Pediatric CRRT
The Ins and Outs

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Epidemiology Of and Indications For Pediatric CRRT

ACUTE KIDNEY INJURY

WHAT IS IT**?**

HOW COMMON?

WHO DOES IT HAPPEN TO**?**

CRRT

WHO GETS IT**?**

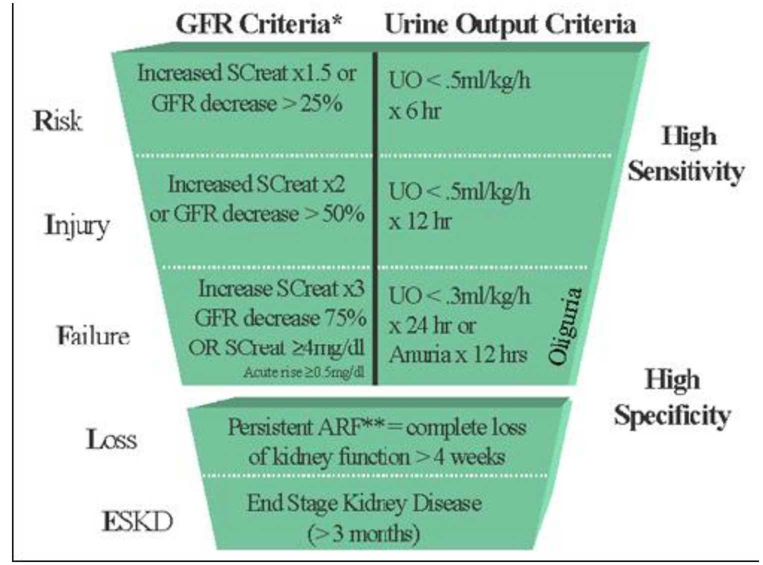
WHAT DO THEY GET**?**

WHO SHOULD GET IT**?**

Pediatric AKI: Definition

Past: So many definitions....

Risk Injury Failure End-Stage Kidney Disease (RIFLE)



Crit Care. 2005; 9(5): 523–527

Pediatric RIFLE (pRIFLE)

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)	

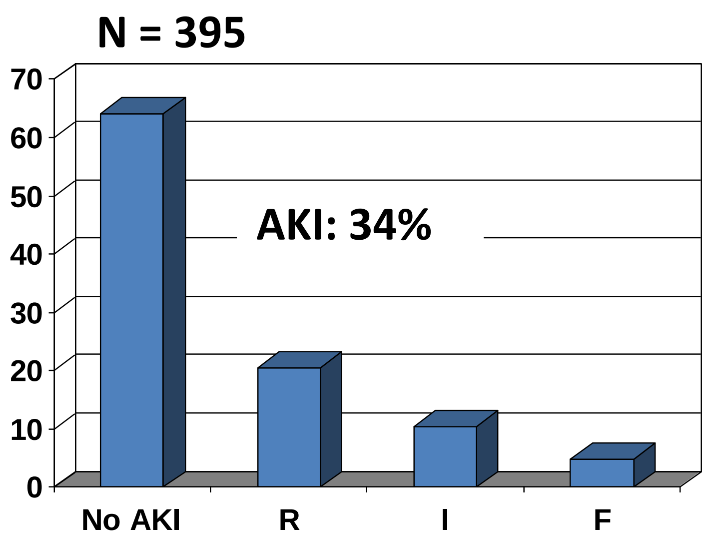
eCCl, estimated creatinine clearance; pRIFLE, pediatric risk, injury, failure, loss and end-stage renal disease.

Kidney International (2007) **71,** 1028–1035.

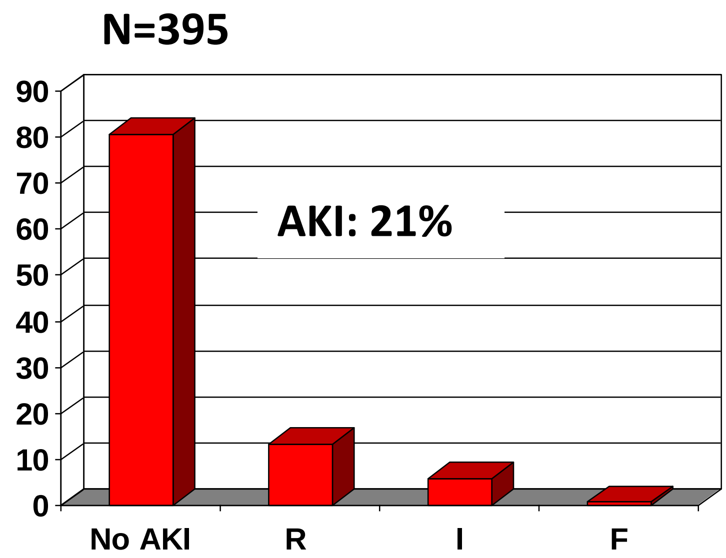
Acute Kidney Injury Network definition

Pediatric AKI: Incidence in PICU Population & Definition-dependent

- Cardiac Surgery



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



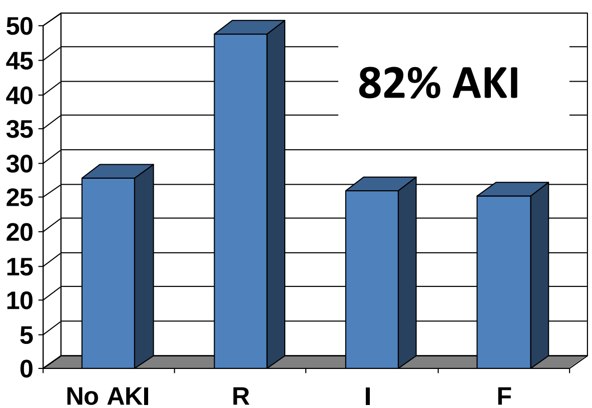
Anesth Analg 2009;109:45–52
(Aprotinin study)

Pediatric AKI: Incidence in PICU Population & Definition-dependent

- General PICU

Most Critically ill children
Vasopressors/Ventilated
Urinary catheter

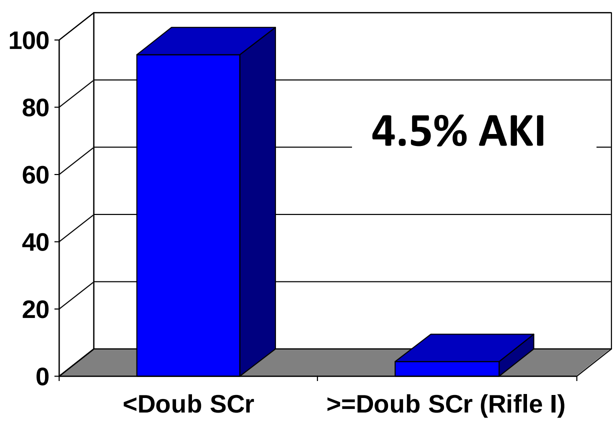
pRIFLE



Kid Int 2007; 71: 1028-35

All PICU
Admx SCr baseline

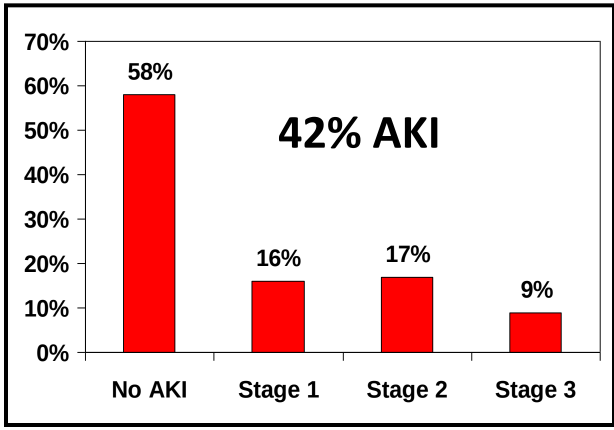
SCr Doubling (pRIFLE I)



Pediatr Crit Care Med 2007; 8:29 –35

All PICU stay>48hrs

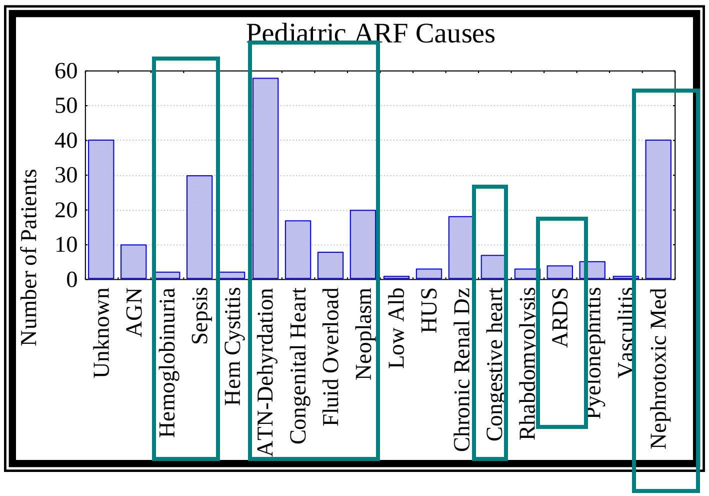
pRIFLE



Al-Kandari et al, ASN, 2008

Pediatric AKI: *Changing Epidemiology*

Previously: Primary renal diseases



Stickle SH et al: Am J Kid Dis 45:96-101, 2005

Table 4. Characteristics and outcome of the acute renal failure (ARF) cases (n = 44)

Etiologies of ARF	
HUS	8 (18.2)
Hematology: oncology pathologies	8 (18.2)
Cardiac surgery	5 (11.4)
Sepsis	4 (9.1)
Trauma	3 (6.8)
Diabetic ketoacidosis	3 (6.8)
Chronic renal failure	3 (6.8)
Others	10 (22.7)

Pediatr Crit Care Med 2007 Vol. 8, No. 1

Table 2 Causes of acute kidney injury

Cause	Numbers and percentages=100
Bone marrow transplantation related	27
Primary renal disease	14
Dehydration	10
Nephrotoxic medication	8
After cardiac surgery	8
Congenital anomalies of the urinary tract	2
Multiple etiologic factors with underlying chronic diseases	31
Total	100

Pediatr Nephrol (2009) 24:1379–1384

CRRT Diagnoses

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]$P(\chi^2) < 0.001$.

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

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

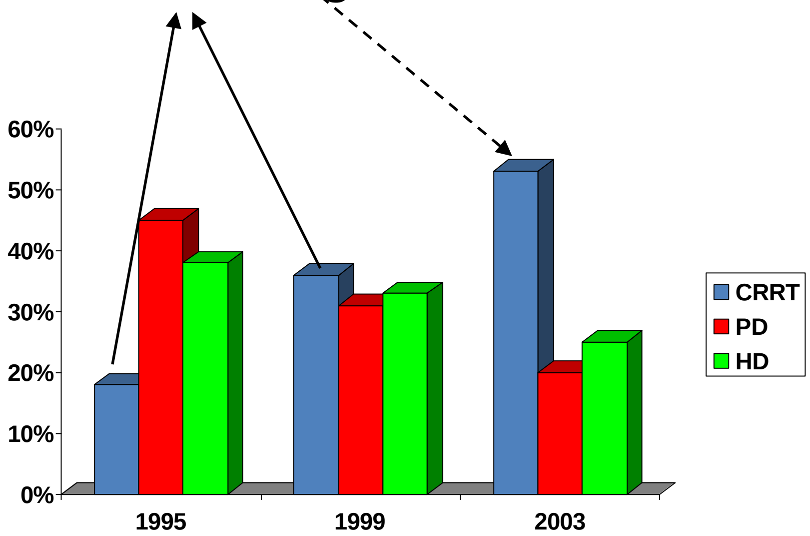
RRT Options

- Hemodialysis, Peritoneal Dialysis, CRRT
  - Each has advantages & disadvantages
  - Choice is guided by
    - Patient Characteristics
      - Disease/Symptoms
      - Hemodynamic stability
    - Goals of therapy
      - Fluid removal
      - Electrolyte correction
      - Both
    - Availability, expertise and cost

Pediatr Nephrol (2009) 24:37–48

Trends in Pediatric RRT

CRRT Increasing



Warady et al, Pediatr Neph 2000, 15:11-3

12-US Multicentre ppCRRT
Most include Dialysis

Table 2. CRRT technical characteristics[a]

Characteristic	n (Circuits)	%
Modality		
CVVHD	746	48
CVVHDF	466	30
CVVH	321	21
SCUF	16	1

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

Why CRRT?

- Reduces hemodynamic instability preventing secondary ischemia
  - Precise Volume control/immediately adaptable
  - Uremic toxin removal
  - Effective control of uremia, hypophosphatemia, hyperkalemia
- Acid base balance
  - Rapid control of metabolic acidosis
- Electrolyte management
  - Control of electrolyte imbalances
- Allows for improved provision of nutritional support
- Management of sepsis/plasma cytokine filter
- Safer for patients with head injuries

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 (hypervolemia with pulmonary edema/respiratory failure)

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

- Independently associated with mortality in children at CRRT initiation.

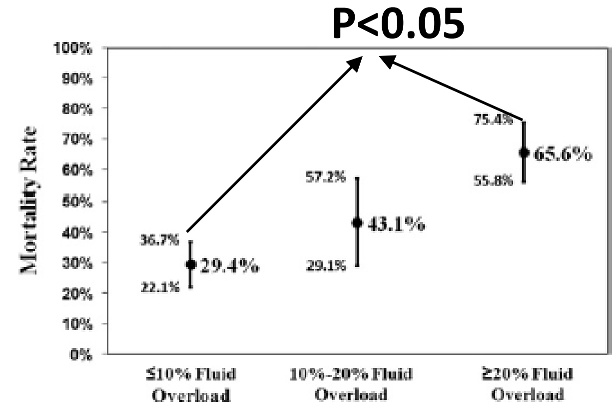


Figure 1. Mortality rates of pediatric intensive care unit patients receiving continuous renal replacement therapy subdivided by degree of fluid overload. Error bars represent 95% confidence intervals for the mortality rate in each fluid overload group. There was a statistically significant difference 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 ($P = 0.07$).

American Journal of Kidney Diseases, Vol 55, No 2 (February), 2010: pp 316-325

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

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.

Timing of Pediatric RRT

- ?????????

- AKI definition may help.

- The decision to initiate RRT affected by

  – strongly held physician beliefs

  – Patient characteristics : age, race, illness acuity, and co-morbidities.

  – Organizational characteristics

Considerations

- Emerging importance of fluid overload prevention.

- Children develop MODS early in ICU course
  - Maximum number of organ failures occurs within 72 hours of ICU admission (87% of patients)

- Children die with MODS very early in ICU course
  - 88.4% of deaths occur within 7 days of MOSF diagnosis

Proulx et al: Crit Care Med 22:1025, 1994

Children are not small adults

- 0 days to 21+ years
- 2 kg to 200 kg

- Not present
  - Diabetes
  - Older age
  - Atherosclerotic disease
  - Hypertension
  - Volume of patients
- Present
  - Size/Access variation
  - Less frequent than adults/less experience
  - Machinery is adapted (not made) for pediatrics
  - Blood priming
    - UF, thermic controls

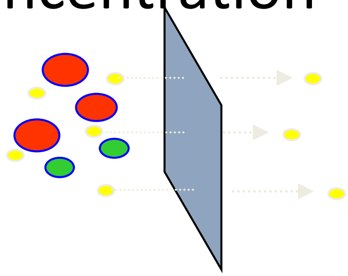
Summary: Pediatric CRRT Epidemiology and Indications

- 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 therapy for renal failure
  - Useful in setting of volume overload
  - Best time to start remains uncertain
- Better AKI definitions will help answer ??s

CRRT Terminology and Modalities

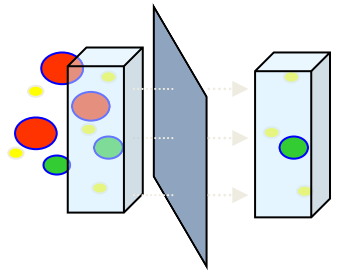
Diffusion vs. Convection

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



Effective for small molecule clearance

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

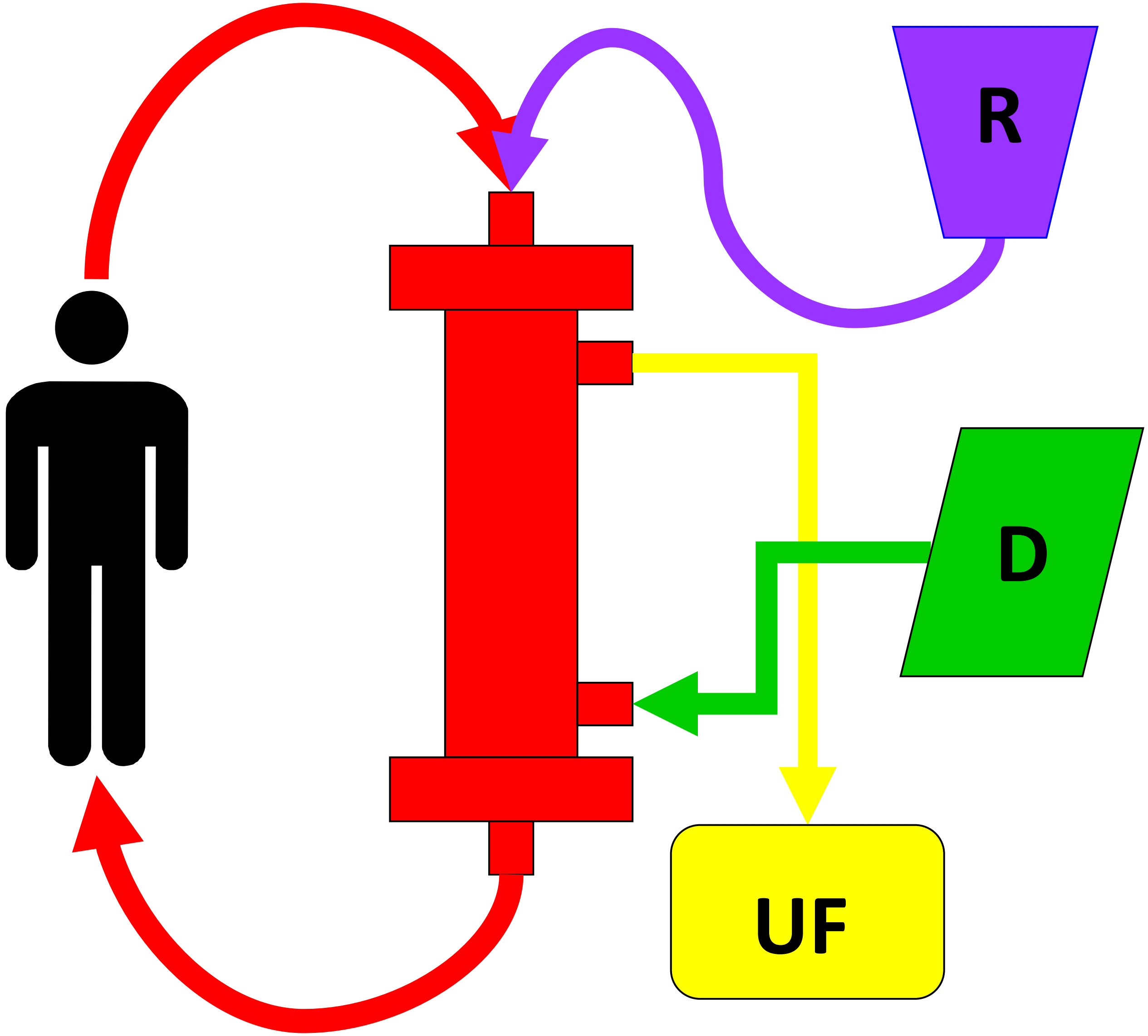


Effectiveness less dependent on molecular size

Current Nomenclature for CRRT

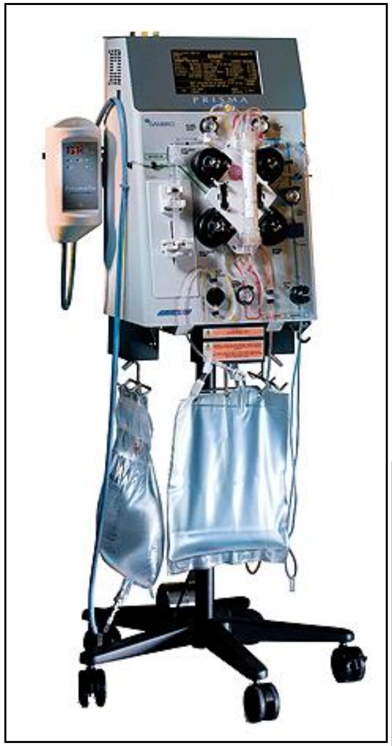
SCUF:	Slow Continuous Ultrafiltration
CVVH:	Continuous Veno-Venous Hemofiltration
CVVHD:	Continuous Veno-Venous Hemodialysis
CVVHDF:	Continuous Veno-Venous Hemodiafiltration

CRRT Schematic



- SCUF
- CVVH
- CVVHD
- CVVHDF

CRRT Machines



Convection vs. Diffusion

Are there advantages of one type of therapy over another?

Solute (MW)	Convective Coefficient	Diffusion Coefficient
Urea (60)	1.01 ± 0.05	1.01 ± 0.07
Creatinine (113)	1.00 ± 0.09	1.01 ± 0.06
Uric Acid (168)	1.01 ± 0.04	0.97 ± 0.04*
Vancomycin (1448)	0.84 ± 0.10	0.74 ± 0.04**
Cytokines (large)	adsorbed	minimal clearance

*P<0.05 , **P<0.01

Summary: CRRT Terminology and Modalities

- CRRT employs physical principles of diffusion and/or convection
- Nomenclature depends on methods used
  - SCUF, CVVH, CVVHD, CVVHDF
- All methods that employ solutions are effective at removing small molecules
- Convection improves large particle removal
- Still unclear about “best” modality

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.

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

Artificial Kidney and Dialysis/Pediatrics

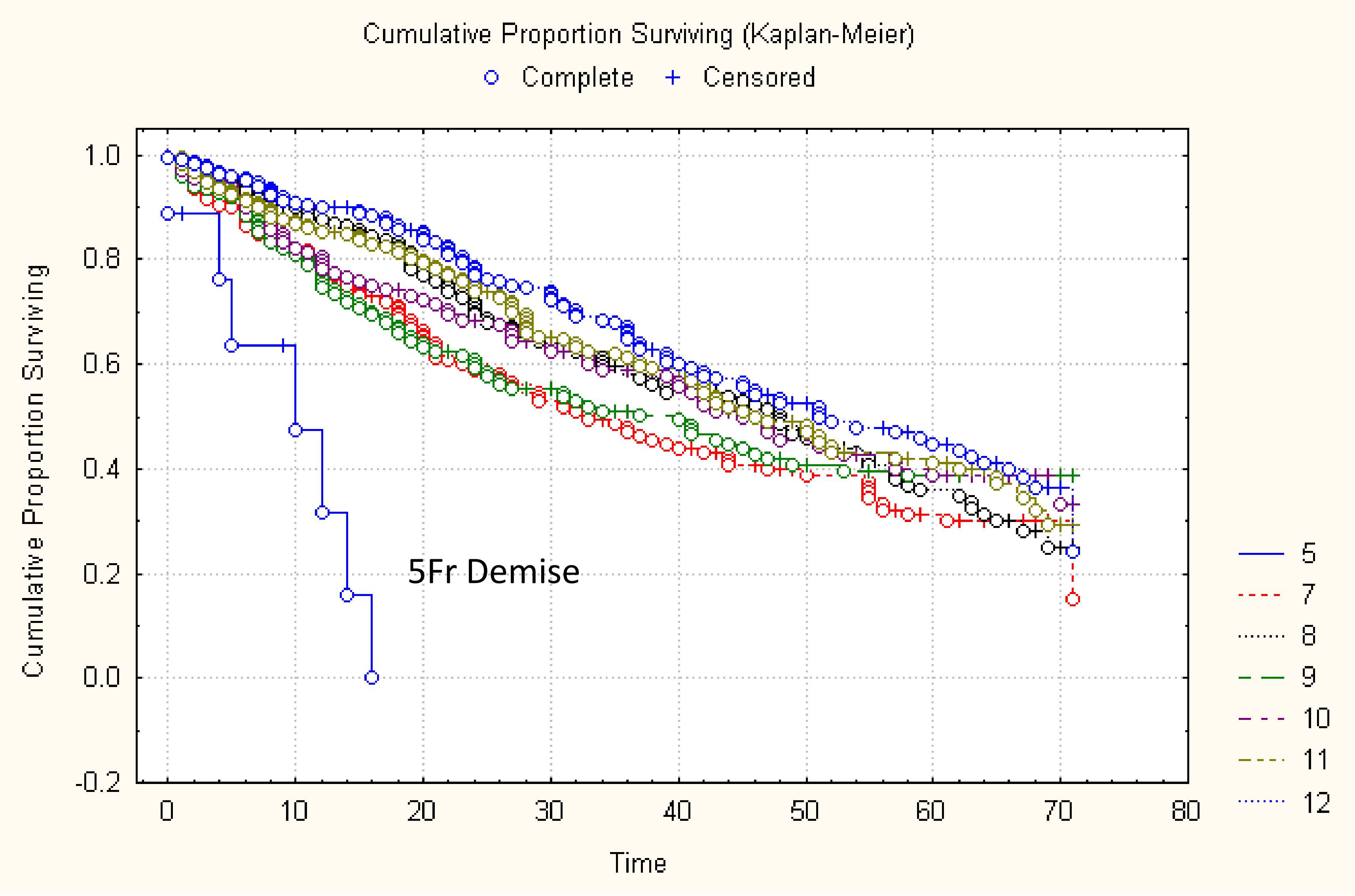
The effect of vascular access location and size on circuit survival in pediatric continuous renal replacement therapy: A report from the PPCRRT registry

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



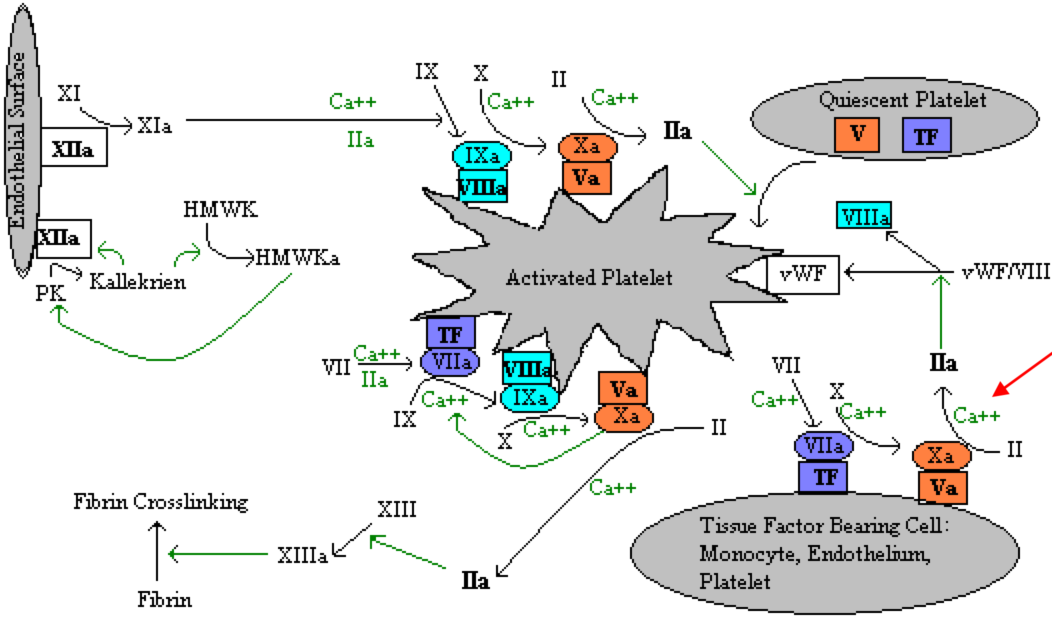
Hackbarth R et al: *IJAIO* December 2007

Summary: Vascular Access for Pediatric CRRT

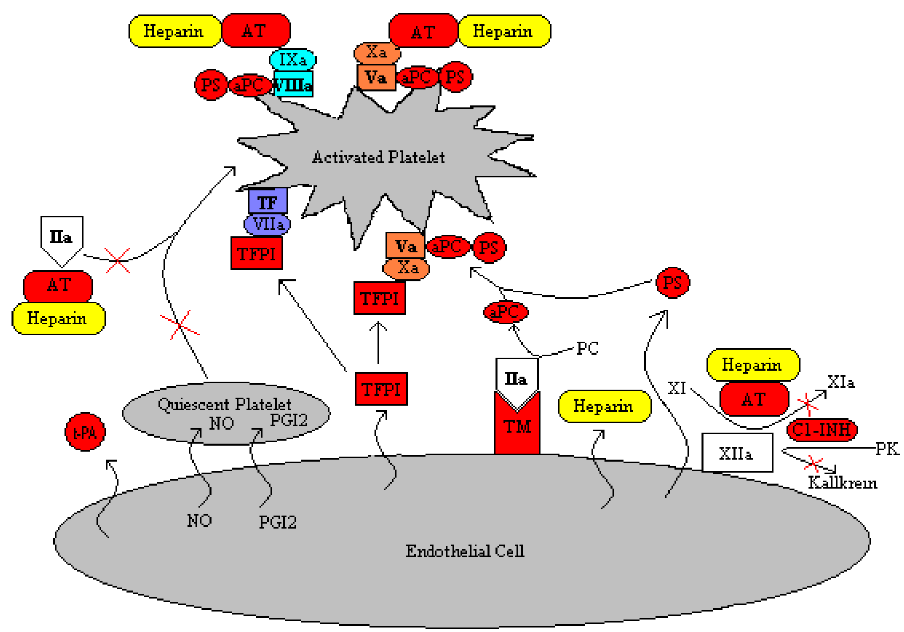
- Put in the largest and shortest catheter when possible
  - Caveat: short femoral catheters have been shown to have high rate of recirc in adult patients. (Little et al. AJKD 2000;36:1135-9)
- The IJ site is preferable (over femoral) when clinical situation allows
- Avoid double lumen 5Fr Catheters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

Anticoagulation

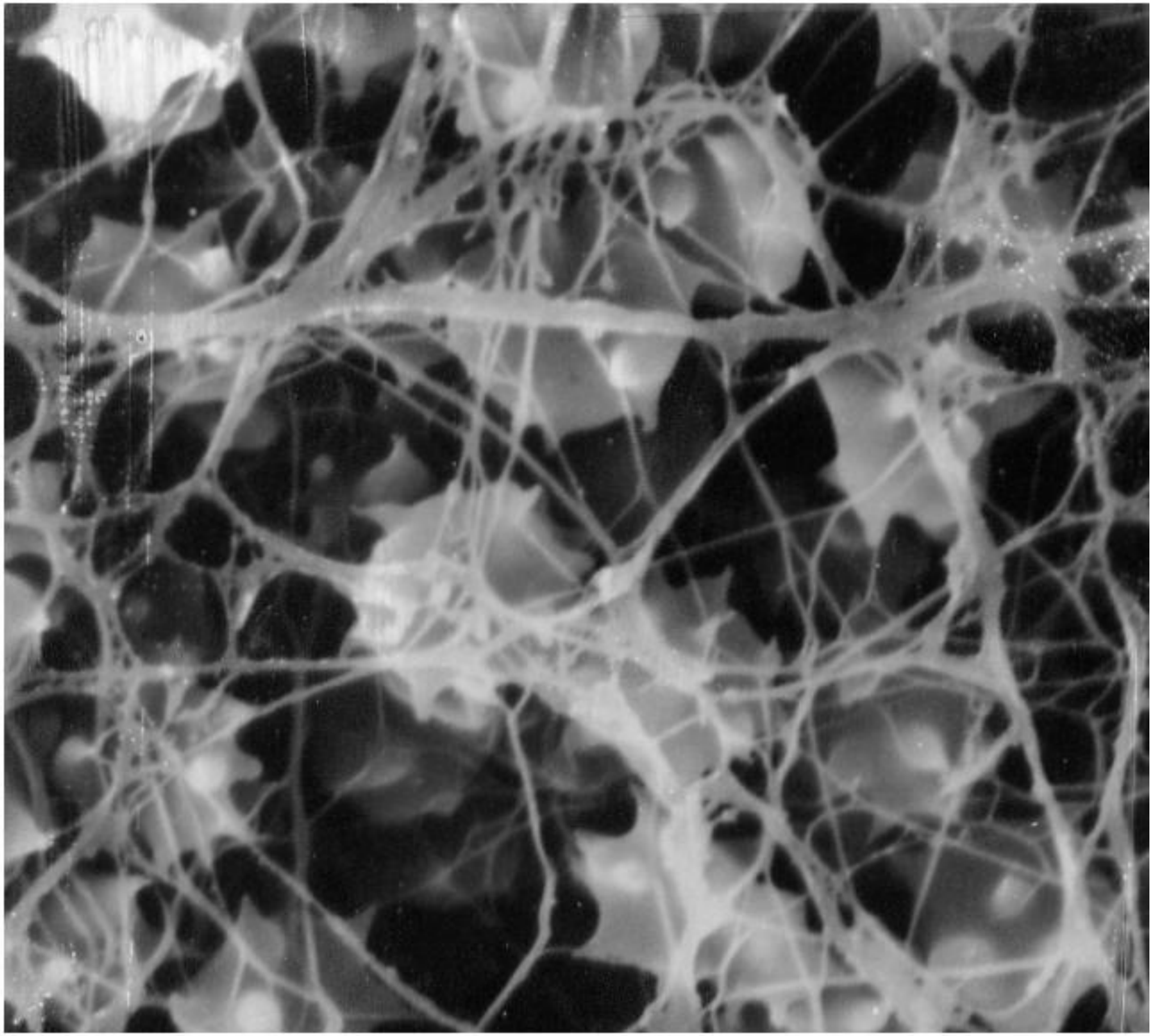
- Another crucial step in delivering the prescribed dose (reducing downtime)
- Critically ill patients are at risk for both increased and decreased clot formation simultaneously



Calcium is necessary for each event in the cascade.



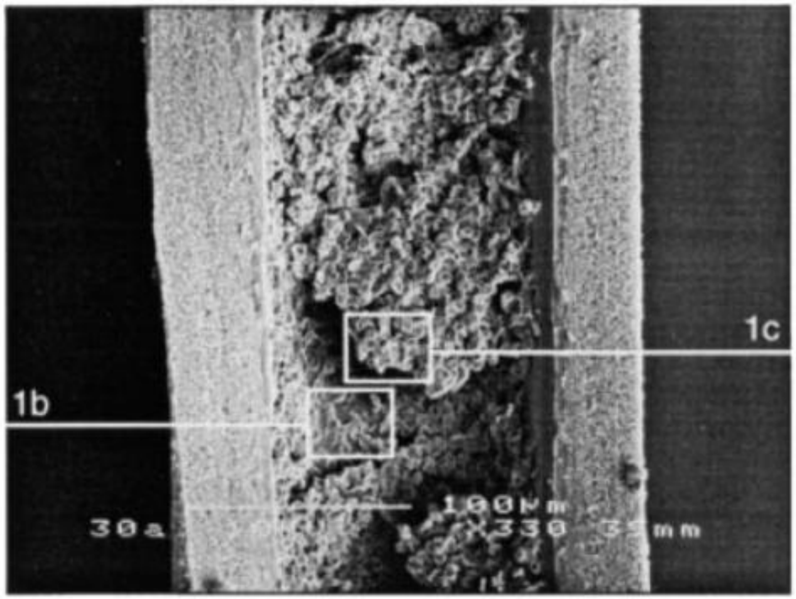
Heparin acts in conjunction with ATIII on thrombin and F IX, FX, FXII



The Clot

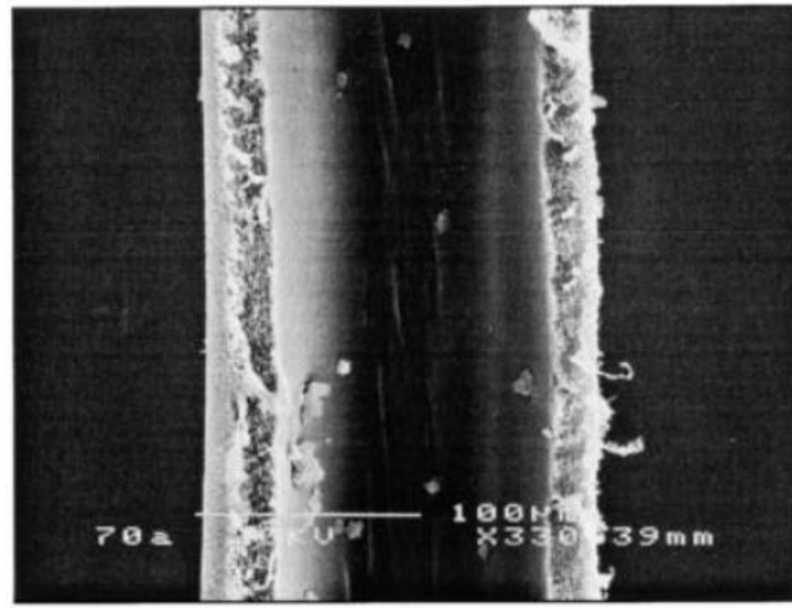
What the filter looks like

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

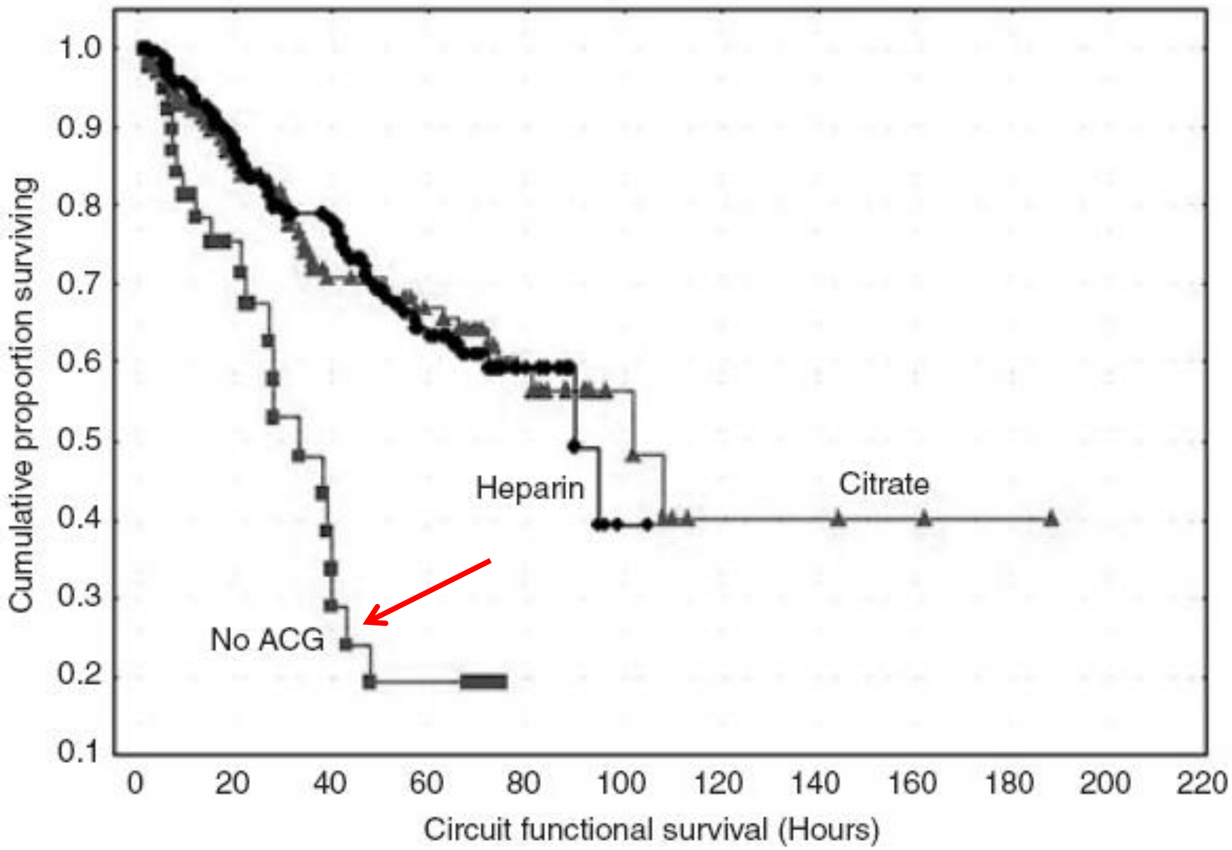
Nephrology Dialysis Transplantation

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

Citrate Specific Issues

- Alkalosis and Hypernatremia
  - Increase diffusion clearance (increase dialysate flow)
  - Or substitute normal saline for some of the high bicarb containing dialysate
  - Others use pharmacy made citrate solutions with 0.67% Citrate vs 2% standard citrate solution (Tolwani AJ et al. Clin J Am Soc Nephrol 2006;1:79-87)

Hypocalcemic Citrate Toxicity

- Rising Total Calcium
- Declining iCal
- Usually see with infants (more Qb hence citrate than total clearance) and in those with liver failure
- Risk for severe hypocalcemia
- Rx by decreasing citrate, and/or a period of increased clearance (D or UF)

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

Thanks

- Geoffrey Fleming- slides
- Jordan Symons- slides
- Michael Zappitelli- slides
- ppCRRT members