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Neuraxial anesthesia compared to general anesthesia on postoperative results in subjects with hip fracture surgery: A meta-analysis

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Abstract

Background:

We performed a meta-analysis to evaluate the effects of neuraxial anesthesia compared to general anesthesia on postoperative results in hip fracture surgery subjects.

Methods:

A systematic literature search up to March 2022 was done and 20 studies included 298785 subjects with hip fracture surgery at the start of the study; 80783 of them were under neuraxial anesthesia, and 218002 of them were under general anesthesia. They were reporting relationships between the effects of neuraxial anesthesia compared to general anesthesia in subjects with hip fracture surgery. We calculated the odds ratio (OR) or the mean difference (MD) with 95% confidence intervals (CIs) to assess the effects of neuraxial anesthesia compared to general anesthesia in subjects with hip fracture surgery using the dichotomous or continuous method with a random or fixed-effect model.

Results:

Neuraxial anesthesia in subjects with hip fracture surgery was significantly related to lower acute myocardial infarction (OR, 0.73; 95% CI, 0.54-0.99, p=0.04), hypotension (OR, 0.37; 95% CI, 0.20-0.70, p=0.002), and postoperative cognitive dysfunction postoperative 1day (OR, 0.27; 95% CI, 0.17-0.42, p<0.001) compared to general anesthesia.

However, no significant difference was found between neuraxial anesthesia and general anesthesia in subjects with hip fracture surgery in a postoperative cognitive dysfunction postoperative 7days (OR, 0.64; 95% CI, 0.37-1.09, p=0.10), pneumonia (OR, 0.69; 95% CI, 0.29-1.62, p=0.39), length of hospital stay (MD, 0.75; 95% CI, -1.39-2.90, p=0.49), deep venous thrombosis (OR, 1.21; 95% CI, 0.50-2.95, p=0.68), 30-day mortality (OR, 1.12; 95% CI, 0.53-2.34, p=0.77), blood loss (MD, -57.47; 95% CI, -123.36-8.41, p=0.09), and delirium (OR, 0.98; 95% CI, 0.32-2.49, p=0.96).

Conclusions:

Neuraxial anesthesia in subjects with hip fracture surgery may decrease the risk of acute myocardial infarction, hypotension, and postoperative cognitive dysfunction postoperative 1 day compared to general anesthesia. Furthers studies are required to validate these findings.

Keywords: hip fracture surgery; neuraxial anesthesia; general anesthesia; epidural anesthesia; spinal anesthesia; postoperative results

Introduction

Hip fracture is one of the most frequent harms that happen in around 1.5 million subjects yearly worldwide; the number is to increase up to 5 million by 2050. [1] Hip fracture in elderly subjects with high comorbidities increases the risk of illness and death. [2] Most hip fractures should be managed surgically that need anesthesia. [3] The choice between neuraxial and general anesthesia is still conflicting. Numerous studies showed that neuraxial anesthesia has many advantages e.g. airway management avoidance, no intubation necessity, and prolonged postoperative analgesia compared to general anesthesia. [4] Also, neuraxial anesthesia can reduce

blood loss; possibly decrease the risk of postoperative nausea and vomiting, and deep venous thrombosis. [4] On the other hand, general anesthesia is shown to offer a more stable hemodynamic state, quicker induction, and avoid some complications e.g. pneumonia, epidural hematoma, and infection. [5] Though, the influence of the two anesthesia methods on subjects with hip fracture is debatable in postoperative results. A recent meta-analysis study including 15 studies showed that neuraxial anesthesia was related to a shorter length of hospital stay in subjects experiencing hip fracture surgery. This study highlighted the statistical significance of the length of hospital stay preferring spinal anesthesia, and the descriptions of the results differed extensively between studies, making assessment very hard. [6] Additional systematic review showed a decrease in-hospital mortality with neuraxial anesthesia with no significant difference for longer-term mortality. [7] Both studies suggested the need for further studies to clarify the difference. The present meta-analysis aimed to evaluate the effects of neuraxial (spinal/epidural) compared to general anesthesia in subjects with hip fracture surgery.

Methods

The present study followed the meta-analysis of studies in the epidemiology statement, [8] which was performed following an established protocol.

Study selection

Included studies were that with statistical measures of association (odds ratio [OR], frequency rate ratio, or relative risk, with 95% confidence intervals [CIs]) between the effects of neuraxial (spinal/epidural) compared to general anesthesia in subjects with hip fracture surgery.

Human studies only in the English language were considered. Inclusion was not restricted by study size or type. Publications excluded were review articles and commentary and studies that did not supply a degree of relationship. Figure 1 shows the whole study process.

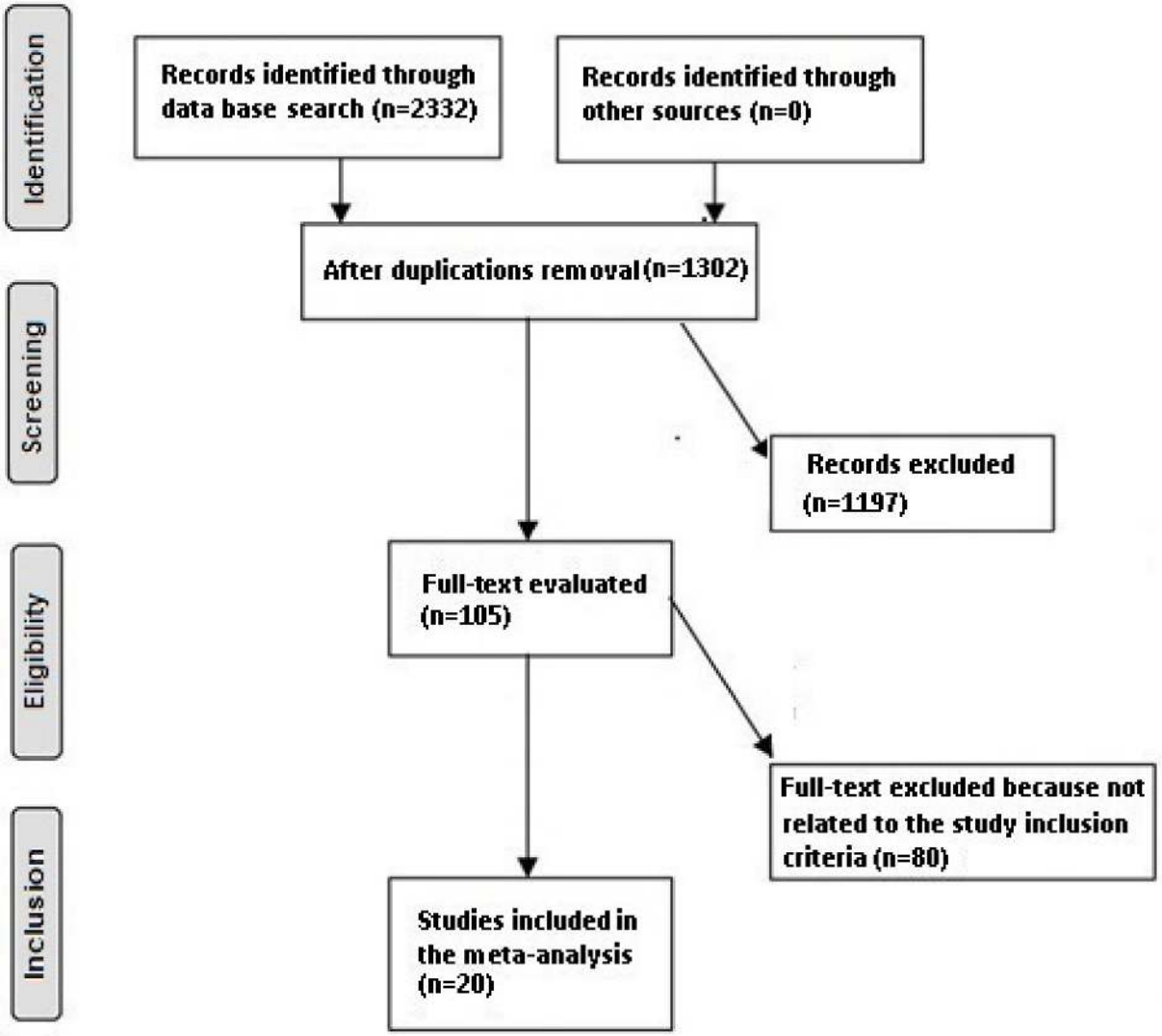

Figure 1. Schematic diagram of the study procedure

The articles were integrated into the meta-analysis when the following inclusion criteria were met:
1. The study was a randomized controlled trial or retrospective study.
2. The target population is subjects with hip fracture surgery
3. The intervention program was the neuraxial (spinal/epidural) and general anesthesia
4. The study included comparisons between the effects of neuraxial anesthesia compared to general anesthesia in subjects with hip fracture surgery on different variables
The exclusion criteria for the intervention groups were:
1. Studies that did not compare neuraxial to general anesthesia
2. Studies with surgery other than hip fracture surgery
3. Studies did not focus on the effect on postoperative results.

Identification

A protocol of search strategies was prepared according to the PICOS principle, [9] and we defined it as follow: P (population): subjects with hip fracture surgery; I (intervention/exposure): neuraxial anesthesia and general anesthesia; C (comparison): effects of neuraxial anesthesia compared to general anesthesia in subjects with hip fracture surgery on different variables; O (outcome): postoperative results; and S (study design): no restriction. [10] First, we conducted a systematic search of Embase, PubMed, Cochrane Library, OVID, and Google scholar till March 2022, by a blend of keywords and related words for hip fracture surgery, neuraxial anesthesia, general anesthesia, epidural anesthesia, spinal anesthesia, and postoperative results as shown in Table 1. All detected studies were gathered in an EndNote file, duplicates were removed, and the title and abstracts were revised to eliminate studies that did not show any relationship between the effects of neuraxial anesthesia compared to general anesthesia in subjects with hip fracture surgery. The remaining studies were examined for related information.

Table 1. Search Strategy for Each Database

Database	Search strategy
Pubmed	#1 "hip fracture surgery"[MeSH Terms] OR "neuraxial anesthesia"[All Fields] OR "general anesthesia"[All Fields] OR " spinal anesthesia"[All Fields] #2 "epidural anesthesia"[MeSH Terms] OR "hip fracture surgery"[All Fields] OR "postoperative results"[All Fields] OR " local recurrence rate "[All Fields] #3 #1 AND #2
Embase	'hip fracture surgery'/exp OR 'neuraxial anesthesia'/exp OR 'general anesthesia'/exp OR ' spinal anesthesia' #2 'epidural anesthesia'/exp OR 'ICBG'/exp OR 'postoperative results' OR 'local recurrence rate' #3 #1 AND #2
Cochrane library	#1 (hip fracture surgery):ti,ab,kw OR (neuraxial anesthesia):ti,ab,kw OR (general anesthesia):ti,ab,kw OR (spinal anesthesia):ti,ab,kw (Word variations have been searched) #2 (epidural anesthesia):ti,ab,kw OR (postoperative results):ti,ab,kw OR (local recurrence rate):ti,ab,kw (Word variations have been searched) #3 #1 AND #2

Screening

Data were abridged on the following bases; study-related and subject-related characteristics onto a standardized form. Last name of the primary author, period of study, year of publication, country, region of the studies, and study design; population type, the total number of subjects, demographic data and clinical and treatment characteristics; categories, qualitative and quantitative method of evaluation, information source, and outcome evaluation; and statistical analysis.[11] If a study qualified for inclusion based upon the aforementioned principles, data were extracted

independently by two authors. In case of disagreement, the corresponding author provided a final option. When there were different data from one study based on the assessment of the relationship between the effects of neuraxial anesthesia compared to general anesthesia in subjects with hip fracture surgery, we extracted them separately. The risk of bias in these studies; individual studies were evaluated using two authors who independently assessed the methodological quality of the selected studies. The “risk of bias tool" from the Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 was used to assess methodological quality. [12] In terms of the assessment criteria, each study was rated and assigned to one of the following three risks of bias: low: if all quality criteria were met, the study was considered to have a low risk of bias; unclear: if one or more of the quality criteria were partially met or unclear, the study was considered to have a moderate risk of bias; or high: if one or more of the criteria were not met, or not included, the study was considered to have a high risk of bias. Any inconsistencies were addressed by a reevaluation of the original article.

Eligibility

The main result concentrated on the effects of neuraxial anesthesia compared to general anesthesia in subjects with hip fracture surgery. An assessment of the effects of neuraxial anesthesia compared to general anesthesia in subjects with hip fracture surgery was extracted forming a summary.

Inclusion

Sensitivity analyses were limited only to studies reporting the relationship between the effects of neuraxial anesthesia compared to general anesthesia in subjects with hip fracture surgery. For subcategory and sensitivity analysis, we compared the effect of neuraxial anesthesia compared to general anesthesia.

Statistical analysis

We calculate the odds ratio (OR) and mean difference (MD) and 95% confidence interval (CI) using the dichotomous or continuous method with a random or fixed-effect model. We calculated the I^2 index and the I^2 index was ranged between 0% and 100%. When the I^2 index was about 0%, 25%, 50%, and 75% that specifies no, low, moderate, and high heterogeneity, respectively. [9] If the I^2 was > 50%, we used the random-effect; if it was < 50%, we used the fixed-effect. We used stratifying the original assessment per result categories as described previously to complete the subgroup analysis. A p-value for differences among subcategories of <0.05 was considered statistically significant. Publication bias was assessed quantitatively using the Egger regression test (publication bias is present if p≥0.05), and qualitatively, by visual inspection of funnel plots of the logarithm of odds ratios versus their standard errors.[11] the entire p-values were 2 tailed. Reviewer manager version 5.3 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark) was used to do all calculations and graphs.

Results

A total of 2332 unique studies were identified, of which 20 studies (between 2003 and 2020) fulfilled the inclusion criteria and were included in the study. [13-32]

The 20 studies included 298785 subjects with hip fracture surgery at the start of the study; 80783 of them were under neuraxial anesthesia, and 218002 of them were under general anesthesia. All studies evaluated the effects of neuraxial anesthesia compared to general anesthesia in subjects with hip fracture surgery.

Study size ranged from 20 to 280100 subjects with hip fracture surgery at the start of the study. The details of the 20 studies are shown in Table 2. 4 studies reported data stratified to acute myocardial infarction, 7 studies stratified to the hypotension, 4 studies stratified to the postoperative cognitive dysfunction postoperative 1day, 3 studies stratified to postoperative cognitive dysfunction postoperative 7days, 4 studies stratified to pneumonia, 6 studies stratified to the length of hospital stay, 4 studies reported data stratified to deep venous thrombosis, 7 studies stratified to 30-day mortality, 7 studies stratified to the blood loss, 8 studies stratified to 30-day mortality, and 5 studies reported data stratified to delirium.

Neuraxial anesthesia in subjects with hip fracture surgery was significantly related to lower acute myocardial infarction (OR, 0.73; 95% CI, 0.54-0.99, p=0.04) with no heterogeneity (I^2 = 0%), hypotension (OR, 0.37; 95% CI, 0.20-0.70, p=0.002) with moderate heterogeneity (I^2 = 53%), and postoperative cognitive dysfunction postoperative 1day (OR, 0.27; 95% CI, 0.17-0.42, p<0.001) with low heterogeneity (I^2 = 18%) compared to general anesthesia as shown in Figures 2-4.

However, no significant difference was found between neuraxial anesthesia and general anesthesia in subjects with hip fracture surgery in a postoperative cognitive dysfunction postoperative 7days (OR, 0.64; 95% CI, 0.37-1.09, p=0.10) with low heterogeneity (I^2 = 45%), pneumonia (OR, 0.69; 95% CI, 0.29-1.62, p=0.39) with moderate heterogeneity (I^2 = 56%), length of hospital stay (MD, 0.75; 95% CI, -1.39-2.90, p=0.49) with high heterogeneity (I^2 = 90%), deep venous thrombosis (OR, 1.21; 95% CI, 0.50-2.95, p=0.68) with high heterogeneity (I^2 = 95%), 30-day mortality (OR, 1.12; 95% CI, 0.53-2.34, p=0.77) with high heterogeneity (I^2 = 96%), blood loss (MD, -57.47; 95% CI, -123.36-8.41, p=0.09) with high heterogeneity (I^2 = 94%), and delirium (OR, 0.98; 95% CI, 0.32-2.49, p=0.96) with moderate heterogeneity (I^2 = 58%) as shown in Figures 5-11.

Selected studies stratified analysis that did and did not adjust for age, ethnicity, the effect of different neuraxial anesthesia, the need for perioperative blood transfusions, and prognosis between the two groups was not performed since no studies reported or adjusted for these factors.

Based on the visual inspection of the funnel plot as well as on quantitative measurement using the Egger regression test, there was no evidence of publication bias (p = 0.86). However, most of the included randomized

controlled trials were assessed to be of a low methodological quality. All studies did not have selective reporting bias, and no articles had incomplete outcome data and selective reporting.

Table 2. Characteristics of the selected studies for the meta-analysis

Study	Country	Total	Neuraxial anesthesia	General anesthesia
Casati, 2003 [13]	Italy	30	15	15
Rasmussen, 2003 [14]	UK	314	158	156
Hoppenstein, 2005 [15]	Palastine	60	30	30
Heidari, 2011 [16]	Iran	387	190	197
Biboulet, 2012 [17]	France	43	15	28
Messina, 2013 [18]	Italy	20	10	10
Silbert, 2014 [19]	Australia	98	48	50
Parker, 2015 [20]	UK	322	158	164
Shi, 2015 [21]	China	100	50	50
Sun, 2016 [22]	China	193	95	98
Haghighi, 2017 [23]	Iran	100	50	50
Meuret, 2018 [24]	France	40	21	19
Chen, 2018 [25]	China	63	31	32
Norouzi, 2018 [26]	Iran	165	135	30
Desai, 2018 [27]	USA	16226	6597	9629
Tzimas, 2018 [28]	Greece	68	35	33
Zhang, 2019 [29]	China	80	40	40
Turan, 2019 [30]	USA	280100	72930	207170
Shin, 2020 [31]	Korea	118	58	60
Akcan, 2020 [32]	Turkey	258	117	141
	Total	**298785**	**80783**	**218002**

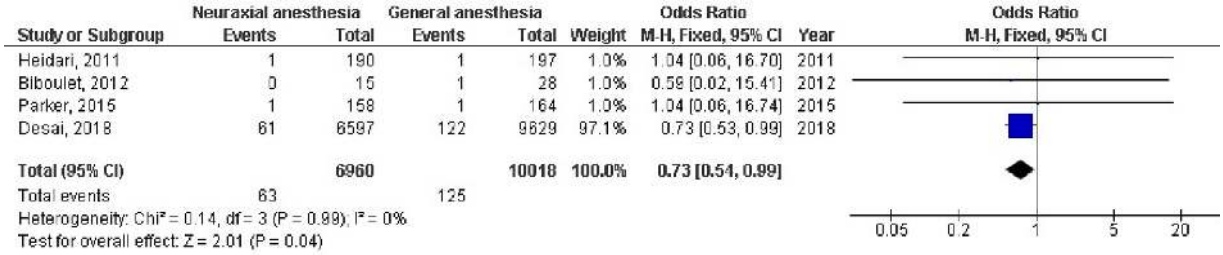

Figure 2. Forest plot of the effect of neuraxial anesthesia compared to general anesthesia on acute myocardial infarction in subjects with hip fracture surgery

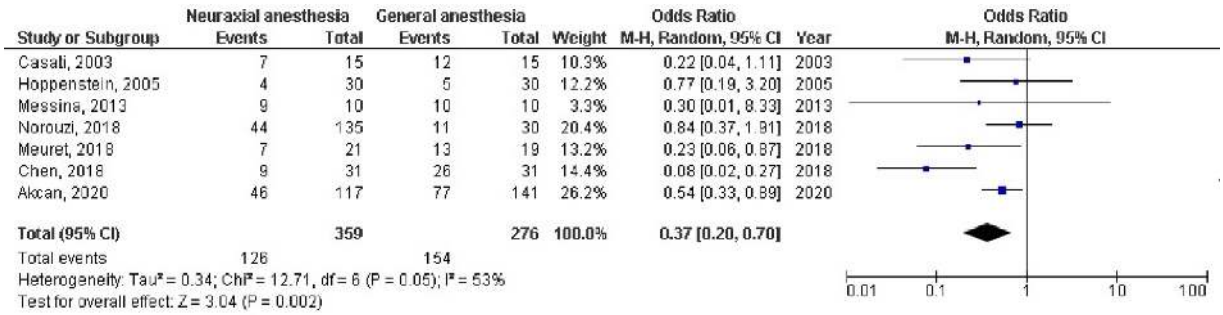

Figure 3. Forest plot of the effect of neuraxial anesthesia compared to general anesthesia on hypotension in subjects with hip fracture surgery.

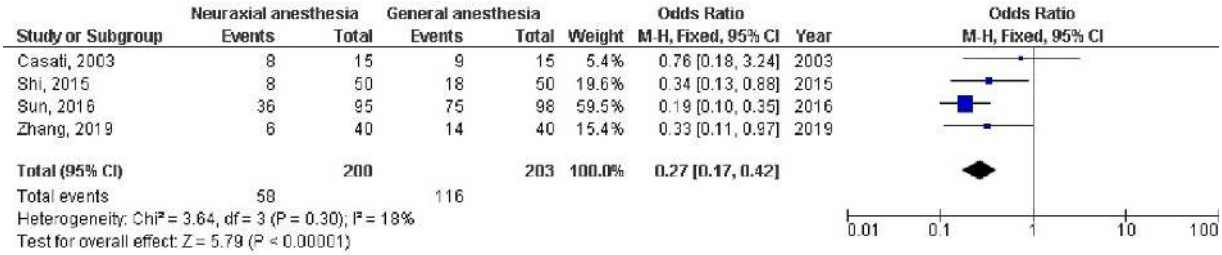

Figure 4. Forest plot of the effect of neuraxial anesthesia compared to general anesthesia on postoperative cognitive dysfunction postoperative 1day in subjects with hip fracture surgery.

Figure 5. Forest plot of the effect of neuraxial anesthesia compared to general anesthesia in on postoperative cognitive dysfunction postoperative 7days in subjects with hip fracture surgery

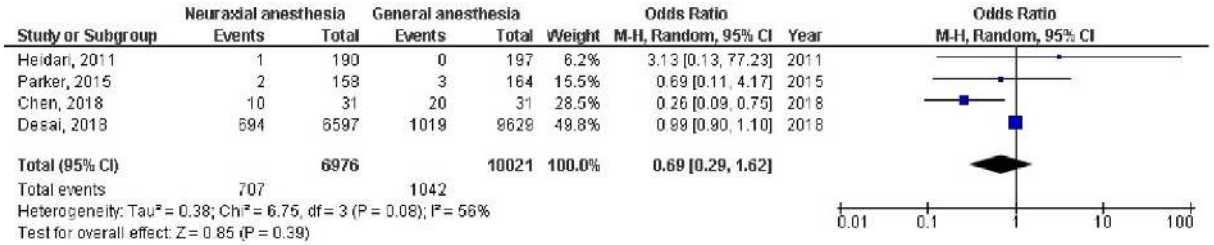

Figure 6. Forest plot of the effect of neuraxial anesthesia compared to general anesthesia on pneumonia in subjects with hip fracture surgery.

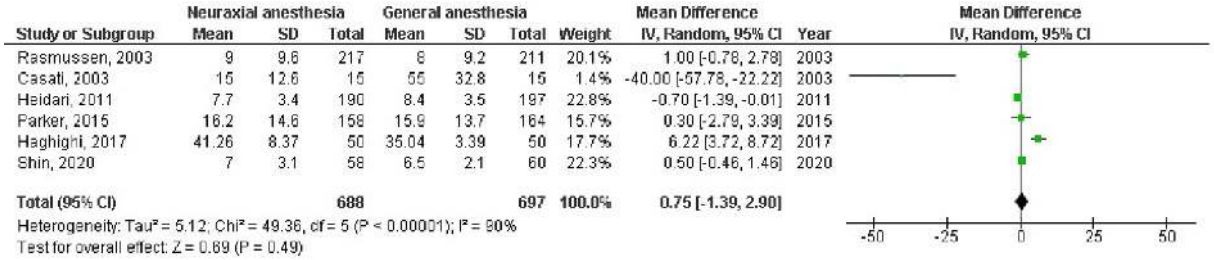

Figure 7. Forest plot of the effect of neuraxial anesthesia compared to general anesthesia on length of hospital stay in subjects with hip fracture surgery.

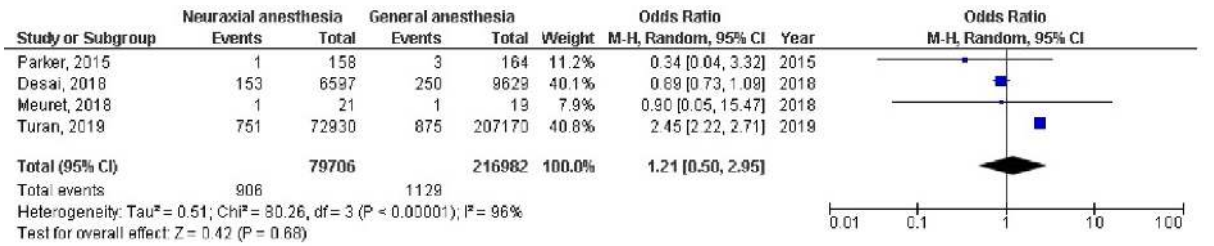

Figure 8. Forest plot of the effect of neuraxial anesthesia compared to general anesthesia on deep venous thrombosis in subjects with hip fracture surgery

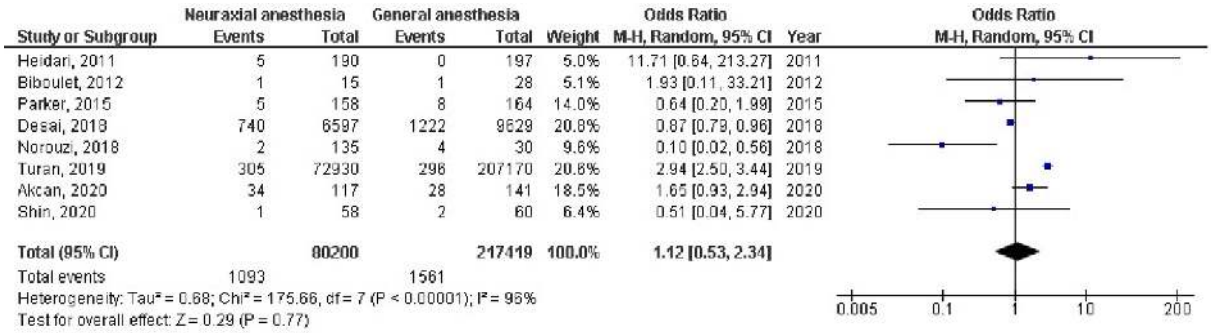

Figure 9. Forest plot of the effect of neuraxial anesthesia compared to general anesthesia on 30-day mortality in subjects with hip fracture surgery.

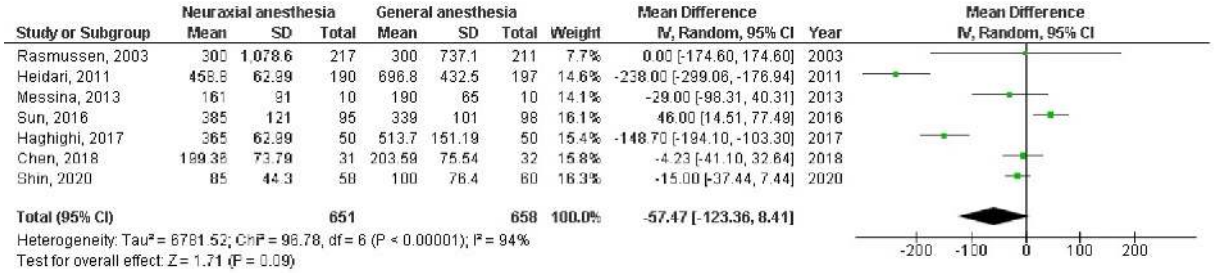

Figure 10. Forest plot of the effect of neuraxial anesthesia compared to general anesthesia on blood loss in subjects with hip fracture surgery.

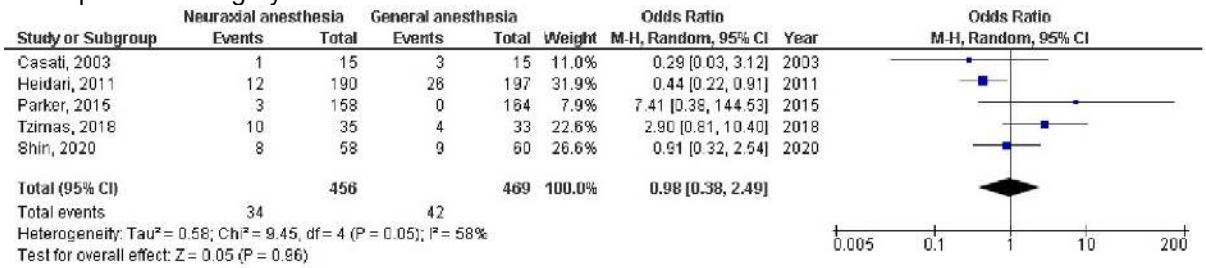

Figure 11. Forest plot of the effect of neuraxial anesthesia compared to general anesthesia on delirium in subjects with hip fracture surgery.

Discussion

This meta-analysis study based on 20 studies included 298785 subjects with hip fracture surgery at the start of the study; 80783 of them were under neuraxial anesthesia, and 218002 of them were under general anesthesia. [13-32] Neuraxial anesthesia in subjects with hip fracture surgery was significantly related to lower acute myocardial infarction, hypotension, and postoperative cognitive dysfunction postoperative 1day compared to general anesthesia.

However, no significant difference was found between neuraxial anesthesia and general anesthesia in subjects with hip fracture surgery in a postoperative cognitive dysfunction postoperative 7days, pneumonia, length of hospital stay, deep venous thrombosis, 30-day mortality, blood loss, and delirium. [13-32] Though the analysis of outcomes should be done with caution because of the low number of studies in each parameter evaluated in our meta-analysis, suggesting more studies relating the type of anesthesia, and postoperative results in subjects with hip fracture surgery to validate these findings. The need for more studies are very obvious in the results of postoperative cognitive dysfunction postoperative 7days and, blood loss wither their low p-values (p=0.10, and p=0.09, respectively) The number of studies in each analysis was small; hence the overall evidence was low, showing the need of further research possibly to significantly influence confidence in the effect evaluation. Present practice showed that the number of subjects who needed blood transfusion was larger in the general anesthesia group, which means subjects getting Neuraxial anesthesia had lower blood loss than those getting general anesthesia. [23] A systematic review with 66 articles revealed that the use of neuraxial anesthesia caused a significant reduction in assessed blood loss. [33] Though similar to our results, a meta-analysis study indicated that there was an insufficient difference between neuraxial anesthesia and general anesthesia in reducing intraoperative blood loss. [34]

The explanations for these findings are likely multi-factorial. Neuraxial anesthesia can cause lower heart rate and blood pressure than general anesthesia by blocking α and β adrenergic receptors; so, controlled blood pressure

lead to intraoperative lower blood loss and acute myocardial infarction in neuraxial anesthesia subjects. [17] Urwin et al. proposed that the frequency of myocardial infarction and pneumonia was lower in subjects with neuraxial anesthesia, and a significantly lower frequency of intraoperative hypotension was identified in subjects receiving general anesthesia. [35] Though, Sutcliffe et al. assessed 1333 hip surgery subjects and found no significant difference. [36] Delirium is a common postoperative complication, which leads to lasting cognitive and functional decline, and increasing length of hospital stay. [20] However, there was a significant reduction in postoperative cognitive dysfunction postoperative 1 day and a relative reduction in postoperative cognitive dysfunction postoperative 7days in neuraxial anesthesia subjects compared to general anesthesia subjects these effects were not extended to delirium. There are several additional factors in developing delirium, e.g. urinary retention, pain, infection, myocardial and cerebral ischemia, constipation, and electrolyte imbalance. [37] Numerous studies have assessed the frequency of delirium in elderly subjects admitted to being in the hospital for different reasons, and the frequency was assessed to range from 30 to 60%. [37-39] Some subject features are easy to have delirium e.g. sleep deprivation, medical immobilities, pre-existing cognitive impairment, visual impairment, hearing impairment, and poly-pharmacy. [40, 41]

A retrospective study stated that the anesthesia method has a slight effect on postoperative mortality, and the anesthesia type must be selected based on the subject physical characteristics. [42] The previous randomized clinical trials study with 425 subjects showed that their comorbid conditions had a great effect on the 30-day mortality in old subjects e.g. diabetes, and cardiovascular disease. [43] Surgery delay for >24 hours was the main factor affecting postoperative mortality in old hip fracture subjects. [44] Another retrospective cohort study assessing 42230 subjects with hip fracture surgery showed that a preoperative delay time of >24 hours was related to a high risk of 30-day mortality and other postoperative complications. [45] Zuo et al. recommended that neuraxial anesthesia may be better in hip fracture surgery. [46] Also, Neuman et al. performed a matched retrospective cohort study with 56729 subjects and found a relatively shorter length of hospital stay with neuraxial anesthesia. They also suggested that the fracture type and conducted surgery procedure were important factors e.g. minimally invasive approaches and optimal quality of fracture decrease might reduce the length of hospital stay. [47] Though, Grant et al. confirmed that the pain severity was lower in subjects with general anesthesia, resulting in a shorter length of hospital stay. [48] Also, the waiting time for surgery increases the length of hospital stay. [49] Perioperative deep venous thrombosis is common in hip fracture subjects. Numerous studies showed that neuraxial anesthesia was related to a lower frequency of deep venous thrombosis compared to general anesthesia. [35, 50, 51] That might be due to that in neuraxial anesthesia sympathetic block can cause vasodilatation of the lower limbs, and increased blood flow to the lower limbs that decrease the coagulability and viscosity of blood. [52] However, we did not find any significant difference, and that might be due to the low number of studies found evaluating this factor (4 studies). Yet, a Cochrane review published in 2016 with 31 randomized controlled trials indicated a decrease in the risk of deep venous thrombosis in the neuraxial group with no potent thromboprophylaxis with a very low level of evidence. [53] Another Cochrane review showed that there was a minimal advantage for neuraxial anesthesia in the frequency of deep venous thrombosis. [54]

This meta-analysis showed the relationship between the type of anesthesia and postoperative results in subjects with hip fracture surgery. However, further studies are needed to validate these potential relationships. Also, further studies are needed to deliver a clinically meaningful difference in perioperative and postoperative results in subjects with hip fracture surgery. These studies must comprise larger with more homogeneous samples. This was suggested also in a previous similar meta-analysis study which showed a similar effect of type of anesthesia on postoperative results in subjects with hip fracture surgery. [55] Well-conducted randomized controlled trials are also needed to assess these factors and the combination of different age, ethnicity, the effect of different neuraxial anesthesia, the need for perioperative blood transfusions, and prognosis between the two groups; since our meta-analysis study could not answer whether they are associated with the results.

In summary, the data suggest that neuraxial anesthesia in subjects with hip fracture surgery may decrease the risk of acute myocardial infarction, hypotension, and postoperative cognitive dysfunction postoperative 1day compared to general anesthesia. Further studies are needed to validate these findings.

Limitations

There may be selection bias in this study since so many of the studies found were excluded from the meta-analysis. However, the studies excluded did not satisfy the inclusion criteria of our meta-analysis. Also, we could not answer whether the results are associated with age, ethnicity, the effect of different neuraxial anesthesia, the need for perioperative blood transfusions, and prognosis between the two groups or not. The study designed to assess the relationship between the effects of neuraxial anesthesia compared to general anesthesia in subjects with hip fracture surgery was based on data from previous studies, which might cause bias induced by incomplete details. The meta-analysis was based on 20 randomized control trials; 10 studies were small, ≤ 100. Variables including age, ethnicity, and nutritional status of subjects were also the possible bias-inducing factors. Some unpublished articles and missing data might lead to a bias in the pooled effect. Also, the criteria of surgical treatment choice were not fully explained. Subjects were using different treatment schedules, dosage of the anesthesia, sedation use, and health care systems. Also, the varying definition of the length of hospital stay and delirium might cause biases.

Conclusions

Neuraxial anesthesia in subjects with hip fracture surgery may decrease the risk of acute myocardial infarction, hypotension, and postoperative cognitive dysfunction postoperative 1 day compared to general anesthesia. However, no significant difference was found between neuraxial anesthesia and general anesthesia in subjects with hip fracture surgery in a postoperative cognitive dysfunction postoperative 7days, pneumonia, length of hospital stay, deep venous thrombosis, 30-day mortality, blood loss, and delirium. Though the analysis of outcomes should be done with caution because of the low number of studies in each parameter evaluated in our meta-analysis, suggesting the need for more studies relating the effects of neuraxial anesthesia compared to general anesthesia in subjects with hip fracture surgery to validate these findings.

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