

The efficacy and safety of desflurane versus sevoflurane in elderly patients during general anaesthesia: a meta-analysis randomized controlled trials

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Research Article

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Abstract

Background: The objective of the study was to systematically screen the literature and to identify of the results of randomized controlled trials (RCTs) comparing the efficacy and safety of desflurane versus sevoflurane in elderly patients during general anaesthesia.

Methods: Databases including PUBMED, EMBASE, Web of Science and Cochrane Library were searched until July 2018 to identify relevant studies. Two authors independently reviewed each study. After literature screening and data extraction, a meta-analysis was conducted using the RevMan 5.2 software. Five RCTs, including 324 patients, met the inclusion criteria and were included in the final analysis.

Results: Our pooled analysis showed that elderly patients during desflurane general anaesthesia could reduce time taken to open eyes (SMD, -0.63; 95% CI, -1.23 to -0.03; P=0.04), follow commands (SMD, -0.97; 95% CI, -1.76 to -0.19; P=0.01), extubation (SMD, -0.77; 95% CI, -1.35 to -0.19; P=0.009) and orientation (SMD, -1.49; 95% CI, -2.43 to -0.54). However, there was no difference between desflurane and sevoflurane groups with regard to anesthesia time (SMD, -0.10; 95% CI, -0.35 to 0.15; P=0.43) and the length of postanesthetic care unit (PACU) PACU stay (SMD, -4.65; 95% CI, -10.31 to 1; P=0.11).

Conclusions: Our results show that elderly patients during desflurane general anaesthesia offers several potential advantages over anaesthesia in terms of the time to open the eyes, follow commands, extubation and orientation. However both anesthetics appear to be equivalent with regard to the anesthesia time and length of PACU stay.

Keywords: Desflurane, sevoflurane, efficacy, safety, elderly patients, meta-analysis

Introduction

With increasing life expectancy, more and more patients over 65 years of age account for an ever increasing need of surgical procedures, especially in developed countries [1, 2]. Ageing has been recognized for years as a process of intrinsic deterioration that results in functional and structural with an irreversible and progressive changes[3, 4]. These changes usually result in increasing the morbidity of the elderly patients and delayed recovery from general anesthesia[5]. Furthermore, Dogru et al have reported that the postoperative recovery from general anesthesia is related to the time spent in the postanesthetic care unit (PACU)[6]. However, owing to the service fees of PACU are double the ward fees[5]. Normally, shortening the time of a PACU stay decreases the service fees, which has an obvious economic benefit[7]. Additionally, using fast elimination anesthetics may lead to less postoperative cognitive dysfunction and faster recovery from anesthesia[8, 9]. Therefore, anesthesia for elderly patients poses a grim challenge for the anesthesiologist and surgeons, due to reduced respiratory reserves and cardiovascular and associated organ system diseases.

Currently, new volatile anaesthetics such as sevoflurane and desflurane are in widespread clinical use for maintenance of general anesthesia[10, 11]. The advantage of these anaesthetics is their low blood solubility, which accounts for its extremely rapid onset of action and recovery from general anesthesia[10, 12, 13]. Since 2001, several randomized controlled trials (RCT) have been carried out to assess the efficiency and safety of desflurane and sevoflurane anesthesia in elderly patients[1, 8, 14-16]. As each type of anesthesia has some advantages and/or disadvantages, and the conclusions have not been completely consistent.

Therefore, the present meta-analysis was performed to systematically compare the efficacy and safety of desflurane and sevoflurane in elderly patients under general anesthesia based on currently available clinical trials. We hope these findings would produce more interest in this topic and provide some help for anesthesiologists, surgeons, elderly patients, and policymakers in making relevant decisions in the future.

Background

Search strategy

The PUBMED, EMBASE, Web of Science and Cochrane Library databases were systematically searched by two independent authors (LYP and DRM) from inception to July 2018. Only articles published in English language were screened. The search keywords were used as follows: “general anaesthesia”, “sevoflurane”, “desflurane”, “elderly patients”, “elderly”, “randomized controlled trials” and “RCT”. In addition, references list of retrieved articles were also searched manually.

Inclusion and exclusion criteria

Eligibility studies that met the following criteria were included: (1) randomized controlled trial; (2) desflurane versus sevoflurane; (3) elderly patient population (>65 years); (4) access to the full text of the study and available data for analysis; (5) including at least one of the following outcomes: Anesthesia time; open eyes, extubation, following commands, orientation and postanesthetic care unit (PACU) time. The exclusion criteria were list as follow: (1) abstracts, case reports, reviews and letters; (2) not randomized controlled trial; (3) animal experiment. (4) Unable to extract original data from the study.

Data Extraction and Quality Assessment

Data were independently extracted by two reviewers (LYP and DRM). The following data items were extracted from each identified study: first author, year of publication, country, number of participants, ages, sex, main results. A quality evaluation of each RCT was conducted by two reviewers (ZJ and HSF) according to the Cochrane Collaboration tool[17]. The following items were used to assess the “risk of bias” of each RCT: random sequence generation, allocation concealment, blinding, incomplete outcome data, free of selective reporting and other bias. Discrepancies were settled by consensus after discussion with one other author (OYAP) when necessary.

Data Synthesis and Analysis

All statistical analyses were conducted using Review Manager 5.2 (Cochrane Collaboration). We estimated the standardized mean difference (SMD) for continuous outcomes with a 95 % confidence interval (CI). Heterogeneity across studies was examined using the Chi squared test and I^2 statistics. If no significant heterogeneity was detected ($I^2 \leq 50\%$), fixed-effect models was applied to pool data. Otherwise, the random-effect model was used. Funnel plot was implemented to assess publication bias.

Results

Study characteristics

Initially, 658 articles were screened through the search of electronic databases. By scanning titles and abstracts, 645 apparently irrelevant reports were excluded. 8 articles were further excluded after carefully reading full text review. Finally, only five RCTs involving 324 patients were included according to the eligibility criteria. Of the patients, 165 and 159 were classified into the desflurane and sevoflurane groups, respectively. The flow diagram of study selection process is presented in Figure 1. The basic characteristics of each included study can be seen in Table 1. Furthermore, the risk of bias across all RCTs is presented in Table 2.

Anesthesia time

Four of the included studies[1, 8, 14, 16] reported data on the anesthesia time. The results are presented in Figure 2a. There was no significant heterogeneity among the studies ($I^2=49\%$, $P=0.12$). The pooled analysis with fixed-effects model

showed no significant difference in the anesthesia time between the two groups (SMD, -0.10; 95% CI, -0.35 to 0.15; P=0.43).

Time taken to open eyes

As shown in Figure 2b, all five included studies[1, 8, 14-16] reported data on the emergence times from the end of anesthesia to eye opening. Our analysis showed that $I^2=85%$ and $P<0.0001$, indicating the studies were significant heterogeneous. Therefore, the random-effect model was used. Pooled results demonstrated that the time taken to open eyes was significantly shorter in the desflurane group when compared with the sevoflurane group (SMD, -0.63; 95% CI, -1.23 to -0.03; P=0.04).

Time taken to extubation

There were five studies[1, 8, 14-16] evaluated the time until extubation. There was significant heterogeneity among the studies ($I^2=84%$, $P<0.0001$), therefore, a random-effects model was applied. Meta-analysis showed that time until extubation was significantly shorter in the desflurane group compared to the sevoflurane group (SMD, -0.77; 95% CI, -1.35 to -0.19; P=0.009). As shown in Figure 2c.

Time taken to follow commands

Among the trials included in our Meta-analysis, 4 studies[8, 14-16] included 288 patients reported the data the emergence times from the end of anesthesia to following commands. There was obvious heterogeneity among these studies ($I^2=90%$, $P<0.00001$), so the random-effects model was applied to pool the outcomes. The pool results indicated the desflurane group had a significantly shorter the time taken to follow commands when compared to the sevoflurane group (SMD, -0.97; 95% CI, -1.76 to -0.19; P=0.01). As shown in Figure 3a.

Time taken to orientation

As shown in Figure 3b, there were four studies[1, 8, 14, 16] reported data on the time taken to orientation. Significant heterogeneity was examined among the studies ($I^2=90%$, $P<0.00001$). Therefore, the pooled analysis with the random-effects model showed that the emergence time from the end of anesthesia to **orientation** was significantly shorter in the desflurane group than the sevoflurane group (fixed-effect model; SMD, -1.49; 95% CI, -2.43 to -0.54).

Length of PACU stay

Four studies[1, 8, 14, 15] with 264 patients compared the length of PACU stay. There was no heterogeneity among studies ($I^2=0%$, $P=0.44$). Results of the pooled data indicated there was no statistically significant difference between the two groups when comparing the PACU time (SMD, -4.65; 95% CI, -10.31 to 1; P=0.11) (Figure 3c).

Publication bias

A funnel plot was used to qualitatively estimate publication bias among the studies that compared the time taken to open eyes between the desflurane and sevoflurane groups. As shown in Figure 4, the funnel plot is basically symmetry, indicating no obvious evidence of publication bias.

Discussion

There is great concern about the efficacy and safety of anesthetics in elderly patients. The present meta-analysis, involving 324 patients included from the five eligible studies, was performed to assess the efficacy desflurane and sevoflurane in elderly patients during general anesthesia. Our analysis screened one study published during the 2 years

since previous meta-analysis[18]. The clinical utility of the previous meta-analyses is still uncertain because of one RCT[19] do not give a complete description of the distribution of hidden, the specific random method. In our present paper, this meta-analysis has been boosted by data from a high quality study[14]. It is well established that desflurane anaesthesia in elderly patients was significantly associated with a faster early recovery than sevoflurane anaesthesia, including shorter the time taken to open the eyes (SMD, -0.63; 95% CI, -1.23 to -0.03; P=0.04), extubation (SMD, -0.77; 95% CI, -1.35 to -0.19; P=0.009), follow commands (SMD, -0.97; 95% CI, -1.76 to -0.19; P=0.01) and orientation (SMD, -1.49; 95% CI, -2.43 to -0.54). However, there was no obvious statically difference in anesthesia time (SMD, -0.10; 95% CI, -0.35 to 0.15; P=0.43) and the length of PACU stay (SMD, -4.65; 95% CI, -10.31 to 1; P=0.11). These results are agreement with to another previous published study[20].

Though the mean time taken to open the eyes, extubation, follow commands and orientation were significantly shorter in the desflurane group than in the sevoflurane group in our analysis, there were high heterogeneity examined among the studies. We speculated the high heterogeneity may be due to each study calculated the time using different criteria. Furthermore, the experience of surgeons and anesthesiologists, and patient characteristics were likely the primary factors affecting the time for recovery.

Despite the studies included in this meta-analysis provided evidence favoring desflurane, several potential limitations should be mentioned. First, Only five RCTs were included, which limited our ability to performed subgroup analyses for some outcomes, therefore, we could not determine the source of heterogeneity. Second, some of the included had a relatively small the sample size, which might have impacted the reliability of the conclusion. Third, each RCT in this meta-analysis was conducted in a different country; therefore, people with different genetic constitutions may have had different responses to identical anaesthetic. Finally, because of lack of adequate data in some studies, we did not assess other possible events, except for those aforementioned results, including Nausea/vomiting, postoperative cognitive dysfunction et al. Although these mentioned shortcomings may lower the reliance of our conclusion, our study systematically assessed the efficacy of of desflurane and sevoflurane in elderly patients under anaesthesia. Meanwhile, some well-designed, large, and multi-center randomized controlled clinical trials are desperately welcomed to obtain further evidence.

In conclusion, this meta-analysis provides some baseline understanding and available information that desflurane had similar efficacy to sevoflurane in terms of the length of PACU stay. However, several potential advantages, such as shorter time to open the eyes, extubation, follow commands and orientation, were observed in desflurane group.

Declarations

Acknowledgements

Not applicable

Statement of human and animal rights

This article does not contain any studies with human participants or animals performed by any of the authors.

Conflict of interest statement

On behalf of all authors, the corresponding author states that there is no conflict of interest.

Informed consent

For this type of study, formal consent is not required.

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Tables

Table 1. Characteristics of the studies included in the review

Author (year)	country	Interventions	Patients (n)	Age(year) (M±SD)	Gender (M/F)	ASA classification	Outcomes included in the meta-analysis
Chen (2001)	USA	Des	35	75±8	20/15	□-□	Anesthesia time; Open eyes; Extubation; Following commands; Orientation; PACU time
		Sev	35	73±9	18/17		
Iannuzzi (2005)	Italy	Des	18	71±3.8	5/9	□	Anesthesia time; Open eyes; Extubation; Orientation; Nausea/vomiting; PACU time
		Sev	18	70±4.2	15/7		
Rortgen (2010)	Germany	Des	40	65-75	Unclear	□-□	Open eyes; Tracheal extubation; Following commands; Orientation; PACU time
		Sev	40	65-75	Unclear		
Deepak (2013)	India	Des	30	69.1±4.7	17/7	□-□	Anesthesia time; Open eyes; Extubation; Following commands; Orientation
		Sev	30	69.4±4.4	12/18		
Pakpirom (2016)	Thailand	Des	42	73.1±5.5	19/11	□-□	Anesthesia time; Open eyes; Following commands; extubation; PACU time
		Sev	36	73.8±6.0	11/25		

M/F□Male/Female; PACU: postanesthetic care unit; Des: Desflurane; Sev: Sevoflurane.

Table 2. Quality assessment of the included studies.

Author (year)	Random sequence Generation	Allocation Concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias
Chen (2001)	Yes	Unclear	Yes	Yes	Yes	Yes	Unclear
Iannuzzi (2005)	Yes	Yes	Yes	Yes	Yes	Yes	Unclear
Rortgen (2010)	Yes	Yes	Yes	Yes	Yes	Yes	Unclear
Deepak (2013)	Yes	Yes	Yes	Yes	Yes	Yes	Unclear
Pakpirom (2016)	Yes	Yes	Yes	Yes	Yes	Yes	Unclear

Figures

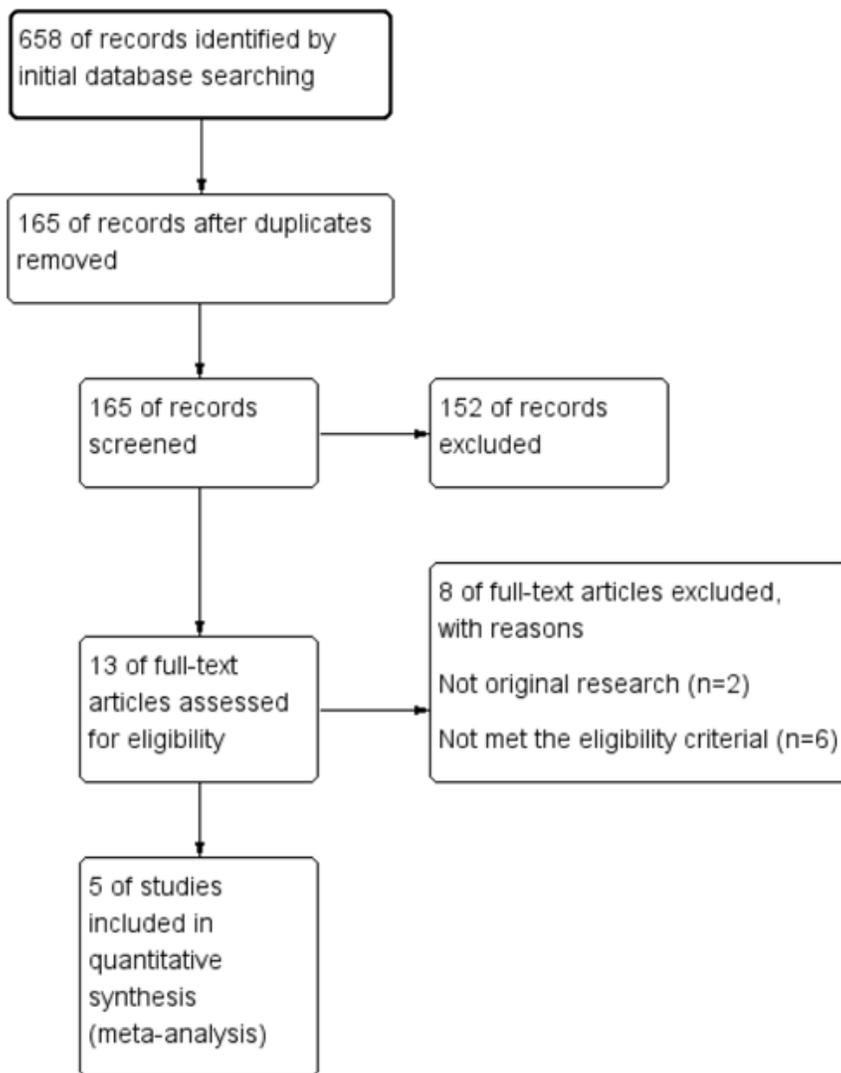


Figure 1

Flow diagram of the study selection process for the meta-analysis.

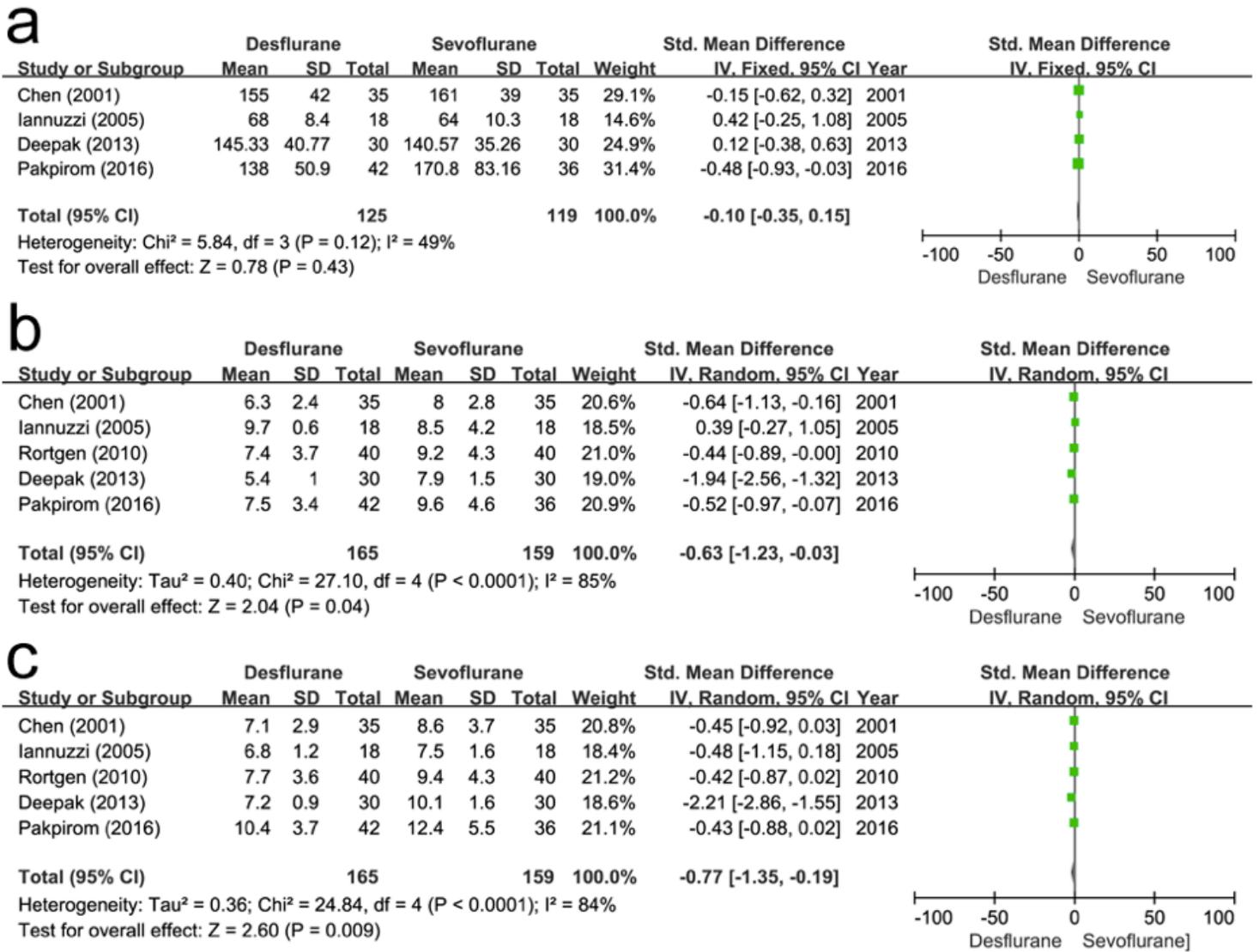


Figure 2

Forest plot of outcome of meta-analysis of RCTs regarding (a) Anesthesia time, (b) Time taken to open eyes, (c) Time taken to extubation.

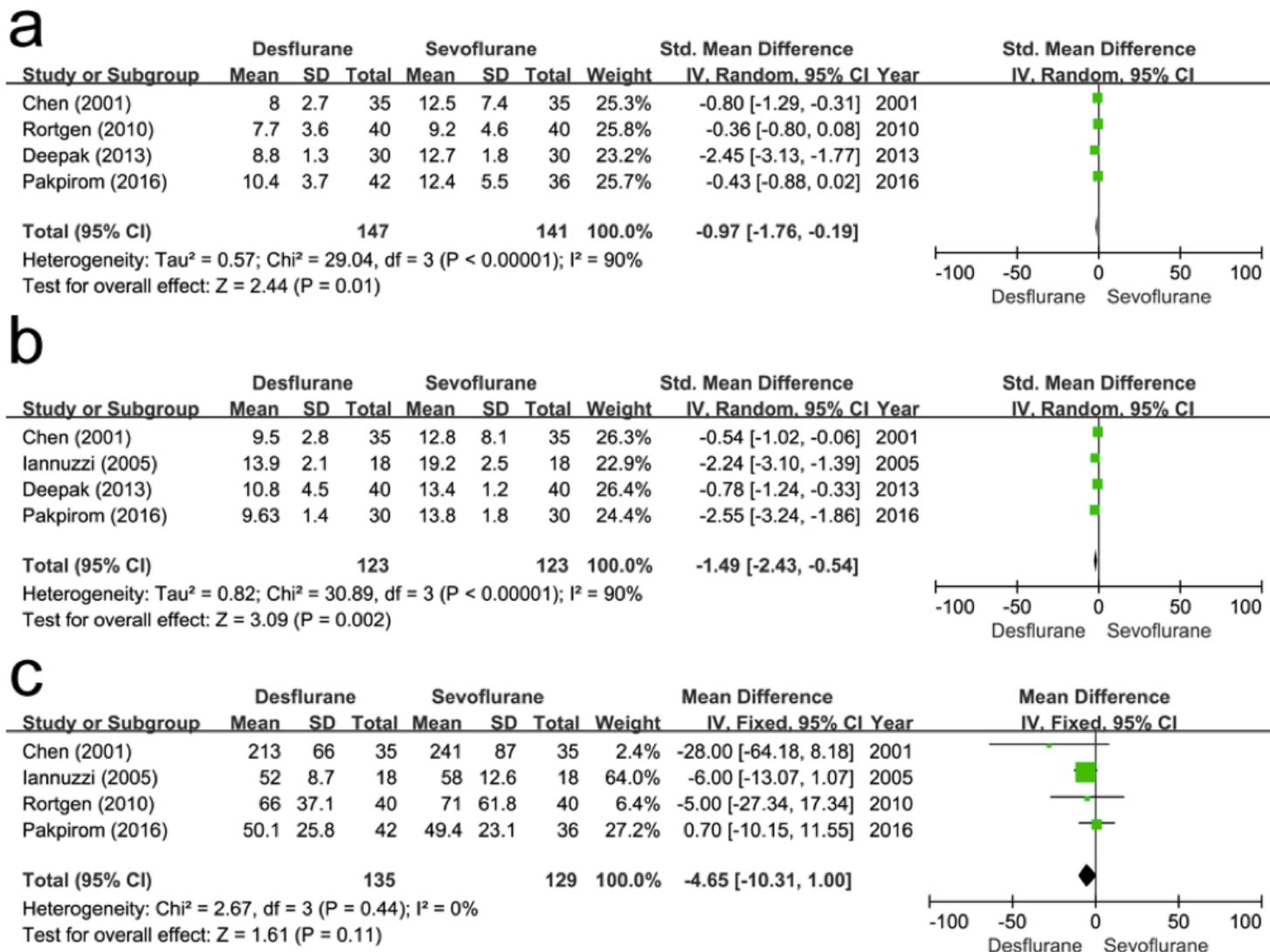


Figure 3

Forest plot of outcome of meta-analysis of RCTs regarding (a) Time taken to follow commands, (b) Time taken to orientation, (c) Length of PACU stay.

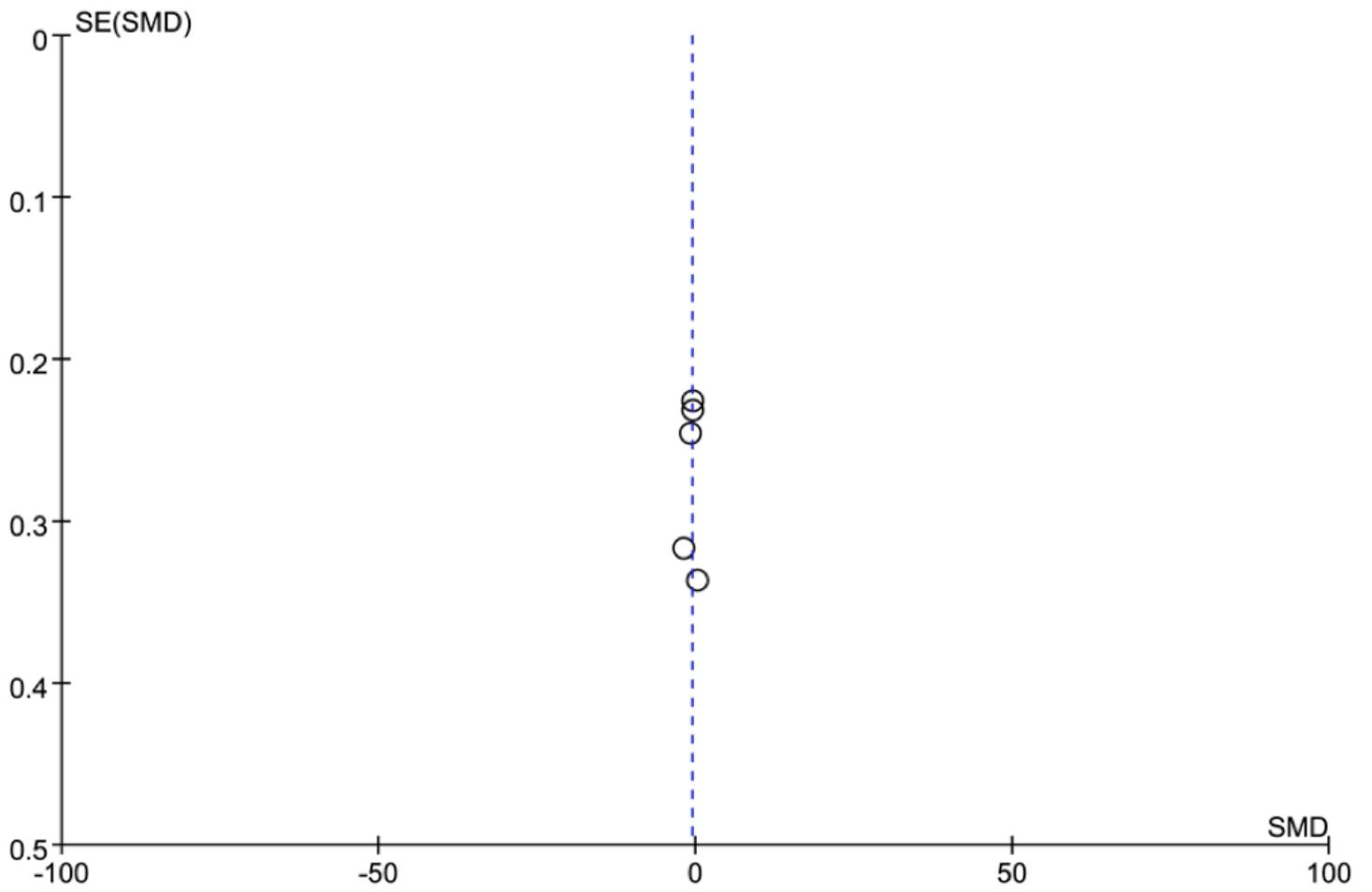


Figure 4

Funnel plot of publication bias analysis.