Delirium and Long-Term Cognitive Impairment in ICU Survivors

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Disclosures:
- NIH and VA U.S. Federal Funding
- Abbott, Hospira, Orion
- Author of PAD Guidelines of SCCM 2013
- Chair of SCCM Delirium section for PAD
- Co-Chair of SCCM ICU Liberation project to aid world-wide implementation
Delirium as a Predictor of Mortality in Mechanically Ventilated Patients in the Intensive Care Unit
Delirium Duration & Mortality

<table>
<thead>
<tr>
<th>Days of Delirium</th>
<th>Relative Hazard of Death</th>
<th>95% CI</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 vs 1</td>
<td>HR 1.7</td>
<td>1.27-2.29</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>0 vs 2</td>
<td>HR 2.69</td>
<td>1.58-4.57</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>0 vs 3</td>
<td>HR 3.73</td>
<td>1.92-7.23</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Cognitive Impairment: Sepsis

Before Sepsis

After Sepsis

% survivors cognitively impaired

Iwashyna T, JAMA 2010;304:1787-1794
Delirium and Cognitive Decline

Delirium accelerates cognitive decline in Alzheimer disease

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ABSTRACT

Objective: To examine the impact of delirium on the trajectory of cognitive function in a cohort of patients with Alzheimer disease (AD).

Methods: A secondary analysis of data collected from a large prospective cohort, the Massachusetts Alzheimer’s Disease Research Center’s patient registry, examined cognitive performance over time in patients who developed (n = 72) or did not develop (n = 336) delirium during the course of their illnesses. Cognitive performance was measured by change in score on the Information-Memory-Concentration (IMC) subtest of the Blessed Dementia Rating Scale. Delirium was identified using a previously validated chart review method. Using linear mixed regression models, rates of cognitive change were calculated, controlling for age, sex, education, comorbid

Delirium in Elderly Patients and the Risk of Postdischarge Mortality, Institutionalization, and Dementia: A Meta-analysis

Joost Witlox; Lisa S. M. Eurelins; Jos F. M. de Jonghe; et al.


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**Analyses of the association between delirium and mortality, institutionalization, and dementia adjusted for age, sex, comorbid illness or illness severity, and baseline dementia. CI indicates confidence interval. Weighting was assigned according to the inverse of the variance. Hazard ratios and odds ratios larger than 1 indicate increased risk of mortality, institutionalization, or dementia among participants who experienced delirium.**
Cognitive Trajectories after Postoperative Delirium


C Sensitivity Analysis with Duration of Delirium

Estimated Score

Days after Surgery

Before Surgery

No delirium
<3 Days delirium
≥3 Days delirium

NEJM 2012;367:30-9
Delirium and Long-Term Cognitive Outcomes

Days of ICU Delirium

Cognitive Function at 1 year (predicted mean T-score)

$p=.005$

Girard T et al CCM 2010; 38:1513–1520
Bringing to light Risk factors And Incidence of Neuropsychological dysfunction in ICU survivors
BRAIN-ICU Hypothesis

• We hypothesized that duration of delirium is a predictor of LTCI in patients at 3 and 12 months after ICU discharge.

• Primary purpose was to identify potentially modifiable risk factors of long-term cognitive impairment such as development of delirium and exposure to sedative medications.
<table>
<thead>
<tr>
<th>INDEPENDENT VARIABLES</th>
<th>DEPENDENT VARIABLES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delirium Duration</td>
<td>Long Term Cognitive Impairment (LTCI) Battery</td>
</tr>
<tr>
<td>Drug Exposure</td>
<td>Health-Related Quality of Life (HRQL) Battery</td>
</tr>
</tbody>
</table>

**Patient enrollment** → **Time** → **12-month follow-up**
Long-Term Cognitive Impairment after Critical Illness


ABSTRACT

BACKGROUND
Survivors of critical illness often have a prolonged and disabling form of cognitive impairment that remains inadequately characterized.
Methods
Prospective Cohort Study

**Included**
- Adults
- Medical/surgical ICU
- Respiratory failure
- Shock

**Excluded**
- Recent ICU time
- Dementia
- Cardiac surgery
- Substance abuse
- Psychiatric disorder

**Enrollment**

**Exposures (ICU)**
- **Primary:** Delirium subtypes
  - CAM-ICU
  - RASS
- **Covariates**
  - Age
  - Education (years)
  - Baseline cognition
  - Comorbid illness
  - Severity of illness
  - Coma
  - Sedatives

**Outcomes (3- & 12-mo)**
- Repeatable Battery Assessment of Neuropsychological Status (RBANS)
- Trailmaking Test, Part B
- MMSE
## Baseline and Clinical Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Hospital Cohort (N=821)</th>
<th>Follow-Up Cohort (N=467)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>61 [51-71]</td>
<td>59 [49-69]</td>
</tr>
<tr>
<td>Education, years</td>
<td>12 [12-14]</td>
<td>12 [12-14]</td>
</tr>
<tr>
<td>Cognitive impairment, %</td>
<td>6%</td>
<td>6%</td>
</tr>
<tr>
<td>Admission diagnoses, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe sepsis</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>Acute respiratory failure</td>
<td>16</td>
<td>15</td>
</tr>
<tr>
<td>Cardiac</td>
<td>17</td>
<td>17</td>
</tr>
<tr>
<td>Other</td>
<td>37</td>
<td>38</td>
</tr>
<tr>
<td>Mechanically ventilated</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients, %</td>
<td>74</td>
<td>75</td>
</tr>
<tr>
<td>Duration, days</td>
<td>3 [1-8]</td>
<td>2 [1-6]</td>
</tr>
<tr>
<td>Hospital length of stay, days</td>
<td>10 [6-17]</td>
<td>10 [6-18]</td>
</tr>
</tbody>
</table>
BRAIN-ICU Outcomes
Long-term cognitive impairment
The Picture of Dementia Following ICU Care

A

<table>
<thead>
<tr>
<th>RBANS Global Cognitive Score</th>
<th>&lt;65 Years</th>
<th>&gt;=65 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=244</td>
<td></td>
<td>N=130</td>
</tr>
<tr>
<td>3 Months</td>
<td>12 Months</td>
<td>3 Months</td>
</tr>
<tr>
<td>12 Months</td>
<td></td>
<td>12 Months</td>
</tr>
<tr>
<td>N=227</td>
<td></td>
<td>N=98</td>
</tr>
</tbody>
</table>

- Normal
- MCI
- TBI
- AD
Global Cognitive Scores by Age and Comorbidity
Delirium and Executive Function

Adjustment Trails B T-Score, 12 Months

Duration of Delirium
Bonn Germany, 2 center 6-24 month follow-up of 25 septic and 19 non-septic ICU survivors

Sepsis survivors showed cognitive deficits in verbal learning and memory

Significant reductions of hippocampal volume vs. controls

More low frequency EEG activity indicating brain dysfunction
“Dementia is perhaps the cruellest manifestation of ageing, inexorably melting away all that which makes us individual and human.”

See Editorial page 177
Delirium

Pain

Agitation

Clinical Practice Guidelines for the Management of Pain, Agitation, and Delirium in Adult Patients in the Intensive Care Unit

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ABCDEs:
Building blocks of managing Pain, Agitation & Delirium
I survived and that is the main thing. And I am so grateful to God that I survived and am now off all oxygen and consider myself all well except that I can’t remember to take my medications...

-SB
The ICU Delirium and Cognitive Impairment Study Group at the Loveless Café, Nashville TN
ICU Delirium and Cognitive Impairment Study Group: selected local members

Pratik Pandharipande
Jim Jackson
Jin Han
Ed Vasilevskis
Chris Hughes
Alessandro Morandi
Paula Watson
Lorraine Ware
Gordon Bernard
Bob Dittus
Ted Speroff
Wes Ely

Leanne Boehm
Joyce Okahashi
Cayce Strength
Brenda Pun
Lauren Hardy
Amy Lipsey
Ryan Black
Jessica McCurley
Michael Santoro
Carrie Jones
Morgan Crawford
Mayur Patel

Tim Girard
John Gore
Baxter Rogers
Stephan Heckers
Cathy Fuchs
Heidi Smith
Ty Berutti
Brad Strohler
Elizabeth Card
Jennifer Thompson
Ayumi Shintani
Stephanie Hamilton