

Incidence, Outcome And Risk Factors of Postoperative Delirium Subtypes, A Systematic Review And Meta-Analysis

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Research

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Abstract

Objective: Systematic review and meta-analysis methodology was used to estimate the pooled incidence, outcome, risk factors of postoperative delirium, including three delirium subtypes: hyperactive delirium, hypoactive delirium, mixed delirium.

Methods: This systematic review and meta-analysis were conducted following the Preferred Reporting Items for Systematic Review and Meta-analyses (PRISMA) guideline. MEDLINE, EMBASE, CENTRAL were searched for relevant studies. Thirty-two studies from 2714 searched results with 9049 patients were enrolled in this systematic review and meta-analysis. Inclusion criteria were: 1) elective surgery population; 2) the incidence of delirium subtypes was recorded; 3) cohort studies; 4) language restricted to English. In addition, studies that were randomized control trials (RCT), case reports, or uncertainty in the incidence of delirium subtypes were excluded. The related information was extracted by two reviewers independently. All the analyses were conducted by the STATA (Version 16.0; Stata Corporation, College Station, TX).

Result: The study we have performed showed that the highest incidence of postoperative delirium was hypoactive (14% [95% CI, 12-16%]), followed by hyperactive (12% [95% CI, 10-14%]), and the lowest was mixed delirium (9% [95% CI, 7-11%]).

Conclusion: The highest incidence of postoperative delirium was hypoactive (14% [95% CI, 12-16%]), followed by hyperactive (12% [95% CI, 10-14%]), and the lowest was mixed delirium (9% [95% CI, 7-11%]). Therefore, it is definitely necessary to update and unify the diagnosis of delirium subtypes based on current tremendous clinical research, thus controlling and adjusting the risk factors of subtypes to reduce the incidence of postoperative delirium and improve patients' prognoses.

Introduction

Delirium is a common acute-onset organ dysfunction characterized by acute and fluctuating impairment of attention and consciousness, which is associated with prolonged hospital stay [1], increased risk of death [2, 3], and long-term cognitive impairment [4, 5]. Based on clinical manifestations, delirium can be divided into three subtypes: hyperactive, hypoactive, and mixed delirium [6–8]. Postoperative delirium is a relatively common and severe complication that occurs 2-5 days after surgery. It can prolong hospital stays by 2-3 days and is associated with a 30-day mortality rate of 7-10% [9]. The incidence of postoperative delirium in the general surgery population is 2-3%, but it is reported that up to 50-70% of high-risk patients will develop postoperative delirium, especially in elderly patients, who have a neurocognitive impairment and complex or emergency surgery [10]. In addition, the significantly increased morbidity and mortality of postoperative delirium are significantly associated with increased expenditures on medical resources [11]. In recent years, tremendous clinical studies have revealed the pathophysiological mechanism of postoperative delirium and provided more treatment options for

reducing the occurrence of postoperative delirium.[12], but there is no corresponding comprehensive research that has reported the incidence, outcome, and risk factors of postoperative delirium.

The primary purpose of this systematic review and meta-analysis is to explore the incidence of postoperative delirium subtypes and further detect the differences in the outcomes and risk factors of each subtype of delirium.

Methods

Search Strategy and Selection Criteria

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) and registered in the prospective international register of systematic reviews (PROSPERO) (registration number is CRD42021230651). MEDLINE, EMBASE, CENTRAL databases were searched for relevant studies from March, 20, 2021 to May, 25, 2021. Search terms included surgery, delirium, motor subtype, and all synonyms related to the terms. Details of the search strategies are provided in **Appendix 1 [see additional file 1]**.

All retrieved studies were independently scanned by two investigators for eligibility. Inclusion criteria were: 1) elective surgery population; 2) the incidence of delirium subtypes was recorded; 3) cohort studies; 4) language restricted to English. In addition, studies that were randomized control trials (RCT), case reports, or uncertainty in the incidence of delirium subtypes were excluded.

Data Extraction And Quality Assessment

Records were managed by EndNote X9.0 software to exclude the duplicate. The following information from eligible studies were extracted by two reviewers independently: study information; preoperative population demographics, perioperative information, postoperative data, sample size and reported evaluation, the scale for delirium and subtype evaluation; the frequency for delirium evaluation.

We used the NEWCASTLE-OTTAWA QUALITY ASSESSMENT SCALE (NOS scale) for quality assessment. Minor modifications, removing two items of the control group, were made to the NOS scale, considering our objective is to explore the incidence of delirium subtype after surgery. A total of six items in the modified version for quality evaluation. Details of six items are provided in **Appendix 2 [see additional file 2]**.

Statistical Analysis

The incidence of postoperative delirium subtypes was calculated by the Stata (Version 16.0; Stata Corporation, College Station, TX). Considering the heterogeneity between studies, random-effect models were used to estimate the average effect and precision, giving a more conservative estimate of the 95%

confidence interval(CI). If $p < 0.05$, the pool was considered statistically significant. The Cochran Q and I^2 statistics were used to assess heterogeneity between studies.

Publication bias was evaluated by visual inspection of the funnel plot, and sensitivity analyses were conducted by removing each included study at one time to obtain the remaining overall estimate of delirium subtype incidence.

Result

A total of 2714 unique studies were identified through systematic search from MEDLINE EMBASE and CENTRAL. After removing duplicates, 2356 results were screened, and 737 published articles met inclusion criteria for full-text review, among which thirty-two studies were retained for the final assessment and quantitative analysis. Figure 1 demonstrates the flowchart of study selection.

Quality Assessment

Based on the modified NOS scale, twenty-six of thirty-two studies scored 4 points or more, demonstrating low or moderate risks of bias. One critical risk of bias came from selection assessment. Twenty-four studies in thirty-two did not use the MMSE to extract the patients who were in delirium before surgery, leading to selection bias. The second bias mainly came from the outcome assessment. Twenty-five studies had diagnosed delirium subtypes, leaving the seven studies missing the data of mixed delirium. Other bias mainly came from the following aspects: the different evaluation scale and the follow-up period, which have been recommended by the 2017 Interpretation of the European Society of Anesthesiology Evidence-Based and Specialist Consensus Guidelines for Postoperative Delirium, the follow-up time changed from three days to seven days [13], aiming to reduce the missing diagnosis of postoperative delirium.

Overall Meta-analysis

All thirty-two studies, including 9049 patients, were enrolled in the meta-analysis for the incidence of postoperative delirium subtype. We have concluded that the highest incidence of delirium was hypoactive (14% [95% CI, 12-16%]), followed by the hyperactive (12% [95% CI, 10-14%]), and the lowest was the mixed type (9% [95% CI, 7-11%]) (Figure 2-4). Heterogeneity between studies was significant, and I^2 was 92.9%, 94.1%, and 95.6% in hypoactive, mixed, and hyperactive delirium, respectively. When tested for publication bias (Figure 5-7), there is an asymmetry funnel plot in the three types of delirium. A sensitivity analysis that ruled out each study at a time provided that no single affected the overall delirium rate significantly.

Outcomes Of Delirium Subtypes

1.1 Duration of ventilation:

We have found that the longest duration of mechanical ventilation was mixed delirium, followed by the hypoactive, and the shortest was hyperactive delirium [14–16]. Compared with the hyperactive delirium, the average mechanical ventilation duration of mixed type was 2.75 days longer, (2.75(-1.26,6.77)($p=0.178$, $I^2=93.9\%$)); and the mixed subtype was 1.46d(1.46(-1.78,4.7) ($p=0.377$, $I^2=84.9\%$)) longer than hypoactive delirium. The average mechanical ventilation time of the hypoactive delirium was 1.11 days longer than that of the hyperactive type (1.11 (0.04, 2.18)($p=0.043$, $I^2=70.6\%$)).

1.2 Length of hospitalization:

Regarding the length of hospitalization, the longest was the mixed subtype, followed by the hypoactive subtype, and the hyperactive was the shortest [14–18]. The average length of stay of the mixed type was 5.57 days longer than that of the hyperactive type (5.57 (-0.7, 11.85) ($p=0.082$, $I^2=77.9\%$)), and 2.92 days longer than the hypoactive type (2.92(-2.13,7.96) ($p=0.257$, $I^2=63.3\%$)); the hypoactive type was 2.02 days longer than the hyperactive type (2.02(-1.53,5.57)) ($p=0.266$, $I^2=46.9\%$)).

1.3 Duration of delirium

We found that the average duration of delirium was the longest in the mixed type, followed by the hypoactive type, and the hyperactive type was the shortest [15, 17, 19–23]. The mixed type was 25.95 hours (25.95(-13.93,65.84) ($p=0.202$, $I^2=89\%$)) longer than the hyperactive type, and 26.53 hours (26.53(6.45, 46.61) ($p=0.01$, $I^2=49\%$)) longer than the hypoactive type, while the duration of hypoactive delirium was longer than that of hyperactive delirium with an average of 2.06 hours (2.06(-19.85,23.98) ($p=0.854$, $I^2=49\%$)).

1.4 Duration of Intensive Care Unit (ICU)

In terms of the duration of ICU, the longest ICU stay was the mixed type, followed by the hypoactive, and the hyperactive was the shortest [14–16]. Among them, the average ICU duration of mixed delirium was 3.89 days (3.89 (1.26, 6.51) ($p=0.004$, $I^2=77.4\%$)) longer than hypoactive delirium, and 3.5 days (3.5 (-1.18, 8.18) ($p=0.143$, $I^2=91.8\%$)) longer than hyperactive delirium. The hypoactive subtype only has prolonged an average of 0.42 days (0.42(-1.31,2.15)($p=0.637$, $I^2=76.3\%$)) than hyperactive delirium.

1.5 Thirty-days and six-month mortality rate

Studies have shown that there is no consistent result about the thirty-days short-term mortality. Robinson T et al. have reported that the hypoactive delirium mortality rate accounted for 14% (7/50), while the mixed delirium was only 4.3% (1/23) [24]. Research by Lee A. et al. has shown that the 30-day mortality rate: the incidence of hyperactive delirium was 4.2%; hypoactive delirium was 3.8%; the mixed type was 0 ($p=0.26$) [15].

In the six months long-term survival rate, the hypoactive and the mixed subtypes were the worst. Bellelli et al. have shown that the six-month survival rate of the hypoactive (36.8%) was higher than that of the mixed type (29.1%), and the hyperactive (10.7%). And They also performed another Cox survival regression analysis, showing that after adjusting for covariates for the duration, hypoactive subtype (HR = 1.12, 95% CI, 1.01-1.25) and mixed delirium (HR = 1.11, 95% CI, 1.01-1.21) was independently associated with an increase in 6-month mortality [20].

1.6 Incidence of secondary intubation and accidental extubation of delirium subtypes

The enrolled studies have shown that the incidence of secondary intubation and accidental extubation were the worst in hyperactive delirium. Van den Boogaard M. et al. have demonstrated that the incidence of secondary intubation and unintentional removal of the tubes was the highest in hyperactive delirium. In the secondary intubation of per 1000 delirium days, the hyperactive delirium (68 persons/1000 days) was the most, followed by the hypoactive (22 persons/1000 days), and the mixed subtype (16 persons/1000 days); the incidence of accidental, unplanned removal tubes was also highest in hyperactive delirium (227 persons/1000 days), hypoactive subtype (35 persons/1000 days); mixed (40 persons/1000 days) [16]. Another study by Robinson. TN has shown that the incidence of accidental extubation was higher in the mixed subtype (90.0% (9/10)) than that of the hypoactive subtype (22.2% (2/9)) (P=0.006) [24].

Risk Factors Contributed To The Delirium Subtypes

According to a comprehensive analysis of the enrolled studies, the results have shown that the ASA score, intraoperative blood loss, duration of anesthesia, duration of operation, and the level inflammatory factors IL-6, which may be the risk factors contributed to the mixed delirium.

Preoperative ASA classification: Bellelli, G. et al. have shown that mixed delirium (86.1%) was more severe than hypoactive type (77.2%), and hyperactive type (70.2%) [20]. Another study by Santana Santos has shown that preoperative ASA classification in hyperactive was worse than hypoactive subtype [18]. In terms of intraoperative blood loss (ml, mean \pm sd) the mixed subtype mixed (207 \pm 236.6) blood loss was higher than hypoactive (177 \pm 197.8), hyperactive (103.3 \pm 154.2) (p=0.6) [18]. Anesthesia time (hours, median [IQR]): Lee, A. et al. have found that the average anesthesia time was the longest in the mixed delirium (6.2 [4.7-8.1]), followed by the hyperactive type (5.4 [4.2-7.0]), and the hypoactive (4.3 [4.0-4.6]) (p < 0.001) [15]. Another study by Santana Santos, F. et al was consistent with above results (min, mean \pm sd) : mixed subtype (164.6 \pm 12.6), hyperactive (162.1 \pm 15.2), hypoactive (155 \pm 15.8) (p = 0.7) [18].

Concerning operation duration (hours, mean \pm sd or median [IQR]): Bellelli, G. et al. have reported that the operation time of the delirium subtype was the longest in the mixed type (96.0 \pm 51.7), followed by the hypoactive (84.3 \pm 41.0) and hyperactive (79.2 \pm 34.6) delirium [20]. Lee, A. et al. have also found that the average operation duration was the longest in the mixed subtype (4.9 [3.3-7.0]). Still, the hyperactive (4.3 [3.2-5.7]) was longer than the hypoactive delirium (3.3 [2.9-3.9]) (p < 0.001) [15]. Another study by

Robinson, T. N. et al has shown that the operation duration was longest in mixed delirium (325 [155]) compared with hypoactive delirium (268 [177]) ($p = 0.12$)[24].

Regarding the level of inflammatory factors, a study has shown that the IL-6 factor was the highest in the mixed type. Van Munster, B. C et al. have shown that IL-6 was highest in mixed (73pg/mL), followed by hyperactive (71pg/mL), and lowest in hypoactive delirium(16pg/mL) ($P=0.02$)[19].

Additionally, we have found that pain score and type of surgery were associated with hyperactive delirium. Studies have reported that the higher the pain score, the more likely it is to develop hyperactive delirium[25]. And the incidence of hyperactive delirium was highest in cardiac surgery[16]. For hypoactive delirium, Stransky M. et al. reported that preoperative treatment with β -blockers was significantly associated with reducing hypoactive delirium[26], which had been reported that highest incidence in was neurological surgery [16].

Discussion

In this systematic review and meta-analysis, 32 studies involving 9049 surgical patients and quantitative analysis were used to evaluate postoperative delirium subtypes' incidence, outcome, and risk factor. The study we have performed showed that the highest incidence of postoperative delirium was hypoactive delirium, followed by hyperactive, and the lowest incidence was the mixed type. The results are consistent with a study focusing on the incidence of delirium subtypes in adult ICU [27]. Both medical and surgical patients are more prone to hypoactive delirium, which is more likely to be overlooked in clinical practice. That may ascribe to the following reasons: Firstly, the clinical features of hypoactive are more indifferent than the hyperactive and mixed types, leading to hypoactive delirium being difficult to recognize. Secondly, the nature of the health care system. The scarcity of continuity care, the difficulty of obtaining the latest records (such as drug changes, recent hospital admissions, or other risk factors such as dementia), and the delayed assessment. Thirdly, misunderstandings within the workforce. It is considered normal for older patients to be disoriented, and hyperactivity symptoms must be present to make a diagnosis; to a certain degree, hypoactive delirium is somehow beneficial to the patient, protecting them from worsening diseases[28].

To our knowledge, this is the first quantitative analysis of the clinical outcomes and risk factors of postoperative delirium subtypes, making the results of this analysis are more accurate and more convincing than the previous qualitative studies. Regarding the clinical outcome of postoperative delirium, we have summarized that mixed delirium was the worst, including duration of mechanical ventilation, length of hospitalization, ICU stay, and delirium duration. Additionally, it is also worth noting that the highest incidence of accidental removal of the tubes and secondary intubation was hyperactive delirium. Our results indicate that the worst clinical outcome was mixed delirium. The reasons may come from the following aspects. Firstly, the mixed delirium fluctuates between the hyperactive and hypoactive[19, 30], making it challenging to identify. Secondly, due to the endogenous (severity of the condition, age, sex) and exogenous (surgery, drugs, anesthesia, intubation) and other factors of the

patients[29], it is more likely to occur the mixed delirium, leading to prolonged mechanical ventilation time, hospital stay, ICU stay time and duration of delirium,

In terms of the risk factors of postoperative delirium subtypes, our findings suggested that mixed delirium was associated with ASA score, intraoperative blood loss, duration of anesthesia, duration of surgery, and the level of the inflammatory factor IL-6; hyperactive delirium had a relation with pain score and type of surgery; and hypoactive delirium was significantly related to preoperative treatment with β -blockers. Regarding other risk factors, a systematic review by Krewulak, K. D has analyzed the risk factors of delirium subtypes in adult ICU: age, gender, APACHE-II disease severity score [27]. However, the study results have not shown the relationship between the risk factors and delirium subtypes. Additionally, studies have also concluded that mixed delirium was more related to drug poisoning and metabolic disorders ($p < 0.001$). Patients with hyperactive delirium were younger, related to drug withdrawal and other systemic causes ($p < 0.001$), and hypoactive delirium was associated with dementia, cerebrovascular and systemic infections ($p < 0.001$) [30]. The most significant difference between this meta-analysis and the studies mentioned above is that we have focused on surgical patients and have found modifiable risk factors during surgery. Among them, the worst outcome was mixed delirium, to which more attention should be paid. Therefore, corresponding measures should be taken to modify risk factors, such as reducing perioperative blood loss[31, 32], shortening the duration of anesthesia and surgery as much as possible, controlling inflammatory reactions to reduce the level of inflammatory factors [33–35]. In addition, for hyperactive delirium, the risk factor is pain, for which appropriate management could be taken to relieve the pain of the patients[36–39]. For hypoactive delirium, preoperative use of β -blocker drugs can significantly reduce the incidence of hypoactive delirium after surgery. Whether considering the use of beta-blockers preoperative needs further investigation and depends on the actual clinical situation[40, 41]. Concerning the risk factors derived from the above analysis, effective measures could be taken to prevent delirium, improve the prognosis of patients, and reduce the incidence of postoperative delirium in surgical patients.

When it comes to the heterogeneity of this article, there are several aspects for consideration. Firstly, one of the sources of heterogeneity may attribute to the different scales of the diagnosis of delirium. Among them, CAM-ICU($n=8$), and DSM-IV($n=9$). CAPD Scale($n=1$), ICDSC($n=1$), RASS($n=3$). According to the latest guidelines, the gold standard for diagnosing delirium is recommended to be diagnosed according to the fifth edition [8]. Secondly, another source of heterogeneity may be the frequency of the diagnostic for delirium. Among the included studies: eleven enrolled studies did not specify the frequency of use of the scale, three of the studies have reported that the frequency of use of the scale was twice a day, and the six studies were three times/day, eleven studies was once a day, what is more, the frequency of a study has reached four times/day. Although the guidelines do not specify the frequency of use of the delirium scale [17, 42], a standard frequency delirium diagnostic scale is conducive to the diagnosis of delirium, especially for hypoactive delirium. Third, the source of heterogeneity may also be the difference in the location and year of the research.

This systematic review has the following limitations. Although major databases have been searched, it is still possible that some grey documents have not been explored. At the same time, this meta-analysis is quite heterogeneous after a comprehensive analysis, but we have elaborated the possible reasons for the heterogeneity. On the other hand, papers published by author Krewulak, K. D. et al., executed in October 22, 2017 and August 13, 2018, respectively, have reported the incidence, risk factors and outcome of delirium subtype in adult ICU. However, our data and the enrolled aim population differs from the above studies, great significance has been attached to the postoperative delirium subtypes, which still need more investigation.

Conclusion

The highest incidence of postoperative delirium was hypoactive type, followed by hyperactive delirium, and the lowest was mixed delirium. What's more, our overall analysis of enrolled studies indicate that the worst outcome was mixed delirium. Thus, supposing adequate measures are taken to control the intraoperative risk factors. In that case, it may be beneficial to reduce the incidence of postoperative delirium, improve the prognosis of patients, and increase the long-term survival rate of patients.

Declarations

Ethical Approval and Consent to participate

No applicable

Consent for publication

All the authors are consent to publish the manuscript in *critical care*

Availability of supporting data

Supported data in appendix

Competing interests

There is no compete interests.

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Authors' contributions

QL and JF G contributed euqually to the whole process of the manuscript, including the conceptualization and methodology, QL contributed the software, Jf G helped in inveatigation; QL contributed to writing—

original draft preparation, Jf G and JS contributed to writing—review and editing, Jf G contributed to visualization; JS contributed to supervision and administered the project.

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References

1. Thomason JW, Shintani A, Peterson JF, et al: **Intensive care unit delirium is an independent predictor of longer hospital stay: a prospective analysis of 261 non-ventilated patients.** *Critical care (London, England)* 2005, **9**(4):R375-381.
2. Park EA, Kim MY: **Postoperative Delirium is Associated with Negative Outcomes and Long-Term Mortality in Elderly Koreans: A Retrospective Observational Study.** *Medicina (Kaunas, Lithuania)* 2019, **55**(10).
3. Hamilton GM, Wheeler K, Di Michele J, et al: **A Systematic Review and Meta-analysis Examining the Impact of Incident Postoperative Delirium on Mortality.** *Anesthesiology* 2017, **127**(1):78-88.
4. Wacker P, Nunes PV, Cabrita H, et al: **Post-operative delirium is associated with poor cognitive outcome and dementia.** *Dementia and geriatric cognitive disorders* 2006, **21**(4):221-227.
5. Goldberg TE, Chen C, Wang Y, et al: **Association of Delirium With Long-term Cognitive Decline: A Meta-analysis.** *JAMA neurology* 2020, **77**(11):1373-1381.
6. Meagher DJ, Trzepacz PT: **Motoric subtypes of delirium.** *Seminars in clinical neuropsychiatry* 2000, **5**(2):75-85.
7. Liptzin B, Levkoff SE: **An empirical study of delirium subtypes.** *The British journal of psychiatry : the journal of mental science* 1992, **161**:843-845.
8. Sachdev PS, Blacker D, Blazer DG, et al: **Classifying neurocognitive disorders: the DSM-5 approach.** *Nature reviews Neurology* 2014, **10**(11):634-642.
9. Jin Z, Hu J, Ma D: **Postoperative delirium: perioperative assessment, risk reduction, and management.** *British journal of anaesthesia* 2020, **125**(4):492-504.
10. Inouye SK, Westendorp RG, Saczynski JS: **Delirium in elderly people.** *Lancet (London, England)* 2014, **383**(9920):911-922.
11. Zywił MG, Hurley RT, Perruccio AV, et al: **Health economic implications of perioperative delirium in older patients after surgery for a fragility hip fracture.** *The Journal of bone and joint surgery American volume* 2015, **97**(10):829-836.

12. Mauri V, Reuter K, Körber MI, *et al*: **Incidence, Risk Factors and Impact on Long-Term Outcome of Postoperative Delirium After Transcatheter Aortic Valve Replacement.** *Frontiers in cardiovascular medicine* 2021, **8**:645724.
13. 曹 磊: **2017 中国老年痴呆症流行病学调查**
J Clin Surg 2018, **Vol**26.
14. Zhang W, Hu W, Shen M, *et al*: **Profiles of delirium and the clinical outcomes of patients who underwent coronary artery bypass grafting: a prospective study from China.** *Journal of clinical nursing* 2016, **25**(5-6):631-641.
15. Lee A, Mu JL, Chiu CH, *et al*: **Effect of motor subtypes of delirium in the intensive care unit on fast-track failure after cardiac surgery.** *The Journal of thoracic and cardiovascular surgery* 2018, **155**(1):268-275.e261.
16. van den Boogaard M, Schoonhoven L, van der Hoeven JG, *et al*: **Incidence and short-term consequences of delirium in critically ill patients: A prospective observational cohort study.** *Int J Nurs Stud* 2012, **49**(7):775-783.
17. Slor CJ, Adamis D, Jansen RWMM, *et al*: **Delirium motor subtypes in elderly hip fracture patients: Risk factors, outcomes and longitudinal stability.** *Journal of Psychosomatic Research* 2013, **74**(5):444-449.
18. Santana Santos F, Wahlund LO, Varli F, *et al*: **Incidence, clinical features and subtypes of delirium in elderly patients treated for hip fractures.** *Dementia and geriatric cognitive disorders* 2005, **20**(4):231-237.
19. van Munster BC, Korevaar JC, Zwinderman AH, *et al*: **Time-course of cytokines during delirium in elderly patients with hip fractures.** *Journal of the American Geriatrics Society* 2008, **56**(9):1704-1709.
20. Bellelli G, Carnevali L, Corsi M, *et al*: **The impact of psychomotor subtypes and duration of delirium on 6-month mortality in hip-fractured elderly patients.** *International journal of geriatric psychiatry* 2018.
21. Ishibashi-Kanno N, Takaoka S, Nagai H, Okubo-Sato M, *et al*: **Postoperative delirium after reconstructive surgery for oral tumor: a retrospective clinical study.** *International journal of oral and maxillofacial surgery* 2020, **49**(9):1143-1148.
22. Horacek R, Krnacova B, Prasko J, *et al*: **Delirium as a complication of the surgical intensive care.** *Neuropsychiatric disease and treatment* 2016, **12**:2425-2434.
23. Scholtens RM, van Munster BC, Adamis D, *et al*: **Variability of Delirium Motor Subtype Scale-Defined Delirium Motor Subtypes in Elderly Adults with Hip Fracture: A Longitudinal Study.** *Journal of the American Geriatrics Society* 2017, **65**(2):e45-e50.

24. Robinson TN, Raeburn CD, Tran ZV, et al: **Motor subtypes of postoperative delirium in older adults.** *Archives of surgery (Chicago, Ill : 1960)* 2011, **146**(3):295-300.
25. Munjupong S, Sripon T, Siripoonyothai S, et al: **Incidence and risk factors of emergence delirium after general and regional anesthesia in elective non-cardiac surgery patients.** *Journal of the Medical Association of Thailand* 2018, **101**(12):1653-1658.
26. Stransky M, Schmidt C, Ganslmeier P, et al: **Hypoactive delirium after cardiac surgery as an independent risk factor for prolonged mechanical ventilation.** *Journal of Cardiothoracic and Vascular Anesthesia* 2011, **25**(6):968-974.
27. Krewulak KD, Stelfox HT, Ely EW, et al: **Risk factors and outcomes among delirium subtypes in adult ICUs: A systematic review.** *Journal of critical care* 2020, **56**:257-264.
28. Hosker C, Ward D: **Hypoactive delirium.** *BMJ (Clinical research ed)* 2017, **357**:j2047.
29. FitzGerald JM: **Delirium clinical motor subtypes: a narrative review of the literature and insights from neurobiology.** *Aging & mental health* 2018, **22**(4):431-443.
30. Glynn K, McKenna F, Lally K, et al: **How do delirium motor subtypes differ in phenomenology and contributory aetiology? a cross-sectional, multisite study of liaison psychiatry and palliative care patients.** *BMJ Open* 2021, **11**(4):e041214.
31. Desai N, Schofield N, Richards T: **Perioperative Patient Blood Management to Improve Outcomes.** *Anesthesia and analgesia* 2018, **127**(5):1211-1220.
32. Ghadimi K, Levy JH, Welsby IJ: **Perioperative management of the bleeding patient.** *British journal of anaesthesia* 2016, **117**(suppl 3):iii18-iii30.
33. Segal JP, Tresidder KA, Bhatt C, et al: **Circadian control of pain and neuroinflammation.** *Journal of neuroscience research* 2018, **96**(6):1002-1020.
34. Saxena S, Maze M: **Impact on the brain of the inflammatory response to surgery.** *Presse medicale (Paris, France : 1983)* 2018, **47**(4 Pt 2):e73-e81.
35. Helander EM, Webb MP, Menard B, et al: **Metabolic and the Surgical Stress Response Considerations to Improve Postoperative Recovery.** *Current pain and headache reports* 2019, **23**(5):33.
36. Mitra S, Carlyle D, Kodumudi G, et al: **New Advances in Acute Postoperative Pain Management.** *Current pain and headache reports* 2018, **22**(5):35.
37. Elmallah RK, Chughtai M, Khlopas A, et al: **Pain Control in Total Knee Arthroplasty.** *The journal of knee surgery* 2018, **31**(6):504-513.

38. Duning T, Ilting-Reuke K, Beckhuis M, et al: **Postoperative delirium - treatment and prevention.** *Current opinion in anaesthesiology* 2021, **34**(1):27-32.
39. Tsaousi GG, Logan SW, Bilotta F: **Postoperative Pain Control Following Craniotomy: A Systematic Review of Recent Clinical Literature.** *Pain practice : the official journal of World Institute of Pain* 2017, **17**(7):968-981.
40. Wang X, Fernandez Robles C, Kertai MD: **Perioperative β -blocker use: what is new in 2020?** *Current opinion in anaesthesiology* 2020, **33**(3):417-422.
41. Blessberger H, Kammler J, Domanovits H, et al: **Perioperative beta-blockers for preventing surgery-related mortality and morbidity.** *The Cochrane database of systematic reviews* 2018, **3**(3):Cd004476.
42. Albrecht JS, Marcantonio ER, Roffey DM, et al: **Stability of postoperative delirium psychomotor subtypes in individuals with hip fracture.** *Journal of the American Geriatrics Society* 2015, **63**(5):970-976.

Figures

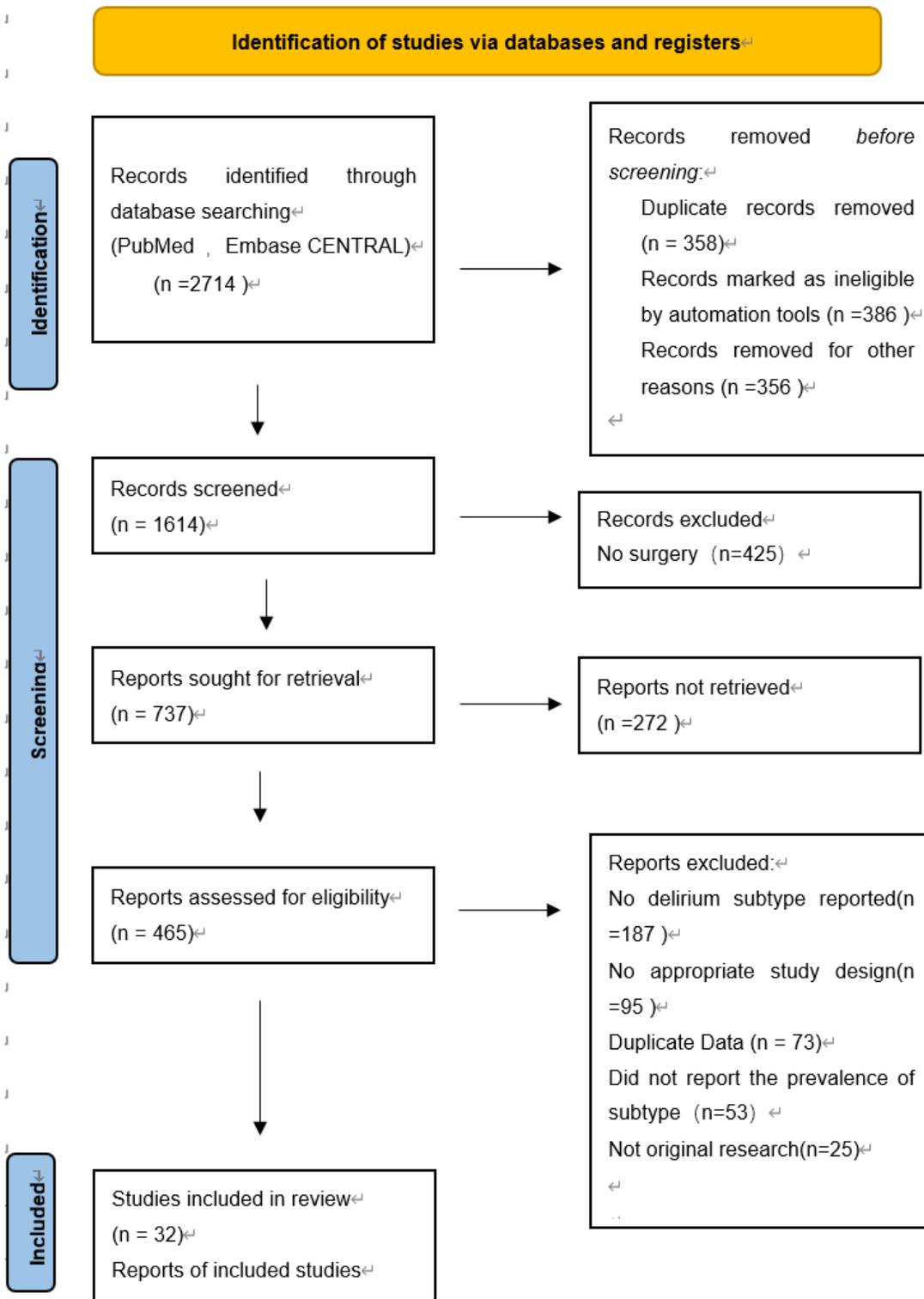


Figure 1

The flow-chart of the whole screening and including process

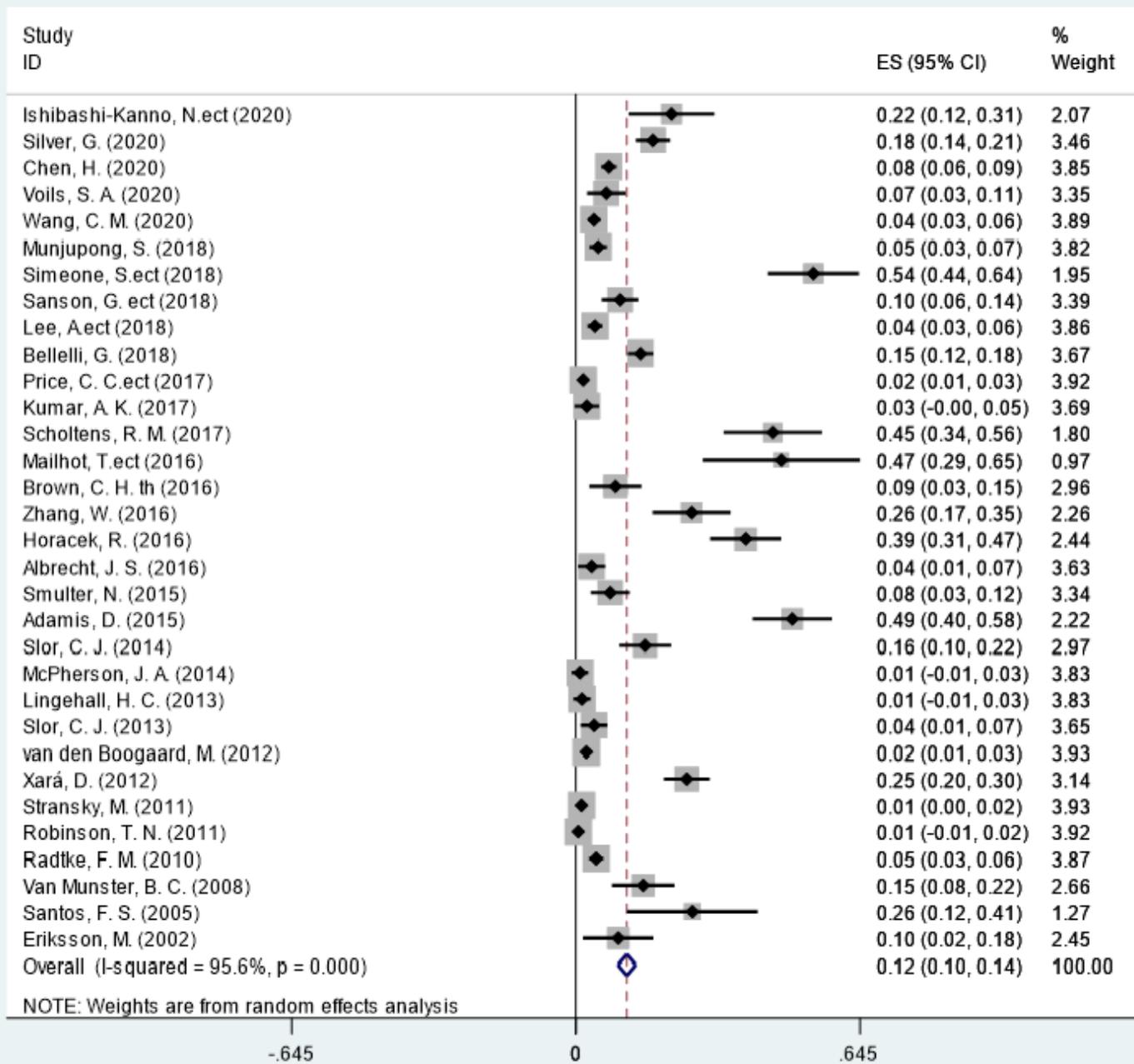


Figure 2

The forest plot of the incidence in hyperactive delirium

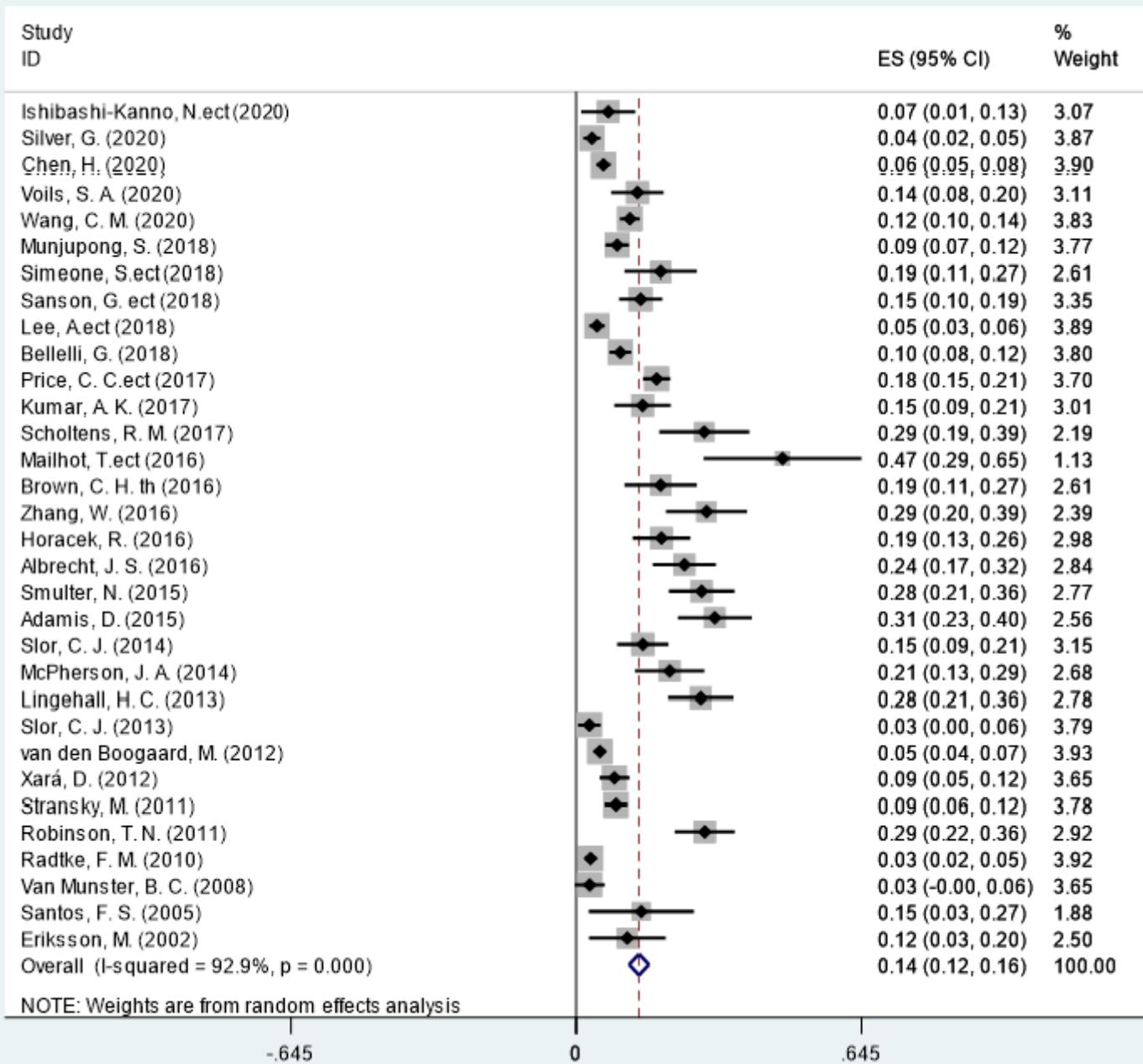


Figure 3

The forest plot of the incidence in hypoactive delirium

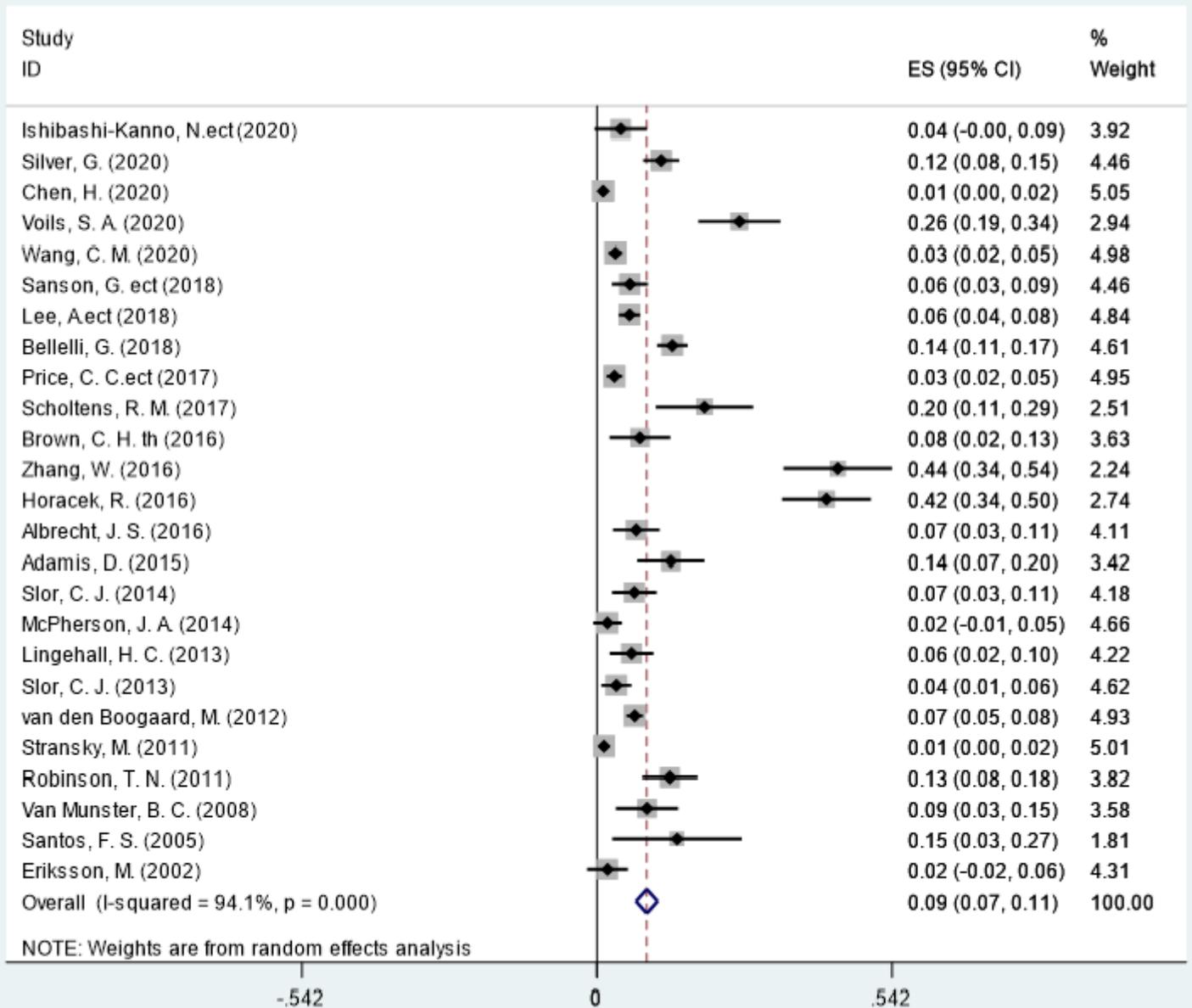


Figure 4

The forest plot of the incidence mixed delirium

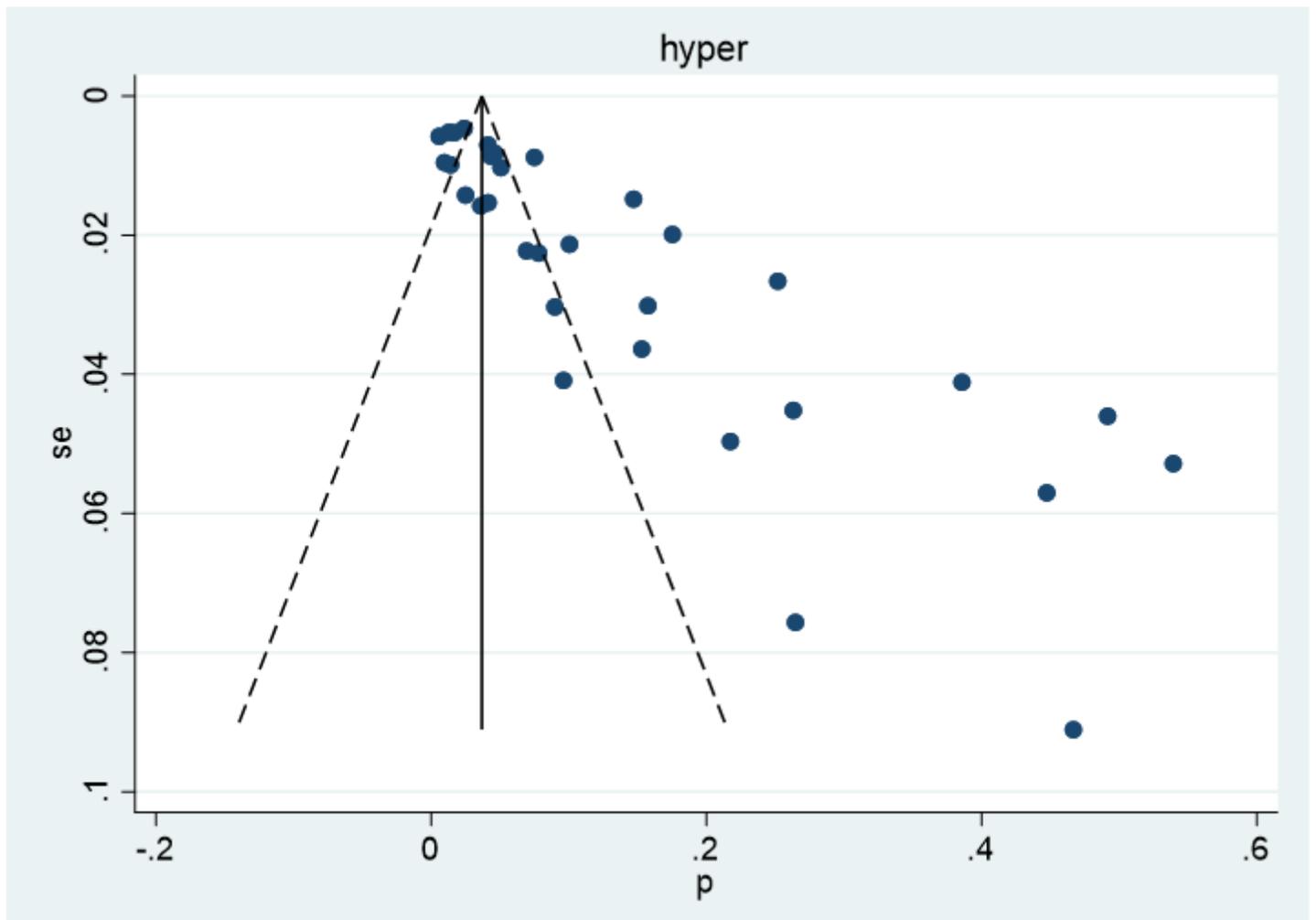


Figure 5

The funnel plot of hyperactive delirium

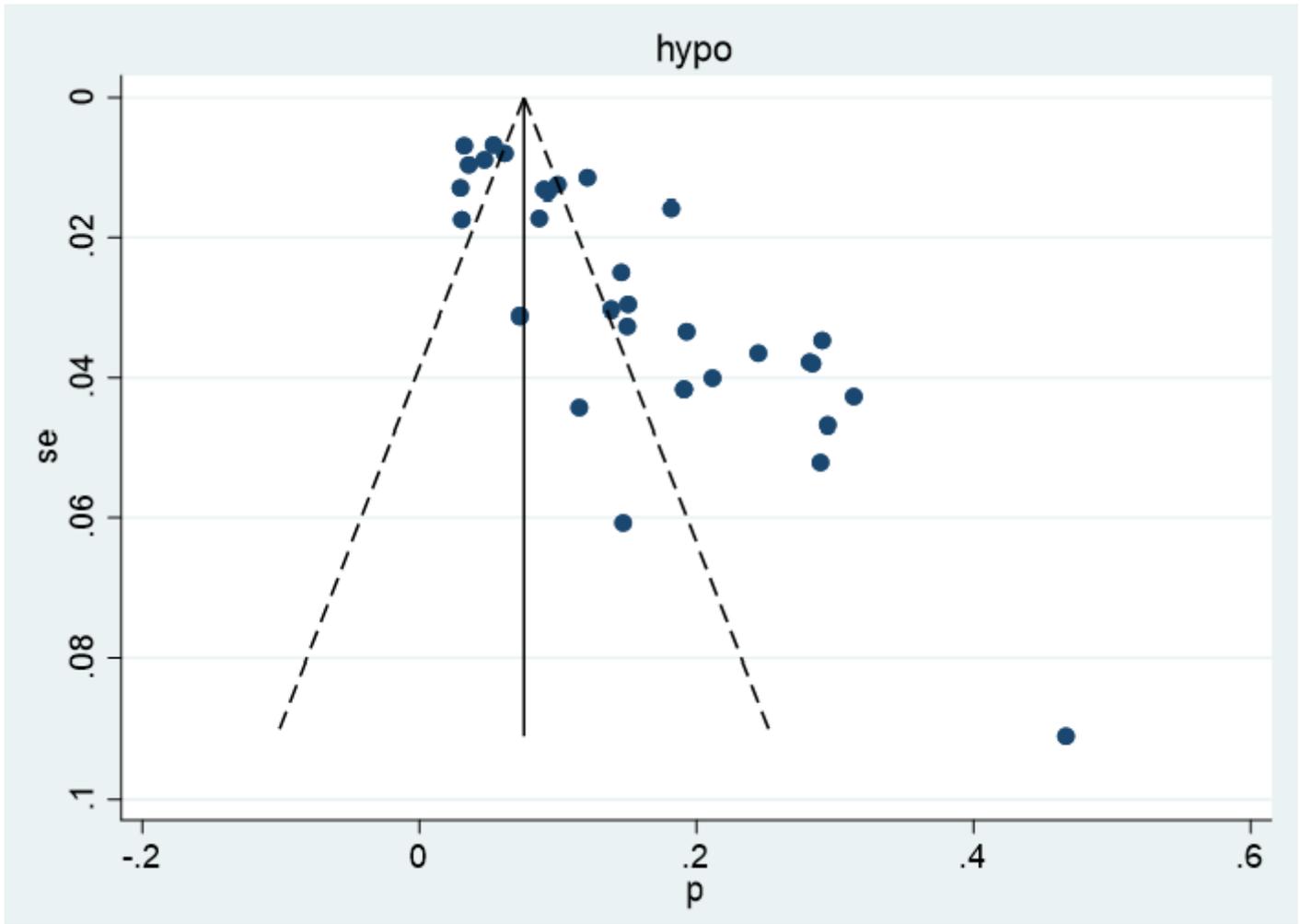


Figure 6

The funnel plot of hypoactive delirium

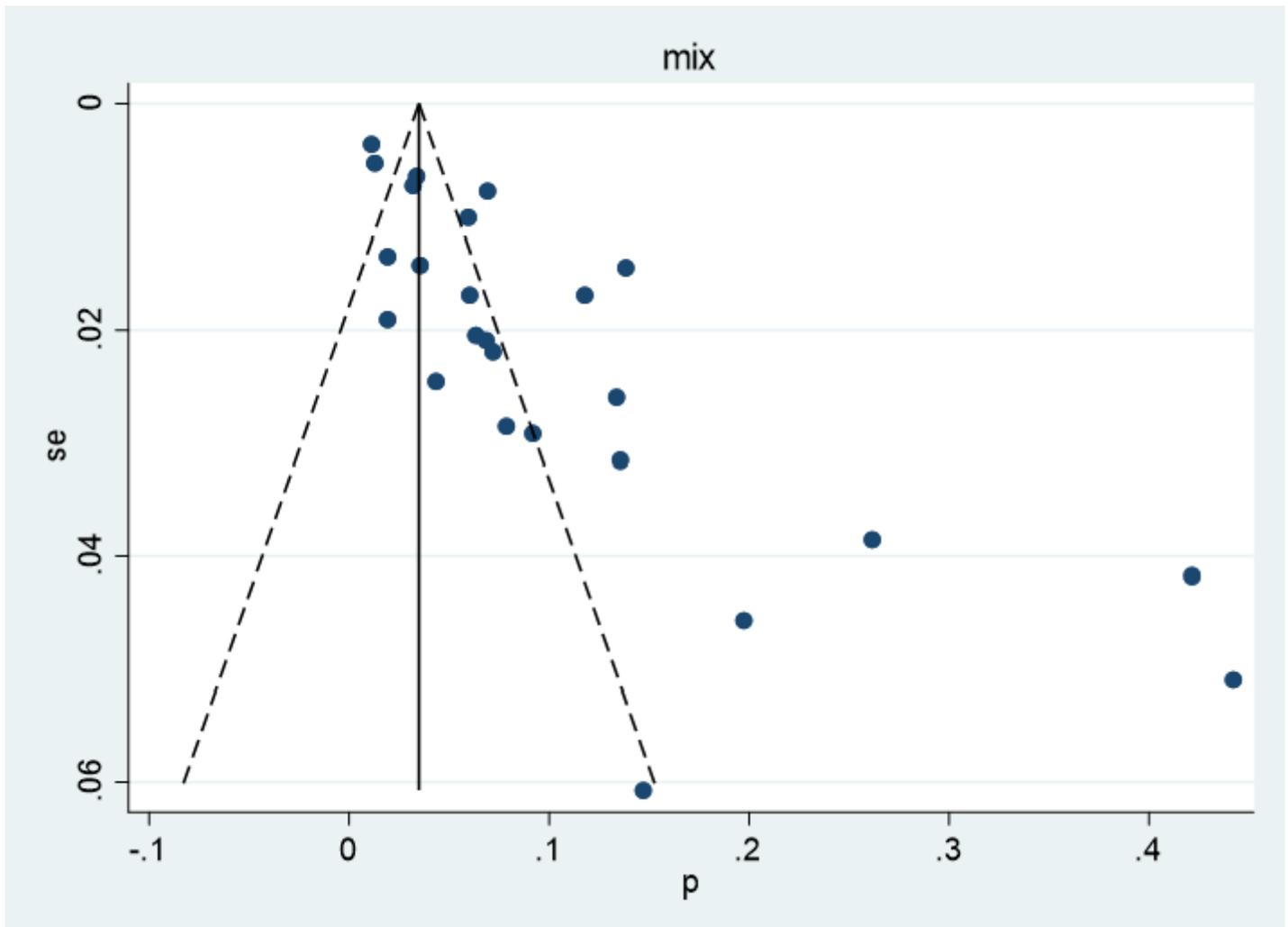


Figure 7

The funnel plot of mixed delirium

Supplementary Files

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- [Additionalfile1.docx](#)
- [Additionalfile2.docx](#)