Pediatric CRRT
The Ins and Outs

Patrick D. Brophy MD, MHCDS
William H. Elinger Professor and Chair
Department of Pediatrics
University of Rochester
Rochester, New York
President, American Society of Pediatric Nephrology
Epidemiology Of and Indications For Pediatric CRRT
ACUTE KIDNEY INJURY

CRRT

WHAT IS IT?
HOW COMMON?
WHO DOES IT HAPPEN TO?
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)

Pediatric RIFLE (pRIFLE)

Acute Kidney Injury Network definition

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**Table 6 | Pediatric-modified RIFLE (pRIFLE) criteria**

<table>
<thead>
<tr>
<th>Risk</th>
<th>Estimated CCl</th>
<th>Urine output</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk</td>
<td>eCCl decrease by 25%</td>
<td>&lt;0.5 ml/kg/h for 8 h</td>
</tr>
<tr>
<td>Injury</td>
<td>eCCl decrease by 50%</td>
<td>&lt;0.5 ml/kg/h for 16 h</td>
</tr>
<tr>
<td>Failure</td>
<td>eCCl decrease by 75% or eCCl &lt;35 ml/min/1.73 m²</td>
<td>&lt;0.3 ml/kg/h for 24 h or anuric for 12 h</td>
</tr>
<tr>
<td>Loss</td>
<td>Persistent failure &gt; 4 weeks</td>
<td></td>
</tr>
<tr>
<td>End stage</td>
<td>End-stage renal disease</td>
<td></td>
</tr>
<tr>
<td>stage</td>
<td>(persistent failure &gt; 3 months)</td>
<td></td>
</tr>
</tbody>
</table>

eCCl, estimated creatinine clearance; pRIFLE, pediatric risk, injury, failure, loss and end-stage renal disease.
Pediatric AKI: Incidence in PICU
Population & Definition-dependent

• Cardiac Surgery


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

All PICU
Admx SCr baseline

All PICU stay>48hrs

Kid Int 2007; 71: 1028-35
Al-Kandari et al, ASN, 2008
Pediatric AKI: Changing Epidemiology

Previously: Primary renal diseases

<table>
<thead>
<tr>
<th>Pediatric ARF Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Patients</td>
</tr>
<tr>
<td>Unknown</td>
</tr>
<tr>
<td>AGN</td>
</tr>
<tr>
<td>Hemoglobinuria</td>
</tr>
<tr>
<td>Sepsis</td>
</tr>
<tr>
<td>Hem Cystitis</td>
</tr>
<tr>
<td>ATN-Dehydration</td>
</tr>
<tr>
<td>Congenital Heart</td>
</tr>
<tr>
<td>Fluid Overload</td>
</tr>
<tr>
<td>Neoplasm</td>
</tr>
<tr>
<td>Low Ab</td>
</tr>
<tr>
<td>HUS</td>
</tr>
<tr>
<td>Chronic Renal Dz</td>
</tr>
<tr>
<td>Congestive heart</td>
</tr>
<tr>
<td>Rhabdomyolysis</td>
</tr>
<tr>
<td>ARDS</td>
</tr>
<tr>
<td>Rhabdomyolysis</td>
</tr>
<tr>
<td>Vasculitis</td>
</tr>
<tr>
<td>Nephrotic Med</td>
</tr>
</tbody>
</table>


Table 2. Causes of acute kidney injury

<table>
<thead>
<tr>
<th>Cause</th>
<th>Numbers and percentages = 100</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone marrow transplantation related</td>
<td>27</td>
</tr>
<tr>
<td>Primary renal disease</td>
<td>14</td>
</tr>
<tr>
<td>Dehydration</td>
<td>10</td>
</tr>
<tr>
<td>Nephrotoxic medication</td>
<td>8</td>
</tr>
<tr>
<td>After cardiac surgery</td>
<td>8</td>
</tr>
<tr>
<td>Congenital anomalies of the urinary tract</td>
<td>2</td>
</tr>
<tr>
<td>Multiple etiologic factors with underlying chronic diseases</td>
<td>31</td>
</tr>
</tbody>
</table>

CRRT Diagnoses

Table 5. Principal diagnoses and survival

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

*P (x²) < 0.001.

Table 2 Primary underlying diagnosis

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Admissions</th>
<th>Survivors (%)</th>
<th>Median % FO (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All diagnoses</td>
<td>76</td>
<td>42 (55.3%)</td>
<td>12.9 (0-66.4)</td>
</tr>
<tr>
<td>Primary renal disease</td>
<td>15</td>
<td>10 (66.7%)</td>
<td>4.6 (0-60.4)</td>
</tr>
<tr>
<td>Secondary renal disease</td>
<td>61</td>
<td>32 (52.5%)</td>
<td>16.7 (0-66.4)</td>
</tr>
<tr>
<td>Sepsis without underlying condition</td>
<td>9</td>
<td>6 (66.7%)</td>
<td>21.8 (4.2-41.2)</td>
</tr>
<tr>
<td>Oncology patients (including TLS)</td>
<td>17</td>
<td>13 (76.5%)</td>
<td>7.4 (2.2-64)</td>
</tr>
<tr>
<td>Oncology patients (not including TLS)</td>
<td>6</td>
<td>3 (50%)</td>
<td>21.5 (7.4-64)</td>
</tr>
<tr>
<td>TLS</td>
<td>11</td>
<td>10 (90.1%)</td>
<td>2.9 (0.2-10)</td>
</tr>
<tr>
<td>BMT recipient</td>
<td>12</td>
<td>2 (16.7%)</td>
<td>25.1 (8.5-65.6)</td>
</tr>
<tr>
<td>Cardiac</td>
<td>7</td>
<td>2 (28.5%)</td>
<td>28.2 (0-66.4)</td>
</tr>
<tr>
<td>Liver</td>
<td>5</td>
<td>2 (40%)</td>
<td>22.5 (5-34)</td>
</tr>
<tr>
<td>Other*</td>
<td>11</td>
<td>7 (63.6%)</td>
<td>12.9 (1.5-54.1)</td>
</tr>
</tbody>
</table>

* Central nervous system, n = 3; diabetic ketoacidosis, n = 2; metabolic, n = 2; sphincter gastrointestinal surgery, n = 2; rhabdomyolysis, n = 1; burns, n = 1.
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
Trends in Pediatric RRT

CRRT Increasing

12-US Multicentre ppCRRT
Most include Dialysis

<table>
<thead>
<tr>
<th>Table 2. CRRT technical characteristics(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristic</td>
</tr>
<tr>
<td>----------------</td>
</tr>
<tr>
<td>Modality</td>
</tr>
<tr>
<td>CVVHD</td>
</tr>
<tr>
<td>CVVHDF</td>
</tr>
<tr>
<td>CVVH</td>
</tr>
<tr>
<td>SCUF</td>
</tr>
</tbody>
</table>

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

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

<table>
<thead>
<tr>
<th>Indication</th>
<th>n</th>
<th>Survivors</th>
<th>% Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluid overload and electrolyte imbalance</td>
<td>157</td>
<td>80</td>
<td>51</td>
</tr>
<tr>
<td>Fluid overload only</td>
<td>100</td>
<td>61</td>
<td>61</td>
</tr>
<tr>
<td>Electrolyte imbalance only</td>
<td>44</td>
<td>30</td>
<td>68</td>
</tr>
<tr>
<td>Prevent fluid overload to allow intake</td>
<td>11</td>
<td>7</td>
<td>64</td>
</tr>
<tr>
<td>Other</td>
<td>32</td>
<td>23</td>
<td>72</td>
</tr>
</tbody>
</table>

**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*

### Table 3

<table>
<thead>
<tr>
<th>Variable</th>
<th>Survivors, n = 42</th>
<th>Nonsurvivors, n = 34</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;20% FO</td>
<td>8 (19.1%)</td>
<td>20 (58.8%)</td>
<td>6.1</td>
<td>(2.2-17.0)</td>
<td>.0006</td>
</tr>
<tr>
<td>Sepsis</td>
<td>13 (31%)</td>
<td>29 (85.3%)</td>
<td>12.9</td>
<td>(4.1-41.0)</td>
<td>.0001</td>
</tr>
<tr>
<td>MODS</td>
<td>29 (69%)</td>
<td>34 (100%)</td>
<td>a</td>
<td>a</td>
<td>.0003</td>
</tr>
</tbody>
</table>

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

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

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

• 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

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

UF

D
## Convection vs. Diffusion

Are there advantages of one type of therapy over another?

<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>Cytokines (large)</td>
<td>adsorbed</td>
<td>minimal clearance</td>
</tr>
</tbody>
</table>

*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 \( \sim 8\eta/2r^4 \)
  – So, the biggest and shortest catheter should be best

• Vessel size
  – French \( \sim 3 \times \) 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 effect of vascular access location and size on circuit survival in pediatric continuous renal replacement therapy: A report from the PPCRRT registry

376 Patients
1574 circuits

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

Electron microscopy of polysulfone hemodiafilter with two varieties of anticoagulation 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
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

- 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)
• 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
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