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Risk factors for postoperative delirium in elderly urological patients
A meta-analysis

Yaqi Hua, BS[a] , Shoulin Chen, MD[b], Xiaoyun Xiong[c], Chuyang Lin, MD[d], Dongying Li, BS[e], Ping Tu, MM[f,*]

Abstract

Background: Avoiding postoperative delirium (POD) can have a significant detrimental effect on the rehabilitation and prognosis of elderly urological patients. It is necessary to explore the risk factors associated with POD in elderly urology to provide a basis for clinical recognition of delirium.

Methods: For relevant studies, we comprehensively searched Embase, MEDLINE, Ovid, PubMed, Scopus, The Cochrane Library, and Web of Science. The search deadline was September 2021.

Results: We identified 2046 studies, 8 of which were included in the ultimate analysis. A total of 8 articles, including 356 cases in the delirium group and 1813 cases in the non-delirium group, were included in the relevant literature. The 2 groups mentioned above differed significantly in the following factors: history of delirium (odds ratio [OR] = 6.98, 95% confidence interval [CI]: 1.63–29.86, P = .009); Preoperative use of psychotropic drugs (OR = 1.97, 95% CI: 1.11–3.52, P = .02); age (OR = 3.10, 95% CI: 2.08–4.12, P < .0001). The meta-analysis demonstrated that smoking, alcohol consumption, gender (male), mode of anesthesia (general anesthesia) and being unmarried did not have a significant effect on POD in elderly urological patients.

Conclusion: The risk factors for POD in elderly urological patients include history of delirium, preoperative use of psychotropic drugs, and age. The present study provides guidance for taking targeted preventive measures to reduce risks.

Abbreviations: CAM = The Confusion Assessment Method, CAM-ICU = The Confusion Assessment Method-Intensive Care Unit, DSM-IV = Diagnostic and Statistical Manual of Mental Disorders–4th edition, NOS = Newcastle–Ottawa Scale, OR = odds ratios, POD = postoperative delirium; TURP = transurethral prostatectomy.

Keywords: aged, delirium, meta-analysis, neurocognitive disorders, risk factors, urologic surgical procedure

1. Introduction

In recent years, the incidence of urological diseases has been increasing, with elderly patients accounting for the majority of them.[1] At the same time, the treatment of urological diseases is mainly surgical, with relatively high incidence postoperative complications in elderly patients. For elderly surgical patients, postoperative delirium (POD) is a highly prevalent postoperative complications.[2] POD is an acute, fluctuating central nervous system dysfunction,[3] mainly manifested as a decline in consciousness and cognitive function. Currently, the incidence of POD in urology is approximately 8.8%, with radical cystectomy accounting for 29% and transurethral prostatectomy (TUPR) for 21% of cases.[4,5] Although POD can occur at any

age, high-risk factors for POD include advanced age. These studies have shown that[6–8] POD will result in many negative outcomes, including dementia, increased patient mortality, increased financial burden on family and society, and longer hospital stays. Preventing or eliminating associated risk factors in the perioperative period and taking measures in advance for patients with associated risk factors can help reduce the incidence of POD. Although the *Consensus-based Guideline on Postoperative Delirium 2017*[9] of the European Society of Anesthesiology point out the susceptibility factors for POD, there is no international consensus on the risk factors associated with POD in elderly urological patients. Moreover, there is no validated predictive model to access the risk of POD in the elderly urological patients.

[a] School of Nursing, Nanchang University, Nanchang, China, [b] Department of Anesthesia, The Second Affiliated Hospital of Nanchang University, Nanchang, China, [c] Department of Nursing, The Second Affiliated Hospital of Nanchang University, Nanchang, China, [d] Department of Clinical Trial Research Center, The Second Affiliated Hospital of Nanchang University, Nanchang, China, [e] Department of Intensive Care Unit, The Second Affiliated Hospital of Nanchang University, Nanchang, China, [f] Department of Post-Anesthesia Care Unit, The Second Affiliated Hospital of Nanchang University, Nanchang, China.

*Correspondence: Ping Tu, Department of Post-Anesthesia Care Unit, The Second Affiliated Hospital of Nanchang University, 1 Min DE Road, Nanchang 330006, China (e-mail: Tupingoo@126.com).

Therefore, the present study collected studies on factors related to POD in geriatric urology, systematically evaluated the related risk factors through meta-analysis, and discussed the correlation between related risk factors and POD, to provide support for clinical work and reduce its incidence.

2. Materials and Methods

The meta-analysis was conducted according to the Preferred Reporting Items for Systematic Review and Meta-Analysis guidelines.[10] Our research complied with the guidelines for human studies and was conducted ethically in accordance with the principles enshrined in the World Medical Association Declaration of Helsinki. The study protocol was approved by The Second Hospital of Nanchang University Medical Research Ethics committee on human research (No.: 066).

2.1. Search strategy

Searches were performed using the following database: Embase, MEDLINE, Ovid, PubMed, The Cochrane Library, and Web of Science. September 11, 2021 was the last search date. The following terms were used: "urological surgery," "delirium," and "elderly." Our complete search for PubMed was: (urological surgery [MeSH Terms] OR prostatectomy [Text Word] OR TURP [Text Word] OR ultrasound [Text Word] OR percutaneous [Text Word] OR ureteroscopy [Text Word] OR kidney transplantation [Text Word] OR renal transplantation [Text Word]) AND (delirium [MeSH Terms] OR cognitive impairment [Text Word] OR disorder [Text Word] OR delirium during awakening [Text Word]) AND (elder [MeSH Terms] OR elderly [Text Word] OR frail [Text Word]). To retrieve more qualified articles, references to the retrieved articles were also included.

2.2. Eligibility criteria

Articles meeting the following criteria were included: Participants: elderly urological surgery patients (age no <60 years); Outcome measures: delirium was determined using internationally recognized assessment tools (The Confusion Assessment Method, The Confusion Assessment Method-Intensive Care Unit, or Diagnostic and Statistical Manual of Mental Disorders, 4th edition)[11–13]; type of study: retrospective cohort study or case-control study; published English-language literature on risk factors for POD in elderly urological patients. We excluded previously published papers, meta-analyses, animal studies, and papers lacking complete data.

2.3. Data abstraction

Two researchers used EndNote to manage the literature and selected papers that met the needs of this meta-analysis based on eligibility criteria. The 2 researchers independently collected data on the first author, type of study, time of publication, basic characteristics of research objects, and relevant risk factors discussed in the paper. In the event of a disagreement over the literature, a third party had to independently examine and discuss it until all 3 researchers agreed.

2.4. Methodological quality assessment

Quality was assessed using the Newcastle–Ottawa scale[14], which includes 3 major dimensions: selection, comparability, and exposure. The evaluation was scored out of 9, with a score of ≥7 being good-quality literature and <7 being inferior-quality literature.
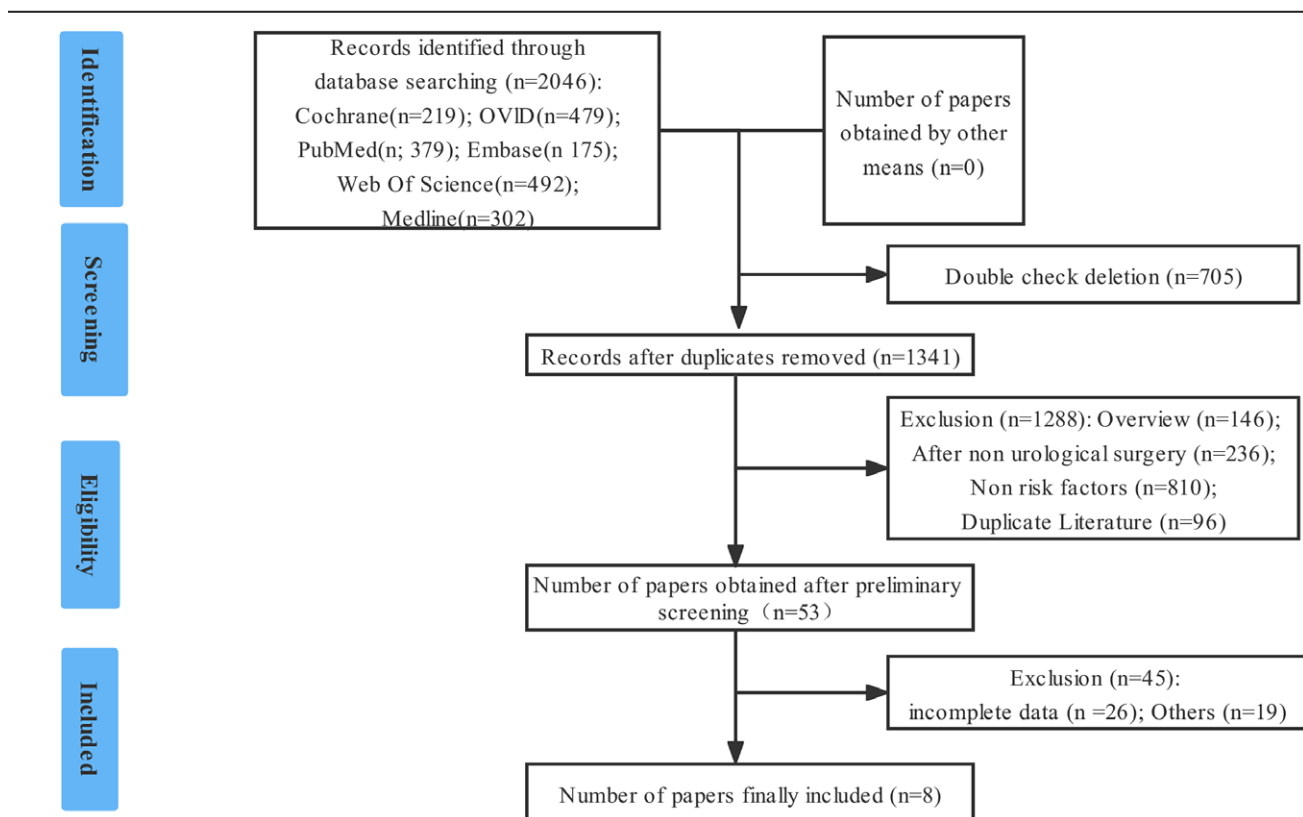

Figure 1. PRISMA flow diagram of study selection process. PRISMA = Preferred Reporting Items for Systematic Review and Meta-Analysis.

Table 1

Basic characteristics and quality evaluation of included studies.

Study	Research type	N	Age range (yr)	Female (n)	Criteria for POD	POD incidence (%)	Risk factors	Statistical method	NOS
Braga et al[15]	Retrospective cohort study	55	≥60	55	CAM	5.45	①②③④⑤	χ2-test、t test and U-test	7
Gani et al[16]	Retrospective cohort study	640	≥65	615	CAM	25.94	⑤⑥	χ2-test、t test	7
Hamann et al[17]2005	Retrospective cohort study	80	≥60	77	CAM	7.00	④⑥⑦	χ2-test、t test	7
Large et al[4]	Case-control study	49	≥65	40	CAM	28.57	④⑥⑧	χ2-test、t test and U-test	7
Peng et al[18]	Retrospective cohort study	558	≥65	358	DSM-IV	7.82	②④⑥⑦⑧	χ2-test、U-test	7
Tai et al[19]	Retrospective cohort study	485	≥65	485	CAM	21.23	②⑤⑧	χ2-test、t test and U-test	8
Sheng et al[5]	Retrospective cohort study	90	66–93	81	CAM	8.89	③⑤⑥⑦	χ2-test、t test	7
Zhang et al[20]	Retrospective cohort study	412	65–84	412	CAM-ICU	6.55	①②④⑤	χ^2 test, t test	9

Note: Risk factors: ① Smoking, ② Alcohol consumption, ③ History of delirium, ④ Preoperative use of psychotropic substances, ⑤ Age, ⑥ Gender (male), ⑦ Mode of anesthesia (general anesthesia), ⑧ Being unmarried.

CAM = The Confusion Assessment Method, DSM-IV = Diagnostic and Statistical Manual of Mental Disorders-4th edition, CAM-ICU = The Confusion Assessment Method-Intensive Care Unit, NOS = The Newcastle–Ottawa Scale, POD = postoperative delirium.

2.5. Statistical analysis

The meta-analysis used Review Manager (version 5.3) to extract research data and generate the forest map. The odds ratio (OR) was selected for secondary classification index, and weighted mean difference was selected as an effective index for continuous index, and the combined OR value and the corresponding 95% CI were calculated. The heterogeneity was detected by the Q test. When $P < .1$ or $I^2 > 50\%$, the random effect model was selected; instead, select the fixed effect model. After combined analysis, it was considered statistically significant when $P < .05$.

3. Results

The researchers initially identified 2046 studies. After screening, the final analysis included 8 studies involving 2169 cases (case group, 356 cases; control group, 1813 cases) (Fig. 1).[4,5,15–20] Of these 8
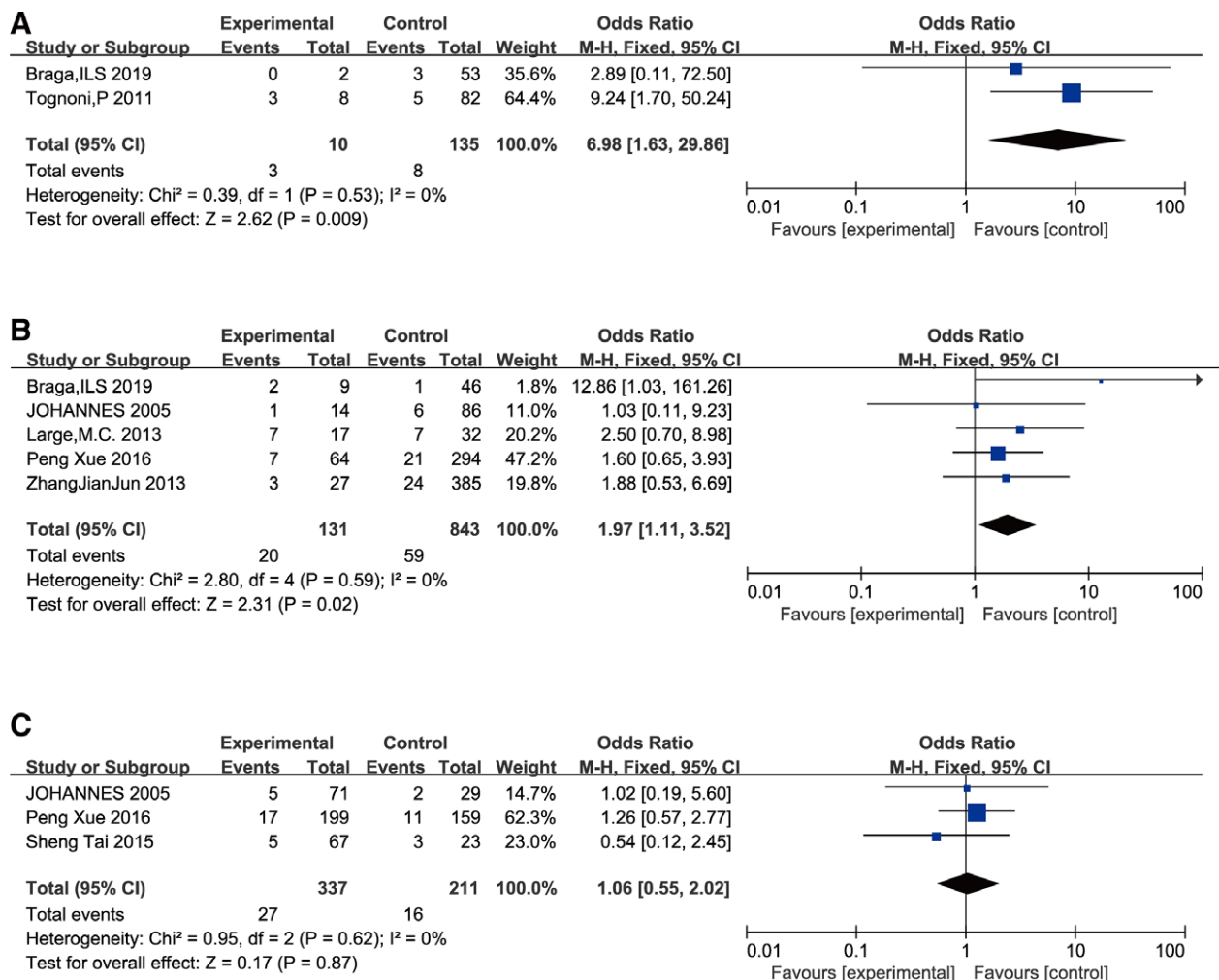

Figure 2. Cumulative meta-analysis of medical and disease factors on postoperative delirium related factors in elderly urological patients.

studies, 7 were retrospective cohort studies and one was a Case-control study. In the evaluation of literature quality, 8 (7 points) were of high-quality. Table 1 summarizes the basic distinguishing features and principal evaluation indicators of the included studies.

3.1. Meta-analysis results

3.1.1. Medical and disease factors. Two studies[5,15] compared the history of delirium (heterogeneity: $P = .53$, $I^2 = 0$). There was a significant difference between the 2 groups (95% CI: 1.63–29.86, $P = .009$) (Fig. 2A).

Five studies[4,15,17,18,20] compared preoperative use of psychotropic substances (heterogeneity: $P = .59$, $I^2 = 0$). There was a significant difference between the 2 groups (95% CI: 1.11–3.52, $P = .02$) (Fig. 2B).

Three studies[5,17,18] compared the mode of anesthesia (general anesthesia) (heterogeneity: $P = .62$, $I^2 = 0$). No significant difference was established between the 2 groups. (95% CI: 0.55–2.02, $P = .87$) (Fig. 2C).

3.1.2.. Basic data. Three studies[5,15,18] compared age (heterogeneity: $P = .83$, $I^2 = 0$). There was a significant difference between the 2 groups. (95% CI: 2.08–4.12, $P < .00001$) (Fig. 3A).

Four studies[15–18] compared gender (male) (heterogeneity: $P = .04$, $I^2 = 65\%$). No significant difference was established between the 2 groups (95% CI: 0.21–9.15, $P = .59$) (Fig. 3B).

Three studies[4,18,19] compared being unmarried (heterogeneity: $P = .008$, $I^2 = 79\%$). No significant difference was established between the 2 groups (95% CI: 0.85–7.83, $P = .09$) (Fig. 3C).

3.1.3. Unhealthy lifestyle. Two studies[15,20] compared smoking (heterogeneity: $P = .68$, $I^2 = 0$). No significant difference was established between the 2 groups (95% CI: 0.67–3.26, $P = .33$) (Fig. 4A).

Four studies[15,18–20] compared alcohol consumption (heterogeneity: $P = .14$, $I^2 = 45\%$). No significant difference was established between the 2 groups (95% CI: 0.74–1.47, $P = .83$) (Fig. 4B).

3.1.4. Sensitivity analysis. Due to the small amount of literature included in the study, we did a sensitivity analysis by changing the data analysis model. After combining the transformation effect of the above risk factors with the model, most of the combined effect values were very close, indicating that the analysis was robust and reliable (Table 2).

3.1.5. Assessment for publication bias. As an example, a funnel diagram was drawn for the risk factor of preoperative use of psychotropic drugs. The results showed that the funnel diagram was symmetrical and the possibility of publication bias was minimal, indicating that the results of the meta-analysis were stable (Fig. 5).

4. Discussion

POD is a common complication in elderly urological patients. Although a single factor can lead to delirium, delirium in the elderly is usually the result of multiple factors. Watt et al[21] conducted a systematic review of 41 studies published between 1948 and 2016 following elective surgery. The study found that a history of delirium, frailty, cognitive impairment, impairment
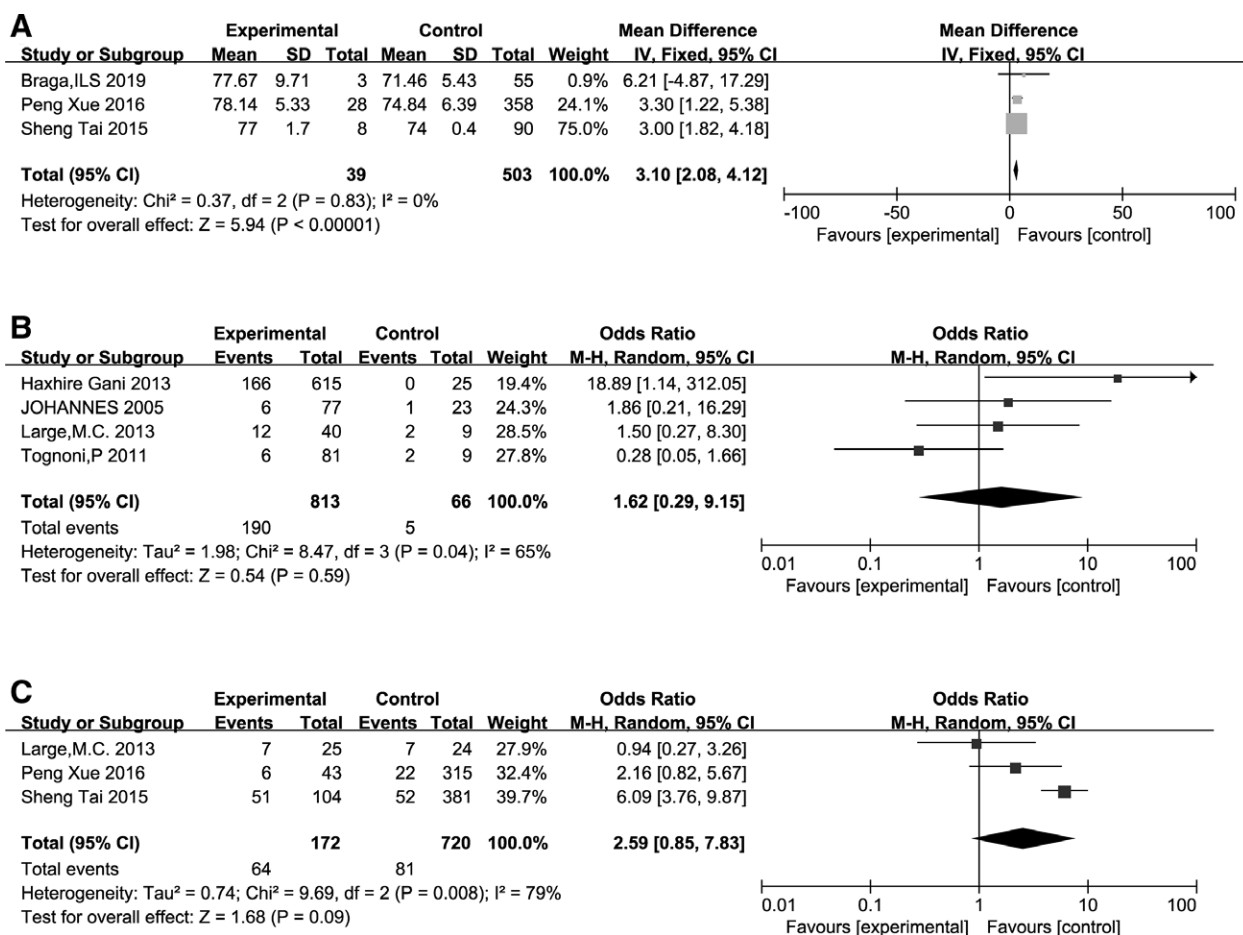

Figure 3. Cumulative meta-analysis of basic data on postoperative delirium related factors in elderly urological patients.
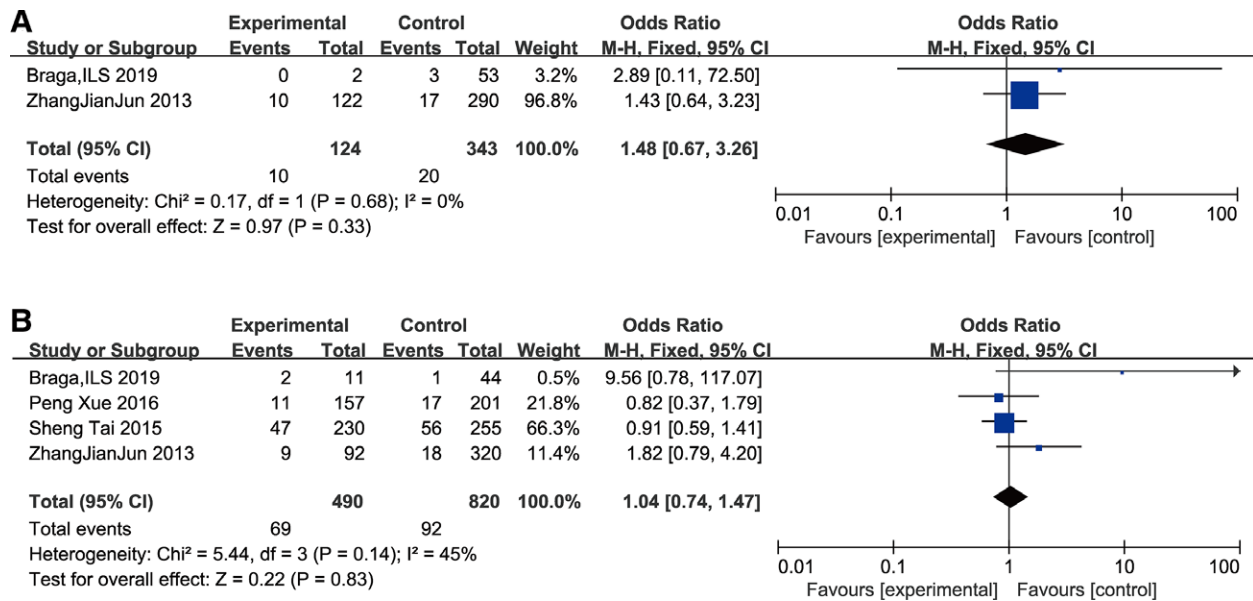
Figure 4. Cumulative meta-analysis of unhealthy lifestyle on postoperative delirium related factors in elderly urological patients.

in activities of daily living, and psychotropic drug use are high-risk factors for delirium. Caregiver support was associated with a low incidence of POD.

Our study found that age was associated with the occurrence of POD. Gender and marital status did not establish a significant difference in the incidence of POD. Age is a risk factor for the development of POD in urological patients. As the population ages, the number of elderly people requiring major surgery increases. At the same time, older patients have decreased physical function and increased susceptibility to stressors, leading to an increased incidence of POD in these patients. According to studies, surgical patients over 65 years of age are more likely to develop POD than younger patients,[9,22] with a 1.15-fold increase in the risk of POD for each additional year of age. Most international and domestic studies have found an association between age and POD.[23] Aging itself is accompanied by a certain degree of increased risk of cognitive impairment and dementia. This is due to changes in neuronal structure and function, aging of nerve cells, reduced cerebral blood perfusion, and failure of neurological signaling as patients age, and the aging brain is also prone to inflammation.[24–26]

Both a history of delirium and preoperative use of psychotropic drugs increase the risk of inducing delirium. There is no international consensus on the effect of preoperative delirium plus other disorders on POD, but some studies have suggested that a history of preoperative delirium and dementia are risk factors for POD.[21,23] Studies have shown that the involvement of delirium, epilepsy and other psychiatric and neurological disorders can affect polyamine levels. Changes in polyamine levels will result in abnormalities in ion channel and ionic glutamate receptors, and subsequent electrolyte disorder.[27] Simultaneously, electrolyte disorder can cause microcirculation disorder, which play a particularly important role in the occurrence of POD.[28] In addition, the development of the POD is also associated with the preoperative use of psychotropic drugs. Studies have demonstrated that long-term use of benzodiazepines before an operation is associated with postoperative mental disorder.[29] Psychotropic drugs mainly act on neurotransmitters in the central nervous system to exert pharmacological effects, and alterations in neurotransmitter levels may be the underlying mechanism of delirium.[30] This meta-study believes that a history of delirium and preoperative use of psychotropic drugs affects the brain's self-regulation ability, decreases the patient's resistance to illness and tolerance to surgery, and lead to a decline of the body's stress capacity, poor tolerance, and easy accumulation of metabolic waste resulting in brain dysfunction, namely delirium. Therefore, for patients with other mental and neurological diseases and preoperative use of psychotropic drugs, medical personnel should strengthen preoperative continuous monitoring, postoperative prevention, and treatment, improve the compensatory ability of various organs, and effectively prevent POD.

This study did not conclude that smoking and alcohol consumption are risk factors for POD in elderly urological patients, which may be related to less literature and fewer cases included in the meta-analysis. However, the unhealthy lifestyle of smoking and drinking has a certain negative impact on patients.[31] Therefore, patients with unhealthy lifestyles such as smoking and drinking should try to improve their lifestyles or quit smoking and drinking.

The quality of the literature collected in this meta-analysis is high, but a number of limitations should be considered when elaborating the results: first and foremost, due to language constraints, only non-English literature was searched in this study; second, the sample size of some risk factors are small, and the results of the meta-analysis need to be further verified; and third, there are some differences in the population included in the studies, leading to heterogeneity among the studies; fourth, the diagnostic criteria and timing of delirium were different among the studies, and bias was not excluded; Fifth, the studies belong to the published literature, and

Table 2

Sensitivity analysis results

Risk factors	OR-Fixed (95% CI)	OR-Random (95% CI)
Smoking	1.48 (0.67, 3.26)	1.49 (0.68, 3.28)
Alcohol consumption	1.04 (0.74, 1.47)	1.17 (0.67, 2.05)
History of delirium	6.98 (1.63, 29.86)	7.18 (1.60, 32.17)
Preoperative use of psychotropic substances	1.97 (1.11, 3.52)	1.98 (1.09, 3.59)
Age	3.10 (2.08, 4.12)	3.10 (2.08, 4.12)
Gender (male)	2.61 (1.06, 6.47)	1.62 (0.29, 9.15)
Mode of anesthesia (general anesthesia)	1.06 (0.55, 2.02)	1.05 (0.55, 2.00)
Being unmarried	3.98 (2.67, 5.95)	2.59 (0.85, 7.83)

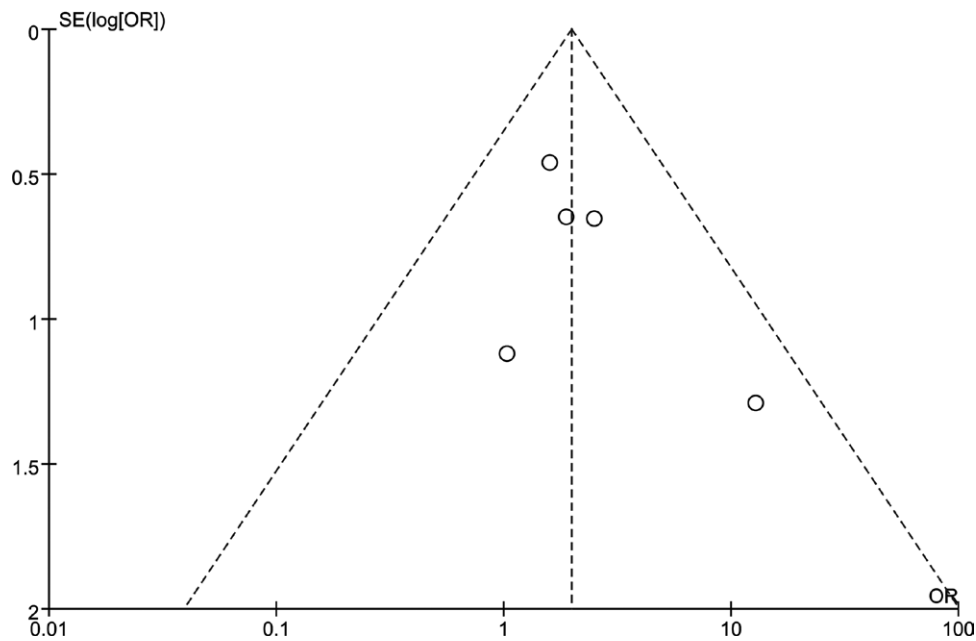CI = confidence interval, OR = odds ratio.

Figure 5. Funnel offset diagram.

potential publication bias is not excluded in this meta-analysis. Therefore, it is suggested that a large-scale, high-grade randomized control trials to be conducted to validate the findings and provide a basis for early clinical identification and prevention of delirium.

In summary, POD in elderly urological patients is strongly correlated with a history of delirium, preoperative use of psychotropic drugs, and old age ($P < .05$); smoking, drinking, gender (male), mode of anesthesia (general anesthesia), and being unmarried were not significantly correlated with it ($P > .05$).

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Author contributions

Conceptualization: Chuyang Lin, Dongying Li, Ping Tu, Shoulin Chen, Yaqi Hua.
Data curation: Chuyang Lin, Yaqi Hua.
Methodology: Chuyang Lin, Shoulin Chen, Xiaoyun Xiong.
Software: Chuyang Lin, Xiaoyun Xiong.
Writing – original draft: Dongying Li, Ping Tu, Shoulin Chen, Yaqi Hua.
Writing – review & editing: Chuyang Lin, Dongying Li, Ping Tu, Shoulin Chen, Xiaoyun Xiong, Yaqi Hua.

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