Risk Factors for Cognitive Decline: Acute Illness, Delirium, and Hospitalization

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Outline

• Hospitalization in older adults
  – Is hospitalization a risk factor for cognitive decline?

• Delirium in hospitalized older adults
  – Is delirium a risk factor for cognitive decline?

• Model for Pathophysiology

• Summary and recommendations
Hospitalization in Older Adults
Hospital use by age group

Population

- Under 15 years
- 15–44 years
- 45–64 years
- 65 years and over

Discharges

- Under 15 years
- 15–44 years
- 45–64 years
- 65 years and over

Days of care

- Under 15 years
- 15–44 years
- 45–64 years
- 65 years and over

NOTE: Population percentages are computed using U.S. Census Bureau 2000-based postcensal estimates of the civilian population of the United States as of July 1, 2007.
SOURCE: CDC/NCHS, National Hospital Discharge Survey.

Figure 2. Distribution of civilian population, hospital discharges, and days of care, by age: United States, 2007
Older adults: High Hospitalization Rates

Figure 1. Hospitalization rates, by age: United States, 1970–2007

NOTE: Rates were calculated using the U.S. Census Bureau estimates of the civilian population. Rates for 1990 and 1995 were based on population estimates adjusted for the net underenumeration in the 1990 census. Rates for 2000, 2005, and 2007 were calculated using 2000-based postcensal civilian population estimates.

SOURCE: CDC/NCHS, National Hospital Discharge Survey.
Hospitalization: relationship to cognitive decline
Two Studies

- Followed large community-based older adult samples:
  - Group Health: N=2929, 6.1 yrs
  - Chicago Health & Aging: N=1870, 9.3 yrs
- Serial cognitive testing: 2,3 yrs
- Hospitalizations → claims data
- Compared those hospitalized with those not hospitalized
Table 2. Difference in Follow-up Cognitive Scores by Hospitalization Status

<table>
<thead>
<tr>
<th></th>
<th>Following Noncritical Illness Hospitalization</th>
<th>$P$ Value</th>
<th>Following Critical Illness Hospitalization</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow-up CASI</td>
<td>−2.27 (−2.61 to −1.93)</td>
<td>&lt;.001</td>
<td>−2.92 (−5.00 to −0.86)</td>
<td>.006</td>
</tr>
<tr>
<td>Adjusted difference</td>
<td>−1.01 (−1.33 to −0.70)</td>
<td>&lt;.001</td>
<td>−2.14 (−4.24 to −0.03)</td>
<td>.047</td>
</tr>
<tr>
<td>Follow-up CASI IRT</td>
<td>−0.28 (−0.32 to −0.24)</td>
<td>&lt;.001</td>
<td>−0.27 (−0.45 to −0.09)</td>
<td>.003</td>
</tr>
<tr>
<td>Adjusted difference</td>
<td>−0.12 (−0.16 to −0.08)</td>
<td>&lt;.001</td>
<td>−0.19 (−0.38 to −0.01)</td>
<td>.04</td>
</tr>
</tbody>
</table>

Abbreviations: CASI, Cognitive Abilities Screening Instrument; CI, confidence interval; IRT, item response theory.

a Linear regression with generalized estimating equations to account for repeated observations, specifying an exchangeable correlation matrix and robust variance estimates.

b The reference category in each comparison was no hospitalization.

c Adjusted for age at study visit, sex, baseline cognitive score, years of education, time since baseline visit, and the baseline comorbidities coronary heart disease and cerebrovascular disease.
# Group Health Study: Dementia

## Table 4. Risk of Incident Dementia by Hospitalization Status

<table>
<thead>
<tr>
<th></th>
<th>No Hospitalizations During Study (n = 1601)</th>
<th>One or More Noncritical Illness Hospitalizations (n = 1287)</th>
<th>One or More Critical Illness Hospitalizations (n = 41)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases of incident dementia, No.</td>
<td>146</td>
<td>228</td>
<td>5</td>
</tr>
<tr>
<td>Risk of incident dementia, HR (95% CI)</td>
<td>1 [Reference]</td>
<td>1.5 (1.3 to 1.9)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Adjusted risk of incident dementia, HR (95% CI)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1 [Reference]</td>
<td>1.4 (1.1 to 1.7)</td>
<td>.001</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; HR, hazard ratio.

<sup>a</sup> Cox proportional hazards regression with age at study visit as the time axis and age at study entry as the beginning of the time period.

<sup>b</sup> Adjusted for age at study entry, sex, baseline Cognitive Abilities Screening Instrument item response theory score, years of education, and baseline comorbidities of coronary heart disease and cerebrovascular disease, with presence of coronary heart disease at baseline included as a time-varying covariate.
Chicago Study: Cognitive Trajectory

Wilson et.al., Neurology 2012
What happens to hospitalized older adults?

Delirium
Delirium

• Confusional state:
  – Acute change/fluctuating course
  – Inattention
  – Disorganized thinking
  – Altered level of consciousness

• Can be diagnosed after a 3-5 minute structured assessment (CAM)

• Acute brain failure (analogous to CHF)

Inouye et. al., Ann Int Med 1990; Lancet 2014
Delirium: Older more vulnerable

Stressor → Compensation → Reserve

Young Reserve

Normal Range

Stressor

Decompensation → DELIRIUM

Old Reserve

OLD
Delirium is Common in Hospitalized Older Adults

<table>
<thead>
<tr>
<th>Population</th>
<th>Prevalence or Incidence</th>
<th>Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical Inpatients &gt;70 yrs</td>
<td>Mixed (50:50)</td>
<td>30-40%</td>
</tr>
<tr>
<td>Major surgery &gt; 70 yrs</td>
<td>Incidence</td>
<td>20-30%</td>
</tr>
<tr>
<td>Hip Fx, CABG &gt; 65 yrs</td>
<td>Incidence</td>
<td>45-55%</td>
</tr>
<tr>
<td>Intensive Care Unit &gt; 18 yrs</td>
<td>Mixed</td>
<td>75-80%</td>
</tr>
</tbody>
</table>

Inouye et. al., Ann Int Med, 1993; Marcantonio et. al., JAMA, 1994; Marcantonio et. al., JAGS, 2000; Ely et. al., JAMA, 2004;
Delirium: relationship to cognitive decline
Two Studies

• TRACS:
  – 225 older cardiac surgery patients
  – enrolled preop, followed for 1 year
  – serial administration of MMSE

• BRAIN-ICU:
  – 467 medical ICU survivors (adults)
  – administered RBANS at 1 year

• Both: daily delirium assessment CAM
TRACS: Cognitive Trajectories

Saczyński, Marcantonio et. al., NEJM, 2012
TRACS: Matched Analysis

Saczyński, Marcantonio et. al., NEJM, 2012
TRACS: Dose Response

C  Sensitivity Analysis with Duration of Delirium

Estimated Score vs. Days after Surgery

- No delirium
- <3 Days delirium
- ≥3 Days delirium

Saczynski, Marcantonio et. al., NEJM, 2012
BRAIN-ICU: Cognition 12 mos. after ICU

Pandharipande et. al, NEJM, 2013
Delirium-related Cognitive Decline

Model for Pathophysiology
Summary

• Hospitalization common in older adults: rate >300/1000 per year
• Delirium: affects 30-40% of hospital stays among older adults
• Epidemiological evidence:
  – Hospitalization → long term cognitive decline
  – Delirium → cognitive decline up to 1 year
  – Assoc. persist despite adjust confounding
• Biological plausibility
Importance

• Preventable:
  – Hospitalization: 10% (per AHRQ)
    • New models: manage acute illnesses at home
  – Delirium: up to 40% (HELP, geriatric consult)

• Even if hospitalized/delirious, cognitive outcomes may be modifiable
  – Improved hospital care, management of delirium
  – Cognitive rehabilitation

Inouye et. al., NEJM 1999; Marcantonio et. al, JAGS, 2001
What we don’t know: Delirium + Decline

Delirium: Marker of Vulnerability?

Aging

Aging + Pre-existing factors

Delirium

Diminished Reserve*

MCI

Dementia

Delirium: Impact on Trajectory?

Aging

Aging + Delirium

Delirium

*Diminished reserve : “usual aging”
Recommendations: Research Agenda

• Epidemiological studies:
  – Go back: better define pre-hospital trajectory
  – Go forward: longer f/u to characterize the decline
  – Identify modifiable risk factors for decline

• Mechanistic studies: pathophysiology

• Intervention studies:
  – Prehabilitation: increase resilience to stress
  – Modify hospital care: prevent/reduce delirium
  – Rehabilitation: treat the decline