

Postoperative Delirium (POD) in Cancer Patients its Incidence and Risk Factors a Prospective Observational Study

SHAH QASIM¹, XU-YING LI², TAO WEI³, KHALID KHAN⁴, QAISAR KHAN⁵

¹Shangla College of Nursing & Health Sciences Alporai, Shangla KPK, Pakistan

²Xiangya School of Nursing, Central South University, Changsha, China

³Hunan Cancer Hospital, Changsha, China

⁴United college of Nursing, Saidu Sharif, Swat, Pakistan

⁵Department of Microbiology, Abdul Wali Khan University, Mardan, KPK, Pakistan

Corresponding author: Shah Qasim, Email: qasim.usn@gmail.com

ABSTRACT

Background: In cancer patients, surgery is an essential part of the multimodality treatment to remove solid tumors and nearly 50% of the cancer patients underwent surgery for the treatment of cancer usually experienced post-operative delirium (POD). Currently, screening for delirium in the surgical wards at many cancer hospitals in China isn't the component of everyday clinical care.

Objectives: This study aims to examine the existing situation of suspected post-operative delirium in cancer patients undergoing surgery during the first 72 hours after surgery, and to identify the risk factors associated with postoperative delirium (POD).

Study Design: Prospective/observational study

Place and Duration: Hunan cancer Hospital. 1st December 2019 and 31st December 2019

Methods: Chinese Cancer patients scheduled for surgery, aged 18 years or elders were prospectively observed by bedside nurses for 03 consecutive postoperative days for the presence of delirium by using Nursing delirium screening scale (Nu-DESC Chinese version).

Results: Among the 319 included cancer patients, 39 (12.2%) developed suspected POD. Univariate analysis showed that cancer surgical patient with comorbidity of hypertension and chronic hepatitis, surgical specialty, duration of surgery >3 hours, post-operative use of benzodiazepine and opioids to be significantly associated with suspected POD. Binary logistic regression model showed hypertension (OR 7.857 95% CI 3.484–17.718 $p < .001$), chronic hepatitis (OR 44.087 95% CI 2.517–772.3 $p = 0.01$), and duration of surgery >3 hours (OR 2.908 95% CI 1.285–6.580 $p = 0.01$), to be independent risk factors for occurrence of suspected POD.

Conclusion: The 12.2% incidence of suspected postoperative delirium (POD) in cancer patients is significant. Recognizing of cancer patients by the nurses and clinicians who may be at risk for developing POD and addressing the modifiable risk factors are extremely essential to lower the risk of its developing.

Keywords: Delirium; Postoperative delirium; Cancer; risk factors; Nu-DESC

INTRODUCTION

In cancer patients, surgery is an essential part of multimodality care to remove solid tumors that require complex, and prolonged surgical procedures.[1] these surgeries mostly lead to postoperative neurobehavioral disorders.[2] Postoperative delirium (POD) is the most common and prevalent form of neurobehavioral disorders characterized by disorganized thinking, altered consciousness levels, sleep-wake pattern disturbance and inattention.[3, 4] POD usually occurs between 1 and 3 post-operative days.[5] In hospital settings, the incidence of delirium may be induced by multiple known risk factors, such as elder patients, neurological disorders, emergency surgery, specific surgical procedures, etc.[6] In research, the prevalence of POD after general surgery is shown to be 9 to 87%.[7] while in cancer patients almost 50% experience post-operative delirium (POD), with older patients being mostly at risk.[8] Since most cancer patients are older and geriatric patients are more prone to delirium, patients with surgical oncology are more likely to develop POD.[2]

Confusion assessment method (CAM), apparently the most widely used in postoperative setup,[13] and the Nursing Delirium Screening Scale (NU-DESC), likely the simplest assessment tool for early detection of delirium especially designed for nurses, are just two examples of the validated assessment tools available for detecting post-operative delirium in patients. Which has a high sensitivity and specificity and takes just about a minute on average to fill out, based on the evaluation of five parameters of Nu-DESC seen by bedside nurses during ordinary clinical practice[14]. The nursing team has greater direct patient contact and is present for longer periods of time than any other medical personnel. Therefore, choosing a screening tool that is ideal for nurses is an apparent and crucial part of integrating delirium care into the daily practise. [15]

With regards to those who have cancer Unfortunately, delirium is often misunderstood, underreported, and misdiagnosed;

and even when it is detected, it is often mistreated or incorrectly thought to be healed. To the best of our knowledge, there are not a lot of published research from China looking at the incidence of POD and its associated risk factors. Moreover, screening for delirium is not yet a standard part of clinical practise in many surgical wards in cancer hospitals in China. In light of this, a prospective observational research was developed to investigate the prevalence of postoperative delirium in surgical oncology and to determine its associated risk factors (POD).

MATERIALS AND METHODS

A prospective observational study design was conducted for a period of 01-month in 10 post-surgical wards at the Hunan cancer hospital, which is a tertiary care teaching "Grade IIIA" specialized cancer hospital in Changsha, China. Ethical authorization for this research study was attained from ethical review board of the Xiangya Nursing School of Central South University China. Participants included in the study recruitment were those; aged 18 years or elders, with good communication capability, who could speak and understand Chinese, pathologically diagnosed with any type of cancer, scheduled for surgery for the treatment of cancer, patients who won't be discharged till 72 hours after surgery and were available & willing to participate in the study. Similarly, patients were excluded from the study if they had history of cognitive impairment, required postoperative intensive care unit admissions, and pathologically diagnosed with gynecological cancer. Informed written consent was obtained by the bedside nurses from each study participant prior to recruitment. Those scheduled surgical patients who were fulfilling the inclusion criteria were identified by the research team, head nurses & bed side nurses in each surgical ward pre-operatively each day, and then postoperatively those patients were observed for 3 consecutive days to score each element of the Nu-DESC,[14] after each nursing shift. The assessment of patient for delirium began during

the first 8-16 hours of patients' arrival into the inpatient surgical wards to allow the participants to have sufficient recovery time from the anesthesia and would regain a higher level of consciousness. The Nu-DESC is basically a scale observing 5-items including orientation disorder, disruptive behavior, defective communication, hallucination/illusion, and psychomotor hindrance. After each observation by the observer, every item is marked on a 3-point Likert (0-2), the values of the items are then added and the score is obtained. The highest score is 10, patient with the score of ≥ 2 is indicated to be positive for delirium.[14] With the threshold of score >1 , Nu-DESC (Chinese version) has the sensitivity and specificity of 85.7% and 86.8%. Nu-DESC rating has shown a reasonable agreement with confusion assessment method (CAM), which is a gold standard for diagnosing the delirium, with $k = 0.521$, ($p < 0.001$).[16] In this study the threshold for delirium diagnosis was kept ≥ 2 , a patient with a score of 2 or above was diagnosed positive for delirium. Further the patients were categorized into two groups based on the presence and absence of delirium for the purpose of analysis.

All patients diagnosed with cancer between December 1, 2019, and December 31, 2019, who satisfied the inclusion and exclusion criteria at the time of the study, were included in the analysis. More than 10 times as many people as there were items on the scale were evaluated for postoperative delirium (POD) in a study of 325 patients. Patients were screened for delirium using the Nu-DESC after surgery, and they also had their demographics, pre-operative features, intra- and postoperative variables recorded.

Only bedside nurses familiar with the Nu-DESC scale were allowed to do the POD assessment and record the score, which helped to reduce the possibility of erroneous information being recorded. Both the head nurse and the bedside nurse were kept in the dark about the delirium score cutoff used to make the diagnosis. The researcher made the final diagnosis. The data was analysed using SPSS 25 — a statistical programme designed specifically for the social sciences. Pre-operative, intra-operative, and post-operative factors were analysed univariately for their relationship to postoperative delirium using the Chi-square test of independence. A binary logistic regression model was then utilised to further describe the important related variables for postoperative delirium after the initial study was completed. The t-test was employed to determine statistical significance for continuous variables, and a value of $p 0.05$ was considered to be significant..

RESULTS

Three hundred and twenty-five (325) patients were identified as eligible for the study and were approached in the pre-operative wards. Of this total, observations of 06 patients by the nurses were incomplete postoperatively and 319 participants (98.1%) had complete data available for analysis.

The mean age of the participants was 53.8 year, including 60% male and 40% female. The frequencies of pre-operative characteristics including the prevalence of comorbidities, substance use and BMI along with intra-and-postoperative factors, which could have possibly influenced POD are listed in **Table 1**.

Table 1: Pre-operative characteristics and intra-and-postoperative factors

Variable	Categories	N umber (%)
Pre-operative C haracteristics		
Comorbidities	Diabetes mellitus	20 (6.3)
	Hypertension	54 (16.9)
	Chronic Hepatitis	4 (1.3)
Substance use	Smoking	108 (33.9)
	Alcohol	67 (21)
BMI	< 18.5	22 (6.9)
	18.5-24.9	171 (53.6)
	25.0-29.9	107 (33.5)
	30.0 & above	19 (6)
Intra-operative factors		
Duration of surgery	≤ 3 hours	228 (71.5)
	> 3 hours	91 (28.5)
Postoperative factors		
Postoperative Hypoxemia		14 (4.4)
Post-operative drugs used	Benzodiazepines	104 (32.6)
	Anti-Convulsant	12 (3.8)
	Anti-Cholinergic	16 (5.0)
	Opioids	154 (48.3)

Using the Nu-DESC, 39 patients were diagnosed with suspected POD, which is equivalent to the 12.2% of the overall incidence. Among all the suspected 39 (12.2%) patients, 38 (11.9%) patients were diagnosed with mixed delirium, while only 1 patient was diagnosed with hyperactive delirium, there was no hypoactive delirium detected. Overall, disorientation seemed to be the maximum observed element in the Nu-DESC score followed by psychomotor retardation, while illusion/hallucination was the least documented element in the Nu-DESC score.

The comparison of demographics and pre-operative categorical variables are displayed in **Table 2**,

whereas the comparison of pre-operative, intra-and-postoperative categorical variables are shown in **Table 3**.

Table 2: Association of demographic characteristics of patients with occurrence of POD

Factors	Category	Total N (%)	Delirium		Statistical value	p-value
			Absent n (%)	Present n (%)		
Gender	Male	190 (59.6)	165 (86.8)	25 (13.2)	0.380	0.537
	Female	129 (40.4)	115 (89.1)	14 (10.9)		
Age	≤ 64	251 (78.7)	222 (88.4)	29 (11.6)	0.495	0.482
	≥ 65	68 (21.3)	58 (85.3)	10 (14.7)		
Marital status	Married	307 (96.2)	269 (87.6)	38 (12.4)	3.260	0.353
	Unmarried	6 (1.9)	6 (100)	0 (0)		
	Divorced	3 (0.9)	2 (66.7)	1 (33.3)		
	Widow	3 (0.9)	3 (100)	0 (0)		
Residence	Rural	219 (68.7)	194 (88.6)	25 (11.4)	0.427	0.513
	Urban	100 (31.3)	86 (86.0)	14 (14.0)		
Education	Master's or higher	37 (11.6)	32 (86.5)	5 (13.3)	1.360	0.507
	Undergraduate	5 (1.6)	5 (100)	0 (0)		
	Middle school or lower	277 (86.8)	243 (87.7)	34 (12.3)		

Table 3: Association of pre-operative characteristics and occurrence of POD

Factors	Category	Total (n)%	Delirium absent n (%)	Delirium present n (%)	Statistic value	p-value
Comorbidities						
Diabetes	Yes	20 (6.3)	16 (80)	4 (20)	—	0.306
	No	299 (93.7)	264 (88.3)	35 (11.7)		
Hypertension	Yes	54 (16.9)	30 (55.6)	24 (44.4)	62.880	$< 0.001^*$
	No	265 (83.1)	250 (94.3)	15 (5.7)		

Chronic Hepatitis	Yes	4 (1.3)	1 (25)	3 (75)	—	0.006*
	No	315 (98.7)	279 (88.6)	36 (11.4)		
Substance use						
Alcohol use	Yes	67 (21)	62 (92.5)	5 (7.5)	1.793	0.181
	No	252 (79)	218 (86.5)	34 (13.5)		
Smoking History	Yes	108 (33.9)	93 (86.1)	15 (13.9)	.421	0.516
	No	211 (66.1)	187 (88.6)	24 (11.4)		
BMI	< 18.5	22 (6.9)	20 (90.9)	2 (9.1)	.938	0.816
	18.5-24.9	171 (53.6)	152 (88.9)	19 (11.1)		
	25.0-29.9	107 (33.5)	92 (93.9)	15 (13.1)		
	≥30.0	19 (6)	16 (84.2)	3 (15.8)		

p-value by likelihood ratio, fisher's exact test or Pearson Chi-square test

Table 4: Association between Intra-and-Postoperative factors with Occurrence of POD

Factors	Total (n)%	Delirium absent n (%)	Delirium present n (%)	Statistic value	p-value
Intra-operative factors					
Duration of surgery					
≤3 hours	228 (71.5)	213 (93.4)	15 (6.6)	23.749	<0.001*
>3 hours	91 (28.5)	67 (73.6)	24 (26.4)		
Postoperative factors					
Postoperative hypoxemia					
Yes	14 (4.4)	13 (92.9)	1 (7.1)	-	1
No	305 (95.6)	267 (87.5)	38 (12.5)		
Postoperative drugs used					
Opioids					
Yes	154 (48.3)	141 (91.6)	13 (8.4)	3.973	0.046*
No	165 (51.7)	139 (84.2)	26 (15.8)		
Benzodiazepines					
Yes	104 (32.6)	101 (97.1)	3 (2.9)	12.547	<0.001*
No	215 (67.4)	179 (83.3)	36 (16.7)		
Anti-convulsant					
Yes	12 (3.8)	12 (100.0)	0 (0)	—	0.373
No	307 (96.2)	269 (87.3)	39 (12.7)		
Anti-cholinergic					
Yes	16 (5.0)	15 (93.8)	1 (6.2)	—	0.703
No	303 (95.0)	265 (87.5)	38 (12.5)		

Note: p-value by fisher's exact test or Pearson Chi-square test

Table 5: Association between Type of Surgery and Occurrence of POD

Surgical department	No.	Delirium present (%)	Delirium absent (%)	Statistic value	P
Hepatobiliary intestinal surgical ward	30	1(3.3)	29(96.7)	129.5	<0.001
Colorectal surgical ward	27	11(40.7)	16(59.3)		
Gastric pancreatic surgical ward	30	0(0)	30(100)		
Orthopedic Surgical ward	26	0(0)	26(100)		
Neurosurgery ward	29	0(0)	29(100)		
Thoracic surgical ward	60	4(18.8)	56(93.3)		
Plastic surgical ward	30	0(0)	30(100)		
Breast surgical ward	26	0(0)	26(100)		
Head & Neck surgical ward	30	23(76.7)	7(23.3)		
Urinary surgical ward	31	0(0)	31(100)		
Total	325	39	286		

Table 6: Multivariate analysis of the variables significantly associated with POD

	B	S.E.	Wald	df	Sig.	Exp (B)	95% C. I. for EXP(B)	
							Lower	Upper
Hypertension	2.061	0.415	24.687	1	0.000	7.857	3.484	17.718
Chronic Hepatitis	3.786	1.461	6.717	1	0.010	44.087	2.517	772.283
Duration of Surgery (>3h)	1.068	0.417	6.568	1	0.010	2.908	1.285	6.580

A p-value of <.05 indicates statistical significance

Patients were examined for the occurrence of postoperative delirium and separated into 64 years or less and 65 or above age groups. POD was more common in patients over 65 (14.7%) than in those under 18 (11.6%), although this difference was not statistically significant ($p=0.482$) when tested with a Chi-squared independence test. POD was also more common in male patients (13.2%) compared to female patients (10.9%), but this difference was not statistically significant ($p=0.537$). The proportion of patients who reported being delirious did not differ by marriage, marital status of the patient had no statistical significance for the development of POD ($p=.353$). Although patients from the urban area were more likely to develop POD (14.0%), as compared to the patient from rural area (11.4%), but this difference was not

statistically significant ($p=.513$). Patients with the education level of master or higher and middle school or lower were found to have almost similar onset of POD, 13.3% and 12.3% respectively ($p=.507$).

All The incidence of POD in diabetic patients (20%) was more than non-diabetic patients (11.7%), yet this difference was not statistically significant ($p=0.306$). POD happened in 44.4% in hypertensive patients as compared to 5.7% in non-hypertensive patients. There was a statistically significant relationship between the two variables. Hypertensive patients were more likely than non-hypertensive patients to have high risk of developing POD, $\chi^2 (1, N = 319) = 62.88, p < .01$. Similarly, the onset of POD among patients with chronic hepatitis was (75%), compared to the patients

without chronic hepatitis (11.4%). By using Fisher's exact test, patients with chronic hepatitis showed a statistically significant higher risk of developing POD, ($p=0.006$).

POD prevalence was 7.5% among drinkers and 13.5% among non-drinkers ($p=0.181$), while the proportion of drinkers in the sample was only 21.0%. The rates of POD among smokers and non-smokers were also quite similar, at 13.9% and 11.4%, respectively ($p=0.516$). Patients' body mass index (BMI) was divided into four categories, with similar POD prevalence throughout the range: 18.5 (9.1%), 18.5-24.9 (11.1%), 25.0-29.9 (13.1%), and 30.0 and above (15.8%). However, there was no statistically significant difference in the prevalence of POD amongst the three BMI categories ($p=0.816$).

As shown in **Table 4**, the duration of surgery was grouped into ≤ 3 hours and > 3 hours. Of the 319 surgeries, 71.1% of the surgeries were performed with in ≤ 3 hours, while 28.5% of the surgeries were done in > 3 hours of time. The incidence of POD in patients with surgery performed with in ≤ 3 hours and > 3 hours was 6.6% and 26.4% respectively. A Chi-square test of independence showed that there was a statistically significant association between duration of surgery and occurrence of POD, $\chi^2 (1, N = 319) = 23.75, p < .01$. Only 1 patient had an incidence of POD in patient with postoperative hypoxemia and 12.5% of POD incidence occurred in postoperative non-hypoxemic patients (Fisher's exact test, $p=1$).

The incidences of POD among patients who were using different medicines post-operatively were also comparable: Of those that required post-operative benzodiazepine was (2.9%), compared to those patients who didn't require post-operative benzodiazepines (16.7%). There was a weak significant association between post-operative benzodiazepine use and onset of POD, Phi and Cramer's V value of .198, $\chi^2 (1, N = 319) = 12.54, p < .01$. Only 12 (3.8%) of the patients were administered anti-convulsant drugs post-operatively, and none of the patient developed POD ($p=0.373$). Similarly, only 1 patient developed POD, as compared to those patients who were not administered anti-cholinergic medicines (12.5%) (Fisher's exact test, $p=0.703$). Among the 319 post-surgical patients, almost half of the participants 154 patients (48.2%) needed post-operative opioids, compared to those patients who didn't require post-operative opioids 165 (51.7%). There was a weak significant association between post-operative opioids use and onset of POD, Phi and Cramer's V value of .112, $\chi^2 (1, N = 319) = 3.973, p=0.046$. The presence of POD in patients belonging to each surgical specialty is analyzed in **Table 5**. Head and Neck surgery had the highest incidence of POD (76.7%), followed by colorectal surgery (40.7%), thoracic surgery (6.7%) and hepatobiliary surgery (3.4%). This difference among the different groups of surgical specialties with occurrence of POD was statistically significant (likelihood ratio 129.5, $df=9, p < 0.001$).

After initially analyzing individual factors for association with POD, the result of five factors identified as significant in univariate analysis were included along with surgical specialty into multivariate analysis, which were comorbidity of hypertension and chronic hepatitis, duration of surgery, and post-operative opioids & benzodiazepine use. A step wise binary logistic regression model was used to determine the factors significantly associated with POD. The adjusted odd ratios, 95% confidence intervals and the p-values of the significant factors associated with POD are depicted in **Table 8**.

DISCUSSION

Prospective research was conducted on the prevalence of delirium in cancer patients. The Nursing Delirium Screening Scale (NUN-DESC Chinese version) was used as the diagnostic tool, with delirium being defined as a score of 2 on this instrument. This study found a considerable POD incidence that is on par with other published studies from other parts of the world. [17] The incidence of POD in the current research (12.2%) was very close to the incidence reported in a prior study (13.3%). [18] This finding is in

line with the pooled incidence of POD found in an analysis of 41 studies (18.4%). [1] Comparatively, reports of POD incidence in the surgical ICU range from 24.4% to 44.4%. [19, 20] These results illustrate how variations in research design, patient demographic, assessment timing, observer competence, surgical subspecialties, and diagnostic instruments all contribute to the wide range in reported postoperative delirium rates.

All research indicates that POD often begins on the first postoperative day, [21-24] less commonly on the second postoperative day and the third day (within 3 days of surgery), and at its latest between 5 and 7 days following surgery. [22-24] Our results are consistent with those of previously published research, which found that POD was most common on the first postoperative day and occurred less frequently on days two and three. In our investigation, nearly all patients were classified as having mixed delirium, the most prevalent of the three delirium subtypes [25].

Patients' post-operative delirium has been linked to circumstances that arise or exist during the pre-operative, intraoperative, or post-operative phases of cancer surgery. The predominance of a few particular characteristics in connection to this study's sample group should be discussed, despite discrepancies and disagreement in the literature about the role of these factors in the development of delirium. The pre-operative, intra-operative, and post-operative times of both the delirium and non-delirium groups are described, along with demographic information such as age, gender, marital status, and kind of operation. Numerous research have established that advancing years are correlated with POD. Patients of any age can be affected [20,21, 26] if the underlying conditions for its onset are met, such as in the case of severe or emergency surgery. [28] In our study elder patients did have high incidence of POD (14.7%) as compared to younger patients (11.6%), however this association was not statistically significant. This is because of 78.7% of our study participants age were ≤ 64 years and the mean age was 53.8, as compared to the previous published studies the median age was 77.8 [22, 24, 27]. The present study also showed that in spite of young participants in our study as compared to the previous studies, still POD happened to the post-operative patient, which showed an agreement with the previous studies [20, 28]. Similarly, male sex has been shown in many large studies as associated with increased risk for the occurrence of POD, [29] yet its association with POD is not clear, studies have found an equal prevalent of POD in both the gender. [2] Recently, based on a systematic review of pooled analysis of 10 studies demonstrated that there is insufficient evidence to support an association between male gender as a preoperative risk factor for the developing of delirium. [30] In our study no statistically significant association between gender and occurrence of POD was found ($p=0.537$).

Marital Status association with delirium is controversial, marital status of the patient is shown as an associative factor with delirium in the study of Tai et al. [27] Their study reported that married percentage was significantly lower in the delirious patients when compared with the non-delirious group (51 vs. 86%, $p = 0.013$). [27] The present study did not find any association of marital status with delirium. In our study 96.2% of the participants were married and only 12 participants were either unmarried, divorced or widowed. The association of marital status with delirium can be best evaluated by having an equal representation of married and unmarried participants.

Surgery itself is a significant precipitating risk factor for delirium occurrence. [31] As shown in Table 5 Head and Neck surgery had the highest incidence of POD (76.7%), followed by colorectal surgery (40.7%), thoracic surgery (6.7%) and hepatobiliary surgery (3.4%) ($p < 0.001$). These findings show an agreement with the study of Hempenius L. (2014) [32] who reported that elective surgery for a solid tumor, cognitive impairment and severity of invasive or surgical procedure were an independent risk factors for postoperative delirium in cancer patients. [32], Delirium is a common complication in patients after major head and neck

cancer surgery with an overall prevalence of 19.26%.[33] The present study also found POD to be occurred more common in patients with major head & neck surgery i.e. 58.9%, the reason behind higher rate in our study is that participants with major head & neck surgeries were only 30, as compared to the previous published studies, the study samples were comparatively large.

Patients with hypertension were more likely to experience POD (44.4%) than those without the condition (5.7%), making hypertension the most common risk factor. Research has found that high blood pressure is associated with an increased likelihood of developing delirium. In line with previous research, we found that hypertension is a significant predictor of delirium in cancer patients having surgery. There is evidence linking chronic hypertension to cognitive decline. [34] Since hypertension is the single most important risk factor for developing dementia, any complications resulting from inadequate intraoperative blood pressure management might have devastating effects on the patient's mental status. [35] A recent Chinese prospective study indicated that ICU- POD was linked to acid-base imbalance, diabetes, hypertension, coma, and the POSSUM score among a sizable group of patients. [36] In commitment with the previous studies our study showed that cancer patients with comorbidity of hypertension were 8 times more likely to have occurrence of POD than patient who don't have hypertension (OR 7.857 95% CI 3.484–17.718 $p < .001$). Our study also found the incidence of POD in diabetic patients (20%) as compared to non-diabetic patients (11.7%), yet this difference was not statistically significant ($p = 0.306$). Along with the significant association of hypertension with POD, our study also found that patients with chronic hepatitis were 46 times more likely to have onset of POD compared to patients who don't have chronic hepatitis (OR 44.087 95% CI 2.517–772.3 $p = 0.01$), which is consistent with the previous studies which also showed the association between hepatic diseases and POD.[37] In our study there were only 4 patients with chronic hepatitis, further study is required with more participants with chronic hepatitis to generalize the result in this cohort.

The significant association between alcohol abuse and increased risk of POD have been shown by two large and many smaller studies. [35] The proportion of alcohol users in our study was only 21.0% compare to 79.0% non-users, because of the small numbers of patient with alcohol use our study did not find any significant association between alcohol use and occurrence of POD.

Other precipitating factors related to the surgical procedure are blood loss, transfusion during or after surgery, and duration of the procedure. All of these are associated with postoperative delirium.[38] Compare to other surgeries, head & neck surgical procedures for cancer treatment, spinal surgeries and orthopedic surgeries are complex and prolonged. Longer surgical duration has been reported associated with the development of postoperative delirium, because the surgical procedure of long duration means more blood loss, need of transfusion and need long duration anesthesia and all of these are the risk factors for developing of POD.[39] Our study is also consistent with the result of previous studies that surgery of duration more than 3 hours is statistically significant with the occurrence of POD. The result of multivariate analysis of our study by step wise binary logistic regression model showed that patients whose surgeries were performed in > 3 hours were 3 times more likely to have occurrence of POD as compared to patients whose surgeries were performed in ≤ 3 hours of surgeries (OR 2.908 95% CI 1.285–6.580 $p = 0.01$).

Patients with old age are at high risk for developing delirium since the aging brain is more susceptible to anesthetic agents. Evidence showed that benzodiazepines, morphine, and anticholinergic are the three common drugs which result in delirium.[40] Kudoh et al. investigated the relationship between postoperative confusion and duration of benzodiazepine exposure, and reported that the incidence of postoperative confusion was significantly more frequent in long-term benzodiazepine users.[41] Our study is also in agreement with Kudoh et al. study, there was a

weak but a significant association between post-operative benzodiazepine use and occurrence of POD in the univariate analysis but no association was found in multi-variate analysis by using stepwise binary logistic regression model.

Opioid use being linked to postoperative confusion is a contentious topic. While Lynch et al. found no correlation between opioid dosage and POD[42], Leung et al. discovered a link between high opioid use and delirium in elderly surgical patients. [43] There was a consensus among trials that opioid administration was linked to postoperative delirium, but researchers were unable to pin down a specific dosage. [44] Studies have shown that the incidence of delirium increases by 40% in cancer patients who are exposed to the equivalent of more than 90 mg of morphine each day. [45] Our sample of 319 patients who had just undergone surgery found that over half of them, 154 patients (48.2%), required post-operative opioids, whereas the other half, 165 patients (51.7%), did not. Using logistic regression analysis, we were unable to uncover any conclusive link. Postoperative hypoxia, hypocarbia, and septic shock all increase the likelihood of delirium. [46] Nursing staff monitored study participants for hypoxemia after surgery; of 319 patients, 14 (4.4% of the total) were diagnosed with hypoxemia, whereas 305 (95.6% of the total) were not hypoxemic and only 1 experienced post-operative delirium (POD).

There are however some caveats worth noting. Firstly, this research was done inside a single setting. Consequently, it's possible that our findings don't apply outside of the context of our study. Second, while the sample size was adequate as a whole, it may not have included a large enough number of individuals from each surgical specialty to reliably detect all relevant variations and relationships between POD and risk variables. Finally, as delirium evaluation was only done for 3 post-op days, the incidence of POD may have been under-estimated. However, delirium can develop after 3 days. As for the fourth, the POD determination was based only on the nurses' observations, without consulting a psychiatrist to double-check the diagnosis. Finally, certain pertinent information, such as previous postoperative delirium and intraoperative drug use, was not gathered and may have influenced our study and conclusions.

CONCLUSION

This study accurately estimated the prevalence (12.2%) of postoperative delirium (POD) in cancer patients following surgery. Patients with a background of hypertension and chronic hepatitis, as well as prolonged surgical length, were shown to be substantially linked with the development of suspected POD. Therefore, it is crucial for nurses and physicians to detect patients who may be at risk for developing POD, and to identify those risk factors that may be addressed, so that prompt steps might be taken to prevent the occurrence of POD and its repercussions.

Author Contributions: S.Q and X.Y.L supervised study design and the implementation of the study, interpretation of results, participated in study design, collecting data, participated in statistical analysis, drafting, and revising the manuscript. T.V., K.H., participated in study design and collecting data. Q.K. participated in interpretation of results, statistical analysis and revision of the manuscript. All authors have read and agreed to the published version of the manuscript

Funding: This research received no external funding.

Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Institutional Review Board of behavioral and nursing research in School of Nursing of Central South University (CSU), China (12019015/16-07-2019).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: Data are available on reasonable request.

Patients Consent for Publication: Obtained.

Conflicts of Interest: The authors declare no conflict of interest.

Ethics Approval: The protocol of the study has been approved by the Research Ethic Committee of the behavioral and nursing research in School of Nursing of Central South University (CSU), China (12019015/16-07-2019).

REFERENCES

1. Watt J, Tricco AC, Talbot-Hamon C, et al (2018) Identifying Older Adults at Risk of Delirium Following Elective Surgery: A Systematic Review and Meta-Analysis. *J Gen Intern Med* 33:500–509. <https://doi.org/10.1007/s11606-017-4204-x>
2. Dhakharia V, Sinha S, Bhaumik J (2017) Postoperative Delirium in Indian Patients Following Major Abdominal Surgery for Cancer: Risk Factors and Associations. *Indian J Surg Oncol* 8:567–572. <https://doi.org/10.1007/s13193-017-0691-9>
3. Sanders RD, Pandharipande PP, Davidson AJ, et al (2011) Anticipating and managing postoperative delirium and cognitive decline in adults. *Bmj* 343:d4331. <https://doi.org/10.1136/bmj.d4331>
4. Steven M. Singer#, Marc Y. Fink VVA (2019) 乳鼠心肌提取 HHS Public Access. *Physiol Behav* 176:139–148. <https://doi.org/10.1056/NEJMcp1605501.Delirium>
5. D Isaacson, J L Mueller JCN and SS (2006) 基因的改变NIH Public Access. *Bone* 23:1–7
6. Zaal IJ, Devlin JW, Peelen LM, Slooter AJC (2015) A systematic review of risk factors for delirium in the ICU. *Crit Care Med* 43:40–47. <https://doi.org/10.1097/CCM.0000000000000625>
7. Maldonado JR (2008) Delirium in the Acute Care Setting: Characteristics, Diagnosis and Treatment. *Crit Care Clin* 24:657–722. <https://doi.org/10.1016/j.ccc.2008.05.008>
8. Joon Yau Leong Ranjith Ramasamy ASP (2017) 乳鼠心肌提取 HHS Public Access. *Physiol Behav* 176:139–148. <https://doi.org/10.1016/j.jgo.2014.10.002.Prevention>
9. Rudolph JL, Jones RN, Rasmussen LS, et al (2007) Independent Vascular and Cognitive Risk Factors for Postoperative Delirium. *Am J Med* 120:807–813. <https://doi.org/10.1016/j.amjmed.2007.02.026>
10. Marcantonio ER, Flacker JM, Michaels M, Resnick NM (2000) Delirium is independently associated with poor functional recovery after hip fracture. *J Am Geriatr Soc* 48:618–624. <https://doi.org/10.1111/j.1532-5415.2000.tb04718.x>
11. Witlox J, Eurelings LSM, De Jonghe JFM, et al (2010) Delirium in elderly patients and the risk of postdischarge mortality, institutionalization, and dementia: A meta-analysis. *JAMA - J Am Med Assoc* 304:443–451. <https://doi.org/10.1001/jama.2010.1013>
12. Vasilevskis EE, Ely EW, Speroff T, et al (2010) Reducing iatrogenic risks: ICU-acquired delirium and weakness - Crossing the quality chasm. *Chest* 138:1224–1233. <https://doi.org/10.1378/chest.10-0466>
13. Wong CL, Holroyd-Leduc J, Simel DL, Straus SE (2010) Does this patient have delirium?: Value of bedside instruments. *JAMA - J Am Med Assoc* 304:779–786. <https://doi.org/10.1001/jama.2010.1182>
14. Gaudreau JD, Gagnon P, Harel F, et al (2005) Fast, systematic, and continuous delirium assessment in hospitalized patients: The nursing delirium screening scale. *J Pain Symptom Manage* 29:368–375. <https://doi.org/10.1016/j.jpainsymman.2004.07.009>
15. Smith MJ, Breitbart WS, Platt MM (1995) A critique of instruments and methods to detect, diagnose, and rate delirium. *J Pain Symptom Manage* 10:35–77. [https://doi.org/10.1016/0885-3924\(94\)00066-T](https://doi.org/10.1016/0885-3924(94)00066-T)
16. Leung J lam ming, Leung V cheuk wing, Leung C ming, Pan P chyou (2008) Clinical utility and validation of two instruments (the Confusion Assessment Method Algorithm and the Chinese version of Nursing Delirium Screening Scale) to detect delirium in geriatric inpatients. *Gen Hosp Psychiatry* 30:171–176. <https://doi.org/10.1016/j.genhosppsych.2007.12.007>
17. Maldonado JR (2008) Delirium in the Acute Care Setting: Characteristics, Diagnosis and Treatment. *Crit Care Clin* 24:657–722. <https://doi.org/10.1016/j.ccc.2008.05.008>
18. Vijayakumar B, Elango P, Ganessan R (2014) Post-operative delirium in elderly patients. *Indian J Anaesth* 58:251–256. <https://doi.org/10.4103/0019-5049.135026>
19. Robinson TN, Raeburn CD, Tran Z V., et al (2009) Postoperative delirium in the elderly: Risk factors and outcomes. *Ann Surg* 249:173–178. <https://doi.org/10.1097/SLA.0b013e31818e4776>
20. Chaiwat O, Chanidnuan M, Pancharoen W, et al (2019) Correction to: Postoperative delirium in critically ill surgical patients: incidence, risk factors, and predictive scores (*BMC Anesthesiology* (2019) 19 (39) 10.1186/s12871-019-0694-x). *BMC Anesthesiol* 19:1–10. <https://doi.org/10.1186/s12871-019-0732-8>
21. Tognoni P, Simonato A, Robutti N, et al (2011) Preoperative risk factors for postoperative delirium (POD) after urological surgery in the elderly. *Arch Gerontol Geriatr* 52:e166-9. <https://doi.org/10.1016/j.archger.2010.10.021>
22. Large MC, Reichard C, Williams JTB, et al (2013) Incidence, risk factors, and complications of postoperative delirium in elderly patients undergoing radical cystectomy. *Urology* 81:123–129. <https://doi.org/10.1016/j.urology.2012.07.086>
23. Sato T, Hatakeyama S, Okamoto T, et al (2016) Slow gait speed and rapid renal function decline are risk factors for postoperative delirium after urological surgery. *PLoS One* 11:e0153961. <https://doi.org/10.1371/journal.pone.0153961>
24. Xue P, Wu Z, Wang K, et al (2016) Incidence and risk factors of postoperative delirium in elderly patients undergoing transurethral resection of prostate: A prospective cohort study. *Neuropsychiatr Dis Treat* 12:137–142. <https://doi.org/10.2147/NDT.S97249>
25. Liptzin B, Levkoff SE (1992) An empirical study of delirium subtypes. *Br J Psychiatry* 161:843–845. <https://doi.org/10.1192/bjp.161.6.843>
26. Logan PGB and GD (2014) 基因的改变NIH Public Access. *Bone* 23:1–7. <https://doi.org/10.1213/ANE.0b013e3182147f6d.Postoperative>
27. Tai S, Xu L, Zhang L, et al (2015) Preoperative risk factors of postoperative delirium after transurethral prostatectomy for benign prostatic hyperplasia. *Int J Clin Exp Med* 8:4569–4574. <https://doi.org/10.1016/j.juro.2016.04.017>
28. Card E, Pandharipande P, Tomes C, et al (2015) Emergence from general anaesthesia and evolution of delirium signs in the post-anaesthesia care unit. *Br J Anaesth* 115:411–417. <https://doi.org/10.1093/bja/aeu442>
29. Zweier (2014) 基因的改变NIH Public Access. *Bone* 23:1–7. <https://doi.org/10.1097/AIA.0000000000000032.Cognition>
30. Tan H, Bi J, Wang Y, et al (2015) Transfusion of old rbc induces neuroinflammation and cognitive impairment. *Crit Care Med* 43:e276–e286. <https://doi.org/10.1097/CCM.0000000000001023>
31. Wang C guang, Qin Y fei, Wan X, et al (2018) Incidence and risk factors of postoperative delirium in the elderly patients with hip fracture. *J Orthop Surg Res* 13:186. <https://doi.org/10.1186/s13018-018-0897-8>
32. Version D (2014) Delirium in frail surgical oncology patients Hempenius , Liesbeth Publisher ' s PDF , also known as Version of record Publication date : Liesbeth Hempenius
33. Zhu Y, Wang G, Liu S, et al (2017) Risk factors for postoperative delirium in patients undergoing major head and neck cancer surgery: A meta-analysis. *Jpn J Clin Oncol* 47:505–511. <https://doi.org/10.1093/jjco/hyx029>
34. Waldstein SR, Manuck SB, Ryan CM, Muldoon MF (1991) Neuropsychological correlates of hypertension: Review and methodologic considerations. *Psychol Bull* 110:451–468. <https://doi.org/10.1037/0033-2909.110.3.451>
35. Beydoun MA, Beason-Held LL (2008) Does hypertension interact with body weight to impact cognitive function in the elderly?: Emerging evidence. *Am J Hypertens* 21:603. <https://doi.org/10.1038/ajh.2008.181>
36. Xing H, Zhou W, Fan Y, et al (2019) Development and validation of a postoperative delirium prediction model for patients admitted to an intensive care unit in China: A prospective study. *BMJ Open* 9:1–9. <https://doi.org/10.1136/bmjopen-2019-030733>
37. Denzik BA (2016) Bedside Nurse Recognition of Delirium in the Medical-Surgical Setting
38. Rodin MB, Flaherty JH (2017) Delirium prevention: Update on multidisciplinary, non-drug prevention of delirium among hospitalized elderly. In: Isik AT, Grossberg GT (eds) *Delirium in Elderly Patients*. Springer International Publishing, Cham, pp 111–123
39. Wang J, Li Z, Yu Y, et al (2015) Risk factors contributing to postoperative delirium in geriatric patients postorthopedic surgery. *Asia-Pacific Psychiatry* 7:375–382. <https://doi.org/10.1111/appy.12193>
40. Young J, Inouye SK (2007) Delirium in older people. *Br Med J* 334:842–846. <https://doi.org/10.1136/bmj.39169.706574.AD>
41. Kudoh A, Takase H, Takahira Y, Takazawa T (2004) Postoperative confusion increases in elderly long-term benzodiazepine users. *Anesth Analg* 99:1674–1678. <https://doi.org/10.1213/01.ANE.0000136845.24802.19>
42. Lynch EP, Lazor MA, Gellis JE, et al (1998) The of impact postoperative pain on the development of postoperative delirium. *Anesth Analg* 86:781–785. <https://doi.org/10.1097/0000539-199804000-00019>
43. Leung JM, Sands LP, Paul S, et al (2009) Does postoperative delirium limit the use of patient-controlled analgesia in older surgical patients? *Anesthesiology* 111:625–631. <https://doi.org/10.1097/ALN.0b013e3181ac7e6>
44. Marcantonio ER, Juarez G, Goldman L, et al (1994) The Relationship of Postoperative Delirium With Psychoactive Medications. *JAMA J Am Med Assoc* 272:1518–1522. <https://doi.org/10.1001/jama.1994.03520190064036>
45. Gaudreau JD, Gagnon P, Roy MA, et al (2007) Opioid medications and longitudinal risk of delirium in hospitalized cancer patients. *Cancer* 109:2365–2373. <https://doi.org/10.1002/cncr.22665>
46. ATLEE JL, BUCKLIN BA, CHANEY MA, et al (2007) Section Editors. In: Atlee JLBT-C in A (Second E (ed) *Complications in Anesthesia*. W.B. Saunders, Philadelphia, p ii