Update on ICU Fluid Resuscitation

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The Importance of Euvolemia

Mortality

Hypovolemia  Euvolemia  Hypervolemia

tissue perfusion
The Volume Expansion Epidemic

- Patients average 2-4 L net positive each ICU day

- “Knee-jerk” reaction to oliguria, tachycardia, hypotension or abnormal laboratory values

- Excess volume results in dysfunction of all organ systems
Volume Overload and Mortality

Fluid resuscitation in septic shock with elevated central venous pressure and mortality*

John H. Boyd, MD, FRCP(C); Jason Forbes, MD, FRCP(C); James A. Russell, MD, FRCP(C)

Table 3. Main Outcome Variables.*

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Conservative Strategy</th>
<th>Liberal Strategy</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death at 60 days (%)</td>
<td>25.5</td>
<td>28.4</td>
<td>0.30</td>
</tr>
<tr>
<td>Ventilator-free days from day 1 to day 28†</td>
<td>14.6±0.5</td>
<td>12.1±0.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ICU-free days†</td>
<td>0.9±0.1</td>
<td>0.6±0.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Days 1 to 7</td>
<td>13.4±0.4</td>
<td>11.2±0.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Organ-failure–free days‡‡</td>
<td>0.9±0.1</td>
<td>0.6±0.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Days 1 to 7</td>
<td>3.9±0.1</td>
<td>4.2±0.1</td>
<td>0.04</td>
</tr>
<tr>
<td>Cardiovascular failure</td>
<td>3.4±0.2</td>
<td>2.9±0.2</td>
<td>0.02</td>
</tr>
<tr>
<td>CNS failure</td>
<td>5.5±0.1</td>
<td>5.6±0.1</td>
<td>0.45</td>
</tr>
<tr>
<td>Renal failure</td>
<td>5.7±0.1</td>
<td>5.5±0.1</td>
<td>0.12</td>
</tr>
<tr>
<td>Hepatic failure</td>
<td>5.6±0.1</td>
<td>5.4±0.1</td>
<td>0.23</td>
</tr>
<tr>
<td>Coagulation abnormalities</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Days 1 to 28</td>
<td>19.0±0.5</td>
<td>19.1±0.4</td>
<td>0.85</td>
</tr>
<tr>
<td>Cardiovascular failure</td>
<td>18.8±0.5</td>
<td>17.2±0.4</td>
<td>0.03</td>
</tr>
<tr>
<td>CNS failure</td>
<td>21.5±0.5</td>
<td>21.2±0.5</td>
<td>0.59</td>
</tr>
<tr>
<td>Renal failure</td>
<td>22.0±0.4</td>
<td>21.2±0.5</td>
<td>0.18</td>
</tr>
<tr>
<td>Hepatic failure</td>
<td>22.0±0.4</td>
<td>21.5±0.4</td>
<td>0.37</td>
</tr>
<tr>
<td>Coagulation abnormalities</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dialysis to day 60</td>
<td>10</td>
<td>14</td>
<td>0.06</td>
</tr>
<tr>
<td>Patients (%)</td>
<td>11.0±1.7</td>
<td>10.9±1.4</td>
<td>0.96</td>
</tr>
</tbody>
</table>

Breaking the Cycle: *Does my Patient Need Fluid?*

1. Is there evidence of tissue hypoperfusion?

2. Is there evidence that tissue hypoperfusion *is due to* hypovolemia?
Markers of Tissue Perfusion

- **Organ Specific:**
  - Venous hemoglobin oxygen saturation ($S_vO_2$)
  - Lactate
  - Base Deficit

- **Global:**
  - Acute respiratory distress syndrome
  - Hypotension, ST segment depression/elevation, elevation of cardiac enzymes
  - Oliguria, decreased fractional excretion of sodium
  - Feeding intolerance, adynamic ileus, stress ulceration/gastritis, enteritis, colitis
  - Hepatitis, centrilobular necrosis, cholestasis, acalculous cholecystitis, pancreatitis
Oxygen Delivery

\[ S_vO_2 \]

Oxygen Consumption

- Anaerobic metabolism
- Normal

\( \downarrow S_vO_2 \)
$S_vO_2$

- Central venous ($S_{cv}O_2$) vs. mixed venous ($S_vO_2$)

- Normal $S_vO_2$ 70%

- $S_{cv}O_2 > S_vO_2$ by 5-15%

- Low values correlate with increased mortality

- Normalization correlates with improved survival

- Trend is more important than absolute value
Advantages
- Early marker of tissue hypoperfusion
- Continuous

Disadvantages
- Invasive
- Labor intensive
- False negatives
Products of Anaerobic Metabolism

Glucose → pyruvate → lactate, $\text{H}^+$, ATP

anaerobic

pyruvate → Acetyl-Co-A → $O_2$, ATP

aerobic

$\text{CO}_2$, $\text{H}_2\text{O}$
Lactic Acidosis

Type A: tissue hypoxia $\rightarrow$ excessive lactic acid production

Type B: insufficient liver metabolism of lactate
- Hepatic insufficiency
- Pharmacologic
  - Propofol
  - Metformin
  - HAART
Base Deficit

The amount of base (mEq) that must be added to each liter of oxygenated blood to return the pH to 7.40 at a temperature of 37.0 and a pCO$_2$ of 40 mm Hg.

Normal range -2 to +2

Correlates with depth of shock

Bicarbonate probably a reasonable substitute

Caution: hyperchloremic non anion gap metabolic acidosis
Anion gap = Na\(^+\) - (Cl\(^-\) + HCO\(_3\)\(^-\))
Resuscitation with chloride-rich fluids can result in a worsening non anion gap, metabolic acidosis due to hyperchloremia.

This can be misinterpreted as worsening shock, which is then treated with chloride-rich fluids.

This misinterpretation is avoided by observing the serum chloride concentrating and calculating the anion gap.

R. Phillip Dellinger, MD; Mitchell M. Levy, MD; Andrew Rhodes, MB BS; Djillali Annane, MD; Herwig Gerlach, MD, PhD; Steven M. Opal, MD; Jonathan E. Sevransky, MD; Charles L. Sprung, MD; Ivor S. Douglas, MD; Roman Jaeschke, MD; Tiffany M. Osborn, MD, MPH; Mark E. Nunnally, MD; Sean R. Townsend, MD; Konrad Reinhart, MD; Ruth M. Kleinpell, PhD, RN-CS; Derek C. Angus, MD, MPH; Clifford S. Deutschman, MD, MS; Flavia R. Machado, MD, PhD; Gordon D. Rubenfeld, MD; Steven A. Webb, MB BS, PhD; Richard J. Beale, MB BS; Jean-Louis Vincent, MD, PhD; Rui Moreno, MD, PhD; and the Surviving Sepsis Campaign Guidelines Committee including the Pediatric Subgroup*
Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock

MANAGEMENT OF SEVERE SEPSIS

A. Initial Resuscitation

1. We recommend the protocolized resuscitation of patients with sepsis-induced tissue hypoperfusion as hypotension or blood lactate concentration should be initiated as soon as possible and should not be delayed pending ICU admission. During the first 6 hours of resuscitation, the goals of initial resuscitation of sepsis-induced hypoperfusion should include all of the following as a part of a treatment protocol (grade 2C).
   a) CVP 8–12 mm Hg
   b) MAP ≥ 65 mm Hg
   c) Urine output ≥ 0.5 mL·kg·hr
   d) Superior vena cava oxygenation saturation (Scvo₂) or mixed venous oxygen saturation (Svo₂) ≥ 70% or 65%, respectively.

2. We suggest targeting resuscitation to normalize lactate in patients with elevated lactate levels as a marker of tissue hypoperfusion (grade 2C).

9. We recommend that all patients requiring vasopressors have an arterial catheter placed as soon as practical if resources are available (UG).

Rationale. In shock states, estimation of blood pressure using a cuff is commonly inaccurate; use of an arterial cannula provides a more appropriate and reproducible measurement of arterial pressure. These catheters also allow continuous analysis so that decisions regarding therapy can be based on immediate and reproducible blood pressure information.
Breaking the Cycle: 

*Does my Patient Need Fluid?*

1. Is there evidence of tissue hypoperfusion?

2. Is there evidence that tissue hypoperfusion *is due to* hypovolemia?
There are Many Causes of Tissue Hypoperfusion (hypovolemia is just one of them)
About 50% of ICU Patients with Evidence of Tissue Hypoperfusion do not Respond to Volume

<table>
<thead>
<tr>
<th>Responders / Non-Responders</th>
<th>% Responders</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calvin (Surgery 81)</td>
<td>20 / 8</td>
</tr>
<tr>
<td>Schneider (Am Heart J 88)</td>
<td>13 / 5</td>
</tr>
<tr>
<td>Reuse (Chest 90)</td>
<td>26 / 15</td>
</tr>
<tr>
<td>Magder (J Crit Care 99)</td>
<td>13 / 16</td>
</tr>
<tr>
<td>Tavernier (Anesthesio 98)</td>
<td>21 / 14</td>
</tr>
<tr>
<td>Magder (AJRCCM 00)</td>
<td>16 / 24</td>
</tr>
<tr>
<td>Tousignant (A Analg 00)</td>
<td>16 / 24</td>
</tr>
<tr>
<td>Michard (Chest 01)</td>
<td>10 / 9</td>
</tr>
<tr>
<td>Mean</td>
<td>211 / 195</td>
</tr>
</tbody>
</table>

Breaking the Cycle: *Does my Patient Need Fluid?*

- In order to determine if volume expansion will improve tissue perfusion, we must estimate *fluid responsiveness*

  ![Frank Starling Curve](image)

  *Traditionally, this has been done with static surrogates such as the CVP or PAOP*
Limitations of Static Measurements of Fluid Responsiveness
CVP does not predict intravascular volume

Marik et al. Chest 2008;134:172
CVP does not predict fluid responsiveness

Does the Central Venous Pressure Predict Fluid Responsiveness? An Updated Meta-Analysis and a Plea for Some Common Sense*

Paul E. Marik, MD, FCCM¹; Rodrigo Cavallazzi, MD²

Background: Despite a previous meta-analysis that concluded that central venous pressure should not be used to make clinical decisions regarding fluid management, central venous pressure continues to be recommended for this purpose.

Aim: To perform an updated meta-analysis incorporating recent studies that investigated indices predictive of fluid responsiveness. A priori subgroup analysis was planned according to the location where the study was performed (ICU or operating room).

Data Sources: MEDLINE, EMBASE, Cochrane Register of Controlled Trials, and citation review of relevant primary and review

ROC AUC 0.56 (95% CI, 0.54–0.58) for those done in the operating room. The summary correlation coefficient between the baseline central venous pressure and change in stroke volume index/cardiac index was 0.18 (95% CI, 0.1–0.25), being 0.28 (95% CI, 0.16–0.40) in the ICU patients, and 0.11 (95% CI, 0.02–0.21) in the operating room patients.

Conclusions: There are no data to support the widespread practice of using central venous pressure to guide fluid therapy. This approach to fluid resuscitation should be abandoned. (Crit Care Med 2013; 41:1774–1781)

Marik et al. Chest 2008;134:172
Dynamic Measurements of Fluid Responsiveness

Predict the response of stroke volume to a physiologic change in pre-load ("auto" volume challenge)

Determine the utility of volume expansion before it is given

Continuous, minimally invasive, and inexpensive

Examples:

- Pulse pressure variability (PPV)
- Systolic pressure variability (SPV)
- Stroke volume variability (SVV)
Dynamic Measurements of Fluid Responsiveness

Physiology

- Left heart preload varies with respiration
  - Decreases with inspiration during spontaneous ventilation
  - Increases with inspiration during mechanical ventilation

- This variability translates into respiratory variability in stroke volume
  - SVV, SPV, PPV

- Variability is greater when the heart operates on the steep portion of the Frank-Starling curve

[Graph showing airway pressure and arterial pressure waves for spontaneous and controlled breaths]
Dynamic Measurements of Fluid Responsiveness

*Physiology*

- Increased SVV predicts fluid responsiveness.
- Typical threshold for SVV is 12%
- Typical definitions of “preload responsiveness:”
  - $\uparrow SV \geq 10\text{-}15\%$
  - $\uparrow CO \geq 10\text{-}15\%$
Respiratory Variation in Arterial Pressure
Dynamic Measurements of Fluid Responsiveness

Clinical Data

Septic shock

Cardiothoracic Surgery

Dynamic Measurements of Fluid Responsiveness
Clinical Data

Craniotomy

Liver Transplantation

Berkenstadt et al. *Anesth Analg* 2001;92:984

Dynamic changes in arterial waveform derived variables and fluid responsiveness in mechanically ventilated patients: A systematic review of the literature*

Paul E. Marik, MD, FCCM; Rodrigo Cavallazzi, MD; Tajender Vasu, MD; Amyn Hirani, MD

- 29 studies, 685 patients
- 56% of patients responded to fluid

Table 2. Ability of dynamic and static hemodynamic variables to predict volume responsiveness: pooled data with 95% confidence intervals

<table>
<thead>
<tr>
<th>Variable</th>
<th>Correlation (r)</th>
<th>AUC</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPV</td>
<td>.78 (.74–.82)</td>
<td>0.94 (0.93–0.95)</td>
</tr>
<tr>
<td>SPV</td>
<td>.72 (.65–.77)</td>
<td>0.86 (0.82–0.90)</td>
</tr>
<tr>
<td>SVV</td>
<td>.72 (.66–.78)</td>
<td>0.84 (0.78–0.88)</td>
</tr>
<tr>
<td>LVEDAI</td>
<td>—</td>
<td>0.64 (0.53–0.74)</td>
</tr>
<tr>
<td>GEDVI</td>
<td>—</td>
<td>0.56 (0.37–0.67)</td>
</tr>
<tr>
<td>CVP</td>
<td>.13 (−.01–.28)</td>
<td>0.55 (0.48–0.62)</td>
</tr>
</tbody>
</table>

AUC, area under the curve; PPV, pulse pressure variation; SPV, systolic pressure variation; SVV, stroke volume variation; LVEDAI, left ventricular end-diastolic area index (derived from transesophageal echocardiography); GEDVI, global end-diastolic volume index (derived from transpulmonary thermodilution); CVP, central venous pressure.
Abilities of pulse pressure variations and stroke volume variations to predict fluid responsiveness in prone position during scoliosis surgery

M. Biais*, O. Bernard, J. C. Ha, C. Degryse and F. Sztark
Sensitivity 82%
Specificity 92%

Fig 3. ROC analysis for the SVV at baseline to discriminate between responders and nonresponders to intravascular volume expansion. The area under ROC curves was 0.900 for SVV (95% confidence interval, 0.809-0.991). The optimal threshold values given by ROC analysis were 10.5% for SVV.
5. We recommend that a fluid challenge technique be applied wherein fluid administration is continued as long as there is hemodynamic improvement either based on dynamic (e.g., change in pulse pressure, stroke volume variation) or static (e.g., arterial pressure, heart rate) variables (UG).

**Rationale.** Dynamic tests to assess patients’ responsiveness to fluid replacement have become very popular in recent years in the ICU (131). These tests are based on monitoring changes in stroke volume during mechanical ventilation or after passive leg raising in spontaneously breathing patients. A systematic review
PPV, SPV or SVV?

- Similar discrimination of fluid responsiveness

- Calculation of SVV may be coupled with continuous CO and SV measurements via arterial waveform contour analysis
  - Aids in determining etiology of shock
  - Allows for dynamic assessment of fluid responsiveness in the setting of SVV limitations (e.g., arrhythmia)
FloTrac (Edwards Lifesciences)

- Platform compatible with any standard arterial line
- Continuous SVV, CI (pulse contour method), SVI information
- Graphical representation of resuscitation progress
- Portable
Arterial Pressure Based vs. Thermodilutional Cardiac Output Determination in 100 Patients During Cardiac Surgery

\[ r^2 = 0.8309, \ p < 0.0001 \]

H. Liu et al. *Internet Journal of Anesthesiology* 2010;22
vs. PAC Thermodilution

vs. Echocardiography
Respiratory-based Measurements of Fluid Responsiveness

Limitations

The limitations of dynamic parameters: SOS

The main limitations to the use of dynamic parameters in surgical patients have been recently summarized as ‘SOS’. The first ‘S’ stands for small tidal volume and spontaneous breathing activity; the ‘O’ stands for open chest. In these conditions, changes in intrathoracic pressure are usually too small to induce significant changes in venous return. As a result, a false-negative may be observed, that is a small PPV or SVV in fluid responders. Several clinical studies have confirmed that the predictive value of PPV and SVV is decreased when patients are breathing spontaneously, when they are mechanically ventilated with a tidal volume \(<7–8 \text{ ml kg}^{-1}\), or when the pericardium and the chest are open. The second ‘S’ stands for sustained cardiac arrhythmias. In this setting, PPV and SVV reflect altered cardiac filling times rather than the effects of mechanical ventilation and then cannot be used to predict fluid responsiveness.

doi:10.1093/bja/aer511
Dynamic Assessment of Fluid Responsiveness

Using $\Delta SV$

$\Delta P = \text{fluid-induced increase in preload}$

$\Delta SV >> 10\%$

$\Delta SV > 10\%$

$\Delta SV < 10\%$

HYPO

HYPER

Preload

Stroke volume
Changes in stroke volume induced by passive leg raising in spontaneously breathing patients: comparison between echocardiography and Vigileo™/FloTrac™ device

- Matthieu Biais, Lionel Vidil, Philippe Sarrabay, Vincent Cottenceau, Philippe Revel and François Sztark

An increase in SV-Flotrac induced by PLR of more than 16% predicted the response to VE (increase in SV-TTE = 15% following VE) with a sensitivity of 85% (95% CI = 62 to 97) and a specificity of 90% (95% CI = 56 to 98). **Areas under the ROC curve for PLR-induced changes in SV-TTE (0.96 ± 0.03) and SV-Flotrac (0.92 ± 0.05).** (n=30 patients)
A Practical Algorithm

- **Tissue hypoperfusion**
  - SVV < 12% or \( \Delta SV < 10\% \)
  - C.I. > 2

- **preload**
  - Stop!

- **contractility**
  - Volume

- **afterload**
  - Inotrope
  - Vasopressor
RCT of SVV < 10% vs. Control in 120 Patients Undergoing “High Risk” Elective Abdominal Surgery

...fewer hypotensive episodes (2 vs. 3.5, p<0.01)

Figure 3

Benes et al. (Czech Rep) Crit Care 2010
RCT of GDT in 40 Patients with Cardiac Disease Undergoing Major Abdominal Operations

Volume challenge for SVV 12%
Dobutamine for CI <2.5l/min/m²

Mayer et.al., Crit Care 2009:13:219 (Germany) (Poster 29th International Symposium Crit Care)
RCT of GDT in 41 Major Abdominal Procedures Using SVV<12%

Return of Gut Function (p<0.01)

Hospital Length of Stay (p=0.04)

Ramsingh et al. Applegate II May 2010, Abstract, Loma Linda, CA
Maximize stroke volume (via boluses of 250ml HES until SV changed by < 10%) and target the oxygen delivery index (DO2I) > 600 ml/min m²
Midwest Organ Transplant Network (11/07-07/08)
Goal-Directed Therapy and Organ Procurement

SVV 8-9

Lori Markham, RN, MSN, CCRN, CPTC Director, Organ Procurement Services 08/2008
Midwest Organ Transplant Network (11/07-07/08)
Goal-Directed Therapy and Organ Procurement

Organs Transplanted = Lives Saved

3.30 OTPD
20 hearts
35 lungs
55 livers
90 kidneys
17 Pancreata

217 Total Organs Transplanted

OTPD

Pre Flotrac

2.80 3.30
Summary

- Both hypovolemia and hypervolemia are associated with morbidity and mortality in the ICU

- Resuscitate only in the face of tissue hypoperfusion

- Resuscitation proceeds systematically, optimizing preload, followed by cardiac output, followed by vascular tone

- To resuscitate effectively, both a dynamic marker of fluid responsiveness (e.g., PPV, ΔSV) and SV/CI is necessary
Limitations of respiratory based dynamic measurements include dysrhythmias and ventilator dysynchrony.

These may be bypassed by using the $\Delta SV$ as marker of fluid responsiveness.

FloTrac (Edwards Lifesciences) provides continuous SVV, SV, and CI measurements, and addresses many of the limitations of traditional resuscitation tools.

But you still need to interpret the data!!!
Update on ICU Fluid Resuscitation

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