Pediatric CRRT
The Basics

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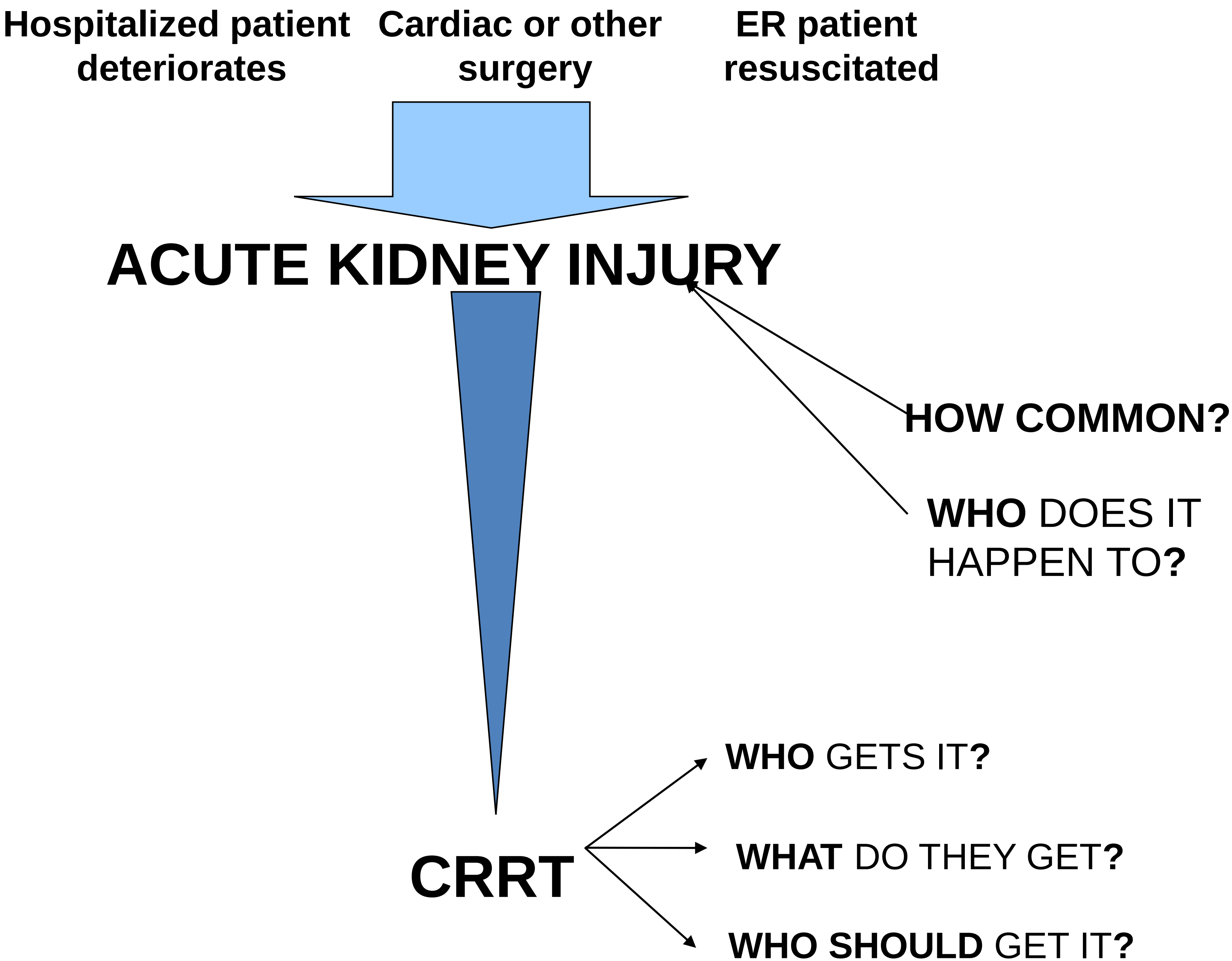
17th International CRRT Conference
San Diego 2012

Epidemiology Of and Indications For Pediatric CRRT



Hospitalized patient deteriorates
Cardiac or other surgery
ER patient resuscitated
ACUTE KIDNEY INJURY
HOW COMMON?
WHO DOES IT HAPPEN TO?
CRRT
WHO GETS IT?
WHAT DO THEY GET?
WHO SHOULD GET IT?

Pediatric AKI: Definition

Pediatric RIFLE (pRIFLE)

Ackan-Arikan et al, Kidney International, 2007

Table 6 | Pediatric-modified RIFLE (pRIFLE) criteria

	Estimated CCl	Urine output
Risk	eCCl decrease by 25%	< 0.5 ml/kg/h for 8 h
Injury	eCCl decrease by 50%	< 0.5 ml/kg/h for 16 h
Failure	eCCl decrease by 75% or eCCl < 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)	

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

Acute Kidney Injury Network

Mehta et al, Crit Care Med, 2007

Table 1

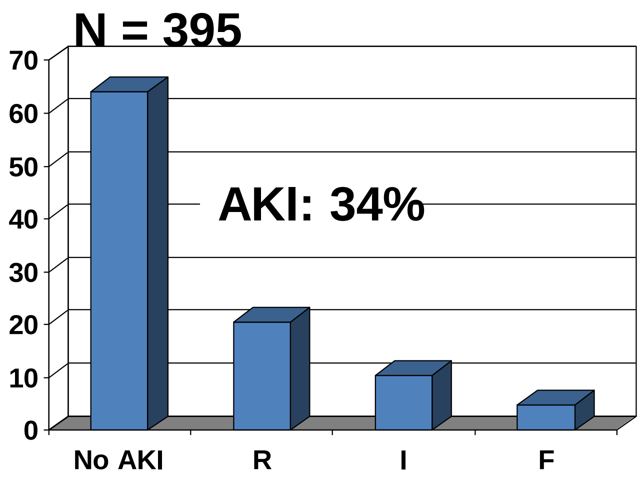
Definition and classification/staging system for acute kidney injury (AKI)*.

AKI stage	Creatinine criteria	Urine output criteria
AKI stage I	Increase of serum creatinine by ≥ 0.3 mg/dl (≥ 26.4 μmol/L) or increase to ≥ 150% – 200% from baseline	Urine output < 0.5 ml/kg/hour for > 6 hours
AKI stage II	Increase of serum creatinine to > 200% – 300% from baseline	Urine output < 0.5 ml/kg/hour for > 12 hours
AKI stage III	Increase of serum creatinine to > 300% from baseline or serum creatinine ≥ 4.0 mg/dl (≥ 354 μmol/L) after a rise of at least 44 μmol/L or treatment with renal replacement therapy	Urine output < 0.3 ml/kg/hour for > 24 hours or anuria for 12 hours

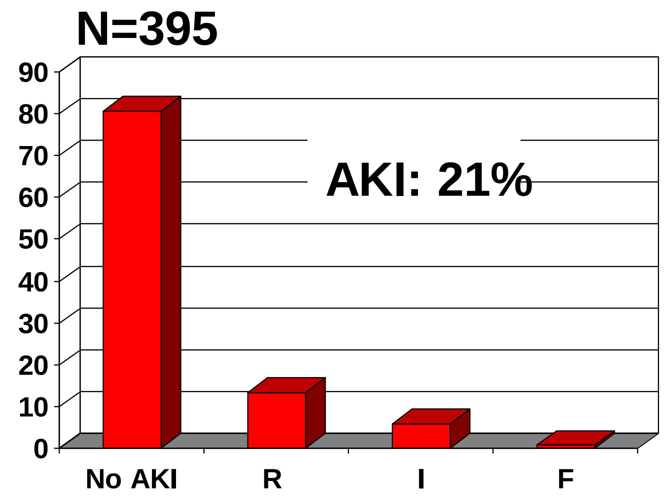
Diagnostic criteria for AKI includes an abrupt (within 48 hours) reduction in kidney function defined as an absolute increase in serum creatinine of either 0.3 mg/dl or more (≥ 26.4 μmol/L) or a percentage increase of 50% or more (1.5 fold from baseline) or a reduction in urine output.
*according to Mehta and colleagues [3]

Pediatric AKI: Incidence in PICU Population & Definition-dependent

- Cardiac Surgery



Kidney Int. 2009 Oct;76(8):885-92



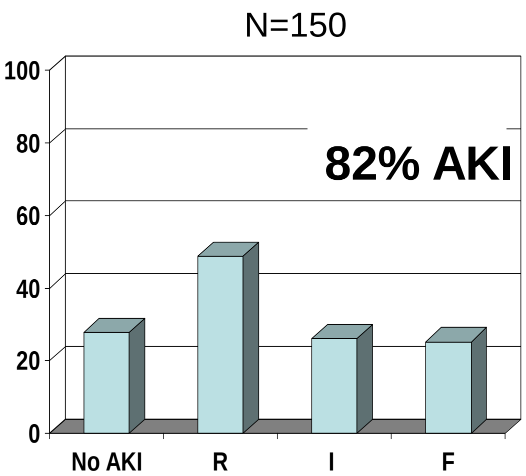
Anesth Analg 2009;109:45–52
(Aprotinin study)

Renal replacement therapy: 1 to 10% - CRRT not very common

Pediatric AKI: Incidence in PICU Population & Definition-dependent

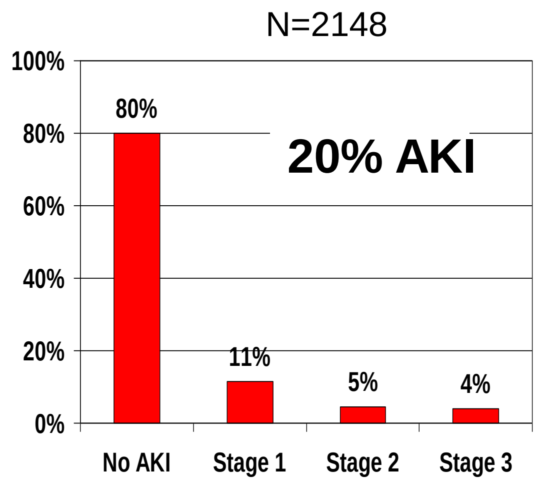
- General PICU

<u>Vasopressors+Ventilated + Catheter</u>



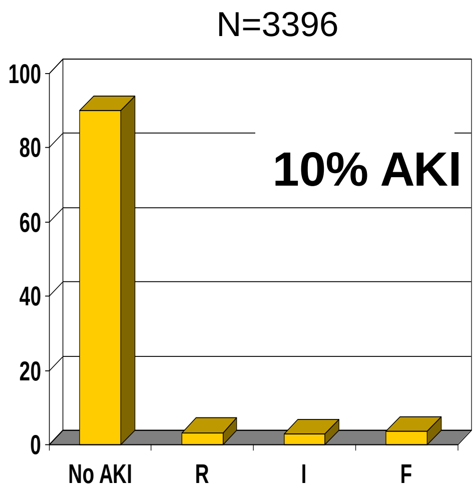
Ackan-Arikan et al, Kid Int 2007; 71: 1028-35

<u>All PICU stay>12hr</u>



Al-Kandari/Eddington, Crit Care, 2011

<u>All PICU admissions</u>



Schneider, Crit Care Med, 2010

Renal replacement therapy: 1 to 9% -- some receive CRRT

CRRT Diagnoses
Mostly secondary renal disease

USA

Table 5. Principal diagnoses and survival[a]

Parameter	n	Survivors	% Survival
Sepsis	81	48	59
Bone marrow transplant	55	25	45
Cardiac disease/transplant	41	21	51
Renal disease	32	27	84
Liver disease/transplant	29	9	31
Malignancy (no tumor lysis syndrome)	29	14	48
Ischemia/shock	19	13	68
Inborn error of metabolism	15	11	73
Drug intoxication	13	13	100
Tumor lysis syndrome	12	10	83
Pulmonary disease/transplant	11	5	45
Other	7	5	71

[a] P (χ^2) < 0.001.

Clin J Am Soc Nephrol 2: 732–738, 2007

USA

Table 2 Primary underlying diagnosis

Diagnosis	Admissions	Survivors (%)	Median % FO (range)
All diagnoses	76	42 (55.3%)	12.9 (0-66.4)
Primary renal disease	15	10 (66.7%)	4.6 (0-60.4)
Secondary renal disease	61	32 (52.5%)	16.7 (0-66.4)
Sepsis without underlying condition	9	6 (66.7%)	21.8 (4.2-41.2)
Oncology patients (including TLS)	17	13 (76.5%)	7.4 (0.2-64)
Oncology patients (not including TLS)	6	3 (50%)	21.5 (7.4-64)
TLS	11	10 (90.1%)	2.9 (0.2-10)
BMT recipient	12	2 (16.7%)	25.1 (8.5-65.6)
Cardiac	7	2 (28.5%)	28.2 (0-66.4)
Liver	5	2 (40%)	22.5 (5-34)
Other[a]	11	7 (63.6%)	12.9 (1-54.1)

[a] Central nervous system, n = 3; diabetic ketoacidosis, n = 2; metabolic, n = 2; s/p gastrointestinal surgery, n = 2; rhabdomyolysis, n = 1; burns, n = 1.

Journal of Critical Care (2009) **24**, 394–400

Other – Spain: Much more in cardiac patients. *Santiago et al, Int Care Med, 2010*

Severe AKI tends to occur EARLY in PICU admission

RRT Options

- Hemodialysis, Peritoneal Dialysis, CRRT
  - Patient Characteristics
    - Disease/Symptoms
    - Hemodynamic stability
  - Goals of therapy
    - Fluid removal
    - Electrolyte correction
    - Both
  - Availability, expertise and cost

Pediatr Nephrol (2009) 24:37–48

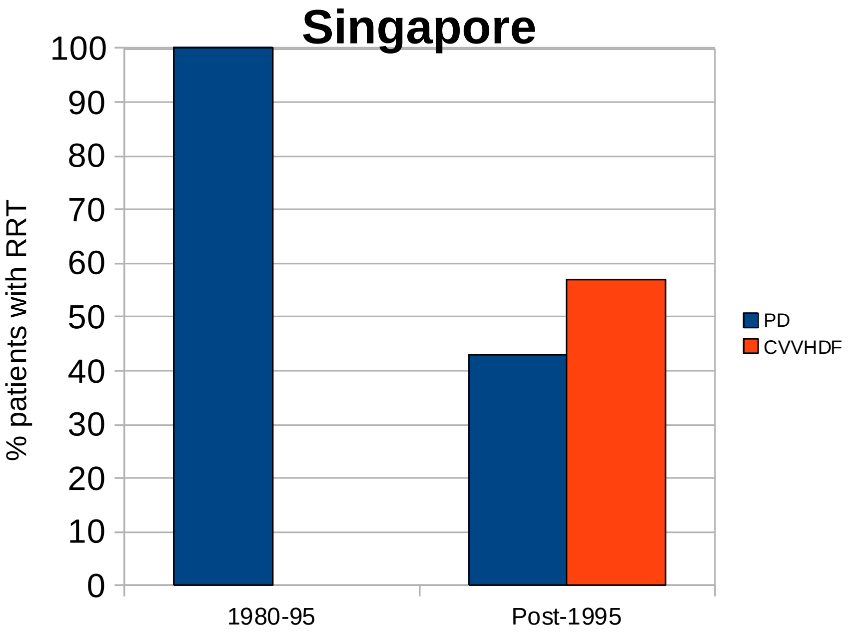
Strazdins et al, Pediatr Nephrol, 2004

RRT Options

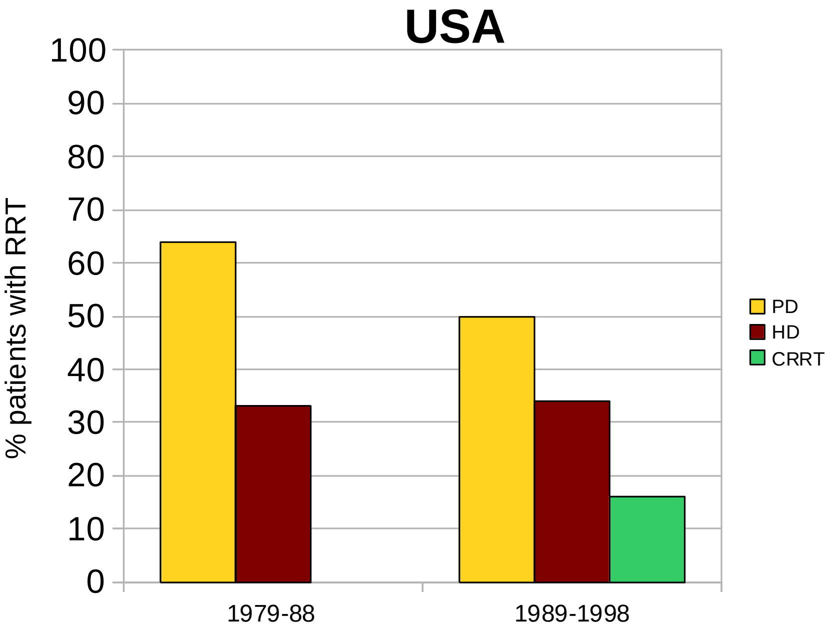
Modality	Advantages	Disadvantages
Acute Hemodialysis	Short treatment	Vascular access necessary
	Accurate UF	Hemodynamic instability
		Heparin
Peritoneal Dialysis	No vascular access	Less efficient
	Minimal equipment	Variable UF
	Minimal training	
	Feasible small infants	
	Continuous	
Continuous renal replacement therapy	Accurate UF, continuous alterations	Vascular access
	Smaller circuit volumes	
	Citrate anticoagulation	

Trends in Pediatric RRT

- CRRT use may be increasing in North America *(Warady & Bunchman, Pediatr Nephrol, 2000)*
- European guidelines *(Strazdins et al, Pediatr Nephrol, 2004)*



Gong et al, Ped Neph, 2001



Williams et al, Arch Ped Adol Med, 2002

Why CRRT?

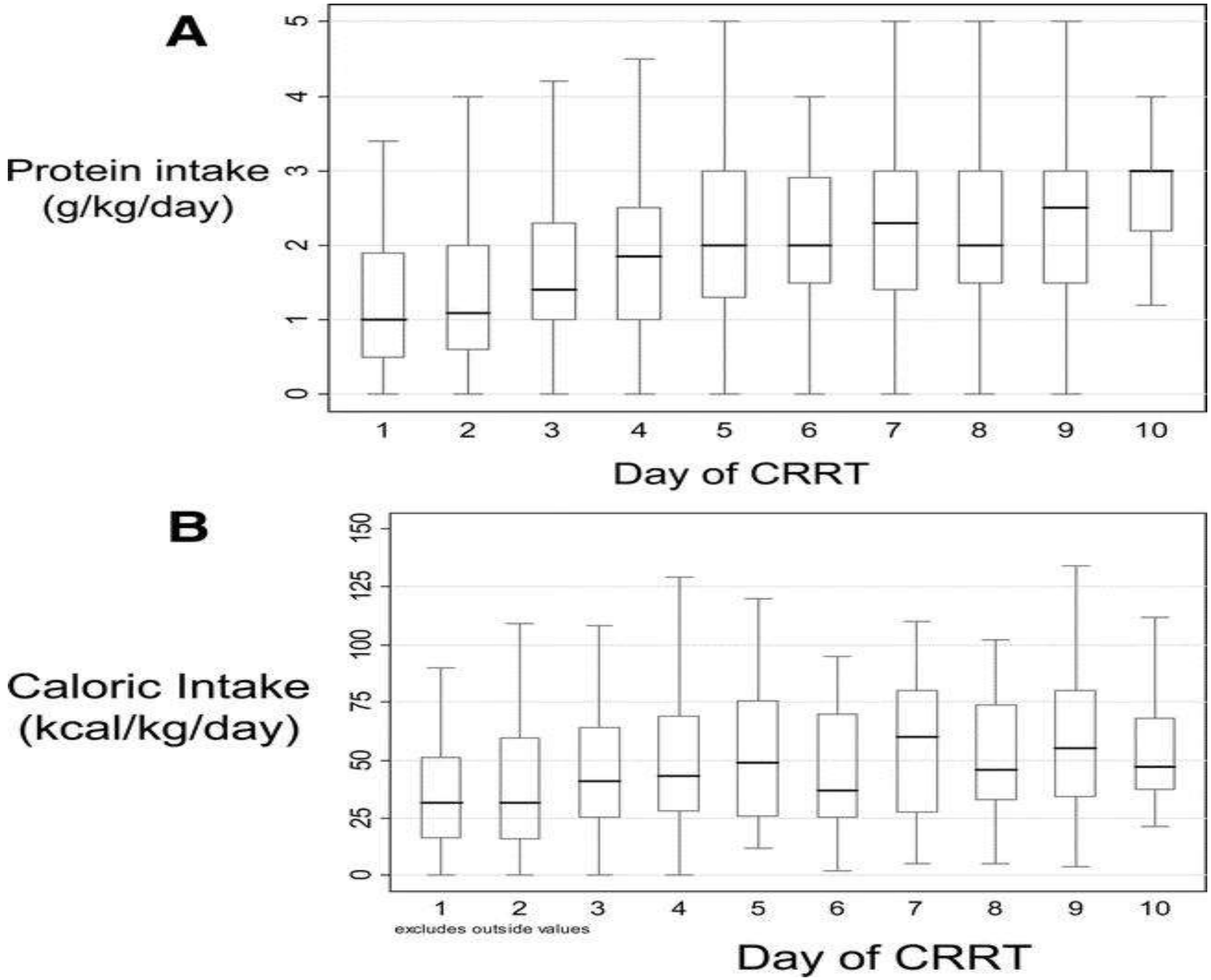
- Deals well with hemodynamic instability
  - Precise Volume control/immediately adaptable
  - Effective control of uremia, hypophosphatemia, hyperkalemia,

  acid base balance

Management of sepsis/plasma cytokine filter

Allows for improved provision of nutritional support

NUTRITION



Zappitelli et all, Crit Care Med, 2008

Indications for Pediatric RRT

- Electrolyte (metabolic) imbalance
- Uremia with bleeding and or encephalopathy
- Acuity/Degree of Kidney Injury
  - reduction in GFR/elevated creatinine
  - reduction in urine output
- Nutritional support
- Intoxications, Inborn errors of Metabolism (IEM)
- Fluid Overload

Table 4. Indications for CRRT and survival[a]

Indication	*n*	Survivors	% Survival
Fluid overload and electrolyte imbalance	157	80	51
Fluid overload only	100	61	61
Electrolyte imbalance only	44	30	68
Prevent fluid overload to allow intake	11	7	64
Other	32	23	72

Clin J Am Soc Nephrol 2: 732–738, 2007

Fluid Overload

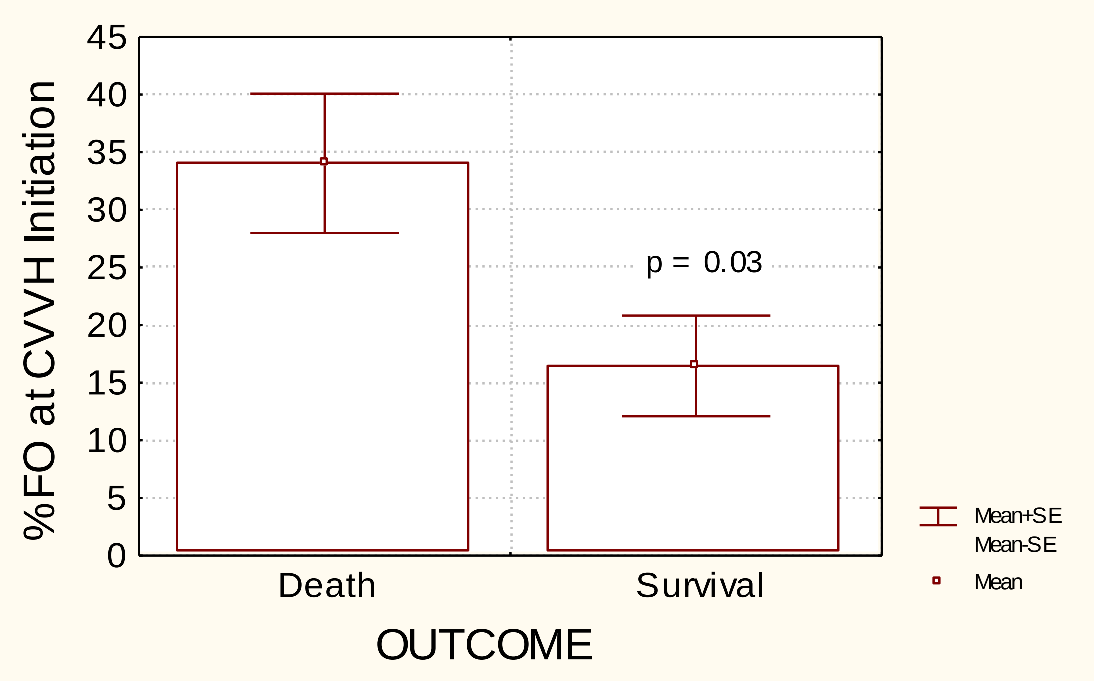
(Total fluid in – Total out)/ weight X 100 = FO %: *Goldstein et al, Pediatrics*

Change in weight: *Selewski et al, Intens Care Med, 2011*

Outcome in Children Receiving Continuous Venovenous Hemofiltration

Stuart L. Goldstein, MD*; Helen Currier, RN, CNN‡; Jeanine M. Graf, MD§; Carmen C. Cosio, MD§; Eileen D. Brewer, MD*; and Ramesh Sachdeva, MD§

Pediatrics 2001;107;1309-1312



Foland et al,Crit Care Med, 2009

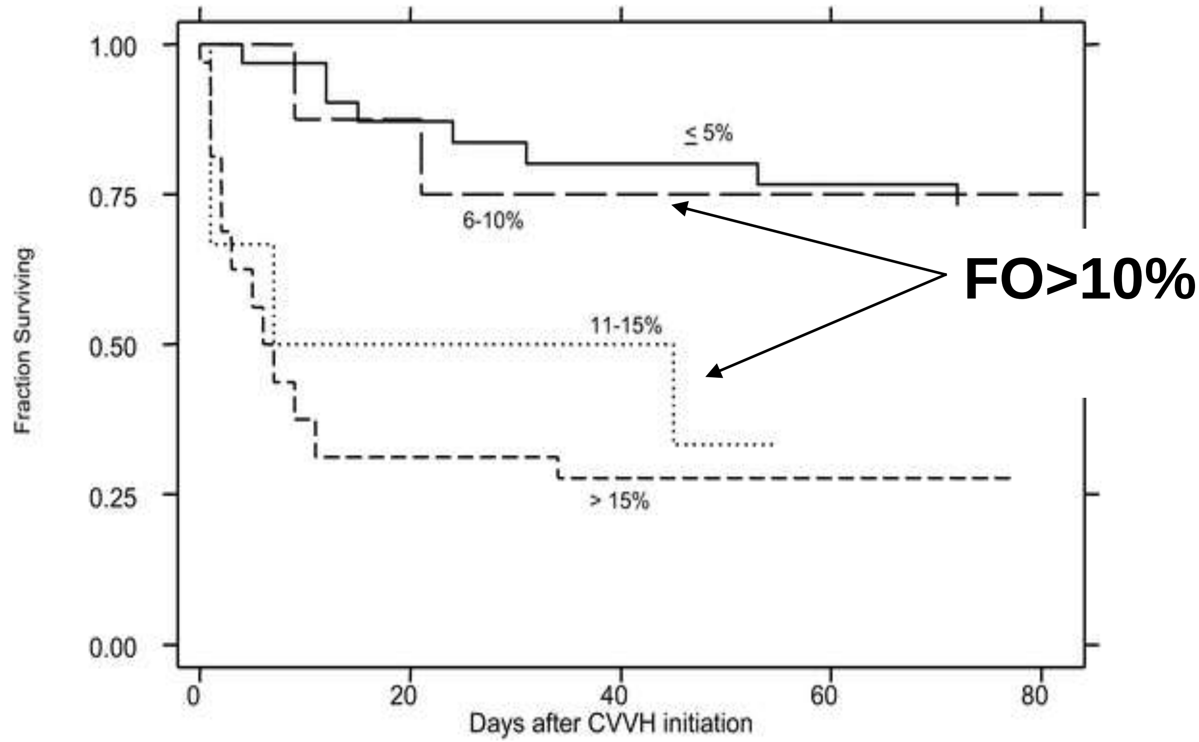
Hayes et al, J Crit Care, 2009

Selewski et al, Int Care Med, 2011

MV analysis: FO – mortality association independent of illness severity

How much is too much?

Gillespie et al, Pediatr Nephrol, 2004



Hayes et al, J Crit Care, 2009

Table 3 Predictors of survival in all patients

Variable	Survivors, n = 42	Nonsurvivors, n = 34	Odds ratio	95% CI	*P* value
>20% FO	8 (19.1%)	20 (58.8%)	6.1	(2.2-17.0)	.0006
Sepsis	13 (31%)	29 (85.3%)	12.9	(4.1-41.0)	.0001
MODS	29 (69%)	34 (100%)	[a]	[a]	.0003

[a] Unable to calculate odds ratio because 100% of nonsurvivors had MODS.

Prospective Pediatric CRRT Registry

Critically ill children + CRRT: FO% predicts mortality

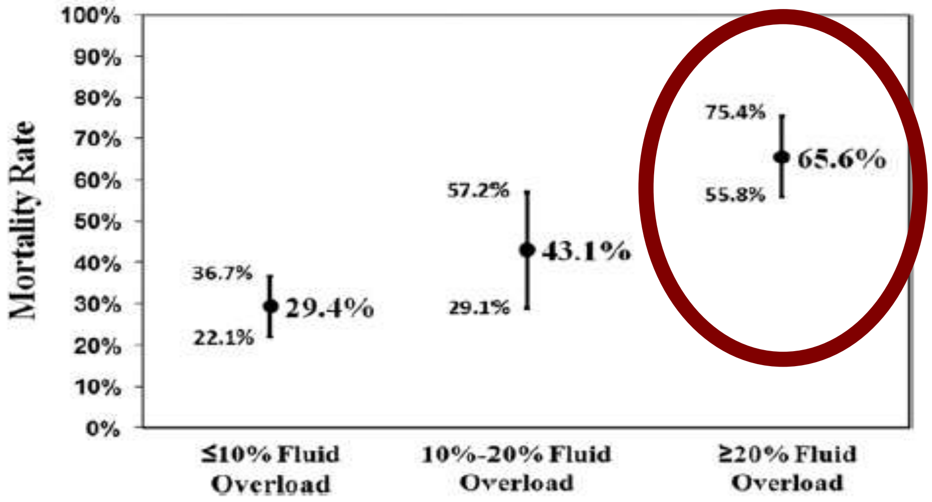


Figure 1. Mortality rates of pediatric intensive care unit patients receiving continuous renal replacement therapy subdivided by degree of fluid overload. Error bars represent 95% confidence intervals for the mortality rate in each fluid overload group. There was a statistically significant difference in mortality among the 3 groups. Patients with ≥ 20% fluid overload had significantly higher mortality than patients with < 10% fluid overload and those with 10%-20% fluid overload. Patients with 10%-20% fluid overload had a trend toward increased mortality compared with patients with < 10% fluid overload; however, this trend did not reach statistical significance ($P = 0.07$).

Sutherland et al, AJKD, 2010

CRRT for FO

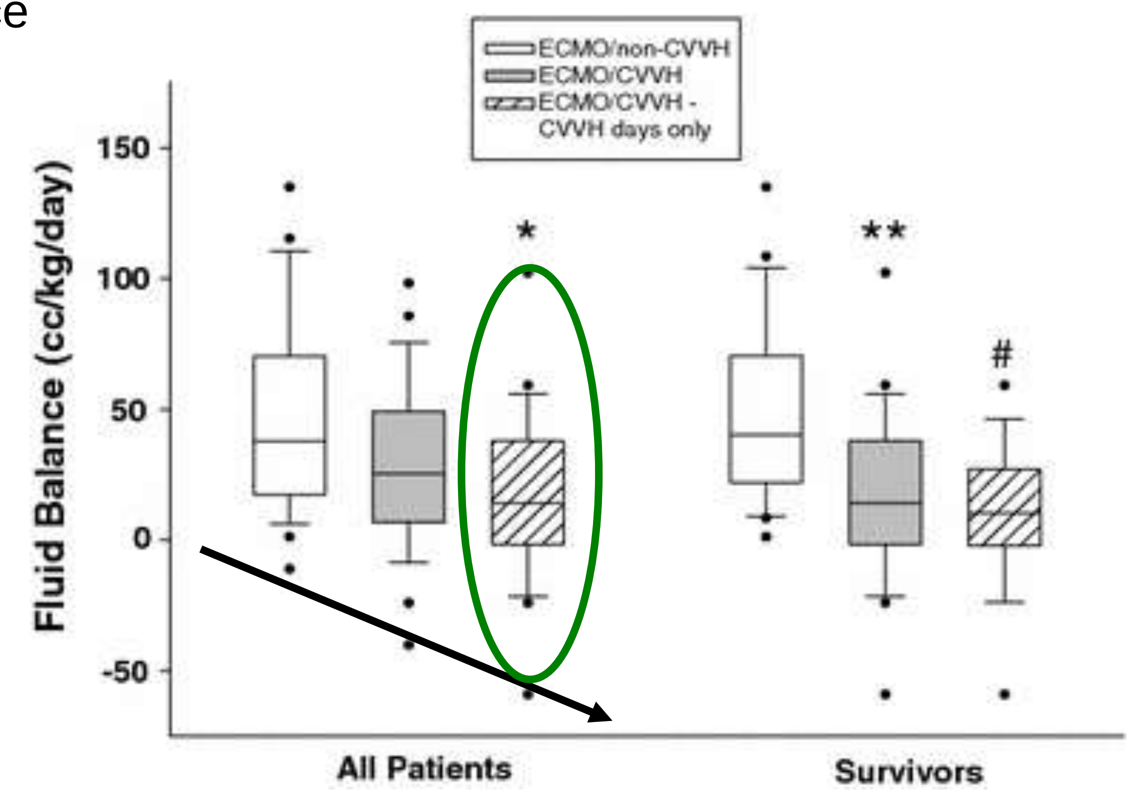
Pediatric Stem Cell Transplant with Acute Lung Injury

Within 24-48 hours of CRRT initiation:

Elbahlawan et al, Pediatr Blood Cancer, 2010

- Better oxygenation (PaO2/FiO2)
- More negative fluid balance

Hoover et al, Intens Care Med, 2008



Timing of Pediatric RRT

???????????????

Will depend on the patient, the individual physician and the place.

Considerations

Emerging importance of fluid overload prevention.

Children develop MODS and severe AKI **early** in ICU course

Children die with MODS very early in ICU course

Feasible in children

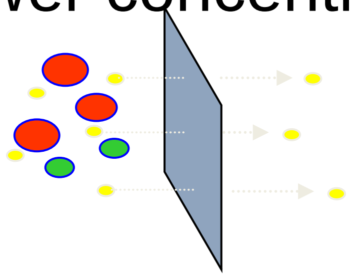
Summary: Pediatric CRRT Epidemiology and Indications

- Pediatric AKI may be more common than previously described
- Primary renal disease giving way to MODS
- CRRT for children continues to expand
  - Advantageous in critically ill child
  - Effective
  - Useful in setting of volume overload
  - Best time to start remains uncertain

CRRT Terminology and Modalities

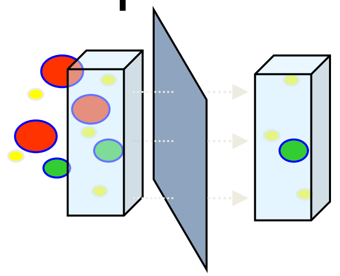
Diffusion vs. Convection

Diffusion is solute transport across a semi-permeable membrane - molecules move from an area of higher to an area of lower concentration



Small molecules diffuse more readily than large molecules

Convection is a process where solutes pass across the semi-permeable membrane along with the solvent in response to a positive transmembrane pressure

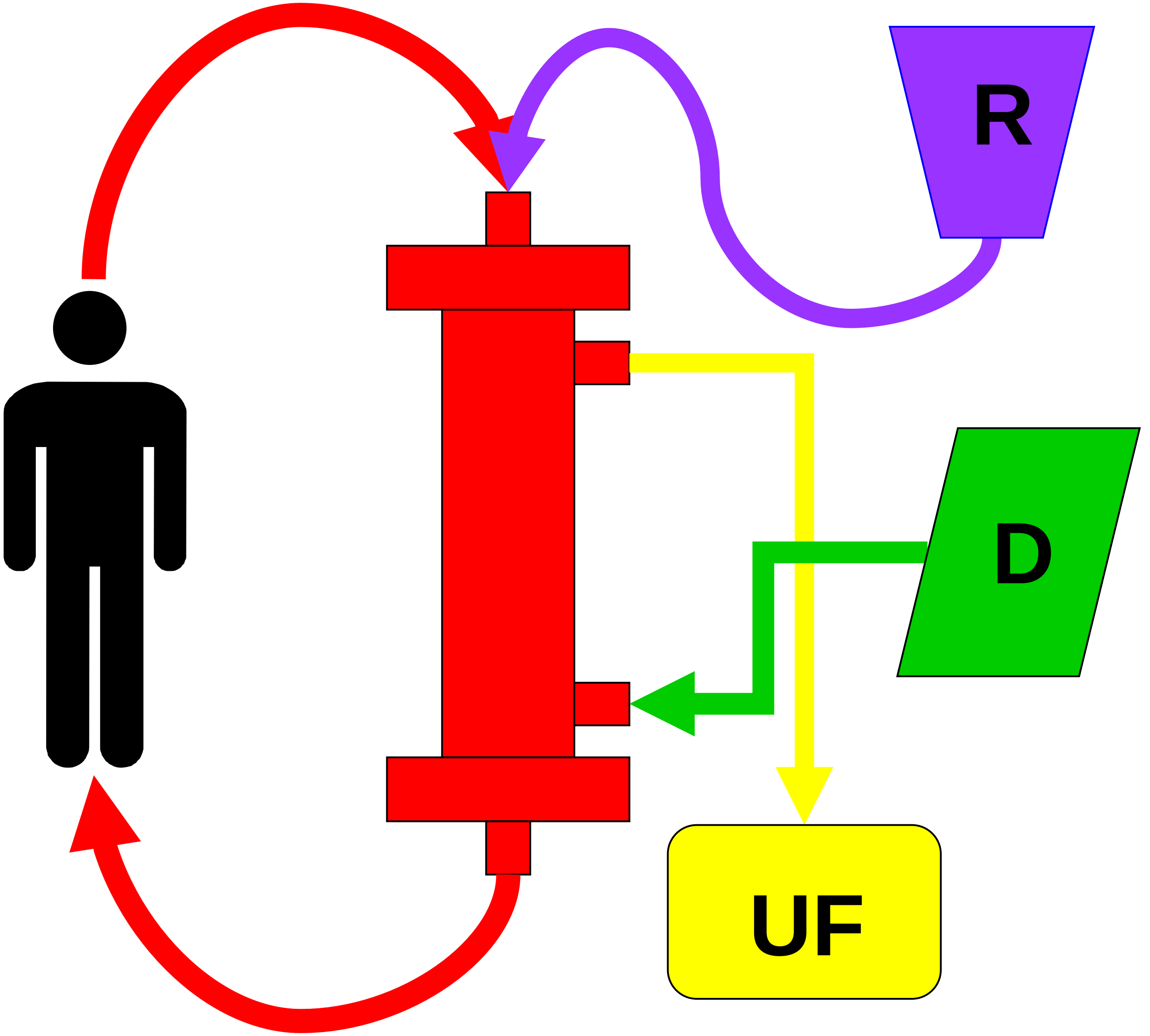


Small and large molecules convect equally well; limit is membrane cut-off

Current Nomenclature for CRRT

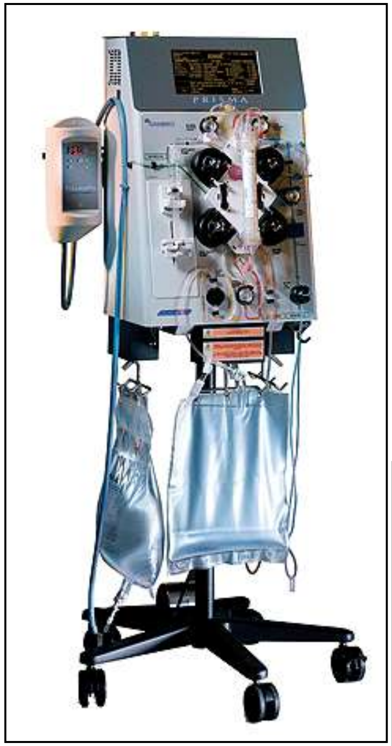
SCUF:	Slow Continuous Ultrafiltration
CVVH:	Continuous Veno-Venous Hemofiltration
CVVHD:	Continuous Veno-Venous Hemodialysis
CVVHDF:	Continuous Veno-Venous Hemodiafiltration

CRRT Schematic



- SCUF
- CVVH
- CVVHD
- CVVHDF

CRRT Machines



Prescribing Pediatric CRRT

Prescribing Pediatric CRRT

- Vascular access
- Hemofilter
- Prime
- Blood pump speed (Q_B)
- Anticoagulation
- Ultrafiltration rate
- Infused fluids
  - CVVH: Pre- and/or post-dilutional replacement
  - CVVHD: Counter-current dialysate
  - CVVHDF: Dialysate and replacement fluid

Hemofilter for CRRT

- Hemofilter size
  - Volume, porosity
- Membrane material
  - Polysulfone, AN-69, PAES, etc.
- Tubing set – integrated or separate?
- “Open” vs. “closed” systems – do you have a choice?

Priming the Circuit for Pediatric CRRT

- Blood
  - Small patient, large extracorporeal volume
- Albumin
  - Hemodynamic instability
- Saline
  - Common default approach
- Self
  - Volume loaded renal failure patient

Choosing Q_B for Pediatric CRRT

- Equation for blood flow rate (Q_B):
  - 3-5ml/kg/min
- Choose from a table:
  - 0-10 kg: 25-50ml/min
  - 11-20kg: 80-100ml/min
  - 21-50kg: 100-150ml/min
  - >50kg: 150-180ml/min
- CRRT device may affect choices for Q_B

The real determinant – <u>the vascular access</u>

Ultrafiltration in Pediatric CRRT

- Choose UF rate to
  - balance input
  - remove excess fluid over time
  - “make room” for IV fluids and nutrition
  - provide solute clearance by convection
- SCUF, CVVHD, post-dilution CVVH: UF rate may be limited by blood flow (filtration fraction)
- Pre-dilution CVVH: High flow of pre-dilution fluid lessens hemoconcentration
- Remember to consider UF limits of the filter, especially in higher-volume hemofiltration

Ultrafiltration Rates

- No study has identified effective, safe UF rates in children
- For HEMODIALYSIS– NET UF rate of 0.2ml/kg/min is tolerated
  - This extrapolates to 1 ml/kg/ hr (NET UF) over 48 hr of continuous hemofiltration

Donckerwolke –Ped Neph 8:103-106,1994

Infused Fluids for Pediatric CRRT

- SCUF: No infused fluids
- CVVHD: Counter-current dialysate
- CVVH: Pre- and/or post-dilution replacement fluid
- CVVHDF: Dialysate and replacement fluids

Rate for Infused Fluid

- Higher rates increase clearance
- Lower rates may simplify electrolyte balance and limit protein loss
- Equations to help choose rate for fluid:
  - 20-60 ml/kg/hr
  - 2000-3000 ml/hr/1.73m2
- May need higher rates to balance citrate delivery

Characteristics of the Ideal CRRT Solution

- Physiological
- Reliable
- Inexpensive
- Easy to prepare
- Simple to store
- Quick to the bedside
- Widely available
- Fully compatible

Purpose of CRRT solutions

- Provide safe and consistent metabolic control
- To be adaptive to the choice of therapy- CVVH, CVVHD, CVVHDF

Options for CRRT Solutions

- Peritoneal dialysate: ***NO***
- Pre-made IV solutions: ***MAYBE***
  - Saline, Lactated Ringers
- Custom-made solutions: ***RARELY***
  - Local pharmacy; outsource
- Commercially available CRRT solutions

Prevalence and Consequences of Errors in Solution Preparation

- 16/31 programs reported errors:
  - 7 errors in replacement solutions
  - 9 errors in dialysate solutions
- Consequences of improper solutions
  - 2 deaths
  - 1 non lethal cardiac arrest
  - 6 seizures (hypo/hypernatremia)
  - 7 without complications

Barletta JF et.al Pediatr Nephrol. 2006 Jun;21(6):842-5

What's the Difference Between Dialysate and Replacement Fluid?

U.S. Food and Drug Administration

Department of Health and Human Services

Dialysate is a Device

Replacement Fluid is a Drug

CRRT Solutions – Many Choices

Name	**Company**	**R / D**	**Bag Size***	**Flavors**
Normocarb HF	DSI	R	3.24 L	2
Prismasate	Gambro	D	5 L	6
Accusol	Baxter	D	2.5 L	5
Prismasol	Gambro	R	5 L	7
Duosol	B Braun	D	5 L	6
PureFlow	NxStage	D	5	5

**after mixing*

Summary: Prescribing Pediatric CRRT

- All modalities (SCUF, CVVH, CVVHD, CVVHDF) are available for treating critically ill children
- Newer solutions make CRRT safer for children as they do for adults
- Devices and equipment are adapted for kids
- Special consideration for flow rates, based on
  – Vascular access

Vascular Access and Anticoagulation for Pediatric CRRT

Why

- Access function is crucial for therapy
- Flows obtained will affect adequacy of blood flow for dose delivered and can affect filter-circuit life
- Downtime from clotted circuits-access is time off therapy

Access Considerations

- Low resistance
  - Resistance ~ $8l\eta/2r^4$
  - So, the biggest and shortest catheter should be best
- Vessel size
  - French ~ 3 x diameter of vessel
  - Beside ultrasound nearly universal
  - SVC is bigger than femoral vein

Access Considerations

- Internal Jugular
  - Very accessible
  - Large caliber (SVC)
  - Great flows
  - Low recirculation rate
  - Risk for Pneumothorax
  - Cardiac monitoring may take precedence.
- Femoral
  - Usually accessible
  - Smaller than SVC
  - Flows may be diminished by:
    - Abdominal Pressures
    - Patient movement
  - Risk for retroperitoneal hemorrhage
  - Higher recirculation rate

•Subclavian: Many feel current double lumen vas cath are too stiff to make the turn into the SVC and I don't personally use them. Although they are used in some centers.

•Better for bigger kids likely

Cincinnati Children's Hospital Center for Acute Care Nephrology
Acute Dialysis/CRRT/Pheresis Access Guideline

1. Provide optimal access for acute dialysis/CRRT/Pheresis to maximize blood flow while minimizing vessel trauma
2. Site – Internal jugular vein preferred, femoral vein second option

Patient size	Catheter size	Special
Neonates	7 French	Triple lumen is available for $CaCl_2$ if providing citrate regional anticoagulation
3-6 kg	7 French	Triple lumen is available for $CaCl_2$ if providing citrate regional anticoagulation
6-12 kg	8 French	
12-20 kg	9 French	
20-30 kg	10 French	
30+ kg	10 French or 11 French	Triple lumen 11.5 Fr **should always** be used for $CaCl_2$ if providing citrate regional anticoagulation

The International Journal of Artificial Organs / Vol. 30 / no. 12, 2007 / pp. 1116-1121

Artificial Kidney and Dialysis/Pediatrics

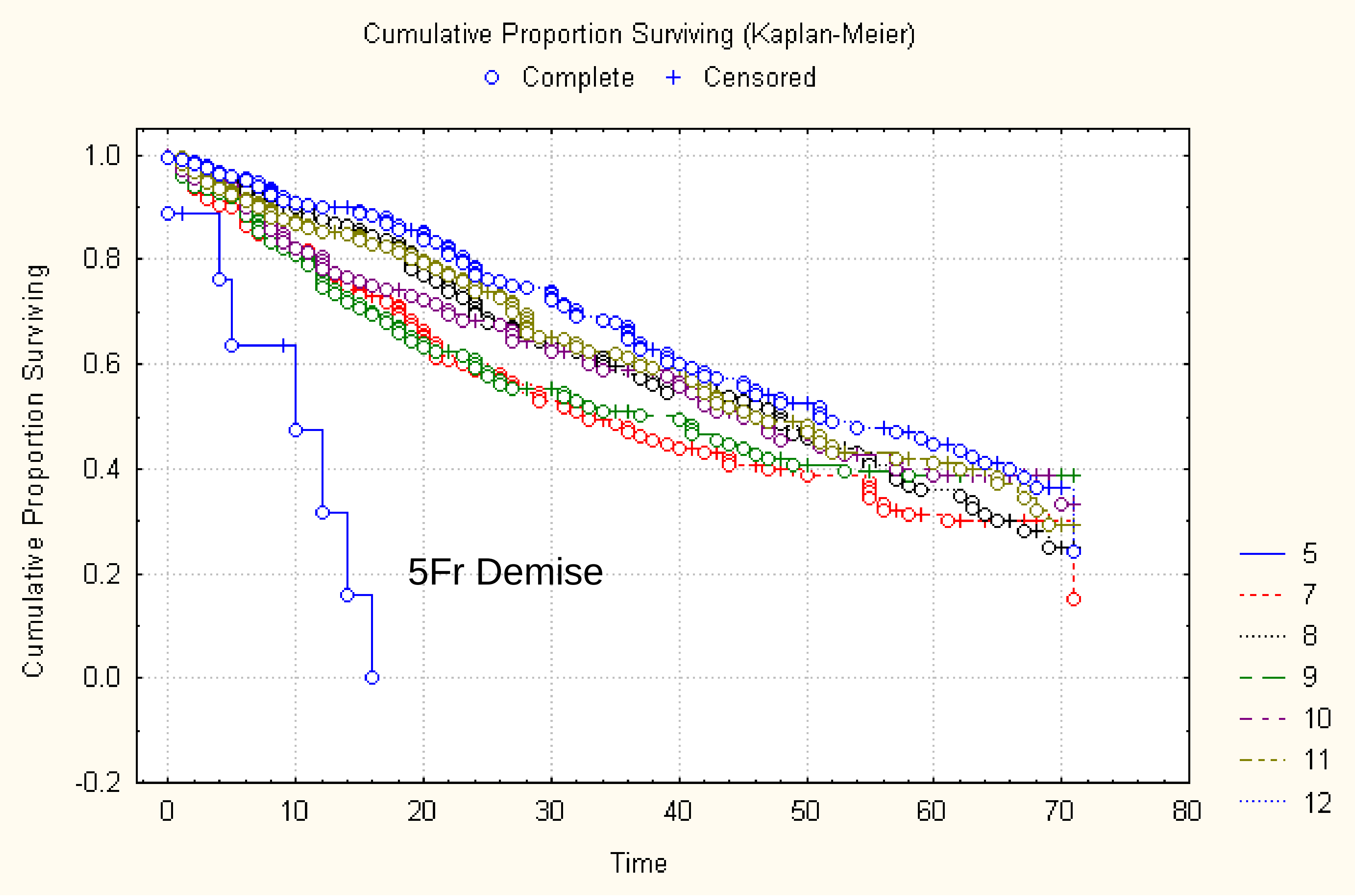
The effect of vascular access location and size on circuit survival in pediatric continuous renal replacement therapy: A report from the PPCRRT registry

R. HACKBARTH[1], T. E. BUNCHMAN[1], A. N. CHUA[2], M. J. SOMERS[3], M. A. BAUM[3], J. M. SYMONS[4], P. D. BROPHY[5], D. BLOWEY[6], J. D. FORTENBERRY[7], D. CHAND[8], F. X. FLORES[9], S. R. ALEXANDER[10], J. D. MAHAN[11], K. D. MCBRYDE[12], M. R. BENFIELD[13], S. L. GOLDSTEIN[2]

- 376 Patients
- 1574 circuits

- Femoral 69%
- IJ 16%
- Sub-Clavian 8%
- Not Specified 7%

Circuit Survival Curves by French Size of Catheter



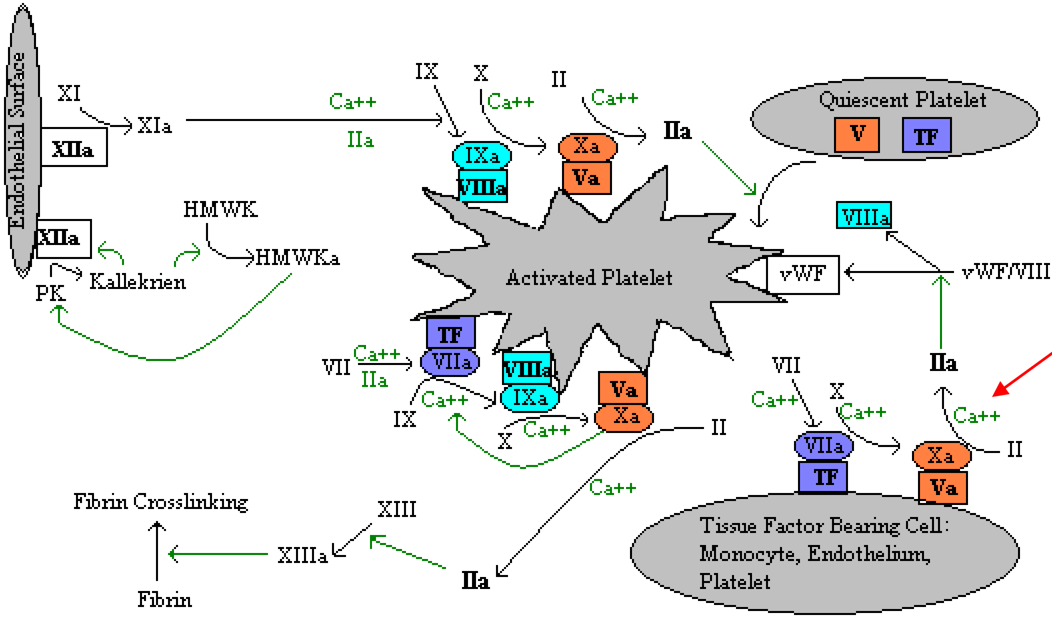
Hackbarth R et al: *IJAIO* December 2007

Summary: Vascular Access for Pediatric CRRT

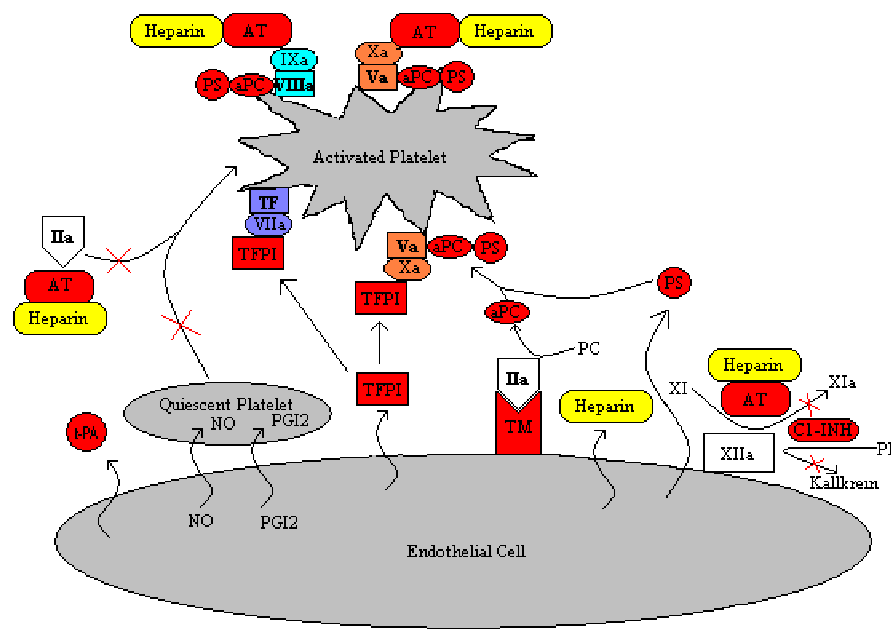
- Put in the largest and shortest catheter when possible
  - Caveat: short femoral catheters have been shown to have high rate of recirc in adult patients. (Little et al. AJKD 2000;36:1135-9)
- The IJ site is preferable (over femoral) when clinical situation allows
- Avoid 5Fr Catheters

Anticoagulation

- Another crucial step in delivering the prescribed dose (reducing downtime)
- Critically ill patients are at risk for both increased and decreased clot formation simultaneously



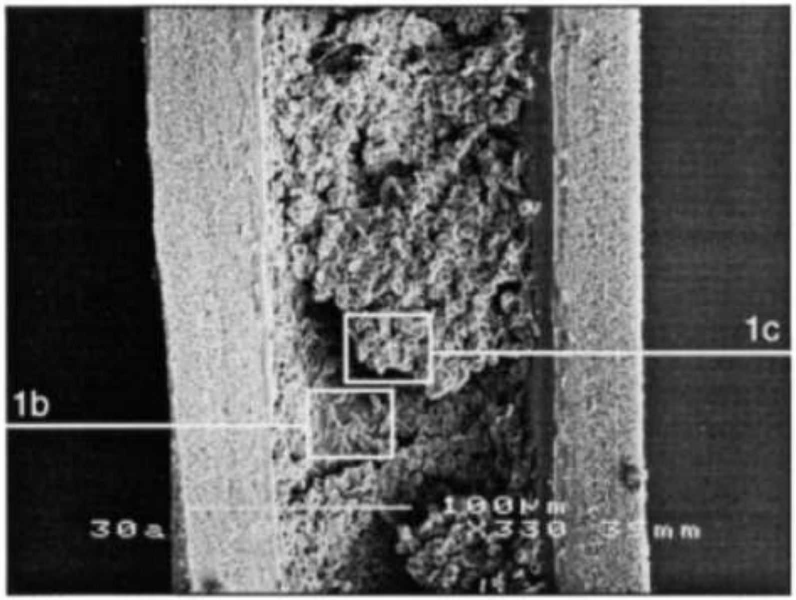
Calcium is necessary for each event in the cascade.



Heparin acts in conjunction with ATIII on thrombin and F IX, FX, FXII

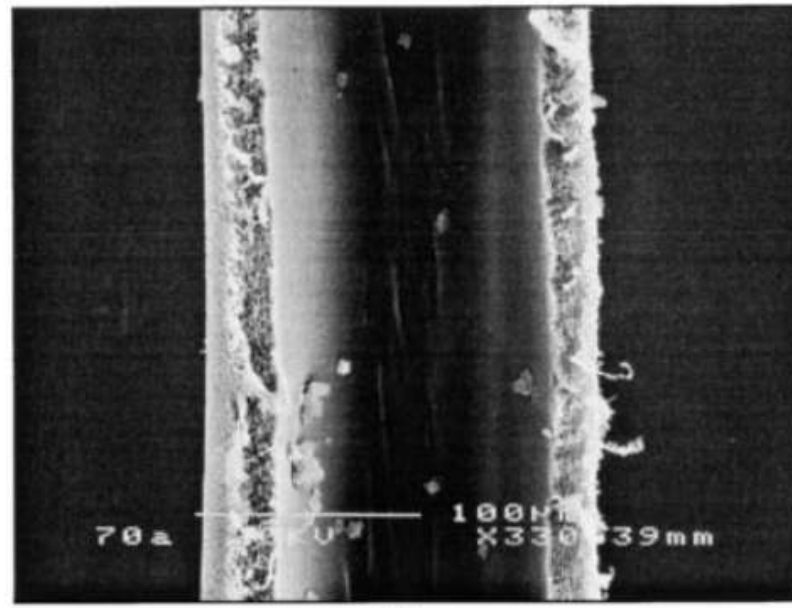
What the filter looks like

Hofbauer R et al. Kid Int 1999;56:1578-83



1a

Heparin



3b

Citrate

Electron microscopy of polysulfone hemodiafilter with two varieties of anticoagualtion during IHD. Granted, no monitoring of degree of anticoagulation was performed to assess adequacy of response.

Anticoagulation

- Systemic Heparin
  - Goal ACT 180-240 sec
  - Patient anticoagulated
    - Risk of bleeding
  - Risk for HIT
- Regional Citrate
  - Goal Circuit iCal 0.3-0.4mmol/L
  - Goal Patient iCal 1.1-1.4 mmol/L
  - Risk for
    - Hypocalcemia
    - Alkalosis
    - Hypernatremia

Nephrol Dial Transplant (2005) 20: 1416–1421
doi:10.1093/ndt/gfh817
Advance Access publication 26 April 2005

Original Article

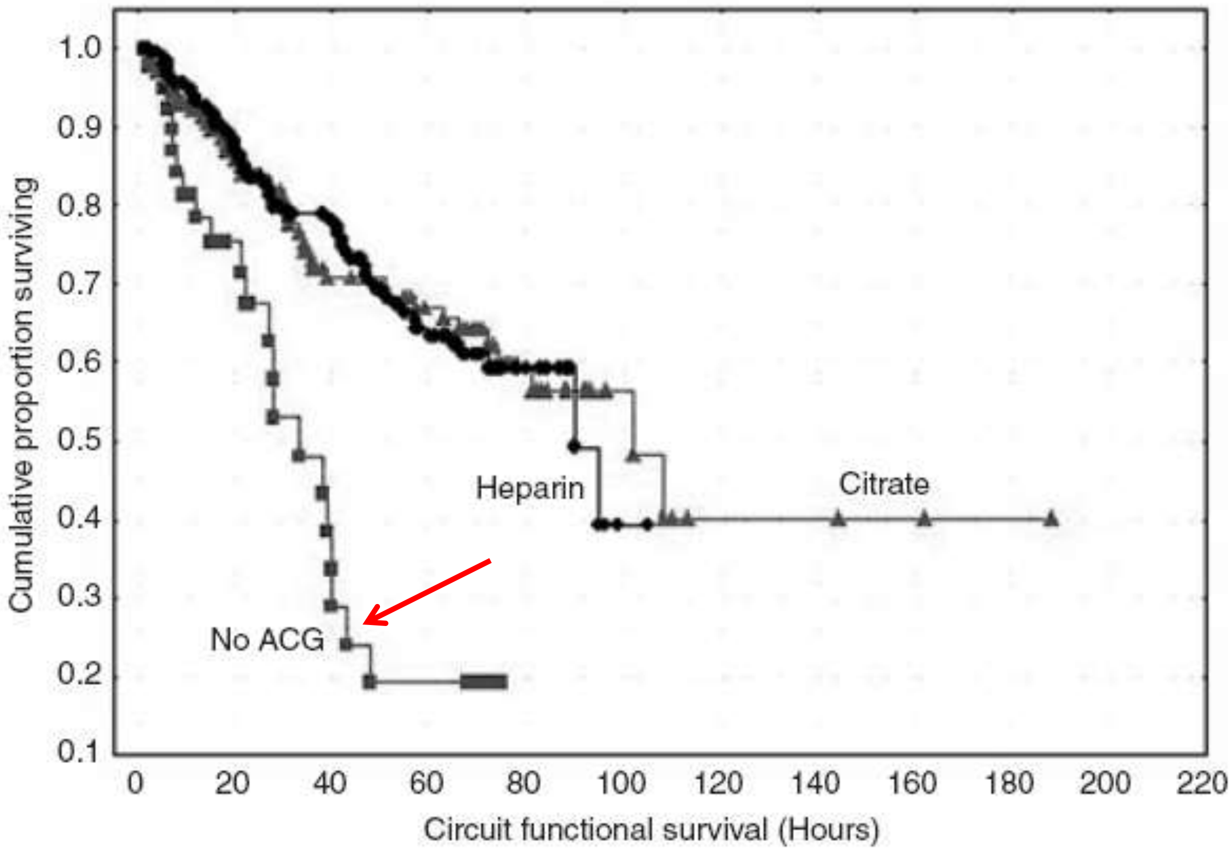
Nephrology Dialysis Transplantation

Multi-centre evaluation of anticoagulation in patients receiving continuous renal replacement therapy (CRRT)

Patrick D. Brophy[1], Michael J. G. Somers[2], Michelle A. Baum[2], Jordan M. Symons[3], Nancy McAfee[3], James D. Fortenberry[4], Kristine Rogers[4], Joni Barnett[5], Douglas Blowey[6], Cheryl Baker[7], Timothy E. Bunchman[8] and Stuart L. Goldstein[7]

- 138 Patients in multicenter registry study
  - 442 Circuits
- Circuit survival time evaluated for three anticoagulation strategies
  - Heparin (52% of circuits)
  - Regional Citrate (36% of circuits)
  - No anticoagulation (12% of circuits)

Brophy PD et al. Nephrol Dial Transplant. 2005;20:1416-21



- Mean circuit survival (42 and 44 hr) were not different for Hep vs Citrate, but both longer than no anticoagulation (27 hr)
- At 60 hr, 69% of Hep and Citrate circuits were functional, but only 28% of the no-anticoagulation circuits
- In this analysis circuit survival was not affected by the access size
- Citrate group had no bleeding complications, 9 Heparin patients with bleeding

Citrate Specific Issues

- Alkalosis
  - 1 mmol Citrate to 3 mmol HCO3
  - Normocarb protocols may exacerbate (35 mEq/L)
- Hypernatremia
  - Tri-Sodium Citrate infusion
- Hypocalcemic Citrate Toxicity
  - Incomplete clearance of citrate, usually due to liver dysfunction
  - Rising total calcium, decreasing iCal

Summary: Anticoagulation for Pediatric CRRT

- Heparin or Citrate is better than no anticoagulation (even in liver failure, DIC, etc)
- Citrate has fewer bleeding complications
- Circuit survival means less downtime hence more delivered therapy
- Pick institutional strategy and learn to use it well
- Consider citrate as the method of choice

Demographics and Outcomes

Demographics

- Provision of CRRT to children requires care of a disparate population

- Prospective Pediatric CRRT Registry (ppCRRT)
  - 344 children from 13 US centers
  - Age range from newborn to 25 years of age
  - Weight range from 1.3kg to 160kg
  - Numerous underlying diseases states
  - Multiple organ systems affected

Symons JM, et. al. (2007) Demographic Characteristics of Pediatric Continuous Renal Replacement Therapy: A Report of the Prospective Pediatric Continuous Renal Replacement Therapy Registry. Clin J Am

Demographics
Which children receive CRRT?

- Mostly critically ill children with AKI and fluid overload

- ppCRRT data
  - 2/3 of kids were receiving vasopressor support
  - 1/2 of patients were receiving diuretics

- Outcome highly dependent on underlying disease and severity of illness

Demographics
Underlying Disease

ppCRRT Registry Cohort (n=344)		
Primary Diagnosis	**Patients**	
Sepsis	81	**23.5%**
Stem Cell Transplant	55	**16.0%**
Cardiac Disease/Transplant	41	**11.9%**
Renal Disease	32	**9.3%**
Liver Disease/Transplant	29	**8.4%**
Malignancy (w/o tumor lysis)	29	**8.4%**
Ischemia/shock	19	**5.5%**
Inborn Error of Metabolism	15	**4.4%**
Drug Intoxication	13	**3.8%**
Tumor Lysis Syndrome	12	**3.5%**
Pulmonary Disease/Transplant	11	**3.2%**
Other	7	**2.0%**

Isolated Renal Disease Uncommon

Majority have systemic disease

Most common diagnoses
- Sepsis (23.5%)
- Oncologic (27.9%)

Symons JM, et. al. (2007) Demographic Characteristics of Pediatric Continuous Renal Replacement Therapy: A Report of the Prospective Pediatric Continuous Renal Replacement Therapy Registry. Clin J Am Soc Nephrol 2:732-738

Outcomes
General Survival Rates

Study	Age	Pt. #	Survival	Associated with Increased Mortality
Bunchman et. al. (2001)	6.2y	106	40%	Vasopressor use, non-renal diagnosis
Goldstein, et. al. (2001)	8.8y	22	43%	Greater FO
Gillespie (2004)	5.1y	77	50%	Greater FO
Foland et. al. (2004)	9.6y	113	61%	MODS, Greater FO
ppCRRT -*Symons et. al. (2007)* -*Sutherland et. al. (2010)*	8.5y	344	58%	Oncologic disease, MODS, Greater FO,
Hayes, et. al. (2009)	5.8y	76	55%	Sepsis, MODS, Greater FO

Survival rate has improved over time from **40-45%** to **55-60%**

Underlying disease, comorbidities, risk factors determine mortality

Outcomes
Question 1

- Does underlying or primary disease matter?
  - Yes
  - No

- What diseases are associated with worse outcomes?

Outcomes
Risk Factors

Variable	**Odds Ratio (Mortality)**	**95% Confidence Interval**	**p-value**
Fluid Overload Group			
≥20% FO vs. <10% FO	21.1	5.2 – 85.7	*<0.001*
≥20% FO vs. 10%-20% FO	11.2	1.8 – 68.4	*0.009*
10%-20% FO vs. <10% FO	1.9	0.33 – 10.8	*0.48*
Oncologic Diagnosis	5.8	2.5 – 13.9	<0.001
Diagnosis of MODS	3.7	1.4 – 9.9	0.008
Sepsis Diagnosis	3.6	1.3 – 9.8	0.01
Convective CRRT Modality	0.49	0.28 – 0.86	0.01
PRISM II PICU Admission	1.04	1.0 – 1.1	0.07
IEM/Intoxication Diagnosis	3.4	0.75 – 15.2	0.11
Inotrope Number	1.2	0.9 – 1.6	0.17
CRRT Initiated to treat FO	1.5	0.66 – 3.4	0.34
Age at CRRT Initiation	1.01	0.97 – 1.05	0.63
Sex	0.96	0.55 – 1.7	0.88

Sutherland SM et. al. (2010) Fluid overload and mortality in children receiving continuous renal replacement therapy: the prospective pediatric continuous renal replacement therapy registry. Am J Kidney Dis 55:316-325

Outcomes

Risk Factors: Oncologic Illness

- 51 patients in ppCRRT w/ stem cell transplant
- 45% survival

- Improved survival w/ convective modality (univariate analysis)

76% also had MODS
Mean FO was over 12%

Flores FX, et. al. (2008) Continuous renal replacement therapy (CRRT) after stem cell transplantation. A report from the prospective pediatric CRRT Registry Group. Pediatr Nephrol Apr 23(4):625-30.

Outcomes
Risk Factors: MODS

- Critically ill kids w/ multi-organ dysfunction syndrome from ppCRRT Registry
- n = 116
- Survival 51.7%
- Causes of AKI necessitating CRRT
  - Sepsis (39.2%)
  - Cardiogenic shock (20%)
- Fluid overload higher in non-survivors (again)

Goldstein SL, et. al. (2005) Pediatric patients with multi-organ dysfunction syndrome receiving continuous renal replacement therapy. Kidney International. 67:653-658.

Outcomes
Underlying Disease

ppCRRT Registry Cohort (n=344)	
Primary Diagnosis	**Survival**
Liver Disease/Transplant	**31%**
Pulmonary Disease/Transplant	**45%**
Stem Cell Transplant	**45%**
Malignancy (w/o tumor lysis)	**48%**
Cardiac Disease/Transplant	**51%**
Sepsis	**59%**
Ischemia/shock	**68%**
Inborn Error of Metabolism	**73%**
Renal Disease	**84%**
Tumor Lysis Syndrome	**83%**
Drug Intoxication	**100%**
Other	**71%**

Symons JM, et. al. (2007) Demographic Characteristics of Pediatric Continuous Renal Replacement Therapy: A Report of the Prospective Pediatric Continuous Renal Replacement Therapy Registry. Clin J Am [illegible]

Outcomes
Question 2

- Does fluid overload matter?
  - Yes
  - No

Outcomes
Risk Factors

Variable	Odds Ratio (Mortality)	95% Confidence Interval	p-value
Fluid Overload Group			
≥20% FO vs. <10% FO	21.1	5.2 – 85.7	*<0.001*
≥20% FO vs. 10%-20% FO	11.2	1.8 – 68.4	*0.009*
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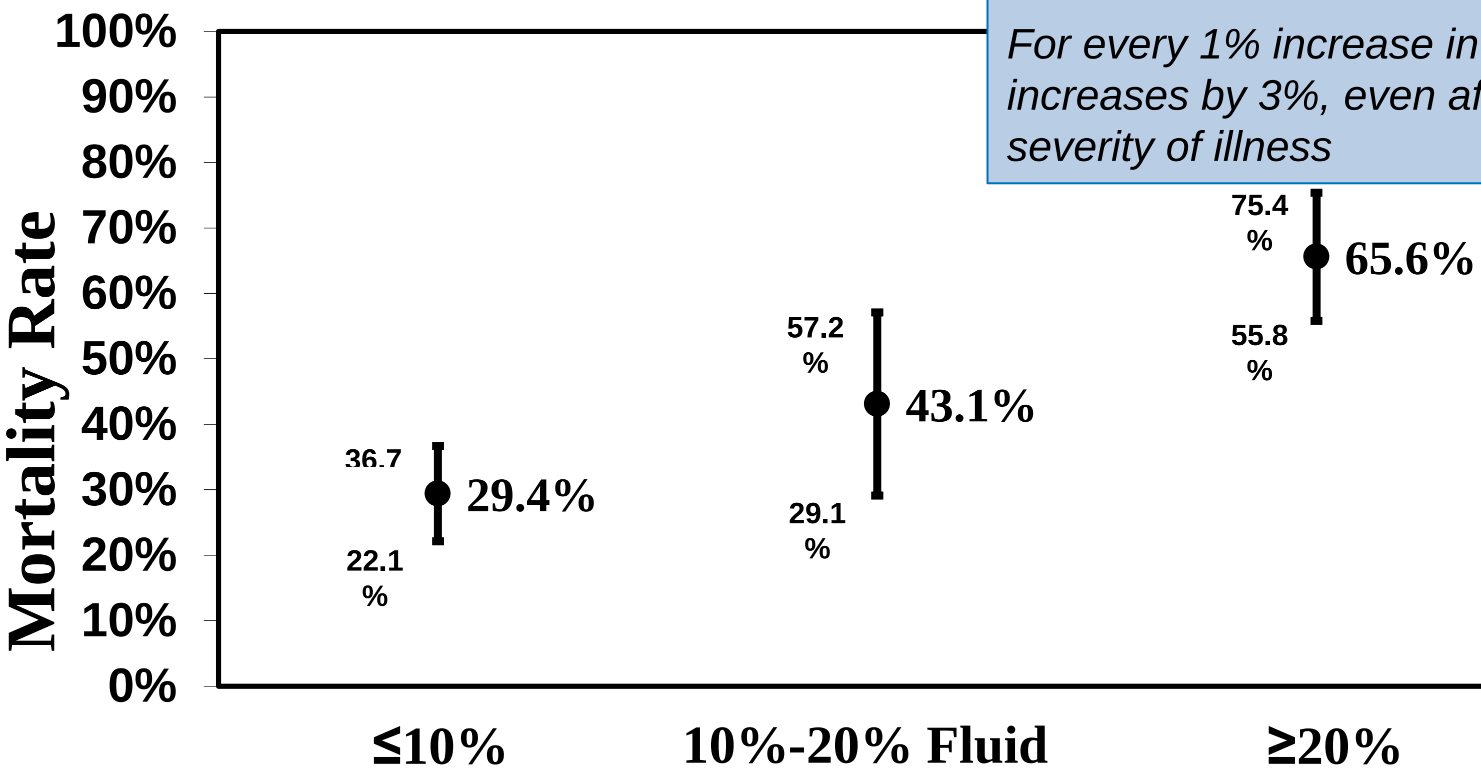
Sutherland SM et. al. (2010) Fluid overload and mortality in children receiving continuous renal replacement therapy: the prospective pediatric continuous renal replacement therapy registry. Am J Kidney Dis 55:316-325

Outcomes

Risk Factors: Fluid Overload

If treated as a continuous variable, odds ratio for FO is 1.03

For every 1% increase in FO, mortality increases by 3%, even after adjusting for severity of illness



Sutherland SM et. al. (2010) Fluid overload and mortality in children receiving continuous renal replacement therapy: the prospective pediatric continuous renal replacement therapy registry. Am J Kidney Dis 55:316-325

Outcomes
Question 3

- Are long term outcomes good or bad?
  - Yes
  - No
  - Nobody Knows

Outcomes
ECMO and CRRT

- Retrospective, single center analysis of ECMO data base
  - 154/378 patients received ECMO and CRRT
  - 68/154 survived to hospital discharge
  - 65/68 (96%) RECOVERED RENAL FUNCTION AND DID NOT REQUIRE RRT AT DISCHARGE

- 3/68 who required RRT at discharge all had primary renal disease

Paden , M., et al. (2010) Recovery of renal function and survival after continuous renal replacement therapy during extracorporeal membrane oxygenation. *Pediatric Critical Care Medicine. epub May 6*

Outcomes
Long term outcomes AKI #1

- Original study of 245 inpatients with AKI
- 174 kids survived to hospital discharge and had long term data available
  - Survival amongst these kids was ~ 80% (139/174)
  - Of these deaths, ~ 70% occurred in the first 12mo
- At 3-5 years post hospital discharge
  - Renal survival ~ 90%
  - WORSE in those with primary renal disease (69% vs. 96%)
  - 60% of patients (n=29) had either microalbuminuria, hyperfiltration, reduced GFR, or hypertension

Askenazi DJ, et al. (2006) 3-5 year longitudinal follow-up of pediatric patients after acute renal failure. *Kidney International. epub Jan 69(1):18417-9.*

Outcomes

Long term outcomes AKI #2

- 37 children with AKI (age 1mo to 10y)
- West Bengal and East India
  - AKI due to glomerulonephritis in 46%
  - AKI due to snakebite in 24%
  - AKI due to sepsis in 8%
- Survival 65%
- 1/3 of survivors with long term data had abnormal creatinine, hematuria, proteinuria, or hypertension

- Patients with AKI requiring CRRT are likely to be on the more severe end of the spectrum and likely have greater incidence of long term sequelae

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Sinha R., et al. (2009) Ten-year follow-up of children after acute renal failure from a developing country. *Nephrol Dial Transplant.24:829-833-9.*

Outcomes
Summary

- The majority of patients who receive CRRT are:
  - Critically ill
  - Have multisystem illness (rather than primary renal disease)
  - Have fluid overload

- Outcome hinges on:
  - Underlying disease and cause of AKI
  - Severity of illness
  - Severity of fluid overload
  - Seems to **not** hinge on CRRT dose

Outcomes
Summary

- Overall survival ranges from 45-60%
- Survivors can expect recovery of renal function and RRT independence
  - Unless cause of AKI is a primary renal disease
- Survivors are likely to have long-term sequelae and require long term follow up
  - Hypertension
  - Proteinuria
  - Chronic kidney disease