Fluid Management of the Critically Ill Patient

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Fluid therapy: an existential conflict

Prevent Fluid Overload!

Resuscitate!
Case

- 55 yr old male presents to ED ‘unwell for 2d’
  - PMH
    - IHD (stent)
    - Type II DM
    - HT
- Acutely tender abdomen, RUQ Peritonism
  - HR 115
  - BP 85/35
  - RR 35
  - Confused
  - Cool peripheries
  - Not passed urine for >6h
- pH 7.25 BE -13
- Lactate 4.5
- PaO₂ 120mmHg on 50% O₂  PaCO₂ 30
- Na⁺ 130 Cl⁻ 101 Alb 25
- Creat 2.1mg/dl

- USS and CT abdo/pelvis
- Dilated extra and intra-hepatic bile ducts, multiple stones in thick-walled Gall Bladder
Resuscitation

- Colloid or Crystalloid?
- Buffered or un-buffered?
- How much initially?
- What resuscitation goals?
- What monitoring?
- What other haemodynamic therapies?
Four Days Later

- In ICU
- Failed attempt ERPC
- PTC Drain (draining and patent)
- 14L +ve FB
- Ventilated
- Sedated with Propofol and Fentanyl
- Piperacillin/Tazobactam, Amikacin and Fluconazole
- BCs *Klebsiella pneumoniae*
Clinical status

- Noradrenaline increased to 0.5µg/kg/min, with MAP 58
- HR 105 SR in and out of AF
  - Amiodarone infusion
- CVP +12 (PEEP +10)
- PaO₂ 60 on 60% O₂
- CI 2.2  SV 45ml (Oesophageal doppler)
- Lactate 3 BE -5
- Remained anuric now on CVVHF pre/post 30/70% at 25ml/kg/hr no fluid off
• Albumin 16
• Bili 116
• CRP 350
• WCC 25
• Temp 35.8
• Not absorbing ng feed
• 20% Dextrose and iv insulin
• IAP +17 but not paralyzed
• Bilateral pulmonary infiltrates and muco-purulent sputum
What next?

• Better CO monitoring?
• Any problematic current therapies
• What is the role of fluid optimisation?
• Colloid (Albumin?) or Crystalloid?
• Inotropes?
• What goals do we set?
  – MAP
  – CO
  – FB
  – Organ function
    • Which ones?
Four phases of intravenous fluid therapy: a conceptual model

**Fig 2** Patients’ volume status at different stages of resuscitation. Reproduced with permission from ADQI (www.ADQI.org).

Too much fluid is bad…
Not Waving but Drowning

- Stevie Smith

Nobody heard him, the dead man,
But still he lay moaning:
“I was much further out than you thought
and not waving but drowning.”
Pathological effects of fluid overload in organ systems

- Cerebral edema
  - Impaired cognition
  - Delirium

- Myocardial edema
  - Conduction disturbance
  - Impaired contractility
  - Diastolic dysfunction

- Pulmonary edema
  - Impaired gas exchange
  - Reduced compliance
  - Increased work of breathing

- Hepatic congestion
  - Impaired synthetic function
  - Cholestasis

- Renal interstitial edema
  - Reduced RBF
  - Increased interstitial pressure
  - Reduced GFR
  - Uremia
  - Salt & water retention

- Gut edema
  - Malabsorption
  - Ileus

- Tissue edema
  - Impaired lymphatic drainage
  - Microcirculatory derangements
    - Poor wound healing
    - Wound infection
    - Pressure ulceration

Critical Illness: Indications for volume expansion

- Direct fluid losses
- Inflammation
  - Redistribution
- Venodilatation
Haemodynamic effects of fluid therapy

- Fluid
- CVP
- Venous compliance
- Capillary leak
- Preload-responsiveness
- Cardiac Output
- Contractility
- Afterload
- Blood Pressure
- Systemic resistance
- Neuroendocrine
- RAA SNS ADH ANP
- Glomerular filtration
- Glomerular haemodynamics
- Urine
- Tubular concentration
Fluid Slots

Diagram: 
- Fluid accumulation: ECM disrupted, Low interstitial pressure, Hydrated Glycosaminoglycans.
- Rapid loss of fluid from vasculature, Systemic Inflammation.
- Fluid therapy, Ultrafiltration.
- Lymphatic return = Fluid loss to Interstitium, Lymphatic return < Fluid loss to Interstitium.
- ANP, TNFα, LPS, Hyperglycemia, Oxidative Stress.
Endothelial Glycocalyx

Figure 2 Glycocalyx characteristics in normal endothelium (left) and during endothelial dysfunction (right). ETC, endothelial cleft.

A

Pressure (mmHg)

Filtration

Absorption?

Net force opposing \( P_c \) in glycosylcalyx model
\[ P_{ce} = (\sigma_{11p} - \sigma_{11g} + P_i) \]

Net force classically opposing \( P_i \)
\[ P_{ce} = (\sigma_{11p} - \sigma_{11i} + P_i) \]

Interstitial forces considered small & negligible
\( P_{eb} = \tau_{lb} = 25 \text{ mmHg} \)
\( P_i = 7.7 \pm 1.9 \text{ mmHg} \) (human arm, heart level)

Net fluid movement

Interstitial forces measured in human subcutis
\( P_i = -2.1 \pm 2.2 \text{ mmHg} \)
\( \tau_l = 15.7 \pm 2.8 \text{ mmHg} \)
\( P_{se} = 6.3 \text{ mmHg} \) (classic Starling sum)
\( P_i = 7.7 \pm 1.9 \text{ mmHg} \) (human arm, heart level)
Revised Starling principle: filtration force = \((P_c - P_i) - \sigma (\Pi_p - \Pi_g)\)
Fluid resuscitation: assessing need and response

- Haemodynamic response to fluid therapy is variable in extent and duration
  - Fluids do not adequately treat vasodilatory hypotension
- Relationship between systemic haemodynamics, RBF & GFR is indirect
- Relationship between GFR and Urine Output is also indirect and confounded by acute stress, CKD, AKI, Drugs
- Urine Output is a poor predictor of Biochemical AKI
Fluid resuscitation in septic shock: A positive fluid balance and elevated central venous pressure are associated with increased mortality.

Table 1. Fluid intake, urine output, and net fluid balance at 12 hrs and cumulative day 4 balance

<table>
<thead>
<tr>
<th></th>
<th>Quartile 1 (Dry)</th>
<th>Quartile 2</th>
<th>Quartile 3</th>
<th>Quartile 4 (Wet)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 hrs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intake, mL</td>
<td>2000 (2050–3900)</td>
<td>4520 (3700–5450)</td>
<td>6110 (5330–7360)</td>
<td>10,100 (8430–12,100)</td>
</tr>
<tr>
<td>Output, mL</td>
<td>2200 (1100–3920)</td>
<td>1590 (960–2560)</td>
<td>1180 (600–2070)</td>
<td>1260 (600–2400)</td>
</tr>
<tr>
<td>Balance, mL</td>
<td>710 (−132–1480)</td>
<td>2880 (2510–3300)</td>
<td>4900 (4290–5530)</td>
<td>8150 (7110–10,100)</td>
</tr>
<tr>
<td>Day 4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intake, mL</td>
<td>16,100 (12,800–19700)</td>
<td>18,500 (15,700–22,500)</td>
<td>22,800 (19,700–26,700)</td>
<td>30,600 (26,200–36,000)</td>
</tr>
<tr>
<td>Output, mL</td>
<td>14,600 (11,500–20100)</td>
<td>11,000 (8210–14,500)</td>
<td>9960 (6940–12,900)</td>
<td>8350 (5100–12,300)</td>
</tr>
<tr>
<td>Balance, mL</td>
<td>1560 (−723–3210)</td>
<td>8120 (6210–9090)</td>
<td>13,000 (11,800–14,700)</td>
<td>20,500 (17,700–24,500)</td>
</tr>
</tbody>
</table>

Volumes are expressed as median (25–75%).

A. Adjusted Survival Curves
   Fluid Balance Quartiles 12 hours

B. Adjusted Survival Curves
   Fluid Balance Quartiles Day 4
Fluid balance and urine volume are independent predictors of mortality in acute kidney injury

Catarina Teixeira, Francesco Garzotto, Pasquale Piccinni, Nicola Brienza, Michele Iannuzzi, Silvia Gramaticopol, Francesco Forfier, Paolo Pelaia, Monica Rocco, Claudio Ronco, Clara Belluomo Anello, Tiziana Bove, Mauro Carlini, Vincenzo Michetti, Dinna N Cruz and for the NEFROlogia e Cura INTensiva (NEFROINT) investigators.

Teixeira et al. Critical Care 2013, 17:R14
http://ccforum.com/content/17/1/R14

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 Vaara, Anna-Maija Korhonen, Kirsia-Maija Kaukonen, Sara Nisula, Oiti Inkinen, Sanna Hoppu, Jouko J Laurila, Leena Mildh, Matti Reinikainen, Vesa Lund, Ilkka Parviainen, and Ville Pettijä for the FINNAKI study group.

Vaara et al. Critical Care 2012, 16:R197
http://ccforum.com/content/16/5/R197
All demonstrate harm associated with fluid overload or benefit from its resolution.
Questions:

- To what extent is fluid overload a marker of illness severity 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?
How are the adverse effects of fluid overload mediated?

*High CVP predicts Renal Dysfunction in Cardiac Failure...*
A total of 145 consecutive patients admitted with ADHF treated with intensive medical therapy guided by pulmonary artery catheter were studied.

WRF was defined as an increase of serum creatinine ≥0.3 mg/dl during hospitalization.
… and in Sepsis
The association between CVP and new or persistent AKI remained after adjustment for fluid balance and PEEP level

(OR = 1.22 (1.08 to 1.39) for an increase of 1 mmHg; P = 0.002)
How might venous congestion cause or worsen renal function?

High venous pressure decreases renal perfusion…
THE INFLUENCE OF VENOUS PRESSURE ON THE ISOLATED MAMMALIAN KIDNEY.

By F. R. WINTON.
Beit Memorial Fellow.

(From the Department of Pharmacology, University College, London.)
...and causes increased renal interstitial pressure
Micropuncture study of pressures in proximal tubules and peritubular capillaries of the rat kidney and their relation to ureteral and renal venous pressures.

Fluids can cause renal swelling...
A Randomized, Controlled, Double-Blind Crossover Study on the Effects of 2-L Infusions of 0.9% Saline and Plasma-Lyte 148 on Renal Blood Flow Velocity and Renal Cortical Tissue Perfusion in Healthy Volunteers

Abeed H. Chowdhury, BSc, MRCS,* Eleanor F. Cox, PhD;† Susan T. Francis, PhD;† and Dileep N. Lobo, DM, FRCS, FACS*
There is already raised interstitial pressure in AKI even without venous congestion…
There is high Renal interstitial pressure in AKI

The Intrinsic Renal Compartment Syndrome: New Perspectives in Kidney Transplantation

anja Herrler,1,4 Anne Tischer,1 Andreas Meyer,1 Sergej Feiler,2 Markus Guba,1 Sebastian Nowak,3 Markus Rentsch,1 Peter Bartenstein,3 Marcus Hacker,3 and Karl-Walter Jauch1

(A)

Subcapsular pressure (mmHg)

0 1 2 3 4 5 6 7 8 9

healthy 6 h 12 h 24 h 48 h 18 days

35 min ischemia 45 min ischemia 35 min ischemia 45 min ischemia 35 min ischemia 45 min ischemia 35 min ischemia 45 min ischemia

Reperfusion time

* p<0.001 vs. healthy, p<0.05 vs. 35 min
** p<0.05 vs. healthy

(Transplantation 2010;89: 40–46)
...and relief of this pressure may attenuate AKI
Renal de-capsulation lessens extent of AKI
Thus,

- **Fluid overload**
- **Raised venous pressure**
- **Interstitial oedema**

may contribute to the maintenance of AKI…
Increased venous pressure

Increased renal vascular resistance

Extrinsic pressure (intra-abdominal hypertension)

Raised interstitial pressure
Renal oedema
- Local inflammation
- Venous congestion
- Tubular leakage

Raised tubular pressure
Reduced ultrafiltration gradient
Increased renal vascular resistance

Prowle, Kirwan, Bellomo *Nat Rev Nephrol* 2013
Management of Fluid Balance in patients with or at risk of AKI...
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
Critically ill patients after immediate resuscitation or perioperative period

Ongoing haemodynamic monitoring

Evidence of inadequate cardiac output?*

Yes

Measure cardiac output?*

Adequate

Assess for fluid overload?§

Yes

Set negative fluid balance target

No

Inadequate

Consider inotropes

No

Assess for hypovolaemia?#

Yes

Give fluid bolus

No

Assess for fluid inputs and insensible losses?*

Set fluid balance target to maintain even fluid balance

Fluid balance achieved?

Yes

Ongoing haemodynamic monitoring

No

Assess expected fluid intake Diuretics

Limit fluid intake

Fluid balance achieved?

Yes

Consider RRT

No

Extra-corporeal fluid removal

AKI-2/3?

Yes

Consider UF or RRT

No

Revise fluid balance target

Prowle, Kirwan, Bellomo Nat Rev Nephrol 2013
Critically ill patients after immediate resuscitation or period of relative stability:

Evidence of inadequate cardiac output?

Yes

Measure cardiac output?²

Adequate

No more fluid boluses required

Inadequate

Consider inotropes

No

Assess for hypovolaemia?³

Yes

Give fluid bolus

No

Assess for fluid overload§

• New organ dysfunction
• Tachycardia
• Hypotension
• Lactic acidosis
• Clinical examination

• Cardiac index
• Stroke volume
• Echo ejection volume
• Central venous oxygen saturation

• Surrogates such as Stroke Volume Variation
• Fluid responsiveness to:
  • Fluid challenges
  • Passive leg raising

Assess for fluid overload®

Set negative fluid balance target™

Assess expected fluid inputs and insensible losses®

Yes

No

Set fluid balance target to maintain even fluid balance

AKI-2/3?

Yes

Consider RRT

No

No

Limit fluid intake Diuretics

Fluid balance achieved?

Yes

Fluid balance achieved?

No

Yes

Extra-corporeal fluid removal

No

Consider UF or RRT

No

Revise fluid balance target

Ongoing haemodynamic monitoring
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
Set negative fluid balance target

AKI-2/3? (Yes/No)
  Yes: Consider RRT
  No: Limit fluid intake Diuretics

Fluid balance achieved? (Yes/No)
  Yes: Extra-corporeal fluid removal
  No: Consider UF or RRT

Revise fluid balance target

Ongoing haemodynamic monitoring
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
Differing clinical circumstances demand different rates of fluid removal


*British journal of anaesthesia* 113: 764-771
Tolerance of fluid removal

- Low tolerance of rapid fluid removal may demand continuous or extended ultrafiltration
Intra-dialytic hypotension
IHD leads to fluid overload
Conclusions

• Management of the critically ill patient involves a existential conflict between need to resuscitate cardiac output and the inevitable sequelae of fluid overload

• We can resolve this dilemma by recognising the fluids are drugs and should be administered appropriately and in the correct dose…

• And also be understanding that while fluid overload is inevitable this does not mean that it should not be recognised, mitigated and managed