

RESEARCH ARTICLE

Effects of propofol and inhaled anesthetics on postoperative complications for the patients undergoing one lung ventilation: A meta-analysis

Jing Yang , Qinghua Huang, Rong Cao, Yu Cui *

Department of Anesthesiology, The Affiliated Hospital, School of Medicine, UESTC Chengdu Women's & Children's Central Hospital, Chengdu, China

* cuiyu19831001@163.com

Abstract

Introduction

With the widespread use of one-lung ventilation (OLV) in thoracic surgery, it is unclear whether maintenance anesthetics such as propofol and inhaled anesthetics are associated with postoperative complications. The purpose of this study was to compare the effects of propofol and inhaled anesthetics on postoperative complications in OLV patients.

Methods

PubMed, EMBASE, Medline, and Cochrane Library were searched for relevant randomized controlled trials until 09/2021. All randomized controlled trials comparing the effect of propofol versus inhaled anesthetics on postoperative complications in OLV patients were included. All randomized controlled trials comparing: (a) major complications (b) postoperative pulmonary complications (c) postoperative cognitive function (MMSE score) (d) length of hospital stay (e) 30-day mortality, were included.

Results

Thirteen randomized controlled trials involving 2522 patients were included in the analysis. Overall, there was no significant difference in major postoperative complications between the inhaled anesthetic and propofol groups (OR 0.78, 95%CI 0.54 to 1.13, $p = 0.19$; $I^2 = 0\%$). However, more PPCs were detected in the propofol group compared to the inhalation anesthesia group (OR 0.62, 95%CI 0.44 to 0.87, $p = 0.005$; $I^2 = 37\%$). Both postoperative MMSE score (SMD -1.94, 95%CI -4.87 to 0.99, $p = 0.19$; $I^2 = 100\%$) and hospital stay (SMD 0.05, 95%CI -0.29 to 0.39, $p = 0.76$; $I^2 = 73\%$) were similar between the two groups. The 30-day mortality rate was also not significantly different between groups (OR 0.79, 95%CI 0.03 to 18, $p = 0.88$; $I^2 = 63\%$).

OPEN ACCESS

Citation: Yang J, Huang Q, Cao R, Cui Y (2022) Effects of propofol and inhaled anesthetics on postoperative complications for the patients undergoing one lung ventilation: A meta-analysis. PLoS ONE 17(10): e0266988. <https://doi.org/10.1371/journal.pone.0266988>

Editor: Antonello Penna, Universidad de Chile, CHILE

Received: March 30, 2022

Accepted: October 7, 2022

Published: October 20, 2022

Copyright: © 2022 Yang et al. This is an open access article distributed under the terms of the [Creative Commons Attribution License](https://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Data Availability Statement: All relevant data are within the article.

Funding: Yu, Cui Chengdu Municipal Health Commission No.2020095 the sponsors or funders play no role in the study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing interests: The authors have declared that no competing interests exist.

Abbreviations: OLV, one lung ventilation; PPCs, postoperative pulmonary complications; MMSE, Mini-mental State Examination.

Conclusions

In patients undergoing OLV, general anesthesia with inhaled anesthetics reduced PPC compared to propofol, but did not provide clear benefits on other major complications, cognitive function, length of hospital stay, or mortality.

Introduction

According to the literature, approximately 3% of surgical patients develop severe complications and 0.4% die postoperatively [1]. And lung cancer is the leading reason of cancer-related death in the United States [2]. One-lung ventilation (OLV) has become a necessary technique in thoracic surgery because it facilitates surgery and prevents contamination of the other lung [3]. However, one-lung ventilation increases the risk of postoperative complications by potentially causing ischemia and hypoxia in the nonventilated lung, pressure trauma and excess fluid in ventilated lung tissue, and alveolar and systemic inflammatory responses [4]. The incidence of postoperative pulmonary complications (PPC) is much higher in patients operated on with OLV than in those without [5].

Christopher, et al. found that in cardiac surgery, inhalation anesthesia was associated with a significant outcome advantage and lower mortality [6]. However, Bassi, A [7] and Modolo, NS [3] found little evidence from randomized controlled trials (RCTs) in 2008 and 2013 that showed significant differences in specific postoperative outcomes between general anesthesia maintained with inhalation and intravenous anesthesia such as propofol in the case of OLV. Subsequently, several RCTs and systematic reviews have suggested that inhaled anesthesia may preserve cardiac function, decrease PPC, and attenuate local alveolar inflammatory responses in patients undergoing OLV [8–10].

Since 2013, more and more clinical RCTs have been published examining the effects of different sedative anesthetics on major complications in OLV patients. Therefore, we conducted this meta-analysis to compare the effects of inhaled anesthetics (Sevoflurane or Desflurane) and propofol on postoperative outcomes.

Methods

We followed the recommendations of the Cochrane Handbook for the Systematic Review [11]. The meta-analysis is also registered at <https://www.crd.york.ac.uk/prospero/> under No. CRD420202222856.

Retrieval strategy

Two authors (JY, QHH) separately searched Pubmed, Medline, Embase, and Cochrane Central registers for relevant RCTs from January 1, 2000, to September 31, 2021. Searches were performed using various combinations of keywords and MeSH terms. The search terms are listed in [Table 1](#), and the search was limited to the English language.

Inclusion criteria

1. Population: Patients (>18 years old) scheduled for standby thoracic surgery under OLV.
2. Intervention: Patients who maintained anesthesia with inhaled anesthetics during OLV.
3. Comparison: Patients received propofol to maintain anesthesia during OLV.
4. Outcomes:

Table 1. The specific keywords and MeSH terms during the screening process.

anesthesia, intravenous	anesthetics, inhalation	one lung ventilation	RCT
intravenous anesthesia	anesthetic gases	single lung ventilation	Randomized controlled trial
intravenous anesthetics	inhalation anesthetics	Ventilation, One-Lung	Controlled clinical trial
intravenous anesthetic agent	inhalation anesthesia	Ventilation, Single-Lung	Randomized
propofol	inhaled anesthesia	lung separation techniques	Randomly
Diprivan	volatile anesthetics	Separation Technique, Lung	Trial
Disoprofol	sevoflurane	Technique, Lung Separation	
	sevoflurane	Lobectomy	
	desflurane	thoracic surgery	
	isoflurane		

We used Boolean operator “OR” to search every potentially eligible article that was relevant to Intravenous anesthetics/ Inhaled anesthetics/ One lung ventilation. Then, we used the operator “AND” to combine the above results to accomplish the screening process.

<https://doi.org/10.1371/journal.pone.0266988.t001>

The primary endpoint was the occurrence of major complications assessed by Clavien-Dindo score (grade III to V) or assessed by surgeon (complications that needs more intensive treatments including overall cardiac events, myocardial infarction, acute renal failure, hepatic failure, disseminated intravascular coagulation, extrapulmonary infection, gastrointestinal failure, coma).

The secondary evaluation items were the number of PPC (hypoxemia, acute respiratory distress syndrome, pulmonary infiltrates, pneumonia, pleural effusions, atelectasis, pneumothorax, bronchospasm, cardiopulmonary edema, aspiration pneumonitis); the scores of Minimal State Examination (MMSE) during hospital admission, length of hospital stay and 30-day mortality.

(5) Study: Randomized controlled studies.

All trials in which the population, intervention, comparison, study, and at least one outcome were reported as described above were included.

Exclusion criteria. Duplicate studies, non-human or pediatric studies, conference abstracts, studies published before the 2000s, and studies from which data could not be extracted.

Data extraction. Based on the above criteria, two authors (JY, QHH) sequentially enrolled in the study and independently extracted data: publication information (first author name, year of publication), participant characteristics (sample size, type of surgery, anesthesia induction scheme, OLV and operation time, OLV strategy) and outcome information. Disagreements regarding eligibility between the two investigators were resolved by discussion. If necessary, a third researcher (RC) was involved in making a determination. Data were extracted or calculated from figures and tables using the Engauge Digitizer 5.1 program (M. Mitchell, Engauge Digitizer, <http://digitizer.sourceforge.net>) as needed. All extracted data were collected in standardized Excel files by the two authors and double-checked by YC for accuracy.

Bias risk assessment and strength of evidence

Two reviewers (JY, QHH) independently assessed the methodological quality of the included trials using methods recommended by the Cochrane Collaboration. For each trial, the criteria used to assess quality were random sequence generation, allocation concealment, performance bias, detection bias, attribution bias, reporting bias, and others. Each criterion was categorized

as "yes," "no," or "unclear," and a simple rating for each trial was classified into three levels (low risk of bias, unclear risk of bias, and high risk of bias). The Grading of Recommendations, Assessment, Development and Evaluations approach (GRADEpro; gdt.gradeapro.org) was approved to comprehensively assess the quality of evidence for each outcome. In this approach, each outcome begins as high-quality evidence, but may be downgraded by one or more of five categories of limitations (risk of bias, inconsistency, indirectness, imprecision, and reporting bias). Finally, this approach depicted the apparent quality of each outcome as low, moderate, or high.

Statistical analysis

According to DerSimonian and Laird method performed by Review Manager 5.3 (RevMan, The Cochrane Collaboration, Oxford, UK), differences were expressed as risk ratio (RR) with 95% confidence intervals (CI) for dichotomous data, and the differences between continuous data were expressed as mean differences (MDs) or standardized mean differences (SMD) with 95% CI. Due to the small number of trials and high heterogeneity among trials, data pooled by five or fewer trials or with heterogeneity values greater than 50% were further subjected to random effects measurement using the Hartung-Knapp-Sidik-Jonkman (HKSJ) method. Since Joanna, et al. [12] found that the HKSJ method was proved superior to the DerSimonian-Laird method in meta-analyses with a smaller number of trials and higher heterogeneity.

Heterogeneity among the pooled studies was expressed as an I^2 value, and the criterion for identifying whether the combined data were more or less heterogeneous was 50%. A random-effects model was performed for significant heterogeneity ($I^2 > 50\%$, $p \leq 0.1$) due to inconsistencies in the surgical process, anesthesia methods, OLV time, and factors that increase heterogeneity. Sensitivity analysis was also performed to explore possible explanations for the high heterogeneity.

Results

Study identification

This search yielded 1945 articles in the initial screening. Based on inclusion and exclusion criteria, 1319 potentially eligible trials were excluded based on title or abstract. Full-text screening excluded 46 studies (10 were not RCTs, 19 did not meet the population criteria, 9 compared intravenous anesthetics with local anesthetics or other agents, and 9 did not report outcomes as previously listed). Finally, 13 studies were included and a meta-analysis was performed [13–25]. The flowchart is shown in Fig 1.

Study characteristics and quality

The main characteristics of the included trials are shown in Table 2. The 13 studies [13–25] included 2522 patients, which published between 2000 and 2021. As showed in Fig 2, 8 of the 13 trials [13, 15–20] showed a low risk of random sequence generation and allocation concealment by describing the randomization method in detail. 6 of the 13 [14, 17, 21–24] did not report details of blinding to participants or outcome assessors, but the impact of lack of blinding on outcomes was considered low. The quality of each outcome was shown in Table 3 by the GRADEpro system. The PPC's level of evidence was high, and the level of evidence for major complications, 30-day mortality, and length of hospital stay was moderate. However, the level of evidence for MMSE score was low.

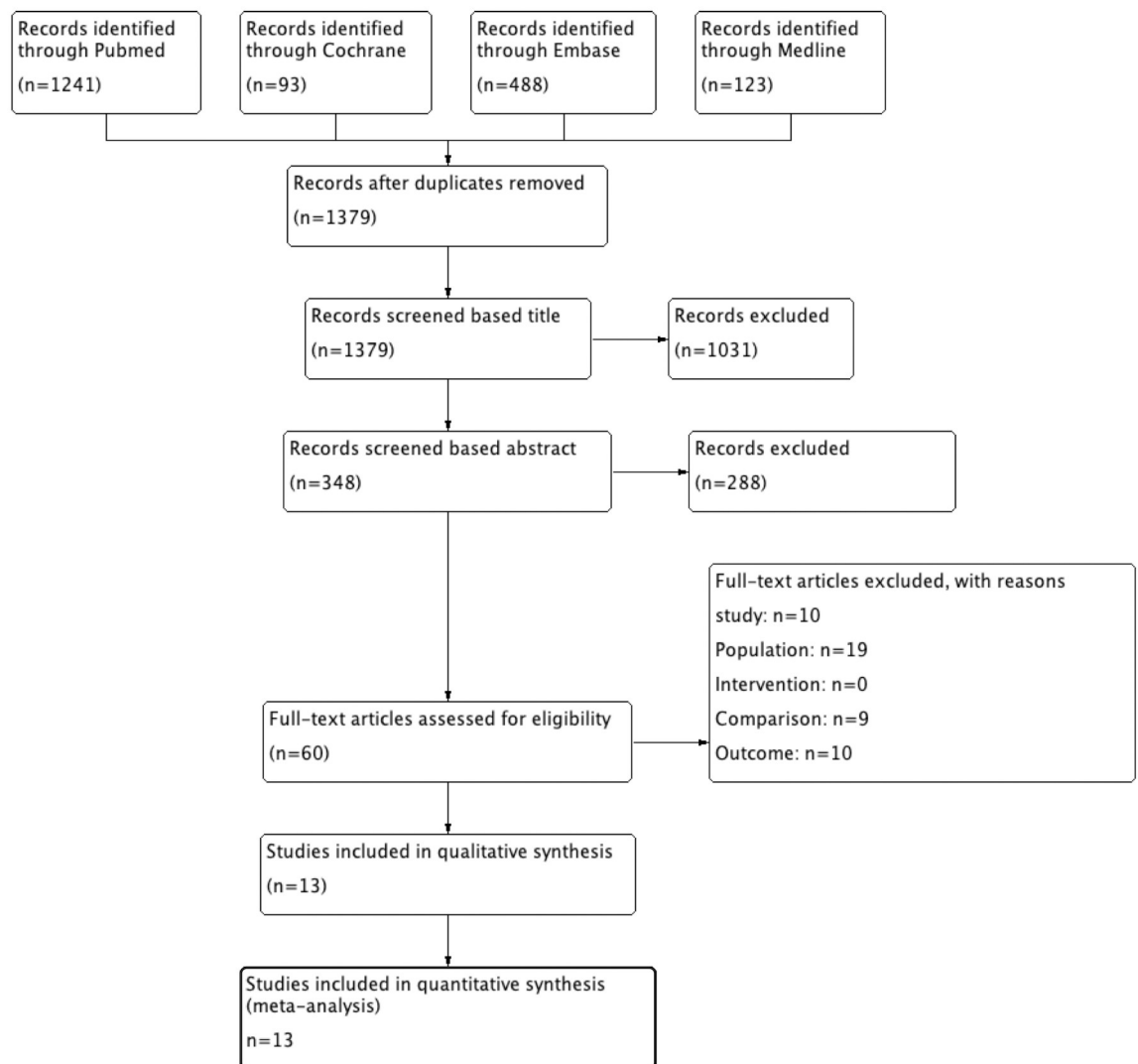


Fig 1. Flow diagram of selecting process.

<https://doi.org/10.1371/journal.pone.0266988.g001>

Primary outcome: major postoperative complications

As mentioned earlier, major complications mean that patients require more intensive care: Five studies [13, 15, 17, 18, 24] evaluated major complications in 1083 patients who underwent OLV. Moreover, the overall incidence of major complications after OLV was 12.37%. However, in our evidence-based analysis, compared to the propofol group, inhaled anesthetics were not associated with a lower incidence of major complications after OLV (OR 0.78, 95% CI 0.54 to 1.13, $p = 0.19$; $I^2 = 0$, Fig 3).

Secondary outcomes

PPC. Seven RCTs [14, 15, 17–20, 24] compared the effect of propofol and inhaled anesthetics on PPC in 763 patients with OLV. Pooled data showed that the incidence of postoperative PPC was 20.9% in the propofol group and 29.6% in the inhaled anesthetic group. And a

Table 2. Trial characteristics.

Trial	Surgery	Intervention(n = 1263)		Control(n = 1259)		OLV strategy	Outcome
		Induction	Maintenance	Induction	Maintenance		
Beck-Schimmer 2016 [13]	Lung surgery	Desflurane(n = 230)		Propofol(n = 230)		Vt ^c 4–6 ml/kg FIO ₂ ^d 0.6–1.0 PEEP ^e 5cmH ₂ O	Complications (Clavien-Dindo classification), Hospital stay
		Etomidate (0.3–0.5mg/kg)	Desflurane (end-tidal concentrations of 4.5–7%)	Etomidate (0.3–0.5 mg/kg)	Propofol TCI ^b (2–6ug/ml)		
Conno 2009 [14]	Lung surgery	Sevoflurane (n = 27)		Propofol(n = 27)		Vt ^c 6–7ml/kg FiO ₂ ^d 1.0	PPCs, Hospital death
		Propofol (1.5–2.5mg/kg)	sevoflurane (1 MAC ^a)	Propofol TCI ^b (3–5ug/ml)	Propofol TCI ^b (1 MAC ^a)		
Gala 2017 [15]	Lung resection surgery	Sevoflurane(n = 86)		Propofol(n = 88)		Vt ^c 6ml/kg FiO ₂ ^d 0.6–1.0 PEEP ^e 5cmH ₂ O	Complications (Clavien-Dindo classification), PPCs, Mortality, Hospital stay
		Propofol (2–3mg/kg)	Sevoflurane (BIS ^f 40–60)	Propofol (2–3mg/kg)	Propofol (BIS ^f 40–60)		
Egawa 2016 [16]	Lung surgery	Sevoflurane(n = 72)		Propofol(n = 72)		Vt ^c 5–6ml/kg FiO ₂ ^d 1.0 PEEP ^e 4–5cmH ₂ O	MMSE score
		Propofol (1–2mg/kg)	Sevoflurane (BIS ^f 40–60)	Propofol TCI ^b (3–4ug/ml)	Propofol (BIS ^f 40–60)		
Lee 2012 [17]	Ivor Lewis operation	Sevoflurane(n = 24)		Propofol(n = 24)		Vt ^c 6ml/kg FIO ₂ ^d (achieve oxygen saturation >95%) PEEP ^e 5cmH ₂ O	Hospital complications, PPCs, Hospital death, Hospital stay
		Thiopental (4–5 mg/kg)	Sevoflurane (end-tidal concentrations of 1–2.5%)	Propofol (BIS ^f 30–50)	Propofol (BIS ^f 30–50)		
Li 2021 [18]	Lung surgery	Sevoflurane(n = 169)		Propofol(n = 167)		Vt ^c 6ml/kg FiO ₂ ^d 0.4–0.5 PEEP ^e 5–8cmH ₂ O	Complications (Clavien-Dindo classification), PPCs, Death,
		Propofol (1.5–2.5mg/kg)	Sevoflurane (BIS ^f 40–60)	Propofol (1.5–2.5mg/kg)	Propofol (BIS ^f 40–60)		
Mahmoud 2011 [19]	Lung surgery	Isoflurane(n = 25)		Propofol(n = 25)		Vt ^c 10ml/kg FiO ₂ ^d 0.8–1.0 PEEP ^e 5cmH ₂ O	PPCs, 30-mortality, Hospital stay
		Propofol (1.5–2 mg/kg)	Isoflurane (1MAC ^a)	Propofol (1.5–2 mg/kg)	Propofol (4–6mg/kg/h)		
Potočnik 2014 [20]	Thoracic surgery	Sevoflurane(n = 17)		Propofol(n = 19)		Vt ^c 4ml/kg FiO ₂ ^d 0.6–0.7 PEEP ^e 3 cmH ₂ O	PPCs, Hospital death
		Sevoflurane (6%)	Sevoflurane (2–2.5%)	Propofol (1.5–2.0 mg/kg)	Propofol (4–6 mg/kg/h)		
Shen 2011 [21]	Thoracic surgery	Sevoflurane (n = 30)		Propofol(n = 30)		Vt ^c 8ml/kg FiO ₂ ^d 0.6	MMSE score
		Sevoflurane (4–6%)	Sevoflurane (0.8–1.2MAC ^a)	Propofol (1.5–2 mg/kg)	Propofol (6–8mg/kg/h)		
Tian 2017 [22]	Lobectomy	Sevoflurane(n = 31)		Propofol(n = 31)		Not reported	Adverse reaction, MMSE score
		Sevoflurane (8%)	Sevoflurane (2%)	Propofol (1mg/kg)	Propofol (6mg/kg)		
Wang 2019 [23]	Lung surgery	Sevoflurane(n = 32)		Propofol(n = 26)		Vt ^c 8–10ml/kg FiO ₂ ^d 1.0	MMSE score
		Sevoflurane (6%)	Sevoflurane (1MAC ^a)	Propofol TCI ^b (3ug/kg)	Propofol TCI ^b (4ug/kg)		
Xu 2014 [24]	Open-chest thoracotomy	Sevoflurane(n = 20)		Propofol(n = 20)		Vt ^c 8ml/kg FiO ₂ ^d 1.0	Complications, PPCs, Hospital death, Hospital stay
		Sevoflurane (8%)	Sevoflurane (BIS ^f 40–60)	Propofol TCI ^b (6ug/ml)	Propofol (BIS ^f 40–60)		
Yu 2017 [25]	Thoracic surgery	Sevoflurane(n = 500)		Propofol(n = 500)		Vt ^c 8ml/kg	MMSE score
		Sevoflurane (2–4%)	Sevoflurane (BIS ^f 45–55)	Propofol (2mg/kg)	Sevoflurane (BIS ^f 45–55)		

MAC^a: minimum alveolar concentration; TCI^b: target controll infusion; Vt^c: tidal volume; FiO₂^d: Fraction of inspiration O₂; PEEP^e: positive end expiratory pressure; BIS^f: bispectral index

<https://doi.org/10.1371/journal.pone.0266988.t002>

fixed effects model showed that inhaled anesthetics were less heterogeneous and significantly reduced the number of patients who developed PPC compared to propofol (OR 0.62, 95%CI 0.44 to 0.87, p = 0.005; I² = 37%, Fig 4).

Postoperative MMSE scores. As shown in Fig 5, five RCTs [16, 21–23, 25] estimated post-operative cognitive function after OLV with MMSE scores in 1324 patients. They found little

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Beck-Schimmer 2016	+	+	+	+	+	?	+
Conno2009	?	?	?	?	?	+	+
Egawa 2016	+	+	+	+	+	+	+
Gala 2017	+	+	+	+	+	+	+
Lee 2012	+	+	?	+	-	+	+
Li 2021	+	+	+	+	+	+	+
Mahmoud 2011	+	+	+	+	+	+	+
Potocnik 2014	+	?	+	+	+	+	+
Shen 2011	+	?	?	?	?	-	+
Tian 2017	?	?	?	?	+	+	?
Wang 2019	?	?	?	?	+	+	?
Xu 2014	?	+	?	?	+	+	+
Yu 2017	?	+	+	+	?	+	?

Fig 2. A summary of assessment of risk bias of each RCT.

<https://doi.org/10.1371/journal.pone.0266988.g002>

Table 3. The details of GRADE evidence among each outcome.

n	Certainty assessment			Number of patients			Effect		Importance		
	Studies, Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Inhaled anesthetics	Propofol		Relative (95%CI)	Absolute (95%CI)
Major complications											
5	randomised trials	not serious	not serious	not serious	serious	none	60/542 (11.1%)	74/541 (13.7%)	OR 0.78 (0.54 to 1.18)	27 fewer per 1,000 (from 58 fewer to 21 more)	⊕⊕⊕○ Moderate
PPCs											
7	randomised trials	not serious	not serious	not serious	not serious	none	80/381 (21.0%)	113/382 (29.6%)	OR 0.62 (0.44 to 0.87)	89 fewer per 1,000 (from 140 fewer to 28 fewer)	⊕⊕⊕⊕ High
MMSE scores											
5	randomised trials	serious	serious	not serious	not serious	none	665	659	-	SMD 1.94 SD lower (4.87 lower to 0.99 higher)	⊕⊕○○ Low
Mortality(30-days)											
5	randomised trials	not serious	serious	not serious	not serious	none	3/335 (0.9%)	4/335 (1.2%)	OR 0.79 (0.03 to 18.00)	2 fewer per 1,000 (from 12 fewer to 167 more)	⊕⊕⊕○ Moderate
Length of hospital stay											
5	randomised trials	not serious	serious	not serious	not serious	none	385	387	-	SMD 0.05 higher (0.29 lower to 0.39 higher)	⊕⊕⊕○ Moderate

PPCs, postoperative pulmonary complications; MMSE, mini-mental state examination; CI, confidence interval; OR, odds ratio; SMD, standard mean difference.

<https://doi.org/10.1371/journal.pone.0266988.t003>

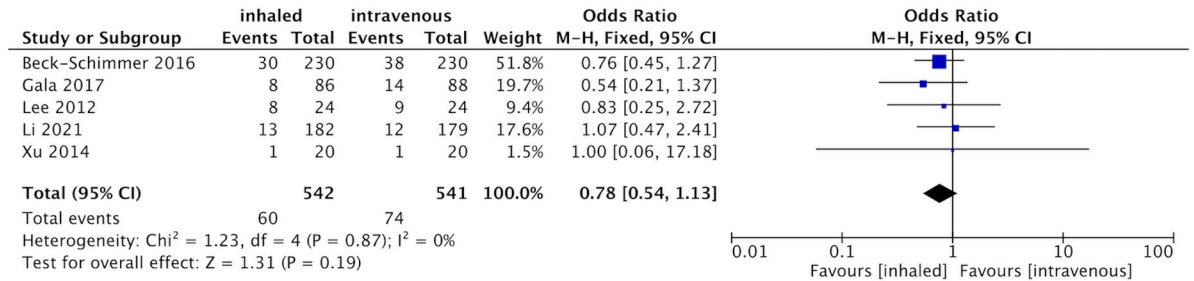


Fig 3. Forest plot for the number of the major postoperative complications between inhaled and propofol groups.

<https://doi.org/10.1371/journal.pone.0266988.g003>

effect of anesthetic type on MMSE scores (SMD -1.94, 95% CI -4.87 to 0.99, p = 0.19; I² = 100%). Due to the very high heterogeneity, further sensitivity analysis and HKSJ methods were performed to reinforce the results. However, removing individual trials did not yield the original heterogeneity, and the HKSJ method reached the same conclusion as before (SMD -1.94, 95%CI -5.11 to 1.23, p = 0.16).

Length of hospital stay. For the length of hospital stay, data were extracted from 5 trials [13, 15, 17, 19, 24] and 772 patients. Fig 6 shows that there was no significant difference at all in the length of hospital stay between different anesthetic types (SMD 0.05, 95% CI -0.29 to 0.39, p = 0.76; I² = 73%, Fig 6). Sensitivity analysis detected that Mahmoud, et al. [19] contributed to the overall heterogeneity. Pooled data excluding this study confirmed that the propofol group had a significantly shorter hospital stay than the inhalation group (SMD 0.19; 95% CI 0.05 to 0.34, p = 0.01; I² = 0). However, the HKSJ method, excluding Mahmoud, et al. led to the conclusion that anesthetics were not related to the length of hospitalization, depicting the instability of the above results (SMD 0.19, 95% CI -0.04 to 0.42, p = 0.07).

30-days mortality rate. Two of five studies [15, 17–19, 24] were designed to evaluate mortality within 30 days postoperatively. The results showed that 3 patients in the inhalation group and 4 patients in the propofol group died within 30 days postoperatively. Due to the small number of papers, we found no difference in mortality within 30 days between the two groups (SMD 0.79, 95% CI 0.03 to 18, p = 0.88; I² = 63%, Fig 7).

Discussion

This analysis included 13 eligible trials [13–25] of 2522 patients undergoing OLV and described substantial evidence, evaluated with the GRADEpro system, that compared to propofol, inhaled anesthetics carry less risk of PPC. However, there were no significant differences

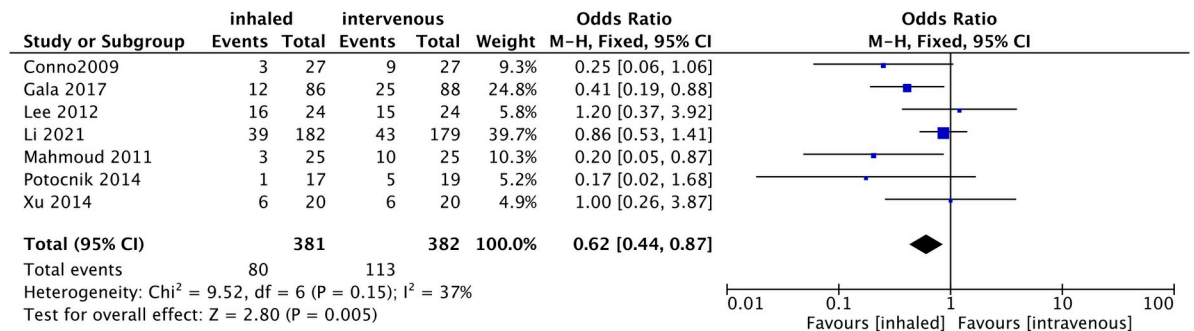


Fig 4. Forest plot for the number of postoperative pulmonary complications between inhaled and propofol groups.

<https://doi.org/10.1371/journal.pone.0266988.g004>

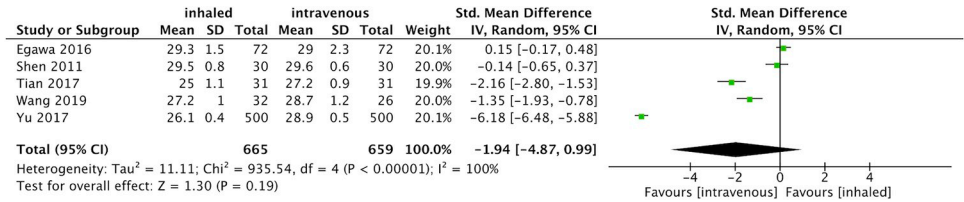


Fig 5. Forest plot for the postoperative MMSE scores between inhaled and propofol groups.

<https://doi.org/10.1371/journal.pone.0266988.g005>

in major complications, postoperative MMSE scores, length of hospital stay, or 30-day mortality by anesthetic type.

In a meta-analysis by Uhlig, et al. [6], in cardiac surgery, general anesthesia with inhaled anesthetics was associated with decreased major complications and mortality, likely due to the cardioprotective effects of volatile anesthetics through coronary vasodilation and decreased stress response [26]. Similarly, Uhlig, et al. [6] concluded that in noncardiac surgery, inhaled anesthetics appear to offer little advantage over intravenous anesthetics in major complications, mortality, and length of hospital stay. However, previous studies have shown that the anti-inflammatory effects of volatile anesthetics can affect other organs such as the lungs, brain, kidneys, and liver [27–29]. For patients undergoing noncardiac surgery (e.g., thoracic, vascular, and abdominal surgery), major complications, length of hospital stay, and mortality may be related more to the type of surgery, patient characteristics, and standardized surgical procedures than to the type of anesthetic. Therefore, the systematic organ protection of inhaled anesthetics was rare for the patients undergoing OLV studied in this study.

To our knowledge, inhaled anesthetics inhibit hypoxic pulmonary vasoconstriction (HPV) and cause hypoxemia when used at a minimum alveolar concentration greater than one during OLV [30]. However, Prakash [31] observed that volatile agents act directly on bronchial smooth muscle, contributing to bronchodilation, and that Cdyn acts to a greater extent at lower pressures during OLV compared to propofol. Thus, there are both advantages and disadvantages of inhaled anesthetics on lung function during OLV.

With regard to in vitro [32] or in vivo [33] inflammatory responses, inhaled anesthetics were found to significantly suppress the inflammatory response to lung injury, contributing to immunomodulatory and organ protective effects. In clinical surgery involving OLV, inhaled anesthetics were also found to exert anti-inflammatory effects by acting on cytokine responses, ischemia-reperfusion, and oxidative stress [15, 34]. A meta-analysis also concluded that compared to intravenous anesthesia, inhaled anesthesia could reduce the alveolar inflammatory response, but has no significant effect on the systemic inflammatory response in the interim [10]. This may contribute to the finding that inhalational agents are more effective in reducing the occurrence of PPC rather than other systemic complications.

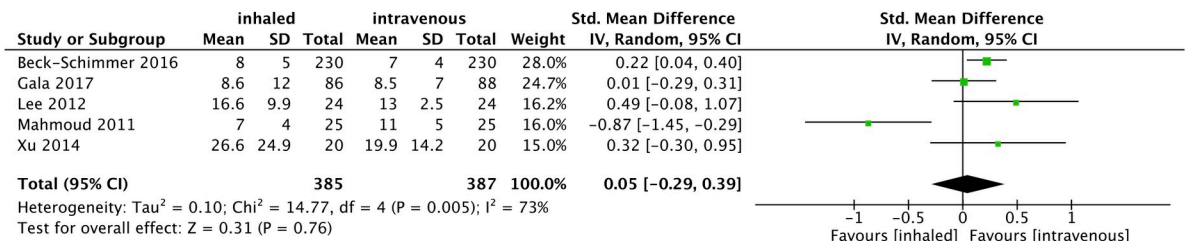


Fig 6. Forest plot for the length of hospital stay between inhaled and propofol groups.

<https://doi.org/10.1371/journal.pone.0266988.g006>

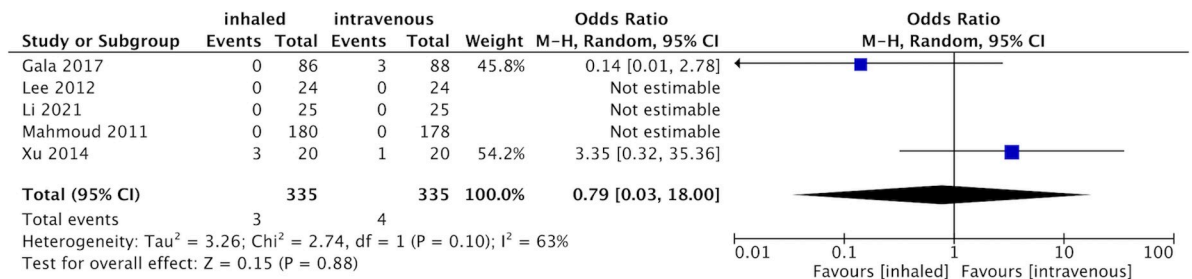


Fig 7. Forest plot for the number of 30-day death between inhaled and propofol groups.

<https://doi.org/10.1371/journal.pone.0266988.g007>

From the reports of the International Working Group on Perioperative Neurotoxicity, little evidence has been detected regarding which anesthetic is preferred for postoperative cognitive function in general anesthesia [35]. Studies have demonstrated that cerebral oxygen saturation is associated with postoperative cognitive dysfunction [36], and OLV is also associated with a definite decrease in partial pressure of oxygen compared to baseline [37]. Furthermore, trials have shown that during the first 30 minutes after OLV, the oxygenation index is higher in the intravenous anesthetic group compared to the inhaled anesthetic group [8]. However, consistent with the recommendations of the working group, we found that postoperative cognitive function screening (MMSE score) after OLV was comparable between the two groups. This may be because MMSE screening is inadequate to measure cognitive function, and postoperative cognitive dysfunction may last for weeks or months, and the follow-up period of the included clinical trials was not long enough. More importantly, desaturation, which could offset differences in the effects of anesthetics on cognitive function, was rare in all participants.

The analysis revealed several limitations. First, all trials did not systematically apply the Clavien-Dindo score in the evaluation of major complications and analyzed complications on a scale of 0 to 5 severity. Due to the limited articles, postoperative events were defined as those requiring more intensive treatment in order to reduce the risk of bias as much as possible. Second, only two trials reported mortality. Mortality rates are relatively low and are more influenced by multiple factors than by anesthetics alone. Therefore, this conclusion can be used as a reference. Next, some of the data obtained were transferred from the median/range and graphs. Although this is a commonly used method, it may increase the risk of error rates since the data are not entirely original. The language is also limited to English, which may increase the risk of publication bias. Therefore, if researchers doubt the prognostic value of different anesthetics during OLV, as recommended by two Cochrane meta-analyses [3, 7], then higher quality, more extensive trials should be designed and conducted in the future to evaluate expected outcomes.

Conclusion

In patients with OLV, inhaled anesthetics had a significant protective effect against PPC compared to propofol, but had no effect on major postoperative complications, cognitive function, length of hospital stay, or mortality at 30 days. Further studies are needed to validate this conclusion.

Author Contributions

Conceptualization: Jing Yang, Qinghua Huang, Yu Cui.

Data curation: Jing Yang, Qinghua Huang.

Formal analysis: Jing Yang.

Funding acquisition: Yu Cui.

Project administration: Yu Cui.

Supervision: Rong Cao.

Validation: Rong Cao.

Writing – original draft: Jing Yang, Qinghua Huang.

Writing – review & editing: Rong Cao, Yu Cui.

References

1. Weiser TG, Regenbogen SE, Thompson KD, Haynes AB, Lipsitz SR, Berry WR, et al. An estimation of the global volume of surgery: a modelling strategy based on available data. *Lancet*. 2008; 372(9633):139–44. Epub 2008/06/28. [https://doi.org/10.1016/S0140-6736\(08\)60878-8](https://doi.org/10.1016/S0140-6736(08)60878-8) PMID: 18582931.
2. Jemal A, Center MM, DeSantis C, Ward EM. Global patterns of cancer incidence and mortality rates and trends. *Cancer Epidemiol Biomarkers Prev*. 2010; 19(8):1893–907. Epub 2010/07/22. <https://doi.org/10.1158/1055-9965.EPI-10-0437> PMID: 20647400.
3. Módolo NS, Módolo MP, Marton MA, Volpato E, Monteiro Arantes V, do Nascimento Junior P, et al. Intravenous versus inhalation anaesthesia for one-lung ventilation. *Cochrane Database Syst Rev*. 2013; 2013(7):Cd006313. Epub 2013/07/13. <https://doi.org/10.1002/14651858.CD006313.pub3> PMID: 23846831; PubMed Central PMCID: PMC6464685.
4. Bernasconi F, Piccioni F. One-lung ventilation for thoracic surgery: current perspectives. *Tumori*. 2017; 103(6):495–503. Epub 2017/06/13. <https://doi.org/10.5301/tj.5000638> PMID: 28604996.
5. Canet J, Gallart L, Gomar C, Paluzie G, Valles J, Castillo J, et al. Prediction of postoperative pulmonary complications in a population-based surgical cohort. *Anesthesiology*. 2010; 113(6):1338–50. Epub 2010/11/04. <https://doi.org/10.1097/ALN.0b013e3181fc6e0a> PMID: 21045639.
6. Uhlig C, Bluth T, Schwarz K, Deckert S, Heinrich L, De Hert S, et al. Effects of Volatile Anesthetics on Mortality and Postoperative Pulmonary and Other Complications in Patients Undergoing Surgery: A Systematic Review and Meta-analysis. *Anesthesiology*. 2016; 124(6):1230–45. Epub 2016/04/12. <https://doi.org/10.1097/ALN.0000000000001120> PMID: 27065094.
7. Bassi A, Milani WR, El Dib R, Matos D. Intravenous versus inhalation anaesthesia for one-lung ventilation. *Cochrane Database Syst Rev*. 2008;(2):Cd006313. Epub 2008/04/22. <https://doi.org/10.1002/14651858.CD006313.pub2> PMID: 18425945.
8. Pang QY, An R, Liu HL. Effects of inhalation and intravenous anesthesia on intraoperative cardiopulmonary function and postoperative complications in patients undergoing thoracic surgery. *Minerva Anesthesiol*. 2018; 84(11):1287–97. Epub 2018/05/15. <https://doi.org/10.23736/S0375-9393.18.12501-6> PMID: 29756694.
9. Sun B, Wang J, Bo L, Zang Y, Gu H, Li J, et al. Effects of volatile vs. propofol-based intravenous anesthetics on the alveolar inflammatory responses to one-lung ventilation: a meta-analysis of randomized controlled trials. *J Anesth*. 2015; 29(4):570–9. Epub 2015/02/27. <https://doi.org/10.1007/s00540-015-1987-y> PMID: 25716536.
10. Yuan JL, Kang K, Li B, Lu J, Miao MR, Kang X, et al. The Effects of Sevoflurane vs. Propofol for Inflammatory Responses in Patients Undergoing Lung Resection: A Meta-Analysis of Randomized Controlled Trials. *Front Surg*. 2021; 8:692734. Epub 2021/07/20. <https://doi.org/10.3389/fsurg.2021.692734> PMID: 34277696; PubMed Central PMCID: PMC8282814.
11. Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ*. 2009; 339:b2535. Epub 2009/07/23. <https://doi.org/10.1136/bmj.b2535> PMID: 19622551; PubMed Central PMCID: PMC2714657.
12. Int'Hout J, Ioannidis JP, Borm GF. The Hartung-Knapp-Sidik-Jonkman method for random effects meta-analysis is straightforward and considerably outperforms the standard DerSimonian-Laird method. *BMC Med Res Methodol*. 2014; 14:25. Epub 2014/02/20. <https://doi.org/10.1186/1471-2288-14-25> PMID: 24548571; PubMed Central PMCID: PMC4015721.
13. Beck-Schimmer B, Bonvini JM, Braun J, Seeberger M, Neff TA, Risch TJ, et al. Which Anesthesia Regimen Is Best to Reduce Morbidity and Mortality in Lung Surgery?: A Multicenter Randomized Controlled Trial. *Anesthesiology*. 2016; 125(2):313–21. Epub 2016/05/21. <https://doi.org/10.1097/ALN.0000000000001164> PMID: 27203279.

14. De Conno E, Steurer MP, Wittlinger M, Zalunardo MP, Weder W, Schneiter D, et al. Anesthetic-induced improvement of the inflammatory response to one-lung ventilation. *Anesthesiology*. 2009; 110(6):1316–26. <https://doi.org/10.1097/ALN.0b013e3181a10731> CN-19417610.
15. de la Gala F, Piñeiro P, Reyes A, Vara E, Olmedilla L, Cruz P, et al. Postoperative pulmonary complications, pulmonary and systemic inflammatory responses after lung resection surgery with prolonged one-lung ventilation. Randomized controlled trial comparing intravenous and inhalational anaesthesia. *Br J Anaesth*. 2017; 119(4):655–63. Epub 2017/11/10. <https://doi.org/10.1093/bja/aex230> PMID: 29121283.
16. Egawa J, Inoue S, Nishiwada T, Tojo T, Kimura M, Kawaguchi T, et al. Effects of anesthetics on early postoperative cognitive outcome and intraoperative cerebral oxygen balance in patients undergoing lung surgery: a randomized clinical trial. *Can J Anaesth*. 2016; 63(10):1161–9. Epub 2016/07/15. <https://doi.org/10.1007/s12630-016-0700-4> PMID: 27412465.
17. Lee JJ, Kim GH, Kim JA, Yang M, Ahn HJ, Sim WS, et al. Comparison of pulmonary morbidity using sevoflurane or propofol-remifentanyl anesthesia in an Ivor Lewis operation. *J Cardiothorac Vasc Anesth*. 2012; 26(5):857–62. Epub 2012/03/03. <https://doi.org/10.1053/j.jvca.2012.01.015> PMID: 22381051.
18. Li XF, Hu JR, Wu Y, Chen Y, Zhang MQ, Yu H. Comparative Effect of Propofol and Volatile Anesthetics on Postoperative Pulmonary Complications After Lung Resection Surgery: a Randomized Clinical Trial. *Anesthesia and analgesia*. 2021. <https://doi.org/10.1213/ANE.0000000000005334> CN-33410611.
19. Mahmoud K, Ammar A. Immunomodulatory Effects of Anesthetics during Thoracic Surgery. *Anesthesiol Res Pract*. 2011; 2011:317410. Epub 2011/11/24. <https://doi.org/10.1155/2011/317410> PMID: 22110498; PubMed Central PMCID: PMC3205595.
20. Potočnik I, Novak Janković V, Šostarič M, Jerin A, Štupnik T, Skitek M, et al. Antiinflammatory effect of sevoflurane in open lung surgery with one-lung ventilation. *Croat Med J*. 2014; 55(6):628–37. Epub 2015/01/07. <https://doi.org/10.3325/cmj.2014.55.628> PMID: 25559834; PubMed Central PMCID: PMC4295075.
21. Shen YF, Wu JX, Xu MY. Effects of anesthesia with propofol and sevoflurane on postoperative cognitive function of elderly patients undergoing thoracic surgery. *Journal of shanghai jiaotong university (medical science)*. 2011; 31(3):322–5. <https://doi.org/10.3969/j.issn.1674-8115.2011.03.017> CN-00980116.
22. Tian HT, Duan XH, Yang YF, Wang Y, Bai QL, Zhang X. Effects of propofol or sevoflurane anesthesia on the perioperative inflammatory response, pulmonary function and cognitive function in patients receiving lung cancer resection. *Eur Rev Med Pharmacol Sci*. 2017; 21(23):5515–22. Epub 2017/12/16. https://doi.org/10.26355/eurrev_201712_13943 PMID: 29243798.
23. Wang G, Liu J, Gao J, Zheng X. Comparison of the effects of sevoflurane and propofol anesthesia on pulmonary function, MMP-9 and postoperative cognition in patients receiving lung cancer resection. *Oncol Lett*. 2019; 17(3):3399–405. Epub 2019/03/15. <https://doi.org/10.3892/ol.2019.9993> PMID: 30867776; PubMed Central PMCID: PMC6396185.
24. Xu WY, Wang N, Xu HT, Yuan HB, Sun HJ, Dun CL, et al. Effects of sevoflurane and propofol on right ventricular function and pulmonary circulation in patients undergone esophagectomy. *International journal of clinical and experimental pathology*. 2014; 7(1):272–9. CN-24427348.
25. Yu W. Anesthesia with propofol and sevoflurane on postoperative cognitive function of elderly patients undergoing general thoracic surgery. *Pak J Pharm Sci*. 2017;30(3(Special)):1107–10. Epub 2017/07/04. PMID: 28671090.
26. Liu KX, Xia Z. Potential synergy of antioxidant N-acetylcysteine and insulin in restoring sevoflurane postconditioning cardioprotection in diabetes. *Anesthesiology*. 2012; 116(2):488–9; author reply 9–90. Epub 2012/01/26. <https://doi.org/10.1097/ALN.0b013e31823fd063> PMID: 22273863.
27. Yang Q, Dong H, Deng J, Wang Q, Ye R, Li X, et al. Sevoflurane preconditioning induces neuroprotection through reactive oxygen species-mediated up-regulation of antioxidant enzymes in rats. *Anesth Analg*. 2011; 112(4):931–7. Epub 2011/03/10. <https://doi.org/10.1213/ANE.0b013e31820bcfa4> PMID: 21385986.
28. Kim M, Park SW, Kim M, D'Agati VD, Lee HT. Isoflurane activates intestinal sphingosine kinase to protect against bilateral nephrectomy-induced liver and intestine dysfunction. *Am J Physiol Renal Physiol*. 2011; 300(1):F167–76. Epub 2010/10/22. <https://doi.org/10.1152/ajprenal.00467.2010> PMID: 20962114; PubMed Central PMCID: PMC3023223.
29. Kim M, Ham A, Kim JY, Brown KM, D'Agati VD, Lee HT. The volatile anesthetic isoflurane induces ecto-5'-nucleotidase (CD73) to protect against renal ischemia and reperfusion injury. *Kidney Int*. 2013; 84(1):90–103. Epub 2013/02/21. <https://doi.org/10.1038/ki.2013.43> PMID: 23423261; PubMed Central PMCID: PMC3676468.
30. Lederman D, Easwar J, Feldman J, Shapiro V. Anesthetic considerations for lung resection: preoperative assessment, intraoperative challenges and postoperative analgesia. *Ann Transl Med*. 2019; 7

- (15):356. Epub 2019/09/14. <https://doi.org/10.21037/atm.2019.03.67> PMID: 31516902; PubMed Central PMCID: PMC6712248.
31. Prakash YS, Iyanoye A, Ay B, Sieck GC, Pabelick CM. Store-operated Ca²⁺ influx in airway smooth muscle: Interactions between volatile anesthetic and cyclic nucleotide effects. *Anesthesiology*. 2006; 105(5):976–83. Epub 2006/10/27. <https://doi.org/10.1097/00000542-200611000-00019> PMID: 17065892.
 32. Yue T, Roth Z'graggen B, Blumenthal S, Neff SB, Reyes L, Booy C, et al. Postconditioning with a volatile anaesthetic in alveolar epithelial cells in vitro. *Eur Respir J*. 2008; 31(1):118–25. Epub 2007/09/28. <https://doi.org/10.1183/09031936.00046307> PMID: 17898018.
 33. Reutershan J, Chang D, Hayes JK, Ley K. Protective effects of isoflurane pretreatment in endotoxin-induced lung injury. *Anesthesiology*. 2006; 104(3):511–7. Epub 2006/03/02. <https://doi.org/10.1097/00000542-200603000-00019> PMID: 16508399.
 34. Schilling T, Kozian A, Senturk M, Huth C, Reinhold A, Hedenstierna G, et al. Effects of volatile and intravenous anesthesia on the alveolar and systemic inflammatory response in thoracic surgical patients. *Anesthesiology*. 2011; 115(1):65–74. Epub 2011/03/15. <https://doi.org/10.1097/ALN.0b013e318214b9de> PMID: 21399490.
 35. Miles Berger KJS, Charles H. Brown IV, Deiner Stacie G., Whittington Robert A., Eckenhoff Roderic G., and for the Perioperative Neurotoxicity Working Group. Best Practices for Postoperative Brain Health: Recommendations From the Fifth International Perioperative Neurotoxicity Working Group. *Anesth Analg*. 2018. 1406–13 p.
 36. Kim J, Shim JK, Song JW, Kim EK, Kwak YL. Postoperative Cognitive Dysfunction and the Change of Regional Cerebral Oxygen Saturation in Elderly Patients Undergoing Spinal Surgery. *Anesth Analg*. 2016; 123(2):436–44. Epub 2016/06/11. <https://doi.org/10.1213/ANE.0000000000001352> PMID: 27285000.
 37. Tanaka N, Katoh RI, Yamamoto M, Hoshino K, Morimoto Y, Ito YM, et al. Changes in cerebral oxygen saturation during one-lung ventilation determined using spatially resolved spectroscopy and contributing factors. *J Clin Anesth*. 2020; 59:99–100. Epub 2019/07/10. <https://doi.org/10.1016/j.jclinane.2019.06.035> PMID: 31288185.