Clinical Interventions in Aging

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ORIGINAL RESEARCH

A Prospective Nested Case-Control Study of Risk Factors for Postoperative Delirium in Elderly Patients with Colorectal Cancer

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Video Abstract

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Purpose: The objective of this study is to investigate the risk factors associated with postoperative delirium (POD) in elderly patients diagnosed with colorectal cancer (CRC).

Patients and Methods: This prospective nested case-control study included elderly patients who underwent CRC surgery at Shanxi Provincial Cancer Hospital between May 2022 and September 2023. A propensity score matching (PSM) method was employed to match patients by age and sex. Univariate and multivariate logistic regression analyses were conducted to identify independent risk factors for POD among elderly patients with CRC.

Results: A total of 443 patients were enrolled, among them, 70 (15.8% of all patients, age: 69.5[64, 73], 55 [78.6%] males) developed POD and 373 did not develop POD (84.2% of all patients, age: 67[62, 71], 234 [62.7%] males). Following PSM at a 1:3 ratio, 70 POD patients and 210 age- and sex-matched non-POD patients were selected for further analysis. The POD group exhibited a significantly higher sleep quality score (9 [6, 15] vs 7.5 [3, 12], P = 0.004), greater intraoperative infusion volume (2041.43±724.37 vs 1814.05 ±653.83, P = 0.015), and elevated peak pain levels post-surgery (1 [0, 2] vs 1 [0, 1], P = 0.001). Univariate and multivariate logistic regression analyses identified higher education level (OR: 0.503 [0.259–0.977]) as an independent factor associated with lower POD risk, whereas higher sleep quality scores (OR: 1.103 [1.040–1.171]) and increased peak pain levels post-surgery (OR: 1.727 [1.295-–2.304]) were identified as independent risk factors.

Conclusion: Elevated peak postoperative pain levels, lower education levels, and sleep dysfunction or disturbance are independent risk factors for developing POD.

Keywords: colorectal cancer, postoperative delirium, risk factors, elderly, sleep quality, pain level, prospective nested case-control study

Introduction

Colorectal cancer (CRC) is a common malignant tumor of the digestive system in clinical practice, and it currently ranks third in the global cancer incidence spectrum and is the second leading cancer type in the cause of death.[1] The incidence and mortality of this disease increase with age and gradually increase with growth.[2] Surgery is the preferred method for the treatment of CRC, studies have shown that surgery could improve patient survival time, and reduce mortality, but it can also lead to a series of postoperative complications. Among them, postoperative delirium (POD) is one of the commonly observed complications, and its prevalence ranged from 7.7% to 25.5% according to previous studies.[3,4] The presentation of POD is a transient organic psychoneurological syndrome characterized by sudden onset, cognitive impairment, sleep-wake cycle disruption, decreased attention and consciousness, and increased/reduced mental activity.[5] Elderly patients are the most susceptible to POD of all ages.[6] With the improvement of China's development level and the trend of population aging, POD has become a thorny problem faced by surgeons in elderly CRC patients.

Received: 22 November 2024
Accepted: 15 May 2025
Published: 21 May 2025

Compared with other types of surgeries, such as orthopedics and cardiac and vascular surgery,[7–9] there are currently few studies focused on the occurrence of delirium after CRC surgery in the elderly,[10,11] moreover, there were many differences among different studies, various settings of exploration focus could affect the independent influencing factors of POD in elderly CRC surgery patients, for example, several studies have shown that prehabilitation could effectively reduce the incidence of POD in elderly CRC patients, however the presence of prehabilitation may affect the exploration of risk factors.[12,13] Even though, there were still some factors have been reported to be associated with POD in patients received CRC surgeries, Sun et al exhibited that postoperative C-reactive protein is an independent indicator for POD.[14] Mosk et al revealed Low skeletal muscle mass was a risk factor for POD in CRC patients,[15] however, these factors have not been examined specifically in the elderly CRC patient group. In addition, POD in elderly patients with CRC will prolong the patient's hospitalization, increase the incidence of dementia and mortality in elderly patients,[10,16] and place a heavy burden on hospitals and families. Therefore, exploration of risk factors and actively preventing POD occurrence is of ultimate importance and requires more detailed research.

Therefore this study aims to adopt a prospective nested case-control study analysis to identify the risk factors for POD in elderly patients with CRC, thereby providing reliable indicators for the management of patients at high risk for POD.

Material and Methods

Study Design and Patients

Elderly patients who underwent CRC surgery at the Shanxi Provincial Cancer Hospital between May 2022 and September 2023 were prospectively selected for this nested case-control study. The inclusion criteria were: 1) patients aged 60 years or above; 2) planning to receive CRC surgery; 3) patients with American Society of Anesthesiologists (ASA) grade I to III; 4) patients able to tolerate anesthesia; 5) patients who volunteer to participate this study. The exclusion criteria were: 1) patients combined with severe neurological diseases or cerebral infarction; 2) long-term use of psychotropic drugs (including alcoholism); 3) preoperative MoCA score < 23; 4) preoperative MMSE score < 23; 5) confirmed or suspected abuse or long-term use of narcotic sedation and analgesia Drug users; 6) have severe visual or hearing or language impairment; 7) have severe organ dysfunction. This study was approved by the Ethics Committee of Shanxi Provincial Cancer Hospital (Approval ID: ChiCTR2200063584), and written informed consent was obtained from all participants. This study complies with the Declaration of Helsinki.

Procedures

According to the 2017 European Society of Anesthesiology recommendations, POD occurs from the patient's recovery period from anesthesia to the fifth postoperative day.[6] This study will assess patients from the moment they enter the recovery room after surgery, and will be assessed at least once a day for 7 consecutive days. Since the 3D-CAM used in this study does not apply to patients admitted to the intensive care unit, if the patient was admitted to the intensive care unit after surgery, the case was also excluded.

The Montreal Cognitive Assessment (MoCA) and Mini Mental State Examination (MMSE) were used to evaluate the cognitive function of all participants, the Pittsburgh Sleep Quality Index (PSQI) was used to assess the sleep quality score, the Visual Analogue Scale (VAS) was used to evaluate the post-surgery pain level, and the 3D-Confusion Assessment Scale (3D-CAM) was used to detect the presence of POD, and the Richmond Agitation-Sedation Scale (RASS) score was used to assess delirium subtypes (hypoactive, hyperactive, and mixed subtypes) (Supplementary Table 1).

This study includes the general characteristics of POD in CRC (age, gender, education level, BMI, and sleep quality score assessed by PSQI), disease-related characteristics (Central nervous system [CNS] disease history), surgery-related characteristics (surgery method, surgery time, anesthesia time, intraoperative infusion volume, intraoperative blood transfusion volume, intraoperative hypotension duration, intraoperative hypertension duration, Intraoperative blood pressure deviation duration, and preventive stoma condition), and post-surgery characteristics (Peak pain level after surgery assessed by VAS). History of CNS diseases includes Alzheimer's disease, epilepsy, encephalitis and meningitis, cerebral infarction, cerebral hemorrhage, cerebral aneurysm, spinal cord disease, etc. The surgical method is divided into laparoscopic surgery and open surgery with or without pneumoperitoneum, with

pneumoperitoneum for laparoscopic surgery and without pneumoperitoneum for open surgery. The surgery time starts from the incision to the end of the stitching. The anesthesia time is from the beginning of induction to the end of extubation. The intraoperative infusion volume is recorded on a special inflow and output record sheet. The record sheet contains key information such as the patient's basic information (such as name, bed number, surgery date, etc), infusion time, infusion volume, and type of infusion. When recording intraoperative infusion volumes, milliliters (mL) are used uniformly as units to ensure the accuracy and comparability of data. In this study, the total amount of fluid transfused during various intraoperatives was used. Intraoperative hypotension duration was recorded to be greater than 5 minutes, and systolic blood pressure was recorded to be ≥20% lower than the baseline value or systolic blood pressure < 90mmHg. The systolic blood pressure recorded for more than 5 minutes with intraoperative hypertension duration increased by ≥20% from the basal value. Therefore, a total of 16 variables were included for further risk factor analysis. The patient's general information and perioperative-related indicators were obtained by consulting the electronic medical record system or on-site records.

Experienced anesthesiologists used sufentanil for intraoperative analgesia management. No neural block technology was used. Patient controlled intravenous analgesia (PCIA) was used after surgery. The analgesic pump was formulated with 2.0 μg/kg sufentanil mixed with 100 mL saline, background infusion speed 2 mL/h, bolus dose 2 mL, lockout time 15 min.

Sample Size Calculation

An event per variable (EPV) of 10 in binary logistic regression analysis is selected in the present study,[17] 16 characteristics were included, therefore the sample size should be at least 160 cases.

Statistical Analysis

All data were analyzed using STATA (version 17.0) and R software (version 4.3.3). For continuous variables, normality and homogeneity tests were conducted, if the data follow a normal distribution, continuous variables are presented as mean ± SD and compared using Student's *t*-test, while non-normally distributed variables are presented as median (interquartile range, IQR) and compared using Mann–Whitney *U*-test. Categorical variables are expressed as numbers and percentages, and the chi-squared (X^2) test was used for comparison between groups. To improve the credibility, an age and sex-matched propensity score matching (PSM) based on the nearest neighbor method was used to eliminate confounding factors, the ratio was set at 1:3, and the caliper value was 0.2. Univariate analysis and multivariate logistic regression were used to analyze the potential risk factors, features with univariate P<0.2 were included in the multivariate analysis, and features with P<0.05 after the multivariate analysis were defined as the independent risk factors. Also, subgroup analyses were performed based on the postoperative pain level and CNS involvement history. A two-tailed P<0.05 indicates statistically significant difference in this study.

Results

Demographic Characteristics

A total of 443 patients were included, including 373 patients (84.2%) who did not develop POD and 70 patients (15.8%) who developed POD, more specifically, among the 70 patients, there were 33, 21, and 16 patients classified as hypoactive, hyperactive, and mixed delirium subtypes. Before PSM, there were significant age differences (P = 0.007), gender (P = 0.011), education level (P = 0.030), sleep quality score (P = 0.003), intraoperative infusion volume (P = 0.009), and peak pain level after surgery (P = 0.002) between the non-POD and POD groups (Table 1). However, the significant differences in age, gender, and education level among the two groups were eliminated after PSM. We still observed that patients in the POD group had a higher PSQI score (9 [6, 15] vs 7.5 [3, 12], P = 0.004), indicating they had worse sleep quality, the Intraoperative infusion volume (2041.43±724.37 vs 1814.05±653.83, P = 0.015), and peak pain level after surgery (1 [0, 2] vs 1 [0, 1], P = 0.001) were also higher in patients at POD group (Table 2).

https://doi.org/10.2147/CIA.S507668

Table 1 Baseline Characteristics Before PSM

Variables	Non-POD Group (N= 373)	POD Group (N=70)	Hypoactive Subtype (N=33)	Hyperactive Subtype (N=21)	Mixed Subtype (N=16)	t/Z/χ 2 value	P value
Age, years	67 [62, 71]	69.5 [64, 73]	69.58±5.57	69.86±6.73	67.38±5.38	7.392	**0.007**
Male, n	234 (80.97%)	55 (19.03%)	22 (40%)	19 (34.55%)	14 (25.45%)	6.5182	**0.011**
BMI, kg/m^2	23.69±3.16	23.43±3.31	23.95±3.91	23.41±2.62	22.38±2.63	0.6272	0.531
Education Level, n						4.73	**0.03**
Junior high school and below	226 (81.29%)	52 (18.71%)	22 (42.31%)	17 (32.69%)	13 (25%)		
High school and above	147 (89.09%)	18 (10.91%)	11 (61.11%)	4 (22.22%)	3 (16.67%)		
Sleep quality score, n	8 [3, 11]	9 [6, 15]	8 [5, 15]	12 [6, 15]	9 [6, 14]	9.057	**0.003**
Anesthesia duration, min	169 [134, 200]	175.5 [150, 218]	174.00 [160.00, 220.00]	175.00 [153.00, 240.00]	182.50 [137.50, 210.00]	3.522	0.061
Operation duration, min	135 [104, 180]	145 [120, 180]	152.64±61.72	159.52±70.79	149.56±64.36	3.257	0.071
Combined history of central nervous system, n	72 (80.90%)	17 (19.10%)	9 (52.94%)	4 (23.53%)	4 (23.53%)	0.9115	0.34
Surgical approach, n						0.0095	0.922
Endoscopic	275 (84.10%)	52 (15.90%)	24 (46.15%)	16 (30.77%)	12 (23.08%)		
Non-endoscopic	98 (84.48%)	18 (15.52%)	9 (50%)	5 (27.78%)	4 (22.22%)		
Blood transfusion during the operation, n	29 (85.29%)	5 (14.71%)	2 (40%)	1 (20%)	2 (40%)	0.0332	0.855
Intraoperative hypotension duration, min	5 [0, 15]	5 [0, 20]	5 [0, 10]	5 [0, 20]	0 [0, 30]	0.52	0.471
Intraoperative hypertension duration, min	0 [0, 0]	0 [0, 0]	0 [0, 0]	0 [0, 0]	0 [0, 0]	0.945	0.331
Intraoperative blood pressure deviation duration, min	10 [0, 20]	10 [0, 20]	10 [0, 20]	10 [0, 20]	2.5 [0, 30]	0.006	0.941
Intraoperative infusion volume, mL	1750 [1500, 2000]	2000 [1500, 2500]	1800.00 [1400.00, 2250.00]	2250.00 [1500.00, 2500.00]	2250.00 [1500.00, 2750.00]	6.749	**0.009**
Peak pain level after surgery, n	1 [0, 1]	1 [0, 2]	1 [1, 2]	1 [0, 2]	2 [1, 3]	9.921	**0.002**
Preventive stoma, n	70 (82.35%)	15 (82.35%)	6 (40%)	7 (46.67%)	2 (13.33%)	0.2693	0.604

Notes: Values are n (%), mean±SD, and median [lower quartile, upper quartile]. The bold P values indicate $P < 0.05$.
Abbreviation: BMI, body mass index.

Table 2 Baseline Characteristics After PSM

Variables	Non-POD Group (N=210)	POD Group (N=70)	Hypoactive Subtype (N=33)	Hyperactive Subtype (N=21)	Mixed Subtype (N=16)	t/Z/χ 2 value	P value
Age, years	69 [63, 72]	69.5 [64, 73]	69.58±5.56	69.86±6.72	67.38±5.37	0.881	0.348
Male, n	167 (75.23%)	55 (24.77%)	22 (40%)	19 (34.55%)	14 (25.45%)	0.0290	0.865
BMI, kg/m^2	23.62±3.08	23.43±3.31	23.95±3.91	23.41±2.62	22.38±2.63	0.4464	0.656
Education Level, n						2.5837	0.108
Junior high school and below	134 (72.04%)	52 (27.96%)	22 (42.31%)	17 (32.69%)	13 (25%)		
High school and above	76 (80.8%)	18 (19.15%)	11 (61.11%)	4 (22.22%)	3 (16.67%)		
Sleep quality score, n	7.5 [3, 12]	9 [6, 15]	8 [5, 15]	12 [6, 15]	9 [6, 14]	8.433	**0.004**
Anesthesia duration, min	171.5 [135, 205]	175.5 [150, 218]	174.00 [160.00, 220.00]	175.00 [153.00, 240.00]	182.50 [137.50, 210.00]	1.974	0.160
Operation duration, min	140 [107, 180]	145 [120, 180]	152.64±61.72	159.52±70.79	149.56±64.36	1.423	0.233
Combined history of central nervous system, n	41 (70.69%)	17 (29.31%)	9 (52.94%)	4 (23.53%)	4 (23.53%)	0.7249	0.395
Surgical approach, n						0.0063	0.937
Endoscopic	157 (75.12%)	52 (24.88%)	24 (46.15%)	16 (30.77%)	12 (23.08%)		
Non-endoscopic	53 (74.65%)	18 (25.35%)	9 (50%)	5 (27.78%)	4 (22.22%)		
Blood transfusion during the operation, n	9 (64.29%)	5 (35.71%)	2 (40%)	1 (20%)	2 (40%)	0.9023	0.342
Intraoperative hypotension duration, min	0 [0, 15]	5 [0, 20]	5 [0, 10]	5 [0, 20]	0 [0, 30]	0.994	0.319
Intraoperative hypertension duration, min	0 [0, 0]	0 [0, 0]	0 [0, 0]	0 [0, 0]	0 [0, 0]	1.524	0.217
Intraoperative blood pressure deviation duration, min	10 [0, 20]	10 [0, 20]	10 [0, 20]	10 [0, 20]	2.5 [0, 30]	0.115	0.734
Intraoperative infusion volume, mL	1814.05±653.83	2041.43±724.37	1800.00 [1400.00, 2250.00]	2250.00 [1500.00, 2500.00]	2250.00 [1500.00, 2750.00]	−2.4516	**0.015**
Peak pain level after surgery, n	1 [0, 1]	1 [0, 2]	1 [1, 2]	1 [0, 2]	2 [1, 3]	10.963	**0.001**
Preventive stoma, n	39 (18.6%)	15 (21.4%)	6 (40%)	7 (46.7%)	2 (13.3%)	0.2753	**0.600**

Notes: Values are n (%), mean±SD, and median [lower quartile, upper quartile]. The bold P values indicate $P < 0.05$.

https://doi.org/10.2147/CIA.S507668

Univariate and Multivariate Logistic Regression Analysis of Patients Developing POD

Univariate analysis was performed in the POD group and the non-POD group after matching. The results showed that 8 features exhibited P < 0.2 and may associated with the POD development, among them, a higher education level (OR: 0.610 [0.333–1.118], P = 0.110), higher intraoperative hypertension duration (OR: 0.965 [0.918–1.015], P = 0.168) are factors potentially associated with POD risk; while higher sleep quality score (OR: 1.092 [1.034–1.154], P = 0.002), anesthesia duration (OR: 1.004 [0.999–1.008], P = 0.107), operation duration (OR: 1.004 [0.999–1.008], P = 0.150), intraoperative hypotension duration (OR: 1.013 [0.997–1.028], P = 0.103), intraoperative infusion volume (OR: 1.000 [1.000–1.001], P = 0.016), and peak pain level after surgery (OR: 1.730 [1.312–2.282], P < 0.001) were risk factors (Table 3).

After multivariate analysis, a higher education level (OR: 0.503 [0.259–0.977], P = 0.042) was revealed to be associated with a decreased risk of developing POD, while a higher sleep quality score (OR: 1.103 [1.040–1.171], P = 0.001) and peak pain level after surgery (OR: 1.727 [1.295–2.304], P < 0.001) were independent risk factors (Table 4).

Subgroup Analysis

PSM-based subgroup analysis was further performed in patients without a history of CNS disease, a total of 222 patients were finally included, and the multivariate analysis showed similar results in all participant groups, higher education level (OR: 0.46

Table 3 Univariate Logistic Regression Analysis of POD Occurrence After PSM

variables	B	SE	Z	OR	P
Age	0.015	0.023	0.680	1.016 [0.971–1.062]	0.499
Male	−0.058	0.338	−0.170	0.944 [0.487–1.830]	0.865
BMI	−0.020	0.044	−0.450	0.980 [0.899–1.069]	0.654
Education level (high school and above)	−0.494	0.309	−1.600	0.610 [0.333–1.118]	0.110
Sleep quality score	0.088	0.028	3.160	1.092 [1.034–1.154]	**0.002**
Anesthesia duration	0.004	0.002	1.610	1.004 [0.999–1.008]	0.107
Operation duration	0.003	0.002	1.440	1.004 [0.999–1.008]	0.150
Combined history of central nervous system	0.279	0.329	0.850	1.322 [0.694–2.518]	0.395
Surgical approach (endoscopic)	−0.025	0.316	−0.080	0.975 [0.525–1.813]	0.937
Blood transfusion during the operation	0.541	0.576	0.940	1.718 [0.556–5.310]	0.347
Intraoperative hypotension duration	0.013	0.008	1.630	1.013 [0.997–1.028]	0.103
Intraoperative hypertension duration	−0.035	0.026	−1.380	0.965 [0.918–1.015]	0.168
Intraoperative blood pressure deviation duration	0.005	0.007	0.670	1.005 [0.991–1.020]	0.504
Intraoperative infusion volume	0.000	0.000	2.410	1.000 [1.000–1.001]	**0.016**
Peak pain level after surgery	0.548	0.141	3.880	1.730 [1.312–2.282]	**<0.001**
Preventive stoma	0.179	0.341	0.520	1.196 [0.613–2.333]	0.600

Note: The bold P values indicate P < 0.05.

Table 4 Multivariate Logistic Regression Analysis of POD Occurrence

Variables	B	SE	Z	OR	P
Education level (high school and above)	−0.686	0.338	−2.03	0.503 (0.259–0.977)	**0.042**
Sleep quality score	0.098	0.030	3.25	1.103 (1.040–1.171)	**0.001**
Anesthesia duration	0.003	0.009	0.37	1.003 (0.986–1.021)	0.714
Operation duration	−0.002	0.009	−0.26	0.998 (0.980–1.016)	0.797
Intraoperative hypotension duration	0.007	0.009	0.83	1.007 (0.990–1.025)	0.408
Intraoperative hypertension duration	−0.031	0.029	−1.08	0.969 (0.915–1.026)	0.282
Intraoperative infusion volume	0.000	0.000	1.73	1.000 (1.000–1.001)	0.083
Peak pain level after surgery	0.546	0.147	3.72	1.727 (1.295–2.304)	**<0.001**

Note: The bold P values indicate P < 0.05.

Table 5 Multivariate Logistic Regression Analysis of POD Occurrence in Patients without Central Nervous System Involvement After PSM

Variables	N=222	
	OR (95% CI)	P
Education level (High school and above)	0.46 (0.21, 0.98)	**0.045**
Sleep quality score	1.14 (1.06, 1.22)	**<0.001**
Peak pain level after surgery	1.75 (1.26, 2.42)	**0.001**

Note: The bold P values indicate P < 0.05.

Table 6 Multivariate Logistic Regression Analysis of POD Occurrence in Patients with Mild to Severe Pain After PSM

Variables	N=204	
	OR (95% CI)	P
Sleep quality score	1.23 (1.08, 1.41)	**0.002**
Intraoperative hypotension duration	1.03 (1.00, 1.06)	**0.026**

Note: The bold P values indicate P < 0.05.

[0.21–0.98], P = 0.045) was in association with lower POD risk, higher sleep quality score (OR: 1.14 [1.06–1.22], P < 0.001) and Peak pain level after surgery (OR: 1.75 [1.26–2.42], P = 0.001) were independent risk factors (Table 5).

In patients who suffered post-surgery pain, after PSM, 204 patients were included, and higher education level was no longer associated with decreased POD risk, but a higher sleep quality score (OR: 1.23 [1.08–1.41], P = 0.002) remained an independent risk factor, and intraoperative hypotension duration (OR: 1.03 [1.00–1.06], P = 0.026) was found as a new independent risk factor (Table 6).

Discussion

The study results showed a 15.8% incidence of POD in elderly patients with CRC. After PSM, univariate analysis and multivariate analysis, higher education level was found in association with lower POD risk, while sleep dysfunction or disturbance and peak pain level after surgery were risk factors for POD development. Subgroup analysis of patients without past CNS diseases and patients without post-surgery pain showed similar results, higher sleep quality scores and peak pain levels after surgery remained independent risk factors.

Firstly, compared with the incidence rates of 13.2% and 10.9% obtained in previous studies by Kim H and Tei M, the results derived from this study are relatively close to them, indicating the results are comparable with previous findings.[10,18] Both univariate and multivariate analyses showed that worse sleep quality is associated with a greater risk of POD. These results are in alignment with the previous studies, Ou-Yang et al showed that poor sleep quality on the night of the operative day was independently associated with increased POD risk;[19] while Zheng et al found that preoperative sleep quality was strongly associated with POD in patients received non-cardiac surgery.[20] The following aspects can partially explain this phenomenon. First, due to experiencing insomnia or sleep deprivation, the brain cannot get adequate rest and recovery, and long-term sleep deprivation can lead to brain dysfunction.[21] Secondly, patients with poor sleep quality may also experience circadian rhythm reversal and sleep fragmentation, which can interfere with the brain's biological clock mechanism.[22] In addition, these patients may have pre-operative impairments in cognitive function or emotion regulation and are therefore more likely to develop POD following the traumatic stimulation of major surgery. These also reflect on the subgroup analysis results, to our knowledge, there is currently no study focused on the CNS involvement history and its association with POD, in the present study, patients without CNS involvement and patients who suffered postoperative pain, poor sleep quality remained a risk factor for POD occurrence.

Postoperative pain is another independent risk factor for POD occurrence, according to a previous study, Hao et al concluded that postoperative pain is a risk factor for POD and is strongly associated with the prognosis of hip fracture patients.[23] Pain may trigger a neuroinflammatory response, including increased neuronal excitability and release of inflammatory mediators. These inflammatory mediators may interfere with neurotransmission and brain function, thereby contributing to the development of POD. At the same time, postoperative pain itself is a type of physical stress response, which may trigger changes in the patient's emotions and cognition. These emotional changes, such as emotional instability, anxiety, and fear, are closely related to the occurrence of delirium.[24] Subgroup analysis was further performed on patients without pain, after PSM, and multivariate analysis, the results revealed that prolonged intraoperative hypotension duration was a risk factor in this population, this finding was in alignment with some previous studies, Chen found intraoperative hypotension could contribute to the occurrence of Burst suppression and further associated with POD,[25] Wang et al revealed that Intraoperative hypotension was associated with POD in elderly patients receiving laryngectomy,[26] and the underlying reason of POD and intraoperative hypotension could be partially explained by reduced cerebral perfusion[27,28] and pre-existing vulnerabilities such as cerebrovascular disease or other comorbidities in elderly patients, although also inclusion criteria strictly ruled out patients with past CNS disease history, the elderly patients are still in a more fragile status.[29,30]

Education level is another important factor associated with delirium, Oliveira showed education level was associated with a decreased risk of delirium (OR = 0.81) in elderly patients who received cardiac surgery;[31] while Wang et al revealed that low education level was a risk factor for POD development.[26] This study also showed that patients with higher levels of education had lower rates of POD. Additionally, other studies indicate that individuals with higher levels of education may have greater cognitive reserve by promoting the growth of synapses and generating new compensatory cognitive strategies compared with patients with lower levels of education. To provide a protection mechanism. In addition, they also have stronger psychological coping skills and can better deal with stress, anxiety and fear.[32] These patients are typically more knowledgeable about postoperative conditions and are willing and able to participate in postoperative care and rehabilitation plans actively. All these factors help prevent the occurrence of POD.[33,34]

Although this study adopted a prospective nested case-control study, and the research subjects focused on elderly patients with CRC who underwent surgery and can more truly reflect the incidence of POD in elderly patients with CRC. However, this study still has several limitations, Firstly, the sample size is relatively small, and all participants were from a single center, further large-scale and multi-center cohorts are necessitated for validation of our findings; secondly, this study only focused on the short-term prognosis (POD), the long term prognosis was not included for analysis; finally, this study excluded ICU-admitted patients and patients with pre-operative cognitive impairment, which could lead to potential selection bias and restrict our findings in a shallower population, however, this strict inclusion criteria ensure a relatively homogenous study population and minimize confounding factors.

Conclusion

This study enrolled revealed that elevated peak postoperative pain levels, lower and poorer sleep quality are independent risk factors for developing POD, while a higher education level was associated with decreased risk of POD.

Data Sharing Statement

All data generated or analysed during this study are included in this published article.

Ethics Approval and Consent to Participate

The study was approved by the Ethics Committee of Shanxi Hospital Affiliated to Cancer Hospital, Chinese Academy of Medical Sciences (Shanxi Province Cancer Hospital) [202229 (ChiCTR2200063584)]. All participants were informed about the study protocol and provided written informed consent to participate in the study.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically

reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

The study was supported by Shanxi Provincial Department of Science and Technology, Shanxi Province Science and Technology Cooperation and Exchange Special Project (Project Number: 202204041101025). The funders had no role in study design, data collection, and analysis, decision to publish, or preparation of the manuscript.

Disclosure

The authors declare that they have no competing interests in this work.

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