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ORIGINAL INVESTIGATION

Effect of seasons on delirium in postoperative critically ill patients: a retrospective analysis

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Abstract

Background and objectives: Postoperative delirium is common in critically ill patients and is known to have several predisposing and precipitating factors. Seasonality affects cognitive function which has a more dysfunctional pattern during winter. We, therefore, aimed to test whether seasonal variation is associated with the occurrence of delirium and hospital Length Of Stay (LOS) in critically ill non-cardiac surgical populations.

Methods: We conducted a retrospective analysis of adult patients recovering from non-cardiac surgery at the Cleveland Clinic between March 2013 and March 2018 who stayed in Surgical Intensive Care Unit (SICU) for at least 48 hours and had daily Confusion Assessment Method Intensive Care Unit (CAM-ICU) assessments for delirium. The incidence of delirium and LOS were summarized by season and compared using chi-square test and non-parametric tests, respectively. A logistic regression model was used to assess the association between delirium and LOS with seasons, adjusted for potential confounding variables.

Results: Among 2300 patients admitted to SICU after non-cardiac surgeries, 1267 (55%) had postoperative delirium. The incidence of delirium was 55% in spring, 54% in summer, 55% in fall and 57% in winter, which was not significantly different over the four seasons ($p = 0.69$). The median

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LOS was 12 days (IQR = [8, 19]) overall. There was a significant difference in LOS across the four seasons ($p = 0.018$). LOS during summer was 12% longer (95% CI: 1.04, 1.21; $p = 0.002$) than in winter.

Conclusions: In adult non-cardiac critically ill surgical patients, the incidence of postoperative delirium is not associated with season. Noticeably, LOS was longer in summer than in winter.

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Introduction

Delirium is characterized by acute change in mental status, including inattention and disorganized processing.¹ It is common in hospitalized patients, with a reported incidence of 11% to 43% in the postoperative population,² and affects up to 80% of critically ill patients.³ Postoperative delirium is independently associated with increased postoperative complications, which may lead to longer Intensive Care Unit (ICU) or hospital stay, and higher postoperative mortality.⁴⁻⁶

Postoperative delirium is a multifactorial cognitive dysfunction.⁷⁻⁹ Recently, it has been shown that even among healthy subjects, cognitive function, especially attention and executive processes, may peak in late summer and early fall, and decline in late winter and early spring, with a more dysfunctional pattern during winter.^{10,11} Furthermore, alteration in cognition was robustly associated with seasonal changes.¹¹⁻¹³ Two previous studies showed a seasonal effect on delirium incidence, with higher incidence in autumn-winter compared to summer months.^{14,15} However, these findings are limited to general medical patients, and the seasonal effect on delirium remains poorly understood in critically ill surgical patients.

Seasonal occurrence of cardiovascular, cerebrovascular, or infectious events, as well as seasonal rhythms in psychological state have been previously reported.¹⁶⁻¹⁹ The possible underlying mechanism of this seasonal influence may be related to changes in light-darkness cycle or lower-vitamin D levels in winter. Previous research also showed seasonal variation in hospitalization rate of patients with chronic conditions, namely longer LOS during winter months.²⁰ However, the influence of seasonal changes on LOS in surgical intensive care patients is unclear.

We therefore aimed to evaluate seasonality in the occurrence of delirium in critically ill non-cardiac surgical populations. Specifically, we tested the primary hypothesis that in surgical ICU patients, admission to ICU during the winter is associated with higher incidence of delirium compared to other seasons. Secondarily, we tested the hypothesis that admission to ICU during the winter is associated with longer hospital LOS. Lastly, we tested the seasonal influence on subtypes of delirium as exploratory outcome.

Methods

Subject selection

With local institutional review board approval (IRB #19-271), we conducted a retrospective analysis of adult patients

(18 years or older), who had elective non-cardiac surgery at Cleveland Clinic between March 21, 2013, and March 20, 2018. To limit bias and clarify the immediate postoperative period for critically ill patients, we included patients who were directly admitted to Surgical ICU (SICU) after surgery and remained in SICU for at least 48 hours and up to 5 days, with delirium assessment during the postoperative period. We excluded patients without any Confusion Assessment Method Intensive Care Unit (CAM-ICU) assessment, or with pre-existing encephalopathy, coexisting Alzheimer's disease, dementia, or other cognitive decline preoperatively, or those who had neurosurgical procedures. Patients admitted to SICU more than once were only evaluated for their first admission.

Exposure and outcome

We defined the exposure as the four seasons classified internationally in the Northern Hemisphere as *Spring*: from March 21st to June 20th; *Summer*: from June 21st to September 20th; *Autumn*: from September 21st to December 20th; and *Winter*: from December 21st to March 20th. On the basis of admission date, all cases were analyzed for seasonal and monthly variation.

Our primary outcome was the incidence of delirium, measured using CAM-ICU^{21,22} during the initial 5 postoperative days, at least once a day by well-trained nurses or physicians. Delirium was defined dichotomically by the presence of at least one positive CAM-ICU assessment accompanied by a Richmond Agitation-Sedation Scale (RAAS) of -3 or greater.^{21,22} CAM-ICU assessments in the first 12-hours after surgery were excluded from the analysis as they might represent residual anesthetic effects.

Our secondary outcome was hospital Length Of Stay (LOS). Additionally, we assessed the seasonal influence on subtypes of delirium as exploratory outcome. We classified delirium events into three motoric subtypes: hypoactive (characterized by sedation, motor slowness, lethargy, and withdrawal from interactions), hyperactive (characterized by agitation, aggression, hallucinations, and disorientation), and mixed (fluctuation between hypoactive and hyperactive subtypes) by using CAM-ICU and RASS.^{23,24} Hypoactive delirium was defined as a positive CAM-ICU assessment associated with a daily RASS score of -3 to 0 points. Hyperactive delirium was defined as a positive CAM-ICU assessment associated with a daily RASS score of 1–4 points. Mixed delirium was defined as a positive CAM-ICU assessment associated with a daily RASS score that fluctuates between the hypoactive and hyperactive ranges.

Data collection

Data was retrospectively collected from Cleveland Clinic electronic medical records, the Perioperative Health Documentation System, including intraoperative information from the electronic anesthesia record keeping system, and ICU registry.

Statistical analysis

Primarily, the incidence of delirium was summarized by season and compared using Chi-Square test for overall pattern of seasonal differences. A logistic regression model was used to assess the association between delirium and seasons, adjusted for all the potential confounding variables listed in [Table 1](#). The odds ratio of delirium in winter, compared to spring, summer and autumn was reported with a 95% Confidence Interval.

Secondarily, the LOS was summarized by season and compared using non-parametric test due to the non-normal distribution of the data. A linear model was used to assess the association between LOS and seasons, adjusted for the potential confounding variables. LOS was log transformed to meet the assumption of the linear regression model. Ratio of LOS comparing winter to spring, summer and autumn was reported with 95% Confidence Interval.

Additionally, we summarized the subtypes of delirium by seasons using the same method as for the primary outcome, among patients with available RASS assessments.

Moreover, to avoid geographical bias, we conducted a sensitivity analysis including only patients from Ohio.

History of anxiety, depression, psychoses, drug abuse, alcohol abuse, surgery duration, year of surgery, and the latitude of residency address were considered as potential confounders.

Sample size and power

We expected about 3,000 ICU patients eligible for this study from March 21, 2013, and March 20, 2018, based on a preliminary query from the electronic medical records. The incidence of delirium in ICU is about 50%. Thus, we would have 90% power at the 0.05 significance level to detect an odds ratio of 1.40 or higher between two seasons.

SAS statistical software version 9.4 (SAS Institute, Cary, NC, USA) was used for all statistical analyses.

Results

In total, 2,300 patients admitted to SICU after non-cardiac surgeries were included in our study. Patient characteristics were summarized in [Table 1](#). The average age was 62 (SD = 15) years, 45% females, about 50% of patients had an American Society of Anesthesiologists (ASA) physical status equal or greater than four, and the mean duration of surgery was about 7 hours. Patients' demographic characteristics, surgical variables, and perioperative management were comparable across the four seasons ([Table 1](#)).

Among the 2300 patients, 1267 (55%) had postoperative delirium. The distribution of eligible patients admitted to

Table 1 Patient characteristics (n = 2300).

	Spring (n = 570)	Summer (n = 574)	Fall (n = 609)	Winter (n = 547)
Age, years	62±15	62±14	61±15	62±14
Sex, female%	257 (45)	257 (45)	284 (47)	245 (45)
Charlson comorbidity index	3 [1,6]	3 [1,5]	3 [1,5]	3 [2,6]
ASA status, %				
≤II	20 (4)	16 (3)	15 (2)	17 (3)
III	249 (44)	238 (41)	274 (45)	251 (46)
IV	290 (51)	307 (53)	314 (52)	268 (49)
V	11 (2)	13 (2)	6 (1)	11 (2)
Disease history of				
Anxiety, %	79 (14)	94 (16)	103 (17)	99 (18)
Psychoses, %	30 (5)	25 (4)	33 (5)	22 (4)
Depression, %	101 (18)	116 (20)	97 (16)	93 (17)
Drug abuse, %	19 (3)	16 (3)	18 (3)	15 (3)
Alcohol abuse, %	35 (6)	37 (6)	40 (7)	21 (4)
Use of Benzos, %	94 (16)	88 (15)	94 (15)	75 (14)
Emergency surgery, %	154 (27)	163 (28)	163 (27)	161 (29)
Type of anesthesia				
General only	523 (92)	531 (93)	548 (90)	483 (88)
Other	47 (8)	43 (7)	61 (10)	65 (12)
Intraoperative information				
Surgery duration, h	6.7±4.0	7.1±5.4	7.1±4.2	7.0±4.0
Estimated blood loss, mL	350 [100–1500]	400 [100–1500]	500 [100–2000]	400 [100–1500]
Total blood given, mL	362 [0–1323]	335 [0–1387]	389 [0–1513]	345 [0–1208]
Total fluid, L	4.5 [2.5–6.8]	4.5 [2.4–7.2]	4.4 [2.5–7.0]	4.4 [2.5–7.0]
Use of urine catheter	10 (2)	6 (1)	20 (3)	11 (2)
APACHE 2 score	61 (24)	62 (25)	60 (25)	60 (23)

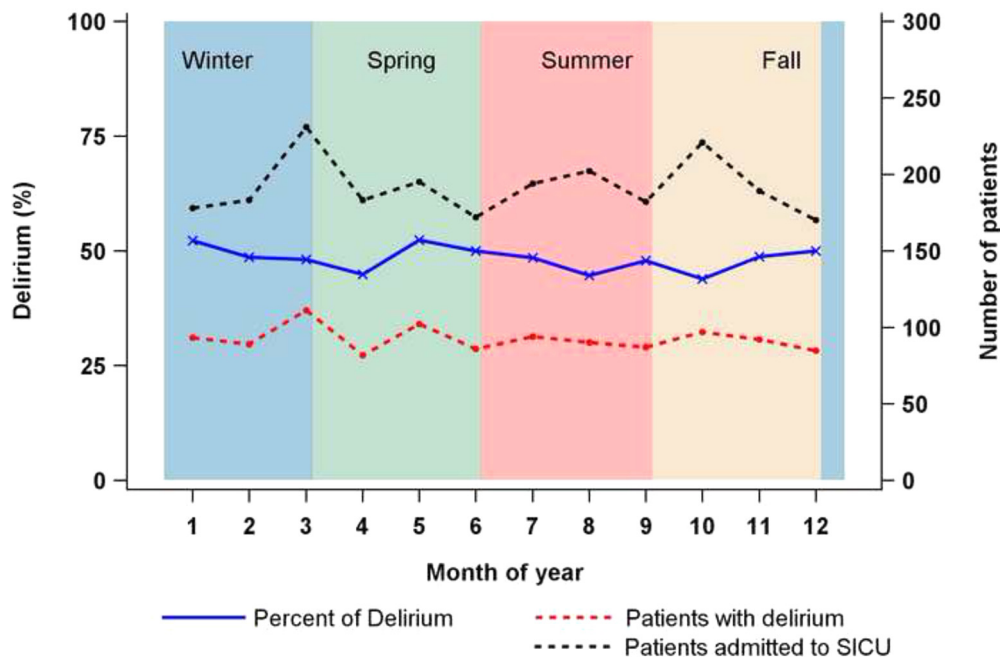


Figure 1 Dash lines show the total number of patients admitted to SICU (black color) and with delirium (red color). Continuous blue line represents the incidence (percentage) of patients with delirium. There are no differences of delirium among seasons (four different colors) nor months (x axis).

ICU and the number of patients who had delirium by month are presented in Figure 1.

According to the seasonal distribution, the incidence of delirium was 55% in spring, 54% in summer, 55% in fall and 57% in winter, which was not significantly different over the four seasons (Chi-Square $p = 0.69$). After adjusting for potential confounding variables, seasonal variation was still not associated with the odds of delirium (joint test $p = 0.81$). The odds ratio of delirium in spring, summer and fall compared to winter are presented in Table 2. The median length of delirium was 24 hours (IQR = [10, 76]) overall and it was not significantly different across the four seasons (Kruskal-Wallis $p = 0.50$).

To eliminate the geographic bias, we conducted a sensitivity analysis by including only patients from Ohio

($n = 1877$), and the result was consistent with the main analyses ($p = 0.39$). Furthermore, we identified the subtypes of delirium among 1104 patients with available RASS assessment and listed the incidence of each subtype in Table 3. The subtypes of delirium were not significantly different across the four seasons (Fisher exact test $p = 0.059$).

The overall median LOS was 12 days (IQR = [8, 19]). We found a marginally significant difference in LOS across the four seasons without adjustment (Kruskal-Wallis $p = 0.024$) and after adjusting for potential confounders ($p = 0.018$). The LOS during summer was 1 day longer (95% CI: 1.04, 1.21; $p = 0.002$) than in winter, adjusted for confounders (Table 2, Fig. 2).

Table 2 Adjusted difference in delirium and length of hospital stay by seasons ($n = 2300$).

	Summary	Estimated difference	p
Delirium incidence		Odds Ratio (95% CI)	
Winter	310 (57%)	ref	
Spring	313 (55%)	1.00 (0.79–1.28)	0.65
Summer	309 (54%)	0.97 (0.76–1.24)	0.96
Fall	335 (55%)	0.91 (0.71–1.15)	0.34
Delirium duration		Ratio of geometric means (95% CI)	
Winter	24 [8, 72]	ref	
Spring	28 [10, 78]	0.94 (0.77–1.15)	0.56
Summer	24 [12, 84]	0.95 (0.77–1.16)	0.61
Fall	24 [12, 60]	0.84 (0.68–1.03)	0.09
Length of hospital stay		Ratio of geometric means (95% CI)	
Winter	11 [8, 18]	ref	
Spring	12 [9, 18]	1.09 (1.02–1.18)	0.018
Summer	12 [9, 20]	1.12 (1.04–1.21)	0.002
Fall	11 [8, 19]	1.08 (1.01–1.16)	0.036

Table 3 Subtypes of delirium by seasons (n = 1104).

Subtypes	Spring (n = 278)	Summer (n = 274)	Fall (n = 282)	Winter (n = 270)
Hyperactive	121 (43%)	110 (40%)	106 (38%)	114 (42%)
Hypoactive	2 (1%)	8 (3%)	3 (1%)	0 (0%)
Mixed	155 (56%)	156 (57%)	173 (61%)	156 (58%)

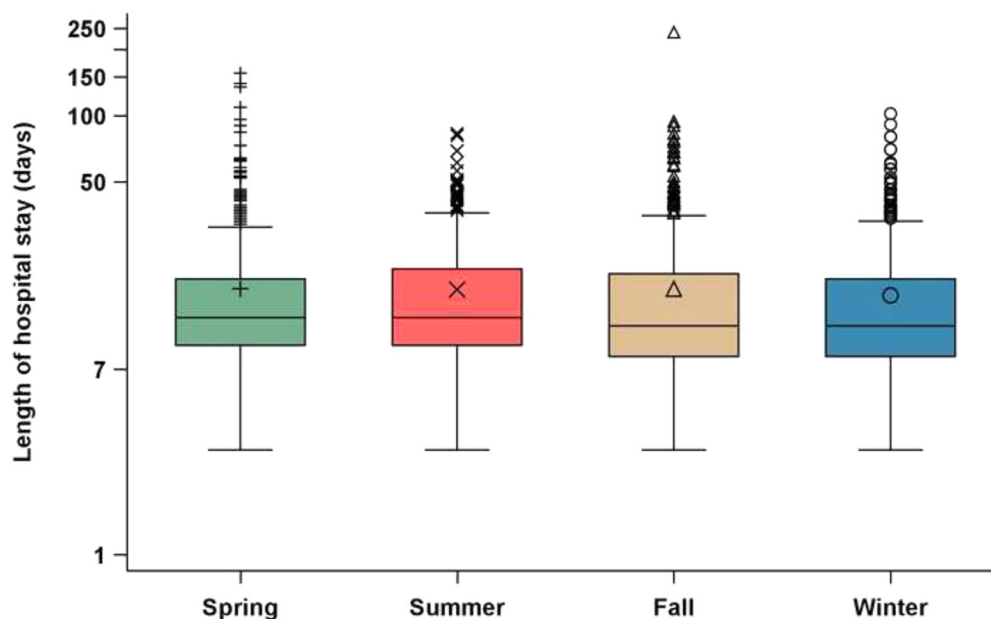
Discussion

In the current study, more than half of patients had postoperative delirium during their postoperative stay in the SICU. In contrast to our expectation, the incidence of postoperative delirium in critically ill patients was not significantly different across the four seasons. Even after adjusting for potential confounding variables and geographical location, seasonal variation was not associated with delirium incidence in this surgical population. Noticeably, hospital LOS was about one day longer in summer than in winter.

We found that the incidence of delirium in SICU is over 50%, which is consistent with previous studies.³ Critically ill surgical patients are at increased risk of delirium owing to the severity of illness, tissue damage associated with the surgical procedure, acute metabolic changes, advanced age, and comorbidities. Nevertheless, SICU-acquired delirium did not differ across the seasons. These results contrast with previous studies^{14,15,17,18} that showed a higher incidence of delirium during autumn and winter months. These inconsistencies may be explained by differences in study populations as previous studies were restricted to elderly¹⁸ and ICU¹⁷ medical patients with higher incidence in winter.^{14,15} Most of our patients had elective surgery. We did not find significant differences in admission rates to SICU along the year. Furthermore, patients' demographics and comorbidities were comparable over the four seasons. Gallerani et al.¹⁴ investigated all admissions to medical intensive care units and found significant variability in cerebral

atherosclerosis or generalized ischemic disease over the year.¹⁴ However, they used discharge International Classification of Diseases and Related Health Problems (ICD-9) codes for delirium diagnosis rather than daily clinical assessments. ICD-9 coding was shown to have good specificity, but low sensitivity.²⁵ One of the main explanations of the seasonal effect on cognitive function is the association with sunlight exposure. Simons et al.²⁶ assessed whether the amount of sunlight exposure before medical ICU admission was associated with delirium during ICU stay. They assessed delirium incidence with CAM-ICU twice a day during ICU stay, and similarly to our results, they did not find a relationship between pre-admission sunlight exposure and the development of ICU-acquired delirium.²⁶

We found a significant difference in LOS across the four seasons, with LOS during the summer about 1 day longer than in the winter. This increment in summer morbidity has been previously reported and might partly be related to the beginning of a new academic year and therefore trainee inexperience.²⁷ The American College of Surgeons-National Surgical Quality Improvement Program (ACS-NSQIP) data over a 3-year period showed worsen surgical morbidity and mortality in July, which contrasts with previously reported literature. In the general non-surgical populations, there is an increase in all-cause mortality during winter months. The underlying explanations may include seasonal variation in blood pressure, lipid levels, changes in activity of the coagulation cascade, and/or seasonal variation in the prevalence of viral or bacterial pneumonia.²⁷ Nevertheless, these

**Figure 2** Boxplot of length of stay in days over the four seasons.

factors do not seem to account for postsurgical morbidity.²⁷ In this setting, trainee inexperience and nurse staffing ratios, as well as the increased incidence of surgical site infections during the summer months, are the main potential factors affecting outcome.²⁸

Strengths and limitations

We selected the widely accepted CAM-ICU tool to diagnose postoperative delirium. This screening tool remains the most feasible test to detect delirium for well-trained nurses or physicians on site. To eliminate the residual effects of anesthetics, we excluded delirium assessments during the initial 12 postoperative hours, and we assessed delirium at least once daily. Moreover, we had robust power to detect seasonal changes in delirium after confounder adjustment, based on our sample size.

Our study has several limitations. The retrospective design is subject to unobserved confounding. Therefore, some bias may still exist even though we adjusted for many demographics and perioperative variables. Our study critically ill population did not include cardiothoracic surgery, vascular surgery, and pediatric patients. Thus, our result cannot be generalized to the entire surgical population. Eighteen of our 30 SICU beds are exposed to sunlight. However, it was not possible to assess delirium incidence according to sunlight exposure because patients often switch to other SICU beds during admission. Similarly, we were unable to adjust for opioid and sedative administration which may lead to delirium. Finally, we only considered overall delirium incidence as well as the type of delirium, but not the severity of delirium. Therefore, our results may be conservative.

Summary

We did not find an association between seasonal variation and occurrence of delirium in critically ill surgical patients. However, we found an association between seasonal variation and hospital length of stay.

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Authorship

YQ, ER: study design, data collection, data interpretation, and manuscript writing; MA, RS, AS, RS, JD, II: data collection and manuscript review; GM: data analysis and interpretation; KR: data interpretation and manuscript writing; and AT: study design, data interpretation, and manuscript writing.

Conflicts of interest

The authors declare no conflicts of interest.

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