Postoperative Delirium & Cognitive Decline

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DEFINITIONS

- Postoperative delirium – acute confusional state with alterations in attention and consciousness
- POCD - Decline in a variety of neuropsychological domains (memory, executive functioning, speed of processing)
- POCD ≠ postoperative delirium?

DELIRIUM vs. POCD

- Older patients undergoing noncardiac surgery who were not delirious were included in this analysis (n = 225)
- 15% developed POCD on either POD 1 or 2

Wang et al., Am J Geriatr Psychiatry 2007;15:50
Delirium & POCD

Incidence of Delirium

<table>
<thead>
<tr>
<th>Population</th>
<th>Incidence</th>
<th>Author</th>
<th>Sample size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hip fracture</td>
<td>44%</td>
<td>Berggren</td>
<td>57</td>
</tr>
<tr>
<td></td>
<td>19%</td>
<td>Edlund</td>
<td>71</td>
</tr>
<tr>
<td></td>
<td>16%</td>
<td>Morrison</td>
<td>541</td>
</tr>
<tr>
<td></td>
<td>20%</td>
<td>Schuurman</td>
<td>92</td>
</tr>
<tr>
<td>Elective orthopedic</td>
<td>18%</td>
<td>Fisher</td>
<td>80</td>
</tr>
<tr>
<td></td>
<td>28%</td>
<td>Rogers</td>
<td>43</td>
</tr>
<tr>
<td>Major elective surgery</td>
<td>9% (46% aortic)</td>
<td>Marcantonio Vaurio</td>
<td>876</td>
</tr>
<tr>
<td></td>
<td>46%</td>
<td>Vaurio</td>
<td>333</td>
</tr>
<tr>
<td></td>
<td>11.4%</td>
<td>Litake</td>
<td>500</td>
</tr>
<tr>
<td>Elective vascular</td>
<td>36% (52% aortic)</td>
<td>Schneider</td>
<td>47</td>
</tr>
</tbody>
</table>

Why is Delirium Important?

- Prolonged hospitalization ($$$)
- Decreased functional status upon discharge
- Cognitive decline post discharge
- Increased institutionalization
- Increased mortality

Inouye, NEJM 2006

Cognitive trajectories

Fong et al., Neurology 2009;72:1570
Etiology of Postoperative Delirium

- 54 of 571 (9.5%) hip fracture patients developed delirium in one study:
  - Only 7% were assigned definite cause: drugs, infection, fluid-electrolyte disorder
  - Majority of cases had no single clear etiology
  - Risk factors: drugs, underlying dementia, sensory deprivation, infection, and fluid-electrolyte disorder


Delirium Risk Factors

- Delirium is a multifactorial syndrome influenced by:
  - Baseline patient risk factors (vulnerability)
  - Precipitating factors

- Patients with more baseline risk factors and exposed to more precipitating factors are much more likely to develop delirium

Delirium Baseline Risk Factors

- Age
- Sensory impairment
- Cognitive impairment
- Depression
- Alcoholism
- Severe illness
- Fever or hypothermia
- Metabolic disorder

Delirium Precipitating Risk Factors

- Use of Restraints
- Psychoactive Medication
  - Anticholinergics
  - Sedative/hypnotics
    - Benzodiazepine
    - Opioids
    - Meperidine
- Polypharmacy
  - >3 meds added
- Malnutrition
- Bladder Catheter
- Urinary Retention
- Pain
Potential surgical risk factors

- Surgical Factors
  - Type of surgery (Cardiac, orthopedic)

Does general anesthesia increased delirium occurrence?

To compare the influence of general, regional or a combination of anesthesia on the development of postoperative delirium or POCD

- 21 studies included, using DSM or ICD criteria

Findings
- No effect of anesthesia on the odds of development postoperative delirium (OR 0.88, 0.51-1.51)
- No effect of anesthesia on the odds of developing POCD (OR 1.34, 0.93-1.95)

General vs. regional anesthesia

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Role of blood pressure during surgery?
Potential anesthetic factors

Anesthetic factors
  • Management (intra- &/or post-op)
    • Williams-Russo, Anesthesiology 1999

MANAGEMENT

Randomized trial of hypotensive epidural anesthesia in 235 older adults (MAP 45-55 vs. 55-70 mm Hg)
• General decline in cognitive function at 1 wk postop, no difference between groups
• Postoperative delirium 9% vs. 4% (power 25%)
  Williams-Russo, Anesthesiology 1999

Pain & postoperative delirium

• Age > 70 years
• Moderate to severe preop rest pain
• Worsened postop pain
• PCA (vs. oral narcotics)
  Vaurio, Anesth & Analg 2006; 102:1267-73

Pain and opioids

Table 3  Hydromorphone Dose by Delirium Status on POD 1 Adjusted for Current Pain at Rest, Preoperative Narcotic Use, Surgical Risk, and Use of Other Medications with CNS Effects

<table>
<thead>
<tr>
<th></th>
<th>No Delirium (n = 226)</th>
<th>Delirium on POD 1 (n = 108)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydromorphone dose on POD 1 (mg)</td>
<td>4.28±0.92</td>
<td>4.34±0.98</td>
<td>0.93</td>
</tr>
<tr>
<td>Hydromorphone dose on POD 2 (mg)</td>
<td>1.38±0.68</td>
<td>1.72±0.68</td>
<td>0.42</td>
</tr>
</tbody>
</table>

Leung, Anesthesiology 2009; 111(3):625-31
Targeting Pain to reduce postoperative delirium

- Non-narcotic adjuvant - gabapentin
- Postop delirium 5/12 in placebo vs. 0/9 in gabapentin treated patients

Leung, Neurology 2006; 67:1-3

Specific anesthetic agent

- Nitrous oxide (Early postoperative delirium 41.9% vs. 43.8% in the oxygen group) - Leung et al, Br J Anaesth 2006
- Sevoflurane vs. desflurane anesthesia – no difference in POCD occurrence – Rortgen et al, Br J Anaesth 2010
- Xenon vs. propofol anesthesia – POCD in 44% of xenon group vs. 50% in propofol group 1 day after treatment – Hocker et al, Anesthesiology 2009

Summary

- Postoperative delirium - etiology likely multi-factorial
- No evidence that anesthesia types, or specific agents make a difference
- Drugs to avoid - meperidine, lorazepam (ICU delirium)
- Clinical trial of postoperative pain management

What is the relationship between surgery and POCD?
Neuropsychological Assessment

<table>
<thead>
<tr>
<th>Commonly used tests in ≈300 studies</th>
<th>Domain</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Trail-making test, Part B (119)</td>
<td>Attention</td>
</tr>
<tr>
<td>2. Trail-making test, Part A (102)</td>
<td>Attention</td>
</tr>
<tr>
<td>3. Digit span (82)</td>
<td>Attention</td>
</tr>
<tr>
<td>4. Grooved pegboard (69)</td>
<td>Motor function</td>
</tr>
<tr>
<td>5. Rey auditory verbal learning (68)</td>
<td>Memory</td>
</tr>
<tr>
<td>6. Mini-mental state examination (61)</td>
<td>General cognitive functioning</td>
</tr>
<tr>
<td>7. Digit symbol (61)</td>
<td>Attention</td>
</tr>
<tr>
<td>8. Stroop color word (56)</td>
<td>Executive function</td>
</tr>
<tr>
<td>9. Controlled word association (55)</td>
<td>Executive function</td>
</tr>
<tr>
<td>10. Symbol digit (30)</td>
<td>Attention</td>
</tr>
</tbody>
</table>

Timing of POCD

Surgery:
- One week Early
- 3 months Intermediate
- 1-2 years Long-term

Questions
- What is cognitive reserve?
- Can we identify who have decreased cognitive reserve preoperatively?
- What are the perioperative “stressors”?

STRESS

COGNITIVE RESERVE

POSTOPERATIVE DELIRIUM, POCD

?  LONG-TERM COGNITIVE DECLINE
### Risk factors for early/intermediate POCD

<table>
<thead>
<tr>
<th>Patient-related Risk Factor</th>
<th>Support</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>ISPOCD, Stockton, Ancelin, Canet, Monk</td>
</tr>
<tr>
<td>Education</td>
<td>ISPOCD, Monk</td>
</tr>
<tr>
<td>Burden of illness</td>
<td>Monk</td>
</tr>
<tr>
<td>Preoperative depression</td>
<td>Leung (delirium only)</td>
</tr>
<tr>
<td>Preoperative cognitive</td>
<td>Bekker, Fong</td>
</tr>
<tr>
<td>Impairment</td>
<td></td>
</tr>
<tr>
<td>Preop habits/drug use</td>
<td>Monk (opioid)</td>
</tr>
<tr>
<td>ApoE4</td>
<td>Heyer, Telis, Leung, Tardiff</td>
</tr>
</tbody>
</table>

### Precipitating factors for early/intermediate POCD

<table>
<thead>
<tr>
<th>Perioperative Risk Factor</th>
<th>Support</th>
<th>Refute</th>
</tr>
</thead>
<tbody>
<tr>
<td>2nd operation</td>
<td>ISPOCD</td>
<td>Monk</td>
</tr>
<tr>
<td>Postop infection</td>
<td>ISPOCD</td>
<td>Monk</td>
</tr>
<tr>
<td>Resp complications</td>
<td>ISPOCD</td>
<td>Monk</td>
</tr>
<tr>
<td>General anesthetic</td>
<td>ISPOCD?</td>
<td>Williams-Russo</td>
</tr>
<tr>
<td>Anesthetic type</td>
<td>?</td>
<td>Leung</td>
</tr>
<tr>
<td>Anesthetic maintenance</td>
<td></td>
<td>Williams-Russo</td>
</tr>
<tr>
<td>Pain management</td>
<td>Wang</td>
<td></td>
</tr>
</tbody>
</table>

### Question

What are the stressors that may precipitate POCD?

Does early POCD leads to longer-term cognitive decline?
Incidence of POCD

Surgery

- One week: Early
- 3 months: Intermediate
- 1-2 years: Long-term

5% (Williams-Russo)
26% (ISPOCD)
10% (ISPOCD)
1% (ISPOCD)
30-41% (Monk)
5-12% (Monk)

JAMA 1995;274:44-50

Risk of general anesthesia & cognitive decline

- Maastricht Aging Study, Netherlands
- 946 patients with at least one operation under general anesthesia
- Results: a history of an operation, # of operations, total duration of anesthesia associated with subjective health complaints but did not predict cognitive performance

Dijkstra, JAGS 1998;46:1258-1265

Surgery and long-term cognitive decline

- Retrospective cohort study
- Subjects recruited from ADRC
- Non-cardiac surgery, illness or neither
- N=575, 214 non demented, 361 had very mild or mild dementia @ recruitment
- Excluded those undergoing cardiac, carotid or neurosurgery
- Median years of follow up 3.1 yrs

Avidan, Anesthesiology 2009;111:964-970
Surgery and long-term cognitive decline

- Demented group declined more markedly
- 25% of non-demented group progressed to a CDR > 0, but not more common after surgery or illness
- Neither demented or mildly demented subjects had accelerated long-term cognitive decline attributable to surgery or major illness when compared with matched controls

Avidan, Anesthesiology 2009;111:964-970

Does mild cognitive impairment increases the risk of POCD?

MCI and POCD

- Retrospective cohort study
- Community-dwelling volunteers participating in aging studies at the NYU ADC
- Subjects divided into normal or MCI (impairment in ≥1 cognitive domains expected for a person’s age, without ADL interference


MCI and POCD

- Post hoc analysis of longitudinal data showed those with MCI had a significantly greater decline in performance on the DS-F test compared with the normal groups and to the MCI group with no surgery
- Significance?

POCD and long-term mortality/cognition

- POCD was associated with increased mortality at 1 yr & 3 months after surgery
- In cardiac surgical patients, cognitive status at discharge was associated with long-term cognitive function

Monk, Anesthesiology 2008;108:18-30
Steinmetz, Anesthesiology 2009;110:548-555

Summary

- Role of cognitive reserve – “good reserve” may be more protected against “stress”
- Etiology of POCD may be multi-factorial (early vs. late)
- Data in animal models (prolonged exposure to some volatile-inhalational anesthetics increase production of amyloid-β and vulnerability to neurodegeneration; neuroinflammation) need clinical confirmation
- Long-term consequence of early POCD on cognition not clear

Future considerations

- Need to have internationally accepted criteria for definitions of POCD
- Timing and duration of assessment of POCD
- Subject exclusion criteria
- Pre-event cognitive trajectory important

Null hypothesis

- Surgery (& anesthesia) have no impact on long-term cognitive status