Fluid Management in Critically Ill Patients with Acute Kidney Injury

Nithin Karakala
Assistant Professor
Nephrology, MUSC
Objective

• Volume resuscitative strategies in critically ill and their impact.
• Crystalloid or colloid?
• Compare balanced and unbalanced crystalloids.
International Guidelines for Management of Severe Sepsis and Septic Shock: 2012

Protocolized, quantitative resuscitation of patients with sepsis-induced tissue hypoperfusion.

   a) Central venous pressure 8–12 mm Hg
   b) Mean arterial pressure (MAP) ≥ 65 mm Hg
   c) Urine output ≥ 0.5 mL/kg/hr
   d) Central venous (superior vena cava) or mixed venous oxygen saturation 70% or 65%, respectively (grade 1C).

Fluid Therapy of Severe Sepsis.

   a) Recommend crystalloids be used as the initial fluid of choice in the resuscitation of severe sepsis and septic shock (grade 1B).
   b) Recommend an initial fluid challenge to achieve a minimum of 30 mL/kg of crystalloids. More rapid administration and greater amounts of fluid may be needed in some patients (grade 1C).
   c) Fluid challenge technique be applied wherein fluid administration is continued as long as there is hemodynamic improvement (grade UG)
Volume Resuscitation in Critically Ill

Sepsis

- Decreased effective circulatory volume
- Increased microvascular permeability
- Venous dilatation

Decreased myocardial contractility

- Decreased renal perfusion
- Decreased oxygen delivery
- Hypoxia and ischemia

Acute tubular injury

Activation of sympathetic pathway

Renal vasoconstriction

Changing What’s Possible
# Early Goal-Directed Therapy in the Treatment of Severe Sepsis and Septic Shock

Emanuel Rivers, M.D., M.P.H., Bryant Nguyen, M.D., Suzanne Havstad, M.A., Julie Ressler, B.S., Alexandria Muzzin, B.S., Bernhard Knoblich, M.D., Edward Peterson, Ph.D., and Michael Tomlanovich, M.D., for the Early Goal-Directed Therapy Collaborative Group

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Intervention</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluids 0-6 hrs</td>
<td>3.5 L</td>
<td>5 L</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fluids 7-72 hrs</td>
<td>10.5 L</td>
<td>8.6 L</td>
<td>0.01</td>
</tr>
<tr>
<td>Fluids 0-3 days</td>
<td>13.3 L</td>
<td>13.4 L</td>
<td>0.73</td>
</tr>
<tr>
<td>Mortality</td>
<td>59 %</td>
<td>38 %</td>
<td>0.009</td>
</tr>
</tbody>
</table>


- A greater degree of positive fluid balance both early in resuscitation (12 hrs) and up to 4 days is associated with an increased risk of mortality in septic shock.
- Optimal survival occurred with a positive fluid balance of approximately 3 L at 12 hrs.

Daily fluid balance

- The daily fluid balance correlates closely with fluid input, but not with urine output.

A

12 hours

R = 0.20

B

Day 4

R = 0.02

- Weak correlation between CVP and degree of fluid overload

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- A Central Venous Pressure of <8 mmHg at 12 hrs is Associated With Improved survival.
Fluid accumulation, recognition and staging of acute kidney injury in critically-ill patients Critical Care 2010, 14:R82 (PICARD)

- In critically-ill patients, the dilution of SCr by fluid accumulation may lead to late diagnosis and underestimation of the severity of AKI.

- Correction of sCr for fluid balance
  - Adjusted creatinine = sCr x correction factor
  - Correction factor = (admission wt (kg) x 0.6 + Σ (daily fluid balance (L))) / admission wt x 0.6.
A positive fluid balance is associated with a worse outcome in patients with acute renal failure (Payen et al, Critical Care Vol 12 No 3).

- Acute renal failure is associated with significantly greater degree of fluid overload.

![Graph showing fluid balance over days for different groups: Late ARF, Early ARF, No ARF.](image-url)
Fluid balance and urine volume are independent predictors of mortality in acute kidney injury. Critical Care 2013, 17:R14 (NEFROlogia e Cura INTensiva Study Group)

- On multivariate analysis, Mean Fluid Balance was an independent predictor of 28-day mortality (HR 1.67, 95%CI 1.33-2.09 per L/day; P<0.001)
Fluid accumulation, survival and recovery of kidney function in critically ill patients with acute kidney injury (KI 2009: 76, (PICARD))

- %FO > 10 associated with 2 fold increase in mortality.
- %FO > 10 at cessation of dialysis associated with 2.5 fold increase in mortality.

### Table: Fluid Accumulation and Mortality

<table>
<thead>
<tr>
<th>Volume</th>
<th>30 d mortality</th>
<th>80 d mortality</th>
<th>Death at hospital discharge</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overload</td>
<td>37%</td>
<td>46%</td>
<td>48%</td>
</tr>
<tr>
<td>No Overload</td>
<td>25%</td>
<td>32%</td>
<td>35%</td>
</tr>
<tr>
<td>P Value</td>
<td>0.02</td>
<td>0.006</td>
<td>0.01</td>
</tr>
</tbody>
</table>

### Graph: Percentage of dialysis days with fluid overload

- P-value for linear trend < 0.0001

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The Importance of Fluid Management in Septic Shock

CHEST 2009; 136:102–109 Murphy

Adequate early Resuscitation
Inadequate early Resuscitation

Conservative late fluid
- Adequate: 18.3%
- Inadequate: 41.9%

Liberal late fluid
- Adequate: 56.1%
- Inadequate: 77.1%

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In patients treated with CRRT negative mean daily fluid balance was consistently associated with improved survival.

During intensive care unit stay, mean daily fluid balance among survivors was -234 mL/day compared with +560 mL/day among nonsurvivors.

- Non survivors had significantly higher % FO.
- In children with ≥ 3 organ failure FO was an independent predictor of mortality, where pressor use and intubation was not associated with mortality.

<table>
<thead>
<tr>
<th>Control Group</th>
<th>Aggressive Diuresis Group</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cumulative Fluid (ml)</td>
<td>8,027</td>
<td>-1,451</td>
</tr>
<tr>
<td>Mortality %</td>
<td>49.1</td>
<td>28.1</td>
</tr>
<tr>
<td>ICU LOS days</td>
<td>37.1</td>
<td>23.6</td>
</tr>
<tr>
<td>Duration of CRRT</td>
<td>6.2</td>
<td>10</td>
</tr>
</tbody>
</table>

![Graphs showing daily fluid balance and cumulative fluid balance over time with statistical comparisons.](image)
• Renal SOFA was not different in both groups.
• Aggressive diuresis is associated with smaller increase in IAP
• Is volume overload the cause of increased mortality?

• We will not know without a prospective randomized trial.
Albumin Vs Crystalloids
Synthesis: 15 g/d

Degradation: 15 g/d

Extravascular

- 25 g/l
- 250 g

Lymphatics

40 g/l
120 g

5%
Human albumin administration in critically ill patients: systematic review of randomized controlled trials
Cochrane Injuries Group Albumin Reviewers, BMJ 1998

- Relative risk of death with albumin administration was 1.68 (1.26 to 2.23).
- For every 17 critically ill patients treated with albumin there is 1 additional death.
• 30 studies were included in this systematic review.
• Total number of patients 1419.
• In 5 studies albumin was not used as volume expander but was added to TPN.
• Only 1 study included septic patients, in which there was no significant change in mortality in patients treated with albumin.
Saline or Albumin for Fluid Resuscitation in Patients with Traumatic Brain Injury

The SAFE Study Investigators NEJM 2007

- 28 day mortality in patients with traumatic brain injury 83.3% in albumin group vs 75.4% in crystalloid group.

P = 0.007
A Comparison of Albumin and Saline for Fluid Resuscitation in the Intensive Care Unit  

The SAFE Study Investigators  
NEJM 2004

- 6997 patients included in the study.
- Severe sepsis 1218 patients.

- No difference in 28 day mortality in the albumin group compared to NS 20.9% vs 21.1%.
A Comparison of Albumin and Saline for Fluid Resuscitation in the Intensive Care Unit

The SAFE Study Investigators

- Sever sepsis RR 0.87
- Trauma with brain injury RR 1.62 (24.5 vs 15.1)
Is there use for albumin in critically ill patients with Hypoalbuminemia?

- Albumin group: 25 grams of albumin/d for 3 days
- Control group: Crystalloids

J Chin Med Assoc May 2009
Chih-Dou Chou
• Albumin infusion improved mortality in septic patients with serum albumin < 2 mg/dl.
• The benefit did ceased to exist when serum albumin > 2 mg/dl
Albumin administration improves organ function in critically ill hypoalbuminemic patients Crit Care Med 2006 MJ Dubois

- In critically ill patients with serum albumin <3.1 mg/dl treatment with albumin was associated with significant improvement in SOFA score.
IS NORMAL SALINE REALLY NORMAL?

Balanced Vs Unbalanced solutions
# History of Intravenous Fluids

<table>
<thead>
<tr>
<th>Year</th>
<th>Name of Solution</th>
<th>Constituents</th>
<th>Modern composition (mmol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1832</td>
<td>Latta’s solution 1</td>
<td>2 drachms muriate of soda, 2 scruples carbonate of soda, 60 ounces of water</td>
<td>Na 106, Cl 78, HCO₃ 14</td>
</tr>
<tr>
<td>1832</td>
<td>Latta’s solution 2</td>
<td>2-3 drachms muriate of soda, 2 scruples subcarbonate of soda, 6 pints of water</td>
<td>Na 48-68, Cl 39-59, HCO₃ 9</td>
</tr>
<tr>
<td>1849</td>
<td>Henry Howlett’s solution</td>
<td>1 drachm common salt, half drachm sulphate of potash, 1 quart water</td>
<td>Na 58, Cl 58, K 19, SO₄ 10</td>
</tr>
<tr>
<td>1883</td>
<td>Ringer’s solution</td>
<td>6 g sodium chloride, 3.1 g sodium lactate, 300 mg potassium chloride and 200 mg calcium chloride in 1000 ml water</td>
<td>Na 130, K 4, Ca 1.5, Cl 109, lactate 28 mmol/l</td>
</tr>
<tr>
<td>1932</td>
<td>Hartmann’s solution</td>
<td>6 g sodium chloride, 3.22 g sodium lactate, 400 mg potassium chloride and 270 mg calcium chloride in 1000 ml water</td>
<td>Na 131, K 5, Ca 2, Cl 111, lactate 29 mmol, in 1 l water</td>
</tr>
<tr>
<td>1921</td>
<td>Hamburger</td>
<td>9 g sodium chloride in 1 l water</td>
<td>Na 154, Cl 154</td>
</tr>
</tbody>
</table>
### Chemical composition of commonly used IV fluids

<table>
<thead>
<tr>
<th></th>
<th>Plasma</th>
<th>NS</th>
<th>Ringer’s lactate</th>
<th>Ringer’s acetate</th>
<th>Plasma-Lyte 148</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Osmolality mOsm/l</strong></td>
<td>290</td>
<td>308</td>
<td>273</td>
<td>277</td>
<td>294</td>
</tr>
<tr>
<td><strong>Na (mEq/l)</strong></td>
<td>140</td>
<td>154</td>
<td>130</td>
<td>145</td>
<td>140</td>
</tr>
<tr>
<td><strong>Cl (mEq/l)</strong></td>
<td>100</td>
<td>154</td>
<td>109</td>
<td>127</td>
<td>98</td>
</tr>
<tr>
<td><strong>K (mEq/l)</strong></td>
<td>4</td>
<td>0</td>
<td>4</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td><strong>Ca (mEq/l)</strong></td>
<td>5</td>
<td>0</td>
<td>3</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td><strong>Mg (mEq/l)</strong></td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td><strong>Lactate (mmol/l)</strong></td>
<td>2</td>
<td>0</td>
<td>28</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Gluconate (mmol/l)</strong></td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>23</td>
</tr>
<tr>
<td><strong>Acetate (mmol/l)</strong></td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>24</td>
<td>27</td>
</tr>
</tbody>
</table>
Effect of balanced and unbalanced solutions on renal function
Effects of NS infusion in healthy volunteers

Randomized, Controlled, Double-Blind Crossover Study.
NS and Plasma-Lyte 148

Annals of Surgery July 2012, Chowdhury
Renal artery flow velocity and renal cortical perfusion measured by Phase contrast MRI.

Annals of Surgery July 2012, Chowdhury
Time to micturition following 50 ml/kg bolus

**Time to first Micturation**

<table>
<thead>
<tr>
<th></th>
<th>Female (n=5)</th>
<th>Male (n=11)</th>
<th>M+F (n=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NS</td>
<td>133±39</td>
<td>79±37</td>
<td>106±11</td>
</tr>
<tr>
<td>LR</td>
<td>80±14</td>
<td>69±40</td>
<td>75±10</td>
</tr>
</tbody>
</table>

Anesth Analg 1999, Williams
Regulation of renal blood flow by plasma Chloride

- Chloride rich solutions cause significant decrease in RBF.

J. Clin. Invest 1983,
### Table: Comparison of Control and Intervention Periods

<table>
<thead>
<tr>
<th></th>
<th>Control Period</th>
<th>Intervention Period</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>NS (l/patient)</td>
<td>3.2</td>
<td>0.06</td>
<td>0.16</td>
</tr>
<tr>
<td>Hartmann (l/patient)</td>
<td>0.6</td>
<td>4.1</td>
<td></td>
</tr>
<tr>
<td>Chloride (mEq/patient)</td>
<td>694</td>
<td>496</td>
<td></td>
</tr>
</tbody>
</table>

### Graph: Incidence of Risk, Injury, Failure, Injury and Failure, and RRT

#### JAMA, October 17, 2012, YONUS

**Changing What’s Possible**

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**MUSC Medical University of South Carolina**
Fluid selection during renal transplant

24 h Cr Cl

4-h UO

Serum Creatinine

D 3 SCr 1 Wk SCr

NS (n=26) LR (n=25)

NS (n=26) LR (n=25)

NS (n=26) LR (n=25)
Balanced Vs Unbalanced solutions in septic shock

In Hospital mortality

Septic Shock

% of treated patients

Balanced Fluids
Unbalanced Fluids

RRT
AKI

Absolute In-Hospital Mortality

Percent of Total Fluid that is Balanced By Day 2

95% CI
Adjusted Mortality (Marginal Fixed Effects)

CCM July 2014, Raghunathan
• Patients treated with unbalanced solutions received more buffer solution and blood transfusion.
• There was higher prevalence lactic acidosis and need for dialysis in patients treated with unbalanced crystalloid solutions.
Unbalanced Solution and Bleeding risk

The risk of major hemorrhage following cardiac surgery was lower in patients who received balanced fluids vs ND (OR 0.7; 0.47-1.2)
Summary

• Volume resuscitation is a critical step in the management of critically ill patients.
• Volume overload should be identified as a major complication and should be managed promptly.
• Albumin should be considered appropriate patient population.
• Balanced crystalloids may be a safer alternative to normal saline.