



Effects of Intrathecal Versus General Anesthesia on Postoperative Cognitive Function in Elderly Hip Fracture Patients: a System Review and Meta Analysis Protocol

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Abstract: Randomized controlled studies have shown that the incidence of postoperative cognitive function in elderly patients undergoing hip fracture surgery varies significantly by anesthesia type. The aim of this study was to assess the effects of intrathecal anesthesia and general anesthesia on postoperative cognitive function in elderly hip fracture by system review and meta-analysis. This study followed the guidance of the Preferred Reporting Items for Systematic Reviews and Meta-analyses. First, the Cochrane Library, Web of Science, PubMed, EMBASE, Chinese Biomedical Literature Database, China National Knowledge Infrastructure, China Science and Technology Journal Database, Wanfang Database, and Clinical Trials Database were searched. Second, the literature was screened and identified for inclusion step by step according to the established inclusion and exclusion criteria using Endnote. Further, Excel 2010 was used to record the basic characteristics and relevant data of the included literature, and the Cochrane Risk of Bias Assessment Tool was used to rate the quality of each included study. Subsequently, meta-analysis was performed using RevMan 5.3 software to assess the effects of intrathecal anesthesia and general anesthesia on postoperative cognitive function of hip fracture in the elderly, and funnel plots were drawn to assess publication bias. The results of this systematic evaluation and meta-analysis will be published in a peer-reviewed journal.

Keywords: intrathecal anesthesia; general anesthesia; hip fracture; cognitive function; systematic evaluation; meta-analysis; protocol

1. Introduction

Hip fractures are a common and debilitating type of fracture in the elderly population[1]. This type of fracture is often accompanied by severe pain, dysfunction, and long-term rehabilitation challenges, which severely impacts the patient's quality of life. In addition, hip fractures in the elderly lead to cognitive dysfunction, including memory loss, poor concentration, and decreased cognitive flexibility[2]. This not only aggravates the physical and psychological burden on the patient, but also slows down the recovery process and even affects the patient's survival rate[3]. The patient's survival rate may even be affected. With the accelerated aging of the population, the number of elderly hip fracture patients is gradually increasing[4]. How to maximize the avoidance and reduction of postoperative cognitive impairment of hip fracture in elderly patients has become a common focus of attention for both clinical workers and researchers. Surgery is one of the main modalities for the treatment of elderly hip fractures, which aims to restore the anatomical structure and function of the fracture site, reduce pain, and promote the early recovery of patients[5]. In orthopedic surgery, the choice of anesthesia is crucial to the patient's postoperative recovery[6]. Currently, intrathecal anesthesia and general anesthesia are two common anesthesia modalities that are widely used in elderly hip fracture surgery[7]. However, the effects of these two anesthesia modalities on postoperative cognitive function are still highly controversial. Some studies have suggested that intrathecal anesthesia may have less impact on cognitive function compared to general anesthesia[8]. However, there are also other studies that offer a different view on this matter, suggesting that there is no significant difference between the two anesthesia modalities on postoperative cognitive functions[9]. Due to the lack of clinical evidence from large samples and multiple centers, the benefits and risks of both intrathecal and general anesthesia on cognitive function after hip surgery in elderly patients remain unclear. Therefore, this protocol proposes to comprehensively assess the effects of intrathecal anesthesia and general anesthesia on postoperative cognitive function after hip fracture in the elderly using system review and meta-analysis, with the aim of providing an evidence-based basis for the choice of anesthesia modality for hip fracture surgery in the elderly.

2. Materials and methods

2.1 Research norms

This study protocol follows the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-analyses[10], and was registered in PROSPERO. No additional ethical approvals were required as the data for this study were all obtained from public databases.

2.2 Search strategy

The Cochrane Library, Web of Science, PubMed, EMBASE, Chinese Biomedical Literature Database, China National Knowledge Infrastructure, China Science and Technology Journal Database, Wanfang Database, and Clinical Trials Database were searched for relevant literature on the effects of intrathecal anesthesia or general anesthesia on cognitive function after hip fracture. The search was conducted using subject terms combined with free terms, including "total hip replacement", "cognitive function", "general anesthesia" as well as "intrathecal anesthesia", and the free terms were obtained from the MeSH database and the China Biomedical Literature Database. The search period was from database establishment to January 2024, with no language or other restrictions.

2.3 Inclusion and exclusion criteria

The details of the inclusion criteria were as follows: (1) The study design was a randomized controlled trial or a case-control study; (2) The inclusion subjects were elderly patients over 65 years of age who underwent hip fracture surgery. (3) The experimental group was elderly patients undergoing hip fracture surgery who received intrathecal anesthesia. (4) The control group was elderly hip fracture surgery patients who received general anesthesia. (5) The outcome indicators included primary and secondary outcomes. The primary outcome was the incidence of POD or POCD at 24 hours, 3 days, and 7 days postoperatively. Secondary outcomes included intraoperative hypotension, blood transfusion, postoperative pulmonary complications, acute myocardial infarction, renal failure, length of hospitalization, and 30-day postoperative mortality.

The details of the exclusion criteria were as follows: (1) duplicate published studies; (2) studies with incomplete data or unavailable data; (3) studies with selective reporting.

2.4 Literature screening

First, two researchers independently used Endnote to perform an initial assessment of the title and abstract of each literature according to the inclusion and exclusion criteria, and to exclude duplicate and irrelevant literature. Second, after the initial screening, two fellows independently reviewed the full text of the remaining literature and further excluded literature that did not meet the inclusion criteria. Finally, the two fellows exchanged and examined their respective included literature and finalized the final included literature. If there was staging between the two researchers, it was resolved through joint discussion or consultation with a third researcher. After the literature screening process and results are finalized, a PRISMA flowchart will be drawn by one of the researchers.

2.5 Data extraction

First, prior to data entry, the research team used Excel 2010 to create a form for extracting and recording data. Second, two researchers collected and entered basic information and study data for inclusion in the study, respectively. In this case, basic information included first author, year of publication, sample size, intervention, age, gender, and American Society of Anesthesiologists classification(ASA); Study data were primary outcomes and secondary outcomes included. If information for a study was unclear or insufficient, the corresponding author was contacted by e-mail and complete data were obtained. Finally, two fellows communicated and checked their respective entered data and finalized the final data. If staging was done between the two fellows, it was resolved through joint discussion or consultation with a third researcher.

2.6 Literature quality assessment

Two researchers rated the quality of each included study separately using the Cochrane Risk of Bias Assessment Tool. Literature quality was evaluated in the following seven areas: randomization methods, allocation concealment, intervention blinding, measurement blinding, significant dropout, selective reporting, and other biases. Each indicator contained three levels of high risk, unclear risk and low risk. At the end of the assessment, two fellows exchanged and examined the results of their respective literature quality evaluations and finalized the final data. If staging was done between the two fellows, it was resolved through joint discussion or consultation with a third fellow.

2.7 Statistical analysis

First, meta-analysis was performed using RevMan 5.4 software. In terms of effect sizes, relative risk (RR) and 95%

confidence interval (CI) were used as effect sizes for dichotomous variables, while weighted mean difference (WMD) and 95% confidence interval (CI) were used as effect sizes for continuous variables. In the heterogeneity test method, I² test and Q test were used to assess the level of heterogeneity. When I² < 50% and P > 0.1, the heterogeneity among combined studies was small; when I² ≥ 50% and P ≤ 0.1, the heterogeneity among combined studies was large. In terms of the combined effect size, the effect model was selected according to the level of heterogeneity. When the level of heterogeneity was low, a fixed-effects model was selected for analysis; when the level of heterogeneity was high, a random-effects effects model was selected. The statistical threshold for the above meta-analysis was P=0.05. Second, Stata 18.0 was used to conduct subgroup and sensitivity analyses to explore the sources of heterogeneity for indicators with significant heterogeneity and to assess the robustness of the results. Further, Stata 18.0 was used to draw funnel plots and perform Egger's test to assess the level of publication bias in the included studies. Symmetric funnel plots indicated no publication bias, whereas asymmetric funnel plots indicated a high likelihood of publication bias. Egger's test results showed that P>0.1 indicated no publication bias, whereas P≤0.1 indicated the presence of potential publication bias. Finally, GRADE was used to evaluate the quality of evidence for each outcome. A starting evidence rating of high was assigned to each outcome, followed by a downward adjustment of the evidence rating based on limitations, inconsistency, indirectness, imprecision, and publication bias, and a final evidence rating for each outcome was determined.

3. Discussion

This study addressed the effects of intrathecal versus general anesthesia on postoperative cognitive function in elderly hip fracture patients in a systematic evaluation and meta-analysis protocol design. Intrathecal and general anesthesia have significant pharmacological differences and may have different mechanisms of neurological effects. Intrathecal anesthesia has relatively little effect on the brain through nerve conduction in the plane of the paralyzed spinal cord, whereas general anesthesia acts on the brain through the blood circulation, and its drugs may cross the blood-brain barrier to directly affect neuronal function. This difference may contribute to the different effects of the two types of anesthesia on cognitive function.

However, the effects of intrathecal and general anesthesia on postoperative cognitive function in elderly hip fracture patients remain ambiguous. The main objective of designing this study protocol was to comprehensively assess the effects of intrathecal versus general anesthesia on postoperative cognitive function in elderly hip fracture patients and to explore possible mechanisms of action and safety issues. By systematically searching and combining available data, the investigators attempted to provide more comprehensive and reliable evidence to guide the choice of anesthesia modality for hip fracture in elderly patients in clinical practice, especially for those at high risk of cognitive impairment. The results of this research protocol are expected to provide important information to clinicians, patients, and policy makers to help them make more informed choices about anesthesia modalities. If the results of this analysis support that intrathecal or general anesthesia has little effect on cognitive function after hip fracture in the elderly, then this will further solidify the place of intrathecal or general anesthesia in clinical practice and provide even stronger support for anesthesia modality selection.

Although this research protocol endeavored to demonstrate the impact of different anesthetic options on postoperative cognitive function in older adults with hip fracture, it still faces some limitations and challenges. First, the impact of surgery itself on postoperative cognitive function is also a complicating factor. Elderly hip fracture surgery is often accompanied by intraoperative and postoperative stresses, such as bleeding, hypoxia, and the use of analgesic medications, all of which may affect patients' cognitive function. Second, there may be methodological differences between studies, including sample selection, dose adjustment, and outcome assessment, which may lead to data heterogeneity, as well as affect the interpretation and generalizability of results. Finally, although meta-analysis aims to synthesize the results of existing studies to improve statistical efficacy, it is still not possible to exclude the influence of potential publication bias and data reporting bias on the results. Therefore, these potential limitations need to be carefully considered when interpreting study results and discussed appropriately in the conclusions.

In summary, this study protocol aims to fill the knowledge gap regarding the effects of intrathecal versus general anesthesia on postoperative cognitive function in elderly hip fracture patients. Future studies can further explore the long-term effects of the two anesthesia modalities on cognitive function, as well as the possible mechanisms of the effects, to provide a more reliable evidence base for clinical practice. Meanwhile, clinicians should consider the patient's age, condition, and type of surgery when choosing anesthesia in order to develop individualized anesthesia protocols to maximize the protection of the patient's cognitive function.

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