Post Anesthesia Care Unit Delirium: Incidence, Risk Factors and Associated Adverse Outcomes

<table>
<thead>
<tr>
<th>Journal:</th>
<th>British Journal of Anaesthesia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manuscript ID</td>
<td>BJA-2017-00602-HH204</td>
</tr>
<tr>
<td>Manuscript Type:</td>
<td>Editorial</td>
</tr>
<tr>
<td>Date Submitted by the Author:</td>
<td>24-May-2017</td>
</tr>
</tbody>
</table>

**Complete List of Authors:**

- Hernandez, Brandon; University of Wisconsin, Anesthesiology
- Lindroth, Heidi; University of Wisconsin, Anesthesiology
- Rowley, Paul; University of Wisconsin, Anesthesiology
- Boncyk, Chistine; University of Wisconsin, Anesthesiology
- Raz, Aeyal; University of Wisconsin, Anesthesiology
- Rambam Health Care Campus, Anesthesiology
- Gaskell, Amy; Waikato District Health Board, Dept of Anaesthesia; University of Auckland, Dept of Anaesthesiology
- Garcia, Paul; Atlanta VA Medical Center, Research and Anesthesiology Service Lines; Emory University School of Medicine, Anesthesiology
- Sleigh, Jamie; University of Auckland, Department of Anaesthesiology
- Sanders, Robert; University of Wisconsin, Anesthesiology

**Mesh keywords:**

- confusion, delirium, anaesthesia
Post Anesthesia Care Unit Delirium: Incidence, Risk Factors and Associated Adverse Outcomes

Brandon B.A. Hernandez, Heidi Lindroth, Paul Rowley, Christina Boncyk, Aeyal A. Raz, Amy A. Gaskell, Paul P.S. García, Jamie Sleigh, Robert R.D. Sanders

1. Department of Anesthesiology, University of Wisconsin, Madison, WI, 53792, USA
2. Department of Anaesthesia, Waikato Hospital, Hamilton, 3240, NZ
3. Department of Anesthesiology, Emory University & Atlanta VA Hospital, Atlanta, GA 30332, USA

Abbreviated title: PACU delirium

*Corresponding author: Dr Robert D Sanders, Department of Anesthesiology, University of Wisconsin School of Medicine and Public Health, 600 Highland Avenue, B6/319 CSC Madison, WI 53792-3272 Telephone: 608-263-8100 Fax: 608-263-0575 Madison, USA. Email: robert.sanders@wisc.edu

Numbers of Figures: 1

Word count: 1303

Conflict of Interest: None
Delirium is a sudden disturbance in attention and orientation to the environment that develops over a short period of time and tends to fluctuate in severity during the course of the day. The acute confusional state of delirium occurs in 50-80% of critically ill patients and postoperatively (from the day after surgery onwards) in up to 54% of elective major non-cardiac surgical patients. It incurs a huge societal burden, due to in part due to its association with increased morbidity and mortality; each additional day of delirium has been independently associated with a 10% increased risk of death. Increased morbidity contributes to prolonged hospital length of stay and significant financial implications: delirium is estimated to total $4-$16 billion annually. Its association with long-term neuropsychological and cognitive deficits mandates a better understanding of the pathogenesis of delirium and the mechanisms underlying the prolonged disruption of cognitive processing. Despite these apparent strong associations, it remains unclear whether delirium identified in the post-anesthetic care unit (PACU) or recovery unit is associated with similar outcomes. For anaesthetists, this is a critical question that remains unanswered. Indeed at least some of these events are of limited duration and hence it could be assumed they would be associated with less severe consequences. In this context, PACU delirium is differentiated from postoperative delirium as the latter occurs from the day after surgery onwards while the former occurs in the PACU on the day of surgery.

In order to illuminate this topic further we conducted a PubMed search using the terms PACU or post-anesthesia care unit or recovery AND delirium or confusion. From this search,
1,293 articles were identified (Supplementary Figure). The search was narrowed by removing 1,196 articles that did not meet inclusion criteria such as those covering an unrelated topic or being published as reviews, opinions, or editorials. After narrowing the search, 97 titles and abstracts were reviewed looking for articles with conclusions as well as containing information specifically pertaining to delirium in the PACU or recovery room. A total of 35 articles were reviewed in full to identify those papers that reported an incidence of diagnosed delirium in the PACU and reported either risk factors for PACU delirium or consequences of PACU delirium.

**Incidence and Diagnosis of PACU Delirium**

Twelve articles were identified that met the criteria of this report. These twelve case control or cohort studies, with a total of 7,439 patients, showed a median incidence of delirium diagnosed in the PACU to be 16.4% (range: 1.3% to 45%). The wide variance appears in part due to heterogeneity in the schemes used for delirium identification (see recommendations in ). Table 1 shows the diagnostic method and corresponding incidence of PACU delirium found by each publication used in this report. Diagnostic methods used include the Nursing Delirium Screening Scale (Nu-DESC), Confusion Assessment Method (CAM/CAM-ICU), the Intensive Care Delirium Screening Checklist (ICDSC), the Delirium Detection Score (DDS), Richmond Agitation-Sedation Scale (RASS), the Riker Sedation Scale, and the DSM IV. We caution here that the RASS and Riker sedation scales are measures of agitation or sedation of a patient and miss important cognitive components of delirium. Indeed one should be hesitant to conclude a non-zero RASS score is an indication of delirium. One study noted a great variety in reported incidence of PACU delirium dependent on the method of assessment. DSM IV criteria found 14% of subjects to be delirious in the PACU, CAM found...
7% of the same subjects to be delirious and the DDS found an incidence of 3%. Interestingly, the more sensitive Nu-DESC found 24% of subjects to be delirious; the Nu-DESC was recommended by the authors to be used for screening. We suggest this recommendation is interpreted cautiously, due to the small study population, the low rate of delirium, and the high potential rate of false positives. Nevertheless, the authors make the argument that a valid assessment tool for delirium screening in the PACU needs to be developed.

A second study looked at the specificity and sensitivity of the CAM-ICU and the Nu-DESC compared to the DSM IV in 91 patients. This study found that neither the CAM-ICU nor the Nu-DESC was sensitive enough to identify delirium post-operatively, with sensitivities of 28% and 32%, respectively. However, both tests performed > 90% for specificity, perhaps reflecting the specific training of personnel in these screens. Regardless of the specificities, inconsistencies in the opinions of delirium diagnosis occur even among experts. From a research perspective this makes clarifying the risk factors and impact of delirium more complex. Our mini-review demonstrates that efforts should be made to develop a screening tool for PACU delirium that is both sensitive, specific, and time-efficient.

Until then, we recommend following the guidelines that suggest making local decisions about relevant tools. It is also interesting that self-reported confusion following anaesthesia in a wide-diverse population is approximately 10%. It would be interesting to see how each measure correlated with this patient-centered, albeit subjective, outcome.

PACU Delirium Risk Factors

From the reviewed publications, both risk factors for patients developing PACU delirium and consequences or negative long-term outcomes of PACU delirium were identified. The risk
factors for developing PACU delirium that were identified were age, longer preoperative fasting times, male gender, type of surgery, preexisting conditions (such as vascular risk factors or ASA score), perioperative drugs administered (such as benzodiazepines, volatile anesthetics and or narcotics), and volume of erythrocytes or fresh frozen plasma administered.

PACU Delirium-Associated Adverse Events

For PACU delirium to be considered an important medical condition it must be associated with either increased morbidity, mortality or costs. PACU delirium is commonly associated with postoperative delirium. Again the effect sizes reported are variable, however the smallest effect size suggested an approximate four-fold increase in the Odds Ratio for postoperative delirium when PACU delirium subsequently was detected. However in this study 18% of the patients without PACU delirium, subsequently demonstrated postoperative delirium. It is unclear whether these constitute missed cases of PACU delirium, or new cases. Hence despite the plausibility of the link between PACU and postoperative delirium, further data is required on the strength of the associations as well as the impact on other healthcare outcomes. One particular study that specifically investigated long-term outcomes of patients with PACU delirium found that there was no association between PACU delirium and mortality 18 months after surgery. However the small sample size (n=91) in this study precludes definitive inference. Additional consequences that were identified in less than two publications include increased length of recovery room (PACU) stay, increased Visual Analog Scale (VAS) for pain at PACU admission, increased VAS score for post-operative nausea and vomiting (PONV) at 24
For Peer Review

h, ours\textsuperscript{25}, \textit{as well as} and one study suggesting that PACU delirium was associated with increased in-hospital mortality.\textsuperscript{26}

Conclusions

On review of the \textit{relevant} literature, \textit{we conclude that} there are hints to the medical importance of PACU delirium, but we suggest that a large perioperative cohort study is needed to confirm the optimal diagnostic approach for \textit{clinically significant} PACU delirium, \textit{to} identify risk factors for PACU delirium, and \textit{to} establish associations with long-term adverse outcomes, \textit{for these patients once a diagnosis is made}. The heterogeneity between study populations, small sample sizes, and lack of long-term follow-up in many studies limits our ability to draw definitive conclusions. The suggestion that PACU delirium could \textit{translate} \textit{transition} to, and hence potentially aid in early identification of patients at increased risk for, postoperative delirium is intriguing. Consistent with the notion that \textit{anaesthesia and surgery may ba}\textsuperscript{re} a stress test for the brain,\textsuperscript{26} early intervention in the PACU \textit{may help} \textit{might} identify a subgroup of patients who are vulnerable to the associated morbidity and mortality of delirium of longer durations. \textit{We propose that a large \textit{multicenter-multicentre} perioperative cohort study is required on this issue.}

Author contributions

\textit{To be completed}

Disclosures of interest

\textit{None declared.}

Funding
Funding came from the Department of Anesthesiology, University of Wisconsin and the James S. McDonnell Foundation (www.jsmf.org) via a collaborative grant (#220023046 lead PI: PSG) to the ACCESS group (Anesthesiologists foCused on Cognition, Emergence, Sleep, and Sedation; www.accesshq.org).
References


5. Sauër A-M. ... aex053

6. Aranake-Chrisinger A ... aex126

7. Sprung J ... aex130


Identified 1293 articles using PubMed

Reviewed 97 Titles and Abstracts

Reviewed full text of 35 articles

12 Included articles

1196 articles removed that did not meet inclusion criteria (unrelated topic, older than 12 years, reviews, opinions, or editorials)

62 citations removed that did not meet inclusion criteria (unrelated topic, not conclusive, not PACU/recovery room specific)

23 articles removed that did not meet inclusion criteria (Risk factors for or consequences of PACU delirium not reported, delirium not quantified in PACU).
Table 1. Diagnostic method and reported incidence of PACU delirium.

<table>
<thead>
<tr>
<th>Publication Author</th>
<th>Incidence of PACU delirium</th>
<th>Sample Size</th>
<th>Diagnostic Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radtke</td>
<td>11%</td>
<td>100</td>
<td>Nu-DESC</td>
</tr>
<tr>
<td>Winter</td>
<td>4.3%</td>
<td>1000</td>
<td>Nu-DESC</td>
</tr>
<tr>
<td>Neufeld</td>
<td>45% 13% 19% 54%</td>
<td>91</td>
<td>DSM IV CAM NuDESC ≥ 2 NuDESC ≥ 1</td>
</tr>
<tr>
<td>Radtke</td>
<td>14% 7% 3% 24%</td>
<td>150</td>
<td>DSM IV CAM DDS Nu-DESC</td>
</tr>
<tr>
<td>Dillon</td>
<td>24%</td>
<td>566</td>
<td>CAM</td>
</tr>
<tr>
<td>Sharma</td>
<td>45%</td>
<td>47</td>
<td>CAM</td>
</tr>
<tr>
<td>Card</td>
<td>31%</td>
<td>400</td>
<td>CAM-ICU</td>
</tr>
<tr>
<td>Veiga</td>
<td>18.8%</td>
<td>680</td>
<td>ICDSC</td>
</tr>
<tr>
<td>Munk</td>
<td>1.3%</td>
<td>1970</td>
<td>RASS</td>
</tr>
<tr>
<td>Xara</td>
<td>6.4%</td>
<td>266</td>
<td>RASS</td>
</tr>
<tr>
<td>Lepouse</td>
<td>4.7%</td>
<td>1359</td>
<td>Riker sedation scale</td>
</tr>
</tbody>
</table>

References


