Role of PoCT in Goal-Directed Therapy in Critical Care Settings

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Sponsored by Instrumentation Laboratory
Contents

- What is Goal-Directed Therapy?
- What are the targets of Goal-Directed Therapy?
- Which PoCT for Goal-Directed Therapy?
- Does Goal-Directed Therapy improve outcome?
- Is PoCT better than central laboratory setting?
A TRIAL OF GOAL-ORIENTED HEMODYNAMIC THERAPY IN CRITICALLY ILL PATIENTS

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Gianni Tognoni, M.D., Antonio Pesenti, M.D., and Roberto Fumagalli, M.D.,
for the SvO2 Collaborative Group

762 critically ill patients, 56 Intensive Care Units

High Postoperative Risk
Septic shock
Acute Respiratory Failure
Massive blood loss
Sepsis Syndrome
COPD
Albumin Replacement in Patients with Severe Sepsis or Septic Shock

Pietro Caironi, M.D., Gianni Tognoni, M.D., Serge Masson, Ph.D., Roberto Fumagalli, M.D., Antonio Pesenti, M.D., Marilena Romero, Ph.D., Caterina Fanizza, M.Stat., Luisa Caspani, M.D., Stefano Faenza, M.D., Giacomo Grasselli, M.D., Gaetano Iapichino, M.D., Massimo Antonelli, M.D., Vieri Parrini, M.D., Gilberto Fiore, M.D., Roberto Latini, M.D., and Luciano Gattinoni, M.D., for the ALBIOS Study Investigators*

1818 critically ill patients, 100 Intensive Care Units

Severe Sepsis  Septic Shock
Prevention or reversal of cellular energetic deficits that can limit the function of one or more vital organs.

Hemodynamic monitoring in shock and implications for management

The definition of shock emerging from this consensus conference does not require the presence of hypotension. Instead, the definition of shock as “failure to deliver and/or utilize adequate amounts of oxygen” may include, but is not limited to, the presence of hypotension.
What is Goal-Directed Therapy?

Protocol-based (or quantitative) strategy to prevent or reverse cellular energetic deficits.
Why do we need monitors?

Physiological variables cannot be accurately predicted based solely on clinical evaluation.

<table>
<thead>
<tr>
<th></th>
<th>Correct prediction (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary Occlusion Pressure</td>
<td>30</td>
</tr>
<tr>
<td>Cardiac Output</td>
<td>51</td>
</tr>
<tr>
<td>Systemic Vascular Resistances</td>
<td>44</td>
</tr>
<tr>
<td>Central venous pressure</td>
<td>55</td>
</tr>
</tbody>
</table>

“Direct measurement of physiological variables lead to changes in therapy in 58% of the cases”.

Eisenberg, Crit Care Med 1984
No monitoring device can improve outcome by itself

- Monitoring technique
- Accurate and relevant data
- Correct interpretation
- Beneficial intervention
- Improved outcome

Vincent, Crit Care 2011
How can we assess “cellular energy metabolism”?

1. Evaluate adequacy of oxygen delivery:

   **CENTRAL VENOUS OXYGEN SATURATION (ScvO₂)**

2. Evaluate adequacy of aerobic energy production:

   **BLOOD LACTATE LEVEL**
What is ScvO₂?

Hemoglobin oxygen saturation of blood drawn from the superior vena cava or right atrium (≈ central venous oxygen content).
What does “low” ScvO₂ mean?

ScvO₂ <70% reveals an imbalance between oxygen delivery and demand (impending or actual hypoxia).

Oxygen delivery

Oxygen consumption

Low cardiac output
Hypoxemia
Anemia

Fever
Anxiety
Exercise
What is ScvO$_2$?

\[ \text{ScvO}_2 \text{ (%) } \]

\[ R^2 0.25 \]

\[ \text{Oxygen delivery (ml/min)} \]

What is ScvO₂?

Oxygen consumption (ml/min)


ScvO₂ (%)

R² 0.07

What is ScvO₂?

R² 0.71

<table>
<thead>
<tr>
<th></th>
<th>ScvO$_2$ &lt;70%</th>
<th>ScvO$_2$ ≥70%</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td>557 (35)</td>
<td>1043 (65)</td>
<td></td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>107 (92-120)</td>
<td>105 (93-120)</td>
<td>0.590</td>
</tr>
<tr>
<td>Mean arterial pressure (mmHg)</td>
<td>70 (60-82)</td>
<td>73 (63-83)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Central venous pressure (cmH$_2$O)</td>
<td>10 (6-13)</td>
<td>10 (7-13)</td>
<td>0.252</td>
</tr>
<tr>
<td>Urine output (ml/h)</td>
<td>50 (20-100)</td>
<td>60 (30-100)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>28-day mortality (%)</td>
<td>36</td>
<td>29</td>
<td>0.004</td>
</tr>
<tr>
<td>90-day mortality (%)</td>
<td>45</td>
<td>39</td>
<td>0.012</td>
</tr>
</tbody>
</table>

Median (IQR); Mann-Whitney rank sum and Chi-square tests

What is lactate?

It is a product of anaerobic, extra-mitochondrial, cellular metabolism.
What does “high” lactate level mean?

Hyperlactatemia (> 2mmol/L) reveals an imbalance between lactate production and clearance.

Aerobic capacity

Energy demand

Low oxygen provision
Impaired oxygen use
(*mitochondrial damage*)

Fever
Anxiety
Exercise
<table>
<thead>
<tr>
<th></th>
<th>Lactate ≤2 mmol/L</th>
<th>Lactate &gt;2 mmol/L</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td>1015 (58)</td>
<td>726 (42)</td>
<td></td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>100 (85-113)</td>
<td>110 (96-123)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean arterial pressure (mmHg)</td>
<td>76 (66-87)</td>
<td>70 (60-80)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Central venous pressure (cmH₂O)</td>
<td>10 (7-12)</td>
<td>10 (6-13)</td>
<td>0.130</td>
</tr>
<tr>
<td>Urine output (ml/h)</td>
<td>69 (32-100)</td>
<td>50 (17-100)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>28-day mortality (%)</td>
<td>22</td>
<td>38</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>90-day mortality (%)</td>
<td>33</td>
<td>48</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Median (IQR); Mann-Whitney rank sum and Chi-square tests

How can we measure ScvO$_2$ and lactate at the bedside?

(Cartridge-type) Blood gas analyzer

Clinically acceptable and immediately available results
Ease to use
Low maintenance time

In-hospital mortality from 41% to 31% (p=0.009)

Rivers, NEJM 2001
Early normalization of ScvO$_2$ decreases mortality

28-day mortality
- 40%
- 26%

Enrollment 6-h later

6-h lactate clearance ≥10%

ScvO₂ ≥70%

In-hospital mortality from 23% to 17% (NS)

Jones, JAMA 2010
Early normalization of lactatemia decreases mortality

Lactate (mmol/L)

28-day mortality 24%

28-day mortality 39%

Enrollment 1-day later

ScvO₂ ≥ 70%

- Fluid responsiveness?
  - Yes
    - Microcirculatory derangement
    - Vasodilators (NTG or ketanserin)
  - No
    - Hypovolemia
    - Fluids (crystalloid or colloid)

ScvO₂ < 70%

- SaO₂ < 92%
- Hb < 7.0 g/dl
- Pain, agitation, fever

\[ \text{2-h lactate clearance} \geq 20\% \]

- Yes
  - Continue therapy and repeat lactate after 2 hours
- No
  - Repeat flow-chart

In-hospital mortality from 44% to 34% (p=0.067)

Jansen, AJRCCM 2010
Review: Quantitative Resuscitation Strategy for Sepsis
Comparison: 01 Quantitative Resuscitation vs. Standard Care
Outcome: 01 Mortality

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment n/N</th>
<th>Control n/N</th>
<th>OR (random) 95% CI</th>
<th>OR (random) 95% CI</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Early</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lin 2006</td>
<td>58/108</td>
<td>83/115</td>
<td>0.46 [0.27, 0.80]</td>
<td>A</td>
<td></td>
</tr>
<tr>
<td>Rivers 2001</td>
<td>38/130</td>
<td>59/133</td>
<td>0.52 [0.31, 0.86]</td>
<td>A</td>
<td></td>
</tr>
<tr>
<td>Alia 1999</td>
<td>23/31</td>
<td>21/32</td>
<td>1.51 [0.51, 4.46]</td>
<td>A</td>
<td></td>
</tr>
<tr>
<td>Yu 1998</td>
<td>15/58</td>
<td>15/29</td>
<td>0.33 [0.13, 0.83]</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>Yu 1993</td>
<td>4/30</td>
<td>6/22</td>
<td>0.41 [0.10, 1.68]</td>
<td>B</td>
<td></td>
</tr>
<tr>
<td>Tuchschmidt 1992</td>
<td>13/26</td>
<td>18/25</td>
<td>0.39 [0.12, 1.24]</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>383</td>
<td>357</td>
<td>0.50 [0.37, 0.69]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events: 151 (Treatment), 202 (Control)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity: Chi² = 5.12, df = 5 (P = 0.40), I² = 2.4%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Test for overall effect: Z = 4.25 (P &lt; 0.0001)</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

| **Late**              |              |             |                    |                    |         |
| Xiao-Zhi 2006         | 4/16         | 7/17        | 0.48 [0.11, 2.11]  | B                  |         |
|Gattinoni 1995         | 84/124       | 37/57       | 1.14 [0.59, 2.20]  | A                  |         |
| Hayes 1994            | 17/24        | 12/23       | 2.23 [0.67, 7.40]  | B                  |         |
| Subtotal (95% CI)     | 164          | 97          | 1.16 [0.60, 2.22]  |         |         |
| Total events: 105 (Treatment), 56 (Control) |
| Test for heterogeneity: Chi² = 2.51, df = 2 (P = 0.29), I² = 20.3% |
| Test for overall effect: Z = 0.43 (P = 0.67) |

| Total (95% CI)        | 547          | 454         | 0.64 [0.43, 0.96]  |         |         |
| Total events: 256 (Treatment), 258 (Control) |
| Test for heterogeneity: Chi² = 14.59, df = 8 (P = 0.07), I² = 45.2% |
| Test for overall effect: Z = 2.16 (P = 0.03) |

Jones, Crit Care Med 2008
Guideline 38. There is fair evidence that POCT of ABG results in the ICU leads to improved clinical outcomes when POCT is found to lead to reduced TTAT compared to that in the central laboratory. Overall, we recommend that POCT of ABG results be considered as a way to improve outcomes in ICU patients. More prospective randomized controlled studies need to be performed. (Literature Search 13)

Strength/consensus of recommendation: B

Level of evidence: II
Is PoCT better than central laboratory testing?

Guideline 46. There is good evidence that more rapid TTAT of lactate results in critical care patient settings leads to improved clinical outcomes. Overall, we strongly recommend that more rapid TTAT of lactate results be considered as a way to improve outcomes in ED, OR, and ICU patients. (Literature Search 21)

Strength/consensus of recommendation: A
Level of evidence: I
Take home messages

- Goal-Directed Therapy is a protocol-based approach to reverse cellular energetic deficit
- ScvO\textsubscript{2} and lactate are useful markers of the balance between cellular energy production and demand
- Central venous blood gas analysis is the most important test to guide therapy
- Early Goal-Directed Therapy improves outcome of critically ill patients
- PoCT may be better than central laboratory testing
Acknowledgements

Prof. Luciano Gattinoni
Prof. Mervyn Singer

Alfredo Lissoni  Stefania Crotti
Giuseppe Breda  Alberto Sicignano
Daniela Tubiolo  Monica Savioli
Nicola Bottino  Riccarda Russo
Mauro Panigada  Federico Polli
Davide Chiumello  Pietro Caironi

Medical students, Fellows and Nurses working with me

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