Endpoints of Resuscitation: Have We Progressed Beyond Lactate?

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Disclosure

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What is Shock?

“Manifestation of the crude unhinging of the machinery of life”

Gross, 1872

“Failure to deliver and/or utilize adequate amounts of oxygen”


“An abnormality of the circulatory system that results in inadequate organ perfusion and tissue oxygenation”

American College of Surgeons Advanced Trauma Life Support Manual, 9E
# Classes of Shock

<table>
<thead>
<tr>
<th>Class</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood loss (ml)</td>
<td>(\leq 750)</td>
<td>750-1500</td>
<td>1500-2000</td>
<td>(\geq 2000)</td>
</tr>
<tr>
<td>Blood loss (% blood volume)</td>
<td>(\leq 15%)</td>
<td>15-30%</td>
<td>30-40%</td>
<td>(\geq 40%)</td>
</tr>
<tr>
<td>Pulse rate</td>
<td>&lt;100</td>
<td>&gt;100</td>
<td>&gt;120</td>
<td>(\geq 140)</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>Normal</td>
<td>Normal</td>
<td>Decreased</td>
<td>Decreased</td>
</tr>
<tr>
<td>Pulse pressure (mmHg)</td>
<td>Normal or increased</td>
<td>Decreased</td>
<td>Decreased</td>
<td>Decreased</td>
</tr>
<tr>
<td>Capillary refill test</td>
<td>Normal</td>
<td>Positive</td>
<td>Positive</td>
<td>Positive</td>
</tr>
<tr>
<td>Respiratory rate</td>
<td>14-20</td>
<td>20-30</td>
<td>30-40</td>
<td>(&gt;35)</td>
</tr>
<tr>
<td>Urine output (ml/hr)</td>
<td>(\geq 30)</td>
<td>20-30</td>
<td>5-15</td>
<td>Negligible</td>
</tr>
<tr>
<td>CNS-mental status</td>
<td>Slightly anxious</td>
<td>Mildly anxious</td>
<td>Anxious and confused</td>
<td>Confused, lethargic</td>
</tr>
<tr>
<td>Fluid replacement (3:1 rule)</td>
<td>Crystalloid</td>
<td>Crystalloid</td>
<td>Crystalloid + Blood</td>
<td>Crystalloid + Blood</td>
</tr>
</tbody>
</table>

ACS ATLS Manual, 9E
Resuscitation

• Restoration of normal physiology
• Standard physiologic values typically used (HR, BP, U/O)
• Values can be normal in setting of tissue hypoxia
• Significant abnormalities at cellular level may continue to exist
Endpoints of Resuscitation

• Developed to better guide resuscitative efforts

• Two general categories:
  • Hemodynamic Markers
    • BP (MAP), CVP, mixed venous oxygenation (SvO₂), pulse waveform analysis
  • Perfusion Markers
    • Base deficit, lactate
HEMODYNAMIC MARKERS
Mean Arterial Pressure

• Intuitive
• Universally available and interpretable
• Sepsis: MAP goals in EGDT showed improved outcomes
• Trauma: Hypotensive resuscitation may improve outcomes
• Normal values?
Hypotension Begins at 110 mm Hg: Redefining “Hypotension” With Data

Increasing mortality at SBP 110

“Hypotension” differs based on age

(<43yo) 108

117 (>43yo)
Mean Arterial Pressure

• Cons
  • Lack of universal MAP goal
  • Oxygenation at cellular level?
  • Hypotensive resuscitation: Not all studies supportive
  • Sepsis: Despite normalization of MAP, lactic acidosis may persist (cryptic septic shock)

• Surviving Sepsis Guidelines
  • MAP ≥ 65 in 1st 6 hours
Central Venous Pressure

- Common measurement
- Preload important determinant of cardiac output
- Surrogate for fluid responsiveness
- Surviving Sepsis guidelines
  - CVP 8-12 is “recommended physiologic target for resuscitation” in 1st 6 hours
Central Venous Pressure

• Reliability as indicator of fluid status controversial
  • Multiple studies: static pressure-derived values (CVP) do NOT accurately predict volume status

• Systematic review, 24 studies (Marik, 2008)
  • No association between CVP and blood volume
  • No association with fluid responsiveness
  • “CVP should not be used to make clinical decisions regarding patient management”
No correlation of CVP with volume status
Mixed/Central Venous Oxygen Saturation

- Systemic O2 is balance between oxygen delivery and consumption
- Venous O2 saturation (SvO2) reflects oxygen extraction
  - Mixed (SvO2) – PA catheter
  - Central (ScvO2) – central line
- Normal SvO2 65-75%
  - Low values suggest hypoxia
Mixed Venous Oxygen Saturation (SvO2)

- **Pros:**
  - True mixed venous sample
  - Data supports use in trauma, cardiac, sepsis

- **Cons**
  - Requires PA catheter
  - Normal SvO2 values do not guarantee adequate tissue oxygenation
    - Severe sepsis: SvO2 normal (or high) due to impaired O2 extraction
  - No survival benefit
  - No benefit in studies comparing lactate and ScvO2-based resuscitation protocols
Central Venous Oxygen Saturation (ScvO2)

- Requires central line placed in SVC, RA
- Regional vs global oxygenation
- Considerable debate on correlation of SvO2 and ScvO2

$\text{ScvO2} \geq \text{SvO2} \sim 7 \pm 4\%$
Central Venous Oxygen Saturation (ScvO2)

Pros
- Decreased in cardiogenic and hypovolemic shock
- Sepsis – EGDT (Rivers, NEJM 2001)
  - ScvO2: 16% reduction in mortality

Cons
- Requires CVC
- Regional vs vs global oxygenation
- Controversy with EGDT study and CVC use/data
  - Single center, reported mortality >20% higher than other studies (46%)
  - Proprietary catheter
  - Other studies have shown improvement in EGDT WITHOUT using ScvO2
• Randomized multicenter trial
• EGDT (including ScvO2) vs “Usual Care” in severe sepsis/shock
• 1260 patients, 56 hospitals
• No difference in 90 day mortality (29% both groups)
• EGDT: Increased IVFs, vasoactive drugs, transfusions, worse organ failure scores, longer ICU days
Arterial Pulse Waveform Analysis

- **Reverse Pulsus Paradoxus**
  - MV: BP increases on inspiration, falls during expiration

- **Stroke volume (SV) derived from arterial waveform**

- **Stroke volume variation (SVV) used to assess fluid responsiveness**

- **Multiple methods available: PiCCO, LiDICO, FloTrac**
Over 25 studies support use of SVV to predict fluid responsiveness (AUC > .84 considered to have good diagnostic accuracy)
Pulse Waveform Analysis: Limitations

- “SOS”
  - Small tidal volumes (<8cc/kg) and Spontaneous Breathing; Open Chest
    - Small changes in intrathoracic pressure/venous return (false negatives)
  - Sustained cardiac arrhythmia (Afib)

- Adequate waveform required
- Ideal patient: Ventilated, high TVs, no spontaneous breaths (paralyzed), no arrhythmia, no RV dysfunction
- Limited large or multicenter studies
BASE DEFICIT

• Marker anaerobic metabolism
• Surrogate marker for lactic acidosis
• Rapidly available as component of ABG

• Normal values -3 to +3 mMol
  • Mild 3-5, moderate 6-14, severe >15
  • Negative values represent acidosis
BASE DEFICIT

- Multiple studies support use in trauma
  - Independent predictor of mortality, ICU, and hospital LOS
  - Severity of deficit directly correlates to volume required in 24h and degree of hemorrhage
  - Failure to normalize BD correlates with mortality and organ failure
  - Complications: Severity correlates with ARF, ARDS, MOF, coagulopathy
BASE DEFICIT

• Limitations:
  • Affected by sodium bicarbonate, hypothermia, CO2 levels
  • Alcohol can artificially worsen BD
  • Other causes of acidosis can affect value (renal failure, DKA, CO2 retention)
  • BD does not correlate well with lactate levels
LACTATE

- Glucose metabolism by-product from pyruvate (aerobic vs anaerobic)
- Marker of anaerobic metabolism
- Balance between production/clearance (Liver>>Kidneys)
  - Hepatic or renal disease may increase lactate
Prolonged lactate clearance is associated with increased mortality in the surgical intensive care unit


- Retrospective review, SICU patients requiring HD monitoring/therapy
- Longer clearance = higher mortality
  - Clearance <24h 3%
  - Clearance 24-28h 13%
  - Clearance 48-96h 42%
  - No clearance 100%
- Time to lactate clearance was ONLY independent predictor of mortality (p<.0001)
Multicenter randomized, 300 pts
- Compared lactate vs ScvO2 in severe sepsis
- All pts normalized to CVP and MAP
- 2 groups: ScvO2 > 70% or lactate clearance ≥ 10%
- Lower mortality in lactate-guided group (17% vs 23%)
Early Lactate-Guided Therapy in Intensive Care Unit Patients

A Multicenter, Open-Label, Randomized Controlled Trial

Am J Respir Crit Care Med  Vol 182. pp 752–761, 2010

• Multicenter randomized, 4 ICUs
• ICU med/surg, lactate ≥ 3.0, 350 pts
• 2 groups: Decrease lactate by >20% q2 hrs for initial 8h vs not following lactate (other resuscitation targets allowed)
• Lactate-guided group
  • Decreased mortality (34% vs 44%)
  • Shorter ICU stay
  • Weaned faster from ventilator and inotropes
LACTATE

• Overall
  • Easily measured laboratory value
  • Provides reliable estimate of hypoperfusion
  • Level I data supports its use as endpoint in goal-directed therapy

• Limitations
  • May be elevated for other etiologies
    • Liver failure, seizures, asthma, cardiac arrest, burns, DKA, malignancy, genetic disorders, drugs (EtOH, cocaine, metformin, B2 agonists, propofol)
  • May lack sensitivity (false negative in mesenteric ischemia, sepsis)
Have We Progressed Beyond Lactate?
Conclusions

• Multiple markers available
• No one single best endpoint
• Resuscitation remains guided by multiple clinical tools
• Global markers (lactate, BD, SvO2) are practical, easily available, and useful as supplements to experienced clinical assessments
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