Comparative Efficacy of Neuraxial and General anesthesia for hip fracture surgery: A meta-analysis of randomized clinical trials

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Xinxun Zheng
Shenzhen Second People's Hospital
ORCiD: 0000-0001-8481-2652

Yuming Tang
Shenzhen Second People's Hospital

Yuan Gao
Shenzhen Second People's Hospital

Zhiheng Liu 873444046@qq.com
Shenzhen Second People's Hospital
Corresponding Author
ORCiD: 0000-0002-2823-543X

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Abstract

Background: The choice of anesthesia technique remains debatable in patients undergoing surgical repair of hip fracture. This meta-analysis was performed to compare the effect of neuraxial (epidural/spinal) versus general anesthesia on perioperative outcomes in patients undergoing hip fracture surgery.

Methods: Medline, Cochrane Library, Science-Direct, and EMBASE databases were searched to identify eligible studies focused on the comparison between neuraxial and general anesthesia in hip fracture patients between January 2000 and May 2019. Perioperative outcomes were extracted for systemic analysis. The sensitivity analyses were performed by the leave-one-out approach. The evidence quality for each outcome was evaluated by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system.

Results: Nine randomized controlled trials (RCTs) including 1084 patients fulfilled our selection criteria. The results showed that there were no significant differences in the 30-day mortality (OR = 1.34, 95% CI 0.56, 3.21; P = 0.51), length of stay (MD = -0.65, 95% CI -0.32, 0.02; P =0.06), and the prevalence of delirium (OR = 1.05, 95% CI 0.27, 4.00; P = 0.95), acute myocardial infarction (OR = 0.88, 95% CI 0.17, 4.65; P = 0.88), deep venous thrombosis (OR = 0.48, 95% CI 0.09, 2.72; P = 0.41), and pneumonia (OR = 1.04, 95% CI 0.23, 4.61; P = 0.96) for neuraxial anesthesia compared to general anesthesia. There was a significant difference in terms of blood loss in favor of the neuraxial anesthesia (MD = -137.8, 95% CI -241.49, -34.12; p = 0.009). The evidence quality for each outcome evaluated by the GRADE system was low.

Conclusions: In summary, our present study demonstrated that neuraxial anesthesia is associated with a reduced blood loss in patients undergoing hip fracture surgery compared to general anesthesia. Due to small sample size and enormous inconsistency in the choice
of outcome measures, more high-quality studies with large sample size are needed to clarify this issue.

**Background**

Hip fracture is one of the most common injuries that occurs in about 1.6 million people around the world each year; the number is estimated to reach more than six million by 2050. Moreover, there are a range of comorbidities in elderly patients with hip fracture, which are associated with an increased risk of morbidity and mortality. Most hip fractures should be treated surgically that requires some type of anesthesia.

Thus far, the ideal choice between neuraxial and general anesthesia has not been identified. Several studies demonstrated that compared with general anesthesia, neuraxial anesthesia has some advantages such as airway management avoidance, no intubation requirement, and prolonged postoperative analgesia. Furthermore, neuraxial anesthesia could provide excellent intraoperative anesthesia, decrease blood loss, potentially reduce risk of postoperative nausea and vomiting (PONV), as well as deep venous thrombosis. Conversely, general anesthesia is reported to provide a more stable hemodynamic state, faster induction, and avoid some complications such as pneumonia, epidural haematoma and infection. However, the effect of the two anesthesia techniques on patients with hip fracture is controversial regarding postoperative outcomes. A recent systematic review including 15 studies revealed that neuraxial anesthesia was only associated with a shorter length of hospital stay in patients undergoing hip fracture surgery. This review emphasized that sensitivity analyses showed marginal statistical significance for length of stay favoring spinal anaesthesia, and the definitions of reported outcomes varied widely or were unclear, making evaluation in a standardized manner very difficult. Another systematic review reported a reduced in-hospital mortality in the neuraxial anaesthesia.
group, but no definitive conclusion can be drawn for longer-term mortality\textsuperscript{10}. Both of them have recommended that further high-quality studies be performed.

To date, several most recent randomized controlled trials (RCTs) have been published, which assessed the effect of the two anesthesia techniques for hip fracture surgery. Through including these RCTs, our study aimed to systematically evaluate perioperative outcomes of patients with hip fracture surgery, and provide more reliable evidence to identify the optimal technique.

**Methods**

This meta-analysis was conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines. A review protocol was written before conducting this study.

**Search Strategy**

Medline, Cochrane Library, Science-Direct, and EMBASE databases were searched by two independent reviewers between January 2000 and May 2019. We selected studies of neuraxial anesthesia compared with general anesthesia in patients undergoing hip fracture surgery. Following items were searched for both alone and in various combinations, “hip fracture” or “femur fracture” or “intertrochanteric” or “femoral neck” AND “regional anesthesia” or “spinal anesthesia” or “neuraxial anesthesia” or “epidural anesthesia”. The “related articles” function in Medline was performed to expand the search. Reference lists were also hand-searched for relevant studies. No language restriction was placed on our search.

**Inclusion and Exclusion Criteria**
Two independent reviewers screened article titles and abstracts based on the following inclusion criteria: (1) randomized controlled trials (RCTs) with no language restriction; (2) studies comparing general anesthesia with neuraxial anesthesia (epidural or spinal) in patients undergoing hip fracture surgery; (3) studies provided numerical data. The following exclusion criteria was used: (1) studies that did not meet the inclusion criteria; (2) unpublished data or repeated data; (3) abstracts, case reports, comments, conference papers, or animal studies, meta-analysis and systematic reviews.

**Data Extraction**

Two independent reviewers designed a structured table and collected all the relevant data into a database. The following information was extracted from each study that met the inclusion criteria: first author’s name, publication year, country, sample size, age, American Society of Anesthesiologists (ASA) physical status, anesthesia technique, surgery type, study outcome measures. We also attempted to contact the corresponding authors to verify the accuracy of the data and to obtain further analytical data. We performed a meta-analysis for blood loss, 30-day mortality, length of hospital stay, and the prevalence of delirium, acute myocardial infarction, deep venous thrombosis, and pneumonia.

**Methodological Quality Assessment**

The methodological quality of each RCT was assessed using the Cochrane Handbook for Systematic Reviews of Interventions 5.1 by two reviewers, which contained the following items: random sequence generation, allocation concealment, blinding, incomplete outcome data, selective reporting, and other sources of bias. It was judged by answering a question, with “yes” indicating low risk of bias, “no” indicating high risk of bias, and
“unclear” indicating unclear or unknown risk of bias\textsuperscript{11}. The corresponding author was also consulted when any disagreement exists, and a consensus was reached by discussion.

**Statistical Analysis**

The statistical analysis of the pooled data were performed using Review Manager software (version 5.1, The Cochrane Collaboration, Oxford, England). For continuous variables, standardized mean difference (SMD) or weighted mean (WMD) difference was calculated with the 95% confidence intervals (CIs) as a summary statistic. For dichotomous variables, relative risk (RR) and 95% CIs were used. The combined effect was considered significant at a 2-sided P < 0.05. The p-value with the Cochrane Q-test was tested, and the \( I^2 \) statistic was used to judge inconsistency of treatment effects across studies. A random effect model was used if high heterogeneity was detected (p<0.10, \( I^2 >50\% \)); otherwise, a fixed effect model was used if low heterogeneity existed (p>0.10, \( I^2 <50\% \)). Sensitivity analyses were performed by leave-one-out approach by STATA 14.0 (STATA Corp, College Station, TX). Publication bias was evaluated by funnel plot, if our meta-analysis included more than 10 studies\textsuperscript{12}.

**Evidence synthesis**

The evidence grade for the main outcomes are assessed using the guidelines of the (GRADE) system working group including the following items: risk of bias, inconsistency, indirectness, imprecision and publication bias. The recommendation level of evidence is classified into the following categories: (1) high, which means that further research is unlikely to change confidence in the effect estimate; (2) moderate, which means that further research is likely to significantly change confidence in the effect estimate but may
change the estimate; (3) low, which means that further research is likely to significantly change confidence in the effect estimate and to change the estimate; and (4) very low, which means that any effect estimate is uncertain. The evidence quality is graded using the GRADEpro Version 3.6 software. The evidence quality was graded using the GRADEpro Version 3.6 software. The strengths of the recommendations were based on the quality of the evidence.

Results

**Study identification and selection**

A total of 1274 relevant studies were identified according to the search strategy. However, 798 publications were excluded after checking for duplicates. Among the 476 remaining articles, 359 articles were excluded after reviewing the titles and abstracts. Then we assessed 17 studies with full texts for eligibility. Eight studies were excluded because four of them included no control groups, and others provided inadequate data. Finally, nine RCTs with a total of 1084 patients between 2003 and 2018 met our inclusion criteria, and were included in the meta-analysis. The flow diagram of study selection is shown in Fig. 1.

Fig. 1 The flow diagram of study selection.

**Study Characteristics**

All the included studies were written in English, which examined perioperative outcomes between hip fracture patients who receive neuraxial or general anesthesia undergoing surgical repair. There were a total of 1084 patients, whose ages were older than 49 years-old. Seven studies looked at outcomes relating to spinal anesthesia compared with
general anesthesia\textsuperscript{13,14,16-19,21}, one study examed outcomes for hypobaric unilateral spinal anesthesia and general anesthesia\textsuperscript{20}, and the other study compared general versus neuraxial anesthesia that encompassed spinal and epidural anesthesia\textsuperscript{15}. In the terms of surgery type, two studies performed arthroplasty, hip screw and intramedullary nail\textsuperscript{18,20}; two studies included hemiarthroplasty only\textsuperscript{13,14}, and one study performed hemiarthroplasty and Intramedullary nail\textsuperscript{16}. Only one study was at a high risk of performance bias\textsuperscript{14}, and the other studies were all at low risk or unclear (Fig. 2). The characteristics of the included studies is shown in Table 1.

Fig. 2 Summary of risk bias assessment. “+” = low risk of bias; “?” = unclear risk of bias; and “-” = high risk of bias.

**Outcomes for meta-analysis**

Delirium rate was reported in four studies with 400 patients in the neuraxial anesthesia group and 409 patients in the general anesthesia group\textsuperscript{13,15,18,21}. The P value with the Cochran’s Q test was 0.03, and the $I^2$ statistic was 66%, which indicated high heterogeneity among these studies. Thus a random effect model was used to analyze the results. The pooled data showed no significant difference in delirium rate between the two groups (OR = 1.05, 95% CI 0.27, 4.00; P = 0.95, Fig. 3)

Three studies examed blood loss during hip fracture surgery with 250 patients in the neuraxial anesthesia group and 257 patients in the general anesthesia group\textsuperscript{15,17,19}. The P value with the Cochran’s Q test was 0.0003, and the $I^2$ statistic was 88%, which indicated high heterogeneity among these studies. Thus a random effect model was used
to analyze the results. There is a significant difference between the two groups in favor of the neuraxial anesthesia (MD = -137.8, 95% CI -241.49, -34.12; p = 0.009, Fig. 4).

Three studies were included in the meta-analysis for 30-day mortality, involving 363 patients in the neuraxial anesthesia group and 389 patients in the general anesthesia group\textsuperscript{15,16,18}. The P value with the Cochran’s Q test was 0.21, and the $I^2$ statistic was 48%, which indicated low heterogeneity among these studies. Thus a fixed effect model was used to analyze the results. The pooled data revealed that there was no significant difference in 30-day mortality between the two groups (OR = 1.34, 95% CI 0.56, 3.21; P = 0.51, Fig. 5).

Acute myocardial infarction rate was reported in three studies with 363 patients in the neuraxial anesthesia group and 376 patients in the general anesthesia group\textsuperscript{15,16,18}. The P value with the Cochran’s Q test was 0.96, and the $I^2$ statistic was 0%, which indicated low heterogeneity among these studies. Thus a fixed effect model was used to analyze the results. The pooled data showed no significant difference in the acute myocardial infarction rate between the two groups (OR = 0.88, 95% CI 0.17, 4.65; P = 0.88, Fig. 6).

Two studies provided the outcome of pneumonia rate, which involved 363 patients in the neuraxial anesthesia group and 389 patients in the general anesthesia group\textsuperscript{15,18}. The P value with the Cochran’s Q test was 0.42, and the $I^2$ statistic was 0%, which indicated low heterogeneity among these studies. Thus a fixed effect model was used to analyze the results. The pooled data showed no significant difference in pneumonia rate between the two groups (OR = 1.04, 95% CI 0.23, 4.61; P = 0.96, Fig. 7).

Two studies reported length of stay in a way that could be comparable by meta-analysis, including 348 patients in the neuraxial anesthesia group and 361 patients in the general anesthesia group\textsuperscript{15,18}. The P value with the Cochran’s Q test was 0.54, and the $I^2$ statistic
was 0%, which indicated low heterogeneity among these studies. Thus a fixed effect model was used to analyze the results. The pooled data revealed that no significant difference was detected in the length of stay between the two groups (MD = -0.65, 95% CI -0.32, 0.02; P = 0.06, Fig. 8)

Two studies were included in the meta-analysis for deep venous thrombosis rate, involving 179 patients in the neuraxial anesthesia group and 183 patients in the general anesthesia group\textsuperscript{18,20}. The P value with the Cochran’s Q test was 0.60, and the $i^2$ statistic was 0%, which indicated low heterogeneity among these studies. Thus a fixed effect model was used to analyze the results. The pooled data revealed that there was no significant difference in deep venous thrombosis rate between the two groups (OR = 0.48, 95% CI 0.09, 2.72; P = 0.41, Fig. 9)

Fig. 3 Forest plot of delirium rate for neuraxial anesthesia versus general anesthesia.
Fig. 4 Forest plot of blood loss for neuraxial anesthesia versus general anesthesia.
Fig. 5 Forest plot of 30-day mortality for neuraxial anesthesia versus general anesthesia.
Fig. 6 Forest plot of acute myocardial infarction rate for neuraxial anesthesia versus general anesthesia.
Fig. 7 Forest plot of pneumonia rate for neuraxial anesthesia versus general anesthesia.
Fig. 8 Forest plot of length of stay for neuraxial anesthesia versus general anesthesia.
Fig. 9 Forest plot of deep venous thrombosis rate for neuraxial anesthesia versus general anesthesia.

**Sensitivity analysis**

Sensitivity analyses were performed by the leave-one-out approach from the aforementioned meta-analyses. No difference was detected in the direction of the
conclusions with each study removed in turn, which showed that our study had good reliability, and the results were statistically robust (Fig. 9).

Fig. 10 Sensitivity analysis of blood loss for neuraxial anesthesia versus general anesthesia.

**Quality of the evidence and recommendation strengths**

A total of seven outcomes in this meta-analysis were evaluated using the GRADE system (Table 2). The evidence quality for each outcome was low. Therefore, we demonstrate that the overall evidence quality is low, which means that further research is likely to significantly change confidence in the effect estimate and may change the estimate.

**Discussion**

In our study, a total of nine RCTs with 1084 patients were included to make an updated meta-analysis. However, no significant difference was detected in the 30-day mortality, length of stay, and the prevalence of delirium, acute myocardial infarction, and pneumonia in patients undergoing hip fracture surgery where either neuraxial or general anesthesia was used. We first focused on the comparison of blood loss between the two anesthesia techniques. We found that neuraxial anesthesia was associated with a significant decrease in blood loss. The sensitivity analysis showed that the result had good reliability. Nevertheless, the sample size was small, and the overall evidence was low, indicating that further research is likely to significantly change confidence in the effect estimate and may change the estimate. Based on the current available evidence, more high-quality RCTs are required for further investigation.

According to methodological quality assessment, eight out of nine RCTs in our study were assessed as high-quality. Moreover, our study included several RCTs, in which the results were published after the most recent systematic review of this topic, making our
results more dependable. Of note, all of the RCTs showed low risk of attrition bias and reporting bias that may contribute to reducing systematic bias. Another strength of our study is low heterogeneity, detected in five out of six outcome measures assessed using $i^2$ statistic, demonstrating consistent outcomes across the comparisons. In addition, some data of previous reviews dated back to the 1980s$^{9,10}$, in which the type of anaesthetic techniques may not reflect current clinical practice, and it may restrain us from finding clinically relevant differences between the two techniques$^{9,46}$, while our study included most recent RCTs.

According to pharmacology, neuraxial anesthesia could lead to lower heart rate, and blood pressure than general anesthesia by blocking alpha and beta adrenergic receptors. Consequently, controlled blood pressure resulted in intraoperative less blood loss in neuraxial anesthesia patients$^{16,28}$. Current practice revealed that the number of patients who needed blood transfusion was larger in general anesthesia group, which means patients receiving spinal anesthesia had less blood loss than those receiving general anesthesia$^{19,29,30}$. In consistent with this result, a systematic review by Richman et al. Including 66 articles demonstrated that the use of neuraxial anesthesia resulted in a significant decrease in estimated blood loss$^{31}$. However, a meta-analysis by Hu er al. including 21 RCTs stated that there was insufficient evidence to support the use of neuraxial anesthesia in decreasing intraoperative blood loss$^{32}$. In our study, only three RCTs involving 507 patients have been summarised. Two out of them showed the neuraxial anesthesia was associated with statistically significant decrease in blood loss, the other showed no significant difference between the two anesthesia techniques. However, a high degree of heterogeneity (88%) and low-quality evidence for this outcome were detected, thus this difference favoring neuraxial anesthesia may not be clinically significant. More
RCTs were needed to focus on this topic.

Delirium is a very common postoperative complication, which leads to lasting cognitive and functional decline, and increasing length of stay\textsuperscript{18,22}. There are many precipitating factors in developing delirium, including infection, myocardial and cerebral ischaemia, urinary retention, pain, constipation as well as electrolyte abnormalities\textsuperscript{23}. Furthermore, several studies have investigated the incidence of delirium in elderly patients, who were admitted to be hospitalized for a variety of reasons, and the prevalence amongst medical wards was estimated to range from 29\% to 64\%\textsuperscript{23-25}. Additionally, the development of delirium is thought to be multifactorial process. Certain patient characteristics are also easy to cause delirium, including pre-existing cognitive impairment, sleep deprivation, medical immobilities, visual impairment, hearing impairment and poly pharmacy\textsuperscript{26,27}. Our study detected no significant difference in delirium rate between general and neuraxial anesthesia. It is noteworthy that none of the included studies represented relative characteristics and potential risk factors that causing delirium in hip fracture patients perioperatively. Thus the result may be underpowered.

Our study detect comparable outcomes in the incidence of 30-day mortality between the two groups. In line with this result, a retrospective study reported that the anesthesia technique has little effect on postoperative mortality, and the type of anesthesia given by the anesthesiologist should be selected based on the individual physical condition\textsuperscript{33}. The study of Lienhart et al. including 425 patients indicated that their coexisting disease has great influence on 30-day mortality in old patients such as diabetes, cardiovascular disease, etc\textsuperscript{34}. Delay of surgery for more than 24h was a main factor affecting postoperative mortality in geriatric hip fracture patients\textsuperscript{35}. The retrospective cohort study of Pincus et al. Investigated 42230 patients undergoing hip fracture surgery, and
demonstrate that a preoperative waiting time of more than 24h was associated with a greater risk of 30-day mortality and other complications\textsuperscript{36}.

In our study, the incidence of myocardial infarction and pneumonia were similar in both groups. Zuo et al. detected the same result, and suggested that the neuraxial anesthesia might be a better choice in hip fracture surgery\textsuperscript{37}. However, Urwin et al. proposed that the incidence of myocardial infarction and pneumonia was lower in patients receiving neuraxial anesthesia, and a significant lower incidence of intraoperative hypotension was detected in patients receiving general anesthesia\textsuperscript{38}. It should be noted that Urwin et al. evaluated 2161 patients retrospectively. Moreover, all of the included studies were performed more than 20 years ago, which are now somewhat dated, since many drugs used for anesthesia techniques and health care systems have been improved a lot. Thus their findings could not provide worthy references to some extent.

There was no significant difference regarding the length of stay between the two anesthesia techniques. Sutcliffe et al. surveyed 1333 volunteers of hip surgery, and found no difference in factors of hospitalization in both groups\textsuperscript{39}. Nevertheless, Neuman et al. conducted a matched retrospective cohort study involving 56729 patients, and found a modestly shorter length of stay in the neuraxial anesthesia group. The authors also proposed that the fracture type and performed surgery procedure were important factors; minimally invasive approaches and optimal quality of fracture reduction may decrease the length of stay\textsuperscript{40}. In addition, Grant et al. declared that the pain severity was lower in patients receiving general anesthesia, resulting in shorter length of stay\textsuperscript{41}. A notable point is that waiting time prior to surgery extended the length of stay\textsuperscript{42}. In our meta-analysis, one study reported the overall length of stay\textsuperscript{18} while the other documented the length of
stay before and after the surgery\textsuperscript{15}. It is difficult to draw a definite conclusion due to the existence of aforementioned multiple factors. Also, the small sample size in our study should be taken into consideration.

Perioperative deep venous thrombosis is common in hip fracture patients. Several studies concluded that neuraxial anaesthesia was associated with fewer incidents of deep venous thrombosis when compared to general anaesthesia\textsuperscript{38,43,44}. It was thought that in neuraxial anaesthesia sympathetic block could lead to vasodilatation of the lower limbs, and then the increased blood flow to the lower limbs was likely to reduce the coagulability and viscosity of blood\textsuperscript{45}. A Cochrane review published in 2016 by pooling the results from 31 RCTs showed a reduced risk of deep venous thrombosis in the neuraxial group without potent thromboprophylaxis. Nevertheless, the level of evidence was very low for this outcome\textsuperscript{46}. Another Cochrane review concluded that there was a marginal advantage for neuraxial anaesthesia regarding the incidence of deep venous thrombosis\textsuperscript{47}. Our study included only two RCTs, and detected no significant difference in the incidence of deep venous thrombosis between the two groups.

Objectively speaking, several limitations of our study should be mentioned. A major limitation is that the sample size was relatively small, and the sample size varied widely among the included studies. Another notable limitation is that most of the included studies did not describe whether additional sedation was used in hip fracture patients receiving neuraxial anesthesia, for instance, the use of propofol sedation could influence the prevalence of postoperative delirium\textsuperscript{48}. Also, no information is available in the terms of the dosage of the anesthesia used. In addition, the inconsistent definition of length of stay and delirium may account for the wide prevalence range for these outcomes. There are numerous confounding factors such as the diversity of patient groups, health care
systems, surgical and anesthetic techniques that may affect the perioperative outcomes, leading to potential biases. This issue would be possibly considered as a weakness. Last but not least, the outcome measures were not identical in each trial, thus we did not have sufficient data to perform other meta-analyses, which potentially affects the current findings of our study. Therefore, more high-quality RCTs with large sample size are required for a firm conclusion.

Conclusion

In summary, our present study demonstrated that neuraxial anesthesia is associated with a reduced blood loss in patients undergoing hip fracture surgery when compared to general anesthesia, however, it was assessed as a low-quality evidence. We suggest that the choice of anaesthesia (neuraxial or general) should be made by the anaesthesiologist based on the individual patient’s requirements, comorbidities, potential postoperative complications, consultation of geriatrician and orthopaedic surgeon, and the clinical experience of the anaesthesiologist. Due to small sample size and enormous inconsistency in the choice of outcome measures, more high-quality studies with large sample size are needed to to clarify this issue.

Abbreviations

ASA: American Society of Anesthesiologists; CI: Confidence interval; GRADE: The grading of recommendations, assessment, development, and evaluation methodology; GA: general anesthesia; HUSA: hypobaric unilateral spinal anesthesia; MMSE: Mini Mental State Examination; NA: neuraxial anesthesia; PONV: Postoperative nausea and vomiting; PRISMA: Preferred reporting items for systematic reviews and meta-analyses; RCT: Randomized controlled trial; RR: Risk ratio; SMD: Standardized mean difference; WMD: weighted mean difference; DVT, deep venous thrombosis
Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Availability of data and materials
All data generated or analyzed during this study are included in this published article.

Competing interests
The authors declare that they have no competing interests.

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Authors’ contributions
XZ and ZL designed and conceived the study, performed the statistical analysis, and drafted the manuscript. YG participated in the interpretation of data, analysis, and drafting of the manuscript. YT participated in the study design and coordination, and helped to draft the manuscript. All authors read and approved the final manuscript.

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Tables

Table 1 The descriptive characteristics of included studies.

| Study | Country | Sample size(male/fe) | Age in years | ASA status | anesthesia | surgery type |
|-------|---------|---------------------|--------------|------------|------------|--------------|

22
| Study                          | Country | Number (Male/Female) | Age | Injury Grade | Treatment | Surgical Approach |
|-------------------------------|---------|----------------------|-----|--------------|------------|------------------|
| Casati et al. (2003)          | Italy   | 30 (7/23)            | 84  | II-III       | GA vs Spinal | Hemiarthroplasty: |
| Hoppenstein et al. (2005)     | Israel  | 60                   | >65 | I-III        | GA vs Spinal | --               |
| Heidari et al. (2011)         | Iran    | 387 (257/130)        | >60 | I-III        | GA vs NA    | --               |
| Biboulet et al. (2012)        | France  | 45 (14/31)           | >75 | III-IV       | GA vs Spinal | Hemiarthroplasty: Intramedullary |
| Messina et al. (2013)         | Italy   | 20 (7/13)            | >75 | III          | GA vs Spinal | --               |
| Parker et al. (2015)          | UK      | 322 (87/235)         | >49 | I-III        | GA vs Spinal | Arthroplasty: Sliding hip screw Intramedullary |
| Haghighi et al. (2017)        | Iran    | 100 (80/20)          | >60 | I-III        | GA vs Spinal | --               |
| Meuret et al. (2018)          | France  | 40 (8/32)            | >75 | I-III        | GA vs HUSA   | Arthroplasty: Dynamic hip screw Intramedullary |
MMSE, Mini Mental State Examination; PONV, Post Operative Nausea And Vomiting; GA, general anesthesia; NA, neuraxial anesthesia; ASA, American Society of Anesthesiologists; HUSA, hypobaric unilateral spinal anesthesia; DVP, deep venous thrombosis.

Table 2 The GRADE evidence quality for main outcome.

| Quality assessment | Delirium rate | Acute myocardial infarction rate | 30-day Mortality |
|--------------------|---------------|---------------------------------|------------------|
| No of studies      | Design        | Risk of bias                    | Indirectness     | Imprecision | Other considerations | Delirium rate |
| Delirium rate      | 4             | randomised trials               | serious          | no serious  | no serious           | none          | 26/4 (6.5%)  |
| Acute myocardial infarction rate | 3          | randomised trials               | no serious risk of bias | no serious | no serious           | none          | 2/3 (0.5%)  |
| 30-day Mortality   | 3             | randomised trials               | serious          | no serious  | serious             | none          | 11/2 (3.3%)  |
| Blood loss (Better indicated by lower values) |
|---------------------------------------------|
| 3 | randomised trials | serious | serious | no serious indirectness | no serious imprecision | none | 25 |

| Pneumonia rate |
|----------------|
| 2 | randomised trials | serious | serious | no serious indirectness | no serious imprecision | reporting bias | 3/3 (0.9%) |

| Length of stay |
|----------------|
| 2 | randomised trials | serious | no serious inconsistency | serious | no serious imprecision | reporting bias | 34 |

**Figures**
Figure 1

The flow diagram of study selection.
Figure 2

Summary of risk bias assessment. “+” = low risk of bias; “?” = unclear risk of bias; and “-” = high risk of bias.
Figure 3

Forest plot of delirium rate for neuraxial anesthesia versus general anesthesia.

Figure 4

Forest plot of blood loss for neuraxial anesthesia versus general anesthesia.

Figure 5

Forest plot of 30-day mortality for neuraxial anesthesia versus general anesthesia.
Figure 6

Forest plot of acute myocardial infarction rate for neuraxial anesthesia versus general anesthesia.

Figure 7

Forest plot of pneumonia rate for neuraxial anesthesia versus general anesthesia.

Figure 8

Forest plot of length of stay for neuraxial anesthesia versus general anesthesia.
Figure 9

Forest plot of deep venous thrombosis rate for neuraxial anesthesia versus general anesthesia.

Figure 10

Sensitivity analysis of blood loss for neuraxial anesthesia versus general anesthesia.

Supplementary Files

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