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ORIGINAL ARTICLE

Probable risk factors for postoperative delirium in patients undergoing spinal surgery

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Abstract Postoperative delirium and its risk factors had been widely reported in several kinds of surgeries; however, there is only one known article relative to postoperative delirium in spinal surgery. We retrospectively examined the incidence of postoperative delirium and the probable risk factors in patients undergoing spinal surgery in our hospital, with the same aged non-delirium patients as controls, over a 6-month period. Studies about postoperative delirium were reviewed and referenced for variable factors collecting in our study. *T* tests, χ^2 test and logistic regression analysis were performed to evaluate the various factors related to postoperative delirium. A total of 18 patients (3.3%), all of them were aged 54 years or older, had postoperative delirium after surgery. Patients without postoperative delirium aged 54 years or older served as the control group. The percentage of patients older than 65 years ($P = 0.003$), with comorbid diseases such as diabetes mellitus ($P = 0.042$) or central nervous system disorders ($P = 0.013$), with a surgical history ($P = 0.028$) in delirium group was larger than the control group. The absolute number of medications being taken before the operation in the delirium patients was also more than the control group ($P = 0.000$). The percentage of patients transfused with 800 mL or more blood was also larger ($P = 0.024$) in delirium group was larger than the control group. Logistic regression analysis showed that central nervous system disorder (OR 6.480), surgical history (OR 3.499), age older than 65 years (OR 3.390), diabetes mellitus (OR 2.981), transfused 800 mL or more blood (OR 2.537), and hemoglobin less than 100 g/L (OR 0.281) were significantly related to the occurrence postoperative delirium. Our findings suggest that postoperative delirium in spinal surgery can also occurred in younger patients and with an acceptable incidence in total. The risk for postoperative delirium is multifactorial. More prospective research is necessary in order to evaluate these and other risk factors in greater detail.

Keywords Postoperative delirium · Spinal surgery · Delirium observation screening (DOS) scale · Logistic regression analysis

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Introduction

It has been previously reported that postoperative delirium can occur following several kinds of surgery, including general surgery [17], head and neck cancer surgery [23], cardiac surgery [5, 13], vascular surgery [19], hip fracture [21, 24], joint replacement [22], and spinal surgery [12]. Postoperative delirium is defined as an acute state of confusion characterized by fluctuating consciousness and inattention, which in most studies occurs shortly after surgery. Diagnosis of this delirious state is usually done according to the confusion assessment method (CAM) criteria, the telephone interview for cognitive status (TICS, a modification of the Mini-Mental Status Exam [MMSE]), specific activity scale (SAS), administration of the delirium rating scale (DRS) or the NEECHAM confusion scale (NCS) [5, 12, 13, 19, 21, 23, 24]. Postoperative delirium has been related to many risk factors, including preoperative factors such as patient's age, drug use, sensory impairment, and the comorbid medical conditions; intraoperative factors such as type of surgery, type of anesthesia, duration of operation, blood loss, and amount of blood transfused; and postoperative factors such as laboratory data, blood pressure, and opiate analgesic drug use [5, 9, 12, 13, 19, 21, 23, 24]. Patients who undergo surgery with these risk factors are considered to be prone to delirium after the operation. The incidence of postoperative delirium in general surgery, hip fracture, joint replacement, and open-heart surgery has been widely reported; however, there is only one known article that describes postoperative delirium in spinal surgery [12]. Delirious patients are often hospitalized longer than other patients and have higher morbidity and mortality rates [4, 14]. Prevention of delirium may help to reduce these problems and the associated costs, and thus there is a need for further understanding of the risk factors. This study was conducted retrospectively to examine the incidence and determine the probable risk factors of postoperative delirium in patients receiving spinal surgery.

Patients and methods

The subjects were 549 patients (302 males and 247 females) who underwent spinal surgery in Changhai Hospital, the Second Military Medical University between 1 May 2007 and 10 November 2007. Their age ranged from 10 to 83 years, with a mean of 48.2 years. Only one patient had a history of delirium prior to the operation. Patients without contraindications of sedatives had the option to receive oral diazepam (5 or 10 mg) on the day prior to the operation to relieve nervousness and anxiety, or to ensure high-quality sleep. All patients underwent the operation under general anesthesia. Phenobarbital (100 mg) and atropine (0.5 mg) via intramuscular injection was given 0.5–1 h before surgery. Anesthetic agents, including propofol and isoflurance, or enflurance complex with fentanyl, rocuronium bromide or vecuronium bromide, were used during the operation. Patients that had a risk for abnormal vital signs were sent to the intensive care unit for at least 12 h after the operation. An adjustable and portable patient or patient-relative controlled analgesic pump (fentanyl) was used on most patients for postoperative pain relief.

Inouye summarized the clinical features of delirium: (1) acute onset, (2) fluctuating course, (3) inattention, (4) disorganized thinking, (5) altered level of consciousness, (6) perceptual disturbances, (7) psychomotor disturbances, (8) altered sleep-wake cycle, and (9) emotional disturbances [9]. Patients with the first and second features, and any two of the other features, were evaluated by nurses. Observations of subjects was conducted each shift and recorded using the delirium observation screening (DOS) scale. This scale was developed based on the DSM-IV criteria for delirium (American Psychiatric Association 1994) [3], literature review, clinical experience, and expert opinion. The DOS scale items can be observed by nurses during the regular care of the patients, and completing the scale takes only a few minutes. The scale shows high internal consistency (Cronbach's alpha, 0.96) and good predictive validity against a DSM-IV diagnosis ($P < 0.001$) [20]. The gold standard in this study was a DSM-IV diagnosis of delirium made by two senior spinal surgeons (Qiang Fu, Ming Li) and one psychiatrist (Yan Han). Each diagnosis was discussed by these three doctors.

Studies about postoperative delirium were reviewed and referenced for variable factors [5, 9, 12, 13, 17, 19, 21–24]. Preoperative factors included age, solitary life condition, drug treatment, preoperative hospitalized days, nutrition status, sensory impairment, comorbid diseases, surgical history, history of delirium, systolic blood pressure (SBP), hemoglobin (HGB), hematocrit (HCT), and blood biochemistry indexes (sodium, potassium, blood sugar). Alcohol and drug use were considered as one measure, with alcohol no less than 30 g per day and drug use as more than three kinds of drugs per day before operation. Hospitalization time in excess of 10 days was considered as a long hospital stay. The malnutrition diagnostic criteria were total protein less than 61 g/L. Patients with sensory impairment were those who had diagnosed glaucoma, cataracts, blindness or deafness. Comorbid diseases were hypertension, diabetes mellitus, pulmonary disease, cardiac disease, central nervous system disorder, psychiatric disorder, chronic kidney disease, and chronic liver disease.

The intraoperative factors included operative time, blood loss, blood transfusion, total infusion, and the use of surgical implants. Postoperative factors included the use of analgesic pumps, fever (temperature higher than 38°C), SBP, HGB, HCT, and blood biochemistry index results of the first day after the operation. All the data was obtained from medical records or nursing records.

Statistical analysis

All data were analyzed by using SPSS 16.0. Numerical variables and ordinal variables were presented as mean and standard deviation (SD). Absolute numbers were for categorical variables. *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 χ^2 test was used for the comparison of the categorical data. A *P* value less than 0.05 was considered statistically significant. Logistic regression analysis was also used to evaluate the various factors related to postoperative delirium. The factors selected for analysis were those *P* values close to or less than 0.2 in the previous univariate analysis, or those had significant clinical relevance. Stepwise forward method was used, and the entry and removal values were 0.10 and 0.15, respectively.

Results

Postoperative delirium occurred in 18 of the 549 patients (3.3%), 10 men and 8 women. The age of the patients with delirium ranged from 54 to 80 years, with a mean of 68.9 years. The delirium was observed between the day of the operation and 3 days after the operation, with a mean of 1.2 days. The duration of delirium ranged from 1 to 8 days, with a mean of 3.1 days. Of these patients, five patients had operation on the cervical spine, two on the cervico-thoracic spine, four on the lumbar-sacral spine, five on the lumbar spine and two on the thoraco-lumbar spine. Three patients required small amounts of perphenazine, between 2 and 4 mg/day. Telephone follow-up interviews were performed every month from 57 days to 250 days. One patient died 36 days after operation in another hospital due to heart failure; this patient underwent an operation for traumatic dislocation of C6 and incomplete paralysis, with comorbid coronary heart disease and pulmonary emphysema. There were no patients requiring medical treatment, nor were there any patients with cognitive complications after discharge.

Since, none of the 549 patients younger than 54 years had delirium after the operation, patients aged 54 years or older who did not have postoperative delirium served as the non-delirium control group (197 patients, one case of a 65 year old man was excluded because he was transported to another hospital upon the request of his relatives on the second day after the operation).

Preoperative factors

The mean age of delirium group and non-delirium group were 68.9 and 63.7 years old ($P = 0.004$), and the difference was also significant for the percentage of patients older than 65 years ($P = 0.003$). Delirium subjects were treated with more medications preoperatively than controls (mean 3.7 vs. 2.4, respectively, $P = 0.000$), and there were more patients with comorbid diabetes mellitus ($P = 0.042$) and central nervous system disorders ($P = 0.013$) in delirium group compared with the control group. Nine patients in delirium group and 46 in non-delirium group had previously undergone operations ($P = 0.028$). No significant differences were found for the other factors (Tables 1, 2).

Intraoperative factors

Eight patients with delirium and 37 patients without delirium were transfused with 800 mL or more blood ($P = 0.024$). There were no differences for the other factors (Tables 1, 2).

Postoperative factors

The sodium level on the first day after the operation in delirium group was lower than what was observed in the control group (139.5 vs. 141, $P = 0.029$) and the blood sugar level was higher in the delirium group compared with the control group (7.9 vs. 6.9, $P = 0.027$). No differences were found between groups for the other factors (Tables 1, 2).

Logistic regression analysis

Variables such as age >65 years, treatment with multiple drugs (>three kinds) on the previous days, audition impairments, diabetes mellitus, central nervous system disorder, pulmonary disease, surgical history, blood loss ≥800 mL, blood transfusion ≥800 mL and postoperative laboratory data including hemoglobin <100 g/L, hematocrit <30%, sodium (dichotomized at 139 mmol/L), blood sugar (dichotomized at 7 mmol/L) were all included in logistic regression analysis according to results of the previous univariate analysis. The results showed that central nervous system disorder (OR 6.480), surgical history (OR 3.499), age >65 years (OR 3.390), diabetes mellitus (OR 2.981), blood transfusion ≥800 mL (OR 2.537), and hemoglobin <100 g/L (OR 0.281) were significantly related to the occurrence postoperative delirium (Table 3).

Discussion

Though postoperative delirium in other surgeries had been widely reported [5, 13, 17, 19, 21–24], there is only one known article relative to postoperative delirium in spinal surgery, which was reported by Kawaguchi [12]. He speculated that there were few articles in this field because the incidence of postoperative delirium is lower in this patient population. In his research, the incidence of postoperative delirium was 3.8%, which is close to our result and lower than hip fracture surgery. This may be because patients who have undergone spinal surgery are exposed to less stressor than patients with hip fracture; most patients with hip fracture go directly from the emergency room to surgery [12, 21].

Postoperative delirium can easily occur in older patients, and this condition has become widely accepted [2, 9]. There were 13 patients older than 65 years who had postoperative delirium, and in logistic regression analysis this factor had a high OR ratio of 3.390. Brown reported approximately one-quarter of adults aged 65 and older experience delirium during hospitalization [3]. Ergina

Table 1 Association between factors of categorical variables and postoperative delirium

	Delirium	Non-delirium	*P* value
Preoperative Data			
Male	10	103	–[a]
Age >65 years	13	71	0.003
Solitary life	3	15	–[a]
Drugs			
Alcohol habit (≥30 g/day)	1	13	–[a]
Sedative-hypnotic drugs use	11	128	–[a]
Treatment with multiple drugs (>three kinds) on the days prior to surgery	7	34	–[a]
Long preoperative hospital stay (>10 days)	3	17	–[a]
Malnutrition	3	12	–[a]
Sensory impairments			
Vision impairments	1	4	–[a]
Audition impairments	2	4	–[a]
Comorbid diseases			
Hypertension	4	58	–[a]
Diabetes mellitus	6	25	0.042
Pulmonary disease	2	7	–[a]
Cardiac disease	2	14	–[a]
Central nervous system disorder	4	9	0.013
Psychiatric disorder	1	1	–[a]
Chronic kidney disease	1	6	–[a]
Chronic liver disease	1	11	–[a]
Surgical history	9	46	0.028
History of delirium	1	0	–[a]
Intraoperative Data			
Operative time ≥180 min	10	80	–[a]
Blood loss ≥800 mL	9	68	–[a]
Blood transfusion ≥800 mL	8	37	0.024
Total infusion ≥3,000 mL	10	102	–[a]
Surgical implants used	17	186	–[a]
Postoperative Data			
Analgesic pumps	18	188	–[a]
Fever (temperature >38°C)	0	4	–[a]
Hemoglobin <100 g/L	7	37	–[a]
Hematocrit <30%	8	42	–[a]

[a] No significant difference

suggested that this may be because older adults have disproportionably more operations than younger adults, and also because the elderly population is growing [7]. All of the patients in our study were under general anesthesia, and one potential candidate mechanism of cognitive impairment is general anesthesia itself [6]. General anesthesia affects brain function at all levels, including neuronal membranes, receptors, ion channels, neurotransmitters, cerebral blood flow, and metabolism [8]. Moreover, the aged brain is more susceptible to anesthetic effects and more sensitive to nonanesthetic drugs [16]. We also found that a greater percentage of patients in delirium group had a history of surgery than in the non-delirium group, with an OR ratio of 3.499 in logistic regression analysis. This finding is in accord with Ergina's research.

In Amador's review, he thought one of the greatest predisposing risk factors for developing postoperative delirium was the presence of neurodegenerative diseases such as Alzheimer's or Parkinson's disease [2]. The same was found in our analysis; central nervous system disorder had the highest OR ratio of 6.480 in logistic regression analysis. Four patients in delirium group had comorbid central nervous system disorders (vs. 9 in the control group, $P = 0.013$). Of the four patients, three had

Table 2 Association between factors of numerical variables/ordinal variables and postoperative delirium

	Delirium	Non-delirium	*P* value
Preoperative Data			
Age (years)	68.9 ± 8.4	63.7 ± 7.3	0.004
Number of medications	3.7 ± 1.4	2.4 ± 1.1	0.000
Preoperative hospital days	7.6 ± 3.9	6.7 ± 3.4	–
Nutrition status (total protein, g/L)	66.1 ± 8.3	67.7 ± 5.9	–
Number of comorbid diseases	1.8 ± 2.0	1.2 ± 1.1	–
Blood pressure (SBP, mmHg)	128 ± 16.4	130 ± 15.7	–
Hemoglobin (g/L)	132 ± 14.3	134 ± 14.8	–
Hematocrit (%)	39.5 ± 4.3	40.4 ± 4.1	–
Blood biochemistry			
Sodium (Na)	141.0 ± 3.2	142.0 ± 2.8	–
Potassium (K)	4.1 ± 0.4	4.0 ± 0.3	–
Blood sugar (mmol/L)	6.0 ± 1.5	5.5 ± 3.0	–
Intraoperative Data			
Operative time (min)	182.8 ± 66.5	167.1 ± 68.1	–
Blood loss (mL)	937.2 ± 795.1	716.9 ± 632.4	–
Blood transfusion (mL)	656.6 ± 796.5	376.9 ± 640.5	–
Total infusion (mL)	3,227.8 ± 1,220.8	3,046.2 ± 1,242.5	–
Postoperative Data			
Blood pressure (SBP, mmHg)	129.1 ± 15.5	125.8 ± 15.1	–
Hemoglobin (g/L)	106.4 ± 15.0	112.7 ± 16.8	–
Hematocrit (%)	31.3 ± 4.2	33.4 ± 3.4	–
Blood biochemistry			
Sodium (mmol/L)	139.5 ± 2.5	141.0 ± 2.82	0.029
Potassium (mmol/L)	3.94 ± 0.5	3.80 ± 0.4	–
Blood sugar (mmol/L)	7.9 ± 2.0	6.9 ± 1.8	0.027

Table 3 Results of logistic regression analysis

Factors	B	Sb	Wald x^2	*P* value	Odds Ratio (95% confidence interval)
Central nervous system disorder	1.869	0.787	5.644	0.018	6.480 (1.387–30.278)
Surgical history	1.253	0.562	4.959	0.026	3.499 (1.162–10.538)
Age >65 years	1.221	0.587	4.323	0.038	3.390 (1.073–10.717)
Diabetes mellitus	1.092	0.604	3.267	0.071	2.981 (0.912–9.746)
Blood transfusion ≥800 mL	0.931	0.577	2.605	0.107	2.537 (0.819–7.856)
Hemoglobin <100 g/L	−1.268	0.608	4.354	0.037	0.281 (0.086- 0.926)

Age >65 years, treatment with multiple drugs (>three) on the days prior to surgery, audition impairments, diabetes mellitus, central nervous system disorder, pulmonary disease, surgical history, blood loss ≥800 mL, blood transfusion ≥800 mL, postoperative hemoglobin <100 g/L, hematocrit <30%, sodium (dichotomized at 139 mmol/L), and blood sugar (dichotomized at 7 mmol/L) were all included in logistic regression analysis

Parkinson's disease (none has the Parkinson's disease in control group), and none had Alzheimer's disease in our study.

Drug toxicity, due to drugs such as meperidine [1], accounts for approximately 30% of all cases of delirium and plays a major role in postoperative delirium [2]. There were no patients treated with meperidine before or after operation in our study. In other reports, alcohol abuse is an important risk factor [1, 2, 4, 5, 18]; however, this does not seem to be the case in our research, possibly because few Chinese people have alcohol problems compared with Western populations.

Operative time more than 10 h, blood transfusion more than 800 mL, and infusion more than 5,000 mL were considered significant risk factors in Yamagata's research [23]. However, there were no generally accepted standards or ranges of values for these factors because different surgeries had different features. Similar results can also be found in the HCT, and sodium levels on the first day after surgery for the delirium group, which were lower than those in the control group in Kawaguchi's research [12]. The present study also demonstrated that the lower concentrations of HGB and HCT on the first day after surgery had close relation to postoperative delirium [12, 17]. Kawaguchi's group stated that the patients with the HCT <30% were at risk for postoperative delirium. A low concentration of HGB and HCT might reduce the oxygen supply to the brain and bring about postoperative delirium. The difference of sodium levels between the delirium and control patients on the first day after surgery has only been presented in these two spinal research reports. Although there was a difference, the sodium levels in both reports were in normal range, so it may have no value in the incidence of postoperative delirium. Morphine used for postoperative pain relief had been related to postoperative delirium [21], and there were no patients treated with morphine in our study. Rather, all were treated with fentanyl, which does not appear to increase the risk for delirium.

The risk for delirium is multifactorial [10, 11]. There still are many factors that we did not assess, such as preoperative mental status, low postoperative oxygen saturation, and pain. Many prospective studies used the Mini-Mental Status Exam [MMSE] for the patients to evaluate the mental status, Lynch et al. [15] found that higher pain scores at rest during the first three postoperative days were associated with an increased risk of delirium. In a retrospective study such as the one that we conducted, data like this cannot be collected. Although we did not evaluate these factors, further prospective studies should be carried out to investigate the relationship between postoperative delirium and these factors in detail.

In conclusion, this study confirms previous findings and suggests that there is an incidence of postoperative delirium in spinal surgery. Older age, comorbid diseases like diabetes mellitus or central nervous system disorder, surgical history, blood transfusion ≥800 mL, and low concentrations of HCT/HGB on the first day after surgery are probable risk factors for postoperative delirium in spinal surgery. Understanding the risk factors of delirium can improve its prevention, diagnosis, and management. Risk of postoperative delirium can be reduced with careful attention to risk factors [2]. However, more prospective research is necessary in order to evaluate factors in greater detail.

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