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**Risk factors of post-anaesthesia care unit delirium in patients undergoing non-cardiac surgery in Singapore**

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**ABSTRACT**

**Introduction:** Post-anaesthesia care unit (PACU) delirium affects 5%–45% of patients after surgery and is associated with postoperative delirium and increased mortality. Up to 40% of PACU delirium is preventable but it remains under-recognised due to a lack of awareness for its diagnosis. Nursing Delirium Screening Scale (Nu-DESC) has been validated in diagnosing PACU delirium but is not routine locally. This study aim was to use the Nu-DESC to establish the incidence and risk factors of PACU delirium in patients undergoing non-cardiac surgery in the surgical population.

**Methods:** With IRB approval and informed consent, we conducted an audit of eligible patients undergoing major surgery in three major public hospitals in Singapore over one week. Patients were assessed for delirium 30–60 minutes following their arrival in the PACU using the Nu-DESC with a score of  $\geq 2$  as indicative of delirium.

**Results:** A total of 478 patients were assessed. The overall incidence rate of PACU delirium was 18/478 (3.8%) and 9/146 (6.2%) in patients over 65 years old. PACU delirium was more common in females, patients with malignancy and those who underwent longer operations. Logistic Regression analysis showed that the use of BIS ( $p < 0.001$ ) and the presence of malignancy ( $p < 0.001$ ) were significantly associated with a higher incidence of PACU delirium.

**Conclusion:** In this first local study, the incidence of PACU delirium was 3.8%, with the incidence increasing to 6.2% in those older than 65 years old. Understanding these risk factors will form the basis for which protocols can be established to optimise resource management and prevent long term morbidities and mortality of PACU delirium.

*Keywords: geriatrics, major non-cardiac surgery, postoperative delirium*

## INTRODUCTION

Post-anaesthesia care unit (PACU) delirium affects 5-45%<sup>(1-3)</sup> of patients after surgery. It is associated with postoperative delirium (POD),<sup>(2,4)</sup> with its attendant poor outcomes of increased hospital length of stay, increased 30-day mortality,<sup>(5)</sup> and long-term progression to dementia.<sup>(6)</sup> Up to 10% of these patients may develop long-term neurocognitive deficits, with diminished quality of life and pose a tremendous socio-economic burden on family and caregivers.<sup>(6,7)</sup>

With an increasingly aging population both globally and locally requiring surgery, the problem of PACU delirium and POD is set to increase. This has led to several guidelines being promulgated to address this issue, including the Brain Health Initiative<sup>(8)</sup> and the Safe Brain Initiative.<sup>(9)</sup>

Up to 40% of POD is preventable,<sup>(10)</sup> but the problem is that POD is often under-diagnosed, partly due to a lack of awareness with no established biomarkers or monitors for detection. The Nursing Delirium Screening Scale (NuDESC) has been validated as a quick and easy screening tool that can be performed within 2 minutes (Figure 1). It has a sensitivity and specificity of 98% and 92% in postoperative patients with a score of  $\geq 2$  being indicative of delirium.<sup>(2)</sup>

Thus, we aimed to use the NuDESC to understand the incidence of PACU delirium after major non-cardiac surgery locally as well as its associated risk factors.

## METHODS

The study was conducted in the National University Hospital, Khoo Teck Puat Hospital and Tan Tock Seng Hospital over a period of 1 week. Ethics approval was obtained from the Domain Specific Review Board (DSRB Reference number 2020/00320) which waived written consent requirement.

All patients aged 21 and above presenting for non-cardiac surgery in major operating theatres were recruited. Exclusions included patients undergoing neurosurgical procedures of the brain or electro-convulsive therapy, those undergoing surgery performed under local anaesthesia, and patients who are mechanically ventilated in the PACU, or those who stayed in the PACU for less than 10 minutes. Other preoperative details such as patient's existing co-morbidities, operative details such as surgical discipline, type of anaesthesia and duration of surgery and PACU details (i.e. length of stay in PACU and discharge destination) were collected. The use of depth of anaesthesia monitoring with bispectral index (BIS) was also recorded.

All eligible patients were assessed for PACU delirium 30-60 minutes upon arrival in PACU using NuDESC. The test is conducted by doctors and nurses participating in the patient's care. NuDESC evaluates delirium based on observation of the following five features: (i) disorientation, (ii) inappropriate behaviour, (iii) inappropriate communication, (iv) illusions/hallucinations, and (v) psychomotor retardation. Each item is scored based on its severity of 0 to 2. A score of  $\geq 2$  was classified as a positive score for postoperative delirium (Figure 1).

All data were entered into a statistical software programme, with analysis, statistical computing and visualisations carried out in the R environment version 1.2.1335 (The R Foundation for Statistical Computing, Vienna, Austria). For continuous variables, median and IQR were presented, and the Mann-Whitney U test was used to test the mean differences between the groups. For categorical variables, the  $\chi^2$  test was used to compare the proportions between the groups. Multivariate logistic regression was performed to determine the independent predictors for postoperative delirium. Factors that had a p-value of  $<0.1$  from the univariate analysis were included in the multivariate regression models. The effect size was reported as an odds ratio (OR) and its 95% confidence interval (CI).

## RESULTS

A total of 478 patients were assessed for PACU delirium over 1 week in three major public hospitals in Singapore. All the patients who were eligible completed their assessment.

The average age was 53.9 ( $\pm 17.2$ ) years, with 146 patients older than 65 years old. Four in ten of the patients were female, and the majority had general anaesthesia (GA). BIS was used in 55 (11.5%) of the patients and the average duration of surgery was 1.68 ( $\pm 1.78$ ) hours. The overall incidence rate of PACU delirium was 18/478 (3.8%) and 9/146 (6.2%) in patients over 65 years old (Table 1).

Logistic regression analysis (Table 2) showed that the use of BIS ( $p < 0.001$ , 9.43(3.17-28.50)) and presence of malignancy ( $p < 0.001$ , 10.7(2.58-40.70)) were significantly associated with a higher incidence of PACU delirium. Of note, the age, gender, type of anaesthesia (general vs regional), pain score in PACU and duration of surgery were not significantly associated with PACU delirium in univariate regression analysis ( $p > 0.05$ ). The other prevalent chronic diseases such as hypertension, diabetes mellitus, ischemic heart disease or chronic kidney disease also did not make a difference in the correlation with PACU delirium.

Further analysis of the 55 patients where BIS was used showed that the population had an average age of 60.9 ( $\pm 12.2$ ) years, and had a higher proportion being female (51.0%). They also had an average of a longer stay in PACU postoperatively (hours) (1.83( $\pm 1.12$ )) compared to the general cohort.

## DISCUSSION

In this one-week cross-sectional observational study of the patients undergoing non-cardiac surgeries in three major public hospitals in Singapore, the incidence of PACU delirium was found to be 3.8%, increasing to 6.2% in those older than 65 years old.

Our study reported a low incidence of 3.8% which could reflect the relatively young age of the postoperative population that was assessed within the time frame across different hospital systems. In comparison, in other studies done in elderly orthopaedic trauma patients, up to 50% of patients have been reported to develop PACU delirium.<sup>(4,5)</sup>

The NuDESC is a validated tool for diagnosing delirium postoperatively and similarly, we found that the implementation of NuDESC as a screening tool is simple, effective, and non-disruptive to the workflow in the PACU.<sup>(2,6,7)</sup> A Swiss study that used this screening tool reported an incidence of 4.8%, similar to our experience.<sup>(3)</sup> In contrast, patients in our cohort were younger and the average duration of surgery shorter. Despite this, the contributors of delirium in our studies differ. The average age of patients with delirium was much higher than our study (72.9 vs 58.0 years), while the average duration of surgery was shorter (85.6 vs 134.22 min). With increasing age, the risk of PACU delirium increases. Similar to other studies, we reported a two-fold increase in its incidence in postoperative patients over 65 years old. The type of anaesthesia did not make a difference in our population and may be due to the relatively short duration of surgery in this overall observational study.

An interesting finding was that the use of BIS was associated with a higher incidence of PACU delirium. The relationship is unlikely to be causal in nature. BIS was more frequently used in patients above 65 years old, reflecting that local anaesthesiologists regarded age as a possible indication for using BIS. BIS-guided anaesthesia has been shown to reduce the rates of

postoperative delirium<sup>(10,11)</sup> particularly in the elderly. Although it was more common for our local anaesthesiologists to utilise BIS for the older patients, there was no evidence that this prevented PACU delirium; and we did not have data on whether BIS was used to guide the depth of anaesthesia.

Patients with malignancy were an at-risk group for developing PACU delirium. They were also more likely to utilise more resources and HD or ICU care. This could reflect the patients' premorbid condition, more extensive surgery, and stress response. Increasingly, the role of chemotherapy and the "chemo-fog" that is reported may also predispose this vulnerable patient group to PACU delirium.<sup>(12)</sup> Further data would be required to identify areas of intervention and prevention.

PACU delirium is a harbinger for POD,<sup>(13)</sup> and early detection and effective triage of these patients is crucial. Patients with PACU delirium and higher Nu-DESC scores were more likely to require more extensive resources and discharge from the PACU to the HD or ICU. Implementing the Nu-DESC in the PACU unit will lay the foundation for using it as a standard of care and optimising resource management for patients in the postoperative period.

This is the first local observational study of PACU delirium and involved three major public institutions in Singapore. Even though the audit was performed over a relatively short time frame, this study has affirmed the importance of PACU delirium, particularly with an increasingly aging population presenting for surgery. Specifically, we identified patients with malignancy as a vulnerable group. Future studies will be designed to understand the role of the disease and treatment in PACU delirium. Understanding these risk factors will form the basis for which protocols can be established to optimise resource management and prevent long term morbidities and mortality of PACU delirium.

This study was not without limitations. All associations are observations, and may indicate, but do not prove, causations. The history of patients with dementia or cognitive impairment, which had been strongly linked with post-operative delirium, was not collated in the study due to the predominantly young population of the study cohort.

In conclusion, in this one-week observational study of 478 patients undergoing non-cardiac surgery in Singapore, we found that we have a low incidence rate of PACU delirium with 3.8% in the general surgical population, and 6.2% in those older than 65 years old. Positive correlation include a history of malignancy and the use of BIS. PACU delirium was associated with a longer duration of PACU stay.

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<b>NuDESC Screening Tool</b>	
<b>Disorientation</b>	
<b>0</b>	Alert, oriented to person, place, and time
<b>1</b>	Disoriented but easily reoriented
<b>2</b>	Disoriented x 2 or x3 but not easily reoriented
<b>Inappropriate behaviour</b>	
<b>0</b>	Calm and cooperative
<b>1</b>	Restless and cooperative
<b>2</b>	Agitated, pulling at devices, or climbing out of bed
<b>Inappropriate Communications</b>	
<b>0</b>	Appropriate
<b>1</b>	Unclear thinking or rambling speech
<b>2</b>	Incoherent, nonsensical, or unintelligible speech
<b>Illusions / Hallucinations</b>	
<b>0</b>	None noted
<b>1</b>	Paranoia or fears
<b>2</b>	Hallucinations or distortions of visual objects
<b>Psychomotor Retardation</b>	
<b>0</b>	None
<b>1</b>	Delayed or slow responsiveness
<b>2</b>	Excessive sleeping, somnolent, or lethargic

Figure 1. NuDESC Screening Tool. Adapted from Gaudreau et al<sup>(14)</sup>

**Table 1: Patient demographics stratified by PACU Delirium**

	<b>Has PACU delirium (N=18)</b>	<b>No PACU delirium (N=460)</b>	<b>Total (N=478)</b>	<b>P value</b>
Gender (Female)	9 (50%)	191(41.6%)	200(41.8%)	0.480
Age	58.0(±19.1)	53.5(±17.1)	53.9(±17.2)	0.277
Age >65 years old	9 (50.0%)	137 (29.8%)	146 (30.6%)	0.069
<b>Chronic diseases</b>				
Hypertension	9(50%)	186(40.5%)	195 (40.8%)	0.422
Diabetes Mellitus	4 (22.2%)	88 (19.2%)	92 (19.2%)	0.748
Ischemic heart disease	3 (16.7%)	42 (9.2%)	45(9.4%)	0.285
Chronic Kidney disease	1(5.6%)	25(5.4%)	26(5.4%)	0.984
Malignancy	5(27.8%)	12(2.6%)	17(3.6%)	<0.001
<b>Anaesthetic method</b>				
General Anaesthesia	18(100%)	396(85.4%)	411(86.0%)	0.572
BIS used	10(55.6%)	45(9.8%)	55(11.5%)	<0.001
Duration of operation	134.22 (72.03)	99.22 (108.05)	100.54	[0.174]
0 - 60 minutes	2 (11.1%)	178 (38.8%)	(107.06)	
60 - 120 minutes	6 (33.3%)	154 (33.6%)	180 (37.7%)	
>120 minutes	10 (55.6%)	127 (27.7%)	160 (33.5%)	
			137 (28.7%)	
<b>Postoperative</b>				
Length of stay in PACU(Hours)	2.72 (±1.72)	1.30 (±1.09)	1.36 (±1.15)	<0.001
Pain score >5	9 (50.0%)	202 (44.0%)	211 (44.1%)	0.606
Discharged to HD / ICU	5(27.8%)	35(7.6%)	40(8.4%)	0.032
Nu-DESC Score	4.8(±1.6)	0.0(±0.2)	0.2(±1.0)	<0.001

HD = High dependency; ICU = Intensive care unit; PACU = Post Anaesthesia Care Unit;

Nu-DESC = Nursing Delirium Screening Scale

Mann-Whitney U test- for continuous variable

Chi Square Test - for discrete variable

Median (±IQR) OR count (%)

**Table 2: Univariate and multivariate logistic/linear regression models for PACU delirium.**

Variables	Univariate		Multivariate	
	p-value	Odds Ratio OR Coeff (95%CI)	p-value	Odds Ratio OR Coeff (95%CI)
Gender (Female)	0.481	1.40(0.54-3.65)		
Age>65	<b>0.0764</b>	2.35(0.90-6.14)	0.470	1.47(0.50-2.34)
Hypertension	0.425	1.47(0.56-3.83)		
Diabetes Mellitus	0.748	1.20(0.33-3.45)		
Ischemic heart disease	0.293	1.99(0.45-6.23)		
Chronic Kidney disease	0.984	1.02(0.06-5.30)		
Malignancy	<b>&lt;0.001</b>	14.3(4.09-45.32)	<b>&lt;0.001</b>	10.90(2.57-24.31)
Use of BIS	<b>&lt;0.001</b>	11.50(4.33-31.58)	<b>&lt;0.001</b>	7.50(2.46-24.31))
Duration of surgery 60-120min >120 min	0.131 <b>0.0129</b>	3.46(0.78-23.9) 7.00(1.81-46.1)	0.395	2.12(0.41-15.73)
Pain score >5 in PACU	0.616	1.27(0.49-3.32)		
Discharge destination(HD/ICU)	<b>0.006</b>	4.52(1.39-12.74)	0.440	1.35(0.32-4.69)

HD = High dependency; ICU = Intensive care unit; PACU = Post Anaesthesia Care Unit; NuDESC = Nursing Delirium Screening Scale

Factors that had a p-value of <0.10 from the univariate analysis were included in the multivariate analysis.