



# **The Analysis of Multiple Outcomes between General and Regional Anesthesia in Hip Fracture Surgery: A Systematic Review and Meta-Analysis of Randomized Controlled Trials**

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Abstract: Surgical interventions in hip fracture have been associated with multiple adverse events, including perioperative hypotension and mortality, making the choice of the anesthetic method for this procedure crucial. There is still no consensus on whether regional (RA) or general (GA) anesthesia should be used to maintain hemodynamic stability and more favorable outcomes. Therefore, this meta-analysis examines the differences between RA and GA groups in the incidence of mortality, intraoperative hypotension, and other intra- and postoperative complications. The comparison is essential given the rising global prevalence of hip fractures and the need to optimize anesthesia strategies for improved patient outcomes, particularly in an aging population. We followed PRISMA guidelines (PROSPERO #CRD42022320413). We conducted the search for studies published in English before March 2022 in PubMed, Google Scholar, and the Cochrane Library. We included RCTs that compared general and regional anesthesia in adult patients having hip fracture surgical interventions. The primary outcome was perioperative mortality. The secondary outcomes were peri- or postoperative complications and duration of hospital stay. We conducted a meta-analysis in RevMan (version 5.4). We examined the quality of the methodology with the Cochrane risk of bias 2 tool, while the quality of evidence was determined with GRADE. Fifteen studies with 4110 patients were included. Our findings revealed no significant difference between general and regional anesthesia in risk of perioperative mortality (RR = 1.42 [0.96, 2.10], *p*-value = 0.08), intraoperative complications, or duration of hospital length of stay. Our results suggest that regional anesthesia and general anesthesia have comparable safety and can be used as alternatives based on specific patient requirements.

**Keywords:** general anesthesia; regional anesthesia; spinal anesthesia; epidural anesthesia; hip fracture; surgery; outcomes

# 1. Introduction

The number of new cases of hip fracture is projected to exceed two and a half million worldwide by the first quarter of the 21st century [1]. Hip fracture is associated with a substantial perioperative complication rate of 6–19% overall [2,3] and a mortality rate of 3–8% [4–7]. Among complications, hypotension poses a particular concern, especially in the frail elderly population, given its association with elevated mortality at 30 days [8,9]. Different methods of anesthetic techniques, fluid therapy, and vasopressors are used to maintain the stability of the mean arterial pressure (MAP) [10,11]. Moreover, directing fluid and vasopressor administration based on a thorough hemodynamic evaluation, conducted through preoperative echocardiography and noninvasive monitoring, is crucial due to the potential adverse events associated with hypo- and hypervolemia. Hypovolemia may lead to decreased preload, resulting in cardiac output reduction and inadequate organ perfusion, while hypervolemia can cause systemic and pulmonary congestion, leading to decreased



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**Copyright:** © 2023 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https:// creativecommons.org/licenses/by/ 4.0/). organ function. Currently, there are several approaches to monitoring fluid responsiveness. One option is the visualization of the inferior vena cava (IVC) diameter with echocardiography from the subcostal region or using a coronal trans-hepatic approach, although more research is needed to determine the appropriate thresholds for fluid responsiveness when employing the latter [12]. Alternatively, continuous noninvasive blood pressure monitoring can be used as it has been associated with a lower incidence of hypotension and hypertension during general anesthesia compared to intermittent cuff measurement [13]. Furthermore, the use of artificial intelligence for continuous noninvasive monitoring of blood pressure during general anesthesia has demonstrated promising results in hemodynamic assessment [14]. Despite the various attempts to prevent hypotensive events and other adverse outcomes, a definitive agreement on the best anesthesia approach for this surgery has not been reached.

General anesthesia (GA) is still widely used in hip fracture surgery, yet multiple regional anesthetic (RA) techniques are also gaining popularity. Thus, spinal anesthesia (SA) is often favored over general anesthesia in patients with a higher susceptibility to complications due to its effectiveness, simplicity, and minimal impact on cognitive and pulmonary function [15]. In fact, between 2007 and 2017, the usage of SA for hip fracture surgery increased by 50% [16]. However, SA is associated with severe hypotension, as it reduces the body's ability to compensate for changes in blood pressure, particularly in frail populations with numerous underlying health conditions [17]. On the other hand, continuous spinal anesthesia (CSA) has been shown to more effectively maintain hemodynamic stability compared with single-shot SA or GA thanks to low-fractionated administration of local anesthetic [10,11,18]. A recent meta-analysis also demonstrated that a 6.5 mg dose of SA was effective and associated with a lower incidence of hypotension compared to a 10.5 mg dose [19]. The authors suggest that a smaller dose provides an effective sensory block in conjunction with opiates through synergistic action of the two while minimizing systemic effects, including hemodynamic outcomes [19]. Similarly, multiple nerve blocks (MNBs) have been used as a GA alternative to minimize hypotensive episodes with some studies reporting promising results [20,21].

This systematic review with meta-analysis (SR&MA) aims to answer two main questions: Are there differences in death rates between the general and regional (SA, CSA, MNB) anesthesia groups? Are there differences in hypotension and other intraoperative and postoperative complications between the two groups?

# 2. Materials and Methods

# 2.1. Protocol

We conducted this study using the PRISMA guidelines [22]. PRISMA diagram is available in Figure 1. The protocol was developed prior to conducting the study and is publicly available in PROSPERO (#CRD42022320413). There were no deviations from the protocol.

#### 2.2. Search Strategy and Criteria

The systematic search for relevant articles published before 15 March 2022 was performed using the following databases: PubMed, Google Scholar, and the Cochrane Library. The search terms used are available in Supplementary Materials. After searching the databases, a manual search was conducted by going through the references of the identified studies.

#### 2.3. Screening

Screening of the articles was conducted by two authors in an independent manner. In case of disagreements, a third author was consulted. The studies were screened based on titles, then abstracts, and finally, by full texts. We included studies based on these criteria:

Inclusion criteria:

- Randomized controlled trials (RCTs);
- Adult patients with hip fractures undergoing surgical procedures;
- Comparing regional anesthesia versus general anesthesia;
- Reporting outcomes of interest: mortality (primary) and intra- and postoperative complications (secondary).

Exclusion criteria:

- Study designs other than RCTs;
- Pediatric studies;
- Not comparing regional to general anesthesia;
- Not reporting outcomes of interest.

Studies that did not meet the specified inclusion criteria were excluded.



Figure 1. PRISMA diagram.

# 2.4. Data Extraction and Statistical Methods

Two authors extracted data independently. Any disagreements were solved by consulting a third author. We extracted study characteristics (country, primary/secondary outcomes, sample size, age) in a data table (Supplementary Table S1). Numeric data on the outcomes of interest were extracted into a spreadsheet for further analysis. If a study did not report data on an outcome of interest for this meta-analysis, we did not include that study in the analysis of that outcome. The primary outcome was death, while the secondary ones were other adverse events and duration of hospitalization. For each outcome, the risk ratio or standardized mean difference was calculated, and sensitivity analysis was conducted. If required, we employed mathematical techniques to calculate the sample mean and standard deviation [23,24]. Given the differences in study populations and procedures, a high level of heterogeneity among the studies was anticipated. Therefore, the random effects model was employed for the analysis. A significance level of p < 0.05 was adopted. Forest plots were constructed for each outcome. To assess statistical heterogeneity, we utilized the  $I^2$  statistic. The data analysis was performed in the software "Review Manager (RevMan) [Computer program]. Version 5.4 (The Cochrane Collaboration, 2020, Copenhagen, Denmark)".

# 2.5. Quality Assessment

The quality of the methodology of the studies included in the review was evaluated with the Cochrane Risk of Bias Tool 2 [25]. We evaluated each study as "low risk", "some concerns", or "high risk" of bias based on the "randomization process", "deviations from the intended intervention", "missing outcome data", "measurement of the outcome", and "selection of the reported results". To assess the quality of the evidence of the main outcomes, we analyzed them with the GRADE [26]. We analyzed each outcome for "risk of bias", "inconsistency", "indirectness", and "imprecision" and summarized the overall quality of the outcome as "high", "moderate", "low", or "very low".

## 3. Results

## 3.1. Included Studies

The systematic search yielded 616 articles. After duplicate removal and title screening, 15 RCTs comprising 4110 patients were identified for inclusion in the MA [27–41] (Figure 1, Table 1).

First Author, Year	Country	Groups	Study Outcomes	Age (Mean $\pm$ SD)	N of Patients: Total (I/C)	Local Anesthetic
Bigler, 1985 [27]	NG	GA SA	Prim.—postoperative mental function and morbidity	$80.1 \pm 1.6$ 77.6 $\pm 2.3$	40 (20/20)	SA: 3 mL bupivacaine 0.75%
Davis, 1981 [28]	New Zealand	GA SA	Prim.—morbidity and mortality	$\begin{array}{c} 81\pm8.2\\ \\ 78\pm8.6\end{array}$	132 (64/68)	SA: tetracaine 0.5% in 6% dextrose with adrenaline 1:100,000 without barbotage in 51 patients Hyperbaric cinchocaine 0.5% in 6% dextrose in 13 patients
Davis, 1987 [29]	New Zealand	GA SA	Prim.—mortality	$79.5\pm8.8$	538 (259/279)	SA: tetracaine, nupercaine or bupivacaine (optional), hyper/iso-baric
Juelsgaard, 1998 [30]	Denmark	GA ISA SDSA	Prim.—incidence of myocardial ischemia in atherosclerotic patients	85.7 (72–94) 82.2 (65–99) 79.6 (72–92)	43 (14/15/14)	ISA: Bupivacaine 0.5% plain SDSA: 2.5 mL bupivacaine plain
Li, 2021 [31]	China	GA SA EA NB	Prim.—delirium within 7 days. Sec.—delirium characteristics, pain intensity in week 1, death at 30 days, hospital LoS, complications, and long-term and financial outcomes	77 (72–82) 77 (71–82)	942 (471/471)	SA: ropivacaine EA, NB: ropivacaine, bupivacaine, lidocaine
McKenzie, 1980 [32]	UK	GA SA	Prim.—postoperative arterial oxygenation and intraoperative mortality	$76.8 \pm 1.38$ $74.5 \pm 2.29$	100 (49/51)	SA: 1.3–1.5 mL hyperbaric cinchocaine 0.5%
McKenzie, 1984 [33]	UK	GA SA	Prim.—mortality at 1 year	$74.2 \pm 1.7$ $75.4 \pm 1.4$	150 (75/75)	SA: 1.3–1.5 mL hyperbaric
McKenzie, 1985 [34]	UK	GA SA	Prim.—incidence of deep vein thrombosis and pulmonaryembolism	$73.9 \pm 4.1$ $72.3 \pm 2.8$	40 (20/20)	SA: 1.2–1.5 mL hyperbaric conchocaine
McLaren, 1978 [35]	UK	GA SA	Prim.—mortality and morbidity	$76 \pm 9.7$ $75.6 \pm 10.3$	55 (26/29)	SA: 0.5 mL hyperbaric cinchocaine (0.5% in 6% dextrose)
Messina, 2013 [36]	Italy	GA SA	Prim.—hemodynamic response	$\begin{array}{c} 81.8\pm 6.3\\ 83.9\pm 9.4\end{array}$	20 (10/10)	SA: 7.5 mg levobupivacaine diluted from 7.5 mg/mL with 2 mL distilled water + preservative-free sufentanil 5 ug
Neuman, 2021 [37]	USA, Canada	GA SA	Prim—death or inability to walk independently at 60 days	$77.7 \pm 10.7$ 78.4 + 10.6	1572 (782/790)	Varied across study sites
Parker, 2015 [38]	UK	GA SA	Prim.—mortality	82.9 (range 52–105) 83.0 (range 59–99)	322 (158/164)	At the discretion of the anesthetist
Svartling, 1986 [39]	Finland	GA SA	Prim.—arterial blood, pressure, arterial oxygen tension, plasma levels of cortisol	$79.6 \pm 2.1$ $75.1 \pm 1.1$	30 (15/15)	SA: 3 mL isobaric bupivacaine hydrochloride 0.5%
Tzimas, 2018 [40]	Greece	GA SA	Prim.—POCD at 30 days after surgery, possible differences Sec.—delirium on days 1, 2, 3, 4	$77.11 \pm 6.5$ $75.09 \pm 6.08$	70 (37/33)	SA: fentanyl 20 mcg + ropivacaine 0.75% based on somatometric characteristics
White, 1980 [41]	South Africa	GA SA PCB	Prim.—pre, intra-, and postoperative events and mortality	$78 \pm 7.8$ $80 \pm 9.1$ $78 \pm 7.3$	56 (20/20/16)	SA: hyperbaric cinchocaine 0.6–0.8 mL

Table 1. Characteristics of the included studies.

Abbreviations: C, control; I, intervention; N, number; POCD, postoperative cognitive dysfunction; prim., primary outcome; sec., secondary outcome; SD, standard deviation; GA, general anesthesia; SA, spinal anesthesia; ISA, incremental spinal anesthesia; SDSA, single-dose spinal anesthesia; PCB, psoas compartment block; EA, epidural block; NB, nerve blocks; NG, not given; LoS, length of stay.

#### 3.2. Mortality

There was no difference in the risk of death in the RA group compared to the GA group (RR = 1.42; 95% CI: [0.96, 2.10], *p*-value = 0.08) (Figure 2). Sensitivity analysis revealed that excluding either Davis et al. (1987) [29] or Li et al. (2022) [31] changed the result favoring RA. We should note that most included studies reported values for the period of four weeks or one month, Neuman et al. (2021) [37] reported values for the period of "after 60 days", and Bigler et al. (1985) [27] did not mention the specific postoperative period.

	GA		RA			Risk Ratio	Ris	k Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Ran	dom, 95% Cl
Bigler 1985	1	24	1	22	2.0%	0.92 [0.06, 13.79]		-
Davis 1981	9	68	3	64	8.3%	2.82 [0.80, 9.97]		
Davis 1987	16	279	17	259	22.4%	0.87 [0.45, 1.69]		•
Juelsgaard 1998	2	14	2	14	4.3%	1.00 [0.16, 6.14]		4
Li 2021	4	464	8	469	9.1%	0.51 [0.15, 1.67]		+
McKenzie 1980	8	51	5	49	11.4%	1.54 [0.54, 4.38]	-	
McKenzie 1984	13	75	8	75	16.6%	1.63 [0.72, 3.69]		- <b> </b>
McLauren 1978	9	29	1	26	3.6%	8.07 [1.10, 59.44]		·
Neuman 2021	13	790	5	782	11.7%	2.57 [0.92, 7.18]		+- <b>-</b>
Parker 2015	8	164	5	158	10.5%	1.54 [0.52, 4.61]	_	<b>+•</b>
Total (95% CI)		1958		1918	100.0%	1.42 [0.96, 2.10]		•
Total events	83		55					
Heterogeneity: Tau <sup>2</sup> = Test for overall effect:	0.06; Ch Z = 1.78	0.02 0.1						
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**Figure 2.** Death. Square—risk ratio for individual studies; line—confidence interval; diamond—pooled risk ratio [27–33,37,38].

#### 3.3. Intraoperative Hypotension

We did not observe a difference between the RA and the GA groups in the risk of hypotension (RR = 1.24 [0.59, 2.60], p = 0.57) (Figure 3). Among the six studies with 1095 patients, there was substantial heterogeneity at I<sup>2</sup> = 76%.

	GA		RA			Risk Ratio	Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl		
Davis 1981	0	68	1	64	4.6%	0.31 [0.01, 7.57]			
Davis 1987	67	279	98	259	27.5%	0.63 [0.49, 0.82]			
Juelsgaard 1998	9	14	2	14	14.8%	4.50 [1.18, 17.21]			
McLauren 1978	1	29	3	26	8.1%	0.30 [0.03, 2.70]			
Messina 2013	9	10	5	10	23.3%	1.80 [0.94, 3.46]			
Parker 2015	17	164	9	158	21.7%	1.82 [0.84, 3.96]	+		
Total (95% CI)		564		531	100.0%	1.24 [0.59, 2.60]	-		
Total events	103		118						
Heterogeneity: Tau² =	0.51; Ch	i² = 20.1	66, df = 5	(P = 0.	0009); <b>i</b> ² :	= 76%			
Test for overall effect: Z = 0.56 (P = 0.57) 0.01 0.1 1 10 10 Favors GA Favors RA									

**Figure 3.** Intraoperative hypotension. Square—risk ratio for individual studies; line—confidence interval; diamond—pooled risk ratio [28–30,35,36,38].

# 3.4. Cardiac and Cerebrovascular Complications

We combined myocardial infarction, cardiac failure, and cardiovascular accident into the overall cardiac and cerebrovascular complications outcome. There was no significant difference between the GA and RA groups in terms of myocardial infarction (RR = 1.23 [0.54, 2.82]), cardiac failure (RR = 0.85 [0.23, 3.07]), or cerebrovascular accident (RR = 0.60 [0.03, 12.83]). The lack of difference was maintained at the exclusion of any study (Figure 4).

## 3.5. Vascular Complications

For deep vein thrombosis, there was no difference between the two groups at RR = 1.36 [0.43, 4.29]. It should be mentioned that the result changed in favor of RA when the study by McKenzie et al. (1985) [34] was excluded. For postoperative pulmonary embolus, the results for the two groups were comparable at RR = 1.59 [0.61, 4.14] (Figure 5). The overall result of the model for vascular complications is in favor of RA.

	GA		RA			Risk Ratio		Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl		M-H, Random, 95% Cl	
1.2.1 Myocardial infa	rction								
Davis 1987	1	279	2	259	7.7%	0.46 [0.04, 5.09]	-		
Juelsgaard 1998	0	14	0	14		Not estimable			
Li 2021	0	471	1	471	4.3%	0.33 [0.01, 8.16]			
McKenzie 1984	2	75	0	75	4.8%	5.00 [0.24, 102.42]			_
Neuman 2021	9	790	6	782	41.6%	1.48 [0.53, 4.15]			
Parker 2015	1	164	1	158	5.8%	0.96 [0.06, 15.27]			
Subtotal (95% CI)		1793		1759	64.2%	1.23 [0.54, 2.82]		-	
Total events	13		10						
Heterogeneity: Tau <sup>2</sup> =	0.00; Ch	i <b>²</b> = 2.2	7, df = 4 (	P = 0.6	9); I <b>²</b> = 09	6			
Test for overall effect:	Z = 0.49	(P = 0.6	62)						
1.2.2 Cardiac failure									
Davis 1987	3	279	3	259	17.4%	0.93/0.19/4.561			
Neuman 2021	ň	790	2	782	4.8%				
Parker 2015	1	164	- 0	158	4.3%	2 89 0 12 70 44			-
Subtotal (95% CI)		1233	-	1199	26.5%	0.85 [0.23, 3.07]			
Total events	4		5					_	
Heterogeneity: Tau <sup>2</sup> =	0.00; Ch	i <sup>2</sup> = 1.4	7. df = 2 (	P = 0.4	8); I <sup>2</sup> = 09	6			
Test for overall effect:	Z = 0.26	(P = 0.8)	30)						
1.2.3 Cerebrovascula	ar accide	nt							
Davis 1987	0	279	3	259	5.0%	0.13 [0.01, 2.56]			
McKenzie 1984	1	75	0	75	4.3%	3.00 [0.12, 72.49]			-
Parker 2015	0	164	0	158		Not estimable			
Subtotal (95% CI)		518		492	9.4%	0.60 [0.03, 12.83]			
Total events	1		3						
Heterogeneity: Tau <sup>2</sup> =	2.45; Ch	i² = 2.0	0, df = 1 (	P = 0.1	6); I <sup>2</sup> = 50	1%			
Test for overall effect:	Z = 0.33	(P = 0.7)	74)						
Total (95% CI)		3544		3450	100.0%	1.04 [0.53, 2.01]		•	
Total events	18		18					Ī	
Heterogeneity: Tau <sup>2</sup> =	0.00: Ch	i <sup>2</sup> = 6.3	1. df = 9 (	P = 0.7	1): <b>I</b> ² = 09	6	L		
Test for overall effect:	Z = 0.10	(P = 0.9)	92)				0.005	U.1 1 10	200
Test for subaroup diff	erences	Chi <sup>z</sup> =	0.38. df =	2 (P =	0.83), <b>i</b> ² =	: 0%		Favors GA Favors RA	

**Figure 4.** Cardiac and cerebrovascular complications. Square—risk ratio for individual studies; line—confidence interval; diamond—pooled risk ratio [29–31,33,37,38].



**Figure 5.** Vascular complications. Square—risk ratio for individual studies; line—confidence interval; diamond—pooled risk ratio [27–29,33,34,37,38].

## 3.6. Acute Kidney Disease

The model does not favor RA over GA (Figure 6) since RR with 95% CI is equal to 1.68 [0.28, 10.27].

# 3.7. Postoperative Pneumonia

The model does not favor RA over GA (Figure 7) since RR with 95% CI is equal to 1.19 [0.73, 1.96].

	GA		RA			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% CI
Davis 1981	1	68	0	64	32.3%	2.83 [0.12, 68.14]	
Davis 1987	0	279	1	259	32.0%	0.31 [0.01, 7.56]	
Parker 2015	2	164	0	158	35.7%	4.82 [0.23, 99.58]	
Total (95% CI)		511		481	100.0%	1.68 [0.28, 10.27]	
Total events	3		1				
Heterogeneity: Tau <sup>2</sup> =	0.00; Ch	i² = 1.6-	4, df = 2 (	P = 0.4	4); l² = 09	6	
Test for overall effect:	Z = 0.56	(P = 0.5	7)				Favors GA Favors RA

**Figure 6.** Acute kidney disease. Square—risk ratio for individual studies; line—confidence interval; diamond—pooled risk ratio [28,29,38].



**Figure 7.** Postoperative pneumonia. Square—risk ratio for individual studies; line—confidence interval; diamond—pooled risk ratio [27–29,33,37,38,41].

## 3.8. Intraoperative Blood Loss (mL)

The model does not favor RA over GA (Figure 8) since the std. mean difference (SMD) with 95% CI is equal to 0.24 [-1.34, 1.83].

		GA			RA			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl
Davis 1981	468	54	68	304	29	64	20.1%	3.73 [3.16, 4.30]	
McKenzie 1980	264	46	51	261	47	49	20.4%	0.06 [-0.33, 0.46]	+
McKenzie 1984	261.7	36.7	75	277.7	36.1	75	20.5%	-0.44 [-0.76, -0.11]	
McKenzie 1985	243	47	20	348	64	20	19.7%	-1.83 [-2.58, -1.08]	_ <b>-</b>
Messina 2013	161	91	10	190	65	10	19.4%	-0.35 [-1.24, 0.53]	
Total (95% CI)			224			218	100.0%	0.24 [-1.34, 1.83]	
Heterogeneity: Tau <sup>2</sup> =	= 3.16; C	hi <b>²</b> = 1							
Test for overall effect	Z = 0.30	) (P = (		Favors GA Favors RA					

**Figure 8.** Intraoperative blood loss (mL). Square—risk ratio for individual studies; line—confidence interval; diamond—pooled risk ratio [28,32–34,36].

## 3.9. Perioperative Blood Transfusion

The model (Figure 9) does not favor RA over GA since RR with 95% CI is equal to 1.04 [0.96, 1.13].

	GA		RA			Risk Ratio	Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% C	I	
Davis 1981	52	68	45	64	15.2%	1.09 [0.88, 1.34]			
Neuman 2021	146	790	130	782	14.1%	1.11 [0.90, 1.38]		-	
Parker 2015	28	164	30	158	3.0%	0.90 [0.56, 1.43]		—	
Tzimas 2018	32	33	35	37	67.8%	1.03 [0.93, 1.13]	-#		
Total (95% CI)		1055		1041	100.0%	1.04 [0.96, 1.13]	•		
Total events	258		240						
Heterogeneity: Tau² =	0.00; Ch	i <sup>z</sup> = 1.3	7, df = 3 (	P = 0.7	1); I² = 09	6		15	$-\frac{1}{2}$
Test for overall effect:	Z = 1.00	(P = 0.3	32)				Favors GA Favors R	A	-

**Figure 9.** Perioperative blood transfusion. Square—risk ratio for individual studies; line—confidence interval; diamond—pooled risk ratio [27,37,38,40].

# 3.10. Duration of Hospital Stay (Days)

The model does not favor RA over GA (Figure 10) since SMD with 95% CI is equal to 0.33 [-0.08, 0.74].

		GA			RA			Mean Difference	Mean Difference	
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Fixed, 95% CI	I IV, Fixed, 95% CI	
Davis 1987	15.9	9	279	15.7	9.6	259	6.8%	0.20 [-1.38, 1.78]	]	
Li 2021	7.7	2.97	470	7.35	3.72	471	91.4%	0.35 [-0.08, 0.78]	] +	
Parker 2015	15.9	13.7	164	16.2	14.6	158	1.8%	-0.30 [-3.39, 2.79]	]	
Total (95% CI)			913			888	100.0%	0.33 [-0.08, 0.74]	ı 🔶	
Heterogeneity: Chi <sup>2</sup> = 0.19, df = 2 (P = 0.91); I <sup>2</sup> = 0% Test for overall effect: Z = 1.56 (P = 0.12)										

**Figure 10.** Duration of hospital stay (days). Green square—risk ratio for individual studies; line—confidence interval; diamond—pooled risk ratio [29,31,38].

#### 3.11. Quality Assessment

We report the Cochrane Risk of Bias 2 in Table 2. Given the nature of the intervention, group assignment could not be concealed from the patients, which contributed to the "risk of bias". Moreover, the randomization process and concealment technique were not described in the older publications. However, these were published in reputable journals. Therefore, all the studies were rated as having "some concerns" in terms of risk of bias.

Table 2. Countaine risk of blas	Table 2.	Cochrane	risk	of bias.
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Study (Author, Year)	Risk of Bias Arising from the Randomization Process	Risk of Bias Due to Deviations from the Intended Interventions	Missing Outcome Data	Risk of Bias in Measurement of the Outcome	Risk of Bias in Selection of the Reported Result	Overall Risk of Bias
Davis et al., 1981 [28]	Some concerns	Low risk	Low risk	Some concerns	Low risk	Some concerns
Bigler et al., 1985 [27]	Some concerns	Low risk	Low risk	Some concerns	Low risk	Some concerns
Davis et al., 1987 [29]	Some concerns	Low risk	Low risk	Some concerns	Low risk	Some concerns
Juelsgaard et al., 1998 [30]	Some concerns	Low risk	Low risk	Some concerns	Low risk	Some concerns
Mckenzie et al., 1980 [32]	Some concerns	Low risk	Low risk	Some concerns	Low risk	Some concerns
Mckenzie et al., 1984 [33]	Some concerns	Low risk	Low risk	Some concerns	Low risk	Some concerns
Neuman et al., 2021 [37]	Low risk	Low risk	Some concerns	Some concerns	Low risk	Some concerns
Parker et al., 2015 [38]	Low risk	Some concerns	Low risk	Low risk	Low risk	Some concerns
White et al., 1980 [41]	Some concerns	Low risk	Low risk	Some concerns	Low risk	Some concerns
Messina et al., 2013 [36]	Low risk	Low risk	Low risk	Some concerns	Low risk	Some concerns
Svartling et al., 1986 [39]	Some concerns	Low risk	Low risk	Some concerns	Low risk	Some concerns
McLaren et al., 1978 [35]	Some concerns	Low risk	Low risk	Some concerns	Low risk	Some concerns
Li et al., 2022 [31]	Low risk	Low risk	Low risk	Some concerns	Low risk	Some concerns
Tzimas et al., 2018 [40]	Some concerns	Low risk	Low risk	Some concerns	Low risk	Some concerns
McKenzie et al., 1985 [34]	Some concerns	Low risk	Low risk	Some concerns	Low risk	Some concerns

The results of the GRADE assessment of the main outcomes are presented in Table 3. The outcomes ranged in the quality of evidence from "low" to "very low" due to "risk of bias" (lack of blinding, lack of information concerning allocation concealment, etc.), "inconsistency" (unexplained heterogeneity and wide variance of point estimates), and "imprecision" (wide confidence intervals). The full description of the assessment is available in the Evidence profile (Table S1).

**Table 3.** Summary of findings. Abbreviations: CI, confidence interval; GA, general anesthesia; GRADE, Grading of Recommendations Assessment, Development and Evaluation; N, number; RA, regional anesthesia; RCT, randomized controlled trial.

	Nof		N of Patients		Effect		
Outcome	Studies	Design	RA	GA	Relative Risk/Mean Difference [95% CI]	Overall Quality	
Death	10	RCT	1918	1958	1.42 [0.96, 2.10]	Low <sup>a</sup> $\oplus \oplus \ominus \ominus$	
Intraoperative hypotension	6	RCT	564	531	1.24 [0.59, 2.60]	Low <sup>a</sup> $\oplus \oplus \ominus \ominus$	
Myocardial infarction	6	RCT	1759	1793	1.23 [0.54, 2.82]	Very low <sup>b</sup> $\oplus \ominus \ominus \ominus$	
Cardiac failure	3	RCT	1199	1233	0.85 [0.23, 3.07]	Very low <sup>b</sup> $\oplus \ominus \ominus \ominus$	
Cerebrovascular accident	3	RCT	492	518	0.60 [0.03, 12.83]	Very low <sup>b</sup> $\oplus \ominus \ominus \ominus$	
Deep vein thrombosis	3	RCT	252	242	1.36 [0.43, 4.29]	Very low <sup>b</sup> $\oplus \ominus \ominus \ominus$	
Postoperative pulmonary embolus	5	RCT	1294	1328	1.59 [0.61, 4.14]	Very low $^{b} \oplus \ominus \ominus \ominus$	

<sup>a</sup> Due to the risk of bias and inconsistency. <sup>b</sup> Due to the risk of bias, inconsistency, and imprecision.  $\oplus \oplus \ominus \ominus$ —low quality;  $\oplus \ominus \ominus \ominus$ —very low quality.

#### 4. Discussion

There are controversies as to the most appropriate anesthetic approach in hip fracture surgeries to minimize the risk of complications, especially among the frail population. In this meta-analysis, we failed to identify the benefits of RA or GA for hip fracture surgery concerning mortality as well as intra- and postoperative complications.

The primary outcome was death. Although there was a trend toward decreased risk of mortality in the RA group at RR = 1.42 [0.96, 2.10], *p*-value = 0.08, we failed to reach statistical significance. Therefore, we observed no difference between the groups. On the contrary, previous observational studies concluded that GA might have an association with reduced incidence of mortality, adverse events, delirium, and shorter length of hospital stay compared with SA [42–46].

The secondary outcomes were intra- and postoperative complications. The results between the two groups were comparable. This finding is in agreement with a recent study that found no difference between the CSA/MNB and GA groups concerning postoperative complications and mortality rates in elderly patients undergoing hip fracture surgery [47]. However, in their study, CSA and MNB offered superior intraoperative blood pressure (BP) control than GA and comparable BP control between the regional anesthesia groups. Moreover, the MNB and CSA groups had a decreased frequency of cases of hypotension below 50 mmHg and requirement in vasopressors compared with the GA group.

One of the reasons for discrepancies in our results with previous literature might be the variations in the characteristics of the patient populations across studies, such as differences in age distribution, baseline health conditions, or comorbidities. These factors may interact differently with the chosen anesthesia methods, influencing mortality and other intra- and postoperative outcomes. Additionally, variations in surgical and anesthetic protocols, including drug dosages, administration techniques, and perioperative care, could contribute to differing results. Methodological dissimilarities, such as study design and blinding procedures, might also play a role in the observed differences. The evolution of medical practices over the study period, spanning three decades, could introduce disparities in outcomes due to advancements in surgical and anesthetic techniques.

Thus, our results suggest that the rate of death and adverse events in patients undergoing surgical procedures for hip fracture did not differ significantly between GA and RA, suggesting comparable safety of the two approaches. This might suggest that either approach can be used as an alternative based on specific patient requirements. For example, RA may be favored in patients with cardiovascular or pulmonary comorbidities, as it can offer better hemodynamic stability. RA was hypothesized to have minimal impact on cognitive function, making it a preferred option for elderly patients. However, a recent meta-analysis did not support this hypothesis [48]. Certain regional techniques, like Continuous Spinal Anesthesia or Multiple Nerve Blocks, may provide superior intraoperative blood pressure control compared to GA. On the other hand, patients with contraindications to regional techniques, such as severe coagulopathy or hemodynamic instability, may be more suitable for general anesthesia. GA might also be preferred in emergency cases or when a rapid onset of anesthesia is crucial. A recent study also proposed that the decision on the anesthesia type for hip fracture surgery may be influenced more by patient preference rather than solely relying on existing evidence and variations in clinical results [46]. For instance, some patients may prefer GA due to a desire for complete unconsciousness during the procedure. Ultimately, the choice between GA and RA should be made on a case-by-case basis, taking into account the patient's medical history, preferences, and the specific clinical context. Shared decision-making between the patient and the healthcare team is crucial to ensure the most appropriate and individualized anesthesia approach for hip fracture surgery.

Thus, the comparable efficacy of GA and RA in hip fracture surgery has substantial implications for clinical decision-making. This finding supports a personalized approach to anesthesia selection, enabling clinicians to consider individual patient characteristics, such as cardiovascular and pulmonary comorbidities or the risk of postoperative cognitive dysfunction. Moreover, the study suggests considering patient preferences in anesthesia choice, promoting shared decision-making processes. Additionally, the study's results suggest that in cases with contraindications to spinal anesthesia, GA remains a viable and safe option. Overall, the study's insights enhance the practical relevance of clinical decision-making by providing a nuanced understanding of when and how to apply GA and RA based on individual patient needs and preferences.

There are several limitations in the body of evidence. The majority of the included studies were conducted over three decades ago, potentially misaligning with current standards in surgical and anesthetic practices. Moreover, the studies demonstrated significant methodological limitations, including a lack of blinding and an inadequate description of the randomization method, which may introduce bias. The review process itself had limitations, as it combined studies with variations in anesthetic regimens and blocks, and there were relative differences in patients' conditions at admission, with some studies defining outcomes differently. Additionally, the inclusion of studies spanning over 40 years may have introduced variations in the quality and safety of surgical and anesthetic techniques. These limitations suggest that generalizing the findings to contemporary clinical settings should be carried out with caution. Moreover, a methodological limitation of our study is the absence of trial sequential analysis (TSA) to assess the robustness of our meta-analysis findings. TSA is an increasingly utilized statistical method in medical literature designed to manage type I and type II errors in meta-analyses [49,50]. It involves cumulative analysis, adjusting significance thresholds, and statistical power throughout the process.

Considering that the majority of the included studies were conducted over three decades ago, future research should involve RCTs that align with current clinical standards. Researchers should also pay careful attention to issues such as blinding and provide detailed descriptions of the randomization method to enhance the quality and reliability of study outcomes. Standardized reporting of outcomes and procedures across studies would facilitate meaningful comparisons and meta-analyses. Long-term outcomes, especially in terms of recovery trajectories, should be investigated to understand the overall impact of anesthesia choice on patient recovery. Patient preferences in anesthesia decision-making are also an issue that should be explored. Addressing these aspects in future research will contribute to a more comprehensive and clinically relevant understanding of the choice

between general and regional anesthesia in hip fracture surgeries. Future meta-analyses could perform a subgroup analysis based on the years of publication to partially solve the issue of including older studies.

The comparable safety and efficacy of general and regional anesthesia observed in our meta-analysis suggest that either approach can be acceptable, depending on individual patient characteristics, preferences, and clinical contexts. Policymakers and guideline developers may find it valuable to acknowledge this flexibility and consider incorporating it into recommendations. This recognition can provide healthcare practitioners with a broader choice of options and encourage shared decision-making between patients and clinicians. Additionally, our study highlights the importance of ongoing updates to clinical guidelines to reflect contemporary evidence and advancements in anesthesia techniques.

## 5. Conclusions

Existing evidence showed that the rate of mortality in patients undergoing hip fracture surgery did not differ significantly between general anesthesia and regional anesthesia. There was no statistically significant difference between RA and GA in cardiac and cerebral complications, including myocardial infarction, cardiac failure, cerebrovascular accident, deep vein thrombosis, postoperative pulmonary embolus, renal failure, postoperative pneumonia, intraoperative hypotension, intraoperative blood loss, intraoperative blood transfusion, or duration of hospital length of stay.

**Supplementary Materials:** The following supporting information can be downloaded at https://www. mdpi.com/article/10.3390/jcm12247513/s1, Document S1: Search terms; Table S1: Evidence profile.

**Author Contributions:** Conceptualization, D.V.; methodology, D.V.; data extraction, M.A.; software, Y.G.A. and F.N.; formal analysis, Y.G.A. and F.N.; quality assessment, M.A.; writing—original draft preparation, D.V.; writing—review and editing, D.V., M.A., F.N. and Y.G.A. All authors have read and agreed to the published version of the manuscript.

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#### References

- Gullberg, B.; Johnell, O.; Kanis, J.A. World-Wide Projections for Hip Fracture. Osteoporos. Int. 1997, 7, 407–413. [CrossRef] [PubMed]
- Haugan, K.; Johnsen, L.G.; Basso, T.; Foss, O.A. Mortality and Readmission Following Hip Fracture Surgery: A Retrospective Study Comparing Conventional and Fast-Track Care. *BMJ Open* 2017, 7, e015574. [CrossRef] [PubMed]
- 3. White, S.M.; Griffiths, R. Projected Incidence of Proximal Femoral Fracture in England: A Report from the NHS Hip Fracture Anaesthesia Network (HIPFAN). *Injury* **2011**, *42*, 1230–1233. [CrossRef] [PubMed]
- 4. Johansen, A.; Tsang, C.; Boulton, C.; Wakeman, R.; Moppett, I. Understanding Mortality Rates after Hip Fracture Repair Using ASA Physical Status in the National Hip Fracture Database. *Anaesthesia* 2017, 72, 961–966. [CrossRef] [PubMed]
- White, S.M.; Moppett, I.K.; Griffiths, R.; Johansen, A.; Wakeman, R.; Boulton, C.; Plant, F.; Williams, A.; Pappenheim, K.; Majeed, A.; et al. Secondary Analysis of Outcomes after 11,085 Hip Fracture Operations from the Prospective UK Anaesthesia Sprint Audit of Practice (ASAP-2). *Anaesthesia* 2016, 71, 506–514. [CrossRef] [PubMed]
- Le Manach, Y.; Collins, G.; Bhandari, M.; Bessissow, A.; Boddaert, J.; Khiami, F.; Chaudhry, H.; De Beer, J.; Riou, B.; Landais, P.; et al. Outcomes After Hip Fracture Surgery Compared with Elective Total Hip Replacement. *JAMA* 2015, 314, 1159. [CrossRef]
- Haentjens, P. Meta-Analysis: Excess Mortality After Hip Fracture Among Older Women and Men. Ann. Intern. Med. 2010, 152, 380. [CrossRef]

- 8. White, S.M.; Griffiths, R. Problems Defining 'Hypotension' in Hip Fracture Anaesthesia. *Br. J. Anaesth.* 2019, 123, e528–e529. [CrossRef]
- 9. Wesselink, E.M.; Kappen, T.H.; Torn, H.M.; Slooter, A.J.C.; Van Klei, W.A. Intraoperative Hypotension and the Risk of Postoperative Adverse Outcomes: A Systematic Review. *Br. J. Anaesth.* **2018**, *121*, 706–721. [CrossRef]
- Biboulet, P.; Jourdan, A.; Van Haevre, V.; Morau, D.; Bernard, N.; Bringuier, S.; Capdevila, X. Hemodynamic Profile of Target-Controlled Spinal Anesthesia Compared with 2 Target-Controlled General Anesthesia Techniques in Elderly Patients with Cardiac Comorbidities. *Reg. Anesth. Pain Med.* 2012, 37, 433–440. [CrossRef]
- Futier, E.; Lefrant, J.-Y.; Guinot, P.-G.; Godet, T.; Lorne, E.; Cuvillon, P.; Bertran, S.; Leone, M.; Pastene, B.; Piriou, V.; et al. Effect of Individualized vs Standard Blood Pressure Management Strategies on Postoperative Organ Dysfunction Among High-Risk Patients Undergoing Major Surgery: A Randomized Clinical Trial. *JAMA* 2017, *318*, 1346. [CrossRef] [PubMed]
- La Via, L.; Astuto, M.; Dezio, V.; Muscarà, L.; Palella, S.; Zawadka, M.; Vignon, P.; Sanfilippo, F. Agreement between Subcostal and Transhepatic Longitudinal Imaging of the Inferior Vena Cava for the Evaluation of Fluid Responsiveness: A Systematic Review. J. Crit. Care 2022, 71, 154108. [CrossRef] [PubMed]
- Sanfilippo, F.; La Via, L.; Dezio, V.; Santonocito, C.; Amelio, P.; Genoese, G.; Astuto, M.; Noto, A. Assessment of the Inferior Vena Cava Collapsibility from Subcostal and Trans-Hepatic Imaging Using Both M-Mode or Artificial Intelligence: A Prospective Study on Healthy Volunteers. *Intensive Care Med. Exp.* 2023, *11*, 15. [CrossRef] [PubMed]
- Juri, T.; Suehiro, K.; Kimura, A.; Mukai, A.; Tanaka, K.; Yamada, T.; Mori, T.; Nishikawa, K. Impact of Continuous Non-Invasive Blood Pressure Monitoring on Hemodynamic Fluctuation during General Anesthesia: A Randomized Controlled Study. J. Clin. Monit. Comput. 2018, 32, 1005–1013. [CrossRef] [PubMed]
- 15. White, S.M.; Moppett, I.K.; Griffiths, R. Outcome by Mode of Anaesthesia for Hip Fracture Surgery. An Observational Audit of 65 535 Patients in a National Dataset. *Anaesthesia* **2014**, *69*, 224–230. [CrossRef] [PubMed]
- 16. Maxwell, B.G.; Spitz, W.; Porter, J. Association of Increasing Use of Spinal Anesthesia in Hip Fracture Repair with Treating an Aging Patient Population. *JAMA Surg.* 2020, 155, 167. [CrossRef]
- 17. Boddaert, J.; Raux, M.; Khiami, F.; Riou, B. Perioperative Management of Elderly Patients with Hip Fracture. *Anesthesiology* **2014**, *121*, 1336–1341. [CrossRef]
- O'Donnell, C.M.; Black, N.; McCourt, K.C.; McBrien, M.E.; Clarke, M.; Patterson, C.C.; Blackwood, B.; McAuley, D.F.; Shields, M.O. Development of a Core Outcome Set for Studies Evaluating the Effects of Anaesthesia on Perioperative Morbidity and Mortality Following Hip Fracture Surgery. Br. J. Anaesth. 2019, 122, 120–130. [CrossRef]
- Messina, A.; La Via, L.; Milani, A.; Savi, M.; Calabrò, L.; Sanfilippo, F.; Negri, K.; Castellani, G.; Cammarota, G.; Robba, C.; et al. Spinal Anesthesia and Hypotensive Events in Hip Fracture Surgical Repair in Elderly Patients: A Meta-Analysis. *J. Anesth. Analg. Crit. Care* 2022, 2, 19. [CrossRef]
- 20. Devisme, V.; Picart, F.; Lejouan, R.; Legrand, A.; Savry, C.; Morin, V. Combined Lumbar and Sacral Plexus Block Compared with Plain Bupivacaine Spinal Anesthesia for Hip Fractures in the Elderly. *Reg. Anesth. Pain Med.* **2000**, *25*, 158–162. [CrossRef]
- Johnston, D.F.; Stafford, M.; McKinney, M.; Deyermond, R.; Dane, K. Peripheral Nerve Blocks with Sedation Using Propofol and Alfentanil Target-Controlled Infusion for Hip Fracture Surgery: A Review of 6 Years in Use. *J. Clin. Anesth.* 2016, 29, 33–39. [CrossRef]
- Page, M.J.; McKenzie, J.E.; Bossuyt, P.M.; Boutron, I.; Hoffmann, T.C.; Mulrow, C.D.; Shamseer, L.; Tetzlaff, J.M.; Akl, E.A.; Brennan, S.E.; et al. The PRISMA 2020 Statement: An Updated Guideline for Reporting Systematic Reviews. *BMJ* 2021, 372, n71. [CrossRef] [PubMed]
- 23. Luo, D.; Wan, X.; Liu, J.; Tong, T. Optimally Estimating the Sample Mean from the Sample Size, Median, Mid-Range, and/or Mid-Quartile Range. *Stat. Methods Med. Res.* 2018, 27, 1785–1805. [CrossRef] [PubMed]
- 24. Wan, X.; Wang, W.; Liu, J.; Tong, T. Estimating the Sample Mean and Standard Deviation from the Sample Size, Median, Range and/or Interquartile Range. *BMC Med. Res. Methodol.* **2014**, *14*, 135. [CrossRef] [PubMed]
- Sterne, J.A.C.; Savović, J.; Page, M.J.; Elbers, R.G.; Blencowe, N.S.; Boutron, I.; Cates, C.J.; Cheng, H.-Y.; Corbett, M.S.; Eldridge, S.M.; et al. RoB 2: A Revised Tool for Assessing Risk of Bias in Randomised Trials. *BMJ* 2019, 366, 14898. [CrossRef] [PubMed]
- Guyatt, G.H.; Oxman, A.D.; Schünemann, H.J.; Tugwell, P.; Knottnerus, A. GRADE Guidelines: A New Series of Articles in the Journal of Clinical Epidemiology. J. Clin. Epidemiol. 2011, 64, 380–382. [CrossRef] [PubMed]
- 27. Bigler, D.; Adelhøj, B.; Petring, O.U.; Pederson, N.O.; Busch, P.; Kalhke, P. Mental Function and Morbidity after Acute Hip Surgery during Spinal and General Anaesthesia. *Anaesthesia* **1985**, *40*, 672–676. [CrossRef]
- 28. Davis, F.M.; Laurenson, V.G. Spinal Anaesthesia or General Anaesthesia for Emergency Hip Surgery in Elderly Patients. *Anaesth. Intensive Care* **1981**, *9*, 352–358. [CrossRef]
- Davis, F.M.; Woolner, D.F.; Frampton, C.; Wilkinson, A.; Grant, A.; Harrison, R.T.; Roberts, M.T.S.; Thadaka, R. Prospective, Multi-Centre Trial of Mortality Following General or Spinal Anaesthesia for Hip Fracture Surgery in the Elderly. *Br. J. Anaesth.* 1987, 59, 1080–1088. [CrossRef]
- Juelsgaard, P.; Sand, N.P.R.; Felsby, S.; Dalsgaard, J.; Jakobsen, K.B.; Brink, O.; Carlsson, P.S.; Thygesen, K. Perioperative Myocardial Ischaemia in Patients Undergoing Surgery for Fractured Hip Randomized to Incremental Spinal, Single-Dose Spinal or General Anaesthesia. *Eur. J. Anaesthesiol.* 1998, 15, 656–663. [CrossRef]

- Li, T.; Li, J.; Yuan, L.; Wu, J.; Jiang, C.; Daniels, J.; Mehta, R.L.; Wang, M.; Yeung, J.; Jackson, T.; et al. Effect of Regional vs General Anesthesia on Incidence of Postoperative Delirium in Older Patients Undergoing Hip Fracture Surgery: The RAGA Randomized Trial. *JAMA* 2022, 327, 50. [CrossRef] [PubMed]
- 32. Mckenzie, P.J.; Wishart, H.Y.; Dewar, K.M.S.; Gray, I.; Smith, G. Comparison of the Effects of Spinal Anaesthesia and General Anaesthesia on Postoperative Oxygenation and Perioperative Mortality. *Br. J. Anaesth.* **1980**, *52*, 49–54. [CrossRef]
- Mckenzie, P.J.; Wishart, H.Y.; Smith, G. Long-Term Outcome after Repair of Fractured Neck of Femur. Br. J. Anaesth. 1984, 56, 581–585. [CrossRef] [PubMed]
- McKenzie, P.J.; Wishart, H.Y.; Gray, I.; Smith, G. Effects of Anaesthetic Technique on Deep Vein Thrombosis. Br. J. Anaesth. 1985, 57, 853–857. [CrossRef]
- McLAREN, A.D.; Stockwell, M.C.; Reid, V.T. Anaesthetic Techniques for Surgical Correction of Fractured Neck of Femur.: A Comparative Study of Spinal and General Anaesthesia in the Elderly. *Anaesthesia* 1978, 33, 10–14. [CrossRef]
- Messina, A.; Frassanito, L.; Colombo, D.; Vergari, A.; Draisci, G.; Della Corte, F.; Antonelli, M. Hemodynamic Changes Associated with Spinal and General Anesthesia for Hip Fracture Surgery in Severe ASA III Elderly Population: A Pilot Trial. *Minerva Anestesiol.* 2013, 79, 1021–1029. [PubMed]
- Neuman, M.D.; Feng, R.; Carson, J.L.; Gaskins, L.J.; Dillane, D.; Sessler, D.I.; Sieber, F.; Magaziner, J.; Marcantonio, E.R.; Mehta, S.; et al. Spinal Anesthesia or General Anesthesia for Hip Surgery in Older Adults. *N. Engl. J. Med.* 2021, 385, 2025–2035. [CrossRef] [PubMed]
- Parker, M.J.; Griffiths, R. General versus Regional Anaesthesia for Hip Fractures. A Pilot Randomised Controlled Trial of 322 Patients. *Injury* 2015, 46, 1562–1566. [CrossRef]
- Svartling, N.; Lehtinen, A.-M.; Tarkkanen, L. The Effect of Anaesthesia on Changes in Blood Pressure and Plasma Cortisol Levels Induced by Cementation with Methylmethacrylate. *Acta Anaesthesiol. Scand.* 1986, 30, 247–252. [CrossRef]
- Tzimas, P.; Samara, E.; Petrou, A.; Korompilias, A.; Chalkias, A.; Papadopoulos, G. The Influence of Anesthetic Techniques on Postoperative Cognitive Function in Elderly Patients Undergoing Hip Fracture Surgery: General vs Spinal Anesthesia. *Injury* 2018, 49, 2221–2226. [CrossRef]
- White, I.W.C.; Chappell, W.A. Anaesthesia for Surgical Correction of Fractured Femoral Neck A Comparison of Three Techniques. Anaesthesia 1980, 35, 1107–1110. [CrossRef] [PubMed]
- 42. Neuman, M.D.; Silber, J.H.; Elkassabany, N.M.; Ludwig, J.M.; Fleisher, L.A. Comparative Effectiveness of Regional *versus* General Anesthesia for Hip Fracture Surgery in Adults. *Anesthesiology* **2012**, *117*, 72–92. [CrossRef] [PubMed]
- Ahn, E.J.; Kim, H.J.; Kim, K.W.; Choi, H.R.; Kang, H.; Bang, S.R. Comparison of General Anaesthesia and Regional Anaesthesia in Terms of Mortality and Complications in Elderly Patients with Hip Fracture: A Nationwide Population-Based Study. *BMJ Open* 2019, 9, e029245. [CrossRef] [PubMed]
- Rosa, R.G.; Falavigna, M.; Da Silva, D.B.; Sganzerla, D.; Santos, M.M.S.; Kochhann, R.; De Moura, R.M.; Eugênio, C.S.; Haack, T.D.S.R.; Barbosa, M.G.; et al. Effect of Flexible Family Visitation on Delirium Among Patients in the Intensive Care Unit: The ICU Visits Randomized Clinical Trial. *JAMA* 2019, 322, 216. [CrossRef] [PubMed]
- Chu, C.-C.; Weng, S.-F.; Chen, K.-T.; Chien, C.-C.; Shieh, J.-P.; Chen, J.-Y.; Wang, J.-J. Propensity Score–Matched Comparison of Postoperative Adverse Outcomes between Geriatric Patients Given a General or a Neuraxial Anesthetic for Hip Surgery. *Anesthesiology* 2015, 123, 136–147. [CrossRef] [PubMed]
- Neuman, M.D.; Rosenbaum, P.R.; Ludwig, J.M.; Zubizarreta, J.R.; Silber, J.H. Anesthesia Technique, Mortality, and Length of Stay After Hip Fracture Surgery. JAMA 2014, 311, 2508. [CrossRef] [PubMed]
- Mounet, B.; Choquet, O.; Swisser, F.; Biboulet, P.; Bernard, N.; Bringuier, S.; Capdevila, X. Impact of Multiple Nerves Blocks Anaesthesia on Intraoperative Hypotension and Mortality in Hip Fracture Surgery Intermediate-Risk Elderly Patients: A Propensity Score-Matched Comparison with Spinal and General Anaesthesia. *Anaesth. Crit. Care Pain Med.* 2021, 40, 100924. [CrossRef]
- 48. Viderman, D.; Aubakirova, M.; Nabidollayeva, F.; Yegembayeva, N.; Bilotta, F.; Badenes, R.; Abdildin, Y. Effect of Ketamine on Postoperative Neurocognitive Disorders: A Systematic Review and Meta-Analysis. *J. Clin. Med.* **2023**, *12*, 4314. [CrossRef]
- 49. Sanfilippo, F.; La Via, L.; Tigano, S.; Morgana, A.; Rosa, V.; Astuto, M. Trial Sequential Analysis: The Evaluation of the Robustness of Meta-Analyses Findings and the Need for Further Research. *EuroMediterr. Biomed. J.* **2021**, *16*, 104–107. [CrossRef]
- Cassai, A.D.; Pasin, L.; Boscolo, A.; Salvagno, M.; Navalesi, P. Trial Sequential Analysis: Plain and Simple. *Korean J. Anesthesiol.* 2020, 74, 363–365. [CrossRef]

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