CRITICAL PATIENT ENCOUNTERS:
USING ETCO₂ TO RECOGNIZE SEVERE SEPSIS IN THE PREHOSPITAL SETTING

Christopher Hunter, MD, PhD
Director, Health Services Department
Associate Medical Director, EMS System
Orange County, FL

Conflict of interest Disclosure

- Authors Conflicts of Interest:
  - C. Hunter, No Conflict of interest
Topics

- Sepsis and acid/base physiology
- Prehospital sepsis care
- ETCO2 as a diagnostic tool in sepsis
- Orange County EMS System Sepsis Alert Protocol
- Preliminary Findings

Sepsis

- End result of an overwhelming infection
- Hypoperfusion leads to end-organ damage and lactic acidosis
  - The severity of lactic acidosis predicts outcomes
- Early Goal Directed Therapy – early identification and aggressive therapy has been shown to improve outcomes
- Surviving Sepsis Campaign – guidelines for best practice
Prehospital Sepsis Care

- Frequent, high-mortality encounters
  - Seymour et al (2012) identified EMS transported more patients diagnosed with sepsis than STEMIs or CVSs, and there was a 19.7% mortality rate

- Prehospital interventions can make a difference
  - EMS transport decreased time to antibiotics and initiation of EGDT Studnek et al., 2012
  - Prehospital IV access and fluid administration improved survival Seymour et al., 2014
  - Prehospital sepsis protocol decreased mortality Guerra et al., 2013

- Early recognition and fluid resuscitation may be most important

Development of Sepsis

- Infection • Internal response (Vitals)
- SIRS • Hypoperfusion (Acidosis)
- Sepsis • Shock (Hypotension)
Respiratory Cycle

Oxygen -> lungs -> alveoli -> blood

breath

CO₂

lungs

CO₂

blood

Oxygen

muscles + organs

Oxygen

energy

Oxygen + Glucose

Oxygenation and Ventilation

Oxygen -> lungs -> alveoli -> blood

breath

CO₂

lungs

CO₂

blood

Oxygen

muscles + organs

Oxygen

energy

Oxygen + Glucose
ETCO2 provides a non-invasive mechanism to detect metabolic acidosis

- ETCO2 correlates with serum bicarbonate and PH levels in children and adults with Diabetic Ketoacidosis (Fearon et al., 2002, Soleimanpour et al., 2013)
- ETCO2 correlates with serum bicarbonate in children with gastroenteritis (Nagler et al., 2006)
- ETCO2 correlates with serum bicarbonate and lactate levels in patient with undifferentiated shock and metabolic disorders (Kehng and Rahman, 2012, Kartel et al., 2006)
- ETCO2 correlates with lactic acidosis and poor outcomes in patient with severe trauma (Deacon, 2004, Caputo et al., 2012)

ETCO2 predicts mortality in Emergency Room patients with suspected sepsis

<table>
<thead>
<tr>
<th>Condition</th>
<th>Correlation Coefficient</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepsis</td>
<td>-0.421</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Severe Sepsis</td>
<td>-0.597</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Septic Shock</td>
<td>-0.482</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
ETCO2 predicts mortality in Emergency Room patients with suspected sepsis

ROC Curve performance of ETCO2 and Lactate in predicting mortality

<table>
<thead>
<tr>
<th>Sepsis Categories</th>
<th>ETCO2 AUC (95%CI)</th>
<th>Lactate AUC (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suspected Sepsis</td>
<td>0.60 (0.37-0.83)</td>
<td>0.61 (0.36-0.87)</td>
</tr>
<tr>
<td>Severe Sepsis</td>
<td>0.67 (0.46-0.88)</td>
<td>0.69 (0.48-0.89)</td>
</tr>
<tr>
<td>Septic Shock</td>
<td>0.78 (0.59-0.96)</td>
<td>0.74 (0.55-0.93)</td>
</tr>
<tr>
<td>Intubation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intubated</td>
<td>0.77 (0.60-0.94)</td>
<td>0.82 (0.68-0.96)</td>
</tr>
<tr>
<td>Not Intubated</td>
<td>0.72 (0.56-0.88)</td>
<td>0.64 (0.46-0.82)</td>
</tr>
</tbody>
</table>

The role of ETCO2 in sepsis

- ETCO2 is a non-invasive outcome predictor in suspected sepsis
- ETCO2 performs as well as serum lactate predicting mortality in septic patients
- ETCO2 may provide a method for earlier identification and intervention in patients with suspected sepsis
A role for ETCO2 in the out of hospital diagnosis of sepsis

<table>
<thead>
<tr>
<th></th>
<th>Infection without Sepsis N=55 (95% CI)</th>
<th>Infection with Sepsis N=31 (95% CI)</th>
<th>Total N=86 (95% CI)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ETCO2</td>
<td>35 (33-37)</td>
<td>21 (20-23)</td>
<td>32 (28-36)</td>
<td>0.013</td>
</tr>
<tr>
<td>Respiratory Rate</td>
<td>29 (28-31)</td>
<td>29 (28-31)</td>
<td>31 (28-34)</td>
<td>0.763</td>
</tr>
<tr>
<td>Systolic BP</td>
<td>143 (136-151)</td>
<td>73 (66-81)</td>
<td>81 (77-85)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>85 (80-90)</td>
<td>74 (69-80)</td>
<td>84 (79-89)</td>
<td>0.006</td>
</tr>
<tr>
<td>Pulse</td>
<td>101 (93-109)</td>
<td>113 (101-125)</td>
<td>104 (98-110)</td>
<td>0.123</td>
</tr>
<tr>
<td>Oxygen Saturation</td>
<td>92 (89-94)</td>
<td>86 (81-92)</td>
<td>91 (88-94)</td>
<td>0.072</td>
</tr>
<tr>
<td>Shock Index</td>
<td>0.74 (0.66-0.82)</td>
<td>1.02 (0.88-1.15)</td>
<td>0.84 (0.76-0.91)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

AUC (95% CI) P-Value

<table>
<thead>
<tr>
<th></th>
<th>AUC (95% CI)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ETCO2</td>
<td>0.74 (0.67-0.81)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Respiratory Rate</td>
<td>0.50 (0.37-0.64)</td>
<td>0.324</td>
</tr>
<tr>
<td>Systolic BP</td>
<td>0.76 (0.65-0.86)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>0.68 (0.55-0.80)</td>
<td>0.007</td>
</tr>
<tr>
<td>Pulse</td>
<td>0.61 (0.49-0.74)</td>
<td>0.006</td>
</tr>
<tr>
<td>Oxygen Saturation</td>
<td>0.62 (0.49-0.75)</td>
<td>0.009</td>
</tr>
<tr>
<td>Shock Index</td>
<td>0.73 (0.62-0.85)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Prehospital ETCO2 predicts mortality in patients with SIRS

<table>
<thead>
<tr>
<th></th>
<th>Survivors N=371 (95% CI)</th>
<th>Non-Survivors N=14 (95% CI)</th>
<th>Total N=385 (95% CI)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ETCO2</td>
<td>32 (28-35)</td>
<td>23 (19-27)</td>
<td>33 (30-36)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Respiratory Rate</td>
<td>29 (26-33)</td>
<td>31 (26-36)</td>
<td>29 (28-33)</td>
<td>0.519</td>
</tr>
<tr>
<td>Systolic BP</td>
<td>142 (138-147)</td>
<td>113 (101-125)</td>
<td>141 (128-144)</td>
<td>0.001</td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>84 (78-88)</td>
<td>74 (60-91)</td>
<td>86 (77-91)</td>
<td>0.711</td>
</tr>
<tr>
<td>Pulse</td>
<td>114 (112-117)</td>
<td>111 (100-123)</td>
<td>114 (112-117)</td>
<td>0.617</td>
</tr>
<tr>
<td>Oxygen Saturation</td>
<td>95 (93-97)</td>
<td>85 (79-90)</td>
<td>95 (93-97)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

AUC (95% CI) P-Value

<table>
<thead>
<tr>
<th></th>
<th>AUC (95% CI)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ETCO2</td>
<td>0.84 (0.77-0.92)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Respiratory Rate</td>
<td>0.55 (0.39-0.71)</td>
<td>0.562</td>
</tr>
<tr>
<td>Systolic BP</td>
<td>0.69 (0.54-0.84)</td>
<td>0.014</td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>0.60 (0.43-0.77)</td>
<td>0.326</td>
</tr>
<tr>
<td>Pulse</td>
<td>0.64 (0.49-0.79)</td>
<td>0.001</td>
</tr>
<tr>
<td>Oxygen Saturation</td>
<td>0.79 (0.66-0.92)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Shock Index</td>
<td>0.57 (0.40-0.73)</td>
<td>0.411</td>
</tr>
</tbody>
</table>
ETCO2 in Emergency Department Sepsis Protocol

- ORMC ED began an internal sepsis screening protocol for those with suspected infection and ≥ 2 SIRS criteria (hold ICU beds, contact pharmacy)
- ETCO2 and serum lactate levels were collected in triage
- Of 54 activations 87% were diagnosed with sepsis
- Mean lactate levels were 3.4 (95%CI 2.6-4.2) vs 2.1 (95%CI 0.5-3.7; p=0.169)
- Mean ETCO2 levels were 31 (95%CI 27-34) vs 47 (95%CI 33-66; p=0.001)
- The AUC for ETCO2 predicting sepsis was 0.87 (95%CI 0.75-0.98) and for lactate was 0.68 (95%CI 0.42-0.93)
- **Low ETCO2 predicted sepsis in a triage screening tool**

Orange County EMS System Sepsis Protocol
Accuracy of a prehospital sepsis alert protocol utilizing ETCO2

- Preliminary pilot study to determine the accuracy of the protocol
- Poor protocol compliance created a study group
- 38 sepsis alert called by single agency to single ED
- 14 (37%) appropriately called based on ETCO2 ≤ 25mmHg, 24 (63%) had ≥ 2 SIRS criteria but ETCO2 > 25mmHg
- Mean ETCO2 in appropriate alerts was 18 (95%CI 15-20) vs 32 (95%CI 29-35; p=0.001). Mean lactate levels in the ED were 5.3 (95%CI 2.5-8.2) vs 2.1 (95%CI 1.7-2.6; p=0.001)
- The correlation between ETCO2 and lactate was -0.50, p=0.008
- The AUC for ETCO2 predicting appropriate activation of sepsis alert was 0.97 (95%CI 0.91-1.0)
- Using the ETCO2 ≤ 25mmHg cut off yielded a sensitivity of 100% and a specificity of 95%
- When appropriately used, the Orange County EMS System sepsis alert was highly sensitive and specific

Effectiveness of a prehospital sepsis alert protocol utilizing ETCO2

- Prospective pilot pre/post intervention study to assess impact of patient care in single ED
- 137 cases (110 pre, 27 post)
- Initiation of prehospital sepsis alert decreased:
  - Time to blood culture 27 (95%CI 18-36) vs 14 (95%CI 9-19)
  - Time to antibiotics 56 (95%CI 39-74) vs 40 (95%CI 24-55)
  - Time to fluids 34 (95%CI 17-52) vs 10 (95%CI 4-16)
  - Length of Stay 13 (95%CI 11-16) vs 9 (95%CI 6-12)
  - ICU Admission 53% (95%CI 43-62%) vs 33% (95%CI 14-52%)
  - Mortality 14% (95%CI 7-20%) vs 7% (95%CI 0-18%)
- Preliminary data, but...
Take Home Points

- Early identification and resuscitation by prehospital providers may improve outcomes for patients with sepsis
- Low ETCO2 is correlated with an acidotic state, and in the setting of suspected sepsis it serves as a similar outcome predictor to serum lactate levels
- ETCO2 may be used as a non-invasive, real time adjunct screening tool to create protocols for prehospital sepsis identification

Works Cited

- McGillicuddy, D, Tang, A, Cataldí, S, Gusev, J, Shapiro, N. Evaluation of end tidal carbon dioxide role in predicting elevated SOFA score and lactate acidosis. Intensive Care Med 2010