J Nepal Health Res Counc 2023 Jan-Mar;21(58): 1-7

Incidence and Predictors of Delirium After Cardiac Surgery

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ABSTRACT

Background: The overall purpose of this study was to determine the incidence and perioperative factors that predispose to cause delirium in postoperative cardiac surgery patients in our Intensive Care Unit.

Methods: We performed a prospective, observational study. Following institutional review board approval, this study included 234 patients above the age of 18 years meeting the inclusion criteria for cardiac surgery in Shahid Gangalal National Heart Center from July 2018 to December 2018. Preoperative, intraoperative and postoperative data for possible risk factors were obtained. Daily assessment of delirium was done during Intensive Care Unit stay of the patient. Collected data were analysed by means of statistical software SPSS-21.

Results: The incidence of delirium was 15.6% (35/224) in our study. Delirium was seen in 14 out of 58 (24.1%) patients with age >60 years which was found to be statistically significant. Preoperative risk factor for developing delirium were carotid artery disease and Hemoglobin level <10gm/dl. Intraoperative risk factor for developing delirium were blood transfusion, longer cardiopulmonary bypass time. Post-operative factors for developing delirium included longer Intensive Care Unit stay, mechanical ventilation time ,duration on inotropes , blood transfusion, use of non-invasive ventilation, sleep deprivation, use of intra-aortic balloon pump, Pao2<70.

Conclusions: As shown in our study, delirium is a frequent occurrence in the cardiac surgical population. The incidence of delirium after cardiac surgery was 15.6%. Several risk factors pre-operatively like age>60 years, carotid artery disease, Hb<10gm/dl, intra-operative factors like longer cardiopulmonary bypass time, blood transfusion and post-operatively longer duration of Mechanical ventilation, Intensive Care Unit stay, blood transfusion, use of intra-aortic balloon pump and Non-invasive ventilation were found to be predictors of delirium.

Keywords: Keywords: Cardiac surgery; delirium; risk factors

INTRODUCTION

Delirium is a common problem that occurs after cardiac surgery. The incidence of delirium after cardiac surgery is estimated to be 26-52%, with a significant percentage being hypoactive delirium.[1,2] Postoperative delirium has been associated with higher hospital costs, longer lengths of hospital stay, increased likelihood of institutionalization, increased risk for dementia, and increased morbidity and mortality.[3,4] Recognizing delirium and those at risk can reduce the impact of delirium through targeted interventions and risk reduction. Understanding the frequency of delirium, the factors associated with it and its complications can help guide future research and resource allocation.[5] The overall purpose of this study was to determine the incidence and perioperative factors that predispose to cause delirium in postoperative cardiac surgery patients in our ICU.

METHODS

Institutional review board approval was done. This was a prospective observational study performed at a cardiac surgical intensive care unit (ICU) of a Heart Center. This study included 224 patients above the age of 18 years meeting the inclusion criteria for cardiac surgery in Shahid Gangalal National Heart Center from July 2018 to December 2018. With the precision (d) of 5% and 95% confidence interval and using the prevalence (P) of 17.5 % from the international study[12,] the sample size was calculated to be 224. Inclusion Criteria included patients 18 years old and above of both sexes; patients who signed an informed consent; patients scheduled

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for cardiac surgery with extracorporeal circulation (coronary-artery bypass grafting (CABG), cardiac valve replacement (CVR), combined CABG + CVR, excision of cardiac myxoma). The exclusion criteria were patients who refused to participate before or after operation; patients in poor general condition; patients with preoperative dementia, delirium or illiterate, psychiatric or mental disorder (epilepsy, schizophrenia, depression, and so on) and patients who might develop withdrawal symptoms like chronic alcoholic and patients who died intraoperatively or within the first 6 hours after the procedure.

Preoperative, intraoperative, and postoperative data for possible risk factors were obtained. Daily assessment of delirium was done during ICU stay of the patient. Anesthesia management was done as per the standard institutional protocol. The choice of monitors, choice of anesthesia induction agents, and maintenance of anesthesia was left to the discretion of the attending team. Data was obtained on each of these facets as per the questionnaire enclosed. Patients were shifted to ICU after the procedure under mechanical ventilation. Patients were then weaned from mechanical ventilation at the discretion of the ICU physician.

Baseline demographics and information regarding preadmission risk factors for delirium were obtained at admission. Intraoperative data such as cardiopulmonary bypass (CPB) time, aortic cross-clamp time (ACX time), and inotrope use was obtained. Postoperatively, the total time on mechanical ventilation and other variables was noted. Daily Richmond Agitation-Sedation Scale (RASS) scoring was done and scores with −4 and -5 was deemed as comatose and not assessable. Those with RASS scores −3 and more were evaluated using the Confusion Assessment Method for the ICU(CAM-ICU). The CAM-ICU scores were obtained on the day of extubation, patients were scored for maximum of 3 days or till ICU discharge, and any change in these scores was recorded. All the critical peri-operative events and ICU course were noted. Delirium assessment was performed by anesthesia residents/registrars/consultants, following rounds each day. Patients with CAM-ICU positive and RASS scores positive (+1 to + 4) manifested delirium in the form of restlessness, agitation, and pulling of devices. Those with CAM-ICU positive and RASS scores negative (0-−3) manifested delirium as lethargy, somnolence, and inattention.

Continuous variables were profiled as mean ± standard deviation (SD), whereas categorical variables described as proportions in the groups with and without delirium. Differences between groups were analyzed using Student's *t*-test or Chi-square test as applicable.

RESULTS

The incidence of delirium was 15.6% (35/224) in our study. Table 1 shows the demographic data and clinical characteristics of patients studied. Based on demographic characteristics, delirium was seen in 14 out of 58 (24.1%) patients with age >60 years compared to 21 out of 166 (12.7%) patients with age equal or less than 60 years and which was found to be statistically significant (p=0.038).

Table 1. Demographic Characteristics.

	Without delirium (n=189)	With delirium (n=35)	Total sample	P value
Age (years)				
≤60	145(76.7%)	21(60%)	166	
>60	44(23.3%)	14(40%)	58	0.038
Gender				
Female	67(35.4%)	15(42.9%)	82	
Male	122(64.6%)	20(57.1%)	142	0.4
Marital status				
Married	167(88.4%)	30(85.7%)	197	
Unmarried	22(11.6%)	5(14.3%)	27	0.65
BMI				
≤25	138(73%)	27(77.1%)	165	
>25	51(27%)	8(22.9%)	59	0.6

Table 2 shows preoperative risk factor for developing delirium in which carotid artery disease (p=0.00) and Hemoglobin level <10gm/dl (p=0.03) were found be statistically significant. History of smoking, drug abuse, alcohol intake, hypertension, diabetes mellitus, thyroid disease, COPD or asthma, previous cardiac surgery, history of stroke, peripheral vascular disease or renal dysfunction were not significantly associated with delirium. NYHA grade 3 or 4, left ventricular ejection fraction of less than 30%, preoperative atrial fibrillation were also not significantly associated with delirium.

Table 3 shows the intra-operative factors. The type of surgery being done was not significant predictor of delirium but the cases with delirium had significantly longer cardiopulmonary bypass time (p=0.01). Delirium was also significantly seen in patients requiring intraoperative blood transfusion (p=0.0). There was

no significant association between cross-clamp time, intraoperative temperature or hemoglobin during cardiopulmonary bypass.

Table 4 showing the post-operative factors such as blood transfusion, use of non-invasive ventilation, use of IABP, hematocrit less than 30%, use of midazolam and PaO2 less than 70mmHg were significantly related to delirium. Postoperative mechanical ventilation time and overall ICU stay were also significantly longer in patients with delirium. Delirium was not significantly associated with factors such as postoperative pain, amount of drain, post-operative atrial fibrillation, infection, Ileus, stroke, Na^+ ≤130, renal dysfunction or the use of CRRT.

Table 2. Preoperative factors.

	Without delirium (n=189), n(%)	With delirium (n=35), n(%)	Total(n=224), n(%)	P value
Smoking	91(48.1%)	22(62.9%)	113(50.4%)	0.11
Drug abuse	1(0.5%)	0	1(0.4%)	0.66
Alcohol intake	57(30.2%)	15(42.9%)	72(32.1%)	0.14
Diabetes mellitus	35(18.5%)	9(25.7%)	44(19.6%)	0.32
Thyroid disease	12(6.3%)	3(8.6%)	15(6.7%)	0.62
History of cardiac surgery	8(4.2%)	3(8.6%)	11(4.9%)	0.27
History of stroke	5(2.6%)	0	5(2.2%)	0.33
Peripheral vascular disease	4(2.1%)	0	4(1.8%)	0.38
Carotid artery disease	35(18.5%)	16(45.7%)	51(22.8%)	0.00
LVEF<30%	7(3.7%)	2(5.7%)	9(4%)	0.57
Atrial fibrillation	18(9.5%)	4(11.4%)	22(9.8%)	0.72
Pre-op Hb<10gm/dl	6(3.2%)	4(11.4%)	10(4.5%)	0.03
NYHA3/4	11(5.8%)	2(5.7%)	13(5.8%)	0.98
Renal dysfunction	2(1%)	0	2(0.9%)	0.54
COPD/Asthma	3(1.6%)	2(5.7%)	5(2.2%)	0.12

Table 3. Intraoperative factors*

			Without delirium (n=189)	With delirium (n=35)	Total (n=224)	P value
Surgery type	Isolated CABG		63(33.3%)	16(45.7%)	79(35.3%)	0.14
	CABG+valve		5(2.6%)	0	5(2.2%)	
	CVR		98(51.9%)	12(34.3%)	110(49.1%)	
	Others		23(12.2%)	7(20%)	30(13.4%)	
Intraoperative temperature		>32°C	26(13.8%)	6(17.1%)	32(14.3%)	0.59
		≤32°C	163(86.2%)	29(82.9%)	192(85.7%)	
Hb during CPB		>10gm%	46(24.3%)	6(17.1%)	52(23.2%)	0.35
		≤10gm%	143(75.7%)	29(82.9%)	172(76.8%)	
Blood transfusion			18(9.5%)	12(34.3%)	30(13.4%)	0.00
CPB time, mean(SD)			96.89(39.85)	115.49(54.08)		0.01
Acx time, mean(SD)			70.40(49.35)	75.9140.92)		0.53

**all values are number(%) of patients unless indicated otherwise*

Table 4. Post-operative factors.

		Without delirium (n=189)	With delirium (n=35)	Total(n=224)	P value
Re-operation		8(4.2%)	1(2.9%)	9(4%)	0.7
Duration of inotropes	<24hrs	66(34.9%)	7(20%)	73(32.6%)	0.05
	24-48 hrs	60(31.7%)	9(25.7%)	69(30.8%)	
	>48hrs	63(33.3%)	19(54.3%)	82(36.6%)	
Blood transfusion		55(29.2%)	23(65.7%)	78(34.8%)	0.00
NRS score >5		29(15.3%)	9(25.7%)	38(17%)	0.13
Use of NIV		1(0.5%)	4(11.4%)	5(2.2%)	0.002
Sleep deprivation		19(10.1%)	15(42.9%)	34(15.2%)	0.00
Drain	<500 ml	119(63%)	18(51.4%)	137(61.2%)	0.41
	500-1000 ml	60(31.7%)	15(42.9%)	75(33.5%)	
	>1000 ml	10(5.3%)	2(5.7%)	12(5.4%)	
Post-operative Atrial fibrillation		26(13.8%)	7(20%)	33(14.7%)	0.33
Infection		2(1.1%)	0	2(0.9%)	0.54
Ileus		1(0.5%)	1(2.9%)	2(0.9%)	0.17
Stroke		1(0.5%)	0	1(0.4%)	0.66
Na^+ ≤130		13(6.9%)	0	13(5.8%)	0.11
Midazolam		3(1.6%)	3(8.6%)	6(2.7%)	0.01
IABP		13(6.9%)	9(25.7%)	22(9.8%)	0.001
CRRT		2(1.1%)	1(2.9%)	3(1.3%)	0.39
Hct<30		30(15.9%)	14(40%)	44(19.6%)	0.001
PaO_2<70		15(7.9%)	11(31.4%)	26(11.6%)	0.00
Renal dysfunction		7(3.7%)	2(5.7%)	9(4%)	0.57
Duration of mechanical ventilation >6hr		74(39.1%)	26(74.3%)	100(44.6%)	0.00
ICU stay	<3 days	68(36%)	4(11.4%)	72(32.1%)	0.00
	3-5 days	74(39.1%)	5(14.3%)	79(35.3%)	
	>5 days	47(24.9%)	26(74.3%)	73(32.6%)	

DISCUSSION

Delirium after cardiac surgery is a fairly common and a major postoperative neurologic complication which is associated with worse post-surgical outcome. However, the risk factors for delirium is affected by multiple factors perioperatively. Several studies have looked into the risk factors and incidence across different populations groups.[6-9] Nevertheless, there seems to be paucity in the information regarding risk factors and incidence for delirium in our population after cardiac surgery. Therefore, identifcation and categorization of high risk patients appears to be an important strategy to reduce the incidence of delirium.

Our present study found that the incidence of delirium after cardiac surgery was 15.6%. The incidence of delirium in previous studies have shown divergence across different patient population.[6,7,10,11] Study by Kumar et al found incidence of 17.5% in their cohort of 120 patients [12] which is comparable to our study.

We found that patients with postoperative delirium were older than patients without delirium which were similar to other studies.[13,14] Advanced age is considered an independent risk factor for delirium.[15] Our study showed that carotid artery disease to be predictor of delirium which is in line with the study done by Bucerius et al.[16] There is increased risk of cerebral embolization with the presence of generalized atherosclerotic diseases especially during manipulation and cannulation of aorta.[17] Additionally our study found that patients with

preoperative hemoglobin level less than 10 gm/dl had increased risk of delirium. Studies have reported that hematocrits under 22–23% on bypass were independent risk factors for neurologic injury.[18] Interestingly, we did not find significant increased risk in delirium with other risk factors like severity of illness by preoperative NYHA class, renal dysfunction, atrial fibrillation which is in contrast to several previous studies.[8,9,16] However, our sample size is clearly a limitation in making conclusive remarks about any of these risk factors.

Our data confirms that the patients in whom postoperative delirium developed had significantly longer time on CPB than patients who did not experience delirium. There has been conflicting results from previous studies which examined whether length of CPB contributes to delirium after cardiac surgery.[19] Other authors have confirmed as we have reported in our study that extended CPB time are risk factors for postoperative delirium after cardiac surgery.[14,20] The data of our study showed that the intraoperative blood transfusion was also found be higher in patients with delirium than in patients without it. A study done by Karkouti et al.[18] observed a 10% increased stroke rate for each percentage decrease from a hematocrit of 21%.

Our study found significant association between longer MV time and ICU stay time with delirium. Patients who had delirium stayed 74.3% more than 5 days than in control group who stayed 24.9% more than 5 days. Similarly, 74.3% of patients with delirium were on mechanical ventilation for more than 6 hours compared to 39.1% who didn't develop delirium. Similar to our study, Norkiene et al reported duration of postoperative mechanical ventilation and ICU stay to be independently associated with postoperative delirium in cardiac surgery.[21] A study done by Arenson et al. showed that the postoperative risk factors associated with in-hospital delirium after cardiac surgery included postoperative stroke or TIA, mechanical ventilation longer than 24 h, the requirement for any transfusion in the postoperative period, and postoperative acute kidney injury.[22] Our data did not replicate all of the above factors which shows that we may have different set of factors from other patient population.

Our study found that the patients with delirium were more likely than those without delirium to receive blood transfusion postoperatively. It is possible to hypothesize that low hemoglobin(Hb) or anemia could impact neuropsychological performance of the patients, by reducing blood oxygen level in the brain impacting cognition .This reduced oxygen-carrying capacity with low Hb can result in tissue malperfusion that can increase susceptibility to postoperative adverse outcomes.[23] However, other comorbidities could confound both anemia and delirium. [24]

Our analysis showed that midazolam administered postoperatively to be associated with delirium. Sockalingam et al [20] reported that benzodiazepines as well as opioid analgesics were associated with the development of postoperative delirium.

In our study, we found no association of higher pain score on numeric rating scale (NRS) with delirium similar to the study by Marcantonio et al.[5] This is in contrast to the study conducted by Lynch et al.[25] and Smulter et al.[26] which reported association of postoperative pain with delirium. Interestingly, our study found significant association of PA02<70 and use of NIV with delirium. A meta-analysis concluded association of delirium with NIV failure.[27] The most likely explanation for this is because cerebral hypoxia is one of the important causes for delirium.

Our study reported that the use of IAPB correlated with an increased risk of delirium similar to study done by Sanders et al. [28] Previous study have shown that patients who demonstrate a low cardiac output during the first several postoperative days experienced hallucinations.[29] Maintaining adequate blood pressure is important, as evidence has emerged of an association between inadequate cerebral perfusion and the development of postoperative delirium. [30]

Similarly, our study has demonstrated that sleep deprivation is stastistically significantly higher in patients who developed delirium. The evidence for the effectiveness of sleep deprivation to reduce delirium specifically in the cardiac surgical ICU is lacking. However, the ICU environment has contributed to the development of postoperative delirium through several factors such as poor sleep quality, lack of natural light, and increased ambient noise.[9]

The present finding is however limited with the fact that it is a single-center, observational study. The sample size is also relatively lower and hence, the data could not be extrapolated to large section of the population. There's need for multicenter studies on larger sample to investigate the cost effectiveness, ease of implementation and the effect on patient outcomes which is likely to give more insight. Future studies are needed in the cardiac surgical population to identify the patients at risk and categorization of high risk patients and to define the optimal approach to managing delirium after cardiac surgery. Recognizing delirium and those at

risk can reduce the impact of delirium through targeted interventions and risk reduction. Despite increasing understanding and advances in knowledge's of delirium, there is still lack of effective therapeutic intervention.

CONCLUSIONS

As shown in our study, delirium is a frequent occurrence in the cardiac surgical population. The incidence of delirium after cardiac surgery was 15.6% with multifactorial etiology some of which are modifiable. Several risk factors pre-operatively like age>60 years, carotid artery disease, Hb<10gm/dl, intra-operative factors like longer CPB time, blood transfusion and post-operatively longer duration of MV, ICU stay, blood transfusion, use of IABP and NIV were found to be predictors of delirium. Hence, optimal approach to preventing and managing delirium is important to prevent ensuing complications from it.

CONFLICT OF INTEREST

The authors declare no conflict of interest

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