Long-term Outcomes in Critical Illness

Pratik Pandharipande, MD, MSCI
Department of Anesthesiology
Vanderbilt University School of Medicine
VA TN Valley Health Care System

Disclosure

• Honoraria from GSK, Hospira and Orion Pharma
• Salary support
  – Vanderbilt Physician Scientist Award (2003-2005)
  – Foundation of Anesthesia Education and Research (2005-2007)
  – VA Career Development Award (2008-2011)

Long-term Outcomes

• ICU Associated Cognitive Impairment and Dementia
• ICU Acquired Weakness and Functional Disability
• ICU Associated Neuropsychological Outcomes

Long-term cognitive impairment (LTCI) after ICU survival

• 10 cohorts (~500 pts) and the largest with neuropsychological testing was 74 patients

• Summary: ~2 out of 3 ICU survivors leave the ICU with long-term cognitive impairments that equates to mild/moderate dementia (sometimes severe)

• Deficits tend to be diffuse and occur in domains including memory, attention/concentration, language, executive functioning

References:

Rothmeiser, Gen Hosp Psych 2001;23:90-96
Hopkins, AJRCCM 1999;160:50-56
Jackson, Crit Care Med 2003;31;1226-34
Hopkins, JINS 2004; 10:1005-1017
Hopkins, AJRCCM 2005; 171:340-347
Marquis, AJRCCM 2000;161:A383 (Curtis)
Al Saidi, AJRCCM 2003 167:A737 (Herridge)
Subarafek, Anesthesiol 2000;90:597-603
Suzuki, AJRCCM 2004; 169:A18
Christie, AJRCCM 2004; 169:A781
Are hospital or ICU related factors predisposing patients to long-term cognitive impairment?

Table 4. Risk of Incident Dementia by Hospitalization Status

<table>
<thead>
<tr>
<th>Cause of Incident Dementia, No.</th>
<th>Nonhospitalized (n = 139)</th>
<th>One or More Noncritical Illness Hospitalizations (n = 138)</th>
<th>P Value</th>
<th>One or More Critical Illness Hospitalizations (n = 41)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Hospitalizations During Study</td>
<td>100</td>
<td>100</td>
<td>.99</td>
<td>100</td>
<td>.99</td>
</tr>
<tr>
<td>Risk of incident dementia, IRR (95% CI)</td>
<td>1.0 (1.0 to 1.9)</td>
<td>1.1 (1.0 to 1.3)</td>
<td>&lt; .001</td>
<td>1.2 (1.1 to 1.2)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Adjusted risk of incident dementia, IRR (95% CI)</td>
<td>1.1 (1.1 to 1.3)</td>
<td>1.2 (1.1 to 1.3)</td>
<td>&lt; .001</td>
<td>1.3 (1.2 to 1.3)</td>
<td>&lt; .001</td>
</tr>
</tbody>
</table>

Table 5. Dementia Subtype Categorized According to DSM-IV-TR by Hospitalization Status

<table>
<thead>
<tr>
<th>No. (%)</th>
<th>No Hospitalizations During Study (n = 139)</th>
<th>One or More Noncritical Illness Hospitalizations (n = 138)</th>
<th>One or More Critical Illness Hospitalizations (n = 41)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alzheimer type</td>
<td>111 (7.6)</td>
<td>126 (9.8)</td>
<td>14 (27)</td>
</tr>
<tr>
<td>Vascular</td>
<td>10 (7.7)</td>
<td>12 (9.2)</td>
<td>2 (4)</td>
</tr>
<tr>
<td>Other</td>
<td>3 (2.2)</td>
<td>4 (3.0)</td>
<td>1 (2.0)</td>
</tr>
</tbody>
</table>

Ehlenbach W, et al. JAMA 2010;303(8):763-770
A neuroanatomical basis for cognitive impairment?

**Delirium and Long-Term Cognitive Outcomes**

- Cognitive Function at 12 Months (Predicted Mean T-score)
- Days of ICU Delirium

**Cognitive Impairment**
- Mild
- Moderate/Severe

- 2nd Survey Before Sepsis
- Last Survey Before Sepsis
- 1st Survey After Sepsis
- 2nd Survey After Sepsis

**Iwashyna TJ, et al. JAMA 2010;304:1787-94**


**Gunther et al. In press CCM 2012**

**Iwashyna TJ, et al. JAMA 2010;304:1787-94**
Morandi et al. CCM in press

White matter integrity (by DTI) in the Genu of the Corpus Callosum (GCC) and Delirium

White matter integrity (by DTI) in the Anterior Limb of Internal Capsule (ALIC) and Delirium

White matter integrity (by DTI) and cognitive impairment

ICU-Acquired Weakness

<table>
<thead>
<tr>
<th></th>
<th>Weakness</th>
<th>Paresis (Severe Weakness)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Berek, 1996</td>
<td>92%</td>
<td>25%</td>
</tr>
<tr>
<td>Leijten, 1995</td>
<td>47%</td>
<td>26%</td>
</tr>
<tr>
<td>Leijten, 1996</td>
<td>58%</td>
<td></td>
</tr>
<tr>
<td>De Jong, 2003</td>
<td>n=95</td>
<td></td>
</tr>
<tr>
<td>Ali, 2004</td>
<td>n=136</td>
<td></td>
</tr>
</tbody>
</table>
Depression and Physical impairment

Risk Factors for Long-term complications

- Aging
- Baseline dementia
- Psychiatric disorders
- Underlying illness
  - Inflammation
  - Coagulation
- Metabolic disturbances
- Hypoxemia
- Genetic predisposition (?)
Recall and cognitive sequelae

Larson MJ. JINS 2007;13:595-605

Cytokines, Acetylcholine, & Delirium/LTCI


Cytokines, Acetylcholine, Delirium/LTCI

Old age, incipient neurodegenerative disease, or anticholinergics


Depression and Physical impairment

Bienvenu et. al. AJRCCM 2012. 185 (5); 517-524
**ADVANCES IN SEDATION FOR THE PERIOPERATIVE AND INTENSIVE CARE SETTING**

**Liberation and Animation**

- Awakening and Breathing Coordination
- Early mobility
- Physical/Cognitive rehabilitation

---

**The ABC Trial**

(Both groups get patient targeted sedation)

<table>
<thead>
<tr>
<th>Control</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical ICU on Ventilator Surrogate Informed Consent</td>
<td>Spontaneous Breathing Trial (SBT) ventilator off safely monitored</td>
</tr>
<tr>
<td></td>
<td>Spontaneous Awakening Trial (SAT) turn sedation/narcotics off monitor safely</td>
</tr>
</tbody>
</table>

**OUTCOMES**

delirium, LOS, 12-mo NPS testing, QOL

---

**Improved 1-Year Survival in ABC Trial**

![Graph showing improved 1-year survival in ABC Trial](https://via.placeholder.com/150)

Hazard Ratio: 0.68 (0.50-0.92), P = .01


---

**Long term cognitive outcomes**

![Graph showing long term cognitive outcomes](https://via.placeholder.com/150)

Jackson JC et al. AJCCM 2010;182(2):183-91
Early Mobilization Protocol

Schweickert et al. Lancet 2009;373:1874-82

Daily Wake-Up + Early Mobility

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Intervention (n=49)</th>
<th>Control (n=50)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Functionally independent at discharge (%)</td>
<td>29 (59%)</td>
<td>19 (38%)</td>
<td>.02</td>
</tr>
<tr>
<td>ICU delirium (days)</td>
<td>2.0 (0.0-8.6)</td>
<td>4.0 (2.0-7.0)</td>
<td>.03</td>
</tr>
<tr>
<td>Time in ICU with delirium (%)</td>
<td>33% (0-88)</td>
<td>56% (33-88)</td>
<td>.02</td>
</tr>
<tr>
<td>Hospital delirium (days)</td>
<td>2.0 (0.0-6.0)</td>
<td>4.0 (2.0-8.0)</td>
<td>.04</td>
</tr>
<tr>
<td>Hospital days with delirium (%)</td>
<td>28% (26)</td>
<td>41% (27)</td>
<td>.01</td>
</tr>
<tr>
<td>Barthel Index score at discharge</td>
<td>75 (7.5-95)</td>
<td>56 (0-85)</td>
<td>.05</td>
</tr>
<tr>
<td>ICU-acquired paresis at discharge</td>
<td>15 (31%)</td>
<td>27 (49%)</td>
<td>.09</td>
</tr>
<tr>
<td>Ventilator-free days</td>
<td>23.5 (17.4-25.6)</td>
<td>21.1 (0.0-23.5)</td>
<td>.05</td>
</tr>
<tr>
<td>Length of stay in ICU (days)</td>
<td>5.9 (4.5-13.2)</td>
<td>7.5 (6.1-12.9)</td>
<td>.08</td>
</tr>
<tr>
<td>Length of stay in hospital (days)</td>
<td>13.5 (8.0-23.1)</td>
<td>12.9 (8.9-19.8)</td>
<td>.93</td>
</tr>
<tr>
<td>Hospital mortality (%)</td>
<td>9 (18%)</td>
<td>14 (25%)</td>
<td>.53</td>
</tr>
</tbody>
</table>


RETURN to Land of the Living

Returning to Everyday Tasks Utilizing Rehabilitation Networks

Cognitive & Physical Rehabilitation: RETURN

**Physical and cognitive rehabilitation**

**ACT RCT**

**Inclusion Criteria:**
Adult patients admitted to the medical or surgical ICU, receiving treatment for any of the following:

- Respiratory failure
- Shock
  - Septic
  - Cardiogenic
  - Hemorrhagic

**Assessment of Pre-Hospital Functional Status**

**Usual Care** (Group 1)

**Physical Activity** (Group 2)

**Physical Activity & Cognitive Therapy** (Group 3)

**Pre-discharge Assessment**

**Post-discharge Assessment**

**3- & 12-month follow-up assessment**

**Used with permission of patient**

**Puzzles & Games**

**Usual Care** (Group 1)

**Physical Activity** (Group 2)

**Physical Activity & Cognitive Therapy** (Group 3)

**3- & 12-month follow-up assessment**

**Used with permission of patient**
Goal-Management Training

- A protocolized approach to rehabilitation of executive functioning.
- Previously used (successfully) in TBI & geriatric patients
- Delivered in the home every other week
- Focuses on enhanced self-awareness and directed practice of compensatory strategies:
  - “Stop” techniques
  - Sequencing and planning activities
- Homework assignments on “off weeks” transfer concepts to real life.


Primary Outcome:

Tower Test: Pre-Discharge vs. 12 weeks

Number of Moves:

Composite Score → T-score

3- & 12-month Follow-up Assessment

- Executive Function
  - Tower Test
  - Dysexec Questionnaire
- Cognitive Impairment
  - IQ-CODE (Cognitive Decline in Elderly)
  - MMSE
  - Trails A & B (Attention & Executive Function)
  - AD8 (Assess changes in cognition)
- Functional Impairment
  - Timed Up & Go Test
  - Katz ADL
  - FAQ
- Health-Related Quality of Life
  - EQ-5