



Risk Factors for Postoperative Delirium in Thoracic Surgery Patients - A Prospective Cross-sectional Study

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Abstract

Background: Postoperative delirium (POD) is a common complication that affects the prognosis and outcome. The risk factors of different surgical types have significance in preventing POD. Still, there are few studies on the risk factors for this complication of thoracic surgery, and further research and exploration are necessary.

Method: This study intends to conduct a prospective cross-sectional study, including patients undergoing elective thoracic surgery. The primary outcome is the incidence of POD 1-7 days after surgery or before discharge. The essential information on patients, surgery, anesthesia, and postoperative details are gathered for statistical analysis. We are exploring the potential relationship between anesthesia-related factors and POD.

Result: One hundred seventy-five patients were included in this study, and 17 (9.7%) patients developed POD. Univariate analysis showed that age-adjusted Charlson Comorbidity Index (aCCI), educational attainment, blood transfusion, artificial blood vessel replacement, and indwelling urinary catheter were statistically different. Logistic regression results showed that the aCCI index (OR 1.811, 95% CI 1.058-3.103; $P=0.030$), the ambulation time (OR 12.303, 95% CI 2.670-56.686; $P=0.001$) increased POD risk. In patients undergoing thoracotomy, blood transfusion (RR 16.875, 95% CI 2.149-132.508; $P=0.012$) was statistically different between POD and non-POD groups.

Conclusion: The results of this study showed that the higher the aCCI index, the later the ambulation time is the risk factor for POD in thoracic surgery patients. The risk of POD may be heightened in thoracic surgery patients who require a blood transfusion. However, additional research is warranted to confirm these findings.

Keywords

Postoperative Delirium, Thoracic Surgery, Risk Factor

Abbreviations

POD: Postoperative Delirium; aCCI: Age-Adjusted Charlson Comorbidity Index; OR: Odds Ratio; CI: Confidence Interval; ASA: American Society of Anesthesiologists; ICU: Intensive Care Unit; NRS: Numerical Rating Scale; 3D-CAM: 3-Minute Diagnostic Confusion Assessment Method; ICU-CAM: ICU-Confusion Assessment Method; Mini-Cog: Mini-Cognitive Assessment; SD: Standard Deviation; LOS: Length of Stay; CCI: Charlson Comorbidity Index; ERAS: Enhanced Recovery After Surgery

Introduction

Postoperative delirium (POD) is a common neuropsychiatric complication that occurs within one week after surgery. According to the International Classification of Disease 10th Revision, the clinical characteristics are acute onset, fluctuating course, patients with fluctuating consciousness, decreased cognitive function, impaired memory, disorientation, and sleep-wake cycle disorders [1,2]. POD is associated with a variety of adverse outcomes, not only increasing the incidence of other postoperative complications such as pneumonia and prolonged ICU stay but also prolonging hospital stay and aggravating economic burden [1,3].

The incidence of POD varies among different types of surgeries, with thoracic surgery patients experiencing an incidence as high as 50% [4]. According to the research report, its occurrence and development are related to various factors, which can be divided into three aspects: preoperative factors, including old age [4-8], squamous cell carcinoma [5], cerebrovascular history [5,8], Preoperative cognitive impairment [7], hypertension and smoking history [8]; Intraoperative factors, such as American Society of Anesthesiologists(ASA) grade III [7], the type of operation [9], duration of operation [6,10], blood loss [10] and cerebral desaturation(defined by the cerebral tissue oxygen saturation, with a baseline of less than 90% for the left and less than 85% for the right) [11]; Postoperative factors included use of clonazepam in intensive care Unit (ICU), postoperative complications [4], abnormal sodium, potassium, and glucose levels, sleep deprivation [6], and extended stay in the ICU [12]. The previous studies identified some factors related to anesthesia, but they were inadequate in offering specific references and guidance for preventing postoperative delirium after thoracic surgery. POD is associated with anesthetic medications, fluctuations in blood pressure, depth of anesthesia/sedation, and respiratory management. Therefore, additional research is required to identify POD risk factors associated with anesthesia in thoracic surgery patients.

Therefore, this study aims to conduct a prospective cross-sectional study to investigate the current occurrence of POD in thoracic surgery patients,

analyze POD factors in thoracic surgery patients, and explore the relationship between anesthesia-related risk factors and POD.

Methods

Study Population:

This single-center prospective cross-sectional study was conducted at a university hospital. This study has been approved by the Medical Ethics Committee of Sichuan University [Approval No. 2018 (164)] and passed the Chinese clinical trial registration, registration number ChiCTR1800019926. Adult patients undergoing elective surgery between September 28, 2020, and November 6, 2020, were included, and those younger than 18 years with preoperative delirium, dementia, mental illness, and inability to communicate were excluded.

Preoperative Evaluation and Postoperative Follow-Up:

Before the expected operation, the researchers evaluated the patients meeting the inclusion criteria; delirium, cognitive function, sleep quality, pain, sensory function, and other assessments were performed at the bedside, and the patient's demographic and clinical information was collected and recorded. After surgery, participants were followed up daily for 1-7 days or until discharge. The occurrence of POD was assessed, the pain was evaluated using the numerical rating scale (NRS), and whether to place an indwelling catheter, the ambulation time, and complications were recorded. All assessments and data collection were conducted by trained researchers, with rigorous quality control implemented and managed throughout the process.

Postoperative Delirium and Assessment of Cognitive Function:

POD Assessment:

The POD was assessed by a dedicated researcher using the 3-minute diagnostic confusion assessment method (3D-CAM). Patients admitted to the ICU after surgery were assessed using the ICU-Confusion assessment method (ICU-CAM).

Cognitive Function Assessment:

Researchers used the Mini-cognitive assessment

(Mini- cog) at the bedside before surgery.

Statistical Analysis:

According to previous literature reports, the POD incidence in thoracic surgery patients is about 5%-50%. Assuming a POD incidence of 30%, the calculation indicates that at least 144 patients need to be included.

Statistical analysis was performed using SPSS statistical software (version 25.0.0.1, IBM). Categorical variables were compared using the Chi-square test or Fisher exact test. Continuous data were expressed as mean $\pm$ variance using t-test or non-parametric tests. The variables considered meaningful and exciting in previous reports were selected for logistic regression analysis. To explore and analyze the relative risk of anesthesia-related factors in thoracic patients.

Result

A total of 175 patients who underwent elective

thoracic surgery from September 28, 2020, to November 6, 2020, were included. All patients completed postoperative follow-up, and all included data analysis. The incidence of POD was about 9.7% (17/175). POD occurred in 13 patients (9.2%) undergoing pulmonary operations, two patients (7.7%) undergoing esophageal surgery, and the highest incidence occurred in patients undergoing mediastinal surgery, with two patients (22.2%) experiencing POD. There was no significant difference in age and gender between the POD group and the non-POD group.

In the preoperative statistical analysis, the age-adjusted Charlson Comorbidity Index (aCCI) of POD patients was significantly higher (4.47 ± 1.586 VS. 3.66 ± 1.583 , $P=0.022$, **Table-1**). More non-POD patients had a high school education or above (46.2% VS. 23.4%, $P = 0.056$). The two groups had no significant differences in visual impairment, preoperative cognitive decline (Mini-cog score less than 2 points), and moderate to severe pain.

Table-1: Demographics and Preoperative Data

Variable	POD	Non-POD	P value
Gender (%)			0.315
Male	9(64.7)	82(51.9)	
Female	8(35.3)	76(48.1)	
Age(mean $\pm$ SD)	60.76 $\pm$ 7.862	56.75 $\pm$ 12.272	0.073
Mini-cog score (%)			1
> 2	12(70.6)	116(73.4)	
< 2	5(29.4)	42(26.6)	
aCCI index (mean $\pm$ SD)	4.47 $\pm$ 1.586	3.66 $\pm$ 1.583	0.022*
Body mass index (%)			0.725
< 18.5	0(0)	12(7.6)	
18.5–24.0	12(70.6)	90(57.0)	
24.0–27.9	4(23.5)	46(29.1)	
> 28	1(5.9)	10(6.3)	
Surgical site (%)			0.262
Pulmonary	13(76.5)	129(81.6)	
Esophagus	2(11.8)	24(15.2)	
Mediastinum	2(11.8)	5(3.2)	
Education background (%)			0.056
Graduate and above	0(0)	36(22.8)	
High school degree	4(23.4)	37(23.4)	
Junior high school diploma	10(58.8)	45(28.5)	
Primary school education	2(11.8)	32(20.3)	
Preschool education	0(0)	1(0.6)	
Uneducated	1(5.9)	7(4.4)	

Radiotherapy and chemotherapy, targeted therapy (%)			0.402
Yes	3(17.6)	13(8.2)	
No	14(82.4)	145(91.8)	
Previous operation history (%)			0.404
Yes	1(5.9)	4(2.5)	
No	16(94.1)	154(97.5)	
Visual impairment (%)			0.835
Yes	1(5.9)	17(10.8)	
No	16(94.1)	141(89.2)	
Preoperative pain score (%)			0.097
NRS > 4	1(5.9)	0(0)	
NRS < 4	16(94.1)	158(100)	

* $P < 0.05$

POD: Postoperative Delirium; SD: Standard Deviation; Mini-cog: Mini-Cognitive Assessment; aCCI: Age-Adjusted Charlson Comorbidity Index; NRS: Numerical Rating Scale

Table-2: Intraoperative Data in Patients with and Without Delirium

Variable	POD	Non-POD	P value
Time of operation(mean±SD)	3.36±1.528	2.83±1.496	0.134
Type of operation (%)			0.332
open thoracotomy	7(41.2)	47(29.7)	
thoracoscope	10(58.8)	111(70.3)	
Operation time over than 3 hours (%)			0.162
Yes	10(58.8)	65(41.1)	
No	7(41.2)	93(58.9)	
Transfer to ICU (%)			0.301
Yes	12(70.6)	91(57.6)	
No	5(29.4)	67(42.4)	
ASA grade (%)			0.26
I	0(0)	1(0.6)	
II	9(52.9)	109(69.0)	
III	8(47.1)	48(30.4)	0.841
Anesthetic mode (%)			
Intravenous anesthesia	0(0)	9(5.7)	
Inhalation anesthesia	8(47.1)	76(48.1)	0.295
Intravenous inhalation combined anesthesia	9(52.9)	73(46.2)	
Dosage of midazolam(mean±SD)	2.324±1.686	2.314±1.068	
Dosage of sufentanil (mean±SD)	42.618±14.350	41.750±11.194	0.768
Dosage of remifentanyl (mean±SD)	1701.7±1064.5	1291.9±714.5	0.19
Dosage of propofol (mean±SD)	415.49±400.70	370.34±443.35	0.7
Dosage of penehyclidine hydrochloride (mean±SD)	0.353±0.285	0.346±0.286	0.927
Apply penehyclidine hydrochloride (%)			0.949
Yes	11(64.7)	101(63.9)	
No	6(35.3)	57(36.1)	
Hypotension (%)			0.418
Yes	17(100)	144(91.1)	
No	0(0)	14(8.9)	
Blood pressure fluctuation by ± 20% above baseline (%)			0.265
Yes	7(41.2)	40(25.3)	
No	10(58.8)	118(74.7)	

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Transfusion (%)			0.007*
Yes	3(17.6)	2(1.3)	
No	14(82.4)	156(98.7)	
Heat preservation (%)			0.591
Yes	3(17.6)	16(10.1)	
No	14(82.4)	142(89.9)	
Vessel replacement (%)			0.025*
Yes	2(11.8)	1(0.6)	
No	15(88.2)	157(99.4)	

* $P < 0.05$

POD: Postoperative Delirium; SD: Standard Deviation; ICU: Intensive Care Unit; ASA: American Society of Anesthesiologists

Regarding surgical methods, POD incidence in patients undergoing thoracotomy was higher than in thoracoscopic surgery (12.3% VS. 8.2%, $P=0.332$), but there was no statistical difference. However, when vascular replacement was involved, there was a significantly higher incidence of POD (66.7% VS. 8.7%, $P = 0.025$). Similarly, POD incidence was also high in transfusion patients (60% VS. 8.2%, $P = 0.007$). There were no significant differences in the methods of anesthesia, anesthetic, blood pressure fluctuation of more than $\pm 20\%$ of baseline, and heat preservation. The results are shown in **Table-2**.

After surgery, 55.4% of the patients had moderate and severe pain. Although the indwelling catheter had

no significant effect on POD, POD patients retained the urinary tube longer after surgery (3.55 ± 2.622 VS. 2.09 ± 1.050 , $P = 0.011$, **Table-3**). There were no significant differences in ambulation time or incidence of complications.

In this study, factors with a P value less than 0.1 were included in the analysis to establish a binary logistic regression model, and the goodness of fit index is pretty good. The results showed that the risk of POD increased by about 0.811 for every one-point increase in the aCCI index (OR 1.811, 95% CI 1.058-3.103; $P=0.030$, **Table-4**), POD risk increases eleven fold for each day of delayed ambulation (OR 12.303, 95% CI 2.670-56.686; $P=0.001$).

Table-3: Postoperative Data in Patients with and Without Delirium

Variable	POD	Non-POD	P value
Postoperative pain score (%)			0.418
NRS > 4	11(64.7)	86(54.4)	
NRS < 4	6(35.3)	72(45.6)	
Ambulation time (mean $\pm$ SD)	2.82 $\pm$ 2.43	1.81 $\pm$ 1.035	0.08
Indwelling catheter (%)			0.51
Yes	11(64.7)	119(75.3)	
No	6(35.3)	39(24.7)	
Catheter indwelling time (mean $\pm$ SD)	3.55 $\pm$ 2.622	2.09 $\pm$ 1.050	0.011*
Complication (%)			0.141
Yes	4(23.5)	14(8.9)	
No	13(76.5)	144(91.1)	
LOS (mean $\pm$ SD)	20.71 $\pm$ 22.039	13.85 $\pm$ 11.840	0.09

* $P < 0.05$

POD: Postoperative Delirium; SD: Standard Deviation; NRS: Numerical Rating Scale; LOS: Length of Stay

Table-4: Results of Logistic Regression Analysis

Variable	OR	95%CI	P value
aCCI index	1.811	1.058-3.103	0.03
Ambulation time	12.303	2.670-56.686	0.001

OR: Odds Ratio; CI: Confidence Interval; aCCI: age-adjusted Charlson Comorbidity Index

Table-5: Exploratory Analysis of Anesthesia-Related Factors

Variable	POD	Non-POD	P value	RR	95% CI
Thoracoscope					
ASA grade (%)			0.215	2.828	0.763-10.479
I~II	5(50.0)	82			
III	5(50.0)	29			
Operation time over than 3 hours (%)			1	1.095	0.292-4.108
Yes	4(40.0)	42(37.8)			
No	6(60.0)	69(62.2)			
Apply penehyclidine hydrochloride (%)			0.795	1.532	0.376-6.245
Yes	7(70.0)	67(60.4)			
No	3(30.0)	44(39.6)			
Blood pressure fluctuation by ± 20% above baseline (%)			0.242	2.7	0.730-9.991
Yes	5(50.0)	30(27)			
No	5(50.0)	81(73)			
Postoperative pain score (%)			1	0.914	0.250-3.334
NRS > 4	5(50)	58(52.3)			
NRS < 4	5(50)	53(47.7)			
Heat preservation (%)			1	0.917	0.107-7.878
Yes	1(10.0)	12(10.8)			
No	9(90.0)	99(89.2)			
Open Thoracotomy					
ASA grade (%)			1	1.105	0.222-5.509
I~II	4(57.1)	28(59.6)			
III	3(42.9)	19(40.4)			
Operation time over than 3 hours (%)			0.108	6.261	0.699-56.104
Yes	6(85.7)	23(48.9)			
No	1(14.3)	24(51.1)			
Apply penehyclidine hydrochloride (%)			0.41	0.51	0.100-2.596
Yes	4(57.1)	34(72.3)			
No	3(42.9)	13(27.7)			
Blood pressure fluctuation by ± 20% above baseline (%)			1	1.48	0.249-8.797
Yes	2(28.6)	10(21.3)			
No	5(71.4)	37(78.7)			
Heat preservation (%)			0.169	4.3	0.622-29.731
Yes	2(28.6)	4(8.5)			
No	5(71.4)	43(91.6)			
Transfusion (%)			0.012*	16.875	2.149-132.508
Yes	3(42.9)	2(4.3)			
No	4(57.1)	45(95.7)			
Vessel replacement (%)			0.041*	18.4	1.406-240.837
Yes	2(28.6)	1(2.1)			
No	5(71.4)	46(97.9)			
Postoperative pain score (%)			0.239	4.071	0.453-36.587
NRS > 4	6(85.7)	28(59.6)			
NRS < 4	1(14.3)	19(40.4)			

* P<0.05

POD: Postoperative Delirium; RR: Relative Risk; CI: Confidence Interval; ASA: American Society of Anesthesiologists; NRS: Numerical Rating Scale

The relative risk of anesthesia-related factors was calculated for patients undergoing thoracoscopic surgery and thoracotomy. None of the patients undergoing endoscopic surgery underwent blood transfusion or vascular replacement. Blood transfusion (RR 16.875, 95% CI 2.149-132.508; $P=0.012$, **Table-5**) may be a risk factor for POD in patients undergoing Open thoracotomy, but logistic regression was not statistically significant.

Discussion

In this study, POD occurred in 9.7% of thoracic surgery patients, with the highest incidence of mediastinal operation (28.57%). The incidence of POD in this study was lower than that reported in the literature, possibly for two reasons: First, advancements in surgical technology have led to the widespread adoption of minimally invasive surgical techniques, particularly in thoracic surgery. Using a thoracoscope reduces the incidence of POD by approximately 30%[10], while the duration of the surgical procedure is also significantly shortened[6], thereby decreasing the likelihood of POD. The second significant difference between this study and previous ones is that the population being studied is dissimilar. In this case, the elderly patients with a high incidence of POD make up 31.43% of the sample, while the lung surgery patients with a lower incidence of POD account for 81% of the cases. Although the sample size has expanded, the probability of POD incidence may not rise for the above reasons. Nevertheless, despite the low incidence, the study still yields positive results.

The analysis of preoperative factors showed that aCCI index was a risk factor for POD. Previous research has indicated that individuals with preoperative complications, including chronic obstructive pulmonary disease and cerebrovascular disease, are more likely to develop POD [5,8,9]. Furthermore, certain diseases have been identified as predictors of POD in various populations; for example, lung disease and cerebrovascular disease in colorectal cancer patients are significant predictors [13]. As POD prevention guidelines have been updated, comprehensive POD risk factor assessment to screen high-risk patients in the subsequent diagnosis and treatment of refined target management is recommended for patients with multiple comorbidities

[14]. Charlson Comorbidity Index(CCI) is the most widely used comorbidities index. The index is mainly selected and weighted according to the relationship between the included diseases and mortality. It can be combined with age to form the age-comorbidities index, which is significantly related to many prognostic outcomes, such as mortality, disability, readmissions, length of stay, etc [15]. According to the findings of this research, the POD risk increases about once for every point increase in the aCCI index. Combined with the recommendations of the guidelines, individual assessment of patients is an essential means of risk screening. Emphasizing the simultaneous consideration of patients' multiple conditions and the severity of their disease while employing relevant metrics to quantify them holds significant implications for subsequent preventative measures and therapeutic interventions.

In the analysis of postoperative factors, the univariate analysis found that POD patients retained urinary tubes longer after surgery, and the ambulation time was later. Logistic regression found that the ambulation time had the most critical effect on POD. Mobilization as soon as possible after surgery is the main content of Enhanced recovery after surgery (ERAS) for thoracic surgery patients [16]. The results of this investigation indicate that attending to patients' postoperative recovery may serve as a means of evaluating their risk of developing POD and that encouraging early ambulation may help to decrease the risk of POD occurring. Consequently, the POD prevention regimen for patients undergoing thoracic surgery should incorporate ERAS as a significant consideration.

In the analysis of intraoperative factors, only blood transfusion and vascular replacement increased POD risk, and no significant effect was shown in multivariate logistic regression. No statistically significant differences were detected after conducting a univariate analysis of anesthesia factors. However, an exploratory analysis utilized the relative risk to explore this area further. Factors related to anesthesia were investigated for patients undergoing thoracoscopic surgery and thoracotomy, as no patients in the thoracoscopic group proceeded with blood transfusion or vascular replacement. The results showed that

blood transfusion would significantly increase the risk of POD in patients undergoing open thoracotomy, similar to some previous studies [17]. In clinical practice, blood transfusion is usually a clinical decision made after weighing the benefits and risks. When patients need transfusion treatment, it often means massive blood loss, oxygen supply, and demand imbalance, etc. Because laboratory tests were not included in this study, the potential relationship between hemoglobin levels and POD in patients undergoing thoracotomy is unclear. Therefore, further studies are needed to explore the relationship between hemoglobin levels, blood transfusion, and postoperative delirium to facilitate the subsequent development of appropriate transfusion indications for patients undergoing thoracic surgery.

This study also has some limitations. First, the sample size is small, and the POD incidence is lower than expected. Second, this study did not evaluate the severity of POD and could not analyze the relationship between POD risk factors and POD severity. Third, this study did not collect laboratory test results such as inflammatory factors or hemoglobin concentration, which might predict POD.

Conclusion

This study found that in patients undergoing thoracic surgery, aCCI index and prolonged postoperative activity were risk factors for POD. Intraoperative blood transfusion may increase POD risk in patients undergoing thoracotomy. The relationship between anesthesia-related factors and POD still needs to be further explored.

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