Predictors of Delirium in ICU: A Comparison Between Cardiac Surgical and Non-Surgical Patients

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Abstract

Aim: The objective of this study was to examine the rate of delirium among patients admitted to the Cardiovascular Surgical Intensive Care Unit (CVICU) as well as identify the patient characteristics associated with delirium.

Methods: This retrospective study utilized electronic medical records of 2393 patients above 18 years admitted in CVICU from January 2017 to December 2017. Group differences between patients with and without delirium were assessed using Chi-Square tests for categorical variables and T-tests for continuous variables. Multivariable logistic regression was used to identify the predictors of delirium among hospitalized patients.

Results: Of the 2393 patients included in the analysis, 1040 (43.46%) had delirium. Patients with delirium were older than those without delirium. Significant predictors of delirium included patients in the age group of 65 - 79, patients above 80 years, anemia, chronic obstructive pulmonary disease, chronic kidney disease, congestive heart failure, peripheral vascular disease, and alcohol use.

Keywords: *Delirium; Cardiovascular Surgical Intensive Care Unit; Older Patients; Comorbidities*

Abbreviations

CVICU: Cardiovascular Surgical Intensive Care Unit; DSM-V: Diagnostic and Statistical Manual of Mental Disorders, 5th Edition; CAM-ICU: Confusion Assessment Method For ICU; RASS: Richmond Agitation Sedation Scale; BMI: Body Mass Index; COPD: Chronic Obstructive Pulmonary Disease; CKD: Chronic Kidney Disease; CHF: Congestive Heart Failure; PVD: Peripheral Vascular Disease; AF: Atrial Fibrillation; OR: Odds Ratio

Introduction

Every 1 in 4 patients in the Intensive Care Unit suffers from delirium [1]. The estimated prevalence of delirium varies between 2% and 73% among the cardiac surgery patients. In patients over the age of 60, nearly 30 - 52% suffer from delirium [2]. In this era of major medical advancements, it has been possible to treat the elderly patients with minimally invasive and improved surgical and anesthetic techniques [3,4]. This has resulted in an increased number of vulnerable patients at risk of developing neurocognitive impairment during their hospitalizations [5].

Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-V) describes delirium as an acute onset of a fluctuating disturbance in the following cognitive functions: attention; environmental awareness; and cognition and/or perception [6]. The exact cause of delirium is unknown. However, its pathogenesis appears to be multifactorial [7]. Furthermore, the development of delirium depends on an interplay of several modifiable and non-modifiable risk factors. The combination of predisposing factors such as age and enabling factors like medical co-morbidities, baseline cognitive, type and length of surgery further increases the risk of developing delirium. The non-modifiable risk factors are then subjected to a second hit by a set of precipitating factors (or trigger factors) that are often modifiable such as pain, medications, infections, immobilization, sensory impairment (hearing/visual), electrolyte imbalance, environment, and emotional distress. In addition, the need for prolonged mechanical ventilation, presence of peripheral and central lines, and use of sedatives like benzodiazepines is documented to increase the likelihood of developing delirium among patients admitted in the Cardiovascular surgical intensive care unit (CVICU) [8].

Given that the delirium occurring in other ICU settings is not generalizable to the CVICU and a limited number of prior studies were conducted in CVICU-specific population. Our primary research objective is to identify the sociodemographic and clinical predictors of delirium among patients admitted in the CVICU. We also aimed to evaluate a mixed CVICU population, comparing cardiac cohort to mix group. A large ICU with cardiac and vascular patients, as well as nonsurgical cardiac patients with mechanical devices, offers us an ideal setting in which to conduct this study.

Materials and Methods

Study design

A retrospective study included patients admitted in the CVICU from January 2017 - December 2017 to determine the prevalence of and the factors associated with delirium. The investigators obtained this data after reviewing electronic health records (EHR) of CVICU patients. The data that support the findings of this study are available on request from the corresponding author. The data is not publicly available due to privacy or ethical restrictions. This study adheres to STROBE guidelines.

Setting and sample

Patients included in this study met the following criteria:

1. Cardiac surgical, non-cardiac vascular surgery, and cardiac medical (nonsurgical) patients requiring mechanical support admitted to CVICU at DeBakey Heart and Vascular Center at Houston from January 2017 to December 2017.

2. Surgical patients were defined as patients who underwent either cardiac or non-cardiac vascular surgery.

3. Above the age of 18 were included.

Study outcome

The primary outcome of this study was the presence or absence of delirium during their course of stay in CVICU. Confusion Assessment method for ICU (CAM-ICU) is a validated clinical tool to qualitatively evaluate the presence or absence of delirium. CAM-ICU screening was performed by ICU-nurses. A patient is identified to have delirium if CAM-ICU is positive i.e if the Richmond Agitation Sedation Scale (RASS) ≥ 3 and alteration/fluctuation in mental status and either altered level of consciousness (i.e. RASS is not 0) and disorganized thinking (combined number of errors to questions is > 1). The presence or absence of delirium was calculated for each patient. Sociodemographic and clinical characteristics of patients were recorded by the investigators. The following baseline characteristics were included: age, sex, race, body mass index (BMI), alcohol abuse and dependence, nicotine dependence, and case type (surgery/medical). Patients' medical records were reviewed for clinical characteristics and comorbidities, and data was extracted. The comorbidities included in the study were chronic anemia, chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD), congestive heart failure (CHF), peripheral vascular disease (PVD), atrial fibrillation (AF) and history of psychosis or current mental or behavioral disease.

Data analysis

Group differences for patients with and without delirium were examined using Chi-square test for categorical variables and t test for continuous variables. The potential predictors of delirium were estimated by multivariable logistic regression model controlling for various baseline confounders. The predictors added in the model include gender, age group, BMI, race, case-type, anemia, COPD, CHF, PVD, CKD, HF, alcohol, nicotine dependence, psychosis and surgery. Outcome variable was defined as the presence/absence of delirium. All analyses were performed using SAS 9.4 (SAS Institute, Inc., Cary, NC, USA), with a statistical significance level of 0.05.

Ethics

This study was approved by the DeBakey Heart and Vascular Center institutional review board with a waiver of written or signed consent.

Results

Descriptive characteristics

A total of 2393 patients met the inclusion criteria from January 2017 through December 2017. Of them, 1040 patients had delirium. The descriptive characteristics of the study population are summarized in table 1. Patients with delirium were older (64.54 years vs 62.80 years; p = 0.0017) as compared with patients without delirium. Patients with and without delirium were significantly different with respect to gender (p = 0.04), race (p = 0.0089), BMI, (p = 0.0038) and use of alcohol (p = 0.01). There was significant difference in the comorbidities like chronic anemia (p < .0001), COPD (p = 0.0022), CKD (p < .0001), CHF (p < .0001) between patients with and without delirium. A significant difference in case type was observed (p = 0.0096).

Variables	With Delirium (N = 1040)	Without Delirium (N = 1353)	P Value
Mean Age in Years (SD)	64.54 (13.40)	62.80 (13.37)	0.0017*
Gender, N (%)			
Female	390 (37.50)	455 (33.63)	0.04*
Male	650 (62.50)	898 (66.37)	
Race, N (%)			
Declined	44 (4.23)	41 (3.03)	
Black	215 (20.67)	212 (15.67)	
Caucasian	743 (71.44)	1046 (77.31)	0.0089*
Asian	30 (2.88)	42 (3.10)	
Native American	8 (0.77)	12 (0.89)	
Age group			
Below 65	456 (43.85)	672 (49.67)	
65 - 79	466 (44.81)	571 (42.20)	0.0031*
Above 80	118 (11.35)	110 (8.13)	

BMI, N (%)			
Underweight (Below 18.5)	22 (1.63)	26 (2.50)	0.0038*
Normal Weight (18.5 - 24.9)	267 (25.67)	278 (20.55)	
Overweight (24.9 - 29.9)	290 (27.88)	396 (29.27)	
Obese (Above 30)	331 (31.83)	424 (31.34)	
Case Type, N (%)			
Surgical	906(87.12)	1127(83.30)	0.0096*
Medical	134(12.88)	226(16.70)	
Anemia, N (%)			
With Anemia	316 (30.38)	237 (17.52)	<.0001*
Without Anemia	724 (69.62)	1116 (82.48)	
COPD, N (%)			
With COPD	247 (23.75)	252 (18.63)	0.0022*
Without COPD	793 (76.25)	1101 (81.37)	
CKD, N (%)			
With CKD	509 (48.94)	445 (32.89)	<0.001*
Without CKD	531 (51.06)	908 (67.11)	
CHF, N (%)			
With CHF	484 (46.54)	472 (34.89)	<.0001*
Without CHF	556 (53.46)	881 (65.11)	
PVD, N (%)			
With PVD	74 (7.12)	119 (8.80)	0.13
Without PVD	966 (92.88)	1234 (91.20)	
AF, N (%)			
With AF	118 (11.36)	137 (10.13)	0.33
Without AF	922 (88.65)	1216 (89.87)	
Alcohol, N (%)			
With Alcohol	30 (2.88)	20 (1.48)	
Without Alcohol	1010 (97.12)	1333 (98.52)	0.01*
Nicotine Dependence			
With Nicotine Dependence	442 (42.50)	594 (43.90)	0.49
Without Nicotine Dependence	598 (57.50)	759 (56.10)	
Psychosis, N (%)			
With Psychosis	3 (0.29)	2 (0.15)	0.45
Without Psychosis	1037 (99.71)	1351 (99.86)	
Surgery, N (%)			
Non-Cardiac Surgery	355 (34.13)	437 (32.30)	
Cardiac Surgery	550 (52.88)	692 (51.15)	0.05
Medical	135 (12.98)	224 (16.56)	

Table 1: *Demographic characteristics of CVICU patients with and without delirium.*

Abbreviations: *BMI: Body Mass Index; COPD: Chronic Obstructive Pulmonary Disease; CKD: Chronic Kidney Disease; CHF: Chronic Heart Failure; PVD: Peripheral Vascular Disease; AF: Atrial Fibrillation.*

Prevalence of delirium

The overall prevalence of delirium among adults admitted in CVICU was found to be 43.46%. Delirium was higher in males (27.12%) as compared to females (16.29%). Prevalence of delirium by age group was as follows: < 65 years (43.85%) ; 65 - 79 years (44.81%); > 80 years (11.35%). Over fourteen percent of patients declined to disclose the race. With that limitation, the prevalence of delirium was highest in Caucasians (31.04%) followed by blacks (8.98%). Delirium was more prevalent in obese (13.83%) and overweight (12.11%) patients. Positive CAM-ICU was reported in 37.86% of surgical patients. Patients who underwent cardiac surgery (22.98%) had the highest prevalence of delirium as compared to noncardiac (14.83%) and medical patients (5.64%). Patients with comorbidities and psychosis reported lower rates of delirium.

Significant predictors that increase the risk of delirium

Table 2 reports the adjusted odds ratio (OR), 95% CI, and P value. The adjusted multivariate logistic regression model shows that the patients between 65 - 79 years (OR, 1.211; [95% CI, 1.010 - 1.452; P = 0.03]), patients above 80 years (OR, 1.605; [95% CI, 1.184 - 2.176; p = 0.002]) vs. those below below 65 years. patients with chronic anemia (OR, 1.733 [95% CI, 1.396 - 2.153; p < 0.0001]), presence of COPD (OR, 1.248 [95% CI, 1.008 - 1.544; p = 0.04]), presence of CKD (OR, 1.575 [95% CI, 1.301 - 1.906; p < 0.0001]), comorbid CHF (OR, 1.262 95% CI, 1.049 - 1.517; p = 0.01]), alcohol abuse and dependence (OR, 2.462 [95% CI, 1.355 - 4.475; p = 0.003]) were significantly associated with increasing the risks of delirium. Patients between 65 - 79 years were 21.1% more likely to develop delirium and patients above 80 years are 60.5% more likely to develop delirium than patients below 65 years. Patients with chronic anemia had 73.3% higher risks of developing delirium. COPD and CHF significantly increased the risks of delirium by 24.8% and 26.2% respectively. Patients with CKD were 57.5% more likely with increased risk of odds of delirium. Heavy alcohol consumption significantly increased the likelihood of delirium by 2.462 times.

Variables	Odds Ratio	95% CI	P Value
Gender			
Female	Reference		0.12
Male	0.869	0.726-1.040	
Age Group			
Below 65	Reference		
65 - 79	1.211	1.010-1.452	0.03
Above 80	1.605	1.184-2.176	0.002
BMI			
Normal Weight (18.5 - 24.9)	Reference		
Underweight (12 - 18.5)	1.332	0.719-2.467	0.36
Overweight (24.9 - 29.9)	0.814	0.643-1.032	0.08
Obese (Above 30)	0.853	0.676-1.077	0.18
Race			
Black	Reference		
Caucasian	0.803	0.637-1.011	0.06
Asian	0.810	0.477-1.378	0.43
Native American	0.830	0.322-2.137	0.69
Declined	1.303	0.801-2.119	0.28
Case Type			

Surgical	Reference		
Medical	0.160	0.016-1.578	0.11
Anemia			
Without Anemia	Reference		<.0001
With Anemia	1.733	1.396-2.153	
COPD			
Without COPD	Reference		0.04
With COPD	1.248	1.008-1.544	
CKD			
Without CKD	Reference		<.0001
With CKD	1.575	1.301-1.906	
CHF			0.01
Without CHF	Reference		
With CHF	1.262	1.049-1.517	
PVD			
Without PVD	Reference		0.009
With PVD	0.655	0.476-0.901	
AF			
Without AF	Reference		0.83
With AF	0.971	0.738-1.277	
Alcohol			
Without Alcohol	Reference		
With Alcohol	2.462	1.355-4.475	0.003
Nicotine Dependence			
Without Nicotine Dependence	Reference		0.34
With Nicotine Dependence	0.919	0.771-1.096	
Psychosis			
Without Psychosis	Reference		0.73
With Psychosis	1.387	0.209-9.209	
Surgery			
Cardiac Surgery	Reference		
Non-Cardiac Surgery	1.042	0.857-1.266	0.67
Medical	3.917	0.397-38.673	0.24

Table 2: *Predictors of delirium in adult patients admitted in CVICU.*

Abbreviations: *BMI: Body Mass Index; COPD: Chronic Obstructive Pulmonary Disease; CKD: Chronic Kidney Disease; CHF: Chronic Heart Failure; PVD: Peripheral Vascular Disease; AF: Atrial Fibrillation; 95% CI, 95% Confidence Interval.*

Significant predictors that decrease the risk of delirium

Patients with peripheral vascular disease (OR, 0.655 [95% CI, 0.476 - 0.901; p = 0.009]) were significantly associated with lower risks of delirium as compared with patients without peripheral vascular disease.

Other non-significant predictors

There was no significant difference between non-cardiac surgery patients and patients who underwent cardiac surgery. The non-surgical cohort were not significantly different from the cardiac surgery cohort.

Discussion

Our results show that the prevalence of delirium was 43% in CVICU patients (n = 1040). Older males with comorbidities such as COPD, CHF, chronic anemia and CKD were at greater risk of developing delirium.

Despite the growing critical care burden in the CVICU, there is not much known about delirium in this specialized setting. A wide variation in the incidence rates was reported among CVICUs due to differences in study design, sample size, population characteristics, and screening techniques used for diagnosis [9]. Prior CVICU-specific delirium studies had emphasized on the prevalence of delirium and its implications on patient morbidity and mortality. Delirium is known to be associated with poor patient outcomes, an increased length of hospital stays, and increased morbidity and mortality [10].

Furthermore, these studies have been limited by small sample size. Pauley., *et al.* in their single-center, retrospective observational study enrolled 590 patients and reported prevalence of delirium to be 20.3% and in-hospital mortality of 33% in a CVICU setting [11]. Likewise, Lahariya and his colleagues reported the incidence of delirium to be 28% in a sample of 309 patients [12]. Naksuk., *et al.* studied delirium in a sample of 11,079 patients, which is the largest to date sample size, and reported that 8.3% of their patients developed delirium [13]. None of these studies exclusively enrolled CVICU patients, nor did they look into patient demographics and risk factors associated with the development of delirium in a CVICU setting.

Our work is an extension of prior studies done with the inclusion of CVICU-specific risk factors studied in a moderate sample size of 2393 patients. Our aim in this study was to identify the proportion of the population at increased risk of delirium in order to proactively manage such patients with pharmacological and non-pharmacological interventions. This study identified that the incidence of delirium increased in patients with COPD, CHF, anemia and CKD, managing these comorbidities preoperatively can have significant implications in reducing the incidence, severity and duration of delirium [14]. Several studies suggest that the vulnerability of ICU delirium is believed to result from the complicated interplay of patient-related, environmental, and disease-associated factors [15,16]. Although delirium in the ICU has been the subject of great interest, the knowledge base discussing acute confusion state after cardiac surgery is very limited. One unique factor that comes into play is the rapidly evolving CVICU management and technology that has made the etiology of delirium more complex. As a result of patient improvisation, we have inadvertently introduced a number of modifiable risk factors that contribute to delirium [17,18]. For example, patients with heart failure can now be treated with ventricular support devices. As a consequence, such patients remain hospitalized and immobile for longer periods of time and receive higher doses of sedatives. These sedatives have significant deleriogenic potential. As patients with heart failure have decreased clearance of medications, it magnifies the risk of developing delirium to the to the extent that nearly 1 in 3 patients with CHF develop delirium [19].

The scope of our study is limited as it is a single-center study, retrospective nature of the study design, and moderate sample size. However, our research opens up more avenues for future studies to investigate how each of the aforementioned demographic and risk factors is associated with delirium. Based on these factors, prediction models can be designed and implemented in acute cardiac care settings which will substantially decrease the incidence of delirium. The need of the hour is to stay vigilant and proactively predict and intercept the course of delirium to reduce the further hospitalization and economic burden. Risk factor modification along with non-pharmacological interventions need to be introduced to help treat and prevent delirium in the CVICU setting.

Conclusion

Our retrospective, observational study demonstrates that the prevalence of delirium is 43% in our CVICU patients. Older male patients with comorbidities such as COPD, CHF, anemia, and CKD were at greater risk of developing delirium. Given the impact of medical advancements in increasing the incidence of delirium in CVICU patients, larger, more recent, prospective clinical trials are warranted to identify patients at high risk of developing delirium. The efforts should be focused on developing tools to prevent delirium in this specialized population cohort.

The incidence of delirium is often unrecognized and overlooked. It results in functional disability and other long-term consequences like cognitive impairment, increased hospitalizations, and poor prognosis. Routine assessment and proactive management of delirium among hospitalized patients should be integrated into the treatment plan to reduce the morbidity and mortality associated with delirium. This study will aid the clinicians and critical care nurses identify the high-risk population and detect the early signs of delirium. The study also adds to the existing knowledge by providing additional insight into the patients' risk factors related to the development of delirium among the patients admitted in CVICU. Incorporating effective nursing care interventions will improve health outcomes and reduce the cognitive impairment of critically ill patients.

Conflict of Interest

Bibliography

1. McPherson JA., *et al*. "Delirium in the cardiovascular ICU: exploring modifiable risk factors". *Critical Care Medicine* 41.2 (2013): 405-413.

2. Sockalingam S., *et al.* "Delirium in the postoperative cardiac patient: a review". *Journal of Cardiac Surgery* 20.6 (2005): 560-567.

3. Burkhart CS., *et al.* "Modifiable and nonmodifiable risk factors for postoperative delirium after cardiac surgery with cardiopulmonary bypass". *Journal of Cardiothoracic and Vascular Anesthesia* 24.4 (2010): 555-559.

4. Tan MC., *et al*. "Incidence and predictors of post-cardiotomy delirium". *The American Journal of Geriatric Psychiatry* 16.7 (2008): 575-583.

5. Bakker RC., *et al.* "Preoperative and operative predictors of delirium after cardiac surgery in elderly patients". *European Journal of Cardio-Thoracic Surgery* 41.3 (2012): 544-549.

6. European Delirium A and S American Delirium. "The DSM-5 criteria, level of arousal and delirium diagnosis: inclusiveness is safer". *BMC Medicine* 12 (2014): 141.

7. Steiner LA. "Postoperative delirium. Part 1: pathophysiology and risk factors". *European Journal of Anaesthesiology* 28.9 (2011): 628-236.

8. Ibrahim K., *et al*. "Delirium in the Cardiac Intensive Care Unit". *Journal of the American Heart Association* 7.4 (2018).

9. Girard TD., *et al*. "Delirium in the intensive care unit". *Critical Care* 12.3 (2008): S3.

10. Francis J and WN Kapoor. "Prognosis after hospital discharge of older medical patients with delirium". *Journal of the American Geriatrics Society* 40.6 (1992): 601-606.

11. Pauley E., *et al*. "Delirium is a robust predictor of morbidity and mortality among critically ill patients treated in the cardiac intensive care unit". *American Heart Journal* 170.1 (2015): 79-86.

12. Lahariya S., *et al*. "Delirium in patients admitted to a cardiac intensive care unit with cardiac emergencies in a developing country: incidence, prevalence, risk factor and outcome". *General Hospital Psychiatry* 36.2 (2014): 156-164.

13. Naksuk N., *et al*. "Editor's Choice-Clinical impact of delirium and antipsychotic therapy: 10-Year experience from a referral coronary care unit". *European Heart Journal. Acute Cardiovascular Care* 6.6 (2017): 560-568.

14. Lee A., *et al*. "Risk prediction models for delirium in the intensive care unit after cardiac surgery: a systematic review and independent external validation". *British Journal of Anaesthesia* 118.3 (2017): 391-399.

15. Van den Boogaard M., *et al*. "Development and validation of PRE-DELIRIC (PREdiction of DELIRium in ICu patients) delirium prediction model for intensive care patients: observational multicentre study". *British Medical Journal* 344 (2012): e420.

16. Khazanie P., *et al*. "Trends in the use and outcomes of ventricular assist devices among medicare beneficiaries, 2006 through 2011". *Journal of the American College of Cardiology* 63.14 (2014): 1395-1404.

17. Mossello E., *et al*. "Predictors and prognosis of delirium among older subjects in cardiac intensive care unit: focus on potentially preventable forms". *European Heart Journal. Acute Cardiovascular Care* 9.7 (2020): 771-778.

18. Khera R., *et al*. "Trends in the use of percutaneous ventricular assist devices: analysis of national inpatient sample data, 2007 through 2012". *JAMA Internal Medicine* 175.6 (2015): 941-950.

19. Honda S., *et al*. "Prevalence, determinants, and prognostic significance of delirium in patients with acute heart failure". *International Journal of Cardiology* 222 (2016): 521-527.