Incidence and Risk Factors for Postoperative Delirium in Patients Undergoing Spine Surgery: A Systematic Review and Meta-Analysis

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Background. The present study aims to investigate the incidence and risk factors associated with postoperative delirium in patients undergoing spine surgery. Methods. PubMed, EMBASE, Cochrane Library, and Science Citation Index were searched up to August 2019 for studies examining postoperative delirium following spine surgery. Incidence and risk factors associated with delirium were extracted. Odds ratios (OR) and 95% confidence intervals (CI) were calculated for outcomes. The Newcastle–Ottawa Scale (NOS) was used for the study quality evaluation. Results. The final analysis includes a total of 40 studies. The pooled analysis reveals that incidence of delirium is 8%, and there are significant differences for developing delirium in age (OR 1.07; 95% CI 1.04–1.09), age more than 65 (OR 4.77; 95% CI 4.37–5.16), age more than 70 (OR 15.87; 95% CI 6.03–41.73), and age more than 80 (OR 1.91; 95% CI 1.78–2.03) years, male (OR 0.81; 95% CI 0.76–0.86), a history of alcohol abuse (OR 2.11; 95% CI 1.67–2.56), anxiety (OR 1.74; 95% CI 1.04–2.44), congestive heart failure (OR 1.4; 95% CI 1.21–1.6), depression (OR 2.5; 95% CI 1.52–3.49), hypertension (OR 1.12; 95% CI 1.04–1.2), kidney disease (OR 1.41; 95% CI 1.16–1.66), neurological disorder (OR 4.66; 95% CI 4.22–5.11), opioid use (OR 1.86; 95% CI 1.18–2.54), psychoses (OR 2.77; 95% CI 2.29–3.25), pulmonary disease (OR 1.81; 95% CI 1.27–2.35), higher mini-mental state examination (OR 0.7; 95% CI 0.5–0.89), preoperative pain (OR 1.88; 95% CI 1.11–2.64), and postoperative urinary tract infection (OR 5.68; 95% CI 2.41–13.39). Conclusions. A comprehensive understanding of incidence and risk factors of delirium can improve prevention, diagnosis, and management. Risk of postoperative delirium can be reduced based upon identifiable risk factors.

1. Introduction

Postoperative delirium is a common complication after surgery in the elderly and causes difficulty in postoperative care [1, 2]. It is defined as an acute change in the cognitive status characterized by fluctuating consciousness, attention, memory, perceptions, and behavior postoperatively [3]. Postoperative delirium often brings out many adverse outcomes, such as functional disability, increased health care costs, and higher morbidity and mortality rates [4]. Thus, a further understanding and prevention of delirium may help reduce these problems and the associated costs. Some previous studies have reported the incidence and risk factors for delirium. However, incidences of postoperative delirium differ greatly, and risk factors of these studies are inconsistent. Therefore, we perform a systematic review and meta-analysis to explore incidence and risk factors for developing postoperative delirium following spine surgery.

2. Materials and Methods

2.1. Search Strategy. The systematic review and meta-analysis were done according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline and AMSTAR (assessing the methodological quality of systematic reviews) Guidelines [5, 6]. PubMed, EMBASE, Cochrane Library, and Science Citation Index were searched exhaustively with inception to August 2019.
2.2. Selection Criteria. Studies included in this systematic review and meta-analysis met the following criteria: (1) original articles on patients who underwent spine surgery, (2) observational, case series or cohort study design, (3) at least incidence reported or one risk factor identified as being associated with delirium, and (4) full text available. If the inclusion criteria were not met, the study was excluded. If the same study was published in different years or various journals, then the most frequently cited study was included for this meta-analysis. The potentially qualified studies were selected independently by 2 authors according to the inclusion and exclusion criteria. Any discrepancy was resolved by discussion to reach a consensus.

2.3. Data Extraction. Data were extracted by two independent authors. By discussion or by involving a third author, disagreements were addressed. The general features cover the first author, publication year, country, study type, sample size, patient characteristics, patients who underwent surgery, delirium diagnosis tool, incidence duration of delirium, and significant factors.

2.4. Quality Assessment. Two authors independently evaluated the quality of the studies, and the level of agreement between them was recorded. Any disagreements between the 2 authors were resolved by discussion with a third author. Newcastle–Ottawa Scale (NOS) was utilized to assess the quality of each study [7] since no studies were randomized controlled trials. Studies with 7–9 points could be identified as high quality, 5–6 points as moderate quality, and 0–4 as poor quality.

2.5. Statistical Analysis. The meta-analysis of comparable data was performed using Stata/SE version 15.0 software. All adjusted odds ratio (OR) with 95% confidence interval (CI)
| Author          | Publication year | Country | Study type     | Sample size | Age mean (SD, range) years | Sex ratio (M : F) | Patients who underwent surgery | Delirium diagnosis tool | Delirium incidence | Duration of delirium (days) | Significant factors                                                                 | Study quality |
|-----------------|------------------|---------|----------------|-------------|---------------------------|------------------|-------------------------------|------------------------|-------------------|----------------------------|-----------------------------------------------------------------------------------|--------------|
| Pan et al. [8]  | 2019             | Korea   | Prospective    | 83          | 71.4 ± 4.6                | 27 : 56          | Lumbar spine                  | CAM                    | 12/83 (14.5%)      | 2.6 (1–5)                | Male, parkinsonism, lower baseline MMSE score                                        | 8            |
| Oe et al. [9]   | 2019             | Japan   | Retrospective  | 319         | >18                       | 85 : 234         | Spinal deformity               | —                      | 30/319 (9.4%)        | —                          | Age, PNI                                                            | 7            |
| Elsamadicy et al. [10] | 2019           | USA     | Retrospective  | 138         | ≥18                       | 40 : 98          | Complex spinal fusion (≥5 levels) | —                      | 15/138 (10.9%)      | —                          | Age, intraoperative ketamine use                                                   | 7            |
| Takenaka et al. [11] | 2019           | Japan   | Prospective    | 13188       | 11–94                     | 7174 : 6014      | Lumbar spine                  | —                      | 65/13188 (4.9%)      | —                          | CVD, dural tear                                                      | 8            |
| Kin et al. [12] | 2019             | Japan   | Retrospective  | 67          | 69.6 ± 12.0               | 49 : 18          | Cervical spine                 | CAM, DSM-IV        | 10/67 (14.9%)       | <3                         | Low general health perception                                                 | 8            |
| Ouchi et al. [13] | 2019            | Japan   | Retrospective  | 88370       | ≥65                       | 47408 : 40962    | Lumbar spine                  | —                      | 450/88370 (5.1%)     | —                          | Age >80                                                             | 8            |
| Watanabe et al. [14] | 2019            | Japan   | Retrospective  | 322         | 75.7 years (67–89)        | 69 : 253         | Thoracic, lumbar spine         | —                      | 26/322 (8.1%)       | —                          | Parkinsonism                                                      | 7            |
| Morino et al. [15] | 2018            | Japan   | Retrospective  | 532         | 64.2 (10–89)              | 283 : 249        | Thoracolumbar deformity        | DSM-IV               | 59/532 (11.1%)     | <5                         | Blood loss                                                        | 8            |
| Adogwa et al. [16] | 2018            | USA     | Retrospective  | 82          | ≥65                       | 33 : 49          | Lumbar spine                  | CAM                   | 22/82 (18%)        | —                          | Cognitive impairment                                                | 7            |
| Adogwa et al. [17] | 2018            | USA     | Retrospective  | 293         | ≥18                       | 105 : 188        | Lumbar spine                  | —                      | 28/293 (9.6%)       | —                          | CKD                                                                | 7            |
| Susano et al. [18] | 2018            | Portugal| Retrospective  | 715         | 73.6 ± 6.0                | 351 : 400        | Cervical, lumbar spine        | —                      | 127/715 (17.8%)    | —                          | Age, ASA physical status ≥3, METs <4, depression, non-elective surgery, invasiveness tier 3 or 4, BIS monitoring, mean pain score postoperative day 1 | 7            |
| Elsamadicy et al. [19] | 2018            | USA     | Retrospective  | 204         | ≥60                       | 204 : 0          | Elective complex spinal fusion (≥3 levels) | —                      | 25/204 (12.3%)     | —                          | Preoperative hgb level <13.5 g/dl                                              | 7            |
| Ouchi et al. [20] | 2018            | Japan   | Retrospective  | 2712        | ≥20                       | 1738 : 974       | Lumbar spine                  | —                      | 52/2712 (1.9%)      | —                          | Open laminectomy                                                  | 7            |
| Kobayashi et al. [21] | 2018           | Japan   | Retrospective  | 35          | 91.3 (90–98)              | 14 : 21          | Cervical, thoracic, lumbar spine | —                      | 11/35 (31.43%)     | —                          | Age, operative time ≥6 hours                                                  | 6            |
| Yoshida et al. [22]    | 2018            | Japan   | Retrospective  | 304         | 62.9 (18–84)              | 64 : 240         | Spinal deformity               | —                      | 34/304 (11.2%)      | —                          | Hyposmia (CCSIT score <9) and RBD (RBDSQ-K >4)                                   | 8            |
| Kim et al. [23]    | 2018             | Korea   | Prospective    | 104         | 71.7 ± 4.7                | 36 : 68          | Cervical, thoracic, lumbar spine | CAM                   | 15/104 (14.4%)     | —                          | —                                                                    | 8            |
Table 1: Continued.

| Author          | Publication year | Country | Study type | Sample size | Age mean (SD, range) years | Sex ratio (M:F) | Patients who underwent surgery | Delirium diagnosis tool | Delirium incidence | Duration of delirium (days) | Significant factors                                           | Study quality |
|-----------------|------------------|---------|------------|-------------|---------------------------|----------------|--------------------------------|------------------------|---------------------|-------------------------|-------------------------------------------------------------|---------------|
| Ramos et al.    | 2017             | USA     | Retrospective | 11043       | 67 ± 9                    | 2981:8062      | Spinal deformity                | —                      | 269/11043           | (2.4%)                  | Movement disorder, parkinsonism                           | 7             |
| Oichi et al.    | 2017             | Japan   | Retrospective | 6921        | ≥20                       | 3324:3597      | Lumbosacral, thoracic, cervical, unspecified | —                      | 670/6921           | (9.7%)                  | Parkinsonism                                                  | 7             |
| Elsamadicy et al. | 2017            | USA     | Retrospective | 453         | ≥65                       | 211:242        | Spine                          | DSM-V                  | 17/453              | (3.75%)                | Superficial surgical site infection, UTI, length of hospital stay | 8             |
| Elsamadicy et al. | 2017            | USA     | Retrospective | 923         | ≥18                       | 333:590        | Spinal deformity                | —                      | 66/923              | (7.15%)                | Depression, age, operative time, postoperative UTI          | 7             |
| Elsamadicy et al. | 2017            | USA     | Retrospective | 839         | ≥18                       | 329:510        | Elective complex spinal fusion (≥3 levels) | —                      | 67/839              | (7.98%)                | —                                                           | 6             |
| Radcliff et al. | 2017             | USA     | Retrospective | 2792        | ≥65                       | 1487:1305      | Cervical spine                  | —                      | 157/2792            | (5.6%)                  | Dementia, TIA/stroke, age ≥ 85 in cervical decompression patients Intraoperative hypotension <80 mmHg, intraoperative use of dezocine | 7             |
| Jiang et al.    | 2017             | China   | Retrospective | 451         | 65.1 (45–84)              | 226:225        | Cervical and lumbar spine       | ICDSC; CAM-ICU         | 42/451              | (9.3%)                  | —                                                           | 7             |
| Soh et al.      | 2017             | Korea   | Prospective | 109         | >70                       | 56:53          | Cervical, thoracic, lumbar spine | CAM; CAM-ICU; DRS-98-R | 9/109              | (8.2%)                  | Pulmonary disease                                             | 7             |
| Adogwa et al.   | 2017             | USA     | Prospective e | 125         | ≥65                       | 50:75          | Spinal deformity                | —                      | 22/125              | (17.6%)                | —                                                           | 7             |
| Adogwa et al.   | 2017             | USA     | Retrospective | 82          | ≥65                       | 33:49          | Spinal deformity                | —                      | 13/82               | (15.9%)                | Cognitive impairment                                          | 7             |
| Kobayashi et al. | 2017            | Japan   | Retrospective | 262         | 82.7 (80–91)              | 142:140        | Cervical, thoracic, and lumbar spine | —                      | 15/262              | (5.72)                  | Cervical lesion surgery, blood loss>300 mL Lower baseline MMSE score, higher average baseline pain, more intravenous fluid, baseline, antidepressant medication | 7             |
| Brown et al.    | 2016             | USA     | Prospective  | 195         | 74 (72–78)                | 47:42          | Cervical, lumbar spine          | CAM; CAM-ICU; DRS-98-R | 36/195              | (18.5%)                | —                                                           | 7             |
| Lee et al.      | 2016             | Korea   | Retrospective | 129         | 73.5 (70 to 85)           | 51:78          | Lumbar spine                    | CAM; DSM-IV            | 18/129              | (13.9%)                | Cognitive impairment                                          | 7             |
| Balabaud et al. | 2015             | France  | Retrospective | 121         | 83.2 ± 2.4               | 48:73          | Lumbar spine                    | —                      | 16/13(13%)          | —                       | Instrumentation, blood loss                                 | 7             |
TABLE 1: Continued.

| Author            | Publication year | Country | Study type | Sample size | Age mean (SD, range) years | Sex ratio (M:F) | Patients who underwent surgery | Delirium diagnosis tool | Delirium incidence | Duration of delirium (days) | Significant factors | Study quality |
|-------------------|------------------|---------|------------|-------------|---------------------------|----------------|-------------------------------|-----------------------|-------------------|----------------------|---------------------|--------------|
| Glennie et al. [37] | 2015             | Canada  | Retrospective | 276         | 42.9 ± 18.8               | 190:86         | Thoracic, lumbar spine        | —                     | 38/276 (13.8%)   | —                    | Age, male, head injury | 7           |
| Dea et al. [38]   | 2014             | Canada  | Prospective | 101         | 62 (33–85)                | 50:51          | Thoracic, lumbar, sacral spine | —                     | 21/101 (20.8)    | —                    | —                   | 6           |
| Seo et al. [39]   | 2014             | Korea   | Prospective | 70          | 70.1 ± 5.8                | 32:38          | Cervical, lumbar spine        | ICDSC; CAM-ICU        | 17/70 (24.3%)    | —                    | Preoperative GDS, BIS measured intraoperatively under 40 | 8           |
| Kelly et al. [40] | 2014             | Canada  | Prospective | 92          | 66.08 ± 10.59             | —              | Lumbar spine                  | —                     | 5/92 (5.4%)      | —                    | CCI, dural tear       | 8           |
| Fineberg et al. [41] | 2013            | USA     | Retrospective | 57,8457     | >18                       | 285520:292937 | Lumbar spine                  | —                     | 4857/57,8457 (0.84%) | —                    | —                   | 6           |
| Imagama et al. [42] | 2011            | Japan   | Retrospective | 918         | 54 (11–87)                | 521:397        | Lumbar spine                  | —                     | 5/918 (0.54%)     | —                    | Cerebral vascular disease, low hemoglobin and hematocrit levels at 1 day after surgery, bad nutritional status Age >70, high-dose methylprednisolone (>1000 mg), hearing impairment | 6           |
| Lee et al. [43]   | 2010             | Korea   | Retrospective | 87          | 73.5 (70–85)              | 27:50          | Lumbar spine                  | CAM, DSM-IV           | 11/81 (13.6%)    | 13.2 (1 to 92)      | Age >65, teaching hospital, alcohol abuse, deficiency anemia, congestive heart failure, coagulopathy, depression, DM with end-organ damage, drug abuse, hypertension, fluid/electrolyte disorders, metastatic neoplasm, neurological disorder, psychoses, pulmonary circulation disorders, renal failure, weight loss | 7           |
| Ushida et al. [44] | 2009             | Japan   | Retrospective | 122         | 52–86                     | —              | Cervical spine                | DOS, DSM-IV           | 26/122 (21.3%)   | —                    | Central nervous system disorder, surgical history, age >65, DM, blood transfusion ≥800 ml, hemoglobin <100 g/L | 6           |
| Gao et al. [45]   | 2008             | China   | Retrospective | 549         | 48.2 (10–83)              | 302:247        | Cervical, thoracic, lumbar, sacral spine | DOS, DSM-IV           | 18/549 (3.3%)    | 3.1 (1 to 8)        | —                   | 7           |
| Author           | Publication year | Country | Study type | Sample size | Age mean (SD, range) years | Sex ratio (M:F) | Patients who underwent surgery | Delirium diagnosis tool | Delirium incidence | Duration of delirium (days) | Significant factors | Study quality |
|------------------|------------------|---------|------------|-------------|---------------------------|----------------|-------------------------------|------------------------|----------------|---------------------------|---------------------|--------------|
| Kawaguchi et al. [46] | 2006             | Japan   | Retrospective | 341         | 59.2 (14–88)              | 186:155        | Cervical, thoracic, lumbar, sacral spine | CAM, DSM-III-R         | 13/341 (3.8%) | ≤7                        | Low concentrations of hemoglobin and hematocrit 1 day after surgery, ambulatory status at admission | 8              |

DOS, delirium observation screening scale; DSM, diagnostic and statistical manual of mental disorders; MMSE, mini-mental state examination; CVD, cardiovascular disease; CKD, chronic kidney disease; CAM-ICU, confusion assessment method for the intensive care unit; DRS-98-R, delirium rating scale revised-98; ICDSC, intensive care delirium screening checklist; PNI, Prognostic Nutritional Index; ASA, American Society of Anesthesiologists physical status; BIS, Bispectral Index; METs, metabolic equivalents of task; UTI, urinary tract infection; RBD, rapid eye movement sleep behavior disorder; CTSST, cross-cultural smell identification test; RBDSQ-K, Korean version of RBD screening questionnaire; TIA, transient ischemic attack; GDS, global deterioration scale; BIS, Bispectral Index; CCI, Charlson Comorbidity Index.
Note: weights are from random effects analysis

| Study ID                      | Incidence (95% CI) | % weight |
|-------------------------------|--------------------|----------|
| Asia                          |                    |          |
| Pan et al. (2019)             | 0.14 (0.07, 0.22)  | 1.01     |
| Oe et al. (2019)              | 0.09 (0.06, 0.13)  | 2.70     |
| Takenaka et al. (2019)        | 0.00 (0.00, 0.01)  | 4.26     |
| Kin et al. (2019)             | 0.15 (0.06, 0.23)  | 0.83     |
| Oichi et al. (2019)           | 0.05 (0.05, 0.05)  | 4.26     |
| Watanabe et al. (2019)        | 0.08 (0.05, 0.11)  | 2.84     |
| Morino et al. (2018)          | 0.11 (0.08, 0.14)  | 3.04     |
| Oichi et al. (2018)           | 0.02 (0.01, 0.02)  | 4.20     |
| Kobayashi et al. (2018)       | 0.31 (0.16, 0.47)  | 0.30     |
| Yoshida et al. (2018)         | 0.11 (0.08, 0.15)  | 2.50     |
| Kim et al. (2018)             | 0.14 (0.08, 0.21)  | 1.19     |
| Oichi et al. (2017)           | 0.10 (0.09, 0.10)  | 4.15     |
| Jiang et al. (2017)           | 0.09 (0.07, 0.12)  | 3.03     |
| Soh et al. (2017)             | 0.08 (0.03, 0.13)  | 1.70     |
| Kobayashi et al. (2017)       | 0.06 (0.03, 0.09)  | 2.95     |
| Lee et al. (2016)             | 0.14 (0.08, 0.20)  | 1.41     |
| Seo et al. (2014)             | 0.24 (0.14, 0.34)  | 0.64     |
| Imagama et al. (2011)         | 0.01 (0.00, 0.01)  | 4.21     |
| Lee et al. (2010)             | 0.14 (0.06, 0.21)  | 1.03     |
| Ushida et al. (2009)          | 0.21 (0.14, 0.29)  | 1.07     |
| Gao et al. (2008)             | 0.03 (0.02, 0.05)  | 3.79     |
| Kawaguchi et al. (2006)       | 0.04 (0.02, 0.06)  | 3.46     |
| Subtotal ($I^2 = 97.6\%, P = 0.000$) | 0.08 (0.07, 0.10)  | 54.57 |
| - América                     |                    |          |
| Elsamadicy et al. (2019)      | 0.11 (0.06, 0.16)  | 1.69     |
| Adogwa et al. (2018)          | 0.27 (0.17, 0.36)  | 0.69     |
| Adogwa et al. (2018)          | 0.10 (0.06, 0.13)  | 2.60     |
| Elsamadicy et al. (2018)      | 0.12 (0.08, 0.17)  | 1.99     |
| Ramos et al. (2017)           | 0.02 (0.02, 0.03)  | 4.24     |
| Elsamadicy et al. (2017)      | 0.04 (0.02, 0.06)  | 3.63     |
| Elsamadicy et al. (2017)      | 0.07 (0.05, 0.09)  | 3.69     |
| Elsamadicy et al. (2017)      | 0.08 (0.06, 0.10)  | 3.58     |
| Raddiff et al. (2017)         | 0.06 (0.05, 0.06)  | 4.09     |
| Adogwa et al. (2017)          | 0.18 (0.11, 0.24)  | 1.21     |
| Adogwa et al. (2017)          | 0.16 (0.08, 0.24)  | 0.94     |
| Brown et al. (2016)           | 0.40 (0.30, 0.51)  | 0.62     |
| Glennie et al. (2015)         | 0.14 (0.10, 0.18)  | 2.21     |
| Dea et al. (2014)             | 0.21 (0.13, 0.29)  | 0.94     |
| Kelly et al. (2014)           | 0.05 (0.01, 0.10)  | 1.93     |
| Fineberg et al. (2013)        | 0.01 (0.01, 0.01)  | 4.26     |
| Subtotal ($I^2 = 97.6\%, P = 0.000$) | 0.08 (0.07, 0.10)  | 38.33 |
| - Europe                      |                    |          |
| Susano et al. (2018)          | 0.18 (0.15, 0.21)  | 2.95     |
| Balabaud et al. (2015)        | 0.01 (0.01, 0.02)  | 4.15     |
| Subtotal ($I^2 = 99.2\%, P = 0.000$) | 0.10 (−0.06, 0.26) | 7.11 |
| - Overall ($I^2 = 99.2\%, P = 0.000$) | 0.08 (0.07, 0.09)  | 100.00 |

Note: weights are from random effects analysis

(a)  

Figure 2: Continued.
### Study ID

| Study ID |
|----------|
| Pan et al. (2019) |
| Takenaka et al. (2019) |
| Kim et al. (2018) |
| Soh et al. (2017) |
| Adogwa et al. (2017) |
| Brown et al. (2016) |
| Dea et al. (2014) |
| Seo et al. (2014) |
| Kelly et al. (2014) |
| Oichi et al. (2017) |
| Watanabe et al. (2019) |
| Susano et al. (2018) |
| Elsamadicy et al. (2018) |
| Ouchi et al. (2019) |
| Kin et al. (2019) |
| Ramos et al. (2017) |
| Ouchi et al. (2017) |
| Elsamadicy et al. (2017) |
| Elsamadicy et al. (2017) |
| Elsamadicy et al. (2017) |
| Adogwa et al. (2018) |
| Adogwa et al. (2018) |
| Adogwa et al. (2018) |
| Susano et al. (2018) |
| Ouchi et al. (2018) |
| Oichi et al. (2019) |
| Kin et al. (2019) |
| Ramos et al. (2017) |
| Ouchi et al. (2017) |
| Elsamadicy et al. (2017) |
| Elsamadicy et al. (2017) |
| Elsamadicy et al. (2017) |
| Adogwa et al. (2018) |
| Adogwa et al. (2018) |
| Adogwa et al. (2018) |
| Susano et al. (2018) |
| Ouchi et al. (2018) |
| Y oshida et al. (2018) |
| Y oshida et al. (2018) |
| L ucas et al. (2015) |
| Balabaud et al. (2015) |
| Glennie et al. (2015) |
| F ineberg et al. (2013) |
| I magama et al. (2011) |
| L ee et al. (2010) |
| U shida et al. (2009) |
| G ao et al. (2008) |
| K awaguchi et al. (2006) |
| Subtotal ($I^2 = 99.4\%, P = 0.000$) |
| Overall ($I^2 = 99.2\%, P = 0.000$) |

### Incidence (95% CI) and % weight

| Study ID |
|----------|
| Incidence (95% CI) |
| % weight |
| 0.14 (0.07, 0.22) |
| 0.00 (0.00, 0.01) |
| 0.14 (0.08, 0.21) |
| 0.08 (0.03, 0.13) |
| 0.18 (0.11, 0.24) |
| 0.20 (0.12, 0.31) |
| 0.08 (0.04, 0.13) |
| 0.10 (0.06, 0.13) |
| 0.16 (0.08, 0.23) |
| 0.09 (0.06, 0.13) |
| 0.11 (0.06, 0.16) |
| 0.15 (0.06, 0.23) |
| 0.05 (0.05, 0.05) |
| 0.08 (0.05, 0.11) |
| 0.11 (0.08, 0.14) |
| 0.27 (0.17, 0.36) |
| 0.10 (0.06, 0.13) |
| 0.18 (0.15, 0.21) |
| 0.12 (0.08, 0.17) |
| 0.02 (0.01, 0.02) |
| 0.31 (0.16, 0.47) |
| 0.11 (0.08, 0.15) |
| 0.02 (0.02, 0.03) |
| 0.10 (0.09, 0.10) |
| 0.04 (0.02, 0.06) |
| 0.07 (0.05, 0.09) |
| 0.08 (0.06, 0.10) |
| 0.06 (0.05, 0.06) |
| 0.09 (0.07, 0.12) |
| 0.16 (0.08, 0.24) |
| 0.06 (0.03, 0.09) |
| 0.14 (0.08, 0.20) |
| 0.01 (0.01, 0.02) |
| 0.14 (0.10, 0.18) |
| 0.01 (0.01, 0.01) |
| 0.01 (0.00, 0.01) |
| 0.14 (0.06, 0.21) |
| 0.21 (0.14, 0.29) |
| 0.03 (0.02, 0.05) |
| 0.04 (0.02, 0.06) |
| 0.08 (0.07, 0.09) |
| 0.08 (0.07, 0.09) |

### Note

Weights are from random effects analysis.

Figure 2: Continued.
This page contains data related to the incidence of spinal deformity and its subcategories. The data is presented in a table and a graph, with percentages and confidence intervals (95% CI) for each study included.

### Study ID
- Lumbar spine
  - Pan et al. (2019)
  - Takenaka et al. (2019)
  - Adogwa et al. (2018)
  - Ouchi et al. (2018)
  - Lee et al. (2016)
  - Balabaud et al. (2015)
  - Kelly et al. (2014)
  - Fineberg et al. (2013)
  - Imagama et al. (2011)
  - Lee et al. (2010)

### Incidence (95% CI) % weight

| Study ID                        | Incidence (95% CI) | % weight |
|-------------------------------|-------------------|----------|
| Lumbar spine                  |                   |          |
| Pan et al. (2019)             | 0.14 (0.07, 0.22) | 1.01     |
| Takenaka et al. (2019)        | 0.00 (0.00, 0.01) | 4.26     |
| Adogwa et al. (2018)          | 0.10 (0.06, 0.13) | 2.60     |
| Ouchi et al. (2018)           | 0.02 (0.01, 0.02) | 4.20     |
| Lee et al. (2016)             | 0.14 (0.08, 0.20) | 1.41     |
| Balabaud et al. (2015)        | 0.01 (0.01, 0.02) | 4.15     |
| Kelly et al. (2014)           | 0.05 (0.01, 0.10) | 1.93     |
| Fineberg et al. (2013)        | 0.01 (0.01, 0.01) | 4.26     |
| Imagama et al. (2011)         | 0.01 (0.00, 0.01) | 4.21     |
| Lee et al. (2010)             | 0.14 (0.06, 0.21) | 1.03     |

### Subtotal (I² = 92.8%, P = 0.000)
- 0.01 (0.01, 0.02) 29.06

### Spinal deformity
- Oe et al. (2019)
- Yoshida et al. (2018)
- Ramos et al. (2017)
- Elsamadicy et al. (2017)
- Adogwa et al. (2017)
- Adogwa et al. (2017)

### Incidence (95% CI) % weight

| Study ID                        | Incidence (95% CI) | % weight |
|-------------------------------|-------------------|----------|
| Spinal deformity              |                   |          |
| Oe et al. (2019)              | 0.09 (0.06, 0.13) | 2.70     |
| Yoshida et al. (2018)         | 0.11 (0.08, 0.15) | 2.50     |
| Ramos et al. (2017)           | 0.02 (0.02, 0.03) | 4.24     |
| Elsamadicy et al. (2017)      | 0.07 (0.05, 0.09) | 3.69     |
| Adogwa et al. (2017)          | 0.18 (0.11, 0.24) | 1.21     |
| Adogwa et al. (2017)          | 0.16 (0.08, 0.24) | 0.94     |

### Subtotal (I² = 95.0%, P = 0.000)
- 0.10 (0.06, 0.14) 15.28

### Mixed
- Elsamadicy et al. (2019)
- Ouchi et al. (2019)
- Watanabe et al. (2019)
- Morino et al. (2016)
- Adogwa et al. (2018)
- Susa et al. (2018)
- Elsamadicy et al. (2018)
- Kobayashi et al. (2018)
- Kim et al. (2018)
- Ouchi et al. (2017)
- Elsamadicy et al. (2017)
- Elsamadicy et al. (2017)
- Jiang et al. (2017)
- Soh et al. (2017)
- Kim et al. (2018)
- Brown et al. (2016)
- Glennie et al. (2015)
- Dea et al. (2014)
- Seo et al. (2014)
- Gao et al. (2008)
- Kawaguchi et al. (2006)

### Incidence (95% CI) % weight

| Study ID                        | Incidence (95% CI) | % weight |
|-------------------------------|-------------------|----------|
| Mixed                         |                   |          |
| Elsamadicy et al. (2019)      | 0.11 (0.06, 0.16) | 1.69     |
| Ouchi et al. (2019)           | 0.05 (0.05, 0.05) | 4.26     |
| Watanabe et al. (2019)        | 0.08 (0.05, 0.11) | 2.84     |
| Morino et al. (2016)          | 0.11 (0.08, 0.14) | 3.04     |
| Adogwa et al. (2018)          | 0.27 (0.17, 0.36) | 0.69     |
| Susa et al. (2018)            | 0.18 (0.15, 0.21) | 2.95     |
| Elsamadicy et al. (2018)      | 0.12 (0.08, 0.17) | 1.99     |
| Kobayashi et al. (2018)       | 0.31 (0.16, 0.47) | 0.30     |
| Kim et al. (2018)             | 0.14 (0.08, 0.21) | 1.19     |
| Ouchi et al. (2017)           | 0.10 (0.09, 0.10) | 4.15     |
| Elsamadicy et al. (2017)      | 0.04 (0.02, 0.06) | 3.63     |
| Elsamadicy et al. (2017)      | 0.08 (0.06, 0.10) | 3.58     |
| Jiang et al. (2017)           | 0.09 (0.07, 0.12) | 3.03     |
| Soh et al. (2017)             | 0.08 (0.03, 0.13) | 1.70     |
| Kobayashi et al. (2017)       | 0.06 (0.03, 0.09) | 2.95     |
| Brown et al. (2016)           | 0.40 (0.30, 0.51) | 0.62     |
| Glennie et al. (2015)         | 0.14 (0.10, 0.18) | 2.21     |
| Dea et al. (2014)             | 0.21 (0.13, 0.29) | 0.94     |
| Seo et al. (2014)             | 0.24 (0.14, 0.34) | 0.64     |
| Gao et al. (2008)             | 0.03 (0.02, 0.05) | 3.79     |
| Kawaguchi et al. (2006)       | 0.04 (0.02, 0.06) | 3.46     |

### Subtotal (I² = 95.3%, P = 0.000)
- 0.11 (0.09, 0.13) 49.65

### Cervical spine
- Kim et al. (2019)
- Radcliff et al. (2017)
- Ushida et al. (2009)

### Incidence (95% CI) % weight

| Study ID                        | Incidence (95% CI) | % weight |
|-------------------------------|-------------------|----------|
| Cervical spine                |                   |          |
| Kim et al. (2019)             | 0.15 (0.06, 0.23) | 0.83     |
| Radcliff et al. (2017)        | 0.06 (0.05, 0.06) | 4.09     |
| Ushida et al. (2009)          | 0.21 (0.14, 0.29) | 1.07     |

### Subtotal (I² = 90.9%, P = 0.000)
- 0.13 (0.03, 0.24) 6.00

### Overall (I² = 99.2%, P = 0.000)
- 0.08 (0.07, 0.09) 100.00

Note: weights are from random effects analysis.

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Figure 2: Continued.
were collected and pooled to evaluate the relationships between various risk factors and postoperative delirium in patients undergoing spine surgery. In addition, crude ORs with 95% CIs were calculated based on the frequency reported in the original literature. Inconsistency was quantified with $I^2$ statistic, and an $I^2$ of $>50\%$ was considered to indicate substantial heterogeneity. The random-effects model or the fixed-effect model was used depending on the heterogeneity of studies included. A random-effects model was used for heterogeneous data. Otherwise, a fixed-effect

![Begg's funnel plot with pseudo 95% confidence limits](Image)

**Figure 2:** Pooled result of incidence of delirium: (a) subgroup analysis based on the factor of country; (b) subgroup analysis based on the factor of study type; (c) subgroup analysis based on the factor of surgical site; (d) result of sensitive analysis; (e) Begg’s funnel plot.
model was used. Begg’s and Egger’s test were used to estimate publication bias, when 10 or more studies are presented. For any variable presenting with large heterogeneity, sensitive analysis or subgroup analysis was used to investigate the potential origin of heterogeneity.

2.6. Search Results. There were 1360 relevant studies included according to the search strategy. After the titles and abstracts were reviewed, 1256 of them were removed. A full-text review was evaluated in the 104 records maintained, and 64 of them were excluded because they did not meet the inclusion criteria. Finally, 40 studies representing 712820 patients were included in the present meta-analysis (Figure 1).

2.7. Study Characteristics and Quality Assessment. The characteristics of the included studies are summarized in Table 1. 22 studies were conducted in Asian countries, 16 studies in North America, and 2 studies in Europe. 31 studies were retrospective, and 9 were prospective in design. The sample size ranged from 35 to 578457 patients. The reported incidence of delirium ranged from 0.49% to 31.43% for patients after spinal surgery. To evaluate the quality of each study, the NOS was utilized. In those studies, all of them were of moderate to high quality (range, 6–8) (Table 1).

2.8. Incidence of Postoperative Delirium after Spine Surgery. The final meta-analysis included 40 studies [1, 8–46] from 7 different countries, and the pooled incidence was 8% (Figure 2). There was high heterogeneity (I-squared > 50%, P < 0.001). Interestingly, the heterogeneity remained high with each of the subgroups of study type, countries, or operated levels (Figure 2(a)–2(c)). After sensitive analysis, 3 studies [11, 25, 41] showed great influence on the pooled result (Figure 2(d)). The asymmetry Begg’s funnel plot suggested the presence of publication bias for incidence of postoperative delirium after spine surgery (P < 0.001) (Figure 2(e)).

2.9. Risk Factors for Postoperative Delirium after Spine Surgery. The ORs and 95% CIs of the risk factors are displayed in Table 2. Among these, 33 factors were examined in 2 or more studies and 18 factors demonstrated statistical significance.

| Risk factors                          | No. of studies | Pooled OR (95% CI) | Heterogeneity I² (%) | P value | Effects model |
|---------------------------------------|----------------|--------------------|----------------------|---------|---------------|
| Admission to ICU                      | 3              | 2.51 (0.38–4.64)   | 0                    | 0.944   | Fixed         |
| Age                                   | 7              | 1.07 (1.04–1.09)   | 16.5                 | 0.304   | Fixed         |
| Age >65                                | 3              | 4.77 (4.37–5.16)   | 0                    | 0.383   | Fixed         |
| Age >70                                | 3              | 15.87 (6.03–41.73) | 48                   | 0.14    | Fixed         |
| Age >80                                | 2              | 1.91 (1.78–2.03)   | 0                    | 0.844   | Fixed         |
| Alcohol abuse                         | 4              | 2.11 (1.67–2.56)   | 0                    | 0.397   | Fixed         |
| Anxiety                               | 2              | 1.74 (1.04–2.44)   | 0                    | 0.773   | Fixed         |
| Blood loss                            | 5              | 1 (0.99–1.01)      | 83.9                 | <0.001  | Random        |
| Blood transfusion                     | 3              | 0.62 (0.07–1.17)   | 74.4                 | 0.02    | Random        |
| Cardiovascular comorbidity            | 10             | 0.81 (0.34–1.29)   | 0                    | 0.697   | Fixed         |
| CCI                                   | 2              | 1.26 (0.56–1.96)   | 0                    | 0.355   | Fixed         |
| Cervical surgery                      | 6              | 0.97 (0.45–1.48)   | 0                    | 0.514   | Fixed         |
| Congestive heart failure              | 3              | 1.4 (1.21–1.6)     | 0                    | 0.708   | Fixed         |
| Depression                            | 7              | 2.5 (1.52–3.49)    | 76                   | <0.001  | Random        |
| DM                                    | 13             | 1.09 (0.6–1.59)    | 0                    | 0.978   | Fixed         |
| Dural tear                            | 2              | 3.21 (0.07–6.35)   | 0                    | 0.864   | Fixed         |
| Gender (male)                         | 17             | 0.81 (0.76–0.86)   | 44.6                 | 0.025   | Fixed         |
| History of surgery                    | 6              | 1.09 (0.55–1.64)   | 0                    | 0.617   | Fixed         |
| Hypertension                          | 13             | 1.12 (1.04–1.2)    | 28.3                 | 0.16    | Fixed         |
| Kidney disease                        | 6              | 1.41 (1.16–1.66)   | 0                    | 0.92    | Fixed         |
| MMSE score                            | 3              | 0.7 (0.5–0.89)     | 51.7                 | 0.126   | Random        |
| Neurological disorder                 | 4              | 4.66 (4.22–5.11)   | 0                    | 0.521   | Fixed         |
| Operated levels                       | 2              | 1.02 (0.81–1.22)   | 0                    | 0.523   | Fixed         |
| Operation time                        | 4              | 1 (0.99–1)         | 0                    | 0.725   | Fixed         |
| Parkinsonism                          | 5              | 5.37 (0.63–10.1)   | 88                   | <0.001  | Random        |
| Preoperative VAS                      | 2              | 1.88 (1.11–2.64)   | 0                    | 0.816   | Fixed         |
| Previous cerebral vascular diseases   | 7              | 1.82 (0.7–2.94)    | 0                    | 0.952   | Fixed         |
| Previous mild cognitive impairment    | 5              | 2.43 (0.99–3.86)   | 0                    | 0.967   | Fixed         |
| Previous opioid use                   | 3              | 1.86 (1.18–2.54)   | 0                    | 0.659   | Fixed         |
| Psychoses                             | 5              | 2.77 (2.29–3.25)   | 0                    | 0.474   | Fixed         |
| Pulmonary disease                     | 6              | 1.81 (1.27–2.35)   | 0                    | 0.925   | Fixed         |
| Postoperative UTI                     | 2              | 5.68 (2.41–13.39)  | 0                    | 0.463   | Fixed         |
| Superficial surgical site infection   | 2              | 0.28 (-3.25–3.81)  | 0                    | 0.433   | Fixed         |

CCI, Charlson Comorbidity Index; DM, diabetes mellitus; MMSE, mini-mental state examination; VAS, Visual Analogue Scale; UTI, urinary tract infection.
After synthesis of 7 studies, it revealed that patients who developed delirium were significantly older (OR 1.07; 95% CI 1.04–1.09). Meanwhile, age older than 65 (OR 4.77; 95% CI 4.37–5.16), 70 (OR 15.87; 95% CI 6.03–41.73), and 80 (OR 1.91; 95% CI 1.78–2.03) years were significantly associated with the risk of developing delirium. Another demographic factor male was considered to be associated with less delirium risk in the pooled analysis (OR 0.81; 95% CI 0.76–0.86).

A history of alcohol abuse (OR 2.11; 95% CI 1.67–2.56), anxiety (OR 1.74; 95% CI 1.04–2.44), congestive heart failure (OR 1.4; 95% CI 1.21–1.6), depression (OR 2.5; 95% CI 1.52–3.49), hypertension (OR 1.12; 95% CI 1.04–1.2), kidney disease (OR 1.41; 95% CI 1.16–1.66), neurological disorder (OR 4.66; 95% CI 4.22–5.11), opioid use (OR 1.86; 95% CI 1.18–2.54), psychoses (OR 2.77; 95% CI 2.29–3.25), and pulmonary disease (OR 1.81; 95% CI 1.27–2.35) were more likely to develop delirium than controls. Assessment of mental state, as measured by mini-mental state examination (MMSE), demonstrated a significantly lower risk to develop delirium in patients with higher scores (OR 0.7; 95% CI 0.5–0.89). In addition, preoperative pain and postoperative urinary tract infection (UTI) were related to the development of delirium.

| Study ID          | OR (95% CI)     | % weight |
|-------------------|-----------------|----------|
| Prospective       |                 |          |
| Pan et al. (2019) | 0.10 (0.01, 0.66) | 1.98     |
| Kim et al. (2018) | 1.16 (0.22, 6.17) | 0.02     |
| Soh et al. (2017) | 0.74 (0.20, 2.71) | 0.13     |
| Brown et al. (2016)| 0.69 (0.30, 1.59) | 0.50     |
| Seo et al. (2014) | 0.78 (0.27, 2.31) | 0.20     |
| Subtotal (I² = 10.2%, P = 0.348) | | |
| Retrospective     |                 |          |
| Oe et al. (2019)  | 1.74 (0.75, 4.06) | 0.08     |
| Elsamadicy et al. (2019) | 2.98 (0.78, 11.40) | 0.01     |
| Kin et al. (2019) | 2.46 (0.58, 10.44) | 0.01     |
| Morino et al. (2018) | 1.93 (1.00, 3.70) | 0.11     |
| Jang et al. (2017) | 0.90 (0.48, 1.68) | 0.58     |
| Elsamadicy et al. (2017) | 1.02 (0.40, 2.61) | 0.17     |
| Kobayashi et al. (2017) | 1.00 (0.37, 2.75) | 0.15     |
| Glennie et al. (2015) | 10.00 (2.50, 33.33) | 0.00     |
| Fineberg et al. (2013) | 0.82 (0.78, 0.87) | 96.04    |
| Lee et al. (2010)  | 2.80 (0.81, 9.68) | 0.01     |
| Gao et al. (2008)  | 5.19 (2.06, 13.10) | 0.01     |
| Kawaguchi et al. (2006) | 5.39 (0.91, 31.90) | 0.00     |
| Subtotal (I² = 0.0%, P = 0.535) | | 97.17 |

Heterogeneity between groups: P = 0.000
Overall (I² = 44.6%, P = 0.025)

Begg's funnel plot with pseudo 95% confidence limits

Figure 3: Pooled result of male: (a) subgroup analysis based on the factor of study type; (b) Begg's funnel plot.
3. Discussion

Delirium is thought to be a less transient disorder than previously believed in several studies [8, 11]. In addition, it has been reported that patients with postoperative delirium have a higher mortality rate than in those without it [4]. Due to the fact that delirium is varying and multifactorial, it will be helpful for prevention of delirium through identifying predictable risk factors.

This systematic review and meta-analysis were performed to pool and identify the incidence and risk factors of postoperative delirium after spine surgery. The pooled incidence of delirium in this meta-analysis is 8%. However, the present study showed wide variation and heterogeneity in incidence of delirium. A previous meta-analysis of 6 studies reported incidence of delirium after spine surgery varies from 0.84% to 21.3% [47]. Interestingly, the heterogeneity remained high with each of the subgroups of study type, countries, or operated levels (Figures 2(a)–2(c)). We found that patients with spinal deformity have higher rate of delirium (10%) and lower rate in patients with lumbar spine (1%). Meanwhile, prospective studies have a higher incidence of postoperative delirium than retrospective studies. After sensitive analysis, 3 studies [11, 25, 41] showed great influence on the pooled result (Figure 2(d)). All these 3 studies have relatively a larger sample size (range, 13188 to 578457), low incidence of delirium (range, 0.49 to 5.1%), and retrospective nature of study design, which may contribute to the heterogeneity.

The asymmetry Begg’s funnel plot suggested the presence of publication bias for incidence of postoperative delirium

| Study ID                  | OR (95% CI)     | % weight |
|---------------------------|-----------------|----------|
| Pan et al. (2019)         | 0.41 (0.11, 1.46)| 48.71    |
| Takenaka et al. (2019)    | 9.91 (2.23, 44.00)| 0.05     |
| Morino et al. (2018)      | 1.03 (0.49, 2.18)| 31.08    |
| Kim et al. (2018)         | 1.97 (0.60, 6.49)| 2.56     |
| Jiang et al. (2017)       | 1.18 (0.36, 3.86)| 7.28     |
| Soh et al. (2017)         | 0.57 (0.00, 3.81)| 6.11     |
| Elsamadicy et al. (2017)  | 2.98 (1.14, 7.80)| 2.00     |
| Brown et al. (2016)       | 2.32 (0.70, 7.59)| 1.87     |
| Lee et al. (2010)         | 4.96 (0.88, 29.06)| 0.11     |
| Gao et al. (2008)         | 4.62 (0.00, 19.92)| 0.22     |
| Overall (I² = 0.0%, P = 0.697) | 0.81 (0.34, 1.29)| 100.00   |

Figure 4: Pooled result of cardiovascular comorbidity: (a) forest plot of cardiovascular comorbidity; (b) Begg’s funnel plot.
after spine surgery, and lower incidence values could be missing (Figure 2(e)).

One of the most important risk factors was older age, especially in patients over 65. This may be attributed to the fact that elderly patients are more likely influenced by age-related physical and psychical changes. Aging is also associated with a higher incidence of comorbidity such as hypertension, diabetes mellitus, and pulmonary disease [12, 30]. The highest rate of delirium in our meta-analysis is 31.43% in a multicenter prospective study with patient’s age more than 90 [21]. Another significant demographic factor is male as a protective factor. Through subgroup analysis, we found that study design may contribute to the heterogeneity and prospective studies showing relatively a higher risk of developing delirium in females (Figure 3(a)). For publication bias, Begg’s funnel plot demonstrated no significant bias (Figure 3(b)).

The present study showed that comorbidities significantly increase the risk of postoperative delirium after spine surgery. A history of alcohol abuse, congestive heart failure, hypertension, neurological disorder, opioid use, psychoses, and pulmonary disease are related to develop delirium. However, diabetes mellitus, history of surgery, and cerebral vascular diseases were not found to be related to developing

| Study ID          | OR (95% CI) | % weight |
|-------------------|-------------|----------|
| Pan et al. (2019) | 1.53 (0.38, 6.19) | 0.08    |
| Kim et al. (2018) | 1.12 (0.35, 3.57) | 0.26    |
| Soh et al. (2017) | 0.39 (0.10, 1.53) | 1.33    |
| Brown et al. (2016)| 4.11 (1.31, 12.79)  | 0.02    |
| Seo et al. (2014) | 1.57 (0.50, 4.91) | 0.14    |
| Subtotal (I² = 0.0%, P = 0.518) | 0.68 (0.07, 1.29) | 1.83    |
| Kin et al. (2019) | 0.50 (0.12, 2.08) | 0.71    |
| Jiang et al. (2017)| 1.03 (0.43, 2.49) | 0.63    |
| Elsamadicy et al. (2017)| 0.44 (0.17, 1.12) | 2.97    |
| Kobayashi et al. (2017)| 2.75 (0.95, 7.92) | 0.06    |
| Fineberg et al. (2013)| 1.15 (1.07, 1.24) | 93.44   |
| Lee et al. (2010) | 1.27 (0.37, 4.31) | 0.17    |
| Gao et al. (2008) | 2.34 (0.84, 7.58) | 0.06    |
| Kawaguchi et al. (2006)| 1.63 (0.53, 5.01) | 0.13    |
| Subtotal (I² = 38.8%, P = 0.120) | 1.13 (1.04, 1.21) | 98.17   |

Heterogeneity between groups: P = 0.152
Overall (I² = 28.3%, P = 0.160) 1.12 (1.04, 1.20) 100.00

Figure 5: Pooled result of hypertension: (a) forest plot of hypertension; (b) Begg’s funnel plot.
delirium, which was consistent with the previous meta-
analysis [47]. For the cardiovascular comorbidity, the pooled
result of 10 studies [8, 11, 15, 23, 26, 30, 31, 34, 43, 45]
showed no significance (OR 0.81; 95% CI 0.34–1.29) with
low heterogeneity (I² 0%) (Figure 4(a)). Only one study
found cardiovascular comorbidity as a risk factor for de-
lirium [11]. The symmetry Begg’s funnel plot suggested no
presence of publication bias for cardiovascular comorbidity
(Figure 4(b)). Interestingly, however, pooled results showed
congestive heart failure as a significant factor. This may be
due to the severity of heart diseases.

Regarding the comorbidity of hypertension, the meta-
analysis of 13 studies [1, 8, 12, 23, 26, 30, 31, 34, 39, 41, 43, 45, 46] identified it as a significant factor, and subgroup analysis
showed heterogeneity comes from study design (Figure 5(a)).
For publication bias, Begg’s funnel plot suggested no significant
bias (Figure 5(b)). Previous study showed that hypertension
leading to microembolization phenomena and cerebral ische-
emia may be responsible for the occurrence of delirium [48].

For neurological or mental diseases, neurological dis-
order, psychoses, anxiety, and depression were found to be
associated with developing delirium. The meta-analysis of 5
studies showed that mild cognitive impairment is not related
to the occurrence of delirium (OR 2.43; 95% CI 0.99–3.86; I²
0%). Meanwhile, parkinsonism was also not found to be
related to postoperative delirium (OR 5.37; 95% CI 0.63–
10.1). However, there is still controversy in the role of
parkinsonism for postoperative delirium. Kim et al. [23]

| Study ID          | OR (95% CI)         | % weight |
|-------------------|---------------------|----------|
| Prospective       |                     |          |
| Pan et al. (2019) | 5.83 (1.03, 32.89)  | 6.87     |
| Kim et al. (2018) | 1.63 (0.26, 10.34)  | 22.80    |
| Subtotal (I² = 0.0%, P = 0.622) | 2.01 (–2.79, 6.82) | 29.66    |
| Retrospective     |                     |          |
| Watanabe et al. (2019) | 8.58 (2.94, 25.25) | 11.37    |
| Ramos et al. (2017) | 2.68 (1.41, 5.10)  | 29.36    |
| Oichi et al. (2017) | 9.56 (8.05, 11.35) | 29.61    |
| Subtotal (I² = 93.3%, P = 0.000) | 6.55 (0.61, 12.49) | 70.34    |
| Overall (I² = 88.0%, P = 0.000) | 5.37 (0.63, 10.10) | 100.00   |

Note: weights are from random effects analysis.

Figure 6: Pooled result of parkinsonism: (a) forest plot of parkinsonism; (b) result of sensitive analysis.
### MMSE score

| Study ID            | OR (95% CI)         | % weight |
|---------------------|---------------------|----------|
| **Asia**            |                     |          |
| Pan et al. (2019)   | 0.71 (0.52, 0.97)   | 34.57    |
| Kim et al. (2018)   | 0.86 (0.66, 1.12)   | 33.86    |
| Subtotal ($I^2 = 0.0\%, P = 0.361$) | 0.78 (0.62, 0.94) | 68.43    |
| **America**         |                     |          |
| Brown et al. (2016) | 0.51 (0.32, 0.81)   | 31.57    |
| Subtotal ($I^2 = \cdot\%, P = \cdot$) | 0.51 (0.26, 0.76) | 31.57    |
| Overall ($I^2 = 51.7\%, P = 0.126$) | 0.70 (0.50, 0.89) | 100.00   |

Note: weights are from random effects analysis

**Figure 7:** Pooled result of MMSE score. Subgroup analysis based on the factor of country.

| Study ID            | OR (95% CI)         | % weight |
|---------------------|---------------------|----------|
| Pan et al. (2019)   | 0.99 (0.99, 1.00)   | 36.66    |
| Kin et al. (2019)   | 1.00 (0.99, 1.01)   | 23.34    |
| Morino et al. (2018)| 0.14 (0.02, 0.97)   | 0.04     |
| Kim et al. (2018)   | 1.00 (1.00, 1.00)   | 39.96    |
| Jiang et al. (2017) | 3.51 (0.15, 10.33)  | 0.00     |
| Overall ($I^2 = 83.9\%, P = 0.000$) | 1.00 (0.99, 1.01) | 100.00   |

Note: weights are from random effects analysis

**Figure 8:** Continued.
Figure 8: Pooled result of blood loss: (a) forest plot of blood loss; (b) result of sensitive analysis.

| Study ID           | OR (95% CI)       | % weight |
|--------------------|-------------------|----------|
| Susano et al. (2018)| 3.04 (1.72, 5.39) | 9.13     |
| Jiang et al. (2017)| 2.68 (0.22, 13.63)| 0.68     |
| Lee et al. (2010)  | 0.36 (0.10, 1.27) | 90.19    |
| Overall ($I^2 = 74.4\%, P = 0.020$) | 0.62 (0.07, 1.17) | 100.00   |

Figure 9: Pooled result of blood transfusion: (a) forest plot of blood transfusion; (b) result of sensitive analysis.
found that that parkinsonism is not a risk factor for postoperative delirium after multivariable analysis. Interestingly, Pan et al. [8] found an opposite result, which may be attributed to relatively a smaller sample of patients with parkinsonism in their study. Notably, the result should be explained with caution since the heterogeneity is high ($I^2$ 88%). After subgroup analysis, there was a high heterogeneity between retrospective studies (Figure 6(a)). Moreover, the result of sensitive analysis showed two studies [24, 25] contributing greatly to the high heterogeneity (Figure 6(b)).

Both studies were retrospective design and focus on patients with parkinsonism, which may result in high heterogeneity.

Mental states, as assessed by MMSE, were associated with the development of delirium (OR 0.7; 95% CI 0.5–0.89). Through subgroup analysis, we found that geographical factors may contribute to heterogeneity (Figure 7). This measure of the state of mental health appears to have a clearer association with postoperative delirium compared to Charlson Comorbidity Index (CCI) which assesses the number of specific medical comorbidities. These findings are also seen in other studies where CCI appears less clearly associated with the incidence of delirium in older patients [12, 49].

The finding that preoperative pain and opioid use is associated with increased probability of delirium has been previously reported in patients with or without hip fracture or patients with cancer [49, 50]. In addition, elderly patients are more sensitive to opioid-related adverse events [51]. In patients with spine disease, pain may lead to stress reaction and changes of nerve conduction if not effectively controlled [34]. However, the accumulation of active metabolites in patients receiving opioid may contribute to the psychotic features such as delirium [52]. Hence, it is suggested that a less toxic drug, buprenorphine patch other than morphine, should be considered for patients with osteoarthritis and other types of lumbago when pain continues despite adequate administrations of nonopioid analgesics [53].

In our study, intraoperative factors do not appear to influence the prevalence of delirium based on normal clinical practice such as blood loss, blood transfusion, cervical surgery, dural tear, operated levels, and operation time. Notably, for intraoperative blood loss, there was high heterogeneity among studies (Figure 8(a)). After sensitive analysis, we found that one study [23] focused on patients with parkinsonism lead to the high heterogeneity. In addition, high heterogeneity was also seen in the meta-analysis of blood transfusion (Figure 9(a)). The sensitive analysis showed that the heterogeneity comes from one study [43], which had more fusion levels (2.27 ± 1.34) and blood loss (1263 ± 903) than other studies (Figure 9(b)). Postoperatively, patients experiencing complications such as UTI had a higher probability to develop delirium.

There are some limitations in our study. First, no randomized controlled trials were included despite our exhausted search from literatures, which may influence the quality of the result. Second, although subgroup analyses were used, the pooled result of incidence was still reported with high heterogeneity, which should be explained with caution.

4. Conclusions

In summary, the study reveals that pooled incidence of delirium is 8% and age, gender, history of alcohol abuse, anxiety, congestive heart failure, depression, hypertension, kidney disease, neurological disorder, opioid use, psychoses, pulmonary disease, MMSE, preoperative pain, and postoperative UTI were significant factors for delirium after spine surgery. A comprehensive understanding of incidence and risk factors of delirium can improve prevention, diagnosis, and management.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors’ Contributions

Mingsheng Tan designed the study, and Xinjie Wu wrote this manuscript. Xinjie Wu and Wei Sun searched database, reviewed studies, and collected and analyzed data. All of the authors have read and approved the final manuscript.

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