Fluid Management of the Critically Ill: When, How Much and What?

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Barts Health NHS Trust
Too much fluid is bad...
Figure 2 Cumulative fluid balance in survivors and non-survivors in the first seven days of ICU stay (mean ± SEM). *$P=0.015$; **$P<0.01$. SEM, standard error of the mean.
Fluid overload is associated with an increased risk for 90-day mortality in critically ill patients with renal replacement therapy: data from the prospective FINNAKI study

Suvi T Vaara¹, Anna-Maija Korhonen¹, Kirsi-Maija Kaukonen¹, Sara Nisula¹, Outi Inkinen², Sanna Hoppu², Jouko J Laurila³, Leena Mildh¹, Matti Reinikainen⁷, Vesa Lund⁶, Ilkka Parviainen⁷ and Ville Pettitla¹,³, for The FINNAKI study group

Vaara et al. Critical Care 2012, 16: R197
http://ccforum.com/content/16/5/R197

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![Graph showing cumulative survival over days from ICU admission with and without fluid overload. Log-rank test P < 0.001.](image)

![Bar chart showing 90-day mortality (%) by fluid accumulation percentage.](image)

*Figure 3 Ninety-day mortality according to the percentage of fluid accumulation prior to renal replacement therapy initiation. Comparison across groups P < 0.001.*
Pathological effects of fluid overload in organ systems

An observational study fluid balance and patient outcomes in the randomized evaluation of normal vs. augmented level of replacement therapy trial*

The RENAL Replacement Therapy Study Investigators

Crit Care Med 2012 Vol. 40, No. 6
All demonstrate harm associated with fluid overload or benefit from its resolution.

Table 1: Studies relating fluid balance to outcomes in AKI since 2008

<table>
<thead>
<tr>
<th>Study</th>
<th>Setting</th>
<th>n</th>
<th>Design</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Teixeira et al. (2013)²²</td>
<td>Critically ill adults</td>
<td>601</td>
<td>Secondary analysis of a</td>
<td>In AKI, higher fluid balance and lower urine volume independently associated with 28-day mortality</td>
</tr>
<tr>
<td>Askenazi et al. (2013)²⁵</td>
<td>Near-term/term sick neonates</td>
<td>58</td>
<td>Prospective single-centre</td>
<td>AKI associated with a net-positive fluid balance and higher mortality</td>
</tr>
<tr>
<td>Basu et al. (2013)³¹</td>
<td>Paediatric patients undergoing arterial</td>
<td>92</td>
<td>Retrospective single-centre</td>
<td>AKI associated with higher postoperative day 1 fluid balance and independently associated with prolonged duration of ventilation and hospitalization</td>
</tr>
<tr>
<td>Hazle et al. (2013)¹³¹</td>
<td>Infants undergoing congenital heart</td>
<td>49</td>
<td>Prospective single-centre</td>
<td>Fluid overload might be an important risk factor for morbidity at all severities of AKI</td>
</tr>
<tr>
<td>Vaara et al. (2012)²⁷</td>
<td>Critically ill adults with AKI requiring</td>
<td>283</td>
<td>Prospective multicentre</td>
<td>Fluid overload at RRT initiation doubled crude 90-day mortality and remained a significant risk for death after adjustment for demographics and illness severity</td>
</tr>
<tr>
<td>Prowie et al. (2012)²⁷</td>
<td>Studies of perioperative GDT reporting</td>
<td>24</td>
<td>Meta-analysis</td>
<td>GDT significantly reduced risk of postoperative AKI. However, only GDT protocols that were overall fluid neutral were associated with a beneficial renal outcome</td>
</tr>
<tr>
<td>Selewski et al. (2012)¹²²</td>
<td>Paediatric ICU patients requiring ECMO</td>
<td>53</td>
<td>Retrospective single-centre</td>
<td>Fluid overload at RRT initiation significantly lower in survivors. Correction of fluid overload after initiation of RRT did not improve outcome</td>
</tr>
<tr>
<td>Bellomo et al. (2012)²⁷</td>
<td>Critically ill patients requiring RRT</td>
<td>1,453</td>
<td>Retrospective analysis of a</td>
<td>Negative mean daily fluid balance on RRT consistently associated with risk of death, survival time, RRT-free days, and ICU and hospital-free days</td>
</tr>
<tr>
<td>Dass et al. (2012)³⁶</td>
<td>Cardiovascular surgery patients</td>
<td>94</td>
<td>Retrospective analysis of a</td>
<td>Positive fluid balance &gt; 849 ml in early postoperative period associated with significantly elevated AKI risk</td>
</tr>
<tr>
<td>Kambhampti et al. (2012)²⁹</td>
<td>Adult patients undergoing cardiovascular surgery</td>
<td>100</td>
<td>Prospective single-centre</td>
<td>Progressive severity of positive fluid balance associated with increased AKI risk</td>
</tr>
<tr>
<td>Heung et al. (2012)³⁸</td>
<td>Patients with AKI requiring initiation of RRT</td>
<td>1.70</td>
<td>Retrospective single-centre</td>
<td>High fluid overload at RRT initiation predicted worse renal recovery at 1 year</td>
</tr>
<tr>
<td>Selewski et al. (2011)¹³³</td>
<td>Critically ill children requiring RRT</td>
<td>1.13</td>
<td>Retrospective single-centre</td>
<td>Fluid overload at initiation of RRT significantly greater in non-survivors</td>
</tr>
<tr>
<td>Grams et al. (2011)²⁵</td>
<td>Critically ill patients with lung injury enrolled into FACTT</td>
<td>1,000</td>
<td>Retrospective analysis of multicentre RCT</td>
<td>A positive fluid balance after AKI strongly associated with mortality in crude and adjusted analyses; post-AKI diuretic therapy associated with 60 day survival</td>
</tr>
<tr>
<td>Fülöp et al. (2010)³⁴</td>
<td>Critically ill adults with AKI requiring RRT</td>
<td>81</td>
<td>Retrospective single-centre</td>
<td>Volume related weight gain &gt; 10% and oliguria significantly associated with mortality in multivariable models adjusting for illness severity and diagnosis</td>
</tr>
<tr>
<td>Sutherland et al. (2010)³⁶</td>
<td>Critically ill children with AKI requiring RRT</td>
<td>297</td>
<td>Prospective observational study</td>
<td>≥20% fluid overload at CRRT initiation associated with higher mortality than 10–20% fluid overload, in turn associated with higher mortality than &lt; 1.0% fluid overload; association between degree of fluid overload and mortality remained after adjusting for intergroup differences in severity of illness</td>
</tr>
<tr>
<td>Bouchard et al. (2009)³¹</td>
<td>Critically ill adults with AKI</td>
<td>618</td>
<td>Secondary analysis of a</td>
<td>In patients with AKI &gt; 10% fluid overload independently associated with 60-day mortality; &gt; 10% fluid overload at peak serum creatinine associated with non-recovery of renal function</td>
</tr>
<tr>
<td>Payen et al. (2008)³⁰</td>
<td>Patients enrolled in the SOAP study</td>
<td>3,147</td>
<td>Secondary analysis of a</td>
<td>Fluid overload an independent risk factor for 60-day mortality in AKI; patients not developing AKI achieved a mean neutral to negative daily fluid balance; AKI associated with daily fluid accumulation</td>
</tr>
</tbody>
</table>

Abbreviations: AKI, acute kidney injury; CRRT, continuous RRT; ECMO, extra-corporeal membrane oxygenation; GDT, goal-directed therapy; ICU, intensive care unit; RCT, randomized controlled trial; RRT, renal replacement therapy.
Questions

• To what extent is fluid overload a marker of illness severity (measure of unknown confounders) and to what extent an avoidable cause of iatrogenic morbidity and mortality?

• Does fluid overload itself contribute to the initiation or persistence of AKI?
  – Can we treat this?

• Does the avoidance or treatment of fluid overload with RRT (or diuretics) improve outcomes?
  – If so when?
Section 5: Dialysis Interventions for Treatment of AKI

5.1.1: Initiate RRT emergently when life-threatening changes in fluid, electrolyte, and acid-base balance exist. (Not Graded)

5.1.2: Consider the broader clinical context, the presence of conditions that can be modified with RRT, and trends of laboratory tests—rather than single BUN and creatinine thresholds alone—when making the decision to start RRT. (Not Graded)

5.2.1: Discontinue RRT when it is no longer required, either because intrinsic kidney function has recovered to the point that it is adequate to meet patient needs, or because RRT is no longer consistent with the goals of care. (Not Graded)

5.2.2: We suggest not using diuretics to enhance kidney function recovery, or to reduce the duration or frequency of RRT. (2B)

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)

5.8.3: We recommend delivering a Kt/V of 3.9 per week when using intermittent or extended RRT in AKI. (1A)

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)
Fluid overload and interstitial oedema may contribute to the maintenance of AKI.
Association between systemic hemodynamics and septic acute kidney injury in critically ill patients: a retrospective observational study

Critical Care 2013, 17:R278  doi:10.1186/cc13133

Matthieu Legrand (matthieu.m.legrand@gmail.com)
Systematic approach to fluid management in critical illness

• Resuscitate appropriately early
• Avoid need for removal as much as possible by then appropriately limiting intake
• Ultrafiltration as a component in an active fluid management strategy
• Indication of potentially inadequate oxygen delivery
  • New or worsening organ dysfunction
  • Lactic acidosis
  • Clinical examination
  • Measures of tissue oxygenation (Near Infra-red Spectrocopy, Gastric tonometry)

• Measures of Cardiac Output / Tissue Perfusion
  • Cardiac index
  • Stroke volume
  • Ejection volume
  • Venous saturation of oxygen
  • Microcirculatory imaging
Measures of Potential Volume Responsiveness

- Stroke volume or pulse pressure variation
- Echocardiography
- Passive straight leg raising
- Haemodynamic response to fluid challenge
- Central venous or pulmonary artery pressure
- Real-time haematocrit changes to fluid removal
Quantification of fluid overload

- Clinical Examination
- Serial Weights
- Cumulative Fluid Balance

- Chest X-ray
- Oxygenation indices
- Lung Ultrasound
- Intra-abdominal pressure

- Echocardiography
- Bioimpedance body composition analysis
Goals in mechanical fluid removal

- Resolve fluid overload and its adverse effects on organ function
- Allow necessary interventions
  - Nutrition
  - Drugs
- Prevent overt hypovolaemia
  - Secondary ischaemic injury
  - Adverse neuroendocrine responses
- Avoid complications of RRT
It is possible to be both fluid overloaded and volume responsive

• Response needs to be tailored to
  – Stage of and severity of illness
  – Acute and chronic organ dysfunction
  – Response to fluid administration or removal
Decisions in prescribing ultrafiltration

• Goal (Long term)
  – Extent of fluid overload
  – “Euvolaemia”

• Tolerance of fluid removal (Short term)
  – Rate of removal
  – Rate of vascular refilling
  – Ability of circulation to tolerate transient reduction in intravascular volume
Differing clinical circumstances demand different rates of fluid removal


British journal of anaesthesia 113: 764-771
Conclusions

• Fluid overload is a common occurrence in the critically ill and is linked to adverse outcomes in particular in association with AKI

• Limiting or resolving fluid overload may require earlier recourse to RRT

• Prescribing fluid removal requires attention to
  – Total fluid excess
  – Rate of vascular refilling
  – Haemodynamic stability

• Treatment will need to be individualized and responses frequently reassessed
Methods to guide UF in CRRT
Detection of Recurrent Renal Injury

- Assessment of the target fluid balance and appropriate rate of fluid removal in AKI is challenging

- Absolute serum creatinine provides little information on underlying renal function in critical illness and almost none in patients on RRT

- Renal biomarkers might also allow detection of continued or recurrent renal injury during recovery from AKI, indicating a need for close attention to haemodynamic stability and nephrotoxic medication

- Higher plasma neutrophil gelatinase-associated lipocalin at commencement of RRT has been associated with increased risk of non-recovery of renal function, while a panel of urine biomarkers can improve clinical risk prediction for recovery of renal function after AKI

Monitoring for Fluid removal:

• Bioimpedance analysis techniques
  – quantify the expansion of extracellular and intracellular fluid volume
  – *Quantification of Fluid Overload*

• Relative blood volume monitoring
  – Real-time monitoring of plasma refilling during ultrafiltration is possible using real-time monitoring of blood haematocrit
  – *Tolerance of Fluid Removal*
Bioimpedance

Fricke's circuit
Two parallel electrical conductors:
\[ R_{(ECW)}: \text{H}_2\text{O-Na} \]
\[ R_{(ICW)}: \text{H}_2\text{O-K} \]
isolated by a cell membrane \((X_C)\)
Body Weight

Fat Free Mass (100%)

- Fat mass
- Body Cell Mass
- Extracellular Water (~30%)
- Intracellular Water (~30%)
- Visceral protein
- Bone Mineral (~7%)
Bioimpedance Vector Analysis

- Reactance $X_c$ (Ω)

Phase angle

Impedance $Z$ (Ω)

Resistance $R$ (Ω)

Frequency increases

$R_\infty$ to $R_o$
Relative Blood Volume

Diagnosis and Management of Fluid Overload in Heart Failure and Cardio-Renal Syndrome: The “5B” Approach

Claudio Ronco, MD,* Manish Kaushik, MD,* Roberto Valle, MD,† Nadia Aspromonte, MD,‡ and W. Frank Peacock IV, MD§

RBV MEASUREMENT METHODS

Optical Methods  US Tr. Time  Conductivity  Viscosity

Ab  Sc

Intensity  Time  Conductivity  Intensity

Het %  Het %  Het %  Het %

Seminars in Nephrology, Vol 32, No 1, January 2012, pp 129-141
BIA & RBV In Combination
(maintenance HD - high UF rate)
Pre-procedural R/H ratios were significantly higher in patients with CI-AKI than without CI-AKI, indicating lower fluid volume in the patients with CI-AKI.

Patients who presented with poor BIVA-estimated fluid volume according to R/H ratio had a 3 times higher incidence of CI-AKI (p = 0.002)
Case #1: Managing Fluid Overload in Critical Illness with CRRT
75yr Male Acute Severe Pancreatitis (Gallstone)

- ICU day 10
- Mechanically ventilated, FiO₂ 0.5, PEEP 10 cmH₂O
- Noradrenaline 0.4µg/kg/min
- Dobutamine 5µg/kg/min
- Urine output 5-15ml/hr
- Creatinine 360µmol/L
- Albumin 22g/L
- Intra-abdominal pressure 25mmHg
- ICU cumulative fluid balance +15L
Multi-frequency BIA (5, 50, 100, 200kHz)
BIA measurements

- TBW 50L (Normal 41L by Watson Formula)
- ECW 30L (Normal 18.5L as 45% of TBW)
- ICW 20L (Normal 22.5 as 55% of TBW)
- ECW:ICW 1.5:1 (Normal 0.8)
- 22% Fluid Overload
- Plan UF ~5-10L over 4 days
Day 13

- 7.5L UF over 3 days
- Noradrenaline and Dobutamine off in 36h
- Pressure support ventilation with falling oxygen requirement
- IAP fell to 15mmHg
- UO ~15ml/hr
Day 14-15

- Raised inflammatory markers
- Back on Noradrenaline
- ScVO$_2$ 45%
- SVV 16%
- >10% increase in SV with filling

- New sepsis
- Volume responsive as expected
- New peri-pancreatic collections on CT
- 2.8L fluid given back
Fluid Balance (ml)
Total Body Water (BIA)
Fluid Balance (ml)

Inclusive of 500ml/day insensible losses

TBW (L)
Fluid Balance (ml)
Inclusive of 500ml/day insensible losses

ECW (L)
24h Fluid Balance vs. ΔExtra-cellular water

\[ r^2 = 0.48 \]
Bioimpedance - Conclusions

• Performance appears variable – occasionally very good
• There is a lack of easily applicable gold standard for body fluid assessment
• Plasma volume is a undetermined
• Plasma electrolytes and fluid collections are a challenge

• Can we set a cut off maybe something equivalent to 10% FO as a target for BIA guided therapy??
• We would need to assess this prospectively
Case #2: RRT Prescription in Severe Uraemia

- 22 yr old man 182cm
- Previous fit university rugby player
- Unwell and progressively weak over 1 year
- Saw family practitioner: BP 200/105

- Bloods
  - Creatinine 2100µmol/L (24mg/dl)
  - Urea 75mmol/L (BUN 210mg/dl)
  - \( \text{HCO}_3^- \) 8, K 7.4, Na 142, \( \text{PO}_4 \) 4, Ca 1.85, Hb 7.8
RRT

• Haemodialysis in Renal Ward

• CRRT

• Issues
  – Potassium
  – Disequilibrium
  – Hypocalcaemia
Haemodialysis - Decisions

• Time / Frequency
• Blood flow
• Dialyzer size
• Acid concentrate composition (K and Ca)
• Sodium concentration (130-155mmol/L)
• Bicarbonate concentration (20-40mmol/L plus acetate)
• Ultrafiltration rate
### Liquid Acid Concentrates in Canisters (1 + 44 AC-F)
Composition of ready-to-use dialysis fluid (after mixing with bicarbonate concentrate 8.4% and purified water)

<table>
<thead>
<tr>
<th>Type</th>
<th>Na⁺ (mmol/L)</th>
<th>K⁺ (mmol/L)</th>
<th>Ca²⁺ (mmol/L)</th>
<th>Mg²⁺ (mmol/L)</th>
<th>Cl⁻ (mmol/L)</th>
<th>HCO₃⁻ (mmol/L)</th>
<th>Acetate (mmol/L)</th>
<th>Glucose (g/L)</th>
<th>Osmolarity (mosm/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AC-F 119/5</td>
<td>138.00</td>
<td>1.00</td>
<td>1.250</td>
<td>0.50</td>
<td>107.50</td>
<td>32.00</td>
<td>3.00</td>
<td>1.00</td>
<td>289</td>
</tr>
<tr>
<td>AC-F 113/1</td>
<td>138.00</td>
<td>1.00</td>
<td>1.500</td>
<td>0.50</td>
<td>108.00</td>
<td>32.00</td>
<td>3.00</td>
<td>1.00</td>
<td>290</td>
</tr>
<tr>
<td>AC-F 219/1</td>
<td>138.00</td>
<td>2.00</td>
<td>1.250</td>
<td>0.50</td>
<td>108.50</td>
<td>32.00</td>
<td>3.00</td>
<td>1.00</td>
<td>291</td>
</tr>
<tr>
<td>AC-F 213/4</td>
<td>138.00</td>
<td>2.00</td>
<td>1.500</td>
<td>0.50</td>
<td>109.00</td>
<td>32.00</td>
<td>3.00</td>
<td>1.00</td>
<td>292</td>
</tr>
<tr>
<td>AC-F 313/2</td>
<td>138.00</td>
<td>3.00</td>
<td>1.250</td>
<td>0.50</td>
<td>109.50</td>
<td>32.00</td>
<td>3.00</td>
<td>1.00</td>
<td>293</td>
</tr>
<tr>
<td>AC-F 313/1</td>
<td>138.00</td>
<td>3.00</td>
<td>1.500</td>
<td>0.50</td>
<td>110.00</td>
<td>32.00</td>
<td>3.00</td>
<td>1.00</td>
<td>294</td>
</tr>
</tbody>
</table>
Acute dialysis for severe uraemia

- Low blood flow (150-200 ml/min)
- Small dialyzer (1-1.4 m²)
- K 1 mmol/L, Ca 1.5 mmol/L
- $\text{HCO}_3$ 20
- Na 145
- No fluid off
- 2.5h
- Recheck UEs and repeat dialysis later
- No anticoagulation
A safer way?

DOI 10.1007/s00134-013-3016-7

FROM THE INSIDE

Rinaldo Bellomo

The avoidable death of a boy and the relentless pursuit for evidence
CRRT for treatment of Severe Uraemia

• Only choices are *Dose* and *Potassium* replacement
• Start K 0 and 15-20 ml/kg/h Effluent Flow Rate
• Run continuously
• Monitor Urea, K
• Add in UF, Potassium replacement and increase dose to 25ml/kg/h when appropriate
• This is simply and easily done within existing CRRT protocols
• Only issue is use of heparin (avoid)
  – Pre-dilute - dose is not an issue
  – Citrate – watch pH and Calcium
**CRRT replacement/dialysis solutions**

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Per 1000 ml ACCUSOL 35</th>
</tr>
</thead>
<tbody>
<tr>
<td>Large chamber ‘A’</td>
<td></td>
</tr>
<tr>
<td>Calcium chloride dihydrate</td>
<td>0.343 g</td>
</tr>
<tr>
<td>Magnesium chloride hexahydrate</td>
<td>0.136 g</td>
</tr>
<tr>
<td>Sodium chloride</td>
<td>7.52 g</td>
</tr>
<tr>
<td>Small chamber ‘B’</td>
<td></td>
</tr>
<tr>
<td>Sodium bicarbonate</td>
<td>13.4 g</td>
</tr>
</tbody>
</table>

The 5000 ml of final solution results from the mixing of 3750 ml of solution ‘A’ with 1250 ml of solution ‘B’.

**Ionic Composition of Final Solution is:**

<table>
<thead>
<tr>
<th></th>
<th>Per 1000 ml ACCUSOL 35</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium (Ca$$^{++}$$)</td>
<td>1.75 mmol</td>
</tr>
<tr>
<td>Magnesium (Mg$$^{++}$$)</td>
<td>0.5 mmol</td>
</tr>
<tr>
<td>Sodium (Na$$^{+}$$)</td>
<td>140 mmol</td>
</tr>
<tr>
<td>Chloride (Cl$$^{-}$$)</td>
<td>109.3 mmol</td>
</tr>
<tr>
<td>Bicarbonate (HCO$$_{3}$$^-)</td>
<td>35 mmol</td>
</tr>
<tr>
<td>Theoretical Osmolarity</td>
<td>287 mOsm/l</td>
</tr>
</tbody>
</table>
Urea changes with 25ml/kg/h CRRT