Postoperative cognitive disorders

**Definition:**
- Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (Copyright © 2013), American Psychiatric Association

**Diagnostic criteria:**
- Disturbance in attention (i.e., reduced ability to direct, focus, sustain, and shift attention) and awareness (reduced orientation to the environment)
- develops over a short period of time (h-d), tends to fluctuate
- Disturbance in cognition (e.g., memory deficit, disorientation, language, visuospatial ability, or perception)
- Direct consequence of an underlying organic condition

**Diagnostic methods:**
- Delirium scales (CAM, CAM-ICU, 3D-CAM…)

**Timing:**
- Days to weeks

**Prognosis:**
- reversible if underlying condition is reversible
POD - Definition and Diagnosis
Confusion assessment method

- (at least) 24 diagnostic instruments available
- Confusion assessment method:
  - validated in high-quality studies including more than 1000 patients
  - sensitivity of 94%, specificity of 89%, high inter-rater reliability
  - has been used in more than 4000 published studies
  - has been translated into at least 12 languages

POD - Definition and Diagnosis
Confusion assessment method - ICU

1. Acute onset or fluctuating course of mental status:
   - Is there an acute change from normal baseline?
   - Is the patient's mental status fluctuating during the past 24 hours?

2. Agitation:
   - Does the patient have a history of a提问？
   - Are there behavioral signs of agitation?

3. Aids for confused patients
   - Has the patient been given adequate medication?
   - Has the patient been given appropriate nutrition?

4. Delirium diagnosis:
   - Is the patient alert and oriented?
   - Do they respond appropriately to verbal stimuli?

POD - Definition and Diagnosis
Delirium Observation Screening Scale

<table>
<thead>
<tr>
<th>Observation</th>
<th>Yes</th>
<th>No</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
</tbody>
</table>

Delirium Observation Screening Scale

Score Interpretation

- No delirium
- Delirium: total score ≥ 4

Delirium Observation Screening Scale - Total Score (0-4)

<table>
<thead>
<tr>
<th>Score Range</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1</td>
<td>No delirium</td>
</tr>
<tr>
<td>2-4</td>
<td>Delirium</td>
</tr>
</tbody>
</table>


Postoperative delirium

Psychomotoric subtypes

Delirium in the Cardiovascular ICU: Exploring Modifiable Risk Factors

Delirium Subtype | Cardiology (n = 28) | Cardiac-Surgical (n = 28)
--- | --- | ---
Hypodynamic | 93% (26) | 89% (22)
Hypertensive | 4% (1) | 4% (1)
Mixed | 4% (1) | 6% (2)

*90 Years and Older (N=100) Younger than 65 (N=28)*

- **Hyperactive (agitant) variant**: Infrequent
- Diagnosis rarely missed (patient disrupts flow of care)
- **Hypoactive (quiet) variant**: Frequent
- Diagnosis often missed (patient neither disruptive nor threatening)

Postoperative cognitive disorders

- Most common postoperative complication in older adults (i.e., > 65yrs)
- Incidence up to 50% after an operation
- High in-hospital mortality (4%–17%)
- Increases 1-month, 6-month, 12-month, and long-term mortality
- Is associated with increased postoperative complications, longer hospital LOS, longer ICU-LOS
- Is associated with loss of functional independence and with cognitive decline
- Costs more than US$164 billion p.a. in the USA and more than $182 billion p.a. in 18 European countries combined
- Is preventable in 30–40% of cases

Postoperative delirium

Relevance

- Surgery with urgent nature and high co-morbidity
- Surgery for atherosclerosis patholgy (cardiac, peripheral vascular, aneurysm repair)
POD - Pathophysiology

Resolution factors - patient related

POD - Pathophysiology

Imbalance of neurotransmitters

Table 2. Preoperative Prediction Rules for Delirium After Noncardiac and Cardiac Surgery

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Criteria</th>
<th>Factor points</th>
<th>Total rule points*</th>
<th>Incidence of delirium (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anorexia</td>
<td>Glucose ≤ 90 mg/dL</td>
<td>0</td>
<td>0</td>
<td>1.2</td>
</tr>
<tr>
<td>Cardiac arrest</td>
<td>Sodium ≤ 125 mmol/L</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Age &gt; 65 years</td>
<td>Age &gt; 65 years</td>
<td>1</td>
<td>1</td>
<td>3.2</td>
</tr>
<tr>
<td>Physical function</td>
<td>Physical function</td>
<td>1</td>
<td>1</td>
<td>4.3</td>
</tr>
<tr>
<td>Anesthesia</td>
<td>Anesthesia</td>
<td>1</td>
<td>1</td>
<td>2.1</td>
</tr>
<tr>
<td>Altered mental status</td>
<td>Altered mental status</td>
<td>1</td>
<td>1</td>
<td>3.2</td>
</tr>
</tbody>
</table>

*Rule points: 0-10

POD - Pathophysiology

Imbalance of neurotransmitters

<table>
<thead>
<tr>
<th>Neurotransmitter</th>
<th>Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dopamine</td>
<td>Drugs, Ischemia</td>
</tr>
<tr>
<td>Acetylcholine</td>
<td>Drugs, Ischemia</td>
</tr>
<tr>
<td>GABA</td>
<td>Benzodiazepines, Liver failure, Withdrawal</td>
</tr>
<tr>
<td>Glutamate</td>
<td>Withdrawal, Drugs, Ischemia</td>
</tr>
</tbody>
</table>

POD - Pathophysiology

Imbalance of neurotransmitters

Potassium channels

<table>
<thead>
<tr>
<th>Channel</th>
<th>Intravenous anaesthetics</th>
<th>Inhalational anaesthetics</th>
<th>Major potentiation</th>
</tr>
</thead>
<tbody>
<tr>
<td>GABA</td>
<td>NMIDA</td>
<td>Nicotinic Ach</td>
<td>Muscarinic Ach</td>
</tr>
<tr>
<td>Intravenous</td>
<td>Barbiturates</td>
<td>Inhalational</td>
<td>Nitrous oxide, isoflurane, sevoflurane, desflurane</td>
</tr>
<tr>
<td>Inhalational</td>
<td>Pentobarbital</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Rudolph JL et al.,
Postoperative Delirium: Acute Change with Long-Term Implications.
Anesth Analg 2011;112:1202–11.
**POD - Pathophysiology**

**Neuroinflammation**

- Upregulation of cytokines: IL-1, IL-6, ROS
- Downregulation of anti-inflammatory cytokines: IL-10, BDNF

**Endothelial dysfunction**

- BBB dysfunction
- Toxin exposure
- Increased permeability

**Precipitating factors: Trigger**

- Early complications of operation
- Hypoxemia
- Prolonged intubation
- Sedation management
- Pain
- Late complications of operation
- Low albumin
- Renal failure
- Sleep-wake disturbance

**Association between Endothelial Dysfunction and Acute Brain Dysfunction during Critical Illness**

Christopher G. Hughes, M.D.,* Alessandro Morandi, M.D.,† Timothy D. Skill, M.D.,‡ Bernhard Reil, M.D., Ph.D.,§ Jennifer L. Thompson, M.P.H.,§ Ayum K. Shimizu, Ph.D.,∥ Brenda L. Dunn, M.S.N.,* E. Wesley Ely, M.D.,‡ Pratik P. Khatri, M.D.,∥

Anesthesia 2013; 118:631-9
POD: Non-pharmacologic prevention
Eliminating precipitating factors

Opioids: deliriogenic
Pain: deliriogenic

Non-opioid based pain regimen?

POD: Inconclusive evidence

Intraoperative hemodynamics and oxygenation

Regional anesthesia and POD

The evidence

Evidence-based clinical update: General anesthesia and the risk of delirium and postoperative cognitive dysfunction

Mise à jour clinique fondée sur des données probantes : L'anesthésie générale et le risque de délire et de dysfonctionnement cognitif postopératoires

Gregory L. HYSSOU F.R.C.A., Anna WYANDT H.D.

CAN J ANESTH 2006 / 53: 7 / pp 669-677

Vaurio E. et al.
Postoperative Delirium: The Importance of Pain and Pain Management
Anesth Analg 2006;102:1267–73

Marcantonio ER et al.
The Association of Intraoperative Factors with the Development of Postoperative Delirium

Moller JT et al.
Long-term postoperative cognitive dysfunction in the elderly: ISPOCD1 study

Reade MC et al.
Sedation and Delirium in the Intensive Care Unit
N Engl J Med 2014;370:444-54

Non-pharmacologic prevention
Eliminating precipitating factors: PAIN

Table 6. Factors Associated with Postoperative Delirium by Multivariate Logistic Regression

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt; 70 years</td>
<td>2.50</td>
<td>1.42–4.4</td>
</tr>
<tr>
<td>Moderate pain at rest postoperatively (VAS = 4–7 versus VAS = 0)</td>
<td>2.89</td>
<td>1.30–6.06</td>
</tr>
<tr>
<td>Incident pain at rest (postoperatively) (VAS = 5 versus VAS = 0)</td>
<td>1.72</td>
<td>1.54–1.92</td>
</tr>
<tr>
<td>Increase in pain at rest (baseline vs. postoperative Day 4)</td>
<td>3.31</td>
<td>1.00–10.9</td>
</tr>
</tbody>
</table>

Mannitol vs. patient-controlled analgesia for postoperative pain control
0.85
0.39–1.34

Oral narcotics vs. patient-controlled IV analgesia for postoperative pain control
0.35
0.17–0.73

N = 333, non-cardiac surgery
Age: 74.6 years
POD incidence: 46%

Opioids: Inconclusive evidence

Non-pharmacologic prevention: Inconclusive evidence

No significant increase in the incidence of delirium associated with general anesthesia was found in the available trials.
**Regional anesthesia and POD**

**The evidence**

The Impact of General and Regional Anesthesia on the Incidence of Post-Operative Cognitive Dysfunction and Post-Operative Delirium: A Systematic Review with Meta-Analysis

---

**Prevention of POD**

**Targeting the imbalance of neurotransmitters**

- **Cholinesterase-Inhibitors**
  - Ineffective or dangerous
  - Benzodiazepines
  - Liver failure

- **GABA**
  - Benzodiazepines

- **Dopamine**
  - Drugs
  - Ischemia

- **Acetylcholine**
  - Drugs

- **Serotonin**
  - Drugs
  - Withdrawal

- **Xenon?**
  - Withdrawal
  - Drugs
  - Ischemia

- **Glutamate**

- **Cytokines**
  - Surgery
  - Infection
  - Sepsis

- **Dopamine**
  - Drugs
  - Ischemia

- **Acetylcholine**

- **GABA**
  - Benzodiazepines
  - Liver failure

- **Antipsychotics**
  - No proven benefit in > 16 RCT’s
  - controversial results
  - even if POD-rates were reduced, meaningful clinical outcomes were not improved (transition to hypoactive delirium?)
  - side effects

- **Acetylcholinesterase inhibitors**
  - ineffective († mortality in rivastigmine trial)

---

**Pharmacologic Prevention**

**Targeting the imbalance of neurotransmitters**

- **Antipsychotics:**
  - no proven benefit in > 16 RCT’s
  - controversial results
  - even if POD-rates were reduced, meaningful clinical outcomes were not improved (transition to hypoactive delirium?)
  - side effects

- **Acetylcholinesterase inhibitors:**
  - ineffective

---

**Prevention of POD**

**Avoidance of benzodiazepines**

- **Per equivalent of 2.5mg midazolam:**
  - 260% increase in the odds to develop POD

---

**Table 2. Multivariable Analysis of Additive and Analagous Medications as Risk Factors for Transitioning to Delirium/Cure or Delirium Only**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Transition to Delirium/Cure Odds Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Midazolam</td>
<td>3.76 (2.15–6.55)</td>
<td>0.00</td>
</tr>
<tr>
<td>Pantryne</td>
<td>1.21 (0.9–1.6)</td>
<td>0.20</td>
</tr>
<tr>
<td>Morphine</td>
<td>1.1 (0.9–1.3)</td>
<td>0.24</td>
</tr>
<tr>
<td>Pregablin</td>
<td>1.2 (0.9–1.5)</td>
<td>0.18</td>
</tr>
</tbody>
</table>

---

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

- There is insufficient evidence to recommend for or against the use of antipsychotic medications prophylactically in older surgical patients to prevent delirium.
- The prescribing practitioner should not newly prescribe cholinesterase inhibitors perioperatively to older adults to prevent or treat delirium.
Prevention of POD
Dexmedetomidine

Can dexmedetomidine be a safe and efficacious sedative agent in post-cardiac surgery patients? a meta-analysis

H. Yan, Jiao, B. He, J. Chen, and Z. H. Wang

Volume – Does it make a difference?
Intensivtherapie nach Herz- und Gefäßchirurgie

Prevention of POD
Depth of anaesthesia monitoring

Postoperative Delirium in a Substudy of Cardiothoracic Surgical Patients in the BAG-RECALL Clinical Trial

Elizabeth L. Whitlock, MD; MSc; Brian A. Tomczak, CPH; Nan Lin, PhD; Daniel L. Hebert, MD, MSc; Mary F. Naimark, MD; Daniel L. Hebert, MD, MSc; and Michael B. Avvent, MD, MSc

Recommndations
Depth of sedation

There is evidence that monitoring the depth of anaesthesia can reduce the occurrence of delirium after general anaesthetic.

Cochrane Library
Eating Well, shines above the rest.

Table 6: Published Trials Randomizing Patients to Bis-Guided Anaesthesia or Usual Care or Another Comparator for Reduction of Postoperative Delirium

<table>
<thead>
<tr>
<th>Study</th>
<th>Patient population</th>
<th>Group 1 (n)</th>
<th>Group 2 (n)</th>
<th>Odds ratio for delirium (group 2 vs group 1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gohier et al., 2010</td>
<td>36/346, from 44 centers, major surgical procedures</td>
<td>180/181</td>
<td>180/181</td>
<td>0.39 (0.32–0.56)</td>
</tr>
<tr>
<td>Gohier et al., 2013</td>
<td>210/210, from 44 centers, major surgical procedures</td>
<td>105/105</td>
<td>105/105</td>
<td>0.64 (0.41–0.98)</td>
</tr>
<tr>
<td>Nakada et al., 2013</td>
<td>&gt;600, electrophysiological surgery</td>
<td>210/210</td>
<td>210/210</td>
<td>0.73 (0.54–0.98)</td>
</tr>
<tr>
<td>Mikulas et al., 2014</td>
<td>Electrophysiological and non-surgical procedures</td>
<td>105/105</td>
<td>105/105</td>
<td>0.80 (0.55–1.23)</td>
</tr>
<tr>
<td>Addala et al., 2014</td>
<td>Electrophysiological and non-surgical procedures</td>
<td>105/105</td>
<td>105/105</td>
<td>0.86 (0.52–1.37)</td>
</tr>
</tbody>
</table>

Special Article
Postoperative Delirium in Older Adults: Best Practice Statement from the American Geriatrics Society

The anesthesia practitioner may use processed electroencephalographic monitors of anesthetic depth during intravenous sedation or general anesthesia of older patients to reduce postoperative delirium.
Non-pharmacologic prevention of POD
Multicomponent intervention

Postoperative cognitive dysfunction

Characteristics

- Concept:
  - Subtle and frequently transient cognitive decline, only detectable with appropriate neuropsychological tests and a comparison with preoperative cognition

- Definition:
  - Not described in the Diagnostic and Statistical Manual of Mental Disorders
  - No ICD code

- Diagnostic criteria:
  - Decrease in neuropsychological test scores from before to after surgery (preop. testing mandatory)
  - Tests typically assess 4-8 different cognitive domains

- Diagnostic methods:
  - Neuropsychological test batteries
    - Learning and memory: Rey Auditory Verbal Learning Test
    - Executive function:
      - Mental Flexibility: Trail Making Tests A + B
      - Executive function:
        - Simple Attention: Digit Span Forward
        - Complex attention (working memory): Digit Span Backward
        - Response Inhibition: Stroop Color Word Test
    - Psychomotor function:
      - Manual dexterity & motor speed: Grooved Pegboard test

Summary

I WATCH DEATH
Infectious
Withdrawal –
Acute metabolic disorder –
Trauma (operative trauma)
CSN pathology –
Hypoxia
D eficiencies –
Endocrine pathologies –
Acute vascular
Toxins (e.g. anaesthetics, drugs with anticholinergic side-effects)
Heavy metals

Evaluation of 1193 patients > 65yrs that had undergone general anaesthesia in the previous 5 years

In 120 patients, there were allegations of the family/near friends that the patient had never been the same since operation

▪ Concept:
  - Subtle and frequently transient cognitive decline, only detectable with appropriate neuropsychological tests and a comparison with preoperative cognition

▪ Definition:
  - Not described in the Diagnostic and Statistical Manual of Mental Disorders
  - No ICD code

▪ Diagnostic criteria:
  - Decrease in neuropsychological test scores from before to after surgery (preop. testing mandatory)
  - Tests typically assess 4-8 different cognitive domains

▪ Diagnostic methods:
  - Neuropsychological test batteries
    - Learning and memory: Rey Auditory Verbal Learning Test
    - Executive function:
      - Mental Flexibility: Trail Making Tests A + B
      - Executive function:
        - Simple Attention: Digit Span Forward
        - Complex attention (working memory): Digit Span Backward
        - Response Inhibition: Stroop Color Word Test
    - Psychomotor function:
      - Manual dexterity & motor speed: Grooved Pegboard test

Postoperative cognitive dysfunction

Characteristics

- Concept:
  - Subtle and frequently transient cognitive decline, only detectable with appropriate neuropsychological tests and a comparison with preoperative cognition

- Definition:
  - Not described in the Diagnostic and Statistical Manual of Mental Disorders
  - No ICD code

- Diagnostic criteria:
  - Decrease in neuropsychological test scores from before to after surgery (preop. testing mandatory)
  - Tests typically assess 4-8 different cognitive domains

- Diagnostic methods:
  - Neuropsychological test batteries
    - Learning and memory: Rey Auditory Verbal Learning Test
    - Executive function:
      - Mental Flexibility: Trail Making Tests A + B
      - Executive function:
        - Simple Attention: Digit Span Forward
        - Complex attention (working memory): Digit Span Backward
        - Response Inhibition: Stroop Color Word Test
    - Psychomotor function:
      - Manual dexterity & motor speed: Grooved Pegboard test
Postoperative cognitive dysfunction

Learning effects

- Correction for learning effects:
  - Reliable change index
  - \[ \text{RCI}_{\text{POCD}} = \frac{\Delta X}{\text{SD}_{\text{POCD}}} \]

Incidence

- Among the patients studied, the incidence of cognitive decline was 33 percent at discharge, 13 percent at six months, and 42 percent at five years.

Impact on outcome

- POCD at 3 mo, n = 596
- POCD at 1 wk, n = 198

- Non-cardiac surgery
  - POCD at 3 mo, n = 596
  - POCD at 1 wk, n = 198

- Executive function —> ↑ fall risk
- Ability to make medical appointments
- Ability to follow instructions
- Ability to remember that medication has to be taken

Relevance

- Frequent yet unrecognised postoperative complication
- Incidence highest in older adults (up to 50%)
- Begins at least 1 week after surgery
- Lasts up to 3mo - 6mo -12mo - longer?
- Associated with an increased mortality
- Premature exit from the workforce (earlier retirement)
- Negative impact on quality of life
- Greater utilisation of social financial assistance

- Usually transient
- Related to dementia?

Mashour GA et al.
Neurological complications of surgery and anaesthesia.
Brown IV C, Deiner S
Perioperative cognitive protection.
British Journal of Anaesthesia 117(S3): iii52-iii61 (2016)
Berger M et al.
Postoperative cognitive dysfunction.
Anesthesiology Clin 33 (2015) 517-550

Monk TG et al.
Predictors of Cognitive Dysfunction after Major Noncardiac Surgery.
Anesthesiology 2008; 108:18–30

Johns MW et al.
Postoperative cognitive dysfunction in the elderly: predictors, risk assessment, and prevention.
Anesthesiology 2010; 113:649-662

Marder AR et al.
Predictors of cognitive decline after major noncardiac surgery.
Anesthesiology 2009; 100:10-20

Lewis MS et al.
The influence of different error estimates in the detection of postoperative cognitive dysfunction using reliable change indices with correction for practice effects.
Archives of Clinical Neuropsychology 22 (2007) 249–257

Nadelson MR et al.
Perioperative cognitive trajectory in adults.
Postoperative cognitive dysfunction

Impact on outcome

- Excessive neuroinflammation
- Failure to resolve inflammation
- Blood-brain barrier endothelial dysfunction
- Pre-existing AD pathology

Pathophysiology

- Excessive neuroinflammation
- Failure to resolve inflammation
- Blood-brain barrier endothelial dysfunction
- Pre-existing AD pathology

Risk factors

<table>
<thead>
<tr>
<th>Risk factors for postoperative cognitive dysfunction (POCD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient</td>
</tr>
<tr>
<td>Operation</td>
</tr>
</tbody>
</table>
| Anesthesia | long-acting anesthetic, marked disturbance of homeostasis, organ ischemia due to hypoxia and hypoperfusion, intra- or postoperative anesthesiological complications | }

"The greater the reserve, the more severe the pathology must be to cause functional impairment"


Marcantonio ER. Postoperative Delirium. JAMA. 2012;308(1):73-81
Postoperative cognitive dysfunction prevention

**TABLE 4**

<table>
<thead>
<tr>
<th>Person</th>
<th>Strategies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient</td>
<td>perioperative cognitive training (?)</td>
</tr>
<tr>
<td>Surgeon</td>
<td>meticulous surgical technique to prevent complications; minimally invasive technique (?)</td>
</tr>
<tr>
<td>Anesthesiologist</td>
<td>cautious use of premedicating drugs (sedatives) in elderly patients, short-acting anesthetics during surgery, meticulous anesthetic technique to prevent perioperative disturbances of homeostasis and organ ischemia, tight volumetric balance, EEG monitoring (?)</td>
</tr>
</tbody>
</table>

**No evidence!**
Postoperative cognitive dysfunction

Critique

- POCD frequently reflects patient frailty
- Cognitive trajectories are similar to age- and disease matched controls NOT undergoing surgery
- Link between surgery/anesthesia and POCD is questionable

Postoperative cognitive dysfunction

Critique

- Pain, inflammation, and acute illness carry a cognitive burden
- Postoperative cognitive improvement when surgery results in
  - decreased pain (e.g., from angina pectoris)
  - decreased inflammation (e.g., from arthritis)
  - increased cerebral blood flow (e.g., from TEA of the carotid artery)
  - enhanced ability to function in daily life

Cognitive Outcomes 7.5 Years After Angioplasty Compared With Off-Pump Coronary Bypass Surgery


Twenty-eight published studies, 2043 patients undergoing CABG

Postoperative cognitive dysfunction

Dementia / Long-lasting POCD

Definition

Table 1: The differential diagnosis of postoperative neurocognitive disturbances with impaired cognitive performance

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Diagnostic Tests</th>
<th>Time</th>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dementia</td>
<td>various dementia tests</td>
<td>-</td>
<td>develop progressively over months to years</td>
</tr>
</tbody>
</table>

In animal models / in vitro systems:
1. increased amyloid beta (Aβ) monomer production;
2. increased Aβ oligomerization;
3. decreased Aβ clearance;
4. intracellular calcium ion release and excitotoxic neuronal injury;
5. inflammatory changes;
6. increased tau production, phosphorylation, and neurofibrillary tangle formation.
Postoperative Delirium

Risk of dementia after general anaesthesia and surgery

- n = 135371 patients with dementia
  - n = 24901 with anaesthesia for the first time since 1995 between 1 January 2004 and 31 December 2007
  - n = 110972 without anaesthesia

Dementia / Long-lasting POCD

Population-based evidence

Prospective evidence


"The prevalence of dementia at 7.5 yr after coronary artery bypass graft surgery is greatly increased compared to population prevalence. Impaired cognition before surgery or the presence of cardiovascular disease may contribute to the high prevalence."

Conclusions: The study did not detect long-term cognitive decline independently attributable to surgery or illness, nor were these events associated with accelerated progression to dementia.

Aims: This is a meta-analysis evaluating the effects of the anaesthetic technique (regional vs. general anaesthesia) on POCD of patients undergoing non-cardiac surgery.

Results: Twenty-six RCTs including 2365 patients.

Conclusions: The present meta-analysis does not support the concerns that a single exposure to general anaesthesia in an adult would significantly contribute to permanent POCD after non-cardiac surgery.


CONCLUSIONS: Exposure to general anesthesia for procedures at age ≥40 years was not associated with prevalent MCI in the elderly.

Summary

- **POD**
  - Acute neurocognitive brain failure
  - Up to 50% of patients > 65y
  - Associated with mortality, LOS, POCD, functional decline, costs
  - Diagnosis: Delirium screening tools
  - Pathophysiology: Neurotransmitter imbalance, inflammation, endothelial dysfunction
  - Predisposing factors vs. precipitating factors
  - Prevention: Multimodal approach, depth of anaesthesia monitoring
  - Therapy: causal (if possible) vs. symptomatic (antipsychotics)

- **POCD**
  - Mostly subtle (and transient) cognitive decline
  - Up to 50% of patients, particularly in the elderly
  - In up to 10% of the elderly still present after 3 months
  - Associated with mortality and premature retirement
  - Diagnosis: Neuropsychological test batteries before AND after surgery
  - Pathophysiology: Neuroinflammation
  - Prevention: ?
  - Treatment: None
  - Role of anesthesia/surgery: questionable

- **Dementia**
  - In vitro and animal data suggest a link between anaesthesia/surgery and dementia
  - Epidemiological data do not support this link in humans
Thank you very much for your attention