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Research article

Risk factors of postoperative delirium following spine surgery: A meta-analysis of 50 cohort studies with 1.1 million participants

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ABSTRACT

Objectives: Postoperative delirium (POD) is considered to be a common complication of spine surgery. Although many studies have reported the risk factors associated with POD, the results remain unclear. Therefore, we performed a meta-analysis to identify risk factors for POD among patients following spinal surgery.
Methods: We systematically searched the PubMed, Embase and the Cochrane Library for relevant articles published from 2006 to February 1, 2023 that reported risk factors associated with the incidence of POD among patients undergoing spinal surgery. The Meta-Analysis of Observational Studies in Epidemiology (MOOSE) guidelines were followed, and random effects models were used to estimate pooled odds ratio (OR) estimates with 95 % confidence intervals (CIs) for each factor. The evidence from observational studies was classified according to Egger's *P* value, total sample size, and heterogeneity between studies.
Results: Of 11,329 citations screened, 50 cohort studies involving 1,182,719 participants met the inclusion criteria. High-quality evidence indicated that POD was associated with hypertension, diabetes mellitus, cardiovascular disease, pulmonary disease, older age (>65 years), patients experiencing substance use disorder (take drug ≥1 month), cerebrovascular disease, kidney disease, neurological disorder, parkinsonism, cervical surgery, surgical site infection, post-operative fever, postoperative urinary tract infection, and admission to the intensive care unit (ICU). Moderate-quality evidence indicated that POD was associated with depression, American

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Table 1
Characteristics of studies included in meta-analysis.

First author	Year	Study Design	Region	Observation Period	Sample size	Female %	Measurements of delirium
Kwon, Y. S. [23]	2022	Retrospective study	Korea	2011–2021	3967	46.20	Once patients were suspected to be POD by a nurse, the patients received psychiatric counseling and the diagnosis of POD was confirmed
Gold, C. [24]	2022	Retrospective review	USA	2017–2021	702	48.15	The primary outcome was the presence of postoperative delirium assessed by the DOSS and CAM-ICU
Wang, D. D. [4]	2021	Prospective study	China	2020.05–2020.11	195	46.70	The CAM-CR scale
Arizumi, F. [6]	2021	Retrospective study	Japan	2013–2014	294	43.20	NR
Pernik, M. N. [25]	2020	Retrospective cohort study	USA	2014–2019	324	NR	Postoperative delirium was assessed via a validated retrospective chart review and cases were confirmed by an expert (SAW)
Susano, M. J. [15]	2020	Prospective cohort study	USA	2017–2018	219	43.00	The FRAIL and the Mini-Cog and the Animal Verbal Fluency test and by chart review using published criteria and by direct, independent assessment with the CAM
Ren, Q. [17]	2020	Prospective observational investigation	Canada	2014.06–2014.10	206	61.20	Patients' serum CRP, delirious status (using the CAM), and delirious score (using MDAS) were examined before surgery and 1–2 days after surgery
Kang, T. [26]	2020	Prospective study	Korea	2016.03–2017.07	138	60.14	The presence of delirium was evaluated by consultation with the Department of Psychiatry based on DSM-V. When patients had delirious symptoms, such as disorientation, memory impairment, perceptual disturbances, psychomotor disturbances, emotional disturbances, and disturbance of the sleep-wake cycle, we consulted the psychiatrist and diagnosed the case as postoperative delirium
Pernik, M. N. [27]	2020	Retrospective cohort study	USA	2014–2019	106	NR	Postoperative delirium was assessed via a validated retrospective chart review method and cases were confirmed with an expert geriatrician (SAW)
Onuma, H. [19]	2020	Retrospective study	Japan	2014–2017	299	51.20	The diagnosis of delirium was based on the criteria outlined in the DSM
Wang, J. [28]	2020	Prospective study	China	2019.03–2019.09	64	64.06	POD was determined by a bedside nurse trained in neurology department using the Nu-DESC, performed 1–3 days postoperatively
Zhang, S. [29]	2020	Prospective study	China	NR	25	NR	Postoperative delirium and delirium severity were assessed using validated methods, including the CAM, CAM for the Intensive Care Unit, Delirium Rating Scale-Revised-98, and chart review
Pernik, M. N. [30]	2020	Retrospective cohort study	USA	2017.01–2019.03	147	53.48	All cases that met any of the criteria were reviewed separately by an expert (SAW)
Alhadi, R. [31]	2019	Retrospective study	USA	2016–2014	313	49.50	CAM
Elsamadicy, A. A. [16]	2019	Retrospective cohort study	USA	2010–2015	130	45.90	NR
Oe, S. [10]	2019	Retrospective study	Japan	2010–2017	319	79.90	Delirium was diagnosed according to medical records within 30 days of surgery using the CAM
Hesse,S. [32]	2019	Prospective study	USA	NR	626	38.98	The occurrence of EEG burst suppression during maintenance and the type of EEG emergence trajectory may be predictive of PACU delirium
Susano, M. J. [33]	2019	Retrospective analysis	USA	2015–2017	716	51.00	Three independent investigators using published criteria-12
Elsamadicy, A. A. [34]	2019	Retrospective cohort study	USA	2005–2015	138	NR	NR
Pan, Z. [14]	2019	Prospective study	Korea	2015–2016	83	67.40	Delirium was diagnosed by the previously accepted short CAM
Kang, S. Y. [35]	2019	Retrospective cohort study	Korea	2010–2016	3634	57.40	NR
Song, K. J. [36]	2019	Retrospective cohort study	Korea	2014–2016	3611	50.57	As defined in the fourth edition of the DSM-V
Plyler, S. S. [37]	2018	Prospective study	USA	NR	30	56.67	The CAM, CAM-ICU, and the 3D-CAM

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Table 1 (*continued*)

First author	Year	Study Design	Region	Observation Period	Sample size	Female %	Measurements of delirium
Kang, S. Y. [12]	2018	Prospective study	Korea	2015–2016	104	65.40	Eligible individuals who were scheduled to have spinal surgery the next day were assessed previous or current delirium using the CAM. We used the CAM to exclude people with previous or current delirium. And then the K-MMSE and neurologic examinations were assessed for the baseline evaluation
Morino, T. [38]	2018	Retrospective cohort study	Japan	2012–2014	532	46.80	The presence of delirium was determined based on the DSM-IV criteria
Kobayashi, K. [39]	2018	Retrospective study	Japan	2008–2013	35	60.00	Summary of the Charlson Comorbidity Index
Elsamadicy, A. A. [2]	2017	Retrospective study	USA	2008–2010	453	53.40	DSM-V criteria
Soh, S. [11]	2017	Prospective observational study	Korea	2014–2015	109	48.60	The CAM for the intensive care unit and the intensive care delirium screening checklist. The patients were evaluated for delirium by the ICDSC and CAM-ICU
Nazemi, A. K. [40]	2017	Retrospective analysis	USA	1990–2015	66	NR	The diagnosis of delirium is based on screening tools, and of these, the CAM has been validated as a sensitive, specific, and reliable method of identifying delirium. Other widely used methods of identifying delirium include the DOS scale based on the DSM-IV and the NEECHAM Confusion Scale
Kobayashi, K. [41]	2017	Retrospective database analysis	Japan	NR	262	53.45	Delirium has 4 features acute onset and a fluctuating course, inattention, disorganization of thinking, and an altered level of consciousness and diagnosis requires the presence of features 1 and 2 and either 3 or 4
Adogwa, O. [42]	2017	Retrospective study	USA	NR	82	59.60	NR
Radcliff, K. [43]	2017	Representative cohort Study	USA	2010–2012	2792	46.70	NR
Elsamadicy, A. A. [44]	2017	Retrospective study	USA	2005–2015	923	63.90	NR
Brown, C. H. [7]	2016	Prospective observational study	USA	2012–2014	89	47.20	Postoperative delirium and delirium severity were assessed using validated methods, including the CAM, CAM for the Intensive Care Unit, Delirium Rating Scale-Revised-98, and chart review
Gaudet, J. G. [45]	2016	Prospective study	Columbia	2014–2015	81	39.51	All study subjects were assessed by a trained investigator, who reviewed all results with the principal investigator
Jiang, X. [46]	2016	Retrospective study	China	2010–2015	451	49.89	Patients who had features of acute onset and fluctuating course and any two of the other features were diagnosed with delirium
Lee, Y. S. [47]	2016	Retrospective study	Korea	2012–2014	129	60.46	Postoperative delirium was diagnosed with the CAM
Wang, J. [48]	2015	NR	China	2011–2013	200	52.50	Delirium was assessed by the CAM according to the DSM-IV criteria
Seo, J. S. [9]	2014	Retrospective study	Korea	2012–2013	70	54.28	Postoperative delirium was diagnosed according to DSM-5 criteria
Kelly, A. [49]	2014	Prospective study	Canada	2019.1–2010.12	92	NR	NR
Fineberg, S. J. [8]	2013	Retrospective database analysis	USA	2002–2009	578,457	50.64	Cases of delirium were identified by ICD-9-CM codes transient mental disorders, acute, and subacute delirium, drug-induced delirium, and altered mental status
Cheung, A. [50]	2013	Retrospective cohort study	USA	2008–2010	68	14.70	We followed a rigorous process for the identification of delirium cases that used the prospective SAVES method, consultation with a psychiatrist, who referred to criteria set out by the American Psychiatric Association: DSM-IV and the CAM or CAM-ICU model
Aydogan, M. S. [51]	2013	Prospective study	Turkey	NR	32	46.86	ICU, CAM-ICU
Fineberg, S. J. [52]	2013	Retrospective study	USA	2002–2009	578,457	NR	NR

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Table 1 (*continued*)

First author	Year	Study Design	Region	Observation Period	Sample size	Female %	Measurements of delirium
Li, H. [18]	2012	Retrospective study	China	2007–2011	1216	44.08	Using the two-stage sedation delirium assessment method, the first sedation assessment was performed, and if the RASS was lower than 4, it was excluded. If it was greater than 4, the second step was performed, that is, delirium assessment. If positive, it was the state of delirium. The evaluation began once a day at 24 h after operation and lasted for 72 h
Imagama, S. [53]	2011	Retrospective study	Japan	2001–2011	918	43.24	NR
Lee, J. K. [3]	2010	Retrospective study	Korea	2000–2007	81	66.70	Postoperative delirium was diagnosed according to the DSM-IV diagnostic criteria and CAM
Ushida, T. [5]	2009	Retrospective study	Japan	2003–2007	81	NR	Observations of subjects was conducted each shift and recorded using the DOS that is developed on the basis of DSM-IV diagnostic criteria. The DOS scale is with 13 items that can be rated as present absent in less than 5 min. The highest total score is 13. Three or more points indicate a delirium
Gao, R. [13]	2008	Retrospective analysis	China	2007.05–2007.11	549	44.99	Diagnosis of this delirious state is usually done according to the CAM criteria, the TICS, MMS, SAS, DRS or NCS
Kawaguchi, Y. [54]	2006	Retrospective analysis	Japan	2000–2002	104	45.45	The presence of delirium was diagnosed by the CAM

First author	Delirium definition	Significant factors	Incidence, n (%)	Adjusted variables
Kwon, Y. S. [23]	A mental disorder characterized by acute and fluctuating course of consciousness disturbance	Old age (≥70 years), Parkinson's disease, depression, Intensive care unit stay, anti-psychotics drug	5.90	NR
Gold, C. [24]	An abrupt disturbance of cognition and consciousness and is characterized by a decreased ability to sustain or shift attention, impairment of memory and executive function, and fluctuation in arousal levels	Age, Lower preoperative, Postoperative hemoglobin, Higher ASA grade, Greater extent of surgery, Higher postoperative pain scores	24.60	A binomial logistic regression model was designed using a custom written MATLAB script
Wang, D. D. [4]	An acute condition characterized by reduced awareness of the environment and a disturbance in attention	Restrictive fluid therapy, GDT	8.20	Age, ASA classification, BMI, or postoperative pain are no statistically significant differences which ensures the comparability of the two groups
Arizumi, F. [6]	A common and serious complication after surgery	Patient factors, Surgical factors, Comorbid disease, System disorder	22.00	A *t*-test and a chi-squared test
Pernik, M. N. [25]	An MD, PA, or NP posing the diagnosis of delirium in the patient chart	Older adults	NR	NR
Susano, M. J. [15]	NR	Age, Years, Male, Female, BMI, College degree or higher, ASA physical status≥3, METS<4, Total number of medications, Chronic use of opioids, Alcohol consumption, Depression, Psychiatric history	25.00	Mann-Whitney *U* test for non-normal distributions, the independent samples *t*-test for normally distributed, and Chi-Square test for categorical variables
Ren, Q. [17]	A common complication of the central nerve system after surgical operations in elderly patients, usually characterized by a fluctuating course of inattention, consciousness and disordered thinking	CPR level, Age, Gender, ASA classification, BMI, Surgery type, MDAS, CRP, Postoperative HB, Blood transfusion	5.80	Age, Gender, BMI, Blood transfusion, ASA classification, Anesthesia duration, and Postoperative HB value were adjusted
Kang, T. [26]	A disturbance in attention, awareness, and cognition which develops over a short period of time with a fluctuating course	Age, Male, Preoperative level of hemoglobin, K-MMSE, Operation time, Blood loss, Visual Assessment Score, Visual Assessment Score, Blood transfusion	18.16	Age, Sex, type of admission, ASA classification, METs or ODI are no statistical difference
Pernik, M. N. [27]	NR	UTSW POSH program	11.40	No significant differences is at baseline
Onuma, H. [19]	A disturbance of consciousness and is characterized by an acute onset and fluctuating course of inattention	A history of stroke and mental disorders, Hypnotic drug use, Malnutrition, Hyponatremia, Respiratory dysfunction, Drug or alcohol abuse, Abnormal sodium	17.70	A multivariable logistic regression analysis was performed using the forward-backward stepwise method to determine the independent risk factors

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Table 1 (*continued*)

First author	Delirium definition	Significant factors	Incidence, n (%)	Adjusted variables
Wang, J. [28]	An acute and fluctuating dysfunction of consciousness caused by surgically-associated and individual patient factors	Age, Sex, ASA, Preoperative MMSE score, Hypertension, DM, Blood loss, Urine output, Anesthesia/Operation duration	15.63	NR
Zhang, S. [29]	NR	Baseline pain, Severity of delirium	21.20	NR
Pernik, M. N. [30]	A physician (resident or attending) or midlevel provider documenting a diagnosis of delirium	Age, Sex, BMI, Base WBC, Medication use, ASA score, Depression, Anxiety, Dementia, Smoking, Alcohol, Glasses use, Hearing aid use, Levels of fusion, Pelvic fixation, Hb, Blood loss	11.60	NR
Alhadi, R. [31]	NR	Lower education level, History of dementia, Smoking	15.70	A multivariable logistic regression model was used to adjust for factors found to be statistically significant ($p < 0.05$) on univariate analysis
Elsamadicy, A. A. [16]	NR	Blood transfusion, Age, Number of fusion levels, Gender, Age, BMI, Depression, anxiety, diabetes, CHF, CAD, A-Fib, MI, PVD, HTN, COPD, DVT, PE, CKD	14.60	An adjustment for known covariates
Oe, S. [10]	One of the most common complications for elderly patients who undergo surgical treatment and anesthesia, usually emerging 1–3 days after surgery	Height, Weight,BMI, Total cholesterol, WBC, Operative blood loss, PNI, CONU	9.40	NR
Hesse,S. [32]	NR	Age, Female, Weight, BMI, ASA physical status, Cardiovascular disease, Stroke, Chronic renal insufficiency, Alcohol use, Surgical discipline, Adjunct anesthetic, Burst suppression, Emergence trajectory, Emergence latency, CAM-ICU	19.97	A univariable analysis
Susano, M. J. [33]	NR	Older age, American Society of Anesthesiologists physical status>2, Metabolic equivalents of task<4, Depression, Nonelective surgery	18.00	Using the$\chi 2$ test or the Fisher exact test for small samples between the 2 groups. All the covariates with $P < 0.1$ in the univariate analysis were entered into the multiple logistic model for delirium
Elsamadicy, A. A. [34]	NR	Intraoperative ketamine	10.90	Age, Gender, BMI, LOS, Estimated blood loss, Proportion of patients requiring blood transfusions were similar
Pan, Z. [14]	A well-defined complication in hospitalized patients characterized by an acute change in cognition with fluctuating levels of consciousness	Age, Sex, BMI, MMSE, CVA, Cerebrovascular accident, TIA, Transient ischemic attack, MCI, Mild cognitive impairment, ARB, Hypertension, DM, History of CVA or TIA, Cardiovascular comorbidity, Parkinsonism, Previous dementia or MCI, Psychiatric disorder, Depression, Medications	14.50	MMSE score, medications, surgical methods, intraoperative blood loss, operation time, admission to ICU, and postoperative fever had no significant differences
Kang, S. Y. [35]	NR	Age, Sex, BMI, HTN, DM, Tuberculosis, Heart disease, Stroke, Cancer, Hyperlipidemia, Parkinsonism, Depression, Operation time, ICU stay	18.90	NR
Song, K. J. [36]	An acute and fluctuating impairment of consciousness that is accompanied by disturbances in attention, cognition, and perception	Preexisting dementia, Old age, Functional impairment, Comorbidities, Psychopathological symptoms	4.27	The chi-square test was used to evaluate differences according to etiology
Plyler, S. S. [37]	Acute onset or fluctuating course of mental status and Inattention, and either feature disorganized thinking or altered level of consciousness	LOS, Alcohol, Sleep cycle alterations, Inadequate pain control, Age greater than 65 years, Decreased renal clearance, Infection, Fever, Hearing and vision impairment, Anemia and Electrolyte disturbances	28.60	No statistically significant difference was found between preimplementation
Kang, S. Y. [12]	Eligible individuals who were assessed previous or current delirium using the CAM	RBD, Hypotension, Age, Men, Hypertension, DM, Cardiovascular comorbidity, Psychiatric disease, Previous dementia, MCI, Previous old CVA, TIA MMSE score, Admission to ICU, Blood loss during operation, Operation time, Anxiety disorder	14.40	Logistic regression analysis and univariate logistic regression analysis
Morino, T. [38]	Disturbances in attention and awareness associated with impairment	Large amounts of intraoperative bleeding, Low preoperative	11.10	Multivariate logistic regression models, with backward elimination were

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Table 1 (*continued*)

First author	Delirium definition	Significant factors	Incidence, n (%)	Adjusted variables
	in at least one cognitive function, including memory, orientation, language, visuospatial ability, or perception	concentration of serum Na, Low hematocrit level, Low concentration of albumin, High body temperature		constructed to find independent risk factors
Kobayashi, K. [39]	Acute onset with fluctuations in neuropsychiatric function, inattention, disorganized thinking, and altered levels of consciousness	Different surgical lesions, preoperative motor loss	0.31	Mann Whitney *U* test or Student *t*-test, and Kruskal-Wallis test
Elsamadicy, A. A. [2]	A risk factor that has been associated with increased in-hospital mortality, complications, and length of hospital stay after surgery	Gender, Age, BMI, Smoker, COPD, CHF, CAD, HTN, Fusion Levels, Operative Time, LOS, Postoperative UT, Postoperative Pneumonia	3.75	Nominal data were compared with the Chi-square test and assessed using a multivariate logistic regression model
Soh, S. [11]	An acute confusional state characterized by changed attention and cognitive function as well as fluctuating consciousness	BMI, Educational lever, MMSE score, DM, Hypertension, Cardiac disease, Pulmonary disease, Chronic kidney disease, Chronic liver disease, Neurologic or psychiatric disease, Drugs use	8.00	A linear mixed models with an unstructured covariance matrix
Nazemi, A. K. [40]	NR	Age, Functional impairment, Preexisting dementia, General anesthesia, Surgical duration >3 h, Intraoperative hypercapnia and hypotension, Greater blood loss, Low hematocrit and albumin, Preoperative affective dysfunction	18.60	NR
Kobayashi, K. [41]	An acute confused state with alterations in attention and consciousness in consciousness, memory, attention, perceptions, and behavior	Demographic data, Drug use, Comorbidities, Perioperative factors, Postoperative factors	5.72	NR
Adogwa, O. [42]	NR	Smoker, CHF, congestive heart failure, CAD, Coronary artery disease, CVD, Cardiovascular disease, MI, Myocardial infarction, HTN, Atrial fibrillation, DM	70.00	NR
Radcliff, K. [43]	NR	TiA, stroke	NR	NR
Elsamadicy, A. A. [44]	NR	Age, Number of medications, DM, Central nervous system disorders, Depression, Operative time, UTI	7.15	NR
Brown, C. H. [7]	A common and underrecognized condition after surgery in older adults	Race, Education, Retired, Smoking, Living in own home, Glasses, Hearing aids	40.50	An independent association between each factor and longer postoperative hospital stay age, functional status, ASA risk score
Gaudet, J. G. [45]	NR	Age, Male, BMI, Hypertension, DM, History of cancer, History of coronary disease, Taking aspirin/steroids	32.00	NR
Jiang, X. [46]	An acute change in cognitive status characterized by fluctuating consciousness, attention, memory, perceptions, and behavior occurring after an operation	Comorbid diseases, Anesthetic drugs use, Drug treatment, Surgical history	9.31	NR
Lee, Y. S. [47]	A common neurological complication that presents after surgery	Dementia and severe illness, Major surgery, Anesthesia, Multiple psychoactive medications	14.00	NR
Wang, J. [48]	A disturbance of consciousness (reduced clarity of awareness of the environment) with reduced ability to focus, sustain or shift attention	Age, Anesthesia type, Duration of operation, intraoperative hypercapnia, intraoperative hypotension, Postoperative sleep disorders	8.50	NR
Seo, J. S. [9]	A disturbance in attention and orientation to the environment that develops in a short period without other neurocognitive disorder and as a change in an additional cognitive domain	Preoperative factor and intraoperative factor	24.30	The two groups exhibited no significant difference in either age or male to female ratio. There was no significant difference in the average age of education between the two groups
Kelly, A. [49]	NR	CCI, Dural Tear	5.40	Adjustment for age and gender to avoid any confounding from those variables
Fineberg, S. J. [8]	A common postoperative complication of hospital admissions in the elderly is characterized by an acute confusional state with fluctuations in	Older age, Alcohol/drug abuse, Depression, Psychotic disorders, Neurological disorders, Deficiency	8.40	Independent t tests for continuous variables and x tests for categorical variables, and Binary logistic regression using the stepwise method was

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Table 1 (*continued*)

First author	Delirium definition	Significant factors	Incidence, n (%)	Adjusted variables
	consciousness, memory, attention, perceptions, and behavior	anemia, Fluid/electrolyte disorders, Weight loss, LOS, Costs, Sex,Race		performed to deter-mine independent risk factors
Cheung, A. [50]	An acute fluctuating change in mental function that is characterized by inattention and disorganized thinking	Infections, Spine surgeries, ICU stays, Malnutrition, New disease process, Time from injury to admission	17.70	Bivariate analyses
Aydogan, M. S. [51]	An acute onset of mental status change or a fluctuating course of delirium symptoms and inattention were accompanied by either disorganized thinking or an altered level of consciousness	Dexmedetomidine and midazolam	21.90	An independent samples *t*-test, the Mann–Whitney *U* test and corrected chi-square test for Categorical variable
Fineberg, S. J. [52]	NR	NR	8.40	NR
Li, H. [18]	A mental disorder characterized by fluctuations in the state of attention and cognitive function	Gender, age, operation duration, operation type, blood loss, dosage of morphine, leakage of cerebrospinal fluid, fever	9.50	Logistic regression analysis
Imagama, S. [53]	NR	Age, Sex	0.54	NR
Lee, J. K. [3]	A mental disorder of acute onset with a fluctuating course, characterized by disturbances in consciousness, orientation, memory, thought, perception and behavior	Comorbidities, Diagnosis, Operation method, Central nervous system disorder, Metabolic disorder, Cardiopulmonary disorder, Systemic illness, Gender, Age	13.60	x [2] test and Fisher exact test for statistical processing
Ushida, T. [5]	An acute and relatively sudden decline in attention-focus, perception, and cognition and known to occur usually in the elderly people	Age, Blood urea levels, Cardiothoracic index, Hypertension, Smoking habits, AF, Pneumonia, Hearing impairment, Disturbance of circadian rhythm	28.40	NR
Gao, R. [13]	An acute state of confusion characterized by fluctuating consciousness and inattention which in most studies occurs shortly after surgery	Central nervous system disorder, Surgical history, Age >65 years, DM, Blood transfusion	3.30	T tests were used for statistical analysis of the difference in the mean values between the delirium group and non-delirium control group, and the x^2 test was used for the comparison of the categorical data
Kawaguchi, Y. [54]	An acute confusional state with a fluctuating course involving an acute generalized impairment of cognitive function that affect attention, memory, planning and organizational skills	Age, Sex, Hemoglobin, Sodium, Medications, Status, Low concentrations of hemoglobin	12.50	Hemoglobin, hematocrit, sodium, potassium, calcium, blood sugar, total protein, and albumin did not differ significantly between the delirium group and the control group

Abbreviations: AF: Atrial fibrillation; A-Fib: Atrial fibrillation; ASA: American Society of Anesthesiologists; BMI: Body Mass Index; CAD: Coronary artery disease; CAM: Confusion Assessment Method; CAM-CR: the Confusion Assessment Method-Chinese Revision; CAM-ICU: CAM for the ICU; CHF: Congestive heart failure; COPD: Chronic obstructive pulmonary disorder; CKD:Chronic kidney disease; DOS: Delirium observation screening; DOSS: the Delirium Observation Screening Scale; DM: Diabetes mellitus; DRS: Administration of the delirium rating scale; DSM-IV: the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; DSM-V: the Diagnostic and Statistical Manual of Mental Disorder; DVT: Prior deep vein thrombosis, HTN: Hypertension osteoarthritis; K-MMSE: the Korean version of the Mini-Mental State Examination; MDAS: the Memorial delirium assessment scale; MI: Prior myocardial infarction; MMSE: a modification of the Mini-Mental Status Exam; NCS: the NEECHAM confusion scale; Nu-DESC: the Nursing delirium screening score; LOS: Length of Stay; PE: Prior pulmonary embolism; PVD: Peripheral vascular disease; SAS: Specific activity scale; TIA: Transient Ischemic Attack; TICS: The telephone interview for cognitive status; UTSW POSH: the UT Southwestern Perioperative Optimization of Senior Health; WBC: White blood cell.

Society of Anesthesiologists (ASA) fitness grade (>II), blood transfusion, abnormal potassium, electrolyte disorder, length of stay, inability to ambulate and intravenous fluid volume.
Conclusions: Conspicuous risk factors for POD were mainly patient- and surgery-related. These findings help clinicians identify high-risk patients with POD following spinal surgery and recognize the importance of early intervention.

1. Introduction

Delirium is known as an acute confusional state characterized by disturbances in consciousness and cognitive changes, which usually occur between 24 and 72 h after surgery [1]. Unless effective treatment can be accessed, the consequences of postoperative delirium (POD) are far-reaching, including loss of independence and cognition, prolonged hospitalization, and increased risk of in-hospital morbidity and mortality [2]. Due to a lack of knowledge of delirium, it is often ignored or misdiagnosed as dementia or depression, which may lead to delays in functional restoration and difficulty in postoperative care [3]. Previous studies have revealed

Table 2
Sensitivity analysis for significant factors and class of evidence.

Significant factors	OR (95 % CI)	P for association	T-F adjusted OR (95 % CI)	No. of study	Filled studies	Class of Evidence
Significant patient-related factors						
Hypertension						
No	Ref.					
Yes	1.22 (1.05–1.41)	0.009	1.17 (0.98–1.40)	18	2	I
Diabetes mellitus						
No	Ref.					
Yes	1.50 (1.19–1.88)	0.001	1.50 (1.19–1.88)	20	0	I
Cardiovascular disease						
No	Ref.					
Yes	1.68 (1.22–2.31)	0.001	1.52 (1.06–2.16)	12	2	I
Depression						
No	Ref.					
Yes	1.91 (1.33–2.74)	0.001	1.91 (1.33–2.74)	10	0	II
Pulmonary diseases						
No	Ref.					
Yes	2.52 (1.67–3.81)	0.001	1.92 (1.16–3.18)	9	4	I
Old age (≥65 years)						
No	Ref.					
Yes	1.95 (1.32–2.87)	0.001	1.24 (0.81–1.88)	13	5	I
Drug abuse						
No	Ref.					
Yes	2.48 (1.57–3.92)	0.001	2.48 (1.57–3.92)	6	0	I
Kidney disease						
No	Ref.					
Yes	1.45 (1.25–1.70)	0.001	1.45 (1.25–1.70)	10	0	I
Neurological disorder						
No	Ref.					
Yes	4.78 (2.74–8.33)	0.001	4.78 (2.74–8.33)	10	0	I
Parkinsonism						
No	Ref.					
Yes	5.32 (1.89–15.01)	0.002	5.06 (2.08–12.32)	2	1	I
Significant surgery-related factors						
ASA fitness grade > II						
No	Ref.					
Yes	1.74 (1.15–2.65)	0.010	1.74 (1.15–2.65)	5	0	II
Blood transfusion; ml						
≤500	Ref.					
> 500	1.71 (1.09–2.68)	0.002	1.18 (0.73–1.89)	11	4	II
Cervical surgery						
No	Ref.					
Yes	1.67 (1.26–2.20)	0.001	1.67 (1.26–2.20)	11	0	I
Potassium						
Normal	Ref.					
Abnormal	5.32 (1.89–15.01)	0.002	5.06 (2.08–12.32)	2	1	II
Electrolyte disorders						
No	Ref.					
Yes	3.10 (2.90–3.40)	0.001	NA	1	NA	II
Inability to ambulate						
No	Ref.					
Yes	2.76 (1.02–7.41)	0.045	NA	1	NA	II
Intravenous fluid volume, mL						
Normal	Ref.					
Abnormal	1.52 (1.04–2.23)	0.031	NA	1	NA	II
SSI						
No	Ref.					
Yes	5.75 (2.60–12.70)	0.001	5.75 (2.60–12.70)	4	0	I
Postoperative fever						
No	Ref.					
Yes	8.40 (2.00–35.24)	0.004	8.40 (2.00–35.24)	3	0	I
Postoperative UTI						
No	Ref.					
Yes	5.71 (3.13–10.41)	0.001	5.71 (3.13–10.41)	5	0	I
LOS, days						
Normal	Ref.					
Abnormal	2.30 (1.23–4.28)	0.009	2.30 (1.23–4.28)	5	0	III
Admission to ICU						
No	Ref.					
Yes	2.91 (2.13–3.96)	0.001	2.91 (2.13–3.96)	5	0	I

Abbreviations: NA: Not available; Ref: Reference group; CI: Confidence interval; OR: Odd ratio; T-F: Trim and filled method.

that the incidence of POD in elderly individuals is as high as 40.5 % in patients undergoing spinal surgery [4].

There are various approaches to the treatment of spinal disease and surgical treatment is often the most appropriate method. Recently, the number of people who had spine surgery has reached more than 4.83 million each year worldwide, and a large number of patients develop POD [5]. Compared with patients undergoing other types of surgery, patients undergoing spinal surgery are more likely to experience delirium [6]. The amount of research on risk factors for POD is increasing.

A variety of factors contribute to the development and outcome of patients with POD, including patient-related risk factors (e.g., patient age, hypertension, diabetes, cardiovascular disease, depression, pulmonary disease, patients experiencing substance use disorder (take drug ≥1 month), kidney disease, neurological disorder and parkinsonism) [3,7–14] and surgery-related risk factors (e.g., American Society of Anesthesiologists (ASA) fitness grade, blood transfusion, cervical surgery, electrolyte disturbance, mobility difficulties, intravenous infusion volume, surgical site infection (SSI), postoperative fever, postoperative urinary tract infection (UTI), length of stay (LOS) or admission to intensive care unit (ICU)) [6,7,15–19]. Many modifiable risk factors for POD have been mentioned in various studies, among which hypertension and diabetes are mentioned in many studies as significant risk factors. However, the identification of risk factors for POD remains controversial. To achieve a sufficient sample size to accurately estimate the association between these factors and POD, we hope to conduct a more comprehensive meta-analysis to assess various reported risk factors according to the level of evidence.

2. Methods

2.1. Standard protocol approvals, registrations, and patient consent

The MOOSE (Meta-Analysis of Observational Studies in Epidemiology) (eTable 1 in the Supplement) [20], PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) [21], Cochrane handbook and AMSTAR (Assessing the methodological quality of systematic reviews) guidelines were followed [22].

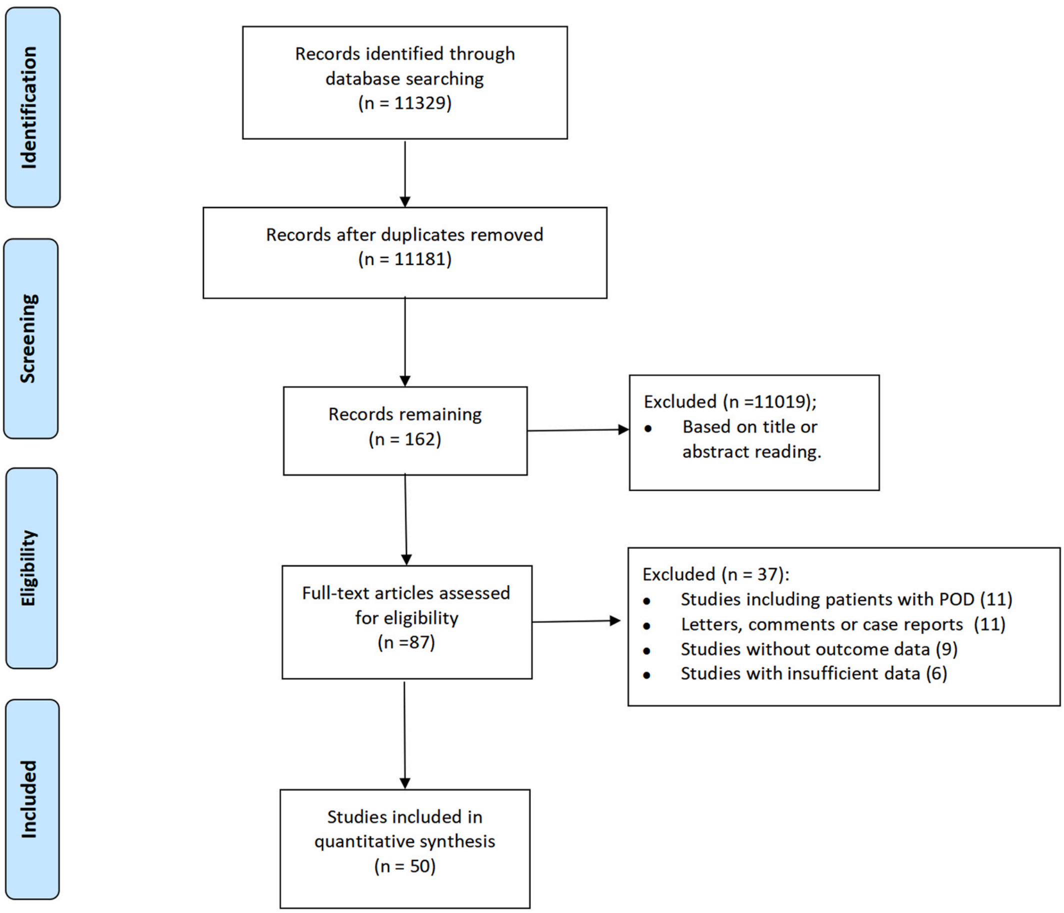

Fig. 1. Flow diagram of the study selection according to the meta-analysis of observational studies in epidemiology.

2.2. Search strategy

PubMed, Embase and Cochrane Library electronic databases were systematically searched by two independent investigators to identify relevant publications from 2006 to February 1, 2023 without language restrictions. Medical subject heading (MESH) terms were used in the PubMed and the Cochrane Library, Embase subject headings (Emtree) were used in Embase, along with text-word terms (including synonyms and closely related words) related to spine surgery, delirium, and risk factors. The detailed searching

Table 3
Sensitivity analysis for No-significant factors and class of evidence.

No-significant Factors	OR (95 % CI)	P for association	T-F adjusted OR (95 % CI)	No. of study	Filled studies	Class of Evidence
No-significant patient-related factors						
Gender						
Female	Ref.					
Male	1.33 (0.95–1.85)	0.097	1.33 (0.95–1.85)	20	0	III
Smoking						
Never	Ref.					
ever	0.87 (0.42–1.77)	0.691	0.87 (0.42–1.77)	10	0	II
Alcohol use						
Never	Ref.					
ever	1.24 (0.86–1.77)	0.247	1.24 (0.86–1.77)	10	0	II
BMI						
Normal	Ref.					
Abnormal	1.06 (0.97–1.16)	0.226	1.01 (0.91–1.12)	2	1	II
Hemoglobin						
Normal	Ref.					
Abnormal	0.60 (0.19–2.00)	0.402	0.60 (0.19–2.00)	2	0	III
Albumin						
Normal	Ref.					
Abnormal	1.07 (0.51–2.24)	0.858	1.07 (0.51–2.24)	6	0	III
Sodium						
Normal	Ref.					
Abnormal	0.86 (0.78–0.96)	0.006	0.83 (0.75–0.98)	5	1	II
Anxiety						
No	Ref.					
Yes	0.94 (0.25–3.48)	0.921	0.94 (0.25–3.48)	3	0	III
Coronary artery disease						
No	Ref.					
Yes	1.08 (0.51–2.28)	0.182	1.08 (0.51–2.28)	3	0	I
Cerebrovascular disease						
No	Ref.					
Yes	1.09 (0.92–1.25)	0.001	2.94 (2.48–3.48)	6	1	I
MMSE score						
≥30	Ref.					
< 30	0.94 (0.71–1.25)	0.660	0.94 (0.71–1.25)	4	0	III
Non-significant surgery-related factors						
Preoperative VAS						
Normal	Ref.					
Abnormal	0.92 (0.71–1.18)	0.490	0.91 (0.71–1.17)	2	1	II
Blood loss; ml						
≤300	Ref.					
> 300	1.00 (0.99–1.01)	0.569	1.00 (0.99–1.01)	14	0	II
Lumbar surgery						
No	Ref.					
Yes	0.59 (0.42–0.82)	0.002	0.59 (0.42–0.82)	8	0	I
Spinal fusion						
No	Ref.					
Yes	0.65 (0.27–1.03)	0.001	0.65 (0.27–1.03)	10	0	II
Spinal decompression						
No	Ref.					
Yes	0.42 (0.40–0.45)	0.001	0.42 (0.40–0.45)	4	0	I
Opioid use						
No	Ref.					
Yes	1.39 (0.74–2.62)	0.310	1.39 (0.74–2.62)	2	0	III
Duration of surgery, min						
≤180	Ref.					
> 180	1.00 (0.99–1.00)	0.274	0.99 (0.99–1.00)	9	3	II
Reoperation						
No	Ref.					
Yes	1.43 (0.35–5.81)	0.617	0.73 (0.18–2.93)	2	1	III

Abbreviations: NA: Not available; Ref: Reference group; CI: Confidence interval; OR: Odd ratio; T-F Trim and filled method.

terms and strategy ('spine' or 'surgery' or 'spinal disease') and (delirium or 'awakening-sleep cycle') and ('risk factor' or 'hypertension' or 'blood loss' or 'operation time' or 'cerebrovascular disease' or 'age factor' or 'neurological disorder' or 'diabetes') were displayed in eTable 2 in the Supplement. Fig. 1 presents the literature search and the study selection. To identify any potentially missed relevant studies, we also manually reviewed the reference lists of previous systematic reviews and meta-analyses. If multiple articles were published from the same cohort, we only included the one with the largest sample size or the most informative for analysis.

All citations from the initial search results were downloaded and merged by using Endnote ×9 software to identify and remove potentially duplicate records. Based on the following inclusion and exclusion criteria, two investigators screened the titles and abstracts independently to identify the most eligible literatures. In cases of disagreement, between the two senior reviewers, a third senior member made the final decision.

2.3. Selection criteria

The retrieved studies were judged as eligible if they meet the following PICOS inclusion criteria (participant, invention, comparator, outcome and study design):

(1) Participants: patients undergoing spinal surgery.
(2) Invention: patient-related and surgery-related factors associated with the incidence of POD following spinal surgery.
(3) Comparator: comparison group with lower exposure or no exposure to a modifiable risk factor.
(4) Outcomes: risk factors for POD after spinal surgery were effectively measured by odds ratios (ORs) and corresponding 95 % confidence intervals (CIs).
(5) Study design: prospective or retrospective cohort studies.

Conference papers or reports that used the same study population, studies that did not report risk estimates or studies that had insufficient data to calculate ORs to estimate the risk of POD were excluded (eTable 3 in the Supplement).

2.4. Data extraction and quality assessment

A predesigned data extraction table for independent studies was used for data extraction by two reviewers. Discrepancies between examiners were resolved through discussion or third-party adjudication. The methodological quality of each qualified study was independently evaluated by the two reviewers using the Newcastle–Ottawa scale (NOS) (eTable 4 in the Supplement) [55]. The maximum score for each study was 9. A score ≥8 indicates high quality (low risk of bias) [56].

2.5. Evaluation of the strength of evidence

The strength of the evidence in the identified associations for observational studies was graded using a set of modified criteria (eTable 5 in the Supplement). We classified an association as Class I (high-quality) evidence when the following three conditions were met simultaneously: Egger's P value > 0.1, a total population >1000 and lower between-study heterogeneity I^2 <50 % [57].

2.6. Statistical analysis

All analyses were conducted by using the systematic Meta-Analysis software STATA (version 12.0; Stata, University Station, Texas, USA). In this study, POD was defined as a sharp decline in cognitive ability in the first 7 days. The fully adjusted effect estimates (ORs) of the correlation between risk factors and POD were used to derive pooled risk estimates depicted graphically with forest plots. Meta-analysis was conducted to analyze the risk of POD with each patient-related factor and surgery-related factor. A random effects meta-analysis was applied for all analyses [58], taking into account inherent interstudy heterogeneity in terms of study population, exposure factors, follow-up time, and other factors. We used the Cochrane Q test and I^2 test to evaluate heterogeneity between studies, and heterogeneity was judged statistically significant at $I^2 \geq 50$ % or $P < 0.05$ [27]. Publication bias was assessed by visual assessment of funnel plot symmetry combined with Begg's and Egger's tests [59]. In addition, we performed Duvall and Tweedie's trim and fill method to adjust the results when publication bias was detected [60]. All statistical tests were two-sided, with P values of <0.05 indicating statistical significance.

3. Results

3.1. Literature search and study characteristics

A total of 11,329 citations were identified. Following the removal of duplicates, 11,181 studies remained for review of their titles and abstracts. In the course of this procedure, 11,242 inconsequential studies were omitted, and 87 potentially pertinent studies were examined in full text. Thirty-seven studies were excluded because they examined non-population-based cohorts, they were meta-analyses, they were reviews, or they did not report outcome data. Finally, 50 studies [2–19,23–54] were included in this meta-analysis (Fig. 1 and eTable 3 in the Supplement).

The baseline characteristics of the included studies are shown in Table 1. All the included studies were published from 2006 to

2021, with 76 % of them [2,4,6,7,10–12,14–17,19,25,26,32,35,36,44,34,37,27,23,24,28–31,33,38,40–42,45–48,39,43] published in 2015 or later. Twenty studies [2,7,8,15,16,25,32,44,27,34,37,50,52,30,31,33,40,42,24,43] were conducted in the United States, twenty-six [3,4,6,9–14,18,19,35,26,36,52,28,38,41,46,48,23,29,47,54,39,53] were conducted in Asia, two [17,49] were conducted in Canada, one [45] was conducted in Colombia, and one [51] was conducted in Turkey. 68 % (34 out of 50) of the studies were retrospective cohort studies, and 58 % (29 out of 50) of the studies included were high-quality with an NOS score of ≥8.

The incidence rates of POD ranged from 0.5 % to 40.5 %, and the pooled incidence rate was 7 %, with significant heterogeneity across studies ($I^2 = 98.4$ %, $P < 0.001$) (eFig. 1 in the Supplement). Additionally, incidence rates were significantly different when stratified by some baseline study-level factors (almost all $P < 0.001$), except one according to the study region involved (6 % in Europe and 27 % in others) (eTable 6 in the Supplement).

3.2. *Patient-related risk factors*

Fig. 2 shows that high-quality (Class I) evidence suggested that patients with hypertension (OR 1.22; 95 % CI 1.05 to 1.41), diabetes (OR 1.50; 95 % CI 1.19 to 1.88), cardiovascular disease (OR 1.88; 95 % CI 1.31 to 2.72), pulmonary disease (OR 2.40; 95 % CI 1.67 to 3.46), older age (OR 1.95; 95 % CI 1.32 to 2.87), patients experiencing substance use disorder (OR 2.48; 95 % CI 1.57 to 3.92), cerebrovascular disease (OR 2.96; 95 % CI 2.49 to 3.51), kidney disease (OR 1.45; 95 % CI 1.24 to 1.70), neurological disorder (OR 4.78; 95 % CI 2.74 to 8.33), and parkinsonism (OR 5.32; 95 % CI 1.89 to 15.01) were at higher risk for POD. Moreover, there was moderate-quality (Class II) evidence of a significant association between depression (OR 1.91; 95 % CI 1.33 to 2.74) and POD.

Meta-analysis revealed no association between POD and sex (OR 1.33; 95 % CI 0.95 to 1.85), smoking (OR 0.87; 95 % CI 0.42 to 1.77), alcohol use (OR 1.24; 95 % CI 0.86 to 1.77), obesity (OR 1.06; 95 % CI 0.98 to 1.15) hemoglobin (>100 g/L) (OR 0.86; 95 % CI 0.71 to 1.05), albumin (<3.5 mmol/L) (OR 1.04; 95 % CI 0.43 to 2.56), sodium (<130 mmol/L) (OR 1.24; 95 % CI 0.85 to 1.80), abnormal potassium (OR 1.01; 95 % CI 0.89 to 1.41), anxiety (OR 0.94; 95 % CI 0.25 to 3.48), coronary artery disease (OR1.08; 95 % CI 0.51 to 2.28), or MMSE score (<30) (OR 0.79; 95 % CI 0.47 to 1.33) (Table 2 and eTable 7 in Supplement).

3.3. *Surgery-related risk factors*

Fig. 3 shows that there was high-quality (Class I) evidence of significant associations between POD and cervical surgery (OR 1.71; 95 % CI 1.26 to 2.33), SSI (OR 5.75; 95 % CI 2.60 to 12.70), postoperative fever (OR 8.40; 95 % CI 2.00 to 35.24), postoperative UTI

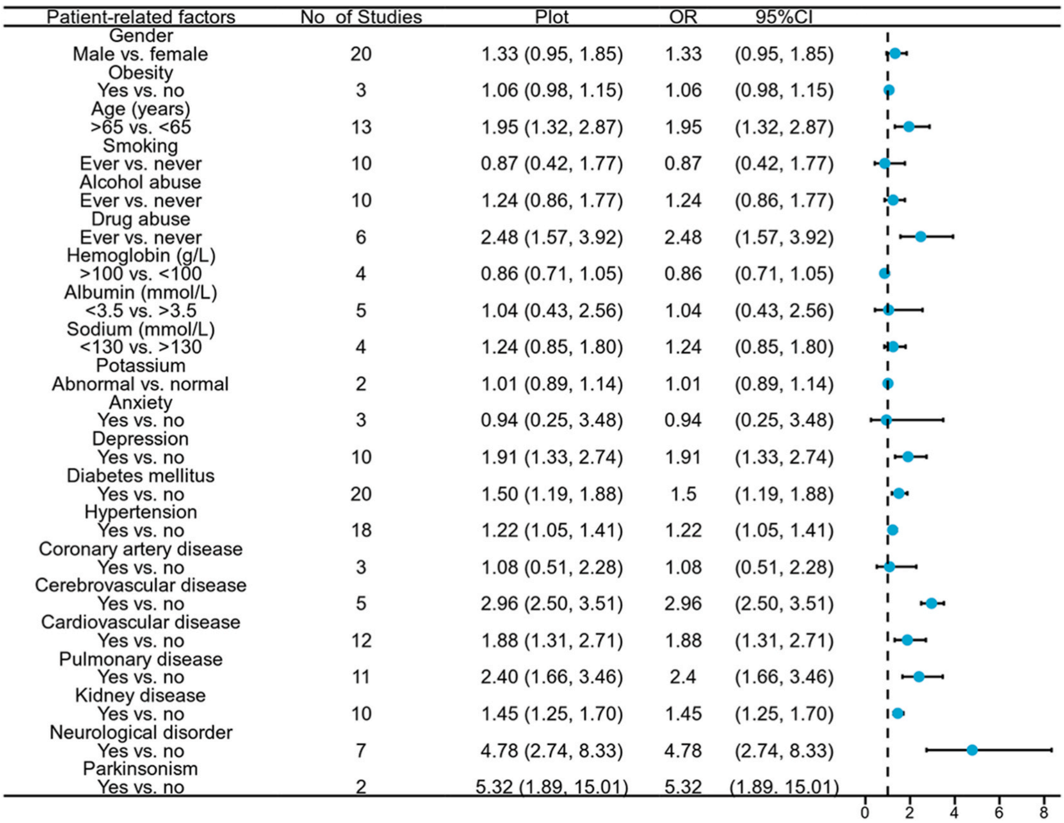

Fig. 2. Meta-analyses of the association between POD and patient-related risk factors.

Surgery-related factors	No of Studies	Plot	OR	95%CI
ASA fitness grade >II vs. I/II	5	1.81 (1.34, 2.45)	1.81	(1.34, 2.45)
MMSE score <30 vs. >30	4	0.79 (0.47, 1.33)	0.79	(0.47, 1.33)
Preoperative VAS Abnormal vs. normal	2	0.92 (0.71, 1.18)	0.92	(0.71, 1.18)
Lumbar surgery Yes vs. no	8	0.59 (0.42, 0.82)	0.59	(0.42, 0.82)
Cervical surgery Yes vs. no	11	1.71 (1.26, 2.33)	1.71	(1.26, 2.33)
Spinal fusion Yes vs. no	9	1.93 (1.30, 2.86)	1.93	(1.30, 2.86)
Spinal decompression Yes vs. no	4	0.76 (0.30, 1.93)	0.73	(0.30, 1.93)
Opioid use Yes vs. no	7	1.36 (0.91, 2.04)	1.36	(0.91, 2.04)
Blood loss (ml) >300 vs.<300	14	1.00 (0.99, 1.01)	1	(0.99, 1.01)
Transfusion Yes vs. no	11	1.71 (1.09, 2.68)	1.71	(1.09, 2.68)
Duration of surgery (min) >180 vs. <180	9	1.00 (0.99, 1.00)	1	(0.99, 1.00)
SSI Yes vs. no	4	5.75 (2.60, 12.70)	5.75	(2.60, 12.70)
Postoperative fever Yes vs. no	3	8.40 (2.00, 35.24)	8.4	(2.00, 35.24)
Postoperative UTI Yes vs. no	5	5.71 (3.13, 10.41)	5.71	(3.13, 10.41)
Reoperation Yes vs. no	2	1.43 (0.35, 5.81)	1.43	(0.35, 5.81)
LOS (days) Abnormal vs. normal	5	3.31 (1.71, 6.41)	3.31	(1.71, 6.41)
Admission to ICU Yes vs. no	5	2.91 (2.13, 3.96)	2.91	(2.13, 3.96)

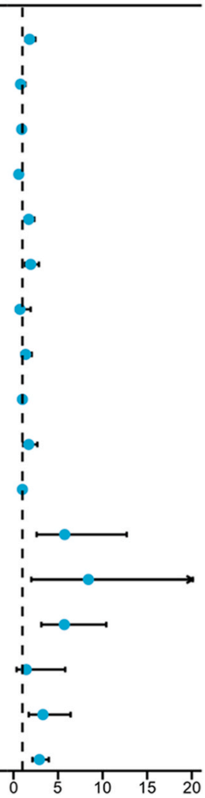

Fig. 3. Meta-analyses of the association between POD and surgery-related risk factors.

(OR 5.71; 95 % CI 3.13 to 10.41) and admission to the ICU (OR 2.91; 95 % CI 2.13 to 3.96). Moderate-quality (Class II) evidence indicates significant correlations between POD and ASA fitness grade > II (OR 1.81; 95 % CI 1.34 to 2.45), blood transfusion >500 ml (OR 1.71; 95 % CI 1.09 to 2.68), electrolyte disorders (OR 3.10; 95 % CI 2.90 to 3.40), inability to ambulate (OR 2.76; 95 % CI 1.02 to 7.41), spinal fusion (OR 1.93; 95 % CI 1.30 to 2.86) and intravenous infusion volume (OR 1.52; 95 % CI 1.04 to 2.23). Furthermore, moderate-quality (Class III) evidence showed that LOS (OR 3.30; 95 % CI 1.71 to 6.41) was significantly correlated with POD (Table 2 and eTable 7 in the Supplement).

High-quality (Class I) evidence revealed that there were no significant associations between POD and lumbar surgery (OR 0.59; 95 % CI 0.42 to 0.82) or spinal decompression (OR 0.76; 95 % CI 0.30 to 1.93). Moderate-quality (Class II) evidence revealed that there were no significant associations between POD and preoperative VAS score (OR 0.92; 95 % CI 0.71 to 1.18), blood loss >300 ml (OR 1.00; 95 % CI 0.99 to 1.01) or operation time (OR 1.00; 95 % CI 0.99 to 1.00). Moderate-quality (Class III) evidence revealed that there were no significant associations between POD and opioid use (OR 1.36; 95 % CI 0.91 to 2.04) or reoperation (OR 1.43; 95 % CI 0.35 to 5.81) (Table 3 and eTable 8 in Supplement).

3.4. Subgroup analyses and sensitivity analyses

We conducted a subgroup analysis of the risk factors if P was <0.05 and a sufficient number of included studies (>12) was provided. Therefore, we performed the subgroup analysis for hypertension, diabetes and older age (eTable 9-11 in Supplement).

We used leave-one-out sensitivity analysis to evaluate the stability of the results for each investigated factor. The results showed that the pooled ORs all remained similar across these analyses for both patient-related risk factors and surgery-related risk factors (eTable 12 in the Supplement).

4. Discussion

4.1. Principal findings

Understanding risk factors for POD can help spinal surgeons and patients coordinate an optimal postoperative management strategy. By pooling 50 studies, we identified significant patient-related factors, including hypertension, diabetes, cardiovascular disease, depression, pulmonary disease, older age (>65 years old), patients experiencing substance use disorder, kidney disease, neurological disorder and parkinsonism, and significant surgery-related factors, including ASA grade > II, blood transfusion>500 ml, cervical surgery, electrolyte disorders, inability to ambulate, intravenous infusion volume, SSI, postoperative fever, postoperative UTI, LOS and stay in the ICU. Despite the results above, our study cannot rule out these potential factors, which have been found to be associated with the risk of postoperative POD in a number of studies (eTable 13 in Supplement).

4.2. Comparisons with previous literature

One of the most important risk factors was advanced age [49]; almost all studies have suggested that older age is a risk factor for postoperative delirium; some studies have targeted patients aged >65 or 70 years at the beginning of the study [38]. Shi et al. revealed that age >65 years was a risk factor for delirium [61]. Kawaguchi et al. reported an incidence of delirium of 12.5 % in patients over 70 years of age who underwent spine surgery, and 2 patients who developed postoperative delirium died during the follow-up period [41]. Brown et al. [7] reported that 40.5 % of patients aged over 70 years developed delirium, and Kobayashi et al. [41] reported that 23 % of patients older than 80 years developed delirium after spine surgery. In general, elderly patients usually have poor general health status, more physical and psychological problems, and decreased functioning [62]; the global aging of the population in recent years may be an important contributor to the increased prevalence of POD over time [63]. All of these factors might contribute to the occurrence of POD after spinal surgery [64]. Depression is a well-established predictor of delirium [65,66]. It has been demonstrated that adult patients with a diagnosis of depression prior to surgery were more likely to develop postoperative delirium than patients without a history of depression [44]. Koskderelioglu et al. demonstrated that depressive mood, as assessed by the Beck Depression Inventory, correlated with the occurrence of postoperative delirium [67]. In the univariate analysis, significant preoperative risk factors for postoperative delirium were higher ASA physical status [68]. Inouye et al. presented a multifactorial model for delirium, which showed a close association of postoperative delirium with anesthesia [69,70]. Cerebral vascular disease is significantly associated with the incidence of delirium, and hypoxic brain injury might cause postoperative delirium in those with cerebral vascular disease [65].

4.3. Potential mechanisms

Although beyond the scope of the current meta-analysis, additional studies concerning the molecular epidemiology of POD are needed to understand the interaction between these patient individual factors and potential mechanisms. Moreover, the crucial mechanism for safe anesthesia management is to maintain the stability of blood pressure [71]. As a highly metabolic organ, the brain is very sensitive to ischemia and hypoxia. Normal adults have an average arterial pressure of 70–105 mmHg during a cardiac cycle, which we refer to as the mean arterial pressure or MAP. Brain autoregulation protects the brain against traumatic injury by maintaining stable blood flow regardless of changes in systemic blood pressure (BP). Beyond its regulatory range, it is common to find insufficient cerebral perfusion, which can induce disorders of micro embolic clearance and hypoxic-ischemic brain damage [72]. Therefore, hypertension is a predictive risk factor for POD in the future, which is consistent with previous studies by Brown and Hesse et al. [7,32]. At the same time, metabolic abnormalities are associated with an increasing risk of POD. Studies by Feinkohl I et al. found that patients with reduced high-density lipoprotein cholesterol and patients with methionine had a significantly increased risk of POD [73]. In addition, serotonin deficiency caused by tryptophan deficiency and increased phenylalanine is associated with the pathogenesis of postoperative delirium, as serotonin is associated with emotional processing and depression [74,75].

4.4. Implications for clinical practice and future studies

Our study’s results provide crucial understanding for future research, clinical approaches, and assessing delirium incidents after spinal surgery, taking into account various risk factors. Prompt assessment of blood pressure and glucose levels pre-surgery, the existence or non-existence of certain concurrent conditions (like cardiovascular disease, depression, pulmonary disease), blood loss during surgery, and successful intervention strategies are crucial for treating and preventing POD. Currently, medical professionals haven’t adequately focused on determining if the occurrence and regularity of POD fall within the normal spectrum or if the control remains constant. The prevention and standardized treatment strategy for patients with POD has not been established, and most patients and doctors are not aware of the link between various risk factors and POD. Maintaining the stability of blood pressure and blood glucose before operation and strengthening the control of other related controllable risk factors are helpful to reduce the incidence of POD risk.

4.5. Strengths

The advantages of the current meta-analysis are as follows. First, it is the largest and most comprehensive meta-analysis we know of. The meta-analysis was strengthened through the implementation of predefined research programs, comprehensive search strategies, strict inclusion criteria, thorough assessment of research quality and transparent reporting of results, thereby improving objectivity and consistency. Secondly, a comprehensive literature search was conducted using MESH/Emtree and free text terms in three main databases, PubMed, Cochrane Library and Embase. A comprehensive database search strategy was developed that was not limited by date or language. In this way, we found as many original articles that met the inclusion criteria as possible to avoid the impact of publication bias on the collection results and improve the repeatability of the results. Third, we assessed the strength of supporting evidence for each investigated risk factor from Class I to Class IV based on interstudy heterogeneity, the *P* value of Egger’s test, and the number of patients, which may help surgeons and patients explain the evidence. Finally, we used the trim-and-fill technique to adjust the pooled estimation according to publication bias, and the result was consistent with the main analysis.

5. Limitations

There are still a number of limitations to our study. First, because most of the included studies were retrospective cohorts and the factors associated with POD were diverse and complex, they were subject to some degree of selection bias. Future studies with more credible evidence will be needed to confirm these findings, such as large prospective cohort studies. Second, we found that effect estimates for some factors were near boundaries with confidence intervals ranging from 0.90 to 1.10 (e.g., obesity, duration of surgery, and blood loss) (Tables 2 and 3). To address this issue, more robust cohort studies with clearer and higher-level evidence are needed. Finally, there is currently no gold standard or guideline to quantitatively assess the strength of evidence from risk factor meta-analyses. Three conditions (Egger's P value, number of included patients and I^2 statistic) were selected to determine the strength of evidence based on previously published criteria [22]. Considering the somewhat arbitrary nature of the choice of any particular thresholds for each item of the criteria, the evidence classification should be used for illustrative purposes rather than absolute rules.

6. Conclusions

Conspicuous risk factors for POD were mainly patient and surgery related. These findings help clinicians identify high-risk patients with POD following spinal surgery and recognize the importance of early intervention.

Author contribution statement

Yuxin Shi: Formal analysis, Data curation. Yudie Xie: Software, Methodology. Di Wang: Resources, Project administration, Formal analysis, Data curation. Ridong Tang: Data curation. Mingjiang Luo: Writing – review & editing, Writing – original draft, Validation, Formal analysis, Data curation, Conceptualization. Yuxin Yang: Methodology. Xin Zeng: Methodology. Gaigai Yang: Software, Resources, Data curation. Zubing Mei: Writing – review & editing, Writing – original draft, Supervision. Beijun Zhou: Software. Jinshan Huang: Data curation. Zhongze Wang: Data curation. Siliang Tang: Formal analysis. Qilong Yi: Formal analysis, Data curation. Jiang Chen: Software. Haoyun Wang: Software. Can Liang: Formal analysis. Juemiao Chen: Formal analysis. Zhihong Xiao: Writing – review & editing, Writing – original draft, Supervision, Software

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Data availability statement

Data included in article/supplementary material/referenced in article.

Ethics approval

Review and/or approval by an ethics committee was not needed for this study because the data sources of this study do not involve any animals or patients.

Informed consent was not required for this study because the data sources of this study do not involve any animals or patients.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e24967.

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