Background physiology

- Patients who are sicker have higher mortality
- Cardiovascular disease is most important
- Assessments of cardiovascular physiology and scoring systems are available
- Older patients have more diseases and less reserve
Surgical Mortality

- Mella BJS 98
- Colorectal surgery audit
- Operations carried out urgently have a higher mortality rate
Surgical Mortality

Farrow, BJA, 82
Death is not immediate for most patients who die within 28 days of surgery.
Patient Selection

Shoemaker in a series of observational studies demonstrated a group of patients that he called “High Risk” and who had a 28 day mortality of 30-40%.
Shoemaker Used Simple Clinical Criteria to Identify These Patients

- Previous severe cardio-respiratory illness
- Late stage vascular disease
- Age > 70 with limited physiological reserve
- Acute abdominal catastrophe
- Septicaemia
- Respiratory failure
- Acute renal failure
- Massive blood loss > 8 units
- Extensive surgery for carcinoma
Shoemaker Asked the Questions

• Which of the commonly measured variables, such Blood pressure, pulse rate, respiratory rate, CVP, blood tests etc., predicted outcome in this “High Risk” group of patients?

• He examined over 30 variables in several thousand patients

  Shoemaker et al. CCM. 1979: 7; 237.
  Shoemaker et al. CCM 1979: 7;424.
  Bland et al. CCM. 1985: 13; 85.
Best prognostic indicators of outcome in these “High Risk” surgical patients

- He demonstrated that only variables related to blood volume and flow had significant prognostic value
  - Blood volume
  - Cardiac output
  - Oxygen delivery
  - Oxygen consumption
Shoemaker and Oxygen Debt

Survivors without complications

Survivors but with complications

Non-survivors

Surgery

Oxygen debt

L/m²
## Results

<table>
<thead>
<tr>
<th></th>
<th>Protocol</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICU Stay (days)</td>
<td>10.2 *</td>
<td>15.8</td>
</tr>
<tr>
<td>Hosp stay (days)</td>
<td>19.3</td>
<td>25.2</td>
</tr>
<tr>
<td>Complications</td>
<td>0.39*</td>
<td>1.30</td>
</tr>
<tr>
<td>Deaths</td>
<td>4%*</td>
<td>33%</td>
</tr>
</tbody>
</table>

*Significant difference
Optimisation of Surgical Patients
- controlled randomised studies.

• To investigate the possible beneficial role of deliberately increasing oxygen delivery in the peri-operative phase for “High Risk” surgical patients
• Historical mortality 33%
Optimisation of Surgical Patients

• **Targets for treatment. Both groups**
  - MAP 80 – 110 mmHg
  - PAWP 12 – 14 mmHg
  - Art Oxygen Sats >94%
  - Haemoglobin >12g/dl
  - Urine output > 0.5 ml/kg.hr

• **Additional targets for protocol group**
  - Oxygen delivery 600 ml/min/m²
Post-operative Mortality
Boyd, Grounds, Bennett, JAMA 1993: 270; 2699.

% age survivors

Days after operation

Kaplan-Meier Survival curve

Protocol (n=53)
Control (n=54)
York Study
Wilson et al. BMJ 1999: 318; 1099

• Wilson and colleagues undertook a trial of pre-operative optimisation of oxygen delivery in major elective surgery

• Patients were randomised to three groups, two were monitored haemodynamically, given fluids ± adrenaline or dopexamine to increase oxygen delivery. The third group were treated conventionally.

• Main outcome measures were hospital mortality and morbidity.
York Study
Wilson et al. BMJ 1999: 318; 1099

Post-operative survival

Days after surgery
Percentage survivors
Adrenaline
Dopexamine
Control
### York Study

Wilson et al. BMJ 1999: 318; 1099

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Adrenaline</th>
<th>Dopexamine</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of patients</strong></td>
<td>46</td>
<td>46</td>
<td>46</td>
</tr>
<tr>
<td><strong>Total bed days</strong></td>
<td>1008</td>
<td>875</td>
<td>596*</td>
</tr>
<tr>
<td><strong>ICU bed days</strong></td>
<td>192</td>
<td>176</td>
<td>152*</td>
</tr>
<tr>
<td><strong>Bed days per patient</strong></td>
<td>22</td>
<td>19</td>
<td>13*</td>
</tr>
</tbody>
</table>
Lobo et al. High Risk Surgical Patients

• Studied effects of increasing DO$_2$ in very high risk surgical patients with an historical mortality of > 50%.

• DO$_2$ was increased pre-operatively and maintained during surgery and post-operatively for 24 hours

• Main outcome criteria was 60 day mortality and morbidity
Lobo et al. High Risk Surgical Patients

Lobo et al. 2000: Crit. Care Med; 28; 3396.
Lobo et al. High Risk Surgical Patients
Lobo et al. 2000: Crit. Care Med: 28; 3396

Percentage of Patients with Complications

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Protocol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percentage</td>
<td>66</td>
<td>32</td>
</tr>
</tbody>
</table>

*Statistically significant difference.
Optimisation of Patients in ITU

- Studied critically ill patients in ICU.
- Mixture of surgical and medical patients.
- Treatment goals using dobutamine were.
  - Oxygen delivery > 600 ml/min/m$^2$.
  - Oxygen consumption > 170 ml/min/m$^2$.
- Outcome. Mortality.
  - Control group 34%.
  - Treatment group 54%.
Optimisation of Patients in ITU

• Multi center study of post-operative patients who had developed sepsis, sepsis syndrome, organ failure or ARDS.

• Patients were entered into the study only after failure of 2 days conventional therapy in ICU.

• Three groups.
  – Conventional therapy.
  – Cardiac Index increased above 4.5 L/min/m^2.
  – Mixed venous saturation above 7%.

• NO DIFFERENCE IN OUTCOME.
Oesophageal Doppler.

- Sinclair et al. BMJ 1997 (# femur)
- Venn et al. BJA 2002 (# femur)
- McKendry et al. BMJ 2004 (cardiac surgery)
- Wakeling et al. BJA 2005 (Bowel surgery)
Randomised controlled trial to investigate influence of the fluid challenge on duration of hospital stay and perioperative morbidity in patients with hip fractures.

• Randomised, prospective controlled trial.
• 90 patients with fracture neck of femur.
• Three groups.
  – Conventional intra-op fluid management
  – Additional colloid guided by CVP
  – Additional colloid guided by Oesophageal doppler
Venn et al BJA 2002.

• Pre-op
  – All necessary medical support
  – Regular analgesia pre-op
  – Maintenance IV fluids 1 litre 12 hourly
  – Blood transfusion if appropriate

• Anaesthesia
  – 3 in 1. inguinal perivascular nerve blockade.
Venn et al. BJA 2002.

- Intra operatively. All patients
  - Continuous monitoring.
  - IV Hartmanns or blood to replace estimated and measured blood loss. AND to maintain heart rate and Blood pressure within 20% of pre-induction baseline.

- PLACEBO GROUP.
  - Clinicians were asked to give IV fluids as they though appropriate within above limits.
<table>
<thead>
<tr>
<th>TIME</th>
<th>CVP ((mmHg))</th>
<th>Gelofusine Challenge</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial reading</td>
<td>&lt;14</td>
<td>200ml</td>
</tr>
<tr>
<td></td>
<td>&gt;14</td>
<td>100ml</td>
</tr>
<tr>
<td>During fluid challenge</td>
<td>Increase &gt; 5</td>
<td>Stop fluid challenge and WAIT</td>
</tr>
<tr>
<td>Following fluid challenge</td>
<td>Increase &gt; 3</td>
<td>WAIT</td>
</tr>
<tr>
<td></td>
<td>≤ 3</td>
<td>Repeat fluid challenge as per initial reading</td>
</tr>
</tbody>
</table>
Venn et al. BJA 2002. Results

Days before being medically fit for discharge

- Control
- CVP
- Doppler
<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>CVP</th>
<th>Doppler</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days before medically fit for discharge</td>
<td>13.9</td>
<td>10</td>
<td>7.7</td>
<td>0.035</td>
</tr>
<tr>
<td>Acute hospital stay</td>
<td>16.7</td>
<td>11.1</td>
<td>12.5</td>
<td>0.17</td>
</tr>
<tr>
<td>Total hospital stay (ortho and Geriatric)</td>
<td>17.5</td>
<td>13.3</td>
<td>13.3</td>
<td>0.27</td>
</tr>
</tbody>
</table>
Early goal directed therapy following major surgery reduces complications and length of hospital stay. A randomised, controlled trial.

R M Pearse, D Dawson, J Fawcett, A Rhodes, R M Grounds ED Bennett
Critical Care 2005

- Pragmatic Study design.
- Randomised, Controlled, Blinded.
- Eight hours of GDT in post-operative period.
- Surgical patients with co-morbidities who were booked to ITU post-operatively.
- Primary endpoint of reduction in complications.
- Prospectively defined morbidity endpoints.
Return from theatre

Randomization

GDT

Control

SaO2 ≥ 94%
Hb 8-10 g dl⁻¹
Temperature ≥ 37 °C
Heart rate <100bpm or <20% above baseline
Urine output > 0.5ml/kg/hour

Administer maintenance crystalloid at 1.5ml kg⁻¹hr⁻¹
Goal Directed Protocol for Control Group

Return from theatre

250 ml fluid challenge
(blood or colloid as appropriate)

Rapid rise in CVP

Yes

Fluid losses > input?

Yes

CI <2.5ml/min/m² or Lactate increase for 2 consecutive hours

No

Blinded Monitoring of cardiac index

Epinephrine and reveal CI to clinicians

No

Yes
Return from theatre

250 ml fluid challenge (blood or colloid as appropriate)

Stroke volume increase >10%

Fluid losses > input?

Yes

No

DO₂I >600 ml/min/m²

Dopexamine to maximum 1 mcg/kg/min

Dopexamine reduced if tachycardia or myocardial ischaemia develop

Observe

Yes

No

DO₂I >600 ml/min/m²

Yes

No

Yes
Oxygen Delivery Index During the Eight Hour Study Period.
Length of Hospital Stay Following Eight Hours of Goal Directed Therapy.

- **Mean**: 17 days (GDT) vs. 29 days (Control)
- **Median**: 11 days (GDT) vs. 14 days (Control)

**41% reduction (95 CI 05% to 81%)**

*P*=0.0015
Total number of complications

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>EGDT</th>
</tr>
</thead>
<tbody>
<tr>
<td>P=0.002</td>
<td>90</td>
<td>43</td>
</tr>
</tbody>
</table>

Mean number complications per patient

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>EGDT</th>
</tr>
</thead>
<tbody>
<tr>
<td>P=0.003</td>
<td>1.5</td>
<td>0.7</td>
</tr>
</tbody>
</table>
Conclusions

• Good evidence to suggest that patients with low cardiac output and oxygen have high mortality when undergoing major surgery.

• Good evidence that increasing cardiac output and oxygen delivery with IV fluids ± inodilators around the time of surgery will improve outcome.
Conclusions

• This improvement in mortality may be due to a reduction in organ failure due to more aggressive therapy at the time of surgery.
• This aggressive therapy also leads to a reduction in postoperative complications.
Optimization Meta-analysis

Improved by protocol

Worsened by protocol

0.33 (CI 0.23-0.49)

For every 100 patients, 11 lives will be saved

Grocott et al 2003
### Meta-analysis

#### Comparison: 01 All Studies

**Outcome: 01 Mortality**

<table>
<thead>
<tr>
<th>Study</th>
<th>n/N</th>
<th>Control n/N</th>
<th>Peto OR (95% CI Fixed)</th>
<th>Weight %</th>
<th>Peto OR (95% CI Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shoemaker 1988</td>
<td>1/28</td>
<td>18/60</td>
<td></td>
<td>17.5</td>
<td>0.21 [0.07, 0.63]</td>
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<tr>
<td>Berlauk 1991</td>
<td>1/68</td>
<td>2/21</td>
<td></td>
<td>2.8</td>
<td>0.09 [0.01, 1.29]</td>
</tr>
<tr>
<td>Boyd 1993</td>
<td>3/53</td>
<td>12/54</td>
<td></td>
<td>17.5</td>
<td>0.26 [0.09, 0.76]</td>
</tr>
<tr>
<td>Mythen 1995</td>
<td>0/30</td>
<td>1/30</td>
<td></td>
<td>1.3</td>
<td>0.14 [0.00, 6.82]</td>
</tr>
<tr>
<td>Sinclair 1997</td>
<td>1/20</td>
<td>2/20</td>
<td></td>
<td>3.8</td>
<td>0.50 [0.05, 5.06]</td>
</tr>
<tr>
<td>Ziegler 1997</td>
<td>3/32</td>
<td>2/40</td>
<td></td>
<td>6.3</td>
<td>1.95 [0.32, 11.98]</td>
</tr>
<tr>
<td>Bender 1997</td>
<td>1/51</td>
<td>1/53</td>
<td></td>
<td>2.7</td>
<td>1.04 [0.06, 16.86]</td>
</tr>
<tr>
<td>Valentine 1998</td>
<td>3/60</td>
<td>1/60</td>
<td></td>
<td>5.2</td>
<td>2.79 [0.38, 20.31]</td>
</tr>
<tr>
<td>Ueno 1998</td>
<td>0/16</td>
<td>2/18</td>
<td></td>
<td>2.6</td>
<td>0.14 [0.01, 2.39]</td>
</tr>
<tr>
<td>Wilson 1999</td>
<td>3/92</td>
<td>8/46</td>
<td></td>
<td>12.2</td>
<td>0.15 [0.04, 0.54]</td>
</tr>
<tr>
<td>Lobo 2000</td>
<td>3/19</td>
<td>9/18</td>
<td></td>
<td>11.2</td>
<td>0.22 [0.06, 0.85]</td>
</tr>
<tr>
<td>Polonen 2000</td>
<td>4/196</td>
<td>9/197</td>
<td></td>
<td>16.9</td>
<td>0.45 [0.15, 1.37]</td>
</tr>
</tbody>
</table>

**Total (95% CI):**

23/665, 67/617

Chi-square 13.33 (df=11) P: 0.35  Z=-4.84 P: <0.00001

#### All studies

<table>
<thead>
<tr>
<th>Mortality</th>
<th>Treatment</th>
<th>Control</th>
<th>Peto OR</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 Mortality</td>
<td>23/665</td>
<td>67/617</td>
<td>0.33</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>3.5%</td>
<td>10.9%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
How to do it

• Individual therapy
• Performance during peri-operative period must attempt to reach goals that are achieved by survivors.
• IV fluids. Individually tailored. Starling curve.
• Inotropes. Vasodilators.
• Endpoints.
What not to use as goals of therapy.

- Interestingly Shoemaker found that the following commonly measured variables were of little predictive value
  - CVP
  - Urine output
  - Pulse rate
  - Blood pressure
  - Respiratory rate
Variables that give a good prediction of outcome

• Blood volume and flow
• Tissue oxygen delivery
• Myocardial performance under stress
  – Cardiac Index greater than 4.5L/min/m²
  – Oxygen delivery greater than 600 ml/min/m²
  – Oxygen consumption greater 170 ml/min/m²
Targets for early studies

- Maximise intravenous fluid therapy to try and achieve “best” position on Starling Curve for each individual patient.
- If this is insufficient to achieve $DO_2I$ of 600ml/min/m$^2$. Then inotropes would be added. (Dobutamine; dopexamine; adrenaline have all been used.)
Pulmonary artery catheters

• A number of studies have used these successfully.
• Used to maximise intravenous volume therapy.
• If goals still not achieved then inotropes or ino-dilators used to achieve goals.
• Reductions in post operative complications and post-operative mortality.
Oesophageal doppler

- Used to monitor cardiac output (or more specifically stroke volume) during surgery.
- Intravenous fluid therapy maximised
- If this fails to achieve goals then inotropes may be added.
- Reduction in hospital stay.
- Reduction in post-operative complications.
LiDDCo. Pulse contour analysis.

- Used to guide therapy in 8 hours immediately following surgery.
- Nurse led Goal Directed Therapy in high risk patients.
- Reduction in hospital stay.
- Reduction in post-operative complications.
Pulmonary Artery Catheters

• Shoemaker et al. Chest 1988
• Boyd et al. JAMA 1993
• Woods et al. BMJ 1999
• Lobo et al. Crit Care Med 2000
• Polonen et al. Anesth Analg 2000
Assess patient as being high risk:
Where possible perform cardiovascular measurements and assess cardiac performance

If cardiac Index less than 4.5L/min or oxygen delivery less than 600 mL.min/m²
Goal–directed therapy may be indicated peri-operatively.
If possible start pre-operative therapy in critical care unit and continue during and post-operatively

1. Increase IV fluids.
   Use flow directed monitoring to maximize intravascular filling pressure
2. Maintain haemoglobin
   Use transfusion if necessary
3. Maintain oxygen saturation
   If necessary intubate and ventilate

If oxygen delivery target still not reached then start inotropes/vasodilators to improve cardiac function until targets are met

If cardiac Index over 4.5L/min or oxygen delivery over 600 mL.min/m²
Then goal directed therapy is unlikely to be needed.

If cardiac Index over 4.5L/min or oxygen delivery over 600 mL.min/m²
Then maintain during peri-operative period until endpoints reached

Frequently re-assess whether patient is achieving targets during peri-operative period

If cardiac Index over 4.5L/min or oxygen delivery over 600 mL.min/m²
Then maintain during peri-operative period until endpoints reached
Intraoperative Optimisation Protocol
Department of Anaesthesia

St George's Healthcare NHS Trust

SV maximisation:
Use LiDCOrapid or CardioQ to monitor the change in SV during a Fluid Challenge.
Achieve maximal stroke volume by repeating Fluid Challenges until the SV does not increase > 10%

Fluid Challenge:
1) 250/500 mL of fluid as a rapid bolus in less than 5 minutes
2) Preferentially use a peripheral cannula
3) Use:
   a) pressure bag or
   b) a 50 mL syringe

Set up monitor:
LiDCOrapid or CardioQ

Give Fluid Challenge

SV increase > 10%  
YES

NO

Recheck SV value every 15 minutes

Has the SV decreased > 10% from last Fluid Challenge?  
PPV>10%?

YES

NO

*C Consider PPV only if patient:
1) is completely ventilated
2) and tidal volumes > 7 ml/Kg of IBW
3) and is in sinus rhythm

<table>
<thead>
<tr>
<th>Time</th>
<th>SV Pre FC</th>
<th>SV Post FC</th>
<th>SV &gt; 10% Yes?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tbody>
</table>

Note:
- CARRY ON
- STOP
- SV > 20% after fluid challenge
- SV > 10% after fluid challenge

Press