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General anesthesia vs spinal anesthesia for patients undergoing total-hip arthroplasty
A meta-analysis

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Abstract
Background: The optimal anesthetic technique remains debated in patients undergoing total-hip arthroplasty (THA). The purpose of this meta-analysis was to test the efficacy of general and spinal anesthesia for patients undergoing THA.

Methods: In January 2018, we searched PubMed, Embase, Web of Science, Cochrane Database of Systematic Reviews, and the Google database. Data from randomized controlled trials (RCTs) that compared the use of general and spinal anesthesia for patients undergoing THA were retrieved. The primary outcome was to compare the total blood loss. The secondary outcomes were the occurrence of deep venous thrombosis (DVT), the occurrence of nausea, and the length of hospital stay. Software Stata 12.0 was used for meta-analysis.

Results: Five RCTs with 487 THAs were finally included for meta-analysis. There was no significant difference between the general anesthesia and spinal anesthesia in terms of the total blood loss (weighted mean difference [WMD] = −20.72, 95% confidence interval [CI] −84.50 to 43.05, $P = .524$; $I^2 = 87.8\%$) and the occurrence of DVT (risk ratio (RR) = 0.85, 95% CI 0.24–3.01, $P = .805$; $I^2 = 70.5\%$). Compared with general anesthesia, spinal anesthesia was a significant reduction in the occurrence of nausea (RR = 3.04, 95% CI 1.69–5.50, $P = .000$; $I^2 = 0.0\%$) and the length of hospital stay (WMD = 1.00, 95% CI 0.59–1.41, $P = .000$; $I^2 = 94.7\%$).

Conclusion: Spinal anesthesia was superior than general anesthesia in terms of the occurrence of nausea and shorten the length of hospital stay. The quality and number of included studies was limited; thus, a greater number of high-quality RCTs is still needed to further identify the effects of spinal anesthesia on reducing the blood loss after THA.

Abbreviations: CENTRAL = Cochrane Central Register of Controlled Trials, CI = confidence interval, DVT = deep venous thrombosis, GRADE = Grading of Recommendations, Assessment, Development and Evaluation, PRISMA = preferred reporting items for systematic reviews and meta-analyses, RCTs = randomized controlled trials, RR = risk ratio, SD = standard deviation, THA = total-hip arthroplasty, WMD = weighted mean differences.

Keywords: general anesthesia, meta-analysis, spinal anesthesia, total-hip arthroplasty

1. Introduction

Total-hip arthroplasty (THA) is a frequently performed and painful procedure.[1,2] Patients undergoing THA may be offered either spinal anesthesia or general anesthesia.[3] Among the various regional techniques, spinal anesthesia is not only common, but also recommended.[4] Recent years, many studies has been published and compared spinal anesthesia and general anesthesia for clinical outcomes of THA. Harsten et al[5] reported that general anesthesia resulted in a more favorable recovery profile compared with spinal anesthesia after THA. However, Maurer et al's[6] spinal anesthesia appears superior to general anesthesia for THA. With more evidence appears, we want to identify whether spinal anesthesia was superior than general anesthesia in terms of the perioperative blood loss, the occurrence of deep venous thrombosis (DVT) and nausea.

2. Materials and methods

This meta-analysis was conducted in accordance with the recommendations of the Cochrane Handbook for Systematic Reviews of Interventions[7] and was written in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) checklist.[8] There was no registered protocol.

2.1. Search strategy and study selection

The following electronic databases were systematically searched from their inception through January 2018: PubMed, Embase, the Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science and the Google database. The detailed PubMed search strategy was as follows: (((spinal anesthesia) AND general anesthesia)) AND (((((("Arthroplasty, Replacement, Hip"[Mesh]) OR THR) OR THA) OR total-hip arthroplasty) OR total-hip

replacement). No language restriction was applied. We manually searched relevant meta-analysis to find any omitting study.

2.2. Eligibility criteria

1. Participants: Patients who underwent THA (including primary THA and THA revisions).
2. Interventions: General anesthesia was used preoperatively for the intervention group.
3. Comparisons: Spinal anesthesia was used preoperatively for the comparison group.
4. Outcomes: Total blood loss, the occurrence of DVT, the occurrence of nausea, and the length of hospital stay.
5. Study design: Only randomized controlled trials (RCTs) were included.

2.3. Data extraction and outcome measures

For each published study included in the meta-analysis, 2 authors (XP and JS) independently extracted the following data: author, publication year, country, cases of spinal anesthesia and general anesthesia, mean age, dose and drugs of general anesthesia and spinal anesthesia, outcomes, duration of the follow-up period, and study type. Any disagreement was resolved by discussion. The outcome measures were total blood loss, the occurrence of DVT, the occurrence of nausea, and the length of hospital stay. If the data were not available and presented in figures or other forms, we extracted the mean and standard deviation values using GetData Graph Digitizer software as needed.[7] If there was any missing data, we contact with authors for missing data.

2.4. Risk of bias assessment

Two reviewers independently evaluated the risk of bias in RCTs according to the recommendations of the Cochrane Handbook for Systematic Reviews of Interventions.[7] There were a total of 7 items need to identify for the risk of bias of the RCTs (random sequence generation, allocation concealment, blinding of the participant and outcome assessment and other bias). Each items were assessed as "low risk of bias," "unclear risk of bias," and "high risk of bias."

2.5. Quality of evidence assessment

To assess the quality of evidence, 2 authors (XP and JS) used the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) methodology.[9] For each outcome, 5 separate factors were rated for quality: risk of bias, inconsistency, indirectness, imprecision, and publication bias.[9,10] And GRADE Profiler (GRADEpro, version 3.6, McMaster University and Evidence Prime Inc, Hamilton) was used to construct summary table.

2.6. Statistical analysis

For dichotomous outcomes (the occurrence of DVT and the occurrence of nausea), we calculated the risk ratio (RR) and the 95% confidence interval (CI). For continuous outcomes (total blood loss and the length of hospital stay), we calculated the weighted mean difference (WMD) and corresponding CIs. Heterogeneity was considered to be statistically significant if the I^2-value was >50%. A fixed-effects model was applied if

the I^2-value was <50%. All statistical analyses were conducted using Stata 12.0 (Stata Corp., College Station, TX). A P-value <.05 was considered statistically significant. We used kappa values to assess the degree of agreement between the 2 reviewers. The criteria was as follows: fair, 0.40 to 0.59; good, 0.60 to 0.74; and excellent, 0.75 or higher.[11] In addition, we calculated numbers needed to treat (NNT) to examine the risk vs benefit of general anesthesia and spinal anesthesia for some endpoints.[12] We used DerSimonian–Laird method to synthesis outcomes with large heterogeneity.[13]

3. Results

3.1. Search results

The literature search and selection process are illustrated in Figure 1. The initial search yielded 158 articles (PubMed = 92, Embase = 18, Web of Science = 32, Cochrane Library = 6, Google database = 10). After excluding duplications, 132 studies were examined. Next, 127 of the 132 studies were excluded based on the inclusion criteria. Finally, a total of 5 studies were finally included in this meta-analysis.[5–17] Kappa value between the 2 reviewers was 0.713 and indicated that degree of agreement was good. There was no missing data for the outcomes.

3.2. Study characteristics

Detailed baseline characteristics of the included studies are presented in Table 1. Four studies were included in the meta-analysis. All articles were published in English between 2011 and 2016. The sample sizes ranged from 10 to 71 (total = 487, SA = 244, GA = 243), and the mean ages ranged from 65.1 to 72.2. The follow-up period was ranged from 72 hours to 1 year.

3.3. Risk of bias among the included studies

Risk of bias can be obtained in Figures 2 and 3. Three studies reported the random sequence generation and only 1 study did not describe the random sequence generation. Three studies were with low risk of bias for the allocation concealment, and 2 studies were with unclear risk of bias. Blinding of the participant and outcome assessment were with low risk of bias in 3 studies. Attrition bias, reporting bias, and other bias were all with low risk of bias.

3.4. Results of meta-analysis
3.4.1. Total blood loss.
Three studies, including 381 patients with THA, tested the effect of general anesthesia and spinal anesthesia on the total blood loss. There was no significant difference between the general anesthesia and spinal anesthesia in terms of the total blood loss (WMD = −20.72, 95% CI −84.50 to 43.05, P = .524; I^2 = 87.8%, moderate evidence, Fig. 4). We use a random-effects model to pool the relevant data.

3.4.2. Occurrence of DVT.
Three studies including 289 patients with THA tested the effect of general anesthesia and spinal anesthesia in terms of the occurrence of DVT. There was no significant difference between the occurrence of DVT between the 2 groups (RR = 0.85, 95% CI 0.24–3.01, P = .805; I^2 = 70.5%, low evidence; Fig. 5) with NNT value is 19.51.

3.4.3. Occurrence of nausea.
Four studies including 369 patients tested the effect of general anesthesia and spinal anesthesia on the occurrence of nausea. Compared with general anesthesia, spinal anesthesia was associated with a significant
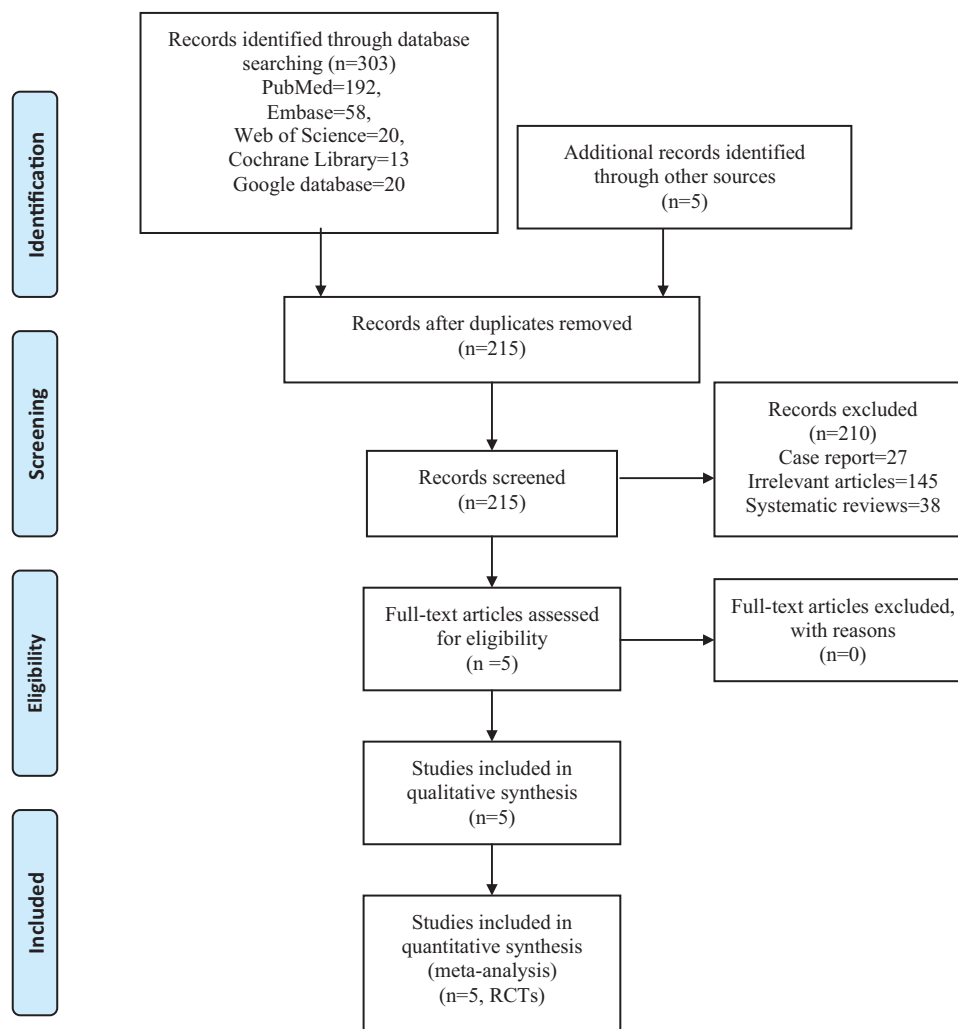
Figure 1. Flowchart of the included studies.

Table 1

General characteristics of the included studies.

Author	Country	Cases (SA vs GA)	Age, yr	Dose and drugs of GA	Dose and drugs of SA	Study	Follow-up	Outcomes
Davis (1989)	New Zealand	69 vs 71	68.3 vs 66.7	Induction with sodium thiopentone, received a narcotic-halothane-muscle relaxant general anesthetic	Tetracaine, supplemented by light basal sedation with a chlormethiazole infusion	RCTs	72 hours	1,2,3,4
Harsten (2015)	Sweden	58 vs 60	68 vs 66	Remifentanil 40 μg/mL and propofol 10 mg/mL using the pharmacokinetic models	Consisting of isobaric bupivacaine 0.5%, 3 mL. An infusion of propofol 10 mg/mL was administered to induce light sedation during surgery	RCTs	1 yr	1, 2, 3, 4
Planes (1991)	France	61 vs 62	66.7 vs 66.8	Fentanyl (2 μg/kg) and thiopentone (5 mg/kg)	100 mL of ringer lactate and etilefrine chlorhydrate (0.01 g), 3.5–4.8 mL (17.5–24 mg) of bupivicaine (0.5%)	RCTs	3 mo	1, 2, 3
Zhou (2014)	China	40 vs 40	65.1 vs 67.4	Midazolam + propofol + sufentanil	0.75 bupivacaine and 50 μg fentayl	RCTs	3 mo	1, 2, 3, 4
Brueckner (2003)	Germany	16 vs 10	70.1 vs 72.2	Remifentanil 40 μg/mL and propofol 10 mg/mL	Bupivacaine 0.5%, 3 mL and infusion of propofol 10 mg/mL	RCTs	1 mo	1, 2, 3, 4

1 = the occurrence of DVT, 2 = the occurrence of nausea, 3 = the length of hospital stay, 4 = total blood loss, RCT = randomized controlled trial.

Figure 2. Risk of bias summary of the included studies. "+" low risk of bias, "−" high risk of bias, "?" unclear risk of bias.

reduction in the occurrence of nausea (RR = 3.04, 95% CI 1.69–5.50, P = .000; I^2 = 0.0%, high evidence; Fig. 6) with NNT value is 6.69.

3.4.4. Length of hospital stay. Four studies including 369 patients tested the effect of general anesthesia and spinal anesthesia on the length of hospital stay. Compared with the

general anesthesia, spinal anesthesia was associated with a significant reduction in the length of hospital stay (WMD = 1.00, 95% CI 0.59–1.41, P = .000; I^2 = 94.7%, low evidence; Fig. 7).

3.4.5. Sensitivity analyses, publication bias, and GRADE evidence. Figure 8 shows the result of sensitivity analyses for total blood loss. Results shown that after omitting each study, the final results did not alter. Since the number of included studies was <10 and thus it was not necessary to perform funnel plot or Begg test. Grade evidences for outcomes were presented in Supplement S1, http://links.lww.com/MD/C918.

4. Discussion

This is the 1st systematic review and meta-analysis that comparing general anesthesia and spinal anesthesia after THA. Current meta-analysis indicated that there was no significant difference between the general anesthesia vs spinal anesthesia in terms of the total blood loss, the occurrence of DVT. Spinal anesthesia was associated with a reduction of the occurrence of nausea and the length of hospital stay.

    General and spinal anesthesia are both commonly used during THA. However, the effects of general and spinal anesthesia for perioperative blood loss and the occurrence of DVT was unknown. Current meta-analysis demonstrated that general anesthesia had no benefit effect on the total blood loss and the occurrence of DVT. There is a high heterogeneity for these outcomes. We performed sensitivity analysis by omitting each study in turn, the final results did not alter. The reason may be as the clinical heterogeneity such as different surgical approach, prosthesis, and surgeons.

    Maurer et al[6] reported that spinal anesthesia was associated with a significantly reduction in blood loss and subsequently blood transfusion. However, Harsten et al[5] reported that there was no significant difference between the hemoglobin level after THA between general anesthesia and spinal anesthesia. Gonano et al[18] compared spinal anesthesia and general anesthesia in terms of the occurrence of DVT and found that spinal anesthesia was associated with a reduction of the occurrence of DVT. Lončarić-Katušin et al[19] revealed that the mode of anesthesia (general vs spinal) has no effect on postoperative mortality, and that the mode of anesthesia should be applied on an individual basis in correlation with associated comorbidities. Accepted benefits of spinal anesthesia include the avoidance of airway
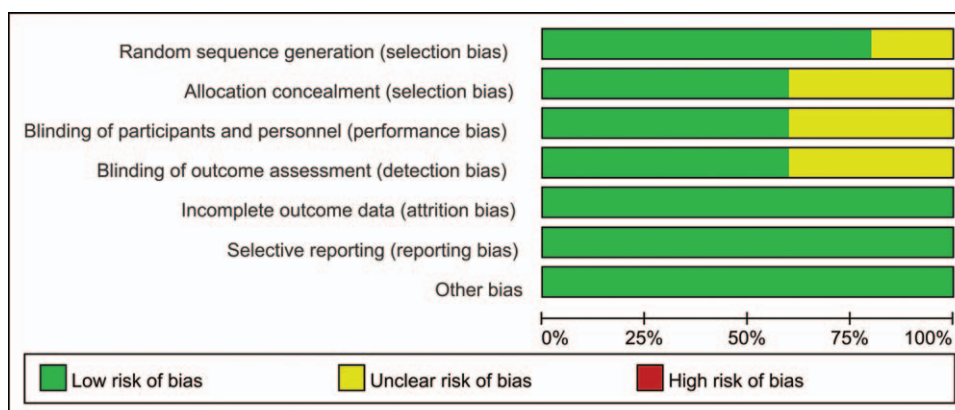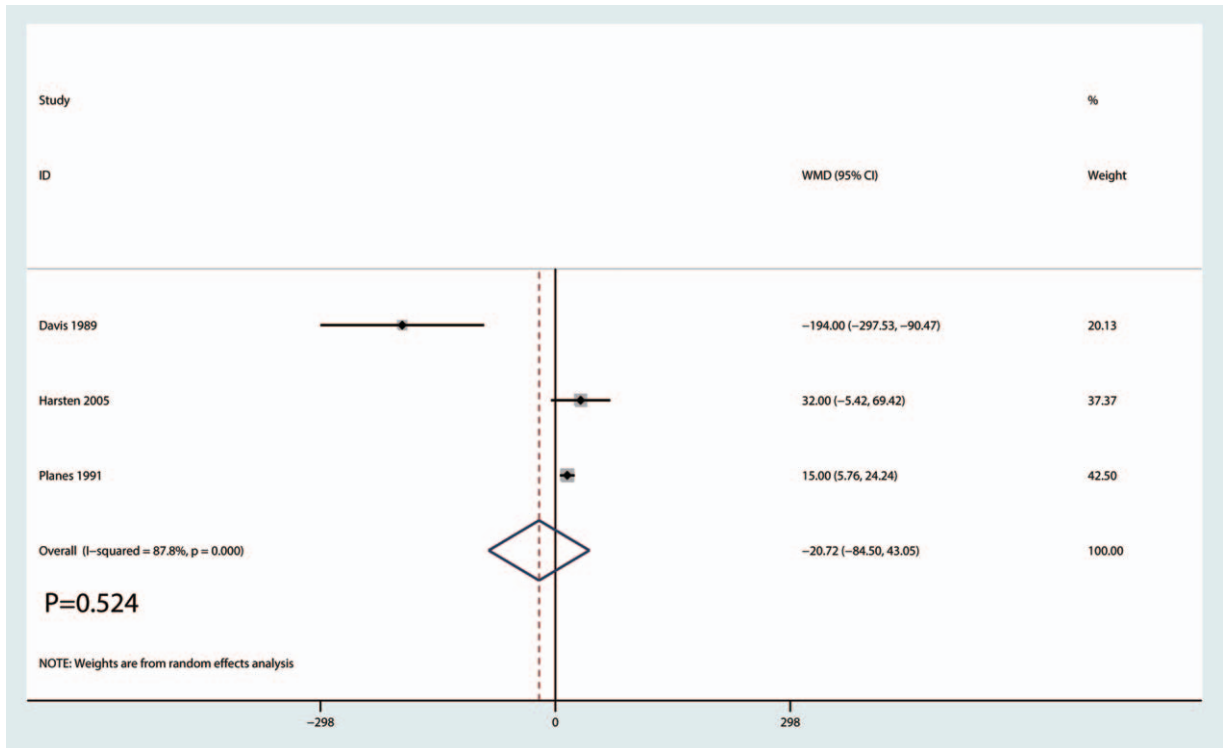

Figure 3. Risk of bias graph.

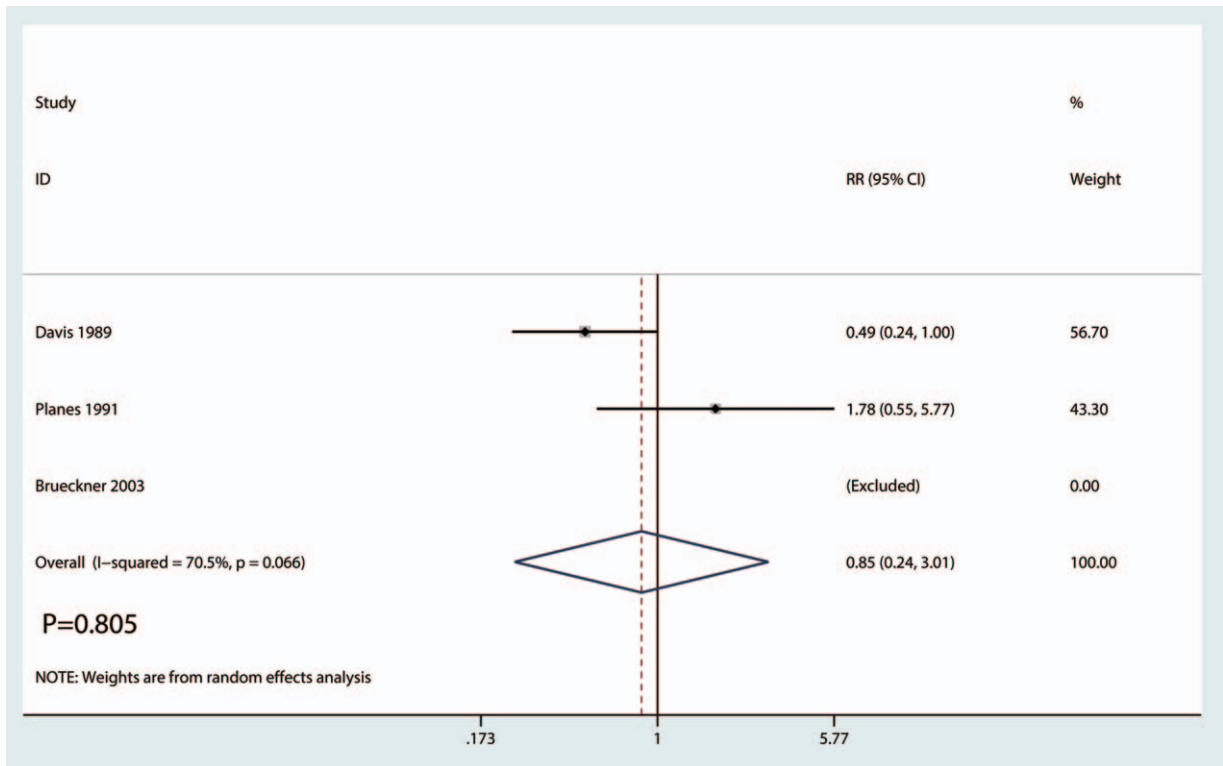**Figure 4.** Forest plot of the total blood loss between the 2 groups.

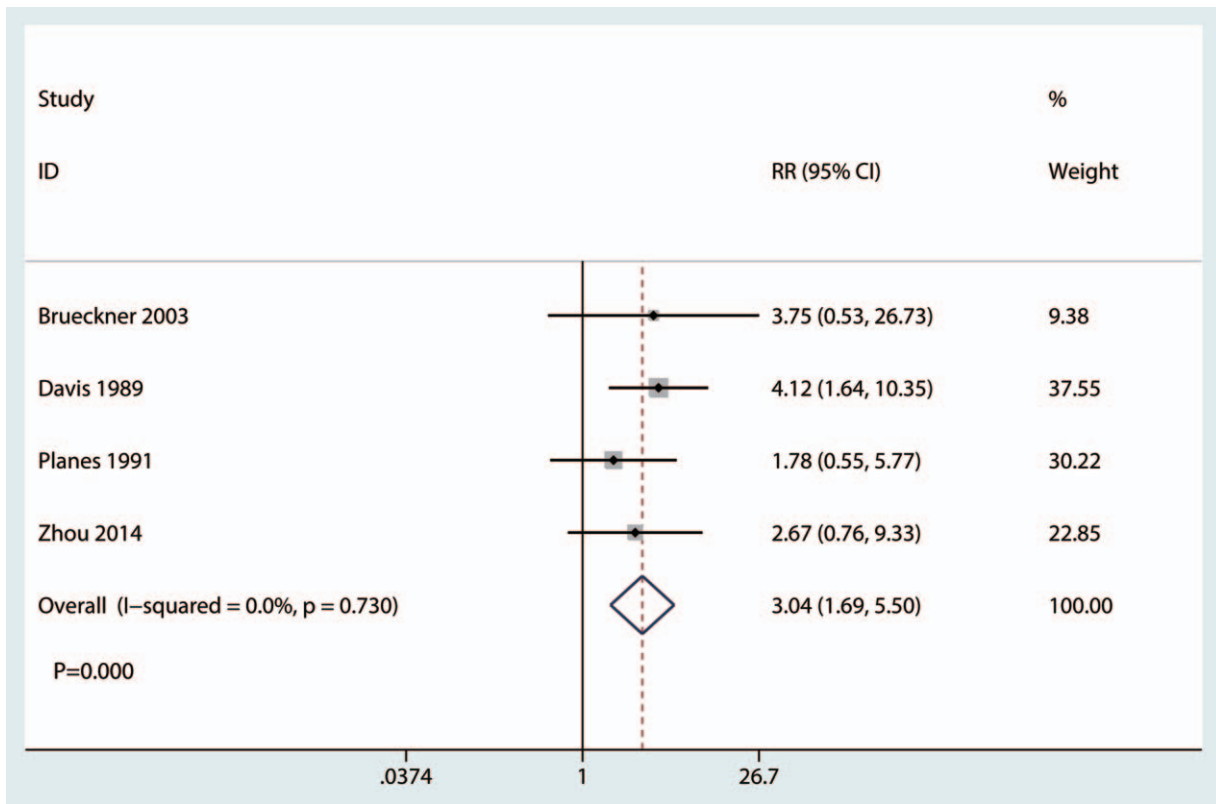**Figure 5.** Forest plot of the occurrence of deep venous thrombosis between the 2 groups.

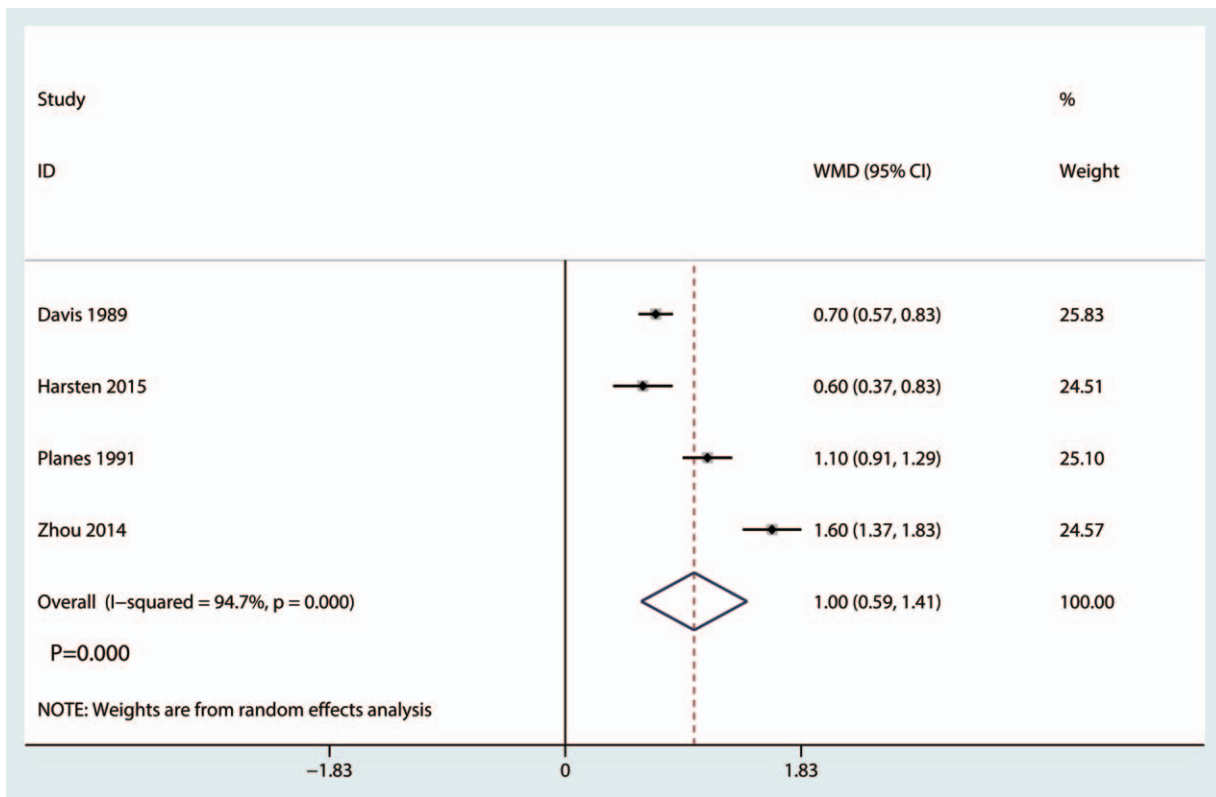**Figure 6.** Forest plot of the occurrence of nausea between the 2 groups.

Figure 7. Forest plot of the length of hospital stay between the 2 groups.
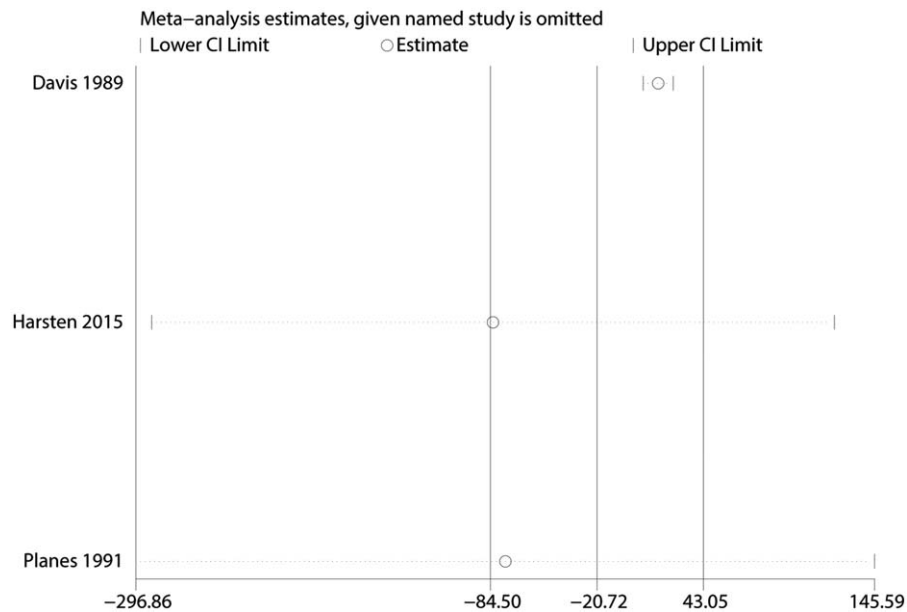
Figure 8. Sensitivity analysis of the total blood loss.

management, decreased perioperative blood loss, and reduction of DVT risk, whereas general anesthesia is recommended for hemodynamically unstable patients.[20,21]

For the occurrence of nausea, we found that spinal anesthesia was associated with a reduction of the occurrence of nausea. Brueckner et al[14] drawn a similar conclusion with our results that spinal anesthesia was associated with a significantly reduction of the occurrence of nausea ($P < .05$). Finsterwald et al[22] reported that the spinal surgery patients in the spinal anesthesia group has lower postoperative nausea and vomiting than general anesthesia group. What's more, lumbar spine surgery in cardiovascular high risk patients with spinal anesthesia is safe.

In addition, we then draw a conclusion that spinal anesthesia was associated with a reduction of the length of hospital stay and further reduce the hospital-related costs. Gonano et al[18] reported that spinal anesthesia was associated with a reduction of the economic costs in THA patients. Kuju et al[23] compared the effectiveness of spinal anesthesia and general anesthesia for open cholecystectomy and results shown that spinal anesthesia is safe and more effective than general anesthesia.

For costs of spinal anesthesia and general anesthesia, many studies shown that spinal anesthesia lead to lower health care costs.[22–24] Since there was no direct comparison between the costs of these 2 approaches. Thus, more studies were needed to identify the economic costs of the 2 methods.

There were a total of 4 main limitations in this meta-analysis: only 5 RCTs with small sample size and overestimation of the intervention effect is more likely compared with larger sample studies; the drug used for spinal anesthesia and general anesthesia were different in the included studies and may cause the heterogeneity for the final outcomes; included studies selected reporting the diagnosis method of DVT and the use of venous thrombosis prophylaxis; perioperative pain management was different in the included studies and thus may cause the heterogeneity.

5. Conclusion

In conclusion, we found that spinal anesthesia was superior than general anesthesia in terms of the occurrence of nausea and shorten the length of hospital stay. There was no significant difference between the perioperative blood loss and the occurrence of DVT. Future research should be aimed at the optimal drug and dose for spinal anesthesia. In addition, more well-designed RCTs should be performed to confirm these results.

Author contributions

Formal analysis: Jian-ming Sun.
Software: Xiang Pu.
Writing – review & editing: Xiang Pu, Jian-ming Sun.

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