

Effect of desflurane–remifentanil or sevoflurane–remifentanil on early recovery in elderly patients: a meta-analysis of randomized controlled trials

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Objective: We conducted a meta-analysis to evaluate different indexes of the postoperative resuscitation period in elderly patients who received desflurane–remifentanil or sevoflurane–remifentanil. **Methods:** A systematic search of the PubMed, Embase, Cochrane Library, China National Knowledge Infrastructure and Wanfang databases for randomized controlled trials (RCTs) of elderly patients who received desflurane–remifentanil or sevoflurane–remifentanil was conducted. Extracted data were analysed using RevMan version 5.3. **Results:** Six studies involving 336 patients were included. Results indicated that the time to open eyes, time to extubation and time to orientation were faster in the desflurane group than in the sevoflurane group ($P < 0.05$). There was no significant difference in the time of discharging from the recovery room between the desflurane and sevoflurane groups ($P > 0.05$). The incidence of vomiting and agitation was lower in the desflurane group than in the sevoflurane group ($P < 0.05$). No significant difference of hypotension and hypertension was found ($P > 0.05$). **Conclusion:** Elderly patients who received desflurane–remifentanil exhibited faster recovery than those who received sevoflurane–remifentanil.

1. Introduction

As the older population constantly grows, the incidence of diseases and cancer, as well as the surgery rate, is greatly increased (Chen et al. 2013). In contrast to adults, the elderly typically have lower basal metabolic rate, degenerated digestive function, atrophied muscles, poor adaptive capacity, decreased immunity, degraded vital organs, and reduced neurotransmitters and neurons. All these factors combined will compromise the recovery from anesthesia and surgery, so the elderly are generally believed to have poor tolerance to anesthesia (Kanazawa et al. 2016; Matsuura et al. 2009). During postoperative recovery and extubation, elderly patients are subject to a higher occurrence rate of agitation, nausea, and vomiting. For this reason, the selection of proper anesthetic drugs is crucial for the postoperative recovery of elderly patients. Combined intravenous–inhalational anesthesia has been more and more widely used in surgery (Ren et al. 2018; Ryu et al. 2018). This type of anesthesia can make full use of the advantages of various anesthetics and techniques to reduce the dose of each anesthetic drug and minimize its side effects. As a result, the patient's physiological stability can be maintained to the greatest extent and safety can be guaranteed. In this study, a meta-analysis of the intravenous–inhalational anesthesia using desflurane–remifentanil or sevoflurane–remifentanil was performed to evaluate the various indicators during postoperative recovery of elderly patients, which would provide a basis for clinical applications.

2. Investigations and results

2.1. Study identification and selection

A total of 388 studies were identified initially. After preliminary and full-text screening, six studies (Çobanoğlu et al. 2013; Dong et al. 2017; Hua and Lin 2006; Iannuzzi et al. 2005; Li et al. 2017; Rörtgen et al. 2010) that included 336 patients (desflurane group $n = 168$; sevoflurane group $n = 168$) were retained. The process of article selection is shown in Fig. 1. The basic information of included studies is presented in the Table.

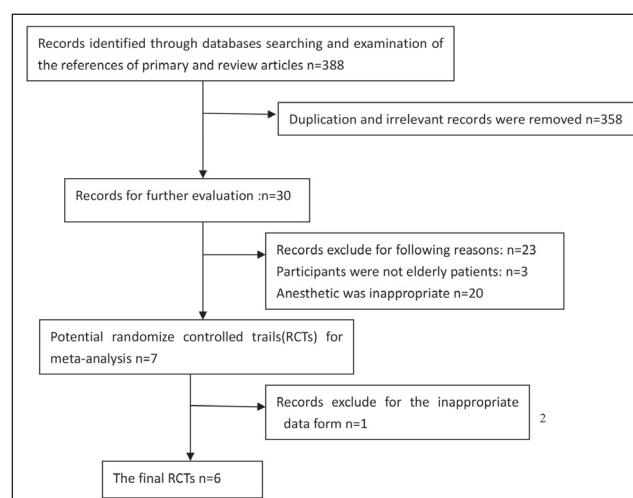


Fig. 1: Flow chart of the study selection procedure

2.2. Literature quality evaluation

Six studies mentioned random sequence generation, of which one described the random sequence generation method. Three studies stated allocation concealment, and two studies explicitly adopted the double-blind method. The data of the six articles were complete, and results were not selectively reported. Other biases were low risk (Fig. 2).

2.3. Results

2.3.1. Time to open eyes

The meta-analysis result is shown in Fig 3. Six studies reported time to open eyes. It was significantly faster in the desflurane group than in the sevoflurane group [MD= -1.97, 95% (CI -3.65,-0.29), $P < 0.05$].

Table: Characteristics of included studies

Study	Year	Country	ASA	Age	DES/Sev (N)	Des Group	Sev Group
Çobanoğlu	2013	Turkey	I–III	65–75	20/20	Des+Rf	Sev+Rf
Dong	2017	China	I–III	65–75	30/30	Des+Rf+Pro	Sev+Rf+Pro
Hua	2006	China	I–II	65–89	30/30	Des+Rf	Sev+Rf
Iannuzzi	2005	Italy	I–II	≥65	18/18	Des+Rf	Sev+Rf
Li	2017	China	I–II	65–75	30/30	Des+Rf+Pro	Sev+Rf+Pro
Rörtgen	2010	Germany	I–III	65–75	40/40	Des+Rf	Sev+Rf

ASA, American Society of Anesthesiologists physical status scale; Des, desflurane; Sev, sevoflurane; Rf, remifentanyl; Pro, propofol

	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
Çobanoğlu2013	+	+	?	+	+	+	+
Dong2017	+	?	?	+	+	+	+
Hua2006	+	?	?	+	+	+	+
Iannuzzi 2005	+	+	+	+	+	+	+
Li2017	+	?	?	+	+	+	+
Rörtgen2010	+	+	+	+	+	+	+

Fig. 2: Methodological quality of the included articles.

2.3.2. Extubation time

The meta-analysis result is shown in Fig. 4. Six studies reported extubation time. It was significantly faster in the desflurane group than in the sevoflurane group [MD= -1.84, 95% (CI -2.98,-0.71), P<0.05].

2.3.3. Orientation recovery

As shown in Fig. 5, three studies reported orientation time, patients in the desflurane group oriented significantly faster than those in the sevoflurane group [MD= -5.58, 95% (CI -7.33,-3.83), P<0.05].

2.3.4. Discharge from the recovery room

As shown in Figure 6, there was no significant difference of patients discharging from the recovery room between the desflurane and sevoflurane groups [MD= -3.46,95% (CI -8.93,2.02), P>0.05].

2.3.5. Postoperative adverse effect

As shown in Fig. 7, four studies reported vomiting and two studies reported agitation. The incidence of vomiting [OR= 0.24, 95 % CI (0.10, 0.58), P<0.05] and agitation [OR= 0.20, 95 % CI (0.06, 0.63), P<0.05] in the desflurane group was lower than in the sevoflurane group. Two studies reported hypotension and hypertension. Meta-analysis showed there was no significant difference in the incidence of hypotension [OR= 0.41, 95 % CI (0.06, 2.88), P>0.05] and hypertension [OR= 0.65, 95 % CI (0.10, 4.09), P>0.05] between the two groups.

3. Discussion

With the increase in age, the functional degradation of vital organs including the liver, kidney, and nervous system in elderly patients will affect the recovery from anesthesia and surgery, delayed recovery is a common phenomenon during resuscitation in elderly patients. Inhalational anesthetics are mainly discharged through the respiratory tract and feature convenient administration, easy control of dosage, and stable hemodynamics (Salawu et al. 2017). Desflurane has the lowest intra-hepatic metabolic rate among the inhalational anesthetics and extremely low toxicity to liver and kidney (Arslan et al. 2009). Therefore, desflurane is suitable for anesthesia in elderly patients. It has been reported that after administration of isoflurane, sevoflurane, and desflurane to experimental animals, the time taken from cessation of anesthesia to standing up of the animals was 26.3±7.2, 18.6 ±7.5, and 11.7±5.1 min (Lopez et al. 2009), respectively. The results showed that the time taken for the recovery from desflurane was the shortest. One study (Chen et al. 2001) has shown that among the elderly patients who had inhaled desflurane or sevoflurane during total knee or hip arthroplasty surgery, those in the desflurane group recovered faster than in the sevoflurane group.

Remifentanyl is an opioid receptor agonist with the advantages of fast onset, short duration of action, rapid metabolism, good controllability, and low incidence of postoperative complications such as respiratory depression (Cascone et al. 2018). It has minimal impact on patients with liver and kidney dysfunction (Glass et al.1999; Beers and Camporesi 2004), and its continuous pumping provides good sedative and analgesic effects (Cavaliere et al. 2002). Remifentanyl also has a certain antitussive effect (Kim et al. 2012; Jun et al. 2010). It has been reported that combined use of remifentanyl could lower the concentration of desflurane and improve the recovery from anesthesia (Kim et al. 2016). Six studies recorded the time to open eyes and extubation time of patients in early recovery. The results of meta-analysis showed that the time to open eyes and extubation were faster in the desflurane group than those in the sevoflurane group, and the difference was statistically significant (P<0.05). Three studies documented the time taken for the patients to recover their sense of direction. The results of meta-analysis showed that the time taken in the desflurane group was shorter than that in the sevoflurane group, and the difference was statistically significant (P<0.05). Three studies recorded the time taken for the patients to discharge from the recovery room. The results of meta-analysis showed no statistically significant difference between the two groups (P>0.05). Furthermore, the results of the meta-analysis showed that the

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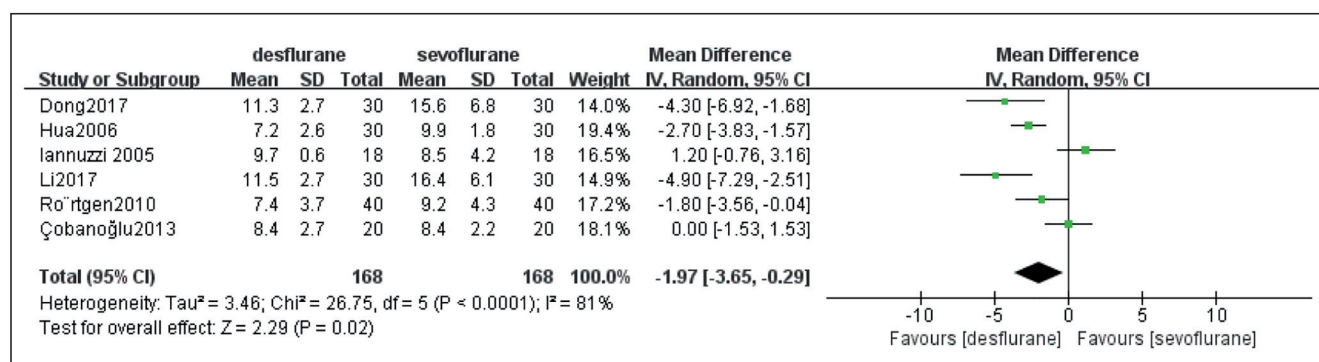


Fig. 3: Meta-analysis of the time to open eyes.

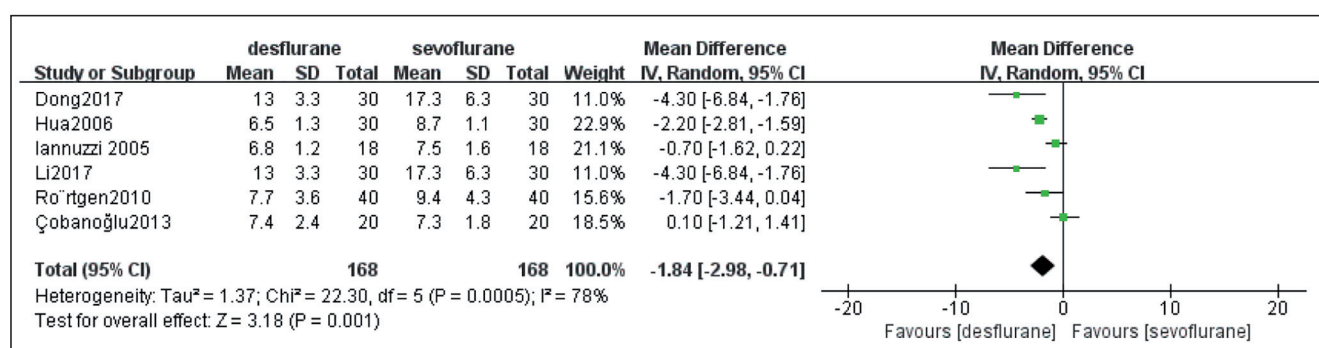


Fig. 4: Meta-analysis of the time to extubation.

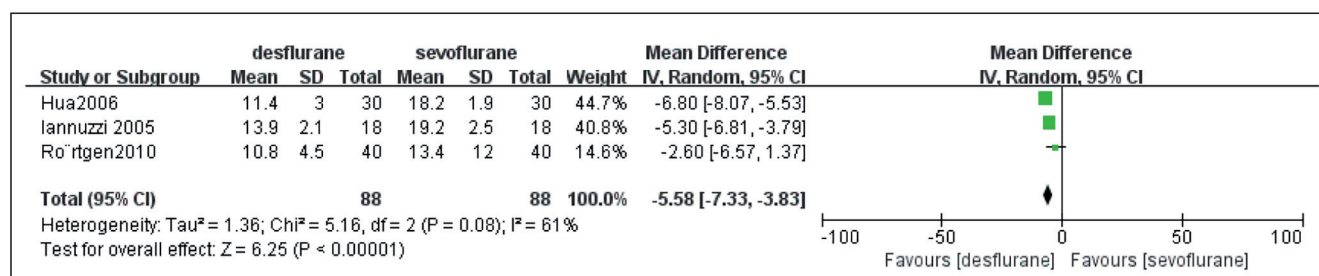


Fig. 5: Meta-analysis of the time to orientation.

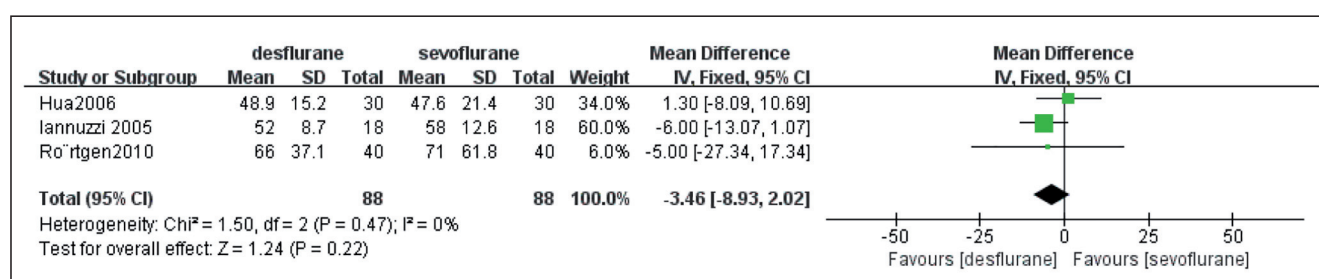


Fig. 6: Meta-analysis of the time to discharge from the recovery room.

incidence of vomiting and agitation in the desflurane group was lower than that in the sevoflurane group, and the difference was statistically significant (P<0.05). There was no significant difference in the incidence of hypotension and hypertension (P>0.05). In summary, according to the findings of this study, compared with sevoflurane–remifentanyl for combined intravenous–inhalational anesthesia, desflurane–remifentanyl is more beneficial for early recovery and has a lower incidence of postoperative adverse effect. However, this study has certain limitations due to the small sample size and the average quality of studies, as the random sequence generation, allocation concealment and blind method were not described in some of them. One study (Tachibana et al.2015) was excluded due to inap-

propriate outcomes indicators. The conclusion still needs to be further supported by including more high-quality studies.

4. Experimental

4.1. Search method

We searched the PubMed, Embase, Cochrane Library, China National Knowledge Infrastructure and Wanfang database from establishment to March 2018, without limitation of language. The following keywords were used: 'sevoflurane', 'desflurane', 'elderly' and their alternative words were combined by the Boolean meaning of 'AND' ('sevoflurane', 'desflurane', 'elderly') and 'OR' (among alternative words). Additionally, references of the included articles were manually searched, and those that met the inclusion criteria were included.

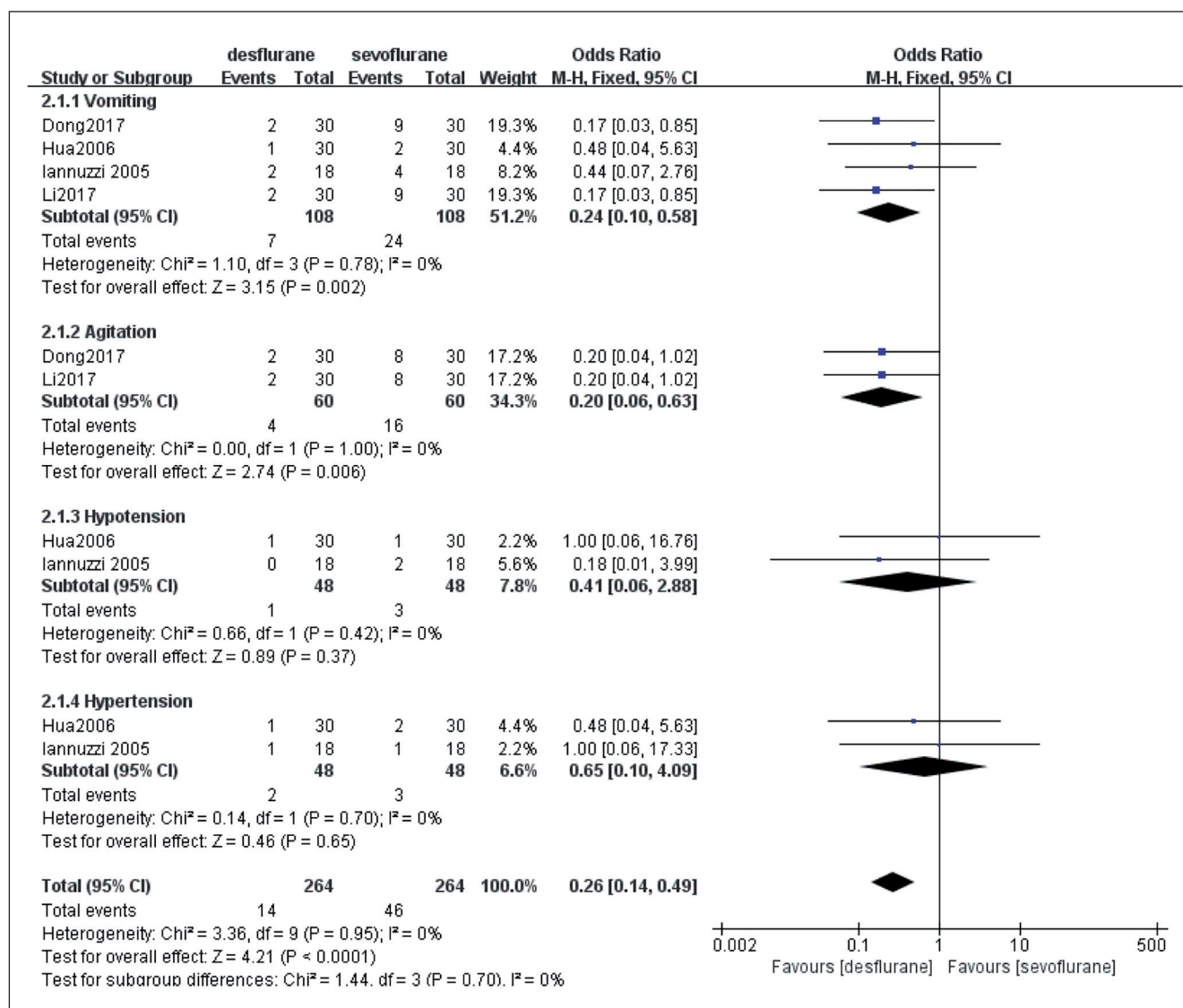


Fig. 7: Meta-analysis of the adverse effect.

4.2. Inclusion criteria and outcome indicator

1) Elderly (≥65 years) patients who received either desflurane–remifentanyl or sevoflurane–remifentanyl; 2) American Society of Anesthesiologists physical status scale (ASA) was I–III; 3) the randomized controlled trials (RCTs). Outcome indicators included time to open eyes, time to extubation, time to orientation, discharge from recovery room and incidence of postoperative adverse effect. Because different terms were used to describe recovery indicators, we reached a consensus that ‘provide birth date clearly’ was equivalent to ‘orientation’.

4.3. Data extraction

Two researchers made dependent decisions by screening the retrieved literature and extracted data. Any disagreement between the two researchers was discussed and resolved. Author was contacted to obtain the original data if the study was incomplete. Otherwise, the publication was excluded.

4.4. Quality evaluation

The methodological quality of the included literature was evaluated by two investigators according to the Cochrane Collaboration’s tool. Any disagreement was resolved by discussion. The risk of bias comprised six items: random sequence generation, allocation concealment, double blind, incomplete outcome data, selective reporting and other bias. These items were assessed ‘low risk’, ‘unclear risk’ and ‘high risk’.

4.5. Statistical analysis

This meta-analysis was conducted using Review Manager version 5.3. Mean difference(MD) was calculated for continuous variables, or odds ratio was calculated for dichotomous variables with corresponding 95% confidence intervals(CI) for each

indicator. I² test were utilised to evaluate heterogeneity. I² < 50% indicated no heterogeneity amongst the studies, the fixed-effect model was used for analysis; otherwise, the random-effect model was applied.

Conflicts of interest: None declared.

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