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Delirium in the Cardiovascular Intensive Care Unit: Exploring Modifiable Risk Factors

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Abstract

Objective—Delirium, an acute organ dysfunction, is common among critically ill patients leading to significant morbidity and mortality; its epidemiology in a mixed cardiology and cardiac surgery intensive care unit (CVICU) is not well established. We sought to determine the prevalence and risk factors for delirium among CVICU patients.

Design—Prospective observational study.

Setting—27-bed medical-surgical CVICU.

Patients—200 consecutive patients with an expected CVICU length of stay >24 hours.

Interventions—None.

Measurements—Baseline demographic data and daily assessments for delirium using the validated and reliable Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) were recorded, and quantitative tracking of delirium risk factors were conducted. Separate analyses studied the role of admission risk factors for occurrence of delirium during the CVICU

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stay and identified daily occurring risk factors for the development of delirium on a subsequent CVICU day.

Main Results—Prevalence of delirium was 26%, similar among cardiology and cardiac surgical patients. Nearly all (92%) exhibited the hypoactive subtype of delirium. Benzodiazepine use on admission was independently predictive of a 3-fold increased risk of delirium [Odds Ratio 3.1 (1, 9.4), p=0.04] during the CVICU stay. Of the daily occurring risk factors, patients who received benzodiazepines [2.6 (1.2, 5.7), p=0.02] or had restraints or devices that precluded mobilization [2.9 (1.3, 6.5), p<0.01] were more likely to have delirium the following day. Hemodynamic status was not associated with delirium.

Conclusions—Delirium occurred in 1 in 4 patients in the CVICU and was predominately hypoactive in subtype. Chemical restraints via use of benzodiazepines or the use of physical restraints/restraining devices predisposed patients to a greater risk of delirium, pointing to areas of quality improvement that would be new to the vast majority of CVICUs.

Keywords

delirium; cardiovascular intensive care unit; acute coronary syndrome; cardiac surgery; benzodiazepines; restraints

Introduction

Since the advent of the modern coronary care unit, severity of illness and comorbidities in cardiac patients have significantly increased (1); patients are now treated in the cardiovascular intensive care unit (CVICU) for a variety of conditions, including myocardial infarction, heart failure, cardiogenic shock, and postoperative cardiac surgical care. While medical cardiovascular care has become more invasive, as demonstrated by the emergence of transcatheter valve replacement, complex coronary intervention and percutaneous life support, surgical care has advanced in parallel, becoming less invasive and increasingly performed in patients with advanced age and comorbidities. As a result, in our experience, the acute and post-procedural clinical course and management of medical and surgical patients in the CVICU is becoming quite similar. While it is well-recognized that pulmonary, hepatic, and renal dysfunction are important causes of morbidity and mortality (2), acute brain organ dysfunction (delirium and coma) and its prevalence, risk factors and impact on outcomes in CVICU patients are poorly understood. In critically ill non-cardiac patients, delirium is the most common organ dysfunction, with rates of up to 80% in mechanically ventilated medical and surgical intensive care unit (ICU) patients (3, 4), and is an independent predictor of poor outcomes, including a longer hospital length of stay, higher costs, increased risk of long-term cognitive impairment, and mortality (4–9).

Delirium can now be reliably diagnosed by non psychiatrists in critically ill patients in under two minutes through the use of validated monitoring instruments such as the Confusion Assessment Method for the ICU (CAM-ICU) (4, 10) and the Intensive Care Delirium Screening Checklist (11). Both methods are used worldwide for delirium monitoring (www.icudelirium.org). The availability of delirium monitoring instruments have advanced research in this field of medicine and we now know that exposure to sedatives such as benzodiazepines (3, 12–14) is one of the strongest modifiable risk factors for developing delirium in medical/surgical and hospitalized patients; strategies to reduce the use of benzodiazepines via the use of alternative agents such as dexmedetomidine (15–17) have reduced the burden of brain dysfunction in non-cardiac patients. Similarly, minimizing physical restraining of patients through early physical therapy (18) has been shown to reduce duration and risk of developing delirium in critically ill patients.

In contrast to the growing literature on delirium in medical and surgical ICU patients (3, 6, 19), the evidence regarding delirium in CVICU patients is sparse, and primarily limited to postoperative coronary artery bypass grafting (CABG) patients (20–30). Studies in cardiac surgical patients have shown that increasing age, preoperative cognitive impairment, depression, cerebrovascular and peripheral vascular disease, preoperative cerebral oxygen saturation, smoking, atrial fibrillation, renal dysfunction, metabolic syndrome, low intraoperative perfusion pressure and cardiogenic shock are associated with increased risk of postoperative delirium (20–30). Similarly, heart failure has been shown to be a risk factor for delirium in hospitalized patients (31). One prospective study of patients hospitalized with ST-elevation MI has reported an incidence of delirium of 5.7%, occurring in patients with advanced age and following cardiac arrest (32). Delirium in cardiac surgical patients has been shown to be associated with longer hospital stays, readmissions, poor cognitive outcomes, and mortality (26, 33–39) attesting to the importance of this organ dysfunction in cardiac patients and pointing to the need to identify potentially modifiable risk factors to focus interventional trials. The goal of the present study was, therefore, to prospectively study the prevalence, motoric subtypes and risk factors associated with the development of delirium in cardiology and cardiac surgical patients admitted to the CVICU, using a validated delirium monitoring instrument.

Materials and Methods

Patient Selection

The study was approved by the Institutional Review Board at Vanderbilt University Medical Center, with a waiver of consent due to the observational nature of the study. We enrolled consecutive patients admitted to the Vanderbilt CVICU, a tertiary level critical care unit managed by a multidisciplinary team that cares for both cardiology and cardiac surgery patients, with an annual volume of 2,800 patients. Enrollment criteria included: (1) age ≥18 years; (2) CVICU admission with a primary cardiac diagnosis or post-cardiac surgery; and (3) an expected CVICU length of stay > 24 hours. Patients were excluded if they had significant baseline neurologic diseases that would confound the evaluation of delirium, an inability to understand English, significant hearing loss, or an expected survival < 24 hours.

Data Collection

Baseline demographics and information regarding preadmission risk factors for delirium were obtained upon admission. Potential risk factors were identified from a review of the literature in medical and surgical ICU patients and post-cardiac surgical patients, as well as from focus group meetings with CVICU staff.

Daily laboratory data and information regarding exposure to medications and anesthesia were collected during patients' CVICU stay. Intraoperative data including length of cardiopulmonary bypass, type of surgery, and transfusion use was recorded. Severity of illness was measured using the modified Acute Physiology Score (APS) of the Acute Physiology and Chronic Health Evaluation II (APACHE II) (40). The APS excludes age, whose effects we planned to analyze separately in our analysis, and the contribution of the Glasgow Coma Scale (GCS), which artificially increases the APACHE score in surgical patients who are comatose immediately after surgery secondary to anesthetics effects and not necessarily metabolic derangements. We also calculated the Sequential Organ Failure Assessment (SOFA) (41) from information obtained within 24 hours of CVICU admission and a daily cardiovascular SOFA (CV SOFA) score was calculated as previously described (42). Other hemodynamic data collected included cardiac output measurements and lowest daily mean arterial pressure.

Delirium Assessment

Patient evaluations were performed using the Richmond Agitation - Sedation Scale (RASS) (43, 44) and the CAM-ICU (4, 10) (as shown in Figure 1) once daily for a maximum of 10 days or until CVICU discharge, whichever occurred first. The assessments were all performed by the research team following rounds each day. That is, these data were not derived from routine bedside nurses' CAM-ICU assessments, but rather they were obtained from RASS and CAM-ICU data conducted explicitly for this investigation by our trained research staff. Patients with a RASS score of −5 (unresponsive to physical and verbal stimulus) and −4 (responsive only to physical stimulus) are considered comatose, and thus ineligible for delirium evaluation; these patients were classified as "unable to assess." Patients with a RASS level greater than −4 were considered either delirious (CAM-ICU positive) or normal (CAM-ICU negative). The CAM-ICU has been validated against the Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV) with high specificity and sensitivity in both ventilated and nonventilated verbal patients (4, 10, 45–53) and can be rapidly and accurately performed by bedside nurses (54, 55). We used the RASS scale in concert with the CAM-ICU as a pragmatic approach to define motoric subtypes of delirium. Patients with positive RASS scores (+1 to +4) with every CAM-ICU positive evaluation were considered to have hyperactive delirium; delirium in these patients was manifested with positive symptoms of restlessness, agitation, combativeness and pulling of devices. Those with RASS scores of 0 to −3 with every CAM-ICU positive evaluation were considered as having hypoactive delirium manifesting negative symptoms such as lethargy, somnolence and inattention. Patients who during their ICU course were found to be delirious on at least one occasion manifesting positive symptoms (hyperactive or "loud" delirium) while on at least one other occasion manifesting negative symptoms (hypoactive, "quiet" or invisible delirium) were considered to have mixed delirium.

Statistical analysis

Patients' baseline demographic and clinical variables are presented using medians and interquartile range (IQRs) for continuous variables and proportions for categorical variables. Delirium prevalence was defined as any patient with at least one CAM-ICU positive assessment during the study period. We labeled these delirium assessments as prevalent cases, since we did not formally assess patients prior to enrollment and thus were unable to assure the cases as incident.

To study the risk factors of delirium, we considered two separate models. The first model was a logistic regression model which assessed baseline risk factors for delirium that occurred at any time during CVICU stay. Independent variables were determined *a priori* and included age, APACHE II APS score, benzodiazepine and dexmedetomidine exposure in the first 24 hours of enrollment, length of cardiopulmonary bypass (in nonsurgical patients this was considered to be 0 minutes), history of peripheral or cerebrovascular disease including prior strokes, and presence of significant cardiac dysfunction defined as cardiac index < 2.0 liters/minute/m^2, ejection fraction ≤35%, admission diagnosis of acute heart failure or cardiogenic shock, use of a ventricular assist device or a CV SOFA score ≥ 3. In our second model, we utilized logistic regression with generalized estimating equations (GEE), and considered the daily occurrence of delirium as the dependent or outcome variable. We included the following list of independent variables (again chosen *a priori*): exposure to sedative medications, such as benzodiazepines and dexmedetomidine, use of restraints or restraining lines (such as a temporary pacemaker, femoral arterial catheter, intra-aortic balloon pump, or ventricular assist device), daily CV SOFA score, and mental status (normal, delirious or comatose) on the previous day. Due to their skewed distributions, sedative doses were log transformed to improve model fit. Standard sedation protocols in our ICU utilize opiates for pain control complemented by propofol or

dexmedetomidine (especially if a patient is delirious) for sedation, with benzodiazepines reserved for only those patients that do not tolerate propofol or dexmedetomidine. At the time of conducting this study, however, there was a nationwide shortage of propofol. As a result, most continuous sedation in the ICU, when required, was with either dexmedetomidine or with benzodiazepines. Our sample size calculation of 200 patients was based on an estimated rate of delirium of 30%. With 60 patients estimated to have the event (delirium), this would have provided us adequate power to study approximately 6 risk factors. Given this limitation and the infrequent use of propofol, we decided not to include it in our multivariable model, thus allowing us to study other important risk factors that occur frequently in cardiac critically ill patients.

Results

Two hundred and eighty two patients met our inclusion criteria. Of these, 82 patients were excluded; these included 8 for anoxic brain injury or stroke, 8 for mechanical ventilation >48 hours prior to hospital arrival, 4 due to deafness/vision loss or inability to understand English and 61 admitted to the CVICU for a non-cardiac diagnosis. Two-hundred consecutive CVICU patients were therefore enrolled into the study; 96 patients (48%) were admitted to the cardiology service and 104 patients (52%) were admitted to the cardiac surgical service; of these 23% (22 patients) of cardiology and 97% (93 patients) of the cardiac surgical service were mechanically ventilated at enrollment. Demographic data and baseline characteristics are presented in Table 1. The APACHE II APS and SOFA scores reflect a critically ill population with organ dysfunctions. The most common admission diagnoses were acute coronary syndrome/myocardial infarction, acute heart failure, off-pump CABG and valve replacement surgery. Analgesia/sedation prescribed by the treating team on Days 1 and 2 of the ICU stay (the period of highest delirium risk in our cohort) comprised of opiates (60% and 58%), benzodiazepines (23% and 23%), and dexmedetomidine (15% and 19%) respectively.

Patient outcomes are summarized in Table 2. The overall prevalence of delirium in the CVICU was 26%, with rates of 29% among the cardiology patients and 24% in the cardiac surgical patients. Of the patients with delirium, 91% of patients suffered hypoactive delirium, 4% with hyperactive delirium and 6% had mixed delirium (Table 3). A smaller number of patients were comatose on at least one evaluation. The duration of delirium was one day or less in most patients; very few patients experienced delirium for a prolonged period (Figure 2). Of all the CAM-ICU positive evaluations, 78% of patients demonstrated presence of all 4 CAM-ICU features (Features 1, 2, 3 and 4 positive), another 7% had disorganized thinking but no altered level of consciousness (LOC) (Features 1, 2 and 3 positive) and only 15% had altered LOC but no disorganized thinking (Features 1, 2 and 4 positive). Thus 85% of our CAM-ICU positive patients had disorganized thinking.

In our evaluation of baseline risk factors and delirium prevalence (Table 4), benzodiazepine use at admission was independently predictive of a 3-fold increased risk of an episode of CVICU delirium (odds ratio, OR [95% CI] 3.1 [1.0, 9.4], p=0.04). Higher age (1.7 [1, 3], p=.04) was also a baseline risk factor for delirium. None of the other pre-specified variables were significantly associated with delirium (Table 4). In the model evaluating daily in-hospital covariates and the risk of development of delirium the following day among eligible patients (excluding discharged, deceased, and comatose patients), there was a greater than 2.5-fold increased risk of developing delirium in patients who received benzodiazepines [2.6 (1.2, 5.7), p=0.02] or had restraints or devices that precluded mobilization [2.9 (1.3, 6.5), p<0.01] (Table 5). Patients who were delirious (OR 11 [5.1, 23.8], p<0.001) or comatose the previous day (OR 13.7 [4.5, 41.7], p<0.001) were more likely to have delirium the following day. Hemodynamic status was not associated with the development of delirium on a

subsequent day. We additionally performed a sensitivity analysis in which we included daily opiate use in addition to the above mentioned variables in our daily risk factor model. This did not change the associations we found between benzodiazepines and restraint use, and the risk of developing delirium; opiate use itself was not associated with an increased risk of developing delirium in this sensitivity analysis.

Discussion

The principal finding of this study was that delirium developed in 1 out of 4 cardiology and cardiac surgical patients admitted to our CVICU for greater than 24 hours. In addition, the hypoactive or "quiet" form of delirium was observed in nearly all cases. This finding is particularly important because hypoactive delirium remains unrecognized in 75% of patients (and thus unaddressed as a form of organ dysfunction) in the absence of standardized assessment (56). In addition, hypoactive delirium has been associated with worse clinical outcomes compared with the more easily recognized hyperactive motoric subtype (39, 56). Modifiable independent risk factors for the development of delirium included the use of benzodiazepines (a chemical restraint), and the use of physical restraints or restraining lines that precluded mobility.

In cardiac surgical patients, variable rates of postoperative delirium have been reported, ranging from 3–70% (34, 57–59). This variability may in part reflect an underestimation of delirium due to lack of frequent assessments and standardized criteria for diagnosis (60). A recent prospective study using CAM-ICU assessment found that 51% of CABG patients developed postoperative delirium (59). While the overall prevalence of delirium of 26% was lower in our cohort, we studied a diverse CVICU population; only 66% of the surgical patients were admitted after CABG or valve surgery. In 1967, Parker and Hodge (61) reported a series of eleven patients experiencing delirium following myocardial infarction. Over the last four decades, little else has been written about this complication in nonsurgical CVICU patients. One observational study of nonagenarians suffering myocardial infarction reported a prevalence of delirium of 28% (62), similar to our much younger cohort.

In contrast to studies in other ICU patients (63), we observed the hypoactive form of delirium almost exclusively. Features of hypoactive delirium include withdrawal, flat affect, apathy, lethargy and decreased responsiveness (64). Given that clinicians fail to detect delirium (especially hypoactive delirium) by clinical exam alone (53), routine monitoring using validated delirium assessment tools may potentially result in earlier identification, management and improved outcomes after major cardiac events.

Our finding that benzodiazepine use was associated with delirium is consistent with previous non-cardiac studies (3, 13) in which lorazepam and midazolam use conferred an increased risk of delirium. Similarly our findings of physical restraints being a risk factor for delirium confirms prior work (65–68). We essentially found that *immobilizing therapies* (benzodiazepines, femoral catheters, intra-aortic balloon pumps, and other ventricular support devices) were associated with CVICU delirium. In other ICUs, delirium has been reduced with lower exposure to benzodiazepines (15, 16, 69, 70) and protocols that incorporate early physical therapy (18). Given the high prevalence of delirium in our CVICU population, strategies perhaps incorporating analgesia-based sedation protocols and early physical therapy (possibly even ergometric exercises in the ICU bed) (71) should be studied for their ability to decrease the burden of brain organ dysfunction (72, 73). This could potentially obviate the needs for restraints, which otherwise are utilized in ICUs to prevent harm to patients through removal of life saving devices.

Interestingly, we did not find an association between clinical variables related to the complexity and severity of acute cardiovascular disease and the development of delirium. The patient population studied was typical for a modern-day CVICU, with a high severity of illness and comorbidities. While the majority of cardiologists and cardiac surgeons are accustomed to managing acute cardiovascular disease and its effects on cardiac, pulmonary, and renal function, and this practice is important, this study illustrates the need to consider the impact of various supportive therapies such as sedation and restraints on the risk of acute brain dysfunction in CVICU patients.

Study limitations

There are several strengths and limitations of our study. We performed a detailed, prospective evaluation of delirium with a standardized bedside instrument and evaluated multiple risk factors daily. We were also able to study the motoric subtypes of delirium in a cohort of both surgical and non-surgical cardiac patients, though we used a pragmatic approach of using the RASS along with the CAM-ICU to define these motoric subtypes. Delirium assessments occurred only once per day, and only while the patients were in the CVICU; given the fluctuating course of delirium, it is possible that we may have under-estimated the prevalence of delirium. It is unlikely that this limitation due to personnel availability actually led to any meaningful changes in our risk factor analyses, yet it is important to realize that, if anything, delirium is an even larger problem in the CVICU patient population that reported in this study. Second, this study was not designed or powered to determine the impact of delirium on adverse outcomes such as length of stay, cost, or mortality. This remains unknown in the mixed CVICU patient population, though the strong relationship between delirium and these outcomes has been repeatedly demonstrated in other studies of critically-ill patients in medical, surgical, geriatric, orthopedic, and other patient populations. While we considered combining cardiology and cardiac surgical patients into one group, given that the acute and post-procedural clinical course and management of medical and surgical patients in the CVICU is becoming quite similar, others might view these as distinct populations and consider the combination to determine risk factors as a limitation. Third, the relatively lower rates of delirium in cardiac patients allowed us to only examine certain risk factors that we had *a priori* deemed as important to study; it is possible that other risk factors could potentially have been missed. In particular, this precluded us from evaluating the role of propofol, opiates and sepsis as risk factors for delirium, though exposure to propofol and our sepsis rates were low in our cohort, and our sensitivity analysis did not show an association between opiate use and risk of delirium. Nevertheless we believe this study advances the knowledge of delirium and its risk factors in cardiology and cardiac surgery patients, with emphasis on risk factors—both chemical and physical restraints—that can potentially be modified to possibly reduce the burden of brain organ dysfunction.

Conclusions

This prospective observational study demonstrates that a significant proportion of cardiology and cardiac surgical CVICU patients experience delirium, predominately in its hypoactive form. Increased dose of benzodiazepines, often administered as a chemical restraint, and the use of physical restraints increased the risk of developing delirium. Given the clinical impact of delirium on long-term outcomes, including cognitive impairment, in other cohorts, a larger prospective trial is warranted to define the independent role of delirium in outcomes in CVICU patients and to plan interventional trials aimed at modifying sedation regimens and nonpharmacologic protocols to limit restraint use.

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Step 1: Sedation and Level of Arousal Assessment with the RASS

Score	Term	Description	
+4	Combative	Overtly combative, violent, immediate danger to staff	
+3	Very agitated	Pulls or removes tube(s) or catheter(s); aggressive	
+2	Agitated	Frequent non-purposeful movement, fights ventilator	
+1	Restless	Anxious but movements not aggressive vigorous	
0	Alert and calm		
-1	Drowsy	Not fully alert, but has sustained awakening (eye-opening/eye contact) to *voice* **(≥10 seconds)**	Verbal Stimulation
-2	Light sedation	Briefly awakens with eye contact to *voice* **(<10 seconds)**	Verbal Stimulation
-3	Moderate sedation	Movement or eye opening to *voice* **(but no eye contact)**	
-4	Deep sedation	No response to voice, but movement or eye opening to *physical* stimulation	Physical Stimulation
-5	Unarousable	No response to *voice or physical* stimulation	

If RASS is -4 or -5, then **Stop** and **Reassess** patient at later time

If RASS is above - 4 (-3 through +4) then **Proceed to Step 2**

Step 2: Delirium Assessment with the CAM-ICU

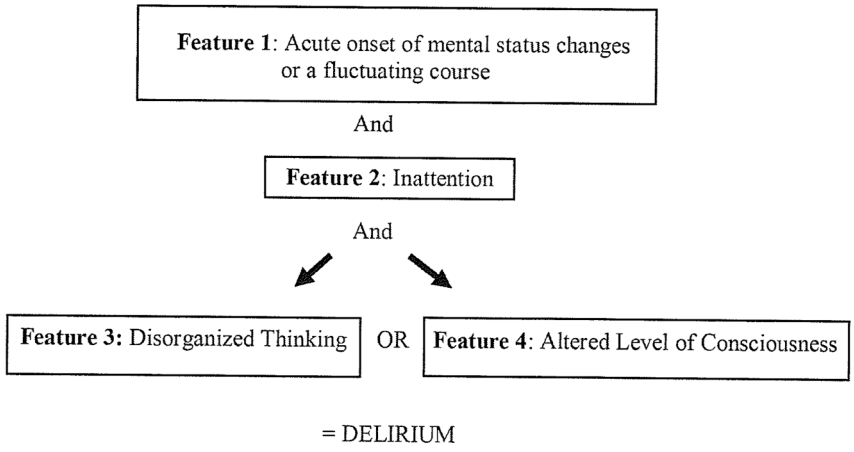

Figure 1. A Two-Step Process of Delirium Assessment

Using the Richmond Agitation-Sedation Scale (RASS), the level of sedation and arousal is assessed (Step 1). If the patient can respond to verbal stimulation (RASS level ≥ −3), then delirium assessment with the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) is performed (Step 2).

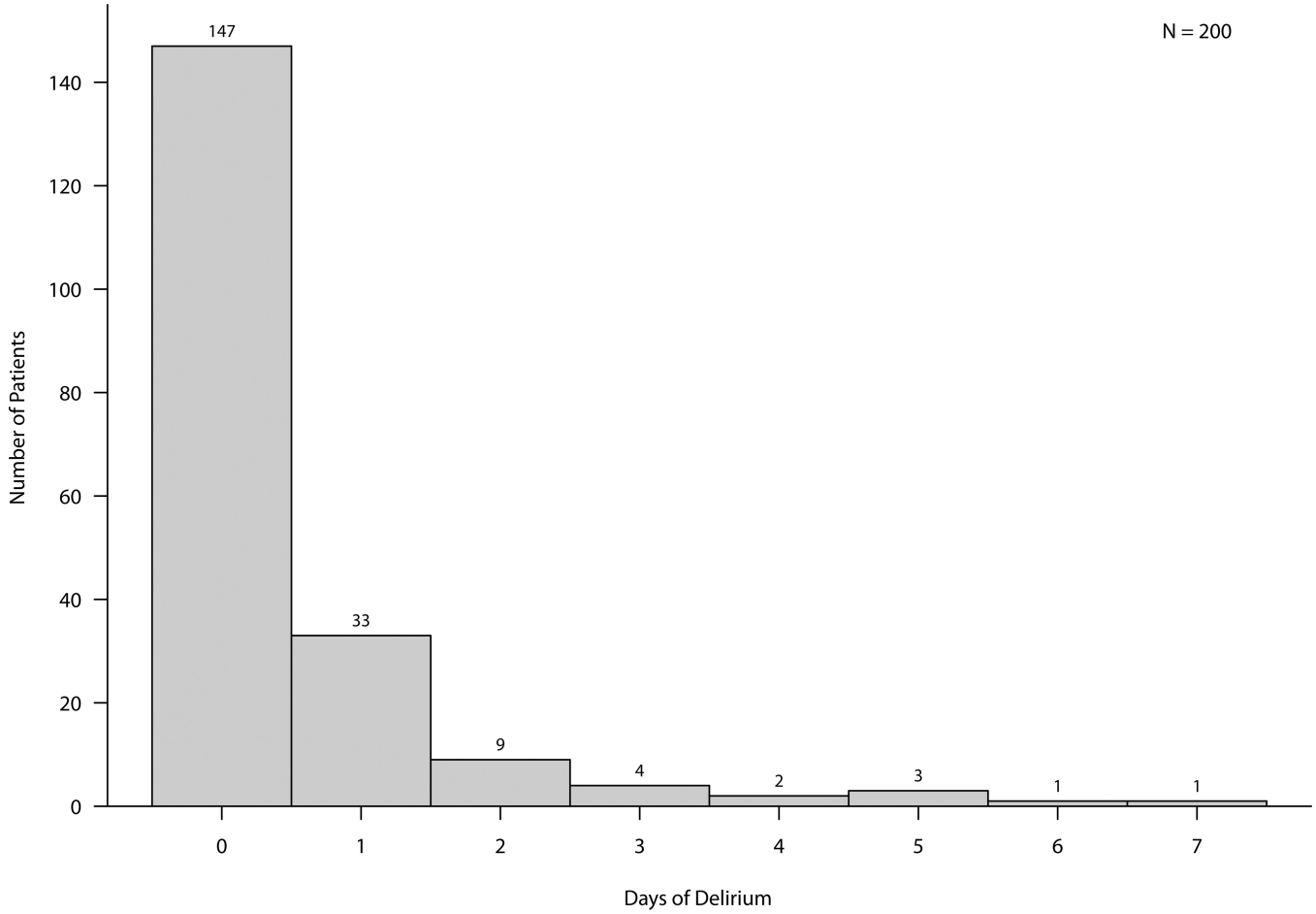

Figure 2. Duration of Delirium in the Cardiovascular Intensive Care Unit

A histogram displaying the duration of delirium in CVICU patients. The X axis represents the days of delirium, and the Y axis the number of patients.

Table 1

Baseline Patient Characteristics

	Cardiology (N = 96)	Cardiac Surgical (N = 104)
Demographic data[a]		
Age (years)	61 [50,72]	65 [56,74]
Female	33% (32)	39% (41)
Active smoker	31% (30)	13% (14)
Significant cardiac dysfunction[b]	47% (45)	79% (82)
SOFA score	5[4,8]	10[9,12]
Cardiovascular SOFA score	1[1,3]	3[2,3]
APACHE II APS score	7 [4,11]	11[9,14]
History of alcohol/drug use	7% (7)	5% (5)
Hypertension	75% (72)	72% (75)
History of dementia	3% (3)	5% (5)
History of depression	16% (15)	15% (16)
History of atrial fibrillation	19% (18)	32% (33)
History of PVD or CVD	21% (20)	25% (26)
Statin use on admission	48% (46)	49% (51)
CVICU admission diagnosis		
Cardiac arrest	6% (6)	0% (0)
Cardiac arrhythmia	9% (9)	3% (3)
Unstable angina	16% (15)	0% (0)
NSTEMI	11% (11)	0% (0)
STEMI	15% (14)	0% (0)
Acute heart failure	12% (12)	1% (1)
Sepsis/septic shock	11% (11)	1% (1)
Minimally invasive valve surgery	0% (0)	12% (12)
Off-pump CABG	0% (0)	34% (35)
On-pump CABG	0% (0)	8% (8)
Valve replacement surgery	0% (0)	24% (25)
Other	18% (18)	19% (19)
CVICU course		
Hematocrit	35 [30,40]	28 [25,31]
Creatinine	1.4 [0.9,2.1]	1 [0.8,1.3]
Sodium	138 [135,140]	139 [136,142]
pH	7.36 [7.28,7.4]	7.31 [7.28,7.35]
PaO_2	95 [72,148]	151 [94,224]

[a] Median (interquartile range) where applicable.

[b] Includes any of the following: cardiac index < 2.0 liters/minute/m^2, ejection fraction ≤35%, admission diagnosis of acute heart failure or cardiogenic shock, use of a ventricular assist device or cardiovascular SOFA score ≥ 3

APACHE IIAPS= Acute Physiology and Chronic Health Evaluation, Acute Physiology Score; CABG = coronary artery bypass graft; CVD = cerebrovascular disease; CVICU = cardiovascular intensive care unit; NSTEMI =non-ST-segment elevation myocardial infarction; PVD = peripheral vascular disease; SOFA = Sequential Organ Failure Score; STEMI = ST-segment elevation myocardial infarction

Table 2

Patient Outcomes

	Cardiology (N = 96)	Cardiac Surgical (N = 104)
Ever delirium	29% (28)	24% (25)
Ever coma[a]	24% (23)	11% (11)
CVICU length of stay (days)	3[2,5]	3[2,4]
Ventilator days	0[0,1.2]	1[1,1]
PRBC transfused (units)	0[0,0]	0[0,2]
CVICU mortality	9% (9)	0% (0)

Values are expressed as median [interquartile range] where applicable.

[a]Defined as RASS ≤ −4

CVICU = cardiovascular intensive care unit; PRBC = packed red blood cells

Table 3

Delirium Subtypesin the CVICU Patients with Delirium*

Delirium Subtype	Cardiology (N = 28)	Cardiac Surgical (N = 25)
Hypoactive	93% (26)	88% (22)
Hyperactive	4% (1)	4% (1)
Mixed	4% (1)	8% (2)

N = number of patients with delirium

* Percentages are rounded to the nearest number.

Table 4

Baseline risk factors for the experiencing delirium in the CVICU[a]

	Low	High	Odds Ratio (95% CI)	P-value
Age	52	73	1.7 (1, 3)	0.04
APACHE II APS	7	12	1.5 (1, 2.2)	0.07
Benzodiazepine use first 24 hours (mg)	0	126.5	3.1 (1, 9.4)	0.04
Dexmedetomidine use first 24 hours (mcg)	0	3360	2.8 (0.8, 9.4)	0.09
Length of pump run (minutes)	0	94.8	1.1 (0.7, 1.7)	0.80
PVD or CVD	No	Yes	1.9 (0.8, 4.1)	0.12
Significant cardiac dysfunction[b]	No	Yes	0.9 (0.4, 1.9)	0.77

Abbreviations: APACHE II = Acute Physiology and Chronic Health Evaluation II, APS= Acute Physiology Score; CI = confidence interval; CVD = cerebrovascular disease PVD = peripheral vascular disease

[b] Includes any of the following: cardiac index < 2.0 liters/minute/m^2·, ejection fraction ≤35%, admission diagnosis of acute heart failure or cardiogenic shock, use of a ventricular assist device orcardiovascular SOFA score ≥ 3

[a] In order to provide a clinically meaningful explanation of model results, odds ratios are calculated to compare the 75th percentile of age, APACHE II APS Scores, and length of pump run to the 25th percentile. For example, a 73-year-old patient has, on average, 1.7 times the odds of experiencing delirium in the CVICU compared with 52-year-old patient.

Because both the 25th and 75th percentiles of the doses of benzodiazepines and dexmedetomidine were 0, we instead compared the minimum and maximum. For dichotomous variables (PVD/CVD and significant cardiac dysfunction) patients with the condition are compared to patients without it.

Table 5

Association between degree of exposure to in-hospital risk factors and odds of developing delirium[a]

Risk Factor	Low Exposure	High Exposure	Odds Ratio (95% CI)	P-value
Any physical restraints[b]	No	Yes	2.9 (1.3, 6.5)	<0.01
Benzodiazepines last 24 hrs	0 mg	2.5 mg	2.6 (1.2, 5.7)	0.02
SOFA CV score	1	3	0.8 (0.4,1.6)	0.62
Dexmedetomidine last 24 hrs[c]	0 mcg	4308 mcg	1.4 (0.5,3.5)	0.53
Mental status previous 24 hours				<0.001
	Normal	Delirium	11 (5.1,23.8)	
	Normal	Coma	13.7 (4.5,41.7)	

Abbreviations: CI = confidence interval; CV SOFA = Cardiovascular Sequential Organ Failure Assessment

[a] In order to provide a clinically meaningful explanation of the results, odds ratios were calculated to compare the 75th percentile to the 25th percentile of benzodiazepines and CV SOFA score. For example, a patient who received 2.5mg of midazolam equivalents (the number shown in the Table) in the last 24 hours has, on average, 2.6 times the odds of developing delirium the next day than a patient who received no benzodiazepines during that period.

[b] Physical restraints included the use of restraints or restraining lines (such as a temporary pacemaker, femoral arterial catheter, intra-aortic balloon pump, or ventricular assist device).

[c] Because both the 25th and 75th percentiles of dexmedetomidine dose were 0, we instead compared the minimum and maximum. For categorical variables (restraints and mental status in the last 24 hours), patients with the condition are compared to patients without it.
As shown, the modifiable risk factors of physical restraints and benzodiazepines (i.e. chemical restraints) were both statistically significant predictors of increased odds of developing delirium.