

19. Ioannidis JP. Why most published research findings are false. *PLoS Med* 2005; **2**: e124
20. Gusmao-Flores D, Salluh JI, Chalhoub RA, et al. The confusion assessment method for the intensive care unit (CAM-ICU) and intensive care delirium screening checklist (ICDSC) for the diagnosis of delirium: a systematic review and meta-analysis of clinical studies. *Crit Care* 2012; **16**: R115
21. van Eijk MM, van den Boogaard M, van Marum RJ, et al. Routine use of the confusion assessment method for the intensive care unit: a multicenter study. *Am J Respir Crit Care Med* 2011; **184**: 340–4
22. Pandharipande P, Cotton BA, Shintani A, et al. Motoric subtypes of delirium in mechanically ventilated surgical and trauma intensive care unit patients. *Intensive Care Med* 2007; **33**: 1726–31
23. Martin BJ, Buth KJ, Arora RC, et al. Delirium: a cause for concern beyond the immediate postoperative period. *Ann Thorac Surg* 2012; **93**: 1114–20
24. Whitlock EL, Torres BA, Lin N, et al. Postoperative delirium in a substudy of cardiothoracic surgical patients in the BAG-RECALL clinical trial. *Anesth Analg* 2014; **118**: 809–17
25. Raats JW, Steunenbergh SL, Crolla RM, et al. Postoperative delirium in elderly after elective and acute colorectal surgery: A prospective cohort study. *Int J Surg* 2015; **18**: 216–9
26. Maniar HS, Lindman BR, Escallier K, et al. Delirium after surgical and transcatheter aortic valve replacement is associated with increased mortality. *J Thorac Cardiovasc Surg* 2016; **151**: 815–23.e1-2
27. Avidan MS, Evers AS. The fallacy of persistent postoperative cognitive decline. *Anesthesiology* 2016; **124**: 255–8
28. Sauèr AM, Nathoe HM, Hendrikse J, et al. Cognitive outcomes 7.5 years after angioplasty compared with off-pump coronary bypass surgery. *Ann Thorac Surg* 2013; **96**: 1294–300
29. Sprung J, Roberts RO, Knopman DS, et al. Mild cognitive impairment and exposure to general anesthesia for surgeries and procedures: a population-based case-control study. *Anesth Analg* 2017; **124**: 1277–90
30. Sprung J, Roberts RO, Knopman DS, et al. Association of mild cognitive impairment with exposure to general anesthesia for surgical and nonsurgical procedures: a population-based study. *Mayo Clin Proc* 2016; **91**: 208–17
31. Sprung J, Jankowski CJ, Roberts RO, et al. Anesthesia and incident dementia: a population-based, nested, case-control study. *Mayo Clin Proc* 2013; **88**: 552–61

British Journal of Anaesthesia 119 (2): 288–90 (2017)
doi:10.1093/bja/oxe197

Post-anaesthesia care unit delirium: incidence, risk factors and associated adverse outcomes

B. A. Hernandez¹, H. Lindroth¹, P. Rowley¹, C. Boncyk¹, A. Raz¹, A. Gaskell², P. S. García³, J. Sleight² and R. D. Sanders^{1,*}

¹Department of Anesthesiology, University of Wisconsin, Madison, WI 53792, USA, ²Department of Anaesthesia, Waikato Hospital, Hamilton 3240, New Zealand and ³Department of Anesthesiology, Atlanta VA Hospital, Emory University, Atlanta, GA 30332, USA

*Corresponding author. E-mail: robert.sanders@wisc.edu

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.¹ 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.¹ It incurs a huge societal burden, because of, in part, a result of its association with increased morbidity and mortality; each additional day of delirium has been independently associated with a 10% increased risk of death.² Increased morbidity contributes to prolonged hospital length of stay and significant financial implications: delirium is estimated to total \$4–16 billion annually.³ Its association with long-term neuropsychological and cognitive deficits^{4–7} mandates a better understanding of the pathogenesis of delirium⁸ and the mechanisms underlying the prolonged disruption of cognitive processing.⁹ Despite these apparent strong associations, it remains unclear whether delirium identified in the post-anaesthetic 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 whereas 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-anaesthesia care unit or recovery AND delirium or confusion. From this search, 1293 articles were identified (Supplementary Fig. S1). The search was narrowed by removing 1196 articles that did not meet the 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

Table 1 Diagnostic method and reported incidence of post-anaesthetic care unit (PACU) delirium

Publication author	Incidence of PACU delirium (%)	Sample size	Diagnostic method
Radtke ¹⁹	11	100	Nu-DESC
Winter ²²	4.3	1000	Nu-DESC
Neufeld ¹²	45	91	DSM IV
	13		CAM-ICU
	19		NuDESC ≥ 2
	54		NuDESC ≥ 1
Radtke ²¹	14	150	DSM IV
	7		CAM
	3		DDS
	24		Nu-DESC
Dillon ²⁶	24	566	CAM
Sharma ¹³	45	47	CAM
Card ²⁴	31	400	CAM-ICU
Veiga ¹⁷	18.8	680	ICDSC
Munk ¹⁰	1.3	1970	RASS
Xara ²⁵	6.4	266	RASS
Lepouse ²³	4.7	1359	Riker Sedation Scale

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 12 case-control or cohort studies, with a total of 7439 patients, showed a median incidence of delirium diagnosed in the PACU to be 16.4% (range: 1.3%¹⁰ to 45%^{11–13}). The wide variance appears in part because of heterogeneity in the schemes used for delirium identification (see recommendations in¹⁴). 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), the Confusion Assessment Method (CAM/CAM-ICU), the Intensive Care Delirium Screening Checklist (ICDSC), the Delirium Detection Score (DDS), the 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:²¹ 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%.²¹ 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 that this recommendation is interpreted cautiously because of 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 with the Diagnosis and Statistical Manual of Mental Disorders, Volume IV (DSM IV) in 91

patients. This study found that the neither the CAM-ICU nor the Nu-DESC was sensitive enough to identify delirium postoperatively, with sensitivities of 28% and 32%, respectively.¹⁸ 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.^{15 16} From a research perspective this makes clarifying the risk factors and impact of delirium more complex. Our Editorial 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.¹⁴ It is also interesting that self-reported confusion following anaesthesia in a diverse population is approximately 10%.²⁰ 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 identified were age,^{13 17} longer preoperative fasting times,^{19 22} male gender,¹⁰ type of surgery,^{13 23} pre-existing conditions (such as vascular risk factors or ASA score),^{13 17} perioperative drugs administered (such as benzodiazepines, volatile anaesthetics or opioids)^{10 13 23 24} and the volume of erythrocytes or fresh frozen plasma administered.¹⁷

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.^{12 13 19 25} Again, the effect sizes reported are variable; however, the smallest effect size¹² 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.¹² 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 are required on the strength of the associations as well as the impact on other healthcare outcomes. One 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.¹¹ However, the small sample size ($n=91$) precludes definitive inference. Additional consequences that were identified in fewer than two publications include increased length of recovery room (PACU) stay,¹⁹ increased Visual Analogue Scale (VAS) for pain at PACU admission,²⁵ increased VAS score for postoperative nausea and vomiting at 24h,²⁵ and one study suggesting that PACU delirium was associated with increased in-hospital mortality.¹⁷

Conclusions

On review of the relevant literature, 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 clinically significant PACU delirium, to identify risk factors for PACU delirium and to establish

associations with long-term adverse outcomes. 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 transition to, and hence potentially aid in the early identification of patients at increased risk for, postoperative delirium is intriguing. Consistent with the notion that anaesthesia and surgery are a stress test for the brain,⁹ early intervention in the PACU might identify a subgroup of patients who are vulnerable to the associated morbidity and mortality of delirium of longer durations. We propose that a large multicentre perioperative cohort study is required on this issue.

Authors' contributions

The project was conceived by RDS, AG, AR, JS, and PSG. Systematic review was conducted by BAH with input from HL, PR, CB and RDS. BAH wrote the manuscript with input from RDS. All authors then edited the manuscript.

Supplementary material

Supplementary material is available at *British Journal of Anaesthesia* online.

Declaration of interest

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 Principal Investigator: P.S.G.) to the ACCESS group (Anesthesiologists foCused on Cognition, Emergence, Sleep, and Sedation; www.accesshq.org).

References

- Sanders RD, Pandharipande PP, Davidson AJ, Ma D, Maze M. Anticipating and managing postoperative delirium and cognitive decline in adults. *Br Med J* 2011; **343**: d4331
- Pisani MA, Kong SY, Kasl SV, Murphy TE, Araujo KL, Van Ness PH. Days of delirium are associated with 1-year mortality in an older intensive care unit population. *Am J Respir Crit Care Med* 2009; **180**: 1092–7
- Leslie DL, Marcantonio ER, Zhang Y, Leo-Summers L, Inouye SK. One-year health care costs associated with delirium in the elderly population. *Arch Intern Med* 2008; **168**: 27–32
- Pandharipande PP, Girard TD, Jackson JC, et al. Long-term cognitive impairment after critical illness. *N Engl J Med* 2013; **369**: 1306–16
- Sauër A-M, Veldhuijzen DS, Ottens TH, Slooter AJC, Kalkman CJ, van Dijk D. The association between delirium and cognitive change after cardiac surgery. *Br J Anaesth* 2017; **119**: 308–15
- Aranake-Chrisinger A, Avidan MS. Postoperative delirium portends descent to dementia. *Br J Anaesth* 2017; **119**: 285–8
- Sprung J, Roberts RO, Weingarten TN, et al. Postoperative delirium in elderly patients is associated with subsequent cognitive impairment. *Br J Anaesth* 2017; **119**: 316–23
- Sanders RD. Hypothesis for the pathophysiology of delirium: role of baseline brain network connectivity and changes in inhibitory tone. *Med Hypotheses* 2011; **77**: 140–3
- Nadelson MR, Sanders RD, Avidan MS. Perioperative cognitive trajectory in adults. *Br J Anaesth* 2014; **112**: 440–51
- Munk L, Andersen G, Moller AM. Post-anaesthetic emergence delirium in adults: incidence, predictors and consequences. *Acta Anaesthesiol Scand* 2016; **60**: 1059–66
- Neufeld KJ, Leoutsakos JM, Oh E, et al. Long-term outcomes of older adults with and without delirium immediately after recovery from general anesthesia for surgery. *Am J Geriatr Psychiatry* 2015; **23**: 1067–74
- Neufeld KJ, Leoutsakos JM, Sieber FE, et al. Outcomes of early delirium diagnosis after general anesthesia in the elderly. *Anesth Analg* 2013; **117**: 471–8
- Sharma PT, Sieber FE, Zakriya KJ, et al. Recovery room delirium predicts postoperative delirium after hip-fracture repair. *Anesth Analg* 2005; **101**: 1215–20. table of contents
- Aldecoa C, Bettelli G, Bilotta F, et al. European Society of Anaesthesiology evidence-based and consensus-based guideline on postoperative delirium. *Eur J Anaesthesiol* 2017; **34**: 192–214
- Numan T, van den Boogaard M, Kamper AM, et al. Recognition of delirium in postoperative elderly patients: a multicenter study. *J Am Geriatr Soc* 2017, DOI: 10.1111/jgs.14933
- Slooter AJC. Delirium, what's in a name? *Br J Anaesth* 2017; **119**: 283–5
- Veiga D, Luis C, Parente D, et al. Postoperative delirium in intensive care patients: risk factors and outcome. *Rev Bras Anesthesiol* 2012; **62**: 469–83
- Neufeld KJ, Leoutsakos JS, Sieber FE, et al. Evaluation of two delirium screening tools for detecting post-operative delirium in the elderly. *Br J Anaesth* 2013; **111**: 612–8
- Radtke FM, Franck M, MacGuill M, et al. Duration of fluid fasting and choice of analgesic are modifiable factors for early postoperative delirium. *Eur J Anaesthesiol* 2010; **27**: 411–6
- Sanders RD, Gaskell A, Raz A, et al. Incidence of connected consciousness after tracheal intubation: a prospective, international, multicenter cohort study of the isolated forearm technique. *Anesthesiology* 2017; **126**: 214–22
- Radtke FM, Franck M, Schneider M, et al. Comparison of three scores to screen for delirium in the recovery room. *Br J Anaesth* 2008; **101**: 338–43
- Winter A, Steurer MP, Dullenkopf A. Postoperative delirium assessed by post anesthesia care unit staff utilizing the Nursing Delirium Screening Scale: a prospective observational study of 1000 patients in a single Swiss institution. *BMC Anesthesiol* 2015; **15**: 184
- Lepouse C, Lautner CA, Liu L, Gomis P, Leon A. Emergence delirium in adults in the post-anaesthesia care unit. *Br J Anaesth* 2006; **96**: 747–53
- Card E, Pandharipande P, Tomes C, et al. Emergence from general anaesthesia and evolution of delirium signs in the post-anaesthesia care unit. *Br J Anaesth* 2015; **115**: 411–7
- Xara D, Silva A, Mendonca J, Abelha F. Inadequate emergence after anesthesia: emergence delirium and hypoactive emergence in the Postanesthesia Care Unit. *J Clin Anesth* 2013; **25**: 439–46
- Dillon ST, et al. Higher C-Reactive Protein Levels Predict Postoperative Delirium in Older Patients Undergoing Major Elective Surgery: A Longitudinal Nested Case-Control Study. *Biol. Psychiatry* **81**: 145–53