Delirium in patients following general anaesthesia

Yi Lin Lee¹ *MMED (Anaes)*, Jolin Wong¹ *FANZCA*, Shin Yi Ng² *MMED (Anaes)*

Delirium is a disturbance of consciousness characterised by an acute onset and fluctuating course of inattention, accompanied by either a change in cognition or a disorganised thinking, resulting in an impaired ability of the patient to receive, process, store and recall information. Delirium develops over a short period of time (hours to days) and is usually reversible. Three subtypes have been described: hypoactive, hyperactive and mixed delirium. Mixed and hypoactive delirium are the most common subtypes and are often undiagnosed if routine screening is not implemented.

The prevalence of delirium in the community is low but can go up to 70% in frail elderly patients undergoing emergency hip fracture surgery in the postoperative period.¹ This increased healthcare burden has profound implications on a rapidly ageing population.

Postoperative delirium comes at a significant cost to both patients and healthcare systems in general. The patient with postoperative delirium may suffer increased mortality, length of hospital stay, long-term cognitive impairment and functional decline, and need for discharge to a long-term care facility.^{1,2}

Risk factors for delirium include patient factors such as advanced age, pre-existing comorbidities such as dementia or cognitive impairment, and a poor functional baseline. Emergency, complex or major abdominopelvic surgery similarly increases the risk of postoperative delirium. Other preoperative triggers for delirium may include polypharmacy, pain, sleep deprivation, and fluid and electrolyte abnormalities.

Post-anaesthetic care unit (PACU) delirium is a subset of perioperative delirium. The difference between PACU and postoperative delirium lies primarily in the definition of the timeframe used, with the former occurring in the PACU on the day of surgery while the latter occurring after surgery. This definition can complicate matters as PACU delirium consists of an inseparable combination of emergence delirium/agitation and postoperative delirium. Emergence agitation refers to restlessness, disorientation, excitation, non-purposeful movement, thrashing, and incoherence during the early recovery from general anaesthesia. It is classically short-

lived, resolves spontaneously and has minimal long-term sequelae. That being said, the presence of emergence agitation remains a strong predictor of postoperative delirium.³

Although PACU delirium carries an association with subsequent postoperative delirium, it remains to be seen whether the former has associations with long-term morbidity and mortality that are similar to postoperative delirium. A study on the long-term outcomes of PACU delirium in elderly patients failed to demonstrate any correlation with mortality, mental or physical function, and utilisation of healthcare resources 18 months following general anaesthesia.⁴ Further studies will be required to determine the long-term significance of PACU delirium in perioperative patient care.

There is an even greater paucity of literature on PACU delirium in the Asian population. In this issue of the *Annals*, Ke et al. described a pragmatic observational study of PACU delirium in a multicentre study in Singapore involving elderly patients above 65 years of age undergoing major non-cardiac surgery.⁵ A total of 98 patients across 4 major hospitals were included in the study. The patients were assessed 30–60 minutes after arrival in the PACU for the presence of delirium, using the Nursing Delirium Screening Scale (Nu-DESC).

The authors highlighted that the Singapore incidence of PACU delirium in patients undergoing major surgery above 65 years of age was 11.4%. This is similar to international data, where a study by Hernandez et al. involving more than 7,000 patients found that the mean incidence of PACU delirium was 16.4%.⁶

Previously identified risk factors for PACU delirium include advanced age, longer preoperative fasting times, male, type of surgery, higher American Society of Anesthesiologists (ASA) scores, type of perioperative drugs administered (such as benzodiazepines, volatile anaesthetics or opioids) and the volume of packed red cells or fresh frozen plasma given.⁶ Similarly, in the study by Ke et al., univariate analysis of the risk factors showed that patients were at higher risk of PACU delirium if they had an ASA score of more than 3 and renal impairment. In addition, moderate to severe depression

¹ Department of Surgical Intensive Care, Singapore General Hospital, Singapore

² Duke-NUS Medical School, Singapore

Correspondence: Adjunct Assoc Prof Shin Yi Ng, Duke-NUS Medical School, 8 College Road, Singapore 169857.

Email: shinyi.ng@duke-nus.edu.sg

and an elevated random blood glucose and HbA1c levels were found to contribute to an increased risk of PACU delirium. In contrast to classical opinion, no association was found between pre-existing dementia and PACU delirium. Furthermore, in contrast to the article by Hernandez, the authors did not find any significant correlation between the type of anaesthesia used, the drugs administered, and the depth of anaesthesia with the incidence of PACU delirium. The former is consistent with recent studies that showed no difference between a general or regional technique with postoperative delirium in a high-risk group of patients undergoing hip fracture surgery.^{7,8}

Controversy remains as to whether depth of anaesthesia is related to postoperative delirium. Evered et al. reported findings from a delirium subset of the Balanced Anaesthesia Study,⁹ showing that the incidence of postoperative delirium was higher in patients who had received a greater depth of anaesthesia.¹⁰ In contrast, the Electroencephalography Guidance of Anesthesia (ENGAGES) trial was a randomised controlled trial that demonstrated no difference in delirium rates when electroencephalography was used to guide anaesthesia.¹¹

Interestingly, Ke et al. found on multivariate analysis that higher random blood glucose ($>9.5\text{mmol/L}$) was positively associated with PACU delirium. This is an easily modifiable factor that may potentially help to reduce any morbidity linked to delirium. The presence and duration of intraoperative hyperglycaemia (blood glucose $>8.3\text{mmol/L}$) has previously been found to have a significant association with postoperative delirium (odds ratio 3.86 confidence interval [CI] 95% [1.13–39.49], $P=0.044$).¹² However, excessively tight control of glucose levels ($4.4\text{--}8.3\text{mmol/L}$) may also be detrimental as the risk of delirium increases (relative risk 1.89, 95% CI 1.06–3.37, $P=0.03$).¹³ It is important to avoid hypoglycaemia and therefore more liberal glycaemic control may be preferred in the perioperative setting (similar to protocols commonly used in intensive care units). At present, not much is known about high random blood glucose as a potentially modifiable risk factor for delirium and therefore more work will need to be undertaken in this aspect.

The diagnosis of PACU delirium can be difficult to make despite the various screening tools available. The gold standard for diagnosing delirium remains the DSM-IV criteria, with Confusion Assessment Method (CAM) and Nu-DESC as 2 of the most commonly utilised screening tools. The diagnosis of delirium is made based on clinical history, behavioural observation and cognitive

assessment. A meta-analysis comparing 6 different delirium assessment tools found that the Nu-DESC had a higher sensitivity than CAM with both having high specificity of more than 0.9, suggesting that the Nu-DESC is an accurate screening tool for delirium.¹⁴ Mimickers of delirium include depression, psychosis and dementia and these should be excluded before the diagnosis is made.

Of late, more importance has been placed on the preservation of brain health in the perioperative setting. To that end, numerous consensus guidelines from organisations such as Brain Health Initiative and Safe Brain Initiative have been formulated to manage the risk of delirium in the perioperative setting. These recommendations are generally divided into (1) preoperative screening and optimisation of risk factors, (2) preoperative care including avoidance of prolonged fasting and the choice for fast-track surgery, (3) intraoperative measures including pain control, and (4) postoperative screening for and prompt treatment of delirium.

The cornerstone in the management of patients with delirium is prevention. Drugs such as benzodiazepines, which may be used in anaesthesia as an anxiolytic or sedative agent, should be switched to an alternative agent or avoided completely in patients at risk of developing delirium. Diabetes mellitus should be optimised and elective surgery may be delayed until blood sugars are better managed. Perioperative euglycaemia should be enforced, avoiding both hyper- and hypoglycaemia. Fasting times should also be reviewed diligently and patients allowed to take food or clear fluids as indicated.

Finally, Ke et al. have shown us that among the elderly in Singapore undergoing major non-cardiac surgery, the incidence of PACU delirium is 11.4%. Patients who experience delirium require a longer hospitalisation stay with a mean increase in hospitalisation cost of SGD10,000. This highlights the importance of channelling more resources to manage risk factors, reducing the incidence of PACU delirium and hence improve health economics for the patient and healthcare system.

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