



Effect of different anesthetic modalities on postoperative delirium in elderly hip fractures

A meta-analysis

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Abstract

Background: Previous findings on the effect of general versus spinal anesthesia on postoperative delirium in elderly people with hip fractures are somewhat controversial. This article included the latest randomized controlled study for meta-analysis to evaluate the effect of general anesthesia (GA) and spinal anesthesia (SA) on delirium after hip fracture surgery in the elderly, so as to guide the clinical.

Methods: Cochrane Library, PubMed, Web Of Science, and Embase were searched from inception up to January 16, 2024. Randomized controlled trial (RCT) was included to evaluate the postoperative results of GA and SA in elderly patients (≥ 50 years old) undergoing hip fracture surgery. Two researchers independently screened for inclusion in the study and extracted data. Heterogeneity was assessed by the I^2 and Chi-square tests, and $P < .1$ or $I^2 \geq 50\%$ indicated marked heterogeneity among studies. The Mantel–Haenszel method was used to estimate the combined relative risk ratio (RR) and the corresponding 95% confidence interval (CI) for the binary variables.

Results: Nine randomized controlled trials were included. There was no significant difference (RR = 0.93, 95% CI = 0.774–1.111, $P > .05$) in the incidence of postoperative delirium between the GA group and the SA group. Intraoperative blood transfusion (RR = 1.0, 95% CI = 0.77–1.28, $Z = 0.04$, $P = .971$), pulmonary embolism (RR = 0.795, 95% CI = 0.332–1.904, $Z = 0.59$, $P = .606$), pneumonia (RR = 1.47, 95% CI = 0.75–2.87, $P = .675$), myocardial infarction (RR = 0.97, 95% CI = 0.24–3.86, $Z = 0.05$, $P = .961$), heart failure (RR = 0.80, 95% CI = 0.26–2.42, $Z = 0.40$, $P = .675$), urinary retention (RR = 1.42, 95% CI = 0.77–2.61, $Z = 1.11$, $P = .267$) were similar between the 2 anesthetic techniques.

Conclusion: There is no significant difference in the effect of GA and SA on postoperative delirium in elderly patients with hip fracture, and their effects on postoperative complications are similar.

Abbreviations: A β = amyloid β , CI = confidence interval, GA = general anesthesia, M-H = Mantel–Haenszel, POD = postoperative delirium, RCT = randomized controlled trial, RR = relative risk, SA = spinal anesthesia.

Keywords: elderly patients, general anesthesia, hip fracture, postoperative delirium, spinal anesthesia

1. Introduction

With the arrival of an aging society, hip fracture has become one of the major health problems facing the elderly. It is estimated that there will be 6.26 million patients with hip fracture every year by 2050.^[1] The prognosis of patients with hip fracture treated conservatively is poor, so surgical treatment is usually considered essential.^[2,3] However, postoperative complications are more frequent in elderly patients, especially the incidence

of postoperative delirium (POD) is high (30%–65%), which is significantly related to the length of hospital stay, mortality and postoperative complications.^[4,5] It has been found that the incidence of POD is lower in spinal anesthesia (SA) compared to general anesthesia (GA).^[6] However, the results of a large randomized controlled trial (RCT) published recently were different. The investigators of that trial concluded that there was no significant difference between the 2 types of anesthesia in

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Special Project of Modernization of Traditional Chinese Medicine in Zhejiang Province (2021ZX009); National TCM Clinical Research Base Support Discipline Construction Plan (2020-JDXK-ZC01).

Informed consent was obtained from all individual participants included in the study.

The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

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How to cite this article: Fan G, Zhong M, Su W, An Z, Zhu Y, Chen C, Dong L, Wu L, Zhang X. Effect of different anesthetic modalities on postoperative delirium in elderly hip fractures: A meta-analysis. *Medicine* 2024;103:23(e38418).

Received: 5 March 2024 / Received in final form: 4 May 2024 / Accepted: 9 May 2024

<http://dx.doi.org/10.1097/MD.000000000038418>

the occurrence of delirium in elderly patients after hip fracture surgery.^[7] Therefore, the correlation between anesthesia methods and POD in elderly patients with hip fracture remains controversial, which deserves further exploration.

The results of META analysis by Zheng et al^[8] on the effect of anesthesia modality on POD after hip fracture showed that there was no significant difference in the occurrence of POD between GA and SA patients. However, its research only included the research from January 2000 to May 2019. The search terms used are too sketchy, the search formula is not explicitly given, and the search strategy has certain limitations. In recent years, several relevant RCTs have been published.^[7-9] These articles may become evidence to support or oppose previous conclusions. Based on a thorough literature search, this study objectively evaluated the effect of GA and SA on the occurrence of POD in elderly patients with hip fractures, providing further evidence-based evidence for clinical practice.

2. Methods

The study protocol has not been previously published. This meta-analysis followed the systematic review and meta-analysis statement of preferred reporting items. All analyses were based on previously published studies, thus no ethical approval and patient consent are required.

2.1. Search strategy and criteria

2.1.1. Bibliography retrieval. References were managed using EndNoteX9.1 software (Thomson Reuters, New York, NY). Two investigators (G. F. and W. S.) independently searched PubMed, Web Of Science, Embase and Cochrane Library up to January 16, 2024, to collect RCTs of GA compared to SA for the treatment of hip fractures in the elderly. Search formula at the end of the text.

2.1.2. Acceptance criteria

Two researchers (G.F. and W.S.) independently screened the literature, and a third author resolved conflicts when they encountered different opinions (Z.A.). Inclusion criteria: Research type: the RCT study on the effect of GA and SA on POD in elderly patients with hip fracture. Research object: elderly patients (age ≥ 50 years) who meet the diagnostic criteria for hip fracture, with no restrictions on race, sex, or fracture classification, etc. Outcome indicators: include any of the required outcome indicators, such as the number of POD, pulmonary embolism, pneumonia, myocardial infarction, etc. Exclusion criteria: repeated published literature and data. Literature with inconsistent research contents. Overviews, abstracts, conference report literature. Literature for which full text is not available or corresponding indicators cannot be obtained from the original data.

2.2. Data extraction

The data extraction is completed by 2 researchers (G.F. and W.S.) independently, and in case of discrepancies, the third author resolved the conflict (Z.A.) and fill in the data extraction form. The following variables were collected from the included papers: Author's name, publication time, experimental country, sample size, intervention measures, number of subjects, basic characteristics of subjects, outcome indicators, etc.

2.3. Quality of included studies

The risk of bias for each RCT was assessed as suggested by the Cochrane Collaboration Handbook for Systematic Reviews of

Interventions.^[10] Risk of bias was classified as high, low, and unclear for each of selection bias types. There are seven scoring items including selection bias-randomization, selection bias-allocation concealment, implementation bias, measurement bias, follow-up bias, reporting bias, and other bias. Generate risk of bias maps via Revman 5.3 (Fig. 1).

2.4. Statistical analysis

We use Mantel-Haenszel method to estimate the combined relative risk ratio (RR) and corresponding 95% confidence interval (CI) of binary variables. Heterogeneity was tested using the Cochran Chi-squared test (Q test) and the I^2 test. If $P > .1$ and $I^2 \leq 50\%$, indicating homogeneity, a fixed-effects model was applied for analysis. If $P \leq .1$, $I^2 > 50\%$, heterogeneity was suggested and a heterogeneity exclusion study was performed. Sensitivity analysis of the research results and bias analysis using Begg test. All analysis procedures were performed by STATA 15.0 software (Stata Corporation, College Station, TX).

2.5. Study characteristics

The flow chart of the study screening is shown in Figure 2. Eight hundred eleven studies were identified from the electronic database. After removing duplicates ($n = 174$), 637 articles were screened. After filtering titles and abstracts, 599 articles were excluded. Of the remaining 38 studies, 29 articles were excluded after full-text review, and 9 studies were finally included. The total incidence of POD in 8 papers^[7,9,11-16] is 0.98% to 43.86%, and the specific characteristics are shown in Table 1.

2.6. Methodological quality assessment and publication bias

The Cochrane risk assessment tool was used to assess the quality of the included study. Among them, 8 studies described the randomization methods, and all 9 papers described the allocation hiding method. Implementation bias is high risk because anesthesia personnel are necessarily informed about the anesthesia method. The results of 1 study were measured directly by the experimenter, and the measurement bias of other items was low risk. There were no follow-up bias, reporting bias and other bias in all 9 studies. We used Begg test to evaluate the publication bias of each outcome. The values of Begg test for each factor are listed in Table 2. We used Begg test to evaluate the publication bias of each outcome. The values and figures of Begg test for each factor are listed in Table 3 and Figure 3, respectively.

3. Meta-analysis results

3.1. Postoperative delirium

Eight studies^[7,9,11-16] reported the POD rate of 3210 patients (1612 in GA group; 1598 in SA group). After the heterogeneity test, $I^2 = 57.0\% > 50\%$ and $P = .023 < .1$ for the Q test, suggesting that the heterogeneity between the literature selected for this study is statistically significant. Further examination of the star diagram suggests that there is a strong possibility of heterogeneity in 1 literature, as shown in the Figure 4. A sensitivity analysis of the 8 papers in this study revealed that Heidari et al^[11] had a greater impact on heterogeneity. After removing this study, the combined effect variables of meta-analysis changed significantly. Therefore, deleting the article and performing the heterogeneity test again after removing the research showed that there was no heterogeneity in the remaining 6 papers ($I^2 = 30.4\% < 50\%$, $P = .196 > .1$). After excluding heterogeneity, meta-analysis was performed with fixed effects. The RR value of the 7 studies was 0.93, and the 95% CI was 0.774 to 1.111, which

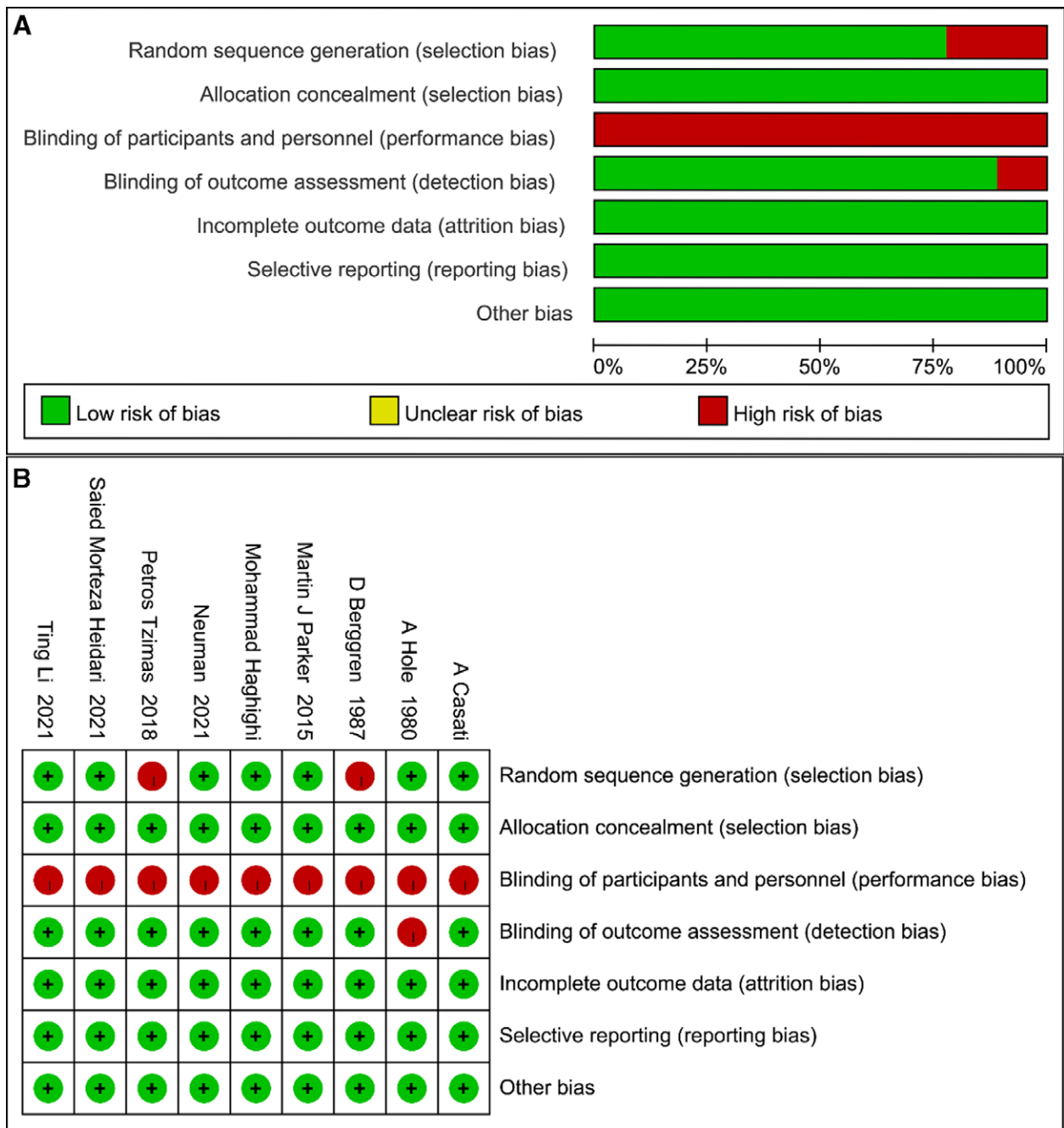


Figure 1. Risk of bias. (A) Risk of bias summary: review authors' judgements about each risk of bias item for each included study. (B) Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

was statistically significant ($Z = 0.82, P > .05$), suggesting that the occurrence of POD was not associated with the choice of general or SA. The details are shown in Figure 5.

3.2. Intraoperative blood transfusion

Three studies^[9,14,17] reported the number of intraoperative blood transfusion, and 1304 patients were included in the study (GA = 656; SA = 648). After the Q test, we got $P = .672, I^2 = 0\%$, indicating that the heterogeneity between studies is not significant, so we use fixed-effect model to combine the results. The combined results showed that there was no significant difference in the occurrence of intraoperative blood transfusion between the 2 groups (RR = 0.98, 95% CI = 0.76–1.27,

$Z = 0.16, P = .872$). The specific situation is shown in Figure 6A. In the 2 studies included, the blood transfusion rate in the GA group was 15.43%, the incidence of delirium was 3.80%, the rate in the SA group was 15.74%, and the incidence of delirium was 5.10%. This may mean that blood transfusion is one of the potential risk factors for delirium.

3.3. Pulmonary embolism

Five studies^[7,11–14] reported the number of patients with post-operative pulmonary embolism, including 1214 cases in GA group and 1188 cases in SA group. Through heterogeneity test, $I^2 = 0.0\% < 50\%$, and $P = .426 > .1$ for the Q test. This suggests that there is no obvious heterogeneity between the selected

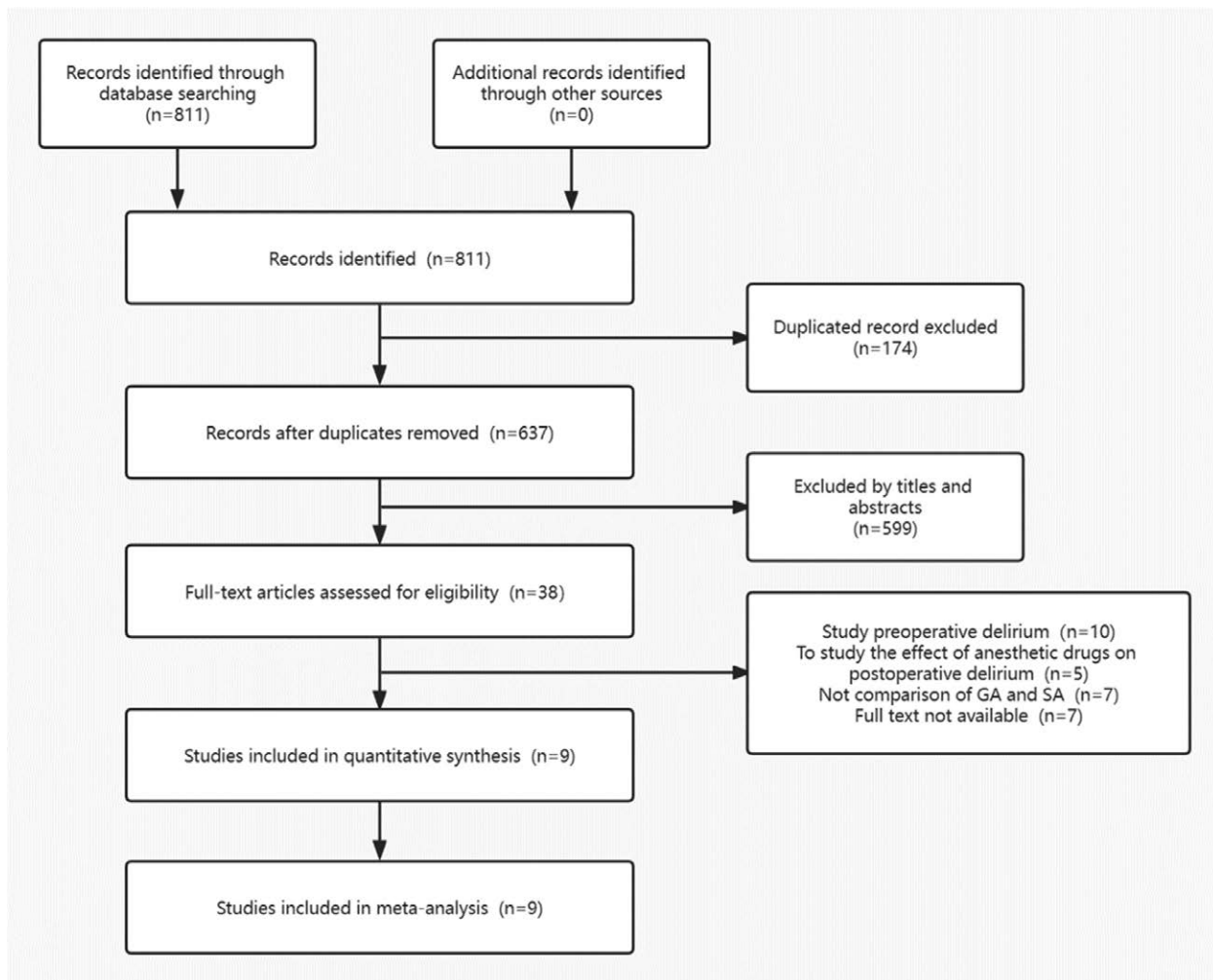


Figure 2. Diagram of study selection. GA = general anesthesia, SA = spinal anesthesia.

Table 1

Incidence of postoperative delirium.

Author	Year	Event_GA	Total_GA	Incidence rate_GA	Event_SA	Total_SA	Incidence rate_SA	Total incidence rate
Hole et al	1980	8	31	25.81%	1	29	3.45%	15%
Berggren et al	1987	11	29	37.93%	14	28	50%	43.86%
Parker and Griffiths	2015	0	157	0.00%	3	148	2.03%	0.98%
Neuman et al	2021	124	629	19.71%	130	633	20.54%	20.13%
Tzimas et al	2018	4	33	12.12%	10	37	27.03%	20.0%
Heidari et al	2021	22	197	11.17%	7	190	3.68%	7.49%
Li et al	2021	24	474	5.06%	29	476	6.09%	5.58%
Casati et al	2003	9	15	60.00%	8	15	53.33%	56.67%

literature in this study. Therefore, the fixed-effect model is used to analyze the results. Combined data showed no significant difference between the 2 groups (RR = 0.795, 95% CI = 0.332–1.904, Z = 0.59, P = .606). The details are in Figure 6B.

3.4. Pneumonia

A total of 5 publications^[7,11–14] were included in studies of postoperative pneumonia, enrolling a total of 2402 patients (GA = 1214, SA = 1188). Through Q test, P = .675, I² = 0.0% < 50%, this suggests that the heterogeneity of these studies is low, so the results were analyzed using the fixed-effects model. Summary data showed no significant difference in the

occurrence of postoperative pneumonia between GA and SA (RR = 1.47, 95% CI = 0.75–2.87, P = .675, Fig. 6C).

3.5. Myocardial infarction

A total of 4 studies^[9,11,12,14] reported 1711 patients with postoperative myocardial infarction (GA = 863; SA = 848). And the Q test showed that the heterogeneity of the 4 studies included was not significant (P = .834, I² = 0.0% < 50%). The combined results of the fixed-effect model showed no significant difference in the occurrence of postoperative myocardial infarction between the 2 anesthetic methods (RR = 0.97, 95% CI = 0.24–3.86, Z = 0.05, P = .961). The specific situation is shown in Figure 6D.

Table 2
The Cochrane Collaboration's tool for assessing risk of bias.

Author	Year	Selection bias-random sequence generation	Selection bias-allocation concealment	Performance bias	Detection bias	Attrition bias	Reporting bias	Other bias
Li et al	2021	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk
Neuman et al	2021	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk
Parker and Griffiths	2015	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk
Tzimas et al	2018	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk
Heidari et al	2021	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk
Berggren et al	1987	High risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk
Hole et al	1980	Low risk	Low risk	High risk	High risk	Low risk	Low risk	Low risk
Mohammad Haghghi	2017	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk

Table 3
Results from the meta-analyses on other result variables.

Variable	Number of study	Total sample	RR	95% CI	P value	I ² (%)	Q test (p)	Begg's test	Statistical method
Postoperative delirium	7	3210	0.93	0.774–1.111	.196	30.4	0.023	0.764	M-H, fixed
Number of intraoperative blood transfusions	2	1304	0.98	0.76–1.27	.872	0	0.672	1	M-H, fixed
Postoperative pulmonary embolism	5	2402	0.795	0.332–1.904	.606	0	0.426	1	M-H, fixed
Postoperative pneumonia	5	2402	1.47	0.75–2.87	.675	0	0.675	0.086	M-H, fixed
Postoperative myocardial infarction	4	1711	0.97	0.24–3.86	.961	0	0.834	1	M-H, fixed
Postoperative heart failure	4	1361	0.8	0.26–2.42	.961	0	0.541	1	M-H, fixed
Postoperative urinary retention	4	1381	1.42	0.77–2.61	.267	41.4	0.163	0.308	M-H, fixed

CI = confidence interval, M-H = Mantel–Haenszel, RR = risk ratio.

3.6. Heart failure

A total of 4 publications^[9,11,12,14] reported the outcome of postoperative heart failure, including 1361 patients (GA = 685; SA = 676). Q test showed $P = .541$ and $I^2 = 0.0\% < 50\%$, which implied no significant heterogeneity between the 4 studies. The fixed-effect model was used to merge. The combined results showed that there was no significant difference in the incidence of heart failure after GA and SA (RR = 0.80, 95% CI = 0.26–2.42, $Z = 0.40$, $P = .961$). The details are in Figure 6E.

3.7. Urinary retention

Four studies^[9,12–14] reported the results of postoperative urinary retention, 695 patients with GA and 686 patients with SA were included in the study. And the Q test showed that the heterogeneity of the 4 studies included was not significant ($P = .163$, $I^2 = 41.4\% < 50\%$). There is no significant difference in the occurrence of urinary retention between GA and SA patients after the combination of fixed-effect models (RR = 1.42, 95% CI = 0.77–2.61, $Z = 1.11$, $P = .267$). The details are shown in Figure 6F.

4. Discussion

POD is a common postoperative complication of hip fracture in the elderly, which poses a psychological and economic burden to patients, and the care of delirious patients is difficult and brings challenges to medical staff. The incidence of POD is higher in patients with hip fractures, thus preventing POD is a key and challenging aspect in the diagnosis and treatment of elderly hip fractures. The mechanism of POD in elderly patients with hip fracture is still not clear, but some risk factors have already been explored.^[18,19] Factors such as intraoperative anesthesia mode, intraoperative blood transfusion and selection of anesthetic have an impact on patients' mental status.^[20,21] The relationship between anesthesia mode and POD is still controversial, so it is worth further exploration.

4.1. Effect of anesthesia mode on postoperative delirium

Common anesthesia methods for hip fractures include GA and SA. GA has the advantage of improving patients' experience during operation and alleviating patients' fear of operation. However, GA also has certain disadvantages, such as long hospital stay, complications of cardiovascular disease, infection, POD, etc.^[22] Among them, POD brings great physical and mental suffering to patients and reduces their quality of life, so it deserves further study. The potential link between GA and postoperative cognitive impairment was first described by Bedford.^[23] Some scholars have since found through research that GA may affect long-term morphological and functional changes in the brain.^[24] The number of patients using SA in hip fracture surgery increased by 50% between 2007 and 2017, which indicates that the prognosis of SA is better.^[25] Several studies have shown a higher incidence of POD with GA compared to SA.^[26,27] However, some scholars believe that SA will lead to changes in the level of Aβ and Tau in cerebrospinal fluid of patients, resulting in cognitive impairment. Through collecting cerebrospinal fluid of patients undergoing total hip replacement during SA, it is found that the lower the Aβ/Tau ratio, the higher the incidence of POD.^[28] Two large RCTs recently published showed that there was no significant difference between GA and SA in the occurrence of delirium after hip fracture surgery in elderly patients.^[7,9] In this study, by comparing SA with GA, we found no significant difference in the occurrence of delirium after hip fracture surgery in the elderly between the 2 anesthesia mode. Compared to previously published studies, we have refined the search terms and included the latest clinical RCTs to provide clinical practitioners with more rigorous and up-to-date evidence to support.^[8] The different types of anesthetic drugs and routes of administration among the studies included in this meta-analysis have some impact on the results, so we conducted heterogeneity tests and sensitivity analyses to obtain more accurate results.

4.2. Effect of anesthesia mode on intraoperative blood transfusion

Because of its special anatomical location, the incidence of massive intraoperative blood loss and intraoperative blood

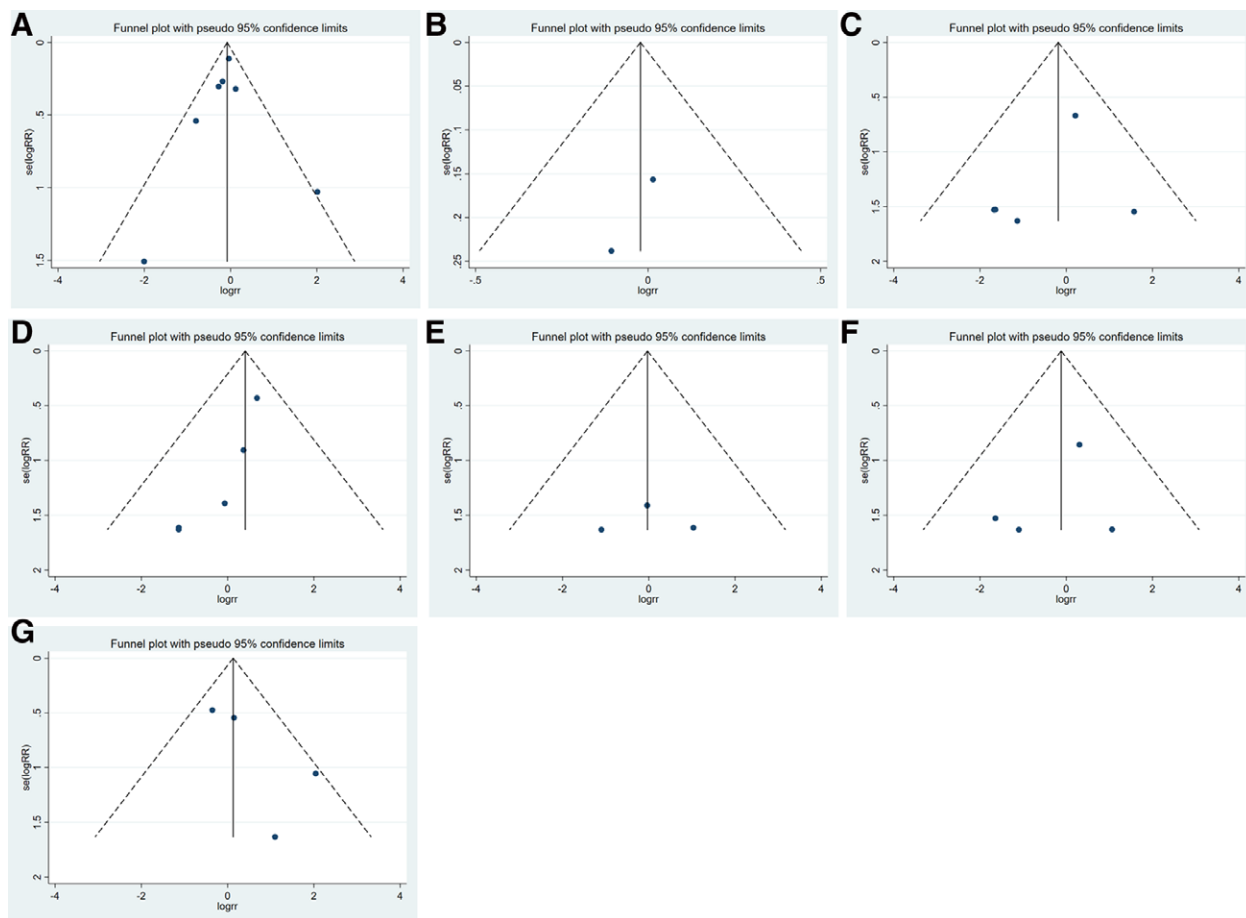


Figure 3. Funnel diagram of each complication. (A) Postoperative delirium. (B) Number of intraoperative blood transfusions. (C) Postoperative pulmonary embolism. (D) Postoperative pneumonia. (E) Postoperative myocardial infarction. (F) Postoperative heart failure. (G) Postoperative urinary retention.

transfusion is high, and intraoperative blood transfusion is closely related to the occurrence of POD.^[29,30] Therefore, it is necessary to study the relationship between anesthetic methods and intraoperative blood transfusion in order to prevent the occurrence of delirium in the elderly after hip fracture surgery. The blood pressure of patients is at a lower level than usual during GA, and intraoperative bleeding is significantly reduced when blood pressure is lower during surgery.^[31,32] Intraoperative blood loss is closely related to intraoperative transfusion, and the use of allogeneic blood transfusion to correct blood loss predisposes to the development of POD.^[33] The author suggests that this anesthesia-blood pressure-transfusion interaction mechanism may be the reason for the lower incidence of delirium in patients who had GA in previously published studies. Some scholars have found that the levels of interleukin 6 and interleukin 8 in peripheral blood of patients with delirium after hip fracture surgery increase.^[34] Blood transfusion activates tumor necrosis factor α , interleukin 6, and interleukin 10 in plasma, which may be the mechanism of blood transfusion leading to the occurrence of POD.^[35] However, the results of this meta-analysis showed that there was no significant difference in the number of intraoperative blood transfusions between the GA and SA, which was inconsistent with the previously published meta-analysis results. The reason for this inconsistency may be the advances of the relevant surgical procedures in recent years and the apparent difference in the sample size included. After including the latest published studies, we obtained the same meta-analysis results as before, namely that SA did not show a significant advantage over GA in preventing postoperative complications such as pulmonary embolism, pneumonia, and heart failure in elderly patients with hip fractures. All of the studies

included in this study are high-quality RCTs. However, there are still some disadvantages such as small sample size, inconsistent anesthetic drugs and anesthetic routes, and there is still an urgent need for more RCTs with large samples to verify the accuracy of the conclusions.

4.3. Effect of anesthesia methods on other postoperative complications

Elderly hip fractures, due to their surgical characteristics, are prone to postoperative complications. Common postoperative complications include pneumonia, pulmonary embolism, heart failure, myocardial infarction, and urinary retention. The occurrence of these postoperative complications poses significant challenges to patient recovery and increases the difficulty of postoperative care. Therefore, while exploring the impact of anesthesia methods on postoperative delirium, we also investigated the effects of anesthesia methods on the occurrence of other complications, aiming to determine the optimal anesthesia method for surgery on elderly hip fractures.

It is generally believed that endotracheal intubation during general anesthesia increases the incidence of postoperative pneumonia. However, according to the results of our meta-analysis, the anesthesia method has no significant effect on postoperative complications such as pneumonia, pulmonary embolism, heart failure, myocardial infarction, or urinary retention. However, the studies included in this analysis are limited, so more research is needed to confirm the relationship between anesthesia method and the occurrence of other postoperative complications.

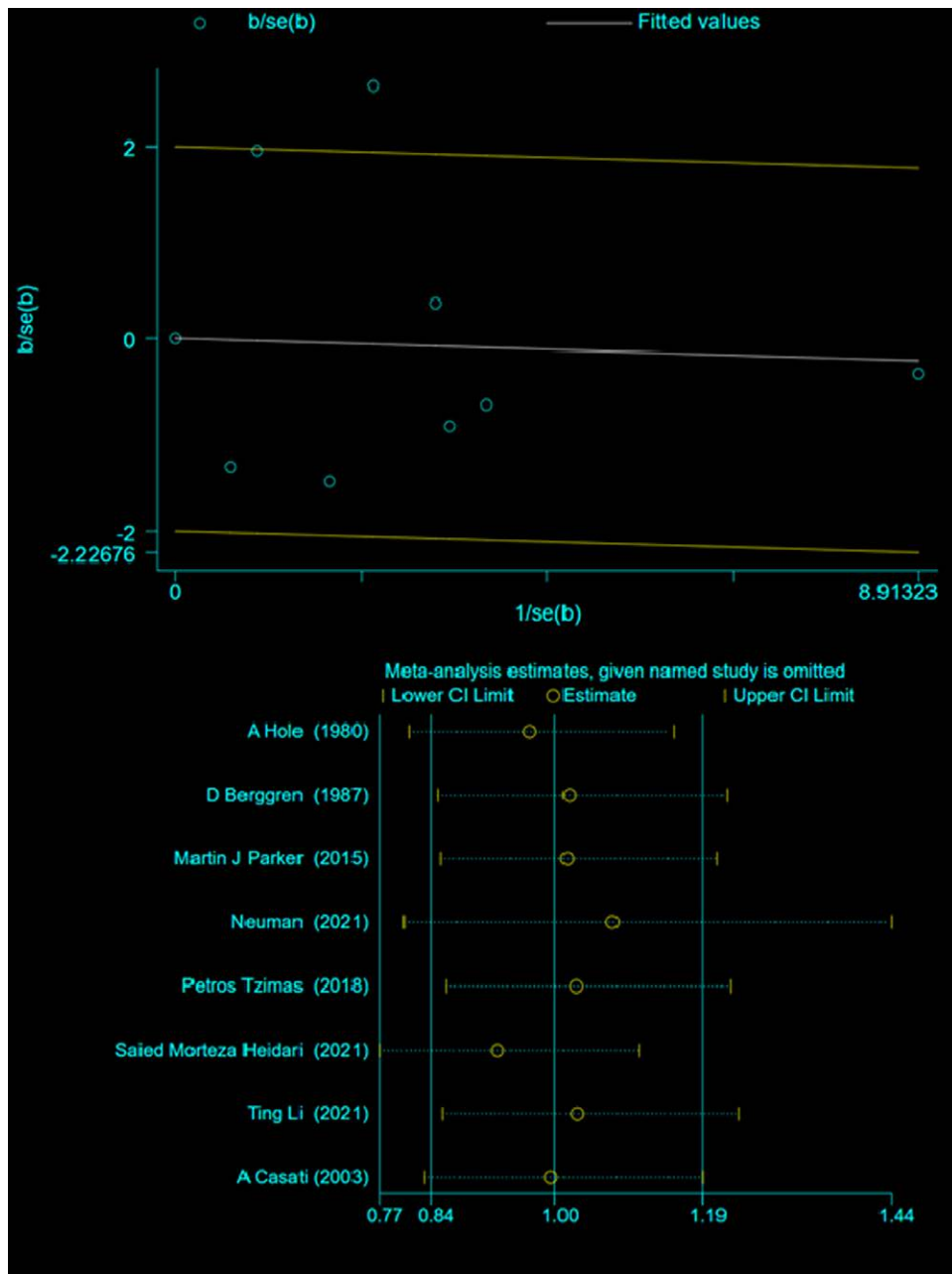


Figure 4. Star diagram of delirium.

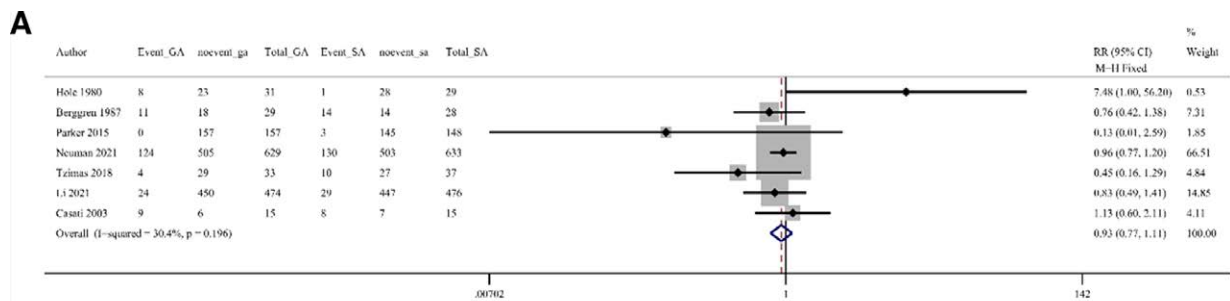


Figure 5. Meta-analysis of the occurrence of delirium after general and spinal anesthesia. CI = confidence interval, GA = general anesthesia, M-H = Mantel-Haenszel, RR = relative risk, SA = spinal anesthesia.

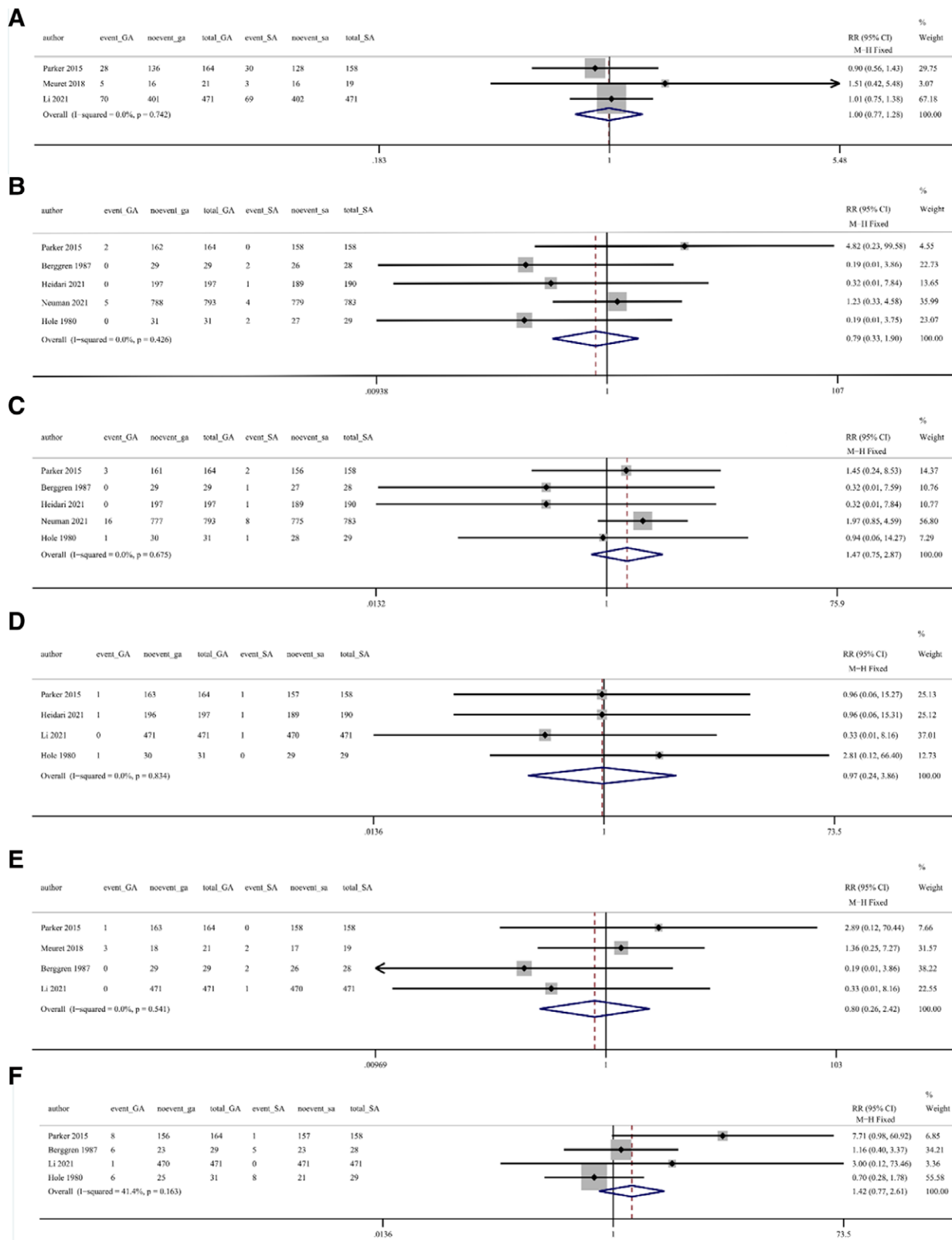


Figure 6. Other meta-analysis results of general anesthesia and spinal anesthesia. (A) Intraoperative blood transfusion. (B) Pulmonary embolism. (C) Pneumonia. (D) Myocardial infarction. (E) Heart failure. (F) Urinary retention. CI = confidence interval, GA = general anesthesia, M-H = Mantel-Haenszel, RR = relative risk, SA = spinal anesthesia.

4.4. Effect of anesthetics on postoperative delirium

The use of intraoperative anesthetics affects the patient's postoperative mental status. Different anesthetics have different advantages and disadvantages. There is evidence that

the incidence of POD varies among patients under different anesthetics for the same procedure.^[36] Therefore, it is essential to investigate the effect of anesthetics on the occurrence of POD. Sevoflurane, propofol and lidocaine are commonly

used anesthetics in the operation of hip fracture in the elderly. There is a certain incidence of POD after sevoflurane anesthesia and propofol anesthesia.^[37] Dexmedetomidine has anxiolytic, sedative and analgesic properties, and it can reduce the incidence of POD.^[38] Therefore, it can be assumed that the addition of dexmedetomidine to sevoflurane anesthesia and propofol anesthesia can reduce the incidence of POD. There is a study confirming the hypothesis that the use of dexmedetomidine reduces the incidence of delirium after sevoflurane anesthesia.^[39] Further studies have found that the triple therapy of dexmedetomidine, midazolam and antiemetic is the best pharmacological strategy to prevent mental disorder after sevoflurane anesthesia.^[40] However, the effect of dexmedetomidine in improving the incidence of delirium after propofol anesthesia is not satisfactory.^[41] Studies have confirmed that the perioperative use of midazolam is not significantly associated with the occurrence of postoperative delirium. Furthermore, the use of midazolam significantly reduces the incidence of cardiac and pulmonary complications.^[42,43] Because of the wide variety of anesthetics selected in the study included in this meta-analysis, it is difficult to conduct data analysis. However, the effect of anesthetics on patients' postoperative mental status is profound, so this may be a direction for future research to prevent the occurrence of POD.

5. Conclusion

Based on the latest clinical RCTs, we meta-analyzed the effect of GA versus SA on the occurrence of delirium after hip fracture in the elderly. The results of the study showed that there was no significant difference in the incidence of delirium after GA and SA. In addition, we reassessed the relationship between GA and SA and pulmonary embolism, pneumonia, myocardial infarction, heart failure, urinary retention, and intraoperative blood transfusion.

Author contributions

Writing—original draft: Guangya Fan, Musen Zhong, Wenshuo Su.

Supervision: Zhongcheng An, Yuchen Zhu, Chen Chen, Liqiang Dong, Lianguo Wu, Xiaoping Zhang.

References

- [1] Curtis EM, van der Velde R, Moon RJ, et al. Epidemiology of fractures in the United Kingdom 1988-2012: variation with age, sex, geography, ethnicity and socioeconomic status. *Bone*. 2016;87:19–26.
- [2] Loggers SAI, Van Lieshout EMM, Joosse P, Verhofstad MHJ, Willems HC. Prognosis of nonoperative treatment in elderly patients with a hip fracture: a systematic review and meta-analysis. *Injury*. 2020;51:2407–13.
- [3] Jay RH, Hipps D. Hip fracture—great steps forward but we still need better evidence. A commentary on NICE CG124 and QS16 on fractured neck of femur. *Age Ageing*. 2018;47:630–2.
- [4] Veronese N, Maggi S. Epidemiology and social costs of hip fracture. *Injury*. 2018;49:1458–60.
- [5] Strøm C, Rasmussen LS, Sieber FE. Should general anaesthesia be avoided in the elderly? *Anaesthesia*. 2014;69(Suppl 1):35–44.
- [6] Griffiths R, Alper J, Beckingsale A, et al. Membership of the Working Party. Management of proximal femoral fractures 2011: association of anaesthetists of Great Britain and Ireland. *Anaesthesia*. 2012;67:85–98.
- [7] Neuman MD, Feng R, Carson JL, et al. REGAIN Investigators. Spinal anesthesia or general anesthesia for hip surgery in older adults. *N Engl J Med*. 2021;385:2025–35.
- [8] Zheng X, Tan Y, Gao Y, Liu Z. Comparative efficacy of neuraxial and general anesthesia for hip fracture surgery: a meta-analysis of randomized clinical trials. *BMC Anesthesiol*. 2020;20:162.
- [9] Li T, Li J, Yuan L, et al. RAGA Study Investigators. Effect of regional vs general anesthesia on incidence of postoperative delirium in older patients undergoing hip fracture surgery: the RAGA randomized trial. *JAMA*. 2022;327:50–8.

- [10] Higgins JPT, Altman DG, Gøtzsche PC, et al. Cochrane Statistical Methods Group. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ*. 2011;343:d5928–d5928.
- [11] Heidari SM, Soltani H, Hashemi SJ, Talakoub R, Soleimani B. Comparative study of two anesthesia methods according to postoperative complications and one month mortality rate in the candidates of hip surgery. *J Res Med Sci*. 2011;16:323–30.
- [12] Hole A, Terjesen T, Breivik H. Epidural versus general anaesthesia for total hip arthroplasty in elderly patients. *Acta Anaesthesiol Scand*. 1980;24:279–87.
- [13] Berggren D, Gustafson Y, Eriksson B, et al. Postoperative confusion after anesthesia in elderly patients with femoral neck fractures. *Anesth Analg*. 1987;66:497–504.
- [14] Parker MJ, Griffiths R. General versus regional anaesthesia for hip fractures. A pilot randomised controlled trial of 322 patients. *Injury*. 2015;46:1562–6.
- [15] Tzimas P, Samara E, Petrou A, Korompilias A, Chalkias A, Papadopoulos G. The influence of anesthetic techniques on postoperative cognitive function in elderly patients undergoing hip fracture surgery: general vs spinal anesthesia. *Injury*. 2018;49:2221–6.
- [16] Casati A, Aldegheri G, Vinciguerra E, Marsan A, Frascini G, Torri G. Randomized comparison between sevoflurane anaesthesia and unilateral spinal anaesthesia in elderly patients undergoing orthopaedic surgery. *Eur J Anaesthesiol*. 2003;20:640–6.
- [17] Meuret P, Bouvet L, Villet B, Hafez M, Allaouchiche B, Boselli E. Hypobaric unilateral spinal anaesthesia versus general anaesthesia in elderly patients undergoing hip fracture surgical repair: a prospective randomised open trial. *Turk J Anaesthesiol Reanim*. 2018;46:121–30.
- [18] Saied NN, Helwani MA, Weavind LM, Shi Y, Shotwell MS, Pandharipande PP. Effect of anaesthesia type on postoperative mortality and morbidities: a matched analysis of the NSQIP database. *Br J Anaesth*. 2017;118:105–11.
- [19] Wu J, Yin Y, Jin M, Li B. The risk factors for postoperative delirium in adult patients after hip fracture surgery: a systematic review and meta-analysis. *Int J Geriatr Psychiatry*. 2021;36:3–14.
- [20] Tanaka P, Goodman S, Sommer BR, Maloney W, Huddleston J, Lemmens HJ. The effect of desflurane versus propofol anesthesia on postoperative delirium in elderly obese patients undergoing total knee replacement: a randomized, controlled, double-blinded clinical trial. *J Clin Anesth*. 2017;39:17–22.
- [21] Evered LA, Chan MTV, Han R, et al. Anaesthetic depth and delirium after major surgery: a randomised clinical trial. *Br J Anaesth*. 2021;127:704–12.
- [22] Short TG, Campbell D, Frampton C, et al. Australian and New Zealand College of Anaesthetists Clinical Trials Network. Anaesthetic depth and complications after major surgery: an international, randomised controlled trial. *Lancet*. 2019;394:1907–14.
- [23] Bedford PD. Adverse cerebral effects of anaesthesia on old people. *Lancet*. 1955;269:259–63.
- [24] Vutskits L, Xie Z. Lasting impact of general anaesthesia on the brain: mechanisms and relevance. *Nat Rev Neurosci*. 2016;17:705–17.
- [25] Maxwell BG, Spitz W, Porter J. Association of increasing use of spinal anesthesia in hip fracture repair with treating an aging patient population. *JAMA Surg*. 2020;155:167–8.
- [26] Urwin SC, Parker MJ, Griffiths R. General versus regional anaesthesia for hip fracture surgery: a meta-analysis of randomized trials. *Br J Anaesth*. 2000;84:450–5.
- [27] Anwer HMF, Swelem SE, el-Sheshai A, et al. Postoperative cognitive dysfunction in adult and elderly patients—general anesthesia vs subarachnoid or epidural analgesia. *Middle East J Anaesthesiol*. 2006;18:1123–38.
- [28] Xie Z, Swain CA, Ward SAP, et al. Preoperative cerebrospinal fluid β -Amyloid/Tau ratio and postoperative delirium. *Ann Clin Transl Neurol*. 2014;1:319–28.
- [29] Magnussen RA, Tressler MA, Obremskey WT, Kregor PJ. Predicting blood loss in isolated pelvic and acetabular high-energy trauma. *J Orthop Trauma*. 2007;21:603–7.
- [30] Scannell BP, Loeffler BJ, Bosse MJ, Kellam JF, Sims SH. Efficacy of intraoperative red blood cell salvage and autotransfusion in the treatment of acetabular fractures. *J Orthop Trauma*. 2009;23:340–5.
- [31] Liu Y, Chen F, Zhao W, et al. Pulmonary artery pressure and variations in arterial blood pressure during the induction period of general anesthesia in elderly patients. *J Coll Physicians Surg Pak*. 2021;31:8–13.
- [32] Pan Y-X, Wang J-C, Lu X-Y, et al. Intention to control low central venous pressure reduced blood loss during laparoscopic hepatectomy: a double-blind randomized clinical trial. *Surgery*. 2020;167:933–41.
- [33] Chou M-Y, Wang Y-C, Peng L-N, et al. Intraoperative blood transfusion predicts postoperative delirium among older patients undergoing

- elective orthopedic surgery: a prospective cohort study. *Int J Geriatr Psychiatry*. 2019;34:881–8.
- [34] van Munster BC, Korevaar JC, Zwinderman AH, Levi M, Wiersinga WJ, De Rooij SE. Time-course of cytokines during delirium in elderly patients with hip fractures. *J Am Geriatr Soc*. 2008;56:1704–9.
- [35] Hensler T, Heinemann B, Sauerland S, et al. Immunologic alterations associated with high blood transfusion volume after multiple injury: effects on plasmatic cytokine and cytokine receptor concentrations. *Shock*. 2003;20:497–502.
- [36] Fodale V, Tripodi VF, Penna O, et al. An update on anesthetics and impact on the brain. *Expert Opin Drug Saf*. 2017;16:997–1008.
- [37] Mei X, Zheng H-L, Li C, et al. The effects of propofol and sevoflurane on postoperative delirium in older patients: a randomized clinical trial study. *J Alzheimers Dis*. 2020;76:1627–36.
- [38] Aldecoa C, Bettelli G, Bilotta F, et al. European Society of Anaesthesiology evidence-based and consensus-based guideline on postoperative delirium. *Eur J Anaesthesiol*. 2017;34:192–214.
- [39] Shi M, Miao S, Gu T, Wang D, Zhang H, Liu J. Dexmedetomidine for the prevention of emergence delirium and postoperative behavioral changes in pediatric patients with sevoflurane anesthesia: a double-blind, randomized trial. *Drug Des Devel Ther*. 2019;13:897–905.
- [40] Wang H-Y, Chen T-Y, Li D-J, et al. Association of pharmacological prophylaxis with the risk of pediatric emergence delirium after sevoflurane anesthesia: an updated network meta-analysis. *J Clin Anesth*. 2021;75:110488.
- [41] Momeni M, Khalifa C, Lemaire G, et al. Propofol plus low-dose dexmedetomidine infusion and postoperative delirium in older patients undergoing cardiac surgery. *Br J Anaesth*. 2021;126:665–73.
- [42] Zarour S, Weiss Y, Kiselevich Y, et al. The association between midazolam premedication and postoperative delirium—a retrospective cohort study. *J Clin Anesth*. 2024;92:111113.
- [43] Greengrass RA. Midazolam and delirium: can you have it both ways? *Reg Anesth Pain Med*. 2022;47:449–50.