Updates in Critical Care

5th Annual Acute Care of the Complex Hospitalized Patient for NPs & PAs
Scottsdale, AZ, February 9th, 2017

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Pulmonary and Critical Care Medicine
Mayo Clinic, AZ
Disclosures

• Nothing to disclose
Overview of Topics

- New sepsis and septic shock definitions
  - JAMA. 2016;315(8):801-810

- Hydrocortisone in severe sepsis

- Acute Hypoxemic Respiratory Failure
  - High Flow NC
  - NIPPV in the Immunocompromised
  - HFNC to prevent re-intubations

- Central venous catheters
  - NEJM 2015;373:1220-9
Question 1

- 59 yo male with longstanding history of BPH and chronic indwelling urinary catheter presents to the Emergency department with 2 days of fever, chills, generalized weakness and left sided flank/lower back pain.

- Tmax 39.9C, BP 78/51, HR 121 regular, 97% RA

- PE: 72kg, somnolent, tachycardic, warm extremities. WBC 18K with left shift. U/A with pyuria. Lactate 1.8 mmol/L

- BP is 80/48 after 3 L of IV crystalloids, urine output of 10 cc in the last 2 hours, lactate level 1.7 mmol/L

- Norepinephrine is started at 0.15 mcg/kg/min with improvement of BP, mentation and urine output
Question 1

• Based on the new sepsis/septic shock definitions, this patient’s findings are consistent with?

A. Systemic inflammatory response syndrome (SIRS)
B. Sepsis
C. Severe sepsis
D. Septic shock
Clinical Review & Education

Special Communication | CARING FOR THE CRITICALLY ILL PATIENT

The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

Mervyn Singer, MD, FRCP; Clifford S. Deutschman, MD, MS; Christopher Warren Seymour, MD, MSc; Manu Shankar-Hari, MSc, MD, FFICM; Djillali Annane, MD, PhD; Michael Bauer, MD; Rinaldo Bellomo, MD; Gordon R. Bernard, MD; Jean-Daniel Chiche, MD, PhD; Craig M. Coopersmith, MD; Richard S. Hotchkiss, MD; Mitchell M. Levy, MD; John C. Marshall, MD; Greg S. Martin, MD, MSc; Steven M. Opal, MD; Gordon D. Rubenfeld, MD, MS; Tom van der Poll, MD, PhD; Jean-Louis Vincent, MD, PhD; Derek C. Angus, MD, MPH

Why and How?

• New knowledge of the pathophysiology of sepsis
• Expert consensus from the ESICM and SCCM
• Systematic literature review and Delphi consensus
• Main concept: sepsis-induced changes in
  ◆ Organ function
  ◆ Cell biology
  ◆ Biochemistry
  ◆ Immunology
  ◆ Circulation
“The need for two or more SIRS criteria to define severe sepsis excluded one in eight otherwise similar patients with infection, organ failure, and substantial mortality”
Sepsis definition challenges

• “Sepsis is a multifaceted host response to an infecting pathogen that may be significantly amplified by endogenous factors”

• No gold standard diagnostic test

• Affected by both host and pathogen factors
New definitions: Sepsis

• “Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection”

• Organ dysfunction can be identified as an acute change in total SOFA score $\geq 2$ points consequent to the infection.
Table 1. Sequential [Sepsis-Related] Organ Failure Assessment Score

<table>
<thead>
<tr>
<th>System</th>
<th>Score</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiration</td>
<td></td>
<td>≥400 (53.3)</td>
<td>&lt;400 (53.3)</td>
<td>&lt;300 (40)</td>
<td>&lt;200 (26.7) with respiratory support</td>
<td>&lt;100 (13.3) with respiratory support</td>
</tr>
<tr>
<td>Pao₂/Fio₂, mm Hg (kPa)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coagulation</td>
<td></td>
<td>≥150</td>
<td>&lt;150</td>
<td>&lt;100</td>
<td>&lt;50</td>
<td>&lt;20</td>
</tr>
<tr>
<td>Platelets, ×10³/μL</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bilirubin, mg/dL (μmol/L)</td>
<td></td>
<td>&lt;1.2 (20)</td>
<td>1.2-1.9 (20-32)</td>
<td>2.0-5.9 (33-101)</td>
<td>6.0-11.9 (102-204)</td>
<td>&gt;12.0 (204)</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MAP ≥70 mm Hg</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MAP &lt;70 mm Hg</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular</td>
<td></td>
<td>Dopamine &lt;5 or dobutamine (any dose)</td>
<td>Dopamine 5.1-15 or epinephrine ≤0.1 or norepinephrine ≤0.1</td>
<td>Dopamine &gt;15 or epinephrine &gt;0.1 or norepinephrine &gt;0.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Central nervous system</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glasgow Coma Scale score</td>
<td></td>
<td>15</td>
<td>13-14</td>
<td>10-12</td>
<td>6-9</td>
<td>&lt;6</td>
</tr>
<tr>
<td>Renal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Creatinine, mg/dL (μmol/L)</td>
<td></td>
<td>&lt;1.2 (110)</td>
<td>1.2-1.9 (110-170)</td>
<td>2.0-3.4 (171-299)</td>
<td>3.5-4.9 (300-440)</td>
<td>&gt;5.0 (440)</td>
</tr>
<tr>
<td>Urine output, mL/d</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: Fio₂, fraction of inspired oxygen; MAP, mean arterial pressure; Pao₂, partial pressure of oxygen.

a Adapted from Vincent et al.

b Catecholamine doses are given as μg/kg/min for at least 1 hour.

c Glasgow Coma Scale scores range from 3-15; higher score indicates better neurological function.
Assessment of Clinical Criteria for Sepsis
For the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

Christopher W. Seymour, MD, MSc; Vincent X. Liu, MD, MSc; Theodore J. Iwashyna, MD, PhD; Frank M. Brunkhorst, MD; Thomas D. Rea, MD, MPH; André Scherag, PhD; Gordon Rubenfeld, MD, MSc; Jeremy M. Kahn, MD, MSc; Manu Shankar-Hari, MD, MSc; Mervyn Singer, MD, FRCP; Clifford S. Deutschman, MD, MS; Gabriel J. Escobar, MD; Derek C. Angus, MD, MPH

<table>
<thead>
<tr>
<th></th>
<th>SIRS</th>
<th>SOFA</th>
<th>LODS</th>
<th>qSOFA</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIRS</td>
<td>0.64</td>
<td>0.43</td>
<td>0.41</td>
<td>0.46</td>
</tr>
<tr>
<td></td>
<td>(0.62-0.66)</td>
<td>(0.41-0.46)</td>
<td>(0.38-0.43)</td>
<td>(0.43-0.48)</td>
</tr>
<tr>
<td>SOFA</td>
<td>&lt;0.01</td>
<td>0.74</td>
<td>0.87</td>
<td>0.65</td>
</tr>
<tr>
<td></td>
<td>(0.73-0.76)</td>
<td>(0.87-0.88)</td>
<td>(0.63-0.66)</td>
<td></td>
</tr>
<tr>
<td>LODS</td>
<td>&lt;0.01</td>
<td>0.20</td>
<td>0.75</td>
<td>0.76</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(0.73-0.76)</td>
<td>(0.75-0.77)</td>
</tr>
<tr>
<td>qSOFA</td>
<td>0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>0.66</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(0.64-0.68)</td>
</tr>
</tbody>
</table>
### Non-ICU encounters (n = 66,522)

<table>
<thead>
<tr>
<th></th>
<th>SIRS</th>
<th>SOFA</th>
<th>LODS</th>
<th>qSOFA</th>
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</thead>
<tbody>
<tr>
<td>SIRS</td>
<td></td>
<td></td>
<td>0.43</td>
<td>0.61</td>
</tr>
<tr>
<td></td>
<td>0.76</td>
<td>0.52</td>
<td>0.43</td>
<td>0.61</td>
</tr>
<tr>
<td>(0.75-0.77)</td>
<td>(0.51-0.53)</td>
<td>(0.42-0.44)</td>
<td>(0.61-0.62)</td>
<td></td>
</tr>
<tr>
<td>SOFA</td>
<td>&lt;.001</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.79</td>
<td></td>
<td>0.80</td>
<td>0.59</td>
</tr>
<tr>
<td>(0.78-0.80)</td>
<td></td>
<td>(0.80-0.81)</td>
<td>(0.58-0.60)</td>
<td></td>
</tr>
<tr>
<td>LODS</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.81</td>
<td>0.68</td>
</tr>
<tr>
<td>(0.80-0.82)</td>
<td>(0.68-0.69)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>qSOFA</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>.72</td>
<td>0.81</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(0.80-0.82)</td>
</tr>
</tbody>
</table>
New concept: Quick SOFA or qSOFA

- Respiratory Rate $\geq 22$/min
- Altered Mental Status
- Systolic Blood Pressure $\leq 100$ mmHg
Table 4. Odds Ratios for Baseline Model and qSOFA Variables for In-Hospital Mortality in the UPMC Derivation Cohort (N = 74,453)

<table>
<thead>
<tr>
<th>qSOFA model</th>
<th>Total No. With Categorical Variable</th>
<th>Deaths, No. (% of Total)</th>
<th>In-Hospital Mortality, Adjusted Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory rate, /min</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;22</td>
<td>45,398</td>
<td>676 (1)</td>
<td>1 [Reference]</td>
</tr>
<tr>
<td>≥22</td>
<td>29,055</td>
<td>2,496 (9)</td>
<td>3.18 (2.89-3.50)</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;100</td>
<td>44,669</td>
<td>789 (2)</td>
<td>1 [Reference]</td>
</tr>
<tr>
<td>≤100</td>
<td>29,784</td>
<td>2,383 (8)</td>
<td>2.61 (2.40-2.85)</td>
</tr>
<tr>
<td>Altered mental status, Glasgow Coma Scale score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14-15</td>
<td>66,879</td>
<td>1,677 (3)</td>
<td>1 [Reference]</td>
</tr>
<tr>
<td>≤13</td>
<td>7,574</td>
<td>1,495 (20)</td>
<td>4.31 (3.96-4.69)</td>
</tr>
</tbody>
</table>
New Definitions: Septic Shock

Developing a New Definition and Assessing New Clinical Criteria for Septic Shock
For the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

Manu Shankar-Hari, MD, MSc; Gary S. Phillips, MAS; Mitchell L. Levy, MD; Christopher W. Seymour, MD, MSc; Vincent X. Liu, MD, MSc; Clifford S. Deutschman, MD; Derek C. Angus, MD, MPh; Gordon D. Rubenfeld, MD, MSc; Mervyn Singer, MD, FRCP; for the Sepsis Definitions Task Force

*JAMA. 2016;315(8):775-787*
Figure 2. Random-Effects Meta-analysis of Studies identified in the Systematic Review, Reporting Septic Shock Mortality

<table>
<thead>
<tr>
<th>Source</th>
<th>Septic Shock Deaths, No.</th>
<th>Patients With Septic Shock, No.</th>
<th>Mortality, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decker et al., 2006</td>
<td>90</td>
<td>125</td>
<td>72.0 (64.1-79.9)</td>
</tr>
<tr>
<td>Aksu et al., 2007</td>
<td>41</td>
<td>78</td>
<td>52.6 (41.5-63.6)</td>
</tr>
<tr>
<td>Netzer et al., 2013</td>
<td>30</td>
<td>91</td>
<td>33.3 (22.8-43.8)</td>
</tr>
<tr>
<td>Sall et al., 2011</td>
<td>85</td>
<td>145</td>
<td>58.6 (50.6-66.6)</td>
</tr>
<tr>
<td>Cancalon-Pereira et al., 2014</td>
<td>418</td>
<td>856</td>
<td>48.8 (46.5-52.2)</td>
</tr>
<tr>
<td>Leipert et al., 2014</td>
<td>4146</td>
<td>7934</td>
<td>52.0 (50.9-53.1)</td>
</tr>
<tr>
<td>Onzi et al., 2014</td>
<td>144</td>
<td>319</td>
<td>53.0 (43.7-62.0)</td>
</tr>
<tr>
<td>Hypotension</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Laplante et al., 2004</td>
<td>81</td>
<td>159</td>
<td>50.9 (43.2-58.7)</td>
</tr>
<tr>
<td>Gospodarcz et al., 2006</td>
<td>44</td>
<td>129</td>
<td>34.1 (25.9-42.3)</td>
</tr>
<tr>
<td>Shihprio et al., 2006</td>
<td>15</td>
<td>53</td>
<td>28.3 (16.2-40.4)</td>
</tr>
<tr>
<td>Pera et al., 2009</td>
<td>202</td>
<td>458</td>
<td>44.1 (36.6-51.7)</td>
</tr>
<tr>
<td>Klein-Enhoff et al., 2012</td>
<td>52</td>
<td>98</td>
<td>53.1 (43.2-62.5)</td>
</tr>
<tr>
<td>Kaskon et al., 2014</td>
<td>14690</td>
<td>11079</td>
<td>28.6 (28.2-29.0)</td>
</tr>
<tr>
<td>Hypotension + Perfusion Abnormalities and/or Vasopressor Therapy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ringle Frauent et al., 1994</td>
<td>67</td>
<td>110</td>
<td>46.4 (37.0-56.7)</td>
</tr>
<tr>
<td>Sain et al., 1995</td>
<td>27</td>
<td>33</td>
<td>81.8 (68.7-95.0)</td>
</tr>
<tr>
<td>Alberti et al., 2002</td>
<td>752</td>
<td>1180</td>
<td>63.8 (60.7-67.0)</td>
</tr>
<tr>
<td>Hypotension + Vasopressor Therapy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rodriguez et al., 2001</td>
<td>129</td>
<td>283</td>
<td>45.6 (39.8-51.4)</td>
</tr>
<tr>
<td>Stoc et al., 2004</td>
<td>106</td>
<td>203</td>
<td>52.2 (46.3-58.3)</td>
</tr>
<tr>
<td>Laplante et al., 2005</td>
<td>28</td>
<td>57</td>
<td>49.1 (36.5-61.8)</td>
</tr>
<tr>
<td>Vincent et al., 2006</td>
<td>250</td>
<td>422</td>
<td>54.3 (46.6-68.7)</td>
</tr>
</tbody>
</table>

Phua et al., 2011

Overall (I^2=99.5%; P = .000)

Mortality, % (95% CI)

Overall (I^2=99.5%; P = .000)

Mortality, % (95% CI)
Figure 4. Serum Lactate Level Analysis

GEE Model Adjusted Odds Ratio (95% CI)

Serum Lactate, mmol/L
New Definitions: Septic Shock

• “Septic shock is a subset of sepsis in which underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality”

• Patients with septic shock can be identified with a clinical construct of sepsis with:
  ◆ Persisting hypotension requiring vasopressors to maintain MAP ≥ 65mmHg AND
  ◆ Serum lactate level >2 mmol/L (18mg/dL) despite adequate volume resuscitation.
Patient with suspected infection

qSOFA ≥2? (see (A))

No

Sepsis still suspected?

No

Yes

Assess for evidence of organ dysfunction

Monitor clinical condition; reevaluate for possible sepsis if clinically indicated
Patient with suspected infection

qSOFA ≥2? (see A)

No

Sepsis still suspected?

No

Monitor clinical condition; reevaluate for possible sepsis if clinically indicated

Yes

No

Assess for evidence of organ dysfunction

SOFA ≥2? (see B)

No

Monitor clinical condition; reevaluate for possible sepsis if clinically indicated

Yes

Sepsis
Patient with suspected infection

qSOFA ≥2? (see A)

- Yes
  - Assess for evidence of organ dysfunction
    - SOFA ≥2? (see B)
      - Yes
        - Sepsis
          - Despite adequate fluid resuscitation, 1. vasopressors required to maintain MAP ≥65 mm Hg AND 2. serum lactate level >2 mmol/L?
            - Yes
              - Septic shock
            - No
              - No

- No
  - Sepsis still suspected?
    - Yes
      - Monitor clinical condition; reevaluate for possible sepsis if clinically indicated
    - No
      - Monitor clinical condition; reevaluate for possible sepsis if clinically indicated
Problems with the new definitions

- How do we call sepsis on vasopressors but normal lactate?
- Poor description of phenotypes
- Derivation and validation cohort mainly from the US
- Gaps in database for qSOFA derivation
- Need for lactate determination
- Risk of “not calling” sepsis when it is present
• **Question:** Does adjunctive early hydrocortisone therapy prevent the development of septic shock in patients with severe sepsis who are not in shock?

• **Findings:** In this randomized clinical trial that included 380 adults, occurrence of septic shock was not significantly different between patients who received hydrocortisone or placebo (21.2% vs 22.9%, respectively).
Figure 2. Time to Septic Shock

Cumulative Probability of Septic Shock

Placebo

Hydrocortisone

Log-rank $P = .69$

Time After Randomization, d

No. at risk

Placebo  176  161  139  136  134  131  130  128

Hydrocortisone  177  163  146  142  138  138  134  130
• No differences in secondary infections between groups
• No differences in patients with or without CIRCI
• **Meaning**: Administration of hydrocortisone did not prevent the development of shock in patients with severe sepsis.
Question 2

• The following patient will likely benefit from the use of NIPPV:

A. 67 yo male with septic shock requiring 3 pressors and developing severe ARDS

B. 54 yo female s/p esophagectomy due to malignancy complicated by aspiration causing hypoxemia and severe mixed acidosis with obtundation

C. 71 yo male with COPD exacerbation, awake and alert, hemodynamically stable, mild respiratory acidosis

D. 58 yo male with pulmonary edema due to acute heart failure in the setting of STEMI with VT storm in need to go to the cath lab
Acute Hypoxemic Respiratory Failure
Non-invasive positive pressure ventilation

- Ventilatory support that does not require an artificial airway
- Mask is used as the interface between the patient and the ventilator
- CPAP and BiPAP
Advantages of NIPPV

• Decrease risks associated with intubation:
  ➢ VAP
  ➢ Trauma of the airway

• Less cost
• Decreased hospital stay
• Less delirium
High flow device: Optiflow

- Flow: 20-50 L/min
- FiO2: up to 1
- Humidification, temp 37°C
High-Flow Oxygen through Nasal Cannula in Acute Hypoxemic Respiratory Failure

Jean-Pierre Frat, M.D., Arnaud W. Thille, M.D., Ph.D., Alain Mercat, M.D., Ph.D., Christophe Girault, M.D., Ph.D., Stéphanie Ragot, Pharm.D., Ph.D., Sébastien Perbet, M.D., Gwénaël Prat, M.D., Thierry Boulain, M.D., Elise Morawiec, M.D., Alice Cottereau, M.D., Jérôme Devaquet, M.D., Saad Nseir, M.D., Ph.D., Keyvan Razazi, M.D., Jean-Paul Mira, M.D., Ph.D., Laurent Argaud, M.D., Ph.D., Jean-Charles Chakarian, M.D., Jean-Darnien Ricard, M.D., Ph.D., Xavier Wittebole, M.D., Stéphanie Chevalier, M.D., Alexandre Herbland, M.D., Muriel Fartoukh, M.D., Ph.D., Jean-Michel Constantin, M.D., Ph.D., Jean-Marie Tonnelier, M.D., Marc Pierrot, M.D., Armelle Mathonnet, M.D., Gaëtan Béduneau, M.D., Céline Delétage-Métreau, Ph.D., Jean-Christophe M. Richard, M.D., Ph.D., Laurent Brochard, M.D., and René Robert, M.D., Ph.D., for the FLORALI Study Group and the REVA Network*
High Flow Oxygen Through Nasal Cannula in Acute Hypoxemic Respiratory Failure

- Multicenter, randomized controlled trial
- 23 ICU’s in France, 310 patients
- Inclusion:
  - P:F < 300
  - PaCO2 < 45
- Exclusion:
  - Asthma exacerbation
  - Cardiogenic pulmonary edema
  - Hemodynamic instability/use of pressors
  - GCS less than 12
  - Contraindication to noninvasive ventilation

High Flow Oxygen Through Nasal Cannula in Acute Hypoxemic Respiratory Failure

• Study Groups:
  • High flow oxygen
  • Standard oxygen
  • Noninvasive ventilation

• Outcomes:
  • Primary: Proportion of patients intubated at day 28
  • Secondary: Mortality in the ICU, at 90 days, and number ventilator free days at day 28

A Overall Population

Cumulative incidence of intubation

Days since Enrollment

P = 0.17 by log-rank test

No. at Risk

<table>
<thead>
<tr>
<th></th>
<th>High-flow oxygen</th>
<th>Standard oxygen</th>
<th>Noninvasive ventilation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>106</td>
<td>94</td>
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<td>0</td>
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</table>

B Patients with a PaO\textsubscript{2}:FiO\textsubscript{2} ≤200 mm Hg

Cumulative incidence of intubation

Days since Enrollment

P = 0.009 by log-rank test

No. at Risk

<table>
<thead>
<tr>
<th></th>
<th>High-flow oxygen</th>
<th>Standard oxygen</th>
<th>Noninvasive ventilation</th>
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<tr>
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</table>
Cumulative Probability of Survival

P = 0.02 by log-rank test

No. at Risk

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<th>45</th>
<th>60</th>
<th>75</th>
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<td>High-flow oxygen</td>
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<td>100</td>
<td>97</td>
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<td>93</td>
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<td>93</td>
<td>86</td>
<td>80</td>
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</tbody>
</table>
Results

• Intubation at day 28 (p=0.18 for all comparisons)
  • 38% in high-flow oxygen group
  • 47% in the standard oxygen group
  • 50% in the NIV group

• Ventilator free days at day 28 (p=0.02)
  • 24 (HF) vs 22 (SO) vs 19 (NIV)

Main conclusions and limitations

• In patients with non-hypercapnic acute hypoxemia respiratory failure, treatment with HF oxygen, standard oxygen or NIPPV did not result in significantly lower intubation rates.

• Important secondary outcomes were better in the HF oxygen group

• Limitations:
  ◆ Negative study for primary outcome
  ◆ Not enough power for secondary outcomes
  ◆ Post-hoc analysis
Research

Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Noninvasive Ventilation vs Oxygen Therapy on Mortality Among Immunocompromised Patients With Acute Respiratory Failure: A Randomized Clinical Trial

Virginie Lemiale, MD; Djamel Mokart, MD; Matthieu Resche-Rigon, MD, PhD; Frédéric Pène, MD, PhD; Julien Mayaux, MD; Etienne Faucher, MD; Martine Nyunga, MD; Christophe Girault, MD, PhD; Pierre Perez, MD; Christophe Guitton, MD, PhD; Kenneth Ekpe, MD; Achille Kouatchet, MD; Igor Théodorese, MS; Dominique Benoît, MD, PhD; Emmanuel Canet, MD; François Barbier, MD, PhD; Antoine Rabbat, MD; Fabrice Brunelle, MD; François Vincent, MD; Kada Klouche, MD, PhD; Kontar Loay, MD; Eric Mariotte, MD; Lila Bouadma, MD, PhD; Anne-Sophie Moreau, MD; Amélie Seguin, MD; Anne-Pascale Meert, MD, PhD; Jean Reignier, MD, PhD; Laurent Papazian, MD, PhD; Ilham Mezhari, MD; Yves Cohen, MD, PhD; Maleka Schenck, MD; Rebecca Hamidfar, MD; Michael Darmon, MD, PhD; Alexandre Demoule, MD, PhD; Sylvie Chevret, MD, PhD; Elie Azoulay, MD, PhD; for the Groupe de Recherche en Réanimation Respiratoire du patient d’Onco-Hématologie (GRRR-OH)

JAMA. 2015;314(16):1711-1719
Effect of Noninvasive Ventilation vs Oxygen Therapy on Mortality Among Immunocompromised Patients With Acute Respiratory Failure: A Randomized Clinical Trial

- Multicenter Randomized Trial
- 374 pts receiving rx for hematologic or solid organ malignancy (85%)
- Acute, non-hypercapneic, hypoxemic RF
- Objective:
  - To determine whether early noninvasive ventilation improved survival
- Outcome:
  - Primary – 28 day mortality
  - Secondary – Intubation, SOFA (day 3), ICU acquired infections, MV duration, ICU LOS.

Effect of Noninvasive Ventilation vs Oxygen Therapy on Mortality Among Immunocompromised Patients With Acute Respiratory Failure: A Randomized Clinical Trial

Effect of Noninvasive Ventilation vs Oxygen Therapy on Mortality Among Immunocompromised Patients With Acute Respiratory Failure: A Randomized Clinical Trial
Effect of Noninvasive Ventilation vs Oxygen Therapy on Mortality Among Immunocompromised Patients With Acute Respiratory Failure: A Randomized Clinical Trial

• No significant difference:
  • 28 day mortality
  • ICU acquired infections
  • Need for and duration of MV
  • ICU LOS
• Study power was limited
• Compared with prior studies, 50% decrease in rates of intubation and mortality
• High flow NC used in about 40% of “Oxygen Group”

To determine whether high-flow nasal cannula oxygen therapy is superior to conventional oxygen therapy for preventing reintubation in mechanically ventilated patients at low risk for reintubation.

Multicenter randomized clinical trial in 7 intensive care units (ICUs) in Spain.

Participants were 527 adult critical patients at low risk for reintubation who fulfilled criteria for planned extubation.
• The primary outcome was reintubation within 72 hours
• Secondary outcomes included postextubation respiratory failure, respiratory infection, sepsis and multiorgan failure, ICU and hospital length of stay and mortality, and time to reintubation.
• HFNC for at least 24 hours
• Goal SpO2 >92%
<table>
<thead>
<tr>
<th>Variable</th>
<th>Oxygen Therapy</th>
<th>Difference Between Groups (95% CI)</th>
<th>P Value</th>
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<tbody>
<tr>
<td></td>
<td>High-Flow (n = 264)</td>
<td>Conventional (n = 263)</td>
<td></td>
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<tr>
<td>Primary Outcome</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All-cause reintubation, No. (%)</td>
<td>13 (4.9)</td>
<td>32 (12.2)</td>
<td>7.2 (2.5 to 12.2)</td>
</tr>
<tr>
<td>Secondary Outcomes</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Postextubation respiratory failure, No. (%)</td>
<td>22 (8.3)</td>
<td>38 (14.4)</td>
<td>6.1 (0.7 to 11.6)</td>
</tr>
</tbody>
</table>

* Wald chi-squared test, adjusting for center.
Among extubated patients at low risk for reintubation, the use of high-flow nasal cannula oxygen compared with conventional oxygen therapy reduced the risk of reintubation within 72 hours.
Question 3

• Ultrasound guidance for central venous catheter placement is possible for the following site:

A. Femoral vein
B. Subclavian vein
C. Jugular vein
D. All of the above
E. None of the above
Intravascular Complications of Central Venous Catheterization by Insertion Site

Jean-Jacques Parienti, M.D., Ph.D., Nicolas Mongardon, M.D., Bruno Mégarbane, M.D., Ph.D., Jean-Paul Mira, M.D., Ph.D., Pierre Kalfon, M.D., Ph.D., Antoine Gros, M.D., Sophie Marqué, M.D., Marie Thuong, M.D., Véronique Pottier, M.D., Michel Ramakers, M.D., Benoît Savary, M.D., Amélie Seguin, M.D., Xavier Valette, M.D., Nicolas Terzi, M.D., Ph.D., Bertrand Sauneuf, M.D., Vincent Cattoir, Pharm.D., Ph.D., Leonard A. Mermel, D.O., and Damien du Cheyron, M.D., Ph.D., for the 3SITES Study Group*

Intravascular Complications of Central Venous Catheterization by Insertion Site

• 10 ICUs, in France from December 2011 through June 2014

• Randomly assigned non-tunneled central venous catheterization in patients in the adult intensive care unit (ICU)
  ➢ Subclavian, jugular, or femoral vein (in a 1:1:1 ratio if all three insertion sites were suitable)
  ➢ 1:1 ratio if two sites were suitable

• The primary outcome measure was a composite of catheter-related bloodstream infection and symptomatic deep-vein thrombosis.
7559 Catheter insertions were screened

- 4088 Were excluded because only one site was available

3471 Underwent randomization
- 2532 Were assigned to 1:1:1
- 939 Were assigned to 1:1

1016 Were assigned to subclavian site
- 843 Had all sites available
- 138 Had femoral site excluded
- 35 Had jugular site excluded

1284 Were assigned to jugular site
- 845 Had all sites available
- 300 Had subclavian site excluded
- 139 Had femoral site excluded

1171 Were assigned to femoral site
- 844 Had all sites available
- 296 Had subclavian site excluded
- 31 Had jugular site excluded

866 Were inserted in assigned site
- 51 Were inserted in the femoral site
- 96 Were inserted in the jugular site
- 3 Were inserted in the contralateral subclavian site

1174 Were inserted in assigned site
- 29 Were inserted in the subclavian site
- 61 Were inserted in the femoral site
- 20 Were inserted in the contralateral jugular site

1114 Were inserted in assigned site
- 4 Were inserted in the subclavian site
- 51 Were inserted in the jugular site
- 2 Were inserted in the contralateral femoral site

843 Were included in the intention-to-treat three-choice comparison
878 Were included in the intention-to-treat pairwise subclavian-versus-femoral comparison
981 Were included in the intention-to-treat pairwise subclavian-versus-jugular comparison
845 Were included in the intention-to-treat three-choice comparison
984 Were included in the intention-to-treat pairwise jugular-versus-subclavian comparison
1145 Were included in the intention-to-treat pairwise jugular-versus-femoral comparison
844 Were included in the intention-to-treat three-choice comparison
875 Were included in the intention-to-treat pairwise femoral-versus-subclavian comparison
1140 Were included in the intention-to-treat pairwise femoral-versus-jugular comparison
The graph shows the percentage of catheters with complications for different insertion sites:

- **Subclavian (N=843):**
  - Mechanical (grade ≥3): 18 (2.1%)
  - Symptomatic deep-vein thrombosis: 4 (0.5%)
  - Bloodstream infection: 4 (0.5%)

- **Jugular (N=845):**
  - Mechanical (grade ≥3): 12 (1.4%)
  - Symptomatic deep-vein thrombosis: 8 (0.9%)
  - Bloodstream infection: 12 (1.4%)

- **Femoral (N=844):**
  - Mechanical (grade ≥3): 6 (0.7%)
  - Symptomatic deep-vein thrombosis: 12 (1.4%)
  - Bloodstream infection: 10 (1.2%)
Main conclusions and limitations

• Subclavian-vein catheterization was associated with a lower risk of bloodstream infection and symptomatic thrombosis and a higher risk of pneumothorax than jugular-vein or femoral-vein catheterization.

• **Limitations:**
  ◆ Ultrasonographic guidance was not randomized.
  ◆ Use of daily chlorhexidine bathing and chlorhexidine-impregnated dressings were not used.
What Was Learned

• New sepsis and septic shock definitions provide better correlation with outcomes but significant limitations persist

• Hydrocortisone did not decrease the development of shock in patients with severe sepsis

• High flow NC may be a reasonable alternative to NIPPV/O₂ in acute hypoxemic respiratory failure and to prevent reintubation

• Benefit of early NIPPV in ICH debatable

• Subclavian-vein catheterization was associated with a lower risk of bloodstream infection and DVT but higher mechanical complications