CRRT for the Experience User 1

Claudio Ronco, M.D.
Rolando Claure-Del Granado, M.D.
AKI & CRRT Conference
February, 2015
Dose in CRRT: Key concepts

• What dose I should prescribe?
• Prescribed *versus* delivered
• Factors influencing clearance
• It is not only urea...
• Practical Considerations
Dose in CRRT: Key concepts

• What dose I should prescribe?
  • Prescribed versus delivered
  • Factors influencing clearance
  • It is not only urea...
  • Practical Considerations
CRRT: treatment goals

- Volume control
- Metabolic control
- Solute clearance
- Safe anticoagulation with minimal clotting
Case

- 70 year old female with no past relevant medical history; presents with acute cholecystitis and sepsis. After cholecystectomy she develop hospital acquired pneumonia, and Ceftazidime plus Vancomycin was started. She required vassopressors. By the time of nephrology consultation she developed AKI, with oliguria. She weighs 70 Kg; she was still on antibiotics, and keterolac was been used as analgesia.

- LABS: Na 138, K 6.5, Cl 109, HCO3 16, BUN 60, CrS 4.7, *GA: pH 7.2 PaCO2 40 PaO2 90 with FiO2 21%, Hb 11 , Hto 30%, WBC 12.500, Plq 104.000.

- She had a positive cumulative fluid balance of 6 liters.
Chapter 5.8: Dose of renal replacement therapy in AKI

5.8.1: The dose of RRT to be delivered should be prescribed before starting each session of RRT. (Not Graded) We recommend frequent assessment of the actual delivered dose in order to adjust the prescription. (1B)
Survey of 26 questions

7 questions for IHD and SLED that included:
- target dosage of therapy
- whether and how frequently delivered dose was assessed

9 questions for CRRT
- characterized dose mL/h vs. mL/kg/h
- no target dosage or assessment of delivered dose was evaluate.

Only 21% of practitioners assessed delivered dialysis dose (IHD).
< 20% of practitioners reported using weight-based dosing of CRRT.

Absence of a consistent standard for prescription and monitoring of RRT during AKI.

Table 2. Management of IHD

<table>
<thead>
<tr>
<th>Site</th>
<th>Respondents Using IHD</th>
<th>Treatment Frequency (%)</th>
<th>Median Treatment Duration (hr)</th>
<th>Median BFR (ml/min)</th>
<th>Monitoring of Delivered Dosage (No. of Practitioners)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VA sites</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>5</td>
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<td>38.1</td>
<td>14.1</td>
<td>4.0</td>
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<tr>
<td>B</td>
<td>2</td>
<td>15.9</td>
<td>25.5</td>
<td>31.8</td>
<td>26.8</td>
</tr>
<tr>
<td>C</td>
<td>3</td>
<td>75.7</td>
<td>0.5</td>
<td>23.8</td>
<td>—</td>
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<tr>
<td>D</td>
<td>1</td>
<td>75.0</td>
<td>13.0</td>
<td>12.0</td>
<td>—</td>
</tr>
<tr>
<td>E</td>
<td>4</td>
<td>69.1</td>
<td>12.7</td>
<td>18.2</td>
<td>—</td>
</tr>
<tr>
<td>F</td>
<td>7</td>
<td>65.4</td>
<td>0.3</td>
<td>29.9</td>
<td>1.6</td>
</tr>
<tr>
<td>G</td>
<td>3</td>
<td>60.6</td>
<td>24.4</td>
<td>11.9</td>
<td>—</td>
</tr>
<tr>
<td>H</td>
<td>7</td>
<td>45.9</td>
<td>5.4</td>
<td>22.5</td>
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</tr>
<tr>
<td>I</td>
<td>4</td>
<td>40.6</td>
<td>29.5</td>
<td>18.9</td>
<td>6.0</td>
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<tr>
<td>J</td>
<td>1</td>
<td>69.0</td>
<td>15.0</td>
<td>10.0</td>
<td>5.0</td>
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<tr>
<td>K</td>
<td>6</td>
<td>13.3</td>
<td>14.8</td>
<td>26.7</td>
<td>29.2</td>
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<tr>
<td>L</td>
<td>3</td>
<td>49.5</td>
<td>7.8</td>
<td>24.5</td>
<td>7.3</td>
</tr>
<tr>
<td>M</td>
<td>4</td>
<td>39.4</td>
<td>38.0</td>
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<td>—</td>
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<td>N</td>
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<td>18.2</td>
<td>18.1</td>
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<td>13.3</td>
</tr>
<tr>
<td>O</td>
<td>3</td>
<td>37.5</td>
<td>22.5</td>
<td>35.0</td>
<td>38.0</td>
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<td>5</td>
<td>90.0</td>
<td>—</td>
<td>—</td>
<td>10.0</td>
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<td>all VA</td>
<td>63</td>
<td>0.7</td>
<td>51.4</td>
<td>5.7</td>
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<td>Non-VA sites</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>O</td>
<td>—</td>
<td>88.9</td>
<td>11.1</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>R</td>
<td>4</td>
<td>56.9</td>
<td>15.7</td>
<td>13.7</td>
<td>6.7</td>
</tr>
<tr>
<td>S</td>
<td>6</td>
<td>73.8</td>
<td>2.9</td>
<td>23.1</td>
<td>18.4</td>
</tr>
<tr>
<td>T</td>
<td>7</td>
<td>23.1</td>
<td>2.5</td>
<td>54.4</td>
<td>15.0</td>
</tr>
<tr>
<td>U</td>
<td>13</td>
<td>16.5</td>
<td>11.6</td>
<td>57.2</td>
<td>8.0</td>
</tr>
<tr>
<td>V</td>
<td>5</td>
<td>81.5</td>
<td>—</td>
<td>14.8</td>
<td>3.7</td>
</tr>
<tr>
<td>W</td>
<td>11</td>
<td>77.2</td>
<td>1.8</td>
<td>13.5</td>
<td>3.9</td>
</tr>
<tr>
<td>all non-VA</td>
<td>46</td>
<td>41.8</td>
<td>8.3</td>
<td>36.7</td>
<td>6.8</td>
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<tr>
<td>Combined VA/non-VA sites</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>X</td>
<td>7</td>
<td>12.9</td>
<td>2.2</td>
<td>17.9</td>
<td>41.2</td>
</tr>
<tr>
<td>Y</td>
<td>12</td>
<td>57.8</td>
<td>1.8</td>
<td>29.9</td>
<td>14.2</td>
</tr>
<tr>
<td>all combined</td>
<td>19</td>
<td>0.9</td>
<td>45.5</td>
<td>1.9</td>
<td>26.6</td>
</tr>
<tr>
<td>All sites</td>
<td>128</td>
<td>0.4</td>
<td>45.4</td>
<td>6.4</td>
<td>31.6</td>
</tr>
</tbody>
</table>

*BFR, blood flow rate; IHD, intermittent hemodialysis.
*Site provided aggregate data for all practitioners.
Dose of CRRT

• For most small solutes, concentration in ultrafiltrate approximates that of plasma water.
• Since dialysate flow \(<\) blood flow, equilibration between plasma and dialysate is nearly complete.
• The concentration of small solutes in the effluent is therefore close to that of plasma water.
• Solute clearance therefore approximates effluent flow rate.
Chapter 5.8: Dose of renal replacement therapy in AKI

5.8.4: We recommend delivering an effluent volume of 20–25 ml/kg/h for CRRT in AKI (1A). This will usually require a higher prescription of effluent volume. (Not Graded)
Post-dilutional CVVH

- $K = \text{[effluent flow rate]} \cdot Q_e \cdot (C_e/C_b)$
- Post-dilutional CVVH:
  - $Q_b$ 100 ml/min.; Hto 30%
  - $Q_{ef}$ 1.5 l/h
  - BUN 60 mg/dl
  - FUN 60 mg/dl
- $K_{urea} = 1500 \text{mL/h} \cdot 60/60$
  - = 1500 mL/h
  - = 25 ml/min.
    (21 mL/kg/hr)

- Filtration fraction:
  - $Q_{UF}/Q_p$
  - $Q_p = Q_b \text{ml/hr } \cdot (1\text{-Hto})$
- Filter clotting $FF=25%$
- $FF = 1500 / (6000 \cdot (1-0.30)) = 0.36 \text{ (36%)}$
- Prevent clotting:
  - Increase $Q_b$
  - Use pre-dilution
Dialysis Dose-Outcome trials and dose measurements

<table>
<thead>
<tr>
<th>Reference</th>
<th>Assessment of Dose</th>
<th>Delivered Dose</th>
<th>Mortality Intensive vs Control (%)</th>
<th>Difference in Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ronco et al,12 2000</td>
<td>Ultrafiltration volume in mL/kg/h</td>
<td>35 and 45 mL/kg/h&lt;sup&gt;a&lt;/sup&gt;</td>
<td>20 mL/kg/h&lt;sup&gt;a&lt;/sup&gt;</td>
<td>42 and 43 vs 59&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Schiff et al,2 2002</td>
<td>Frequency (3×/wk vs daily)</td>
<td>Weekly delivered Kt/V = 5.8 (mean Kt/V per session = 0.94)</td>
<td>Weekly delivered Kt/V = 3.0 (mean Kt/V per session = 0.92)</td>
<td>28 vs 46</td>
</tr>
<tr>
<td>Bouman et al,27 2002</td>
<td>Ultrafiltration volume in mL/kg/h</td>
<td>48.2 mL/kg/h</td>
<td>19.5 mL/kg/h</td>
<td>37 vs 46&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>Saudan et al,28 2006</td>
<td>Ultrafiltration volume in mL/kg/h</td>
<td>CVVHDF (24 mL/kg/h replacement fluid + 18 mL/kg/h dialysate)</td>
<td>CVVH (25 mL/kg/h replacement fluid)</td>
<td>46 vs 61&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Tolwani et al,29 2008</td>
<td>Ultrafiltration volume in mL/kg/h</td>
<td>29 mL/kg/h</td>
<td>17 mL/kg/h</td>
<td>64 vs 60&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>Palevsky et al,3 2008</td>
<td>Ultrafiltration volume in mL/kg/h for CRRT and frequency of session &amp; Kt/V for IHD and SLED</td>
<td>IHD, 5.4 sessions/wk; SLED, 6.2 sessions/wk (session Kt/V = 1.3); CRRT, 35.8 mL/kg/h</td>
<td>IHD, 3 sessions/wk; SLED: 2.9 sessions/wk (session Kt/V = 1.3); CRRT, 22 mL/kg/h</td>
<td>53.6% vs 51.5%</td>
</tr>
<tr>
<td>Faulhaber-Walter et al,32 2009</td>
<td>SUN levels</td>
<td>&lt;90 mg/dL</td>
<td>120-150 mg/dL</td>
<td>70.4% vs 70.7%</td>
</tr>
<tr>
<td>Bellomo et al,30 2009</td>
<td>Ultrafiltration volume in mL/kg/h</td>
<td>40 mL/kg/h&lt;sup&gt;a&lt;/sup&gt;</td>
<td>25 mL/kg/h&lt;sup&gt;a&lt;/sup&gt;</td>
<td>44.7% vs 44.7%</td>
</tr>
</tbody>
</table>
Delivered RRT dose and survival

Kellum JA and Ronco C Nature Reviews Nephrology; 2010
Dose in CRRT: Key concepts

- What dose I should prescribe?
- Prescribed *versus* delivered
- Factors influencing clearance
- It is not only urea...
- Practical Considerations
<table>
<thead>
<tr>
<th>Reference</th>
<th>Dialysis Modality</th>
<th>Prescribed</th>
<th>Delivered</th>
<th>% of Delivered Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evanson et al. 1998</td>
<td>IHD</td>
<td>Kt/V 1.25±0.47</td>
<td>Kt/V 1.04±0.49</td>
<td>83.5%</td>
</tr>
<tr>
<td>Evanson et al. 1999</td>
<td>IHD</td>
<td>Kt/V 1.11±0.32</td>
<td>spKt/V 0.9±60.33</td>
<td>86.4 – 75.5%</td>
</tr>
<tr>
<td>Venkataraman et al. 2002</td>
<td>CRRT</td>
<td>24.5±6.7 mL/Kg/h</td>
<td>16.6±5.4 mL/Kg/h</td>
<td>68%</td>
</tr>
<tr>
<td>Tolwani et al. 2008</td>
<td>CRRT</td>
<td>Standard 20 mL/Kg/h</td>
<td>17 mL/Kg/h</td>
<td>85%</td>
</tr>
<tr>
<td>Vesconi 2009 et al.</td>
<td>CRRT</td>
<td>34.3 mL/Kg/h</td>
<td>27.1 mL/Kg/h</td>
<td>79%</td>
</tr>
</tbody>
</table>
Data from 52 critically ill patients, AKI requiring dialysis (Pre-dilution CVVHDF)

Regional citrate anticoagulation.

Filter efficacy was assessed by calculating FUN/BUN ratios q12 hr.

Prescribed urea clearance (K, ml/min) - Eflluent volume rate = Qd (ml/min) + Qr (ml/min) + Qnet (ml/min)

K Estimated = Effluent volume adjusted for effective time of treatment.

K delivered = FUN (mg/dl)/BUN (mg/dl) x effluent volume rate (ml/min)
Reasons for Discontinuing CRRT and Filter efficacy

Table 3. Reasons for stopping CRRT

<table>
<thead>
<tr>
<th>Reasons</th>
<th>Number of Filters</th>
<th>Percentage (%)</th>
<th>FUN/BUN Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factors affecting treatment time without affecting filter function</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D/C for surgical procedures</td>
<td>10</td>
<td>6.3</td>
<td>0.93 (0.92 to 0.99)</td>
</tr>
<tr>
<td>D/C for medical procedures</td>
<td>9</td>
<td>5.7</td>
<td>1.0 (0.95 to 1)</td>
</tr>
<tr>
<td>routine filter changes</td>
<td>16</td>
<td>10.1</td>
<td>0.95 (0.84 to 1.0)</td>
</tr>
<tr>
<td>machine problems</td>
<td>8</td>
<td>5.0</td>
<td>0.97 (0.85 to 1.0)</td>
</tr>
<tr>
<td>transition to IHD</td>
<td>17</td>
<td>10.7</td>
<td>0.96 (0.82 to 0.97)</td>
</tr>
<tr>
<td>venous access clot</td>
<td>6</td>
<td>3.8</td>
<td>0.97 (0.96 to 0.98)</td>
</tr>
<tr>
<td>physician decision</td>
<td>10</td>
<td>6.3</td>
<td>0.98 (0.94 to 1)</td>
</tr>
<tr>
<td>patient or family decision</td>
<td>11</td>
<td>6.9</td>
<td>0.96 (0.94 to 1)</td>
</tr>
<tr>
<td>patient recovery</td>
<td>6</td>
<td>3.8</td>
<td>0.95 (0.92 to 0.99)</td>
</tr>
<tr>
<td>death</td>
<td>3</td>
<td>1.9</td>
<td>0.98 (0.87 to 1.0)</td>
</tr>
<tr>
<td>access change</td>
<td>9</td>
<td>5.7</td>
<td>0.9 (0.87 to 0.95)</td>
</tr>
<tr>
<td>Factors affecting filter function</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>filter clotted</td>
<td>41</td>
<td>25.8</td>
<td>0.89 (0.83 to 0.94)</td>
</tr>
<tr>
<td>filter leak</td>
<td>1</td>
<td>0.63</td>
<td>0.745</td>
</tr>
<tr>
<td>low-sieving concentration polarization</td>
<td>12</td>
<td>7.5</td>
<td>0.86 (0.79 to 1.0)</td>
</tr>
</tbody>
</table>

Claure-Del Granado et al. CJASN, 2011
• **Conclusion:**

“Measured effluent volume normalized for effective treatment time significantly overestimates delivered dose of small solutes in CRRT. To achieve a prescribed dialysis dose, effluent-based dose should be increased by 20-25%* to account for decreases in treatment time and reduced filter efficacy during CRRT.”
Original Article

Solute clearance in CRRT: prescribed dose versus actual delivered dose

William D. Lyndon¹, Keith M. Wille² and Ashita J. Tolwani¹

A

B

Lyndon W et al Nephrol Dial Transplant, 2011
Dose in CRRT: Key concepts

- What dose I should prescribe?
- Prescribed *versus* delivered
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- It is not only urea...
- Practical Considerations
Factors Influencing CRRT Clearances in the ICU

- Patient factors
- Treatment factors
Treatment Related Factors

- Catheter
- Filter
- Time out of therapy
Treatment Related Factors

- Catheter
  - Filter
  - Time out of therapy
Complications, Effects on Dialysis Dose, and Survival of Tunnelled Femoral Dialysis Catheters in Acute Renal Failure

Kada Klouche, MD, PhD, Laurent Amigues, MD, Sebastien Deleuze, MD, Jean-Jacques Beraud, MD, and Bernard Canaud, MD

Pre-dilution CVVHDF
Filter 0.9 m² AN69
Anticoagulation LMW Heparin
Filter change each 72 hrs. or if clotted

Randomized
-15 patients (46 treatments) PNT catheter
-15 patients (46 treatments) ST catheter

Prescribed and delivered clearance was assessed
No difference in Qb
No difference in recirculation rate
ST catheters less catheter related thrombosis and infection

Klouche K et al. Am J Kidney Dis, 2007
Treatment Related Factors

• Catheter
• Filter
  – Down time due to *filter clotting* is the major reason for reduced RRT dose
  – *Concentration polarization* reduces ultrafiltration rate and the filtrate concentrations of various medium / large sized proteins
  – *Convection – Diffusion interactions*
• Time out of therapy
Assessing and Delivering Dialysis Dose in Acute Kidney Injury

Rolando Claure-Del Granado and Ravindra L. Mehta
Division of Nephrology and Hypertension, Department of Medicine, University of California San Diego, San Diego, California

Claure-Del Granado R and Mehta RL. Sem Dialysis; 2011
Post-dilutional CVVH

- $K = [\text{effluent flow rate}] \frac{Q_e}{C_e/C_b}$

- Post-dilutional CVVH:
  - $Q_b$ 100 ml/min.; Hto 30%
  - $Q_{ef}$ 1.5 l/h
  - BUN 60 mg/dl
  - FUN 60 mg/dl

- $K_{urea} = 1500 \text{ mL/h} \times \frac{60}{60}$
  - $= 1500 \text{ mL/h}$
  - $= 25 \text{ ml/min.}$
  - $(21 \text{ mL/kg/hr})$

- Filtration fraction:
  - $\frac{Q_{UF}}{Q_p}$
  - $Q_p = Q_b \text{ ml/hr } \times (1-\text{Hto})$

- Filter clotting $FF = 25$

- $FF = \frac{1500}{(6000 \times (1-0.30))} = 0.36 \text{ (36\%)}$

- Prevent clotting:
  - Increase $Q_b$
  - Use pre-dilution
  - Citrate
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 Barnett⁴, Douglas Blowey⁵, Cheryl Baker⁷, Timothy E. Bunchman⁸ and Stuart L. Goldstein⁷
**Citrate Anticoagulation for Continuous Renal Replacement Therapy in the Critically Ill**

Heleen M. Oudemans-van Straaten  
Department of Intensive Care Medicine, Onze Lieve Vrouwe Gasthuis, Amsterdam, The Netherlands

**Table 2.** Main results of the randomized controlled trial comparing citrate to low-molecular-weight heparin anticoagulation for CVVH presented for the per-protocol patients [4]

<table>
<thead>
<tr>
<th>Event</th>
<th>Citrate (n = 97)</th>
<th>Nadroparin (n = 103)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse events needing discontinuation of study anticoagulant, %</td>
<td>2</td>
<td>19</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Bleeding, %</td>
<td>6</td>
<td>16</td>
<td>0.08</td>
</tr>
<tr>
<td>Circuit survival time (all reasons), h</td>
<td>27 (13–47)</td>
<td>26 (15–43)</td>
<td>0.68</td>
</tr>
<tr>
<td>Renal recovery (all patients), %</td>
<td>69</td>
<td>52</td>
<td>0.02</td>
</tr>
<tr>
<td>Renal recovery (surviving patients), %</td>
<td>97</td>
<td>86</td>
<td>0.08</td>
</tr>
<tr>
<td>Hospital mortality, %</td>
<td>41 (21–51)</td>
<td>57 (48–62)</td>
<td>0.03</td>
</tr>
<tr>
<td>Three-month mortality, %</td>
<td>45 (35–55)</td>
<td>62 (53–72)</td>
<td>0.02</td>
</tr>
</tbody>
</table>
Anticoagulation, delivered dose and outcomes in CRRT: The program to improve care in acute renal disease (PICARD)

Anticoagulation, delivered dose and outcomes in CRRT:
The program to improve care in acute renal disease (PICARD)

<table>
<thead>
<tr>
<th>Type of anticoagulant</th>
<th>Median (IQR) Filter Life in Hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Citrate</td>
<td>48 (20.3-75.0)</td>
</tr>
<tr>
<td>Heparin</td>
<td>15.9 (8.5 - 27.0)</td>
</tr>
<tr>
<td>No anticoagulant</td>
<td>17.5 (9.5 to 32)</td>
</tr>
</tbody>
</table>

* p value < 0.0001

Claure-Del Granado et al Hemodialysis Int, 2014
OPINION

Effluent volume and dialysis dose in CRRT: time for reappraisal

Etienne Macedo, Rolando Claire-Del Granado and Ravindra L. Mehta

Macedo E et al. Nat Rev Nephrol. 2011
Treatment Related Factors

- Catheter
- Filter
- Time out of therapy
The Impact of Down-Time and Filter Efficacy on Delivered Dose of Continuous Renal Replacement Therapy

Pre-dilution/post-dilution CVVHDF

- \( Q_b \) 100 mL/min.; Hto 30%
- \( Q_{uf} \) 1.0 L/hr
- \( Q_d \) 1.0 L/hr
- \( Q_{r,pre} \) 0.5 L/hr
- \( Q_{r,post} \) 0.2 L/hr

Dilution factor:
\[
\frac{Q_b}{(Q_b+Q_r)}
\]

- Pre-dilution CVVH
  \[ K = Q_e \times (C_e/C_b) \times \left[ \frac{Q_b}{(Q_b+Q_r)} \right] \]
  20 mL/min \( \rightarrow \) 17 mL/kg/hr

- Pre-dilution/post-dilution CVVHDF:
  - \( Q_b = 200 \) ml/min = 12000 mL/hr; Hto 30%
  - \( K_{urea} = 2500 \) ml/hr \( \times 1 \times \left[ \frac{12000}{(12000 + 500)} \right] = 2400 \) mL/hr
    = 40 mL/min (34 mL/kg/hr).
  - FF:
    \[
    \frac{1000}{[(12000(1-0.3)) + 500]} = 0.11
    \]
Dose in CRRT: Key concepts

• What dose I should prescribe?
• Prescribed versus delivered
• Factors influencing clearance
• It is not only urea...
• Practical Considerations
KDIGO Clinical Practical Guideline for Acute Kidney Injury

Chapter 5.8: Dose of renal replacement therapy in AKI

5.8.2: Provide RRT to achieve the goals of electrolyte, acid-base, solute, and fluid balance that will meet the patient’s needs. (Not Graded)
Urea clearance as a single parameter to evaluate dose

• A number of studies have suggested a relationship between small-solute control or clearance and patient outcomes during acute IHD.

• In the 1950s and 1960s, it was conclusively demonstrated during the Korean and Vietnam wars that IHD saved lives
The marker solute (urea) cannot and does not represent all the solutes that accumulate in AKI.

Its kinetics and volume of distribution are also different from those of the solutes of interest.

Its removal during CRRT is not representative of the removal of other solutes.
Dialysis dose in acute kidney injury and chronic dialysis

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Centre for Nephrology, University College London Medical School, Royal Free Campus, London NW3 2PF, UK (AD); and Renal Unit, Lister Hospital, Stevenage, Hertfordshire, UK (KF)

Hours to days
Months to years
Years to decades

Increasing molecule size

K⁺, H⁺, Na⁺, H₂O
Small nitrogenous solute
Middle-sized molecules

Relevant study
VA/NIH² RENAL¹
NCDS study³
MPO study¹¹

HEMO study⁸

Davenport and Farrington Lancet; 2010
618 patients enrolled in a prospective multicenter observational study (PICARD).

Fluid overload was defined as more than a 10% increase in body weight relative to baseline.

\[
\left( \sum \text{daily (fluid intake (L) – total output (L))/body weight (in kilograms)} \right) \times 100.
\]

Dialyzed patients, survivors had significantly lower fluid accumulation when dialysis was initiated compared to non-survivors after adjustments for dialysis modality and severity score.

Non-dialyzed patients, survivors had significantly less fluid accumulation at the peak of their serum creatinine.
Prospective observational study. 297 children from 13 centers across the United States.

Fluid overload from ICU admission to CRRT initiation, defined as a % equal to (fluid in [L] – fluid out [L])/(ICU admit weight [kg]) x 100%.

Patients who developed 20% fluid overload at CRRT initiation had significantly higher mortality. Adjusted mortality OR was 1.03 (95% CI, 1.01-1.05)

Sutherland et al. AJKD; 2010
### Proposed parameters for Dose Assessment

**TABLE 2. Proposed parameters for delivered dose assessment**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Measurement</th>
<th>Tools</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Solute</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Very small waste products</td>
<td>$K^+$, $Na^+$, Phosphate $H^-$</td>
<td>Blood levels of $K$, $Na$, $PO_4$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Phosphate clearance</td>
</tr>
<tr>
<td></td>
<td></td>
<td>pH, $HCO_3$, AG, SIDeff,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SIDapp, SIG, Delta gap, Delta ratio.</td>
</tr>
<tr>
<td>Small waste products</td>
<td>Urea</td>
<td>Clearance (ml/minutes)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EKR (ml/minutes)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Std$Kt/V$</td>
</tr>
<tr>
<td>Middle-sized molecules</td>
<td>Serum $\beta_2$ Microglobulin</td>
<td>$\beta_2$ Microglobulin clearance</td>
</tr>
<tr>
<td>Fluid</td>
<td>Weight (kg)</td>
<td>Weight changes</td>
</tr>
<tr>
<td></td>
<td>Inputs–Outputs</td>
<td>Fluid accumulation</td>
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<tr>
<td></td>
<td>BIA</td>
<td>Fluid overload</td>
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<tr>
<td></td>
<td>BNP</td>
<td>BIVA</td>
</tr>
<tr>
<td></td>
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<td>BNP profile</td>
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</tbody>
</table>
Dose in CRRT: Key concepts

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Dose in CRRT: Practical considerations

- Clearances should be measured as part of routine care delivery as estimated clearances do not equate delivered.

- Optimizing RRT clearances requires constant assessment and adjustment for operational characteristics and treatment factors.

- Delivered Dose is less than Prescribed and consequently prescribed dose should compensate for the anticipated reduction (approximately 15-25%).

- Solute Clearances are not the sole measure of dialysis adequacy. Fluid removal and fluid balance are equally if not more important parameters to be monitored.