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Incidence and risk factors for postoperative delirium after head and neck cancer surgery: an updated meta-analysis

Bo Dong¹, Dongdong Yu¹, Li Jiang¹, Meinv Liu¹ and Jianli Li^{1*}

Abstract

Background Postoperative delirium (POD) is a frequent neurologic dysfunction that often leads to more negative outcomes. Early identification of patients who are vulnerable to POD and early implementation of appropriate management strategies could decrease its occurrence and improve patient prognosis. Therefore, this meta-analysis comprehensively and quantitatively summarized the prevalence and related predictive factors of POD in head and neck cancer surgical patients.

Methods PubMed, Embase, and Cochrane Library were searched for observational studies that reported the prevalence and risk factors for POD after head and neck cancer surgery and were published from their inception until December 31, 2022. Two reviewers independently selected qualified articles and extracted data. The qualities of related papers were assessed using the Newcastle-Ottawa scale (NOS). RevMan 5.3 and Stata 15.0 were applied to analysis the data and conduct the meta-analysis.

Results Sixteen observational studies with 3289 inpatients who underwent head and neck cancer surgery were included in this review. The occurrence of POD ranged from 4.2 to 36.9%, with a pooled incidence of 20% (95% Cl 15–24%, $l^2 = 93.2\%$). The results of this pooled analysis demonstrated that the statistically significant risk factors for POD were increased age (OR: 1.05, 95% Cl: 1.03–1.07, P < 0.001), age > 75 years (OR: 6.52, 95% Cl: 3.07–13.87, P < 0.001), male sex (OR: 2.29, 95% Cl: 1.06–4.97, P = 0.04), higher American Society of Anesthesiologists grade (OR: 2.19, 95% Cl: 1.44–3.33, P < 0.001), diabetes mellitus (OR: 2.73, 95% Cl: 1.24–6.01, P = 0.01), and history of smoking (OR: 2.74, 95% Cl: 1.13–6.65, P = 0.03).

Conclusions POD frequently occurs after head and neck cancer surgery. Several independent predictors for POD were identified, which might contribute to identifying patients at high risk for POD and play a prominent role in preventing POD in patients following head and neck cancer surgery.

Keywords Risk factors, Incidence, Postoperative delirium, Meta-analysis, Systematic review, Head and neck cancer

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Introduction

Head and neck cancer is one of the most frequent malignancies, including cancers of the oral cavity, pharynx, larynx, paranasal sinuses, and nasal cavity [1]. There were more than 878,000 new cases of head and neck cancers in 2020 and approximately 445,000 deaths each year worldwide [2]. Over the past few decades, researchers have made great efforts to explore therapeutic strategies for



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head and neck cancer, such as radiotherapy, chemotherapy, and immunotherapy; however, surgical resection is still the main treatment method [3]. Unfortunately, owing to the complex nature, multiple comorbidities, highly invasive and extensive surgical procedures, and longer operation time, surgery may inevitably lead to postoperative complications, which not only prolong the hospital stay and decrease the quality of life but also increase the total hospital cost and the risk of mortality [4]. Postoperative delirium (POD), a relatively frequent neuropsychiatric disorder after anesthesia and surgery, is an acute and transient cerebral disorder characterized by disturbance of attention, perception, and consciousness [5]. It was reported that approximately 11.50 to 36.11% of inpatients experienced POD after head and neck cancer surgery, depending on the frequency of assessment, age of the patient, and different types of surgical interventions [6]. POD can lead to unfavourable events such as prolonged hospital stay, increased risk of dementia, mortality, high medical expenses, functional impairment, and other clinical complications [7, 8]. Fortunately, 30–40% of POD can be prevented by early identification and treatment of its related risk factors, although the present pathophysiology of POD remains obscure [9]. Therefore, it is reasonable to believe that early identification of patients at risk for POD and timely implementation of targeted intervention strategies might play critical roles in reducing POD incidence and its related detrimental effects.

Based on different clinical psychomotor behaviours, POD could be further categorized into three subtypes: hyperactive, hypoactive, or mixed. The subtype of POD may be influenced by factors related to specific surgical patient populations. For example, hypoactive-type POD, characterized by lethargy, apathy, and reduced motor activity, occurs more frequently after cardiac and hip fracture surgery [10, 11], while hyperactive-type POD, characterized by agitation, restlessness, and insomnia, is common after head and neck cancer surgery [12]. Recently, several meta-analyses demonstrated that some predisposing risk factors (ageing, low albumin, diabetes, history of delirium, preoperative depression, preoperative functional dependence, mild cognitive impairment, and carotid artery stenosis) and precipitating risk factors (time of mechanical ventilation, surgery delay > 48 h, and intensive care unit stay time) could increase the incidence of POD in patients after cardiac and orthopedic surgery [13, 14]. In regard to patients undergoing head and neck cancer surgery, there may be different risk factors for POD. Risk factors for POD after head and neck cancer surgery were reported in the individual studies, but the results were inconsistent or even conflicting [12, 15]. Additionally, in 2017, Zhu et al. identified several potential risk factors for POD after head and neck cancer surgery using univariate analysis [6]. However, this metaanalysis only included 8 articles, which contributed to the unreliability of results. In addition, the majority of included studies in this review were from Japan in this review, which might reduce the generalizability of the conclusions. Furthermore, this review used univariable analysis to summarize the risk factors for POD rather than multivariate analysis, which led to the results being less mathematically robust. Over the past five years, several studies reporting the risk factors for POD after head and neck cancer surgery have been published, which may offer some new evidence. Consequently, this study was conducted to comprehensively and quantitatively analyze the prevalence and related risk factors for POD in patients who underwent head and neck cancer surgery, and thus providing guidance for clinical prevention decision-making.

Methods

Our meta-analysis strictly complied with the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [16].

Literature search

PubMed, Cochrane Library, and Embase were comprehensively searched for articles published from their inception until December 31, 2022. Based on the combination of medical subject heading terms and text words, a basic search strategy was conducted using the following terms: "delirium," "postoperative delirium," "mixed origin delirium," "head and neck," "neoplasms," "cancer," and "risk factors," etc. See Additional File 1 for the detailed search strategies.

Study selection

Inclusion criteria included the following: (1) studies designed as cohort, case-control, or cross-sectional studies; (2) studies including patients undergoing surgery for head and neck cancer; (3) studies reporting the prevalence and risk factors for POD in patients undergoing surgery for head and neck cancer; (4) studies in which POD was diagnosed by some validated methods, such as the Nursing Delirium Screening Scale (Nu-DESC), Intensive Care Delirium Screening Checklist (ICDSC), Confusion Assessment Method (CAM) or Diagnostic and Statistical Manual of Mental Disorders (DSM); (5) studies written in English; and (6) studies with complete data that could be extracted, including ORs of multivariable risk factors with 95%CIs. Exclusion criteria included the following: (1) reviews, letters, abstract-only publications, animal experiments, and case reports; (2) studies with overlapping populations or duplicate publications; (3) studies that did not investigate the predictors for POD

by multivariate logistic regression analysis; and (4) articles with insufficient data for statistics.

Data extraction and quality assessment

Two authors screened the full text of the articles, extracted the data and assessed the quality of the papers separately. The extracted data comprised authors, year of publication, country, study design, sample size, mean age of the patients, diagnostic methods for POD and its incidence, risk factors for POD, and study quality score. Since all the selected studies were observational studies, the quality of the eligible papers was rated using the Newcastle-Ottawa Scale (NOS), which is recognized as a standardized method for the quality assessment of nonrandomized studies [17]. The maximum total score for the included studies was 9 points using the NOS which contains eight items. Papers with NOS scores \geq 7.0 were considered high quality, and NOS scores < 7.0 were regarded as low quality. Any disagreements were eventually resolved through discussion or negotiation.

Statistical analysis

Stata 15.0 and RevMan 5.3 were used to analyze all data. If multivariable risk factors were reported in more than two studies, we performed a meta-analysis. Pooled ORs with corresponding 95% CIs were applied to assess the relationship between the predictors and POD, and P < 0.05 was regarded as statistically significant. I² values and Q-test statistics were applied to detect heterogeneity among articles, where P < 0.1 and $I^2 > 50\%$ were deemed to indicate significant heterogeneity. If the articles showed high heterogeneity, a random-effect model analysis was utilized; otherwise, a fixed-effect model was chosen. The final result for each relevant variable was presented as forest plots. When the heterogeneity of the pooled effect was significant ($I^2 > 50\%$), we further explored the source of heterogeneity using the sensitivity or subgroup analysis. Publication bias with a funnel plot was also conducted.

Results

Literature search

The initial literature search retrieved 542 citations from the PubMed (n=122), Embase (n=354), and Cochrane Library (n=66). After the removal of duplicate articles (n=113) by EndNote X9, 429 articles were retained. After preliminary headline and abstract screening, 394 studies were eliminated. The 35 remaining studies consequently underwent full-text review. Subsequently, 19 papers were eliminated for the following reasons: conference abstract (6 studies); not conducting multivariate analysis (3 studies); systematic review or letter (3 studies); without validated POD tools (3 studies); incomplete data (2 studies); randomized controlled trial (1 study); and duplicated population (1 study). Ultimately, 16 articles were eligible for this meta-analysis. The detailed process of the database search is shown in Fig. 1.

Characteristics of identified studies

In total, 16 observational studies with 3289 patients were published from 2009 to 2022, and the sample size ranged from 69 to 515. Of these 16 observational studies included, 1 was a case-control study, 14 were retrospective cohort studies, and 1 was a prospective cohort study. Of the 16 articles, 12 studies were conducted in Asia (7 in Japan [12, 18-23], 3 in China [24-26], and 2 in South Korea [27, 28]), while 3 studies were performed in the Germany [5, 15, 29] and the remaining 1 study was conducted in the United States [30]. The most common diagnostic method was the DSM-IV in 8 of 16 included studies [12, 18, 19, 21, 22, 24, 27, 30], the DSM-V in 4 studies [5, 15, 20, 29], the CAM in 2 studies [25, 26], and the ICDSC [23] and Nu-DESC [29] in the remaining 2 studies. Table 1 presents the basic information of the selected literature.

Methodological quality evaluation

Data on the quality of the eligible articles based on the NOS is presented in the Table 2. The NOS score of all included studies was no less than 7 points, suggesting that all of these were high-quality.

Incidence of POD

All eligible articles provided the incidence of POD, varying from 4.2 to 36.9% with a pooled incidence of 20% (95% CI 15–24%, $I^2=93.2\%$) (Fig. 2). In addition, subgroup analyses were performed on region, criteria for POD, number of samples, quality of included studies, and study design (Table 3). Furthermore, we performed a sensitivity analysis and the results suggested that none of the included articles had a great influence on the pooled estimates (Fig. 3). Begg's funnel plot provided significant evidence of publication bias (Fig. 4).

Risk factors of POD

Originally, we identified 53 risk factors from included studies based on multivariate analysis. Of these, 8 risk factors were reported in two or more studies, and finally 6 risk factors were considered statistically significant, which are displayed in Table 4. All of these identified factors were divided into 2 categories, including predisposing and precipitating risk factors.



Fig. 1 The flow diagram of the search process of the literature and the results of the literature search

Predisposing risk factors

Age

A total of 5 articles showed that older age was a potential risk factor for POD. The meta-analysis of these articles suggested that older age was a significant predictor for POD (OR: 1.05, 95% CI: 1.03–1.07, P < 0.001, $I^2 = 18\%$, Table 4; Fig. 5). Moreover, age > 75 years was deemed as a risk factor for POD in 2 studies, and the results of this meta-analysis suggested that patients older than 75 years were more prone to experience POD (OR: 6.52, 95% CI: 3.07–13.87, P < 0.001, $I^2 = 0\%$, Table 4; Fig. 6).

Male sex

Five papers reported that male sex was a potential risk factor for POD. The meta-analysis results indicated that male gender was an independent risk factor for POD (OR: 2.29, 95% CI: 1.06-4.97, P = 0.04), with mild heterogeneity (I²= 55%, P= 0.06, Table 4, Fig. 7). Furthermore, the potential sources of heterogeneity were sought through sensitivity analysis, and the results indicated that no single study significantly changed the pooled result.

American society of anesthesiologists (ASA) physical states Three studies reported the association between ASA physical status and POD, and the meta-analysis indicated that a 2.19-fold increased risk of POD in patients with higher ASA grades (OR: 2.19, 95% CI: 1.44–3.33, P < 0.001, I2=31%, Table 4; Fig. 8).

Diabetes mellitus

Diabetes mellitus was recognized as a risk factor for POD in 3 papers. In our meta-analysis, patients with

Table 1 Characteristics of the included studies

Study(year)	Country	Study design	Sample size(n)	Age(years)	POD assessment	POD incidence(%)	Risk factors	Nos score
Shiiba et al. (2009) [18]	Japan	Retrospective	132	63.0±12.6	DSM-IV	18.0	Age, sex	9
Hasegawa et al. (2015) [19]	Japan	Retrospective	188	NR	DSM-IV	15.4	Age, intraopera- tive hemoglobin, excessive hemor- rhage	9
Booka et al. (2016) [20]	Japan	Retrospective	293	61.9±13.6	DSM-V	17.1	Age	9
Choi et al. (2017) [27]	South Korea	Retrospective	341	56±12	DSM-IV	26.0	Age, psychiatric disorder history, marital status, NRS, ASA status, ICU stay period	9
Zhang et al. (2019) [24]	China	Retrospective	287	NR	DSM-IV	4.2	Comorbidity, ASA status	8
Wang et al. (2019) [25]	China	Prospective	323	60.0	САМ	8.7	ASA status, educa- tional level, cancer stage, intraopera- tive hypotension, intraoperative dexmedetomidine use	8
Ishibashi-Kanno et al. (2020) [12]	Japan	Retrospective	69	62.9±11.9	DSM-IV	33.3	Age, sex, diabetes mellitus, COPD, recent hospi- talization, sedation period	9
Densky et al. (2019) [30]	United States	Retrospective	515	60.1±12.8	DSM-IV	10.9	Age, operative time, CCI, sex, tumor N clas- sification, history of smoking,	8
Makiguchi et al. (2020) [21]	Japan	Retrospective	122	60.3±11.2	DSM-IV	36.9	High preoperative albumin, postop- erative insomnia, history of smoking, diabetes mellitus	8
Kong et al. (2021) [<mark>26</mark>]	China	Case-control	98	68	CAM	30.6	Hypertension, irregular medica- tion	7
Takahashi et al. (2021) [22]	Japan	Retrospective	104	63.0	DSM-IV	21.2	Operative time, anesthesia time, blood loss, method of reconstruction, postoperative ambulation, red blood cell count, hemoglobin, hematocrit	8
Kinoshita et al. (2021) [23]	Japan	Retrospective	97	NR	ICDSC	20.6	eq:number of the state	8

(2022) [5]

Study(year)	Country	Study design	Sample size(n)	Age(years)	POD assessment	POD incidence(%)	Risk factors	Nos score
Taxis et al. (2022) [15]	Germany	Retrospective	225	NR	DSM-V	21.8	Operative time, ACCI, sex, ICU stay period, impaired wound healing, positive his- tory of nicotine and alcohol abuse, microvascular surgery, previous head and neck sur- gery, flap success, tracheostomy, postoperative nutritional risk screening score	8
Obermeier et al. (2022) [<mark>29</mark>]	Germany	Retrospective	198	NR	Nu-DESC	32.8	Duration of intuba- tion, gender, fluid intake	8
Kim et al. (2022) [<mark>28</mark>]	South Korea	Retrospective	197	60.0±13.3	DSM-V	9.1	Age, past neu- rological history, time to ambula- tion	9
Kolk et al.	Germany	Retrospective	100	65	DSM-V	18.0	Age, diabetes	9

Abbreviations: CAM Confusion Assessment Method, DSM-V Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, DSM-IV Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, ICDSC Intensive Care Delirium Screening Checklist, Nu-DESC Nursing Delirium Screening Scale, NR Not reported, NRS Numeric rating scale of pain, ASA American Society of Anesthesiologists, ICU Intensive care unit, ACCI Age-adjusted Charlson Comorbidity Index, CCI Charlson Comorbidity Index, COPD Chronic obstructive pulmonary disease, TSH Thyrotropic hormone, NLR Neutrophil-to-lymphocyte ratio, BMI Body mass index, E-PRE-DELIRIC Early Prediction Model for Delirium in an intensive care unit

diabetes mellitus had a 2.73-fold increased risk of POD compared to patients without diabetes mellitus (OR: 2.73, 95% CI: 1.24–6.01, P = 0.01, I2 = 0%, Table 4; Fig. 9).

History of smoking

Two articles reported that the impact of the smoking history on risk of POD. Our results indicated that the pooled OR was 2.74 (95% CI: 1.13–6.65, *P*=0.03) with no heterogeneity (I2=0%, P=0.86, Table 4; Fig. 10).

Precipitating risk factors

In this category, only 2 risk factors were analyzed by meta-analysis, including operative time and ICU stay time. The meta-analysis of 2 risk factors showed that surgery time (OR: 1.00, 95% CI: 1.00-1.01, *P*=0.003, I2=0%, Table 4; Fig. 11) and ICU stay time (OR: 2.08, 95% CI: 0.46-9.46, P=0.34, I2=93%, Table 4; Fig. 12) were not significant risk factors for POD.

Discussion

POD is a common postoperative complication among head and neck cancer surgery patients and is related to notable morbidity and mortality. In light of these adverse prognoses, it is imperative to identify related predictive factors of POD and take appropriate preventive measures to prevent POD in patients undergoing surgery for head and neck cancer. Thus, we conducted this meta-analysis and found several significant predictive factors of POD after head and neck cancer surgery including increased age, age > 75 years, male sex, higher ASA level, diabetes mellitus and history of smoking.

mellitus, preoperative TSH, type of surgery

Our study was not the first systematic review and meta-analysis exploring the risk factors for POD after head and neck cancer surgery. Compared with a previous meta-analysis [6], our systematic review and meta-analysis included articles that were published within the latest 5 years and that summarized the incidence of POD after head and neck cancer surgery. The prevalence of POD varies significantly among surgical

Table 2 The Newca	stle-Ottawa Scale (NO ⁵	s) scoring								
Study(year)	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Outcome not present at baseline	Control for age	Control for other confounding factors	Assessment of outcome	Enough follow-up duration long	Adequacy of follow-up	Total
Shiiba et al. (2009) [18]	-	-	-		-		-	-	-	6
Hasegawa et al. (2015) [19]	-	-	—	-	-	_	-	-	-	6
Booka et al. (2016) [20]	-		-	-	-	-	F	-	-	6
Choi et al. (2017) [27]	-	-	—	-		_	-	-	-	6
Zhang et al. (2019) [24]	-	-	—	-	0	_	-	-	-	∞
Wang et al. (2019) [25]	-	-	—	-	0	-	-	-	-	œ
lshibashi-Kanno et al. (2020) [12]	0	-	—	-		_	-	-	-	œ
Densky et al. (2019) [30]	-	-	—	-		-	-	-	1	6
Makiguchi et al. (2020) [21]	-	—	—	-	0	-	-	-	1	œ
Kong et al. (2021) [26]	0	-	—	-	0	-	-	-	-	2
Takahashi et al. (2021) [22]	-	-	—	-	0	_	-	-	-	œ
Kinoshita et al. (2021) [23]	-	-	—	-	0	_	-	-	-	∞
Taxis et al. (2022) [15]	-	-	—	1	0	-	-	-	-	œ
Obermeier et al. (2022) [<mark>29</mark>]	-	, -	-	-	0	-	—	-	1	Ø
Kim et al. (2022) [28]	-	-		-		-	—	-	-	6
Kolk et al. (2022) [5]	-	-		1	-	-	-	-	-	6



Fig. 2 Forest plots of the incidence of postoperative delirium

Table 3 Subgroup analysis of postoperative delirium after head and neck surgery

Outcomes	Number of studies	ES(95% CI)	l ² (%)
Pooled results			
Subgroup analyses base	ed on region		
Asia	12	0.18 (0.13–0.22)	93.0
Western countries	4	0.26 (0.19–0.33)	75.4
Subgroup analyses base	ed on criteria for F	POD	
DSM-IV	8	0.20 (0.13–0.27)	95.0
DSM-V	4	0.16 (0.10–0.22)	81.8
CAM	2	0.20 (0.02-0.41)	95.0
Others	2	0.27 (0.15–0.39)	80.4
Subgroup analyses base	ed on number of s	sample	
N <200	10	0.23 (0.17–0.29)	87.9
N≥200	6	0.15 (0.08–0.21)	95.1
Subgroup analyses base	ed on quality of in	cluded studies	
NOS 9	7	0.19 (0.13–0.24)	84.4
NOS 7–8	9	0.20 (0.15-0.24)	95.1
Subgroup analyses base	ed on study desig	n	
Retrospective	14	0.20 (0.15–0.25)	93.5
Others	2	0.20 (0.02–0.41)	95.0

Abbreviations: CAM Confusion Assessment Method, DSM-V Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, DSM-IV Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, POD Postoperative delirium, ES Effect size, CI Confidence interval populations; for instance, the incidence of POD is reportedly 5.45 to 28.57% after urological surgery, 10.09 to 51.28% after hip fracture surgery, and 4.1 to 54.9% after cardiac surgery [13, 14, 32]. In our study, the incidence of POD ranged from 4.2 to 36.9% with a pooled incidence of 20% and high heterogeneity (I2=93.2%, P < 0.001), which was consistent with a previous metaanalysis [6]. The heterogeneity of POD incidence may be a consequence of the sample size, the region of surgery, or the POD diagnostic criteria [33]. In addition, the incidence of POD in Western countries was significantly higher than that in Asia, possibly due to ethnic differences.

It is widely accepted that advanced age is an important predisposing predictor for POD [34]. In this metaanalysis, older age was associated with a relatively low risk of POD after head and neck cancer surgery. However, for patients over 75 years old, the risk of POD was 6.52 times higher than that in patients younger than 75 years old, which was in line with a previous meta-analysis [35]. The results may be explained by the presence of more comorbidities such as depression, preexisting cerebrovascular disease, insomnia, and frailty in elderly patients [36]. An alternative explanation might be agerelated inflammatory response changes, which might play a role in the pathophysiology of POD [37]. In addition, the effect of sex differences on POD risk remains



Fig. 3 Sensitivity analysis of the incidence of postoperative delirium



Fig. 4 Begg's funnel plot of the incidence of postoperative delirium

controversial. A previous meta-analysis suggested that female sex was a predictor for POD in patients undergoing spinal surgery [38]. Conversely, our results indicated that male sex was significantly associated with POD development in head and neck cancer surgery patients. A possible explanation was that males were more likely to develop obstructive sleep apnoea and alcohol dependence, which have been confirmed as significant risk factors for POD [39].

ASA classification is a well-known grading system for evaluating patients' tolerance to anesthesia and their physical status before surgery. In line with our recent study [40], our results indicated that an ASA level increase was a strong predictor for POD. Therefore, those who have a higher ASA level should be of great

Table 4 Meta-analysis of risk factors for postoperative delirium after head and neck cancer surgery

Risk factors	Number of studies	Pooled OR	Lower 95% Cl	Upper 95% Cl	P-value	l ² (%)	Statistical method
Age	5	1.05	1.03	1.07	< 0.001	18	Fixed
Age > 75 years	2	6.52	3.07	13.87	< 0.001	0	Fixed
Male gender	5	2.29	1.06	4.97	0.04	55	Random
ASA states	3	2.19	1.44	3.33	< 0.001	31	Fixed
ICU stay	2	2.08	0.46	9.46	0.34	93	Random
Operative time	3	1.00	1.00	1.01	0.003	0	Fixed
History of smoking	2	2.74	1.13	6.65	0.03	0	Fixed
Diabetes mellitus	3	2.73	1.24	6.01	0.01	0	Fixed

Abbreviations: ASA American Society of Anesthesiologists, CI Confidence interval, ICU Intensive care unit, OR Odds ratio



Fig. 5 Forest plot for increased age

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Fixed, 95% C		IV.	Odds Ratio Fixed, 95% Cl	
Hasegawa 2015	1.92132467	0.51911831	55.0%	6.83 [2.47, 18.89]				
Kim 2022	1.81807678	0.57430913	45.0%	6.16 [2.00, 18.99]				
Total (95% CI)			100.0%	6.52 [3.07, 13.87]			•	
Heterogeneity: Chi ² = 0 Test for overall effect:	0.02, df = 1 (P = 0.8 Z = 4.87 (P < 0.000	9); I² = 0% 01)			0.01 Favo	0.1 0.t [experimer	1 10 1 Tal] Favours [control]	100

Fig. 6 Forest plot for age > 75 years



Fig. 7 Forest plot for male sex

concern to clinicians. In our study, we also investigated whether diabetes mellitus was associated with POD after head and neck cancer surgery. Diabetes mellitus is a well-established risk factor for the development of dementia [41]. Additionally, the study by Liu and colleagues demonstrated that the increased risk of POD



Fig. 8 Forest plot for American Society of Anesthesiologists level

				Odds Ratio		Odds	Ratio	
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Fixed, 95% CI	[IV. Fixed	d. 95% CI	
Densky 2020	1.58350453	0.73514237	30.0%	4.87 [1.15, 20.58]				
Kolk 2022	0.66782937	0.59562397	45.7%	1.95 [0.61, 6.27]		_	-	
Makiguchi 2020	0.9242589	0.81588594	24.3%	2.52 [0.51, 12.47]				
Total (95% CI)			100.0%	2.73 [1.24, 6.01]			-	
Heterogeneity: Chi ² =	0.95, df = 2 (P = 0.62	2); I² = 0%			0.01	1	1 10	100
Test for overall effect:	Z = 2.50 (P = 0.01)				Favours	experimental]	Favours [control]	100

Fig. 9 Forest plot for diabetes mellitus

			Odds Ratio			Odds Ratio		
Study or Subgroup	log[Odds Ratio]	SE Weight	IV, Fixed, 95% C		IV	. Fixed. 95% CI		
Ishibashi-Kanno 2019	1.12817109 0.81374	701 30.9%	3.09 [0.63, 15.23]			-		
Makiguchi 2020	0.95551144 0.54373	389 69.1%	2.60 [0.90, 7.55]					
Total (95% CI)		100.0%	2.74 [1.13, 6.65]			-	-	
Heterogeneity: Chi ² = 0.0 Test for overall effect: Z	03, df = 1 (P = 0.86); l ² = 0% = 2.23 (P = 0.03)			0.01 Eavoi	0.1	1 entall Eavours (10	100

Fig. 10 Forest plot for the history of smoking

Study or Subaroup	log[Odds Patio]	SE	Woight	Odds Ratio		n	Odds Ratio	1	
Study of Subgroup	logiouus Ratioj	JE	weight	IV. FIXED. 35% C		1	, Fixed, 35% C		
Ishibashi-Kanno 2019	0.00399202	0.00127106	97.3%	1.00 [1.00, 1.01]					
Takahashi 2021	-0.00424518	0.0075771	2.7%	1.00 [0.98, 1.01]			1		
Taxis 2022	0.3832195	0.44778338	0.0%	1.47 [0.61, 3.53]					
Total (95% CI)			100.0%	1.00 [1.00, 1.01]					
Heterogeneity: Chi ² = 1.8	87, df = 2 (P = 0.39); $I^2 = 0\%$						10	100
Test for overall effect: Z	= 3.01 (P = 0.003)				Favor	Irs [experim	ental] Favours	[control]	100

Fig. 11 Forest plot for operative time

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV. Random. 95% C	I	Oc IV. Ra	dds Ratio ndom. 95% Cl	
Choi 2017	0.00995033	0.00505169	53.3%	1.01 [1.00, 1.02]				
Taxis 2022	1.558776	0.39960353	46.7%	4.75 [2.17, 10.40]				
Total (95% CI)			100.0%	2.08 [0.46, 9.46]				
Heterogeneity: Tau ² = Test for overall effect: 3	1.12; Chi ² = 15.02, Z = 0.95 (P = 0.34)	df = 1 (P = 0.0	0001); l² =	93%	0.01 Eavo	0.1	1 10	100

Fig. 12 Forest plot for length of intensive care unit stay

after hip fracture surgery was explained by diabetes mellitus [42]. Our results also revealed that head and neck cancer surgical patients with diabetes mellitus were more susceptible to POD. Diabetes mellitus could weaken insulin signaling pathways in the regulation of the functions of neurons and glial cells [43]. In addition, diabetes mellitus is characterized by hyperglycemia, oxidative stress, and chronic inflammation that can lead to blood-brain barrier impairment [44]. Thus, it is not surprising that patients with diabetes mellitus had a higher risk for POD after head and neck cancer surgery.

Several studies have demonstrated that a history of smoking was associated with surgical complications, including postoperative pneumonia and wound infection [45]. However, the correlation between a history of smoking and perioperative neurocognitive disorders remains obscure to date. A previous study showed that a preoperative smoking history could decrease the incidence of early postoperative cognitive dysfunction by stimulating the cholinergic anti-inflammatory pathway [31]. Interestingly, our results suggested that a history of smoking was considered as a significant predictor for POD after head and neck cancer surgery. Similar to our current study, Zhou et al. also found that smoking was positively related to POD in patients undergoing non-cardiac and non-obstetric surgery [46], which was associated with the impaired cholinergic function due to nicotine withdrawal resulting from sudden cessation of smoking [47].

This meta-analysis did not conclude that operative time and intensive care unit duration were predictive factors of POD after head and neck cancer surgery, which might be related to the small number of studies included. However, according to the Consensus-based Guideline on POD of the European Society of Anesthesiology, operative time and ICU stay time should be considered as risk factors for POD after surgery [48]. Thus, the connection between the 2 risk factors and POD needs to be validated in future large-sample prospective multicentre cohort studies.

Limitations

There were some limitations in our study. First, only articles published in English were included in the current study, resulting in unavoidable selection bias. Second, we identified several risk factors for POD after head and neck cancer surgery, however, the association between these risk factors and POD in other surgical populations still need to be explored further. Third, some significant risk factors were identified in a few studies with small sample sizes, which should be interpreted with caution.

Conclusions

To sum up, our meta-analysis indicated that POD was common after head and neck cancer surgery. Based on the multivariate analysis, some significant predictors were identified, including increased age, age >75 years, male sex, higher ASA grade, diabetes mellitus, and history of smoking, which might play a critical role in optimizing clinical management of POD.

Abbreviations

POD	Postoperative delirium
NOS	Newcastle-Ottawa scale
OR	Odds ratio
Cls	Confidence intervals
Nu-DESC	Nursing Delirium Screening Scale
ICDSC	Intensive Care Delirium Screening Checklist
CAM	Confusion Assessment Method
DSM	Diagnostic and Statistical Manual of Mental Disorders
ASA	American Society of Anesthesiologists

Supplementary Information

The online version contains supplementary material available at https://doi. org/10.1186/s12883-023-03418-w.

Additional file 1.

Acknowledgements

Not applicable.

Authors' contributions

BD and JLL conceived the study and drafted the manuscript. DDY applied the search strategy. LJ and MNL extracted the data. BD made the figures and tables. BD and JLL drafted this manuscript. All authors reviewed the manuscript.

Funding

The study was supported by the Key Research and Development Program of Hebei Province (Grant No. 19277714D).

Availability of data and materials

All data generated or analyzed during this study are included in this published article and its supplementary information files.

Declarations

Ethics approval and consent to participate Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Received: 5 April 2023 Accepted: 3 October 2023 Published online: 17 October 2023

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