syndrome - decompress
- ❑ rhabdomyolysis - alkalinise, mannitol
- ❑ hypercalcaemia: hydration
- ❑ obstruction: remove obstruction

Investigations

- Urea, creatinine
- Na, K, Ca
- CPK
- ABG
- Renal ultrasound
- Urine dipstick
 - ± microscopy
 - ± renal biopsy

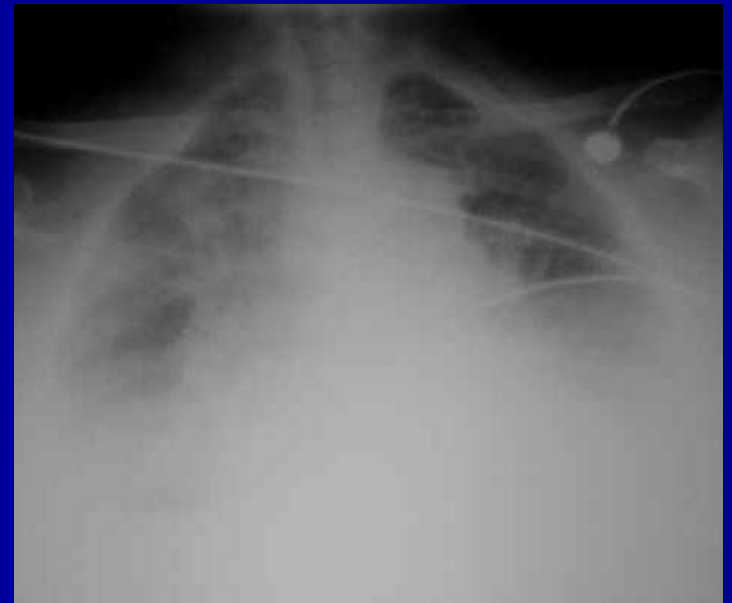


Resuscitation

- correct hypovolaemia
 - ▲ volume repletion
 - ▲ CVP guidance using serial fluid challenges
- restore cardiac output
 - ▲ vasopressors/inotropes if other evidence of tissue hypoperfusion
- restore perfusion pressure
 - ▲ Maintain MBP according to age
 - ▲ volume repletion and vasopressors

Acute renal failure requiring urgent management

- Rapidly rising creatinine
- Fluid overload
- Refractory oliguria
- Acidosis
- Hyperkalaemia
- Uremic pericarditis



Acute renal failure

- volume restrict
- adjust drug doses
- renal replacement therapy
 - ▲ unstable patients may require continuous haemo(dia)filtration rather than intermittent haemodialysis

Dopamine

- inconsistent diuretic effect
 - ▲ but this may cause dehydration
- does not
 - ▲ increase creatinine clearance
 - ▲ prevent acute renal failure
- does cause serious toxicity problems
 - ▲ tachyarrhythmias
 - ▲ exacerbates renal and mesenteric ischaemia
 - ▲ impaired immune function
- **fundamentally not useful**

Furosemide

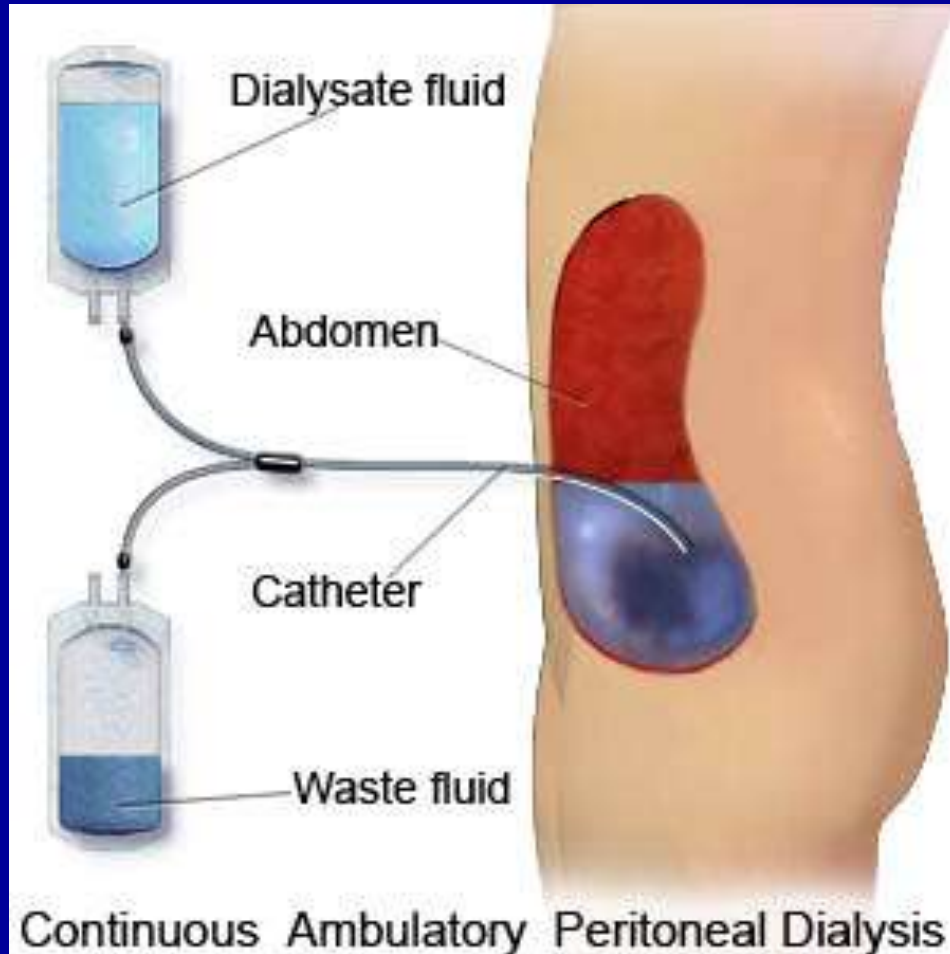
- does
 - ▲ reduce juxtamedullary oxygen consumption
- has not been shown to
 - ▲ improve creatinine clearance
 - ▲ affect survival either way
- disadvantages
 - ▲ of diuresis
- may be used but **ONLY** after adequate volume resuscitation

Mannitol

- volume expansion
- osmotic diuresis
- free radical scavenging
- may have specific role in rhabdomyolysis
- Patient should be making urine to be given

Renal replacement therapy

Peritoneal dialysis, CRRT, Hemodialysis



Selection of Therapy for Acute Renal Failure (ARF)

Renal Replacement Therapy for ARF

peritoneal dialysis

- In small children
- if no vascular access can be obtained

intermittent hemodialysis

- standard haemodialysis
- appropriate for isolated ARF

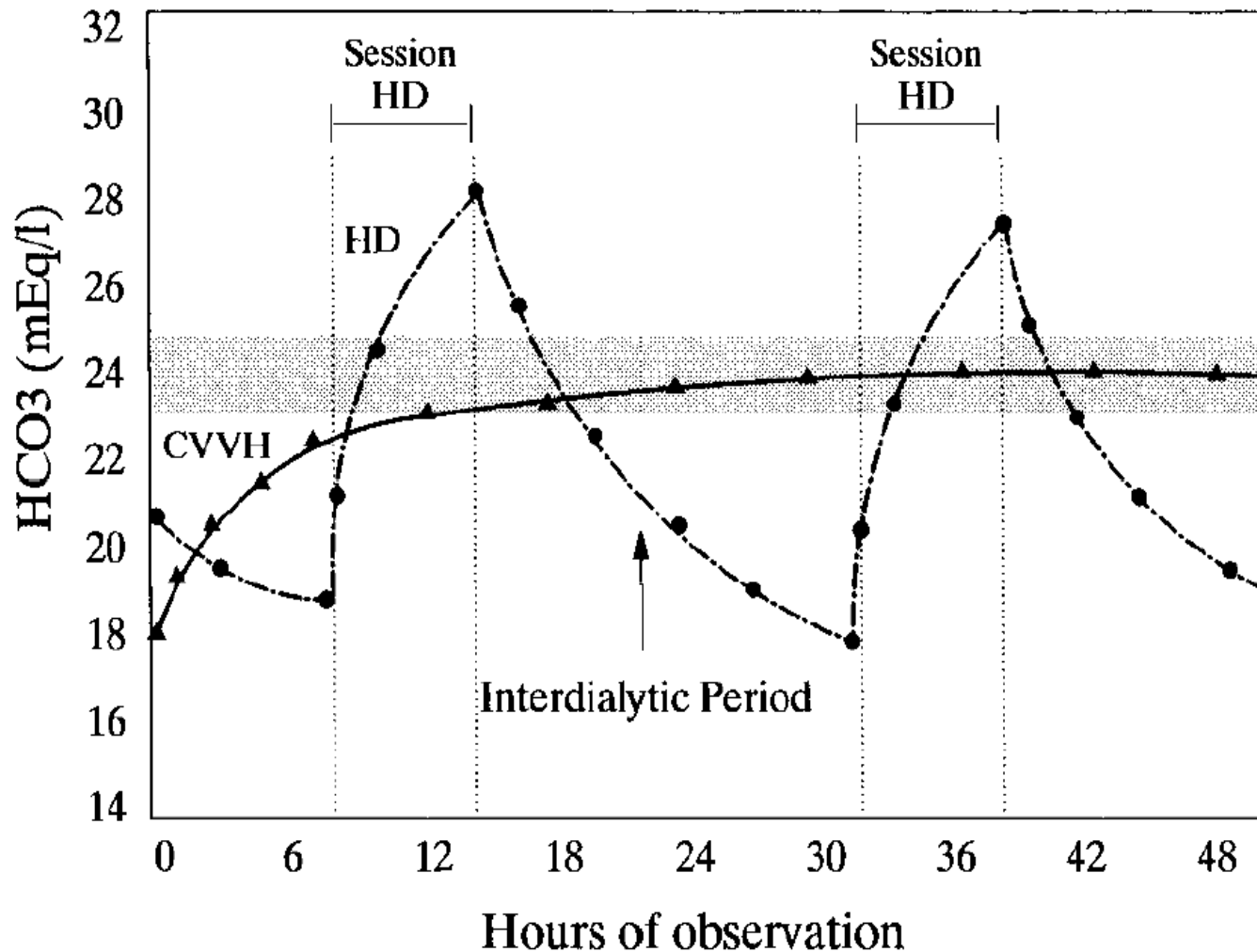
slow extended daily dialysis (SLEDD)

- prolonged, daily haemodialysis
- suitable for most patients

continuous therapies (CRRT)

- mostly haemofiltration
- suitable for all patients

iHD vs. CRRT: No “Saw Tooth”

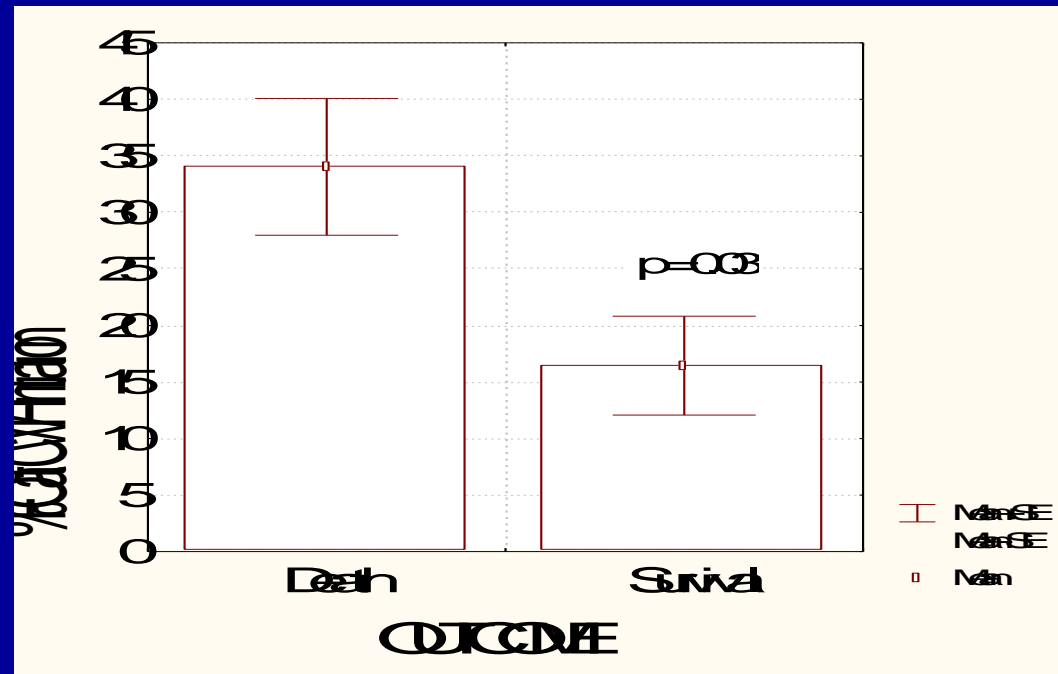


CRRT and Outcome in Children

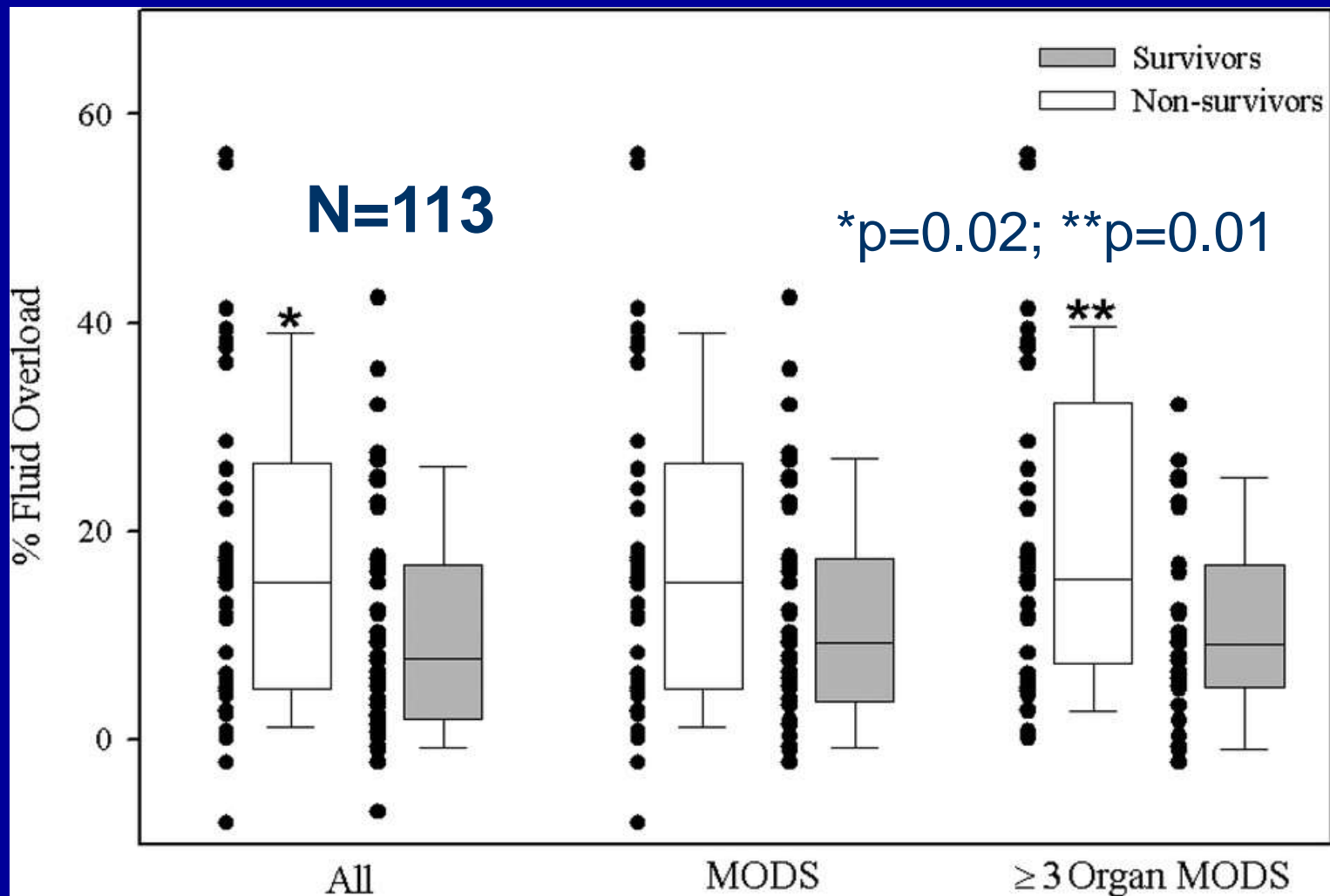
- 22 pt (12 male/10 female) received 23 courses (3028 hrs) of CVVH (n=10) or CVVHD (n=12) over study period.
- Overall survival was 41% (9/22).
- Survival in septic patients was 45% (5/11).
- PRISM scores at ICU admission and CVVH initiation were 13.5 +/- 5.7 and 15.7 +/- 9.0, respectively (p=NS).
- Conditions leading to CVVH (D)
 - Sepsis (11)
 - Cardiogenic shock (4)
 - Hypovolemic ATN (2)
 - End Stage Heart Disease (2)
 - Hepatic necrosis, viral pneumonia, bowel obstruction and End-Stage Lung Disease (1 each)

CRRT and Outcome in Children

- Lesser % Fluid Overload (FO) at CVVH (D) initiation was associated with improved outcome ($p=0.03$)
- Lesser % FO at CVVH (D) initiation was also associated with improved outcome when sample was adjusted for severity of illness ($p=0.03$; multiple regression analysis)



Fluid Overload as a Risk Factor



Foland et al, *CCM* 2004; 32:1771-1776

OUTCOMES

- Impacting on AKI demands that we optimize therapies
- Predict, prevent, treat immediately
- Technology can help, we wouldn't hold ventilation if the need it---so why does this happen in the case of AKI?
 - ▲ Access?
 - ▲ Fear?
 - ▲ Failure to appreciate the consequences of with-holding therapy?
 - ▲ Knowing when to start? (the great debate)
 - ▲ Knowing what modality to use (availability?)
 - ▲ Available data?

Thanks