Update on CRRT: Pearls for the Clinician

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Overview

(Please interrupt me at any time)

- Access
- Solutions
- Anticoagulation
- Nutrition
- Drug Clearance
- Outcome
- ECMO and PCRRT
Convective Clearance

To increase clearance by convection, increase ultrafiltration rate (will require more replacement fluids)
Diffusive Clearance

To increase clearance by diffusion, increase dialysate flow rate
### Sieving Coefficients

<table>
<thead>
<tr>
<th>Solute (MW)</th>
<th>Convective Coefficient</th>
<th>Diffusion Coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urea (60)</td>
<td>1.01 ± 0.05</td>
<td>1.01 ± 0.07</td>
</tr>
<tr>
<td>Creatinine (113)</td>
<td>1.00 ± 0.09</td>
<td>1.01 ± 0.06</td>
</tr>
<tr>
<td>Uric Acid (168)</td>
<td>1.01 ± 0.04</td>
<td>0.97 ± 0.04*</td>
</tr>
<tr>
<td>Vancomycin (1448)</td>
<td>0.84 ± 0.10</td>
<td>0.74 ± 0.04**</td>
</tr>
<tr>
<td>Calcium (protein bound)</td>
<td>0.67 ± 0.1</td>
<td>0.61 ± 0.07</td>
</tr>
<tr>
<td>Cytokines (large)</td>
<td>adsorbed</td>
<td>minimal clearance</td>
</tr>
</tbody>
</table>

*P<0.05  **P<0.01
Comparison of Urea Clearance: CVVH vs CVVHD

(Maxvold et al, Crit Care med. 2000 Apr;28(4):1161-5)

BFR = 4 mls/kg/min
FRF/Dx FR = 2 l/1.73 m2/hr
SAM = 0.3 m2
Clearance: Convection vs. Diffusion
Vascular Access

Figure 2: Mean Patient Weight vs Catheter Size

Hackbarth R et al: *IJAIO* 30:1116-21, 2007
<table>
<thead>
<tr>
<th>Catheter Size*</th>
<th>Number of Patients</th>
<th>% Survival at 60 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>6</td>
<td>0 (p &lt; 0.0000)</td>
</tr>
<tr>
<td>7</td>
<td>57</td>
<td>43 (p &lt; 0.002)</td>
</tr>
<tr>
<td>8</td>
<td>65</td>
<td>55 (NS)</td>
</tr>
<tr>
<td>9</td>
<td>35</td>
<td>51 (p &lt; 0.002)</td>
</tr>
<tr>
<td>10</td>
<td>46</td>
<td>53 (NS)</td>
</tr>
<tr>
<td>11.5</td>
<td>71</td>
<td>57 (NS)</td>
</tr>
<tr>
<td>12.5</td>
<td>64</td>
<td>60 (NS)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Insertion Site*</th>
<th>Number of Patients</th>
<th>% Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Internal Jugular</td>
<td>58</td>
<td>60 (p &lt; 0.05)</td>
</tr>
<tr>
<td>Subclavian</td>
<td>31</td>
<td>51 (NS)</td>
</tr>
<tr>
<td>Femoral</td>
<td>260</td>
<td>52 (NS)</td>
</tr>
</tbody>
</table>

Hackbarth R et al: *IJA/O* 30:1116-21, 2007
<table>
<thead>
<tr>
<th>PATIENT SIZE</th>
<th>CATHETER SIZE &amp; SOURCE</th>
<th>SITE OF INSERTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>NEONATE</td>
<td>Dual-Lumen 7.0 French (COOK/MEDCOMP)</td>
<td>Femoral vein</td>
</tr>
<tr>
<td>3-6 KG</td>
<td>Dual-Lumen 7.0 French (COOK/MEDCOMP)</td>
<td>Internal/External-Jugular, Subclavian or Femoral vein</td>
</tr>
<tr>
<td>6-30 KG</td>
<td>Dual-Lumen 8.0 French (KENDALL/ARROW)</td>
<td>Internal/External-Jugular, Subclavian or Femoral vein</td>
</tr>
<tr>
<td>&gt;15 KG</td>
<td>Dual-Lumen 9.0 French (MEDCOMP)</td>
<td>Internal/External-Jugular, Subclavian or Femoral vein</td>
</tr>
<tr>
<td>&gt;30 KG</td>
<td>Dual-Lumen 10.0 French (KENDALL, ARROW)</td>
<td>Internal/External-Jugular, Subclavian or Femoral vein</td>
</tr>
<tr>
<td>&gt;30 KG</td>
<td>Triple-Lumen 12 French (KENDALL/ARROW)</td>
<td>Internal/External-Jugular, Subclavian or Femoral vein</td>
</tr>
</tbody>
</table>

Access table available at pcrrt.com)
## Chemical Content of PrismaSol

<table>
<thead>
<tr>
<th>Ion (mEq/ L)</th>
<th>BK 0/ 3.5</th>
<th>BGK 2/ 0</th>
<th>BGK 2/ 3.5</th>
<th>BGK 4/ 2.5</th>
<th>BGK 4/ 0</th>
<th>BGK 0/ 2.5</th>
<th>BK 0/ 0</th>
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</thead>
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<tr>
<td>Sodium</td>
<td>140</td>
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<td>140</td>
<td>140</td>
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<tr>
<td>Potassium</td>
<td>0</td>
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<td>2</td>
<td>4</td>
<td>4</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Chloride</td>
<td>109.5</td>
<td>108</td>
<td>111.5</td>
<td>113</td>
<td>110.5</td>
<td>109</td>
<td>106.5</td>
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<tr>
<td>Bicarb</td>
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<td>32</td>
<td>32</td>
<td>32</td>
<td>32</td>
<td>32</td>
<td>32</td>
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<tr>
<td>Lactate</td>
<td>3</td>
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<td>3</td>
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<tr>
<td>Calcium</td>
<td>3.5</td>
<td>0</td>
<td>3.5</td>
<td>2.5</td>
<td>0</td>
<td>2.5</td>
<td>0</td>
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<tr>
<td>Magnesium</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
</tr>
<tr>
<td>Gluc(mg/dL)</td>
<td>0</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>0</td>
</tr>
</tbody>
</table>
Sites of Thrombus Formation

- Any blood surface interface
  - Hemofilter
  - Bubble trap
  - Catheter
  - Areas of turbulence resistance
    - Luer lock connections / 3 way stopcocks
Sites of Action of Heparin

Contact Phase (intrinsic)
- XII activation
- XI IX

Tissue Factor (extrinsic)
- TF:VIIa
- platelets / monocytes / macrophages

UF HEPARIN
- LMWH
- prothrombin
- THROMBIN
- fibrinogen
- CLOT

Tissue Factor (extrinsic)
- TF:VIIa
- platelets / monocytes / macrophages

UF HEPARIN
- LMWH
- prothrombin
- THROMBIN
- fibrinogen
- CLOT

VIIIa
- Ca++
- platelets
Heparin Protocols
Benefit and Risks

- **Benefits**
  - Heparin infusion prior to filter with post filter ACT measurement
  - Bolus with 10-20 units/kg Infuse at 10-20 units/kg/hr
  - Adjust post filter ACT 180-200 secs

- **Risks**
  - Patient Bleeding
  - Unable to inhibit clot bound thrombin
  - Ongoing thrombin generation
  - Activates - damages platelets / thrombocytopenia
(Citrate = 1.5 x BFR 150 mls/hr)

(Ca = 0.4 x citrate rate 60 mls/hr)

(BFR = 100 mls/min)

Normocarb Dialysate

Normal Saline Replacement Fluid

ACD-A/Normocarb Wt range 2.8 kg – 115 kg

Average life of circuit on citrate 72 hrs (range 24-143 hrs)

Calcium can be infused in 3rd lumen of triple lumen access if available.

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

Patrick D. Brophy¹, Michael J. G. Somers², Michelle A. Baum², Jordan M. Symons³, Nancy McAfee³, James D. Fortenberry⁴, Kristine Rogers⁴, Joni Barnett⁵, Douglas Blowey⁶, Cheryl Baker⁷, Timothy E. Bunchman⁸ and Stuart L. Goldstein⁷

Seven ppCRRT centers

- 138 patients/442 circuits
- 3 centers: hepACG only
- 2 centers: citACG only
- 2 centers: switched from hepACG to citACG

- HepACG = 230 circuits
- CitACG = 158 circuits
- NoACG = 54 circuits

Circuit survival censored for

- Scheduled change
- Unrelated patient issue
- Death/withdrawal of support
- Regain renal function/switch to intermittent HD

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Fig. 1. The breakdown of the number of CRRT circuit change requirements. Notably, clotting (29%), scheduled changes (25%) and unrelated patient issues (28%) represented the most common reasons necessitating CRRT circuit change. n = 138 patients receiving 18 208 h of CRRT comprising a total of 442 CRRT circuits. Mean circuit life was 41.2 ± 30.8 h (range 1–188).

Fig. 2. Comparison of CRRT circuit life for all circuits with: no anticoagulation (filled squares), heparin anticoagulation (filled circles) or citrate anticoagulation (filled triangles). Mean circuit survival was no different for circuits receiving hepACG (42.1 ± 27.1 h) and citACG (44.7 ± 35.9 h), but was significantly lower for circuits with noACG (27.2 ± 21.5 h, P < 0.005). Kaplan–Meier analyses revealed no circuit survival difference between hepACG and citACG circuits, but significantly lower survival for noACG circuits (P < 0.001). Circuits were censored for Kaplan–Meier analysis if changed because of scheduled change as per the manufacturer’s recommendations, access malfunction, machine malfunction or unrelated patient issues. Log-rank analysis showed that 69% of hepACG and citACG circuits, but only 28% of noACG circuits, were functional at 60 h. Note, clotting rates were similar for hepACG circuits (58 out of 230, 25%) and citACG circuits (43 out of 158, 27%), but were significantly higher for noACG circuits (27 out of 54, 50%, P < 0.001).

ppCRRT ACG Side Effects

Heparin
- 11 cases of systemic bleeding on heparin
- 5 cases no ACG used secondary to bleeding
- 1 case of HIT

Citrate
- 19 cases of metabolic alkalosis
  - 1 change to heparin for hyperglycemia
  - 1 change to heparin for alkalosis
- 3 cases of citrate lock
Complications of Citrate: Metabolic alkalosis

- Metabolic alkalosis due to
  - 1 mmol of citrate converts to 3 mmol of HCO3
  - PrismaSol BGK 2/0
  - NG losses
  - TPN with acetate component
Complications of Citrate: Rx of Metabolic alkalosis

- Rx Metabolic alkalosis by
  - PrismaSol has a 32 Bicarb bath
    - Decrease bicarbonate dialysis rate and replace at the same rate with NS (pH 5) to allow for the total solution exposure to be identical (ie no change in solute clearance) yet this will give less HCO3 exposure and an acid replacement
  - NG losses
    - Replace with \( \frac{1}{2} - \frac{2}{3} \) NS
  - TPN with acetate component
    - Use high Cl ratio
Metabolic alkalosis

- No longer a clinical issue
- When we moved to Normocarb HF 25 we no longer have this issue
- What is needed is a PrismaSol 22 bicarbonate with 2 K
Complications

- Hemodynamic
- Thermal
  - < 25 kg may mask fever
- Nutritional
Factors effecting hemodynamics-1

- Volume status of patient
  - Excessive Ultrafiltration
    - over aggressive ultrafiltration prescription
    - error of ultrafiltration monitoring
  - Inadequate replacement
  - Accidental disconnect
Ultrafiltration accuracy
2.8 kg infant on PRI SMA

Prescription
BFR 30 mls/min
Dx FR 300 mls/hr
Factors affecting hemodynamics-2

- Vasopressor Enhancement
  - Enhancement of vasopressor effectiveness will occur with improvement of acidosis
  - Other agents (e.g. atracurium) is metabolism is pH dependent therefore drug clearance in general is effected with pH change
pH correction upon Epi effect
Factors effecting hemodynamics-3

- **Vasopressor clearance**
  - Due to proximity of infusion
    - recirculation effecting delivery and clearance
    - be aware of infusing vasopressor agents in immediate proximity to the “arterial” port of the hemofiltration machine
Vascular Access

Note the relationship of the line tips.
Factors effecting hemodynamics

- Vasopressor clearance
  - Vasopressor agents all have in common a small molecular weight and minimal protein binding
    - Epinephrine
    - Norepinephrine
    - Dopamine
    - Dobutamine
Factors effecting hemodynamics-4

- Circuit reaction
  - Circuit compliance
  - Circuit extracorporeal volume
    - more or a problem in pediatrics
- Membrane reaction
  - Bradykinin release syndrome
Membranes Compatibility

- Use of more biocompatible membranes (eg AN-69 polyacrylonitrile) results in less complement activation
- Hemodialysis data has shown that biocompatible membranes (eg AN69 membrane) improve survival in ARF, have a shorter time to recovery of renal function, and is less associated with oliguria
Membranes Compatibility

- AN-69 membranes have been associated with “Bradykinin Release Syndrome” in patients on ACE inhibitors
- This “Bradykinin Release Syndrome” may be pH dependent
- But what about its use in CRRT?
Plasma kallikrein activity kinetics with AN69 membrane: Influence of diluted plasma pH
Bradykinin Release Syndrome
(Brophy et al, AM J Kid Dis, June 2001)

- What is the link
  - Blood bank blood has
    - ICa of 0.04 mmol/l
    - K+ of 40-60 mEq/l
    - pH of 6.4
  - Therefore we hypothesize that if this is a pH blood reaction either we buffer the blood or bypass the membrane
Bypass System to Prevent Bradykinin Release Syndrome

Bradykinin Release Syndrome

- Pts all on ACE inhibitors on AN69 membrane for chronic hemodialysis
- 19 pt events rinse with physiologic soln (pH < 5) prior to HD vs 10 pt events rinsed with HCO3 (pH > 5) based solutions prior to HD
- Less BRS noted with HCO3 pre-rinse
Negating the Bradykinin Factor

AHackbarth et al)

- AN-69 membrane circuit primed with 60% Blood Bank Blood and 40% albumin (5%)
- In separate experiments convective (CVVH) or diffusive (CVVHD) were done for an hour in a recirculation mode
- Replacement/Dialysate fluid was bicarbonate based and run at 2000 mls/hr
- BFR at 100 mls/min
- Samples for pH and Bradykinin taken at 30 mins intervals
Negating the Bradykinin Factor

(Hackbarth et al)

Z-BUF Modality and Bradykinin Levels

Bradykinin (pg/ml) vs Time (minutes)

CVVH Bradykinin
CVVHD Bradykinin
CVVHD pH
CVVH pH
Prismaflex Device with HF 20 Set

- Blood flow (ml/min) 10-100
- Dialysate flow (ml/h) 50-2500
- Subst-flow rate (ml/h) 20-1000
- Subst.prebp (ml/h) 30-1000
- Volume reduction (ml/h) 10-2000
- Heparin-Infusion (ml/h) 0.5-5.0

• treatment options
  • SCUF
  • CVVH
  • CVVHD
  • CVVHDF
  • CVVHDF pre+postdil
Prismaflex HF 20 Set: CRRT
Fluid removal

Scales (g)

-2000 -1800 -1600
-1400
-1200
-1000
-800
-600
-400
-200
0

Patient fluid removal (g)

-200
-400
-600
-800
-1000
-1200
-1400
-1600
-2000

24.10.09 23:00
25.10.09 11:00
25.10.09 23:00
26.10.09 11:00
26.10.09 23:00
27.10.09 11:00

Post Replacement
Dialysate
Effluent
Patient Fluid Removal
Nutritional losses
Replacement fluid vs dialysate


- Study design
  - Fixed blood flow rate-4 mls/kg/min
  - HF-400 (0.3 m2 polysulfone)
  - Cross over for 24 hrs each to pre filter replacement or Dx at 2000 mls/hr/1.73 m2

- Indirect calorimetry to measure REE
- TPN source of nutrition @ 120% of REE
- 10% Aminosyn II
  - 1.5 gms/kg/day of protein
Comparison of **Total** Amino Acid losses: CVVH vs CVVHD

(Maxvold et al, Crit Care Med 2000 Apr;28(4):1161-5 )

![Bar chart showing comparison of Amino Acid Losses between CVVH and CVVHD](chart.png)
Nitrogen losses in CRRT


- 7 adults with MOSF on CVVHDF
- 2.5 gms/kg/day of TPN AA delivered
- 24 hr nitrogen balance, AA clearance, protein catabolism performed
Nitrogen losses in CRRT


- BUNs maintained at 26.6 mmol/l
- Protein catabolic rate avg 235 gms/day
  - (range 107-355 gms)
- Median nitrogen losses 24.3 gms/day
  - (range 21.1-65.5 gms)
- Median nitrogen balance -1.8 gms/day
  - (range -21 to + 17.9 g/day)
D. “Known drug characteristics”

- These recommendations made by panel of nephrologists and pharmacists
- Based on:
  - Protein Binding Information
  - Volume of Distribution
  - Molecular Weight
When in doubt, start here…

- Blood flow, filter type are not very important.

Find out

- In CVVHD: Dialysate flow rate (ml/hr)
  - Usually 2 L/1.73m²/hr (33 mL/1.73m²/min)

- In CVVH: Substitution Fluid rate (ml/hr)
  - Usually 2L/1.73m²/hr (33 mL/1.73m²/min)

- Add this to patient’s native Cr Cl (ml/1.73m²/min)

- This is patient’s new Cr Cl → dose accordingly

- Works in most cases…is good enough for initial estimates. Follow up with drug level monitoring.
## Sieving Coefficient & Protein Binding

<table>
<thead>
<tr>
<th>Drug</th>
<th>Reported SC</th>
<th>Free Fraction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amikacin</td>
<td>0.93</td>
<td>0.95</td>
</tr>
<tr>
<td>Imipenem</td>
<td>0.78</td>
<td>0.80</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>0.84</td>
<td>0.80</td>
</tr>
<tr>
<td>Penicillin</td>
<td>0.68</td>
<td>0.50</td>
</tr>
<tr>
<td>Ranitidine</td>
<td>0.78</td>
<td>0.85</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>0.80</td>
<td>0.90</td>
</tr>
<tr>
<td>Valproic Acid</td>
<td>0.22</td>
<td>0.10</td>
</tr>
</tbody>
</table>
Drug Prescribing in Renal Failure edited by George Aronoff et al

- Commonly carried text by pharmacists
- [http://www.kdp-baptist.louisville.edu/renalbook/](http://www.kdp-baptist.louisville.edu/renalbook/)
- New edition to come out soon
- Recommendations for new drugs
- IHD and CRRT recommendations
- Pediatric recommendations
Small changes in Cr

Chertow et al, cJ ASN, June 2006
**HF vs. Conservative for Ventilator days**

<table>
<thead>
<tr>
<th></th>
<th>EIHF (n = 40)</th>
<th>Control (n = 40)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Successful weaning, n</td>
<td>28 (70%)</td>
<td>15 (37%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Duration of MV, days</td>
<td>11 ± 3</td>
<td>20 ± 5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Independence from vasopressor support, n</td>
<td>30 (75%)</td>
<td>10 (25%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ICU stay, days</td>
<td>12 ± 5</td>
<td>16 ± 4</td>
<td>0.002</td>
</tr>
<tr>
<td>Hospital stay, days</td>
<td>19 ± 5</td>
<td>34 ± 4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ICU survival, n</td>
<td>28 (70%)</td>
<td>16 (40%)</td>
<td>0.003</td>
</tr>
<tr>
<td>Predicted survival based on individual risk of death</td>
<td>41 ± 12</td>
<td>40 ± 10</td>
<td>n.s.</td>
</tr>
<tr>
<td>28-day survival, n</td>
<td>22 (55%)</td>
<td>11 (27.5%)</td>
<td>0.005</td>
</tr>
<tr>
<td>Predicted survival based on individual risk of death</td>
<td>41 ± 12</td>
<td>40 ± 10</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

Reprinted with permission from Piccinni et al. [15].

Chertow et al, CJASN, June 2006
RI FLE Criteria

**GFR Criteria**
- Increased SCreat x1.5 or GFR decrease > 25%
- Increased SCreat x2 or GFR decrease > 50%
- Increase SCreat x3, GFR decrease 75% or SCreat ≥4mg/dl
  - Acute rise ≥0.5mg/dl

**Urine Output Criteria**
- UO < .5ml/kg/h x 6 hr
- UO < .5ml/kg/h x 12 hr
- UO < .3ml/kg/h x 24 hr or Anuria x 12 hrs

**Risk**
- High Sensitivity

**Failure**
- High Specificity

**Loss**
- Persistent ARF** = complete loss of kidney function > 4 weeks
- End Stage Kidney Disease (> 3 months)

**ESKD**
## Modified Pediatric RIFLE

<table>
<thead>
<tr>
<th>Category</th>
<th>Criteria</th>
<th>Urine output</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk</td>
<td>GFR decrease by 25%</td>
<td>&lt;0.5ml/kg/hour for 8 hours</td>
</tr>
<tr>
<td>Injury</td>
<td>GFR decrease by 50%</td>
<td>&lt;0.5ml/kg/hour for 16 hours</td>
</tr>
<tr>
<td>Failure</td>
<td>GFR decrease by 75% or GFR&lt;35ml/min/1.73m²</td>
<td>&lt;0.3 ml/kg/hour for 24 hours or anuric for 12 hours</td>
</tr>
<tr>
<td>Loss</td>
<td>Persistent ARF &gt; 4 weeks</td>
<td></td>
</tr>
<tr>
<td>End stage</td>
<td>End Stage Renal Disease (&gt;3 months)</td>
<td></td>
</tr>
</tbody>
</table>

Goldstein et al, KI 2007
Now validated in 3 additional Pediatric Studies
Creatinine Changes and AKI in Children

- 390 pediatric cardiac surgery patients
- Cr rise at 25-50% above baseline within first 24 hours of surgery
  - Increase LOS
  - Increase ventilator days
- Zappitelli et al, Kid Int 2009 76:885-892
LOS with AKI - Pediatrics

(Alkandari et al Crit Care June 2011)

- 2106 admits/377 with AKI (delta Cr)
- AKI correlated with
  - Higher Pediatric Risk of Mortality Score
  - Ventilation
  - Infections
- AKI mortality 3.7 (OR)
- AKI associated with > LOS and Vent days
Data by RRT Modality in AKI

- Comparison of Modalities
- PD
- HD
- CRRT
- HD + CRRT
PATIENT MORTALITY

Fleming et al., J Thorac Cardiovasc Surg, 1995

Modality
(NS in mortality)
CALORIC INTAKE

% Change From Baseline

Modality(* p < 0.05 compared to PD)

PD

CAVH *

CVVH *

Fleming et al., J Thorac Cardiovasc Surg, 1995
Renal Replacement Therapy in the PICU Pediatric Outcome Literature

- 122 children studied
- No PRISM scores
- Most common diagnosis
  - IHD: primary renal failure
  - CRRT: sepsis
    - 31% survival
- Conclusion: patients who receive CRRT are more ill

Pediatric ARF: Modality and Survival

Ped Neph 16:1067-1071, 2001
Pediatric ARF: Modality and Survival

- Patient survival on pressors (35%) lower than without pressors (89%) ($p<0.01$)
- Lower survival seen in CRRT than in patients who received HD for all disease states

Ped Neph 16:1067-1071, 2001
Unique Situations-CRRT

- When hemodynamic instability and highly catabolic conditions are present
  - Sepsis
  - Bone Marrow Transplantation
    - Goldstein SL, Seminars in Dialysis 2009; 22; 180-184
    - Walters et al, Pediatr Neph 2009 24; 37-38
Stem Cell Transplant: ppCRRT

- 51 patients in ppCRRT with SCT
- Mean %FO = 12.41 ± 3.7%.
- 45% survival
  - Convection: 17/29 survived (59%)
  - Diffusion: 6/22 (27%), p<0.05
- Survival lower in MODS and ventilated patients

Prospective Pediatric Study

- 40 patients with Sepsis/ARF at 4 ppCRRT centers
- Randomized crossover design
  - 24 hours of CVVH or CVVHD, then crossover
- 2500 ml/hr/1.73m² clearance
- Dialysis/Replacement fluid with [HCO₃]=35mmol/l
- Citrate ACG
- Serum collection at 0, 1, 24, 25 and 48 hours
  - TNF-alpha
  - IL-1 beta
  - IL-6, IL-8, IL-10, IL-18
- Six hours of effluent for CK’s for clearance estimation
ppCRRT Sepsis Study

- 10 patients enrolled to date
  - 6 male, 4 female
  - Mean age 12 ± 4.8 years
  - Mean weight 44 ± 21 kg

- PELOD
  - Mean = 27 ± 10
  - Median = 22 (range 11-42)
ppCRRT [Cytokine] % Change: Convection vs. Diffusion

<table>
<thead>
<tr>
<th>Cytokine</th>
<th>Convection</th>
<th>Diffusion</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>TNF-alpha</td>
<td>-3.7 ± 9.6</td>
<td>3.9 ± 9.1</td>
<td>0.08</td>
</tr>
<tr>
<td>IL-1 beta</td>
<td>-2.8 ± 14.8</td>
<td>1.4 ± 12.9</td>
<td>0.46</td>
</tr>
<tr>
<td>IL-6</td>
<td>32.7 ± 102.8</td>
<td>-2.6 ± 18.4</td>
<td>0.21</td>
</tr>
<tr>
<td>IL-8</td>
<td>-29.1 ± 26.0</td>
<td>-8.3 ± 17.2</td>
<td>0.018</td>
</tr>
<tr>
<td>IL-10</td>
<td>-44.6 ± 29.0</td>
<td>3.1 ± 45.0</td>
<td>0.007</td>
</tr>
<tr>
<td>IL-18</td>
<td>-13.6 ± 17.9</td>
<td>16.9 ± 24.7</td>
<td>0.002</td>
</tr>
<tr>
<td>PELOD</td>
<td>-22 ± 34</td>
<td>-6 ± 30</td>
<td>0.26</td>
</tr>
</tbody>
</table>
Early vs Late as defined by RIFLE

Figure 1

Chou et al, Crit Care June 2011

Early = 192R
Late = 259IF

Log rank P = 0.33

Survival probability (%)

Days from RRT initiation to death

Early RRT

Late RRT

RIFLE
Fluid Overload as a Risk Factor

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

N=113

*p=0.02; **p=0.01
**ppCRRT MODS Data: 116 children**
*(ppCRRT KI 2005 Feb;67(2):653-8)*

<table>
<thead>
<tr>
<th>Variable (values mean +/- SD)</th>
<th>Survivors</th>
<th>Non-Survivors</th>
<th>p-value (t-test)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>8.5 ± 6.7</td>
<td>8.5 ± 7.2</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Weight (kg)</strong></td>
<td>34.2 ± 25.4</td>
<td>31.7 ± 25.8</td>
<td>NS</td>
</tr>
<tr>
<td><strong>PRISM at ICU Admit</strong></td>
<td>14.3 ± 8.2</td>
<td>16.2 ± 9.7</td>
<td>NS</td>
</tr>
<tr>
<td><strong>PRISM at CRRT Initiation</strong></td>
<td>13.9 ± 8.2</td>
<td>18.6 ± 7.2</td>
<td>&lt; 0.003</td>
</tr>
<tr>
<td><strong>CVP at CRRT Initiation</strong></td>
<td>16.5 ± 6.1</td>
<td>21.2 ± 6.6</td>
<td>&lt; 0.003</td>
</tr>
<tr>
<td><strong>BUN at CRRT Initiation</strong></td>
<td>61.1 ± 41.8</td>
<td>67.8 ± 45.7</td>
<td>NS</td>
</tr>
<tr>
<td><strong>% FO at CRRT Initiation</strong></td>
<td>14.2 ± 15.9</td>
<td>25.4 ± 32.9</td>
<td>&lt; 0.03</td>
</tr>
<tr>
<td><strong>No. of Pressors</strong></td>
<td>1.4 ± 1.1</td>
<td>1.7 ± 1.1</td>
<td>NS</td>
</tr>
</tbody>
</table>
Urine NGAL as an Early AKI Biomarker after Cardiopulmonary Bypass

AKI = 50% or greater increase in serum creatinine from baseline

Centrifugal circuit design
**ExtraCorporeal Membrane Oxygenation**

- ECMO Neonatal/Pediatric Survival Data: ELSO Registry 1998-2008
- Neonates (≤ 30 days old)
  - N = 8958
  - Survival: 5776 (72.6%)
  - NonSurvival: 2182 (27.4%)
ExtraCorporeal Membrane Oxygenation

ECMO and PCRRRT

- Indications for CRRT tandem with ECMO
- Systems Set Up Design
- Publications reviewing PCRRRT and ECMO Survival and Longterm Renal Outcomes
CRRT on ECMO

“Homemade” system connected to the ECMO circuit

- IV infusion pumps used to control ultrafiltrate
- (if replacement desired) IV infusion pump to add replacement fluids
- Several sites to hook into circuit each with drawbacks (shunting, bubble trap, flows)
- IV pumps are not engineered to maintain accuracy when flow/pressure above the pump is variable.
ECMO/CRRT Arrangement: Homemade System

Patient Return Cannula
("Arterial")

Flow Probe (F)

IV Pump (Set Hourly Rate)

Urometer

UF Drain

IV Pump I Replacement Fluids

Ultraltrate

Hemofilter

ECMO Membrane Oxygenator

ECMO Roller Pump

ECMO Bladder

Patient Venous Drain Cannula
ECMO/CRRT Arrangement: RRT System
<table>
<thead>
<tr>
<th></th>
<th>Hemofilter (Homemade)</th>
<th>CRRT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ultrafiltration control</strong></td>
<td>IV pump controlled</td>
<td>CRRT machine controlled</td>
</tr>
<tr>
<td><strong>Metabolic Control</strong></td>
<td>NO</td>
<td>YES</td>
</tr>
<tr>
<td><strong>ECMO Flow</strong></td>
<td>Blood Shunt - decrease ECMO flow or decreased PaO2 to patient</td>
<td>NO systemic changes</td>
</tr>
<tr>
<td><strong>Anti-coagulation</strong></td>
<td>Heparin</td>
<td>Heparin</td>
</tr>
</tbody>
</table>
CRRT/ECMO in Tandem

**CRRT/ECMO Centrifugal Pump**

Santiago et al  
*Kidney Int* 2009

N= 6 children on VA ECMO

Inlet line after the Centrifugal Pump

Outlet/return line before the Oxygenator

Mean Filter Life = 138 hours
CRRT/ECMO in Tandem

By accessing and returning between the pump head and the lung, we eliminate shunting and flow disturbance to the patient. We chose not to return to the venous line due its tendency to be very negative at high flow creating an increased risk for air entering the circuit.
CRRT/ECMO Outcomes

  - 15/35 (42.9%) neonatal and pediatric survived
    - 14/15 (93%) RENAL RECOVERY
    - 1/15 (7%) – Wegener’s
CRRT/ECMO in Cardiac Newborns

Shah SA et al. ASAIO J 2005

- 41/84 (48.9%) post-operative congenital heart disease patients with AKI
  - CVVH NOT associated with:
    - Ability to wean off ECMO
    - Survival to discharge


- 26/74 (35%) post-operative congenital heart disease patients
  - Hemofiltration = 5.01 X increased risk of death
CRRT/ECMO – Noncardiac Children

  - Case-control study
    - Cases 26/86 - received CVVH for >24 hours
    - Controls - no CVVH
  - Significant differences in fluid balance
  - Significant treatment differences
  - No difference in survival or vent days during or after ECMO
ExtraCorporeal Membrane Oxygenation

- ELSO Pediatric Registry 1998-2008
  \[N = 2514 \quad \text{Survival} = 1410 \ (56\%)\]

- ELSO Accumulative (1985-2008)
  \[N = 4065 \quad \text{Survival} = 2247 \ (55.3\%)\]

  Ped Pts Receiving Dialysis (1985-2008)
  \[N = 1616 \ (39\%) \quad \text{Survival} = 606 \ (37.5\%)\]
ECMO&CRRT Can be Safely done in a variety of setups

- No additional regional Anti-coagulation is needed since the patient and the entire circuit is already heparinized for ECMO
- Circuit prime for the CRRT can usually be saline
  Due to the relative size of the CRRT circuit in ratio to the larger ECMO circuit
  - When starting Ultrafiltration careful monitoring of fluid goals over a time period will prevent ↑ Hct and viscosity changes that are unwanted
  - CRRT Support on ECMO Effect on Mortality is yet to be more clearly defined as to timing of Initiation of both supports and Subsequent Outcomes.
Summary

- Questions still remain on optimal prescription and timing
- The “best” form of RRT is that which you do well
- Research is needed in the area of drug monitoring and nutrition in AKI and RRT
What is on the Horizon

- Wearable HD/CWH systems
- Small (< 12 mls) circuits for CWH