Goal Directed Fluid Therapy is an important component of Enhanced Recovery Protocols

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Disclosure

- Consultant and research funding - Edwards Lifesciences, Cheetah Medical, Grifols
Goals of fluid therapy

1. Maintain central euvolemia
2. Avoid salt and water excess
The Challenge

Adapted from: Bellamy, BJA 2006

Complications

- Hypoperfusion
- Organ Dysfunction
- Adverse outcome

Hypovolemic: 
- BOWEL ISCHEMIA

Optimal:

Volume Load

Overloaded:
- BOWEL WALL EDEMA

Edema:
- Organ Dysfunction
- Adverse outcome
Brandstrup “Restriction” Study
- liberal fluid use causes harm

- Multicenter RCT
- Elective Colorectal Surgery
- 172 patients
  - Standard of Care = liberal fluids
  - Fluid ‘restriction’ = zero balance group (to maintain preop body weight)

Brandstrup study complications

## A rational approach to fluid therapy

<table>
<thead>
<tr>
<th>Maintenance</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative deficits</td>
<td>The deficit after usual fasting is low</td>
</tr>
<tr>
<td>Insensible perspiration</td>
<td>The basal fluid loss via insensible perspiration is approximately 1ml/kg/h during major abdominal surgery</td>
</tr>
<tr>
<td>Third space</td>
<td>A primarily fluid-consuming third space does not exist</td>
</tr>
<tr>
<td>Urine Output</td>
<td>Should be replaced</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Volume</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma losses from the circulation due to fluid shifting of acute bleeding</td>
<td>Timely replacement with an iso-oncotic colloid via a goal-directed approach</td>
</tr>
</tbody>
</table>

Goal no. 1:
Avoidance of fluid excess, especially crystalloid
• Over 5000 patients
• Intra-abdominal procedures
• 2009-2012
• UC Irvine and Vanderbilt
• No departmental guidelines on fluid administration

Variability in practice and factors predictive of total crystalloid administration during abdominal surgery: retrospective two-centre analysis

M. Lilot\textsuperscript{1,2}, J. M. Ehrenfeld\textsuperscript{3}, C. Lee\textsuperscript{1}, B. Harrington\textsuperscript{1}, M. Cannesson\textsuperscript{1} and J. Rinehart\textsuperscript{1*}

Lilot BJA, 2015. doi:10.1093/bja/aeu452
Strongest predictor for the amount of crystalloid given was THE ANESTHESIA PROVIDER.
DOS fluid volumes and outcomes

- Premier database
- Over 100,000 patients
- Low < 1.7L DOS fluids
- High > 5L DOS fluids

Goal-Directed Fluid Therapy

‘It is a source of regret that the measurement of flow is so much more difficult than the measurement of pressure. This has led to an undue interest in the blood pressure manometer. Most organs, however, require flow rather than pressure.’

Jarisch A, 1928.26
Frank-Starling Fluid Challenge

- Stroke Volume
  - $\Delta SV_1$
  - $\Delta SV_2$

- Intravascular Volume
  - $FC_1$
  - $FC_2$

- OPTIMAL ZONE
  - $< 10\% \uparrow$ in SV
  - $> 10\% \uparrow$ in SV
Maintain SV above trigger
GDT reduces complications

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Protocol Events</th>
<th>Protocol Total</th>
<th>Control Events</th>
<th>Control Total</th>
<th>Weight</th>
<th>Odds Ratio M-H, Random, 95% CI</th>
<th>Odds Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bender 1997 (32)</td>
<td>7</td>
<td>51</td>
<td>7</td>
<td>53</td>
<td>4.0%</td>
<td>1.05 [0.34, 3.22]</td>
<td></td>
</tr>
<tr>
<td>Berlau 1991 (31)</td>
<td>11</td>
<td>68</td>
<td>9</td>
<td>21</td>
<td>4.3%</td>
<td>0.26 [0.09, 0.76]</td>
<td></td>
</tr>
<tr>
<td>Bonazzi 2002 (29)</td>
<td>2</td>
<td>50</td>
<td>4</td>
<td>50</td>
<td>1.7%</td>
<td>0.48 [0.08, 2.74]</td>
<td></td>
</tr>
<tr>
<td>Chytra 2007 (26)</td>
<td>15</td>
<td>80</td>
<td>28</td>
<td>82</td>
<td>9.3%</td>
<td>0.45 [0.22, 0.92]</td>
<td></td>
</tr>
<tr>
<td>Conway 2002 (25)</td>
<td>5</td>
<td>29</td>
<td>9</td>
<td>28</td>
<td>3.2%</td>
<td>0.44 [0.13, 1.53]</td>
<td></td>
</tr>
<tr>
<td>Donati 2007 (24)</td>
<td>8</td>
<td>68</td>
<td>20</td>
<td>67</td>
<td>6.1%</td>
<td>0.31 [0.13, 0.77]</td>
<td></td>
</tr>
<tr>
<td>Gan 2002 (23)</td>
<td>0</td>
<td>50</td>
<td>6</td>
<td>50</td>
<td>0.6%</td>
<td>0.07 [0.00, 1.24]</td>
<td></td>
</tr>
<tr>
<td>Lobo 2000 (22)</td>
<td>6</td>
<td>19</td>
<td>12</td>
<td>18</td>
<td>2.7%</td>
<td>0.23 [0.06, 0.91]</td>
<td></td>
</tr>
<tr>
<td>Lobo 2006 (21)</td>
<td>14</td>
<td>25</td>
<td>17</td>
<td>25</td>
<td>3.8%</td>
<td>0.60 [0.19, 1.90]</td>
<td></td>
</tr>
<tr>
<td>Lopes 2007 (20)</td>
<td>7</td>
<td>17</td>
<td>12</td>
<td>16</td>
<td>2.3%</td>
<td>0.23 [0.05, 1.03]</td>
<td></td>
</tr>
<tr>
<td>Malhotra 2008 (19)</td>
<td>1</td>
<td>15</td>
<td>3</td>
<td>15</td>
<td>0.9%</td>
<td>0.29 [0.03, 3.12]</td>
<td></td>
</tr>
<tr>
<td>Mckendry 2004 (18)</td>
<td>17</td>
<td>89</td>
<td>26</td>
<td>85</td>
<td>9.9%</td>
<td>0.54 [0.27, 1.08]</td>
<td></td>
</tr>
<tr>
<td>Mythen 1995 (17)</td>
<td>0</td>
<td>30</td>
<td>6</td>
<td>30</td>
<td>0.6%</td>
<td>0.06 [0.00, 1.15]</td>
<td></td>
</tr>
<tr>
<td>Noblett 2006 (16)</td>
<td>1</td>
<td>51</td>
<td>8</td>
<td>52</td>
<td>1.1%</td>
<td>0.11 [0.01, 0.91]</td>
<td></td>
</tr>
<tr>
<td>Pearse 2005 (15)</td>
<td>27</td>
<td>62</td>
<td>41</td>
<td>60</td>
<td>8.9%</td>
<td>0.36 [0.17, 0.75]</td>
<td></td>
</tr>
<tr>
<td>Polonen 2000 (14)</td>
<td>2</td>
<td>196</td>
<td>11</td>
<td>197</td>
<td>2.2%</td>
<td>0.17 [0.04, 0.80]</td>
<td></td>
</tr>
<tr>
<td>Schultz 1985 (12)</td>
<td>2</td>
<td>35</td>
<td>3</td>
<td>35</td>
<td>1.5%</td>
<td>0.65 [0.10, 4.13]</td>
<td></td>
</tr>
<tr>
<td>Shoemaker 1988 (11)</td>
<td>8</td>
<td>28</td>
<td>30</td>
<td>60</td>
<td>5.4%</td>
<td>0.40 [0.15, 1.05]</td>
<td></td>
</tr>
<tr>
<td>Ueno 1998 (9)</td>
<td>4</td>
<td>16</td>
<td>5</td>
<td>18</td>
<td>2.2%</td>
<td>0.87 [0.19, 4.01]</td>
<td></td>
</tr>
<tr>
<td>Valentine 1998 (8)</td>
<td>15</td>
<td>60</td>
<td>10</td>
<td>60</td>
<td>6.2%</td>
<td>1.67 [0.68, 4.08]</td>
<td></td>
</tr>
<tr>
<td>Venn 2002 (7)</td>
<td>7</td>
<td>30</td>
<td>14</td>
<td>29</td>
<td>4.0%</td>
<td>0.33 [0.11, 1.00]</td>
<td></td>
</tr>
<tr>
<td>Wakeling 2005 (6)</td>
<td>24</td>
<td>67</td>
<td>38</td>
<td>67</td>
<td>10.0%</td>
<td>0.43 [0.21, 0.85]</td>
<td></td>
</tr>
<tr>
<td>Wilson 1999 (5)</td>
<td>38</td>
<td>92</td>
<td>28</td>
<td>46</td>
<td>9.3%</td>
<td>0.45 [0.22, 0.93]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>1228</td>
<td>1164</td>
<td>100.0%</td>
<td></td>
<td>0.44 [0.35, 0.55]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total events 221
Heterogeneity: Tau² = 0.01; Chi² = 22.52, df = 22 (P = 0.43); I² = 2%
Test for overall effect: Z = 7.14 (P < 0.00001)

**OR 0.44 [0.35-0.55] p<0.00001**

Anesth Analg 2011;112:1392–402
Long-term effects of complications

- 69% decrease in median survival if ≥1 30-day complication
- 105,951 patients

NICE Guidelines

Compared with conventional clinical assessment (with or without invasive cardiovascular monitoring) the Esophageal Doppler is associated with reduced:

• postoperative complications
• use of central venous catheters
• in-hospital stay

The case for adopting it in the NHS is supported by the evidence

March 2011
Does GDFT offer any advantage over a non-liberal fluid within an Enhanced Recovery pathway?
Conceptual model of perioperative fluid changes and fluid therapy

Minto, Scott, Miller. Anesthesiology Clinics. 2015; 33:35-4
RCT, 100 patients

Major abdominal surgery with EBL > 500 ml

No ERAS - All patients were fasted and received bowel prep, no laparoscopic surgery, no early feeding

Intraoperative ED-guided GDT vs. Control

GDT group : 10% algorithm with esophageal doppler

Control group: standard care (blinded to ED)

Gan Anesthesiology 2002; 97:820-6
Randomized clinical trial of goal-directed fluid therapy within an enhanced recovery protocol for elective colectomy

S. Srinivasa¹, M. H. G. Taylor², P. P. Singh¹, T.-C. Yu¹, M. Soop³ and A. G. Hill¹

- RCT, 85 patients
- Elective open or laparoscopic colectomy
- ERAS protocol: No routine bowel prep, CHO drink, Thoracic Epidural, Early mobilization and feeding
- Intraoperative EDM-guided GDT vs. Control
- Fluid “restriction” or zero balance group: max 1500ml crystalloid and 500ml colloid
- GDT group: max 1500ml crystalloid (baseline fluid restriction) + 10% algorithm with esophageal doppler

Srinivasa 2013; 100: 66-74
## Gan vs. Srinivasa

<table>
<thead>
<tr>
<th></th>
<th>Gan</th>
<th>Srinivasa</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type of surgery</strong></td>
<td>Major abdominal</td>
<td>Colorectal within ERAS</td>
</tr>
<tr>
<td></td>
<td>All open. No ERAS.</td>
<td>Some laparoscopic</td>
</tr>
<tr>
<td></td>
<td>Fasted. Bowel prep.</td>
<td>No bowel prep. CHO drink</td>
</tr>
<tr>
<td><strong>Total fluid in GDF group</strong></td>
<td>5420</td>
<td>1994</td>
</tr>
<tr>
<td><strong>Total fluid in control group</strong></td>
<td>4775</td>
<td>1614</td>
</tr>
<tr>
<td><strong>Change in FTc during surgery</strong></td>
<td>Increased in GDF group</td>
<td>No change</td>
</tr>
<tr>
<td><strong>Intraoperative SV during surgery</strong></td>
<td>Increased in GDF group</td>
<td>No change</td>
</tr>
<tr>
<td><strong>Outcome</strong></td>
<td>Reduced postop ileus (5 days vs 3 days)</td>
<td>No change</td>
</tr>
<tr>
<td></td>
<td>Reduced LOS (7d vs 5d)</td>
<td></td>
</tr>
</tbody>
</table>

• Multicenter RCT
• 734 medium to high-risk patients
• Primary outcome - composite of postoperative complications and mortality

<table>
<thead>
<tr>
<th>Outcome</th>
<th>GDT (P-value)</th>
<th>Usual care (P-value)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary outcome</td>
<td>134 (0.07)</td>
<td>158 (43.4%)</td>
<td>0.07</td>
</tr>
<tr>
<td>Mortality at 180d</td>
<td>7.7%</td>
<td>11.6%</td>
<td>0.08</td>
</tr>
</tbody>
</table>
So where are we now with GDFT?

- ERAS has made fluid management easier
  - Carb-loaded, hydrated patient
  - Laparoscopic surgery
- Small, single center studies - harder to show benefit
  - Control group management improved
- OPTIMISE - reduction in complications, underpowered
- No evidence that GDFT causes harm
- Complications are expensive!
Economic burden of complications
University HealthSystem Consortium (UHC), 2011

In-hospital mortality, hospital length of stay (HLOS) and direct costs were compared between patients with one or more complications (with) and patients without any complications (without).

<table>
<thead>
<tr>
<th>Surgery</th>
<th>Patients, n</th>
<th>Morbidity, %</th>
<th>Mortality, %</th>
<th>HLOS, days (mean ± SD)</th>
<th>Direct Cost, $ (mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>with</td>
<td>without</td>
<td>with</td>
</tr>
<tr>
<td>AAA open repair</td>
<td>2,040</td>
<td>19.6</td>
<td>20.8</td>
<td>6.0</td>
<td>23.9 ± 17.2</td>
</tr>
<tr>
<td>Vascular bypass</td>
<td>6,765</td>
<td>9.5</td>
<td>10.3</td>
<td>1.1</td>
<td>17.5 ± 15.2</td>
</tr>
<tr>
<td>Esophagectomy</td>
<td>1,794</td>
<td>12.5</td>
<td>6.3</td>
<td>2.4</td>
<td>23.2 ± 15.5</td>
</tr>
<tr>
<td>Gastrectomy</td>
<td>5,995</td>
<td>8.7</td>
<td>11.7</td>
<td>1.0</td>
<td>25.0 ± 21.3</td>
</tr>
<tr>
<td>Colectomy</td>
<td>19,055</td>
<td>15.0</td>
<td>15.2</td>
<td>2.6</td>
<td>23.1 ± 25.2</td>
</tr>
<tr>
<td>Resection of rectum</td>
<td>4,251</td>
<td>9.2</td>
<td>4.9</td>
<td>0.4</td>
<td>16.2 ± 13.0</td>
</tr>
<tr>
<td>Hepatectomy</td>
<td>4,934</td>
<td>7.6</td>
<td>14.8</td>
<td>0.7</td>
<td>17.9 ± 16.6</td>
</tr>
<tr>
<td>Pancreatectomy</td>
<td>6,564</td>
<td>14.6</td>
<td>11.4</td>
<td>0.4</td>
<td>21.7 ± 19.1</td>
</tr>
<tr>
<td>Cystectomy</td>
<td>4,036</td>
<td>10.9</td>
<td>5.2</td>
<td>0.4</td>
<td>19.3 ± 13.0</td>
</tr>
<tr>
<td>F&amp;H fracture repair</td>
<td>19,706</td>
<td>7.3</td>
<td>10.6</td>
<td>0.9</td>
<td>14.6 ± 12.2</td>
</tr>
</tbody>
</table>

Manecke, Critical Care 2014, 18:566
Which patients?

A risk-adapted matrix to match monitoring needs to patient and surgical risk

Duke Enhanced Recovery Pathway for colorectal surgery - Fluids

- **Preoperative**
  - Clear fluids encouraged until 1 hour before arrival at hospital
  - Given Clearfast to drink 1 hours before arrival at hospital

- **Intraoperative**
  - LR infusion 3ml/Kg/hour based on IBW
  - GDFT using boluses of colloid to optimize SV/SVV

- **Postoperative**
  - Maintenance fluids overnight
  - Permissive oliguria (>10ml/hr) as long as other signs ok
  - IV down as soon as drinking adequately
  - Remove Foley on POD1
Summary

• Fluid management is generally still chaotic
  – Wide variability in practice
    • Too little fluid
    • Too much fluid, esp. crystalloid
• Liberal fluid use is associated with harm
• Fluid protocols have advantages
Summary

• Pressure monitoring has significant limitations

• Goal - Directed Fluid Therapy
  – Physiologically sound
  – Right Fluid, Right Amount, Right Time
  – Evidence – based to reduce morbidity, length of stay, and healthcare costs.

• Ultimately the need for GDT is surgeon, patient, and institution specific