

Effect of Dexmedetomidine on Atrial Fibrillation-Based Tachyarrhythmia After Cardiac Surgery: A Systematic Review and Meta-Analysis

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Research

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Abstract

Background: The incidence of tachyarrhythmia with atrial fibrillation as the main manifestation increases after adult cardiac surgery, which leads to an increase in adverse events. Dexmedetomidine has been widely used in the perioperative period, but the effect of dexmedetomidine on tachyarrhythmia after cardiac surgery in adults remains controversial.

Objective: To evaluate the effect of perioperative use of dexmedetomidine on tachyarrhythmia with atrial fibrillation as the main manifestation after cardiac surgery.

Methods: We searched six databases, including Embase, PubMed, Cochrane, CNKI, Wanfang, and Sinomed, for literature published up to November 2020, without restrictions on language. The primary endpoint was the number of patients with atrial fibrillation after cardiac surgery. The secondary endpoints included: the number of patients with supraventricular tachycardia, the number of patients with ventricular tachycardia, the number of patients with ventricular fibrillation, the number of patients with myocardial infarction, the number of dead patients, mechanical ventilation duration, and the length of ICU stay and hospitalization. We used Stata (Version 12.0) and Review Manager (Version 5.3) provided by Cochrane Collaboration for data analysis. If the included studies have high statistical heterogeneity ($P \leq 0.1$, $I^2 > 50\%$), we will use a random-effects model. Otherwise, a fixed-effects model will be used for calculation.

Results: Among the 1388 studies retrieved, a total of 18 studies met our inclusion criteria (N=3171 participants). The use of dexmedetomidine reduced the incidence of atrial fibrillation by 17% (RR=0.83, 95% CI 0.73-0.93; Z=3.06, P=0.002), reduced the incidence of supraventricular tachycardia by about 70% (RR=0.29, 95% CI 0.11-0.77; Z=2.47, P=0.01), reduced the incidence of ventricular tachycardia by about 80% (RR=0.23, 95% CI 0.08-0.63; Z=2.85, P=0.004), but had no effect on the incidence of ventricular fibrillation (RR=1.02, 95% CI 0.14-7.31; Z=0.02, P=0.99). There was no significant difference in the incidence of myocardial infarction between the two groups (RR = 0.90, 95% CI 0.37-2.18; Z = 0.24, P = 0.81). There was no significant difference in mortality between the two groups (RR = 0.86, 95% CI 0.31-2.44; Z = 0.28, P = 0.78). Dexmedetomidine group can reduce the time of patients in ICU (SMD = -0.35, 95% CI -0.69 to -0.02; Z = 2.07, P = 0.04), but the heterogeneity between studies is high ($I^2 = 93\%$). There was no effect on duration of mechanical ventilation (SMD = -0.10, 95% CI -0.25 to 0.06; Z = 1.18, P = 0.24) and length of hospitalization (SMD = -0.46, 95% CI -1.08 to 0.16; Z = 1.46, P = 0.14).

Conclusion: Dexmedetomidine can reduce the incidence of atrial fibrillation, supraventricular tachycardia, and ventricular tachycardia after cardiac surgery in adults but does not affect the occurrence of ventricular fibrillation.

Trial registration: CRD42021233613; Registration: Jan 2021

Introduction

Atrial fibrillation (AF) is a tachyarrhythmia characterized by the deterioration of atrial mechanical function due to uncoordinated activities of the atria. The incidence of AF increases after heart operation. It was reported that the incidence of AF is about 30% in patients with coronary artery bypass grafting, 40% in patients with heart valve repair or replacement, and 50% in patients with combined surgery [1]. The exact mechanism of AF remains unclear. Atrial traction, myocardial ischemia and hypoxia, inflammatory reaction, electrolyte disturbance, and conduction system damage during cardiac surgery all increase the incidence of AF [2]. AF may cause a series of adverse events, including discomfort, anxiety, cognitive impairment, hemodynamic deterioration, myocardial infarction, stroke, prolonged hospitalization, and increased medical expenses [3–7].

As we all know, dexmedetomidine (DEX) is a highly selective α_2 receptor agonist, which has been widely used in the perioperative period. DEX can reduce sympathetic activity, the tension of the sinus node and atrioventricular node [8], thus slowing down patient's heart rate. However, the effect of DEX on AF after adult heart operation is still controversial. Retrospective study [9, 10] found that DEX can reduce the occurrence of AF after heart operation, which was also confirmed by randomized controlled trials (RCTs) [11–14]. However, other studies [15–19] found that DEX had no influence on AF incidence after heart operation. Besides, a meta-analysis [20] suggested that DEX may increase the incidence of AF after heart operation in patients with a history of AF. Given these controversies, we sorted out the relevant literature and did this systematic review and meta-analysis.

1. Methods

1.1 Search strategy

The Preferred Reporting Items for Systematic Reviews and Meta-analyses Protocols (PRISMA) statement was the guideline during this study's design. This study's protocol has been registered in the International Prospective Register of Systematic Reviews (PROSPERO), and the registration number is CRD42021233613.

Two authors (WZW and JL) searched six databases, including Embase, PubMed, Cochrane, CNKI, Wanfang, and Sinomed, for literature published up to November 2020. The combination of subject word and free word retrieval was used for searching the literature. The keywords in PubMed included: ((thoracic surgical procedures [mesh] or cardiovascular surgical procedures [mesh] or ((cardiovascular [title / Abstract] or coronary [title / Abstract] or myographic [title / Abstract] or vascular [title / Abstract] or aorto * [title / Abstract] or valve [title / Abstract] or "vascular reconstructive" [title / Abstract] or "off" pump"[Title/Abstract] OR bypass[Title/Abstract]) AND (surg* [Title/Abstract] OR operat* [Title/Abstract]))) AND ("dexmedetomidine" [Mesh]). The search was performed with no restrictions on language and focused on the type of RCT. We also reviewed the reference lists of the relevant articles and performed the manual search to identify additional studies. Contact the corresponding author or the first author when in doubt or if the data is incomplete.

1.2. Inclusion criteria for study selection

(1) Participants: The adult patients (≥ 18 years) who underwent cardiac surgery and were transferred to intensive care unit (ICU) after surgery, without restrictions on the type of surgery and whether they underwent cardiopulmonary bypass. (2) Intervention measures: DEX was used during the perioperative period, without restrictions on the starting time, dose, loading dose, and drug duration. (3) Control: Placebo or other sedative and analgesic drugs. (4) Outcome indicator: The primary outcome indicator is the incidence of postoperative AF. The collected AF information is observed from electrocardiogram (ECG) monitor or collected from ECG and 24-hour Holter ECG after the operation, without restrictions on the duration and frequency of AF and whether AF is new-onset or not. (5) Design: RCTs.

1.3 Exclusion criteria

(1) Non-human trials or pediatric surgery. (2) Non-cardiac surgery. (3) Use of other α_2 receptor agonists. (4) Outcome indicators have not reported the occurrence of postoperative AF. (5) Retrospective studies, observational studies, reviews or systems evaluation. (6) Repeated publications. (7) Unable to obtain full-text literature.

1.4 Data extraction and quality assessment

Two authors (WZW and JL) performed data extraction independently. The data contained: First author, publication year, number of cases in the two groups, type of surgery, load and maintenance dose of DEX, control group drugs,

follow-up time, the number of patients with AF after cardiac surgery, the number of patients with supraventricular tachycardia (SVT), the number of patients with ventricular tachycardia (VT), the number of patients with ventricular fibrillation (VF), the number of patients with myocardial infarction (MI), the number of reported deaths, the duration of mechanical ventilation (MV), the ICU stay and hospital stay. We pre-extracted the designed data extraction form. If the opinions of the two data extractors were inconsistent and could not be resolved through negotiation, a third researcher (MSW) assisted in the resolution. If data from any category were not reported in the preliminary study, we would contact the corresponding authors or the first author to request the information. We used the Cochrane bias risk assessment tool to assess the methodological quality of the included studies.

1.5 Statistical analysis

We used Stata (Version 12.0) and Review Manager (Version 5.3) provided by Cochrane Collaboration for data analysis. Mantel-Haenszel (M-H) method was used to calculate relative risk (RR) and 95% confidence interval (CI) for binary variables. Continuous variables such as MV time, ICU stay, and hospital stay were expressed as standardized mean difference (SMD) and 95% CI. We used Cochran's Q-statistic and I^2 statistics to assess heterogeneity. If the included studies had high statistical heterogeneity ($P \leq 0.1$, $I^2 > 50\%$), we used a random-effects model. Otherwise, a fixed-effects model was used for calculation. We use funnel plots and Egger's test to assess and quantify publication bias. When $P < 0.1$, we thought there was a significant publication bias.

2. Results

2.1. Study selection and quality assessment

A total of 1388 studies were detected, and 1045 studies remained after removing duplicate documents. 210 studies remained after reading the title and abstract. 10 studies were not found in full text, and 18 [11-19, 21-29] articles were included after a full-text screening of the remaining articles. 18 literatures were included in the meta-analysis (Fig. 1). In one of the articles [25], we contacted the author and obtained data on postoperative AF. The study [12] with the smallest sample size included 60 patients, and the study [29] with the largest sample size included 794 patients. The surgical types of 8 studies were simple coronary artery bypass grafting (CABG) [13, 15-17, 19, 21, 22, 24], 2 studies were simple valve surgery [12, 26], and the type of surgery for the remaining studies were adult cardiac surgery including all types [11, 18, 23, 25, 27-29]. Five studies were sponsored by pharmaceutical companies [16, 17, 25, 28, 29]. For the evaluation of double-blind in the trial's methodological quality, most of the studies were unclear or high-risk, and three studies were "open-label" [11, 16, 22]. The included articles' baseline characteristics were shown in Table 1, and the risk of bias was shown in Fig. 2 and 3.

2.2 Main results

Regarding the incidence of AF, a total of 18 studies with 3171 patients (1603 in the DEX group and 1568 in the control group) were included in the meta-analysis. After cardiac surgery, the total incidence of AF was 22.86%, including 20.59% in the DEX group and 25.19% in the control group. Compared with the control group, DEX decreased the incidence of AF by 17% (RR=0.83, 95%CI 0.73-0.93; Z=3.06, $I^2=31\%$; P=0.002) (Fig. 4). Funnel plot (Fig. 5) and Egger's test [see Additional file 1] showed no publication bias (P = 0.196).

Regarding the incidence of SVT, a total of 2 studies [13, 28] with 461 patients (233 in the DEX group and 228 in the control group) were included. The total incidence of SVT after cardiac surgery was 4.77%, 2.15% in the DEX group, and 7.46% in the control group. The risk of SVT in the DEX group was about 30% of that in the control group (RR = 0.29; 95% CI 0.11-0.77; $I^2 = 32\%$; Z = 2.47, P = 0.01; Fig. 6).

Regarding the incidence of VT, a total of 4 studies [13, 16, 17, 28] with 836 patients (421 in the DEX group and 415 in the control group) were included. The total incidence of VT after cardiac surgery was 2.75%, in which the incidence of the DEX group was 0.95%, and that of the control group was 4.58%. Compared with the control group, the risk of VT in the DEX group was 23% of the control group (RR = 0.23, 95% CI 0.08-0.63; $I^2 = 0\%$; $Z = 2.85$, $P = 0.004$; Fig. 7).

Regarding the incidence of VF, a total of 2 studies [22, 28] with 388 patients (195 in the DEX group and 193 in the control group) were included. The incidence of VF was 0.52%, and there was no difference between the two groups (RR = 1.02, 95% CI 0.14-7.31; $I^2 = 0\%$; $Z = 0.02$, $P = 0.99$; Fig. 8).

We also counted the incidence of MI after surgery. A total of 3 studies [16, 17, 29] with 1169 patients (586 in the DEX group and 583 in the control group) were included. The total MI incidence was about 1.63% (1.54% in the DEX group and 1.72% in the control group). The incidence of MI in the DEX group was slightly lower than that in the control group, but there was no statistical significance (RR = 0.90, 95% CI 0.37-2.18; $I^2 = 23\%$; $Z = 0.24$, $P = 0.81$; Fig. 9).

Regarding the mortality rate, a total of 7 studies [11, 13, 17, 22, 23, 28, 29] with 1679 patients (842 in the DEX group and 837 in the control group) were included. The overall mortality incidence was about 0.66% (0.59% in the DEX group and 0.72% in the control group). The mortality in the DEX group was lower than that in the control group, but there was no statistical significance (RR = 0.86, 95% CI 0.31-2.44; $I^2 = 0\%$; $Z = 0.28$, $P = 0.78$; Fig. 10).

The results showed that DEX could reduce the time of patients in ICU (11 studies [11, 14, 15, 18, 19, 21-23, 25, 27-29] 2341 patients; SMD = -0.35, 95% CI -0.69 to -0.02; $I^2 = 93\%$; $Z = 2.07$, $P = 0.04$; Fig. 11), but the heterogeneity between studies was high. There was no significant difference in postoperative mechanical ventilation time (1967 patients in 13 studies [11, 15, 16, 18, 19, 21-28]; SMD = -0.10, 95% CI -0.25 to 0.06; $I^2 = 65\%$; $Z = 1.18$, $P = 0.24$; Fig. 12) and hospitalization (1158 patients in 8 studies [11, 14, 15, 18, 21, 23, 27, 28]; SMD = -0.46, 95% CI -1.08 to 0.16; $I^2 = 96\%$; $Z = 1.46$, $P = 0.14$; Fig. 13). The publication bias of ICU time ($P = 0.135$) and MV time ($P = 0.666$) was evaluated by funnel plot (Fig. 14, 15) and Egger's test [see Additional file 1]. There was no publication bias in both groups.

4. Discussion

Our study had achieved remarkable results on DEX's effect on the incidence of AF in adult patients after heart surgery. The meta-analysis of 18 RCTs and 3171 participants confirmed the anti-arrhythmic effect of DEX, which is not only reflected in the effect on AF, but also in the impact on SVT and VT.

Various types of arrhythmia often occur after heart surgery, but AF and malignant ventricular arrhythmia have the most significant influence on postoperative hemodynamics. Studies have confirmed that the autonomic nervous system is closely related to the occurrence of postoperative AF [30]. Stimulation of vagus nerves and sympathetic nerves can cause AF. High-intensity vagal nerve stimulation can induce the atrium and pulmonary veins' electrical remodeling, thus promoting AF [31]. Drugs that increase sympathetic nerve tension can also increase the incidence of postoperative AF, while perioperative use of beta-blockers can decrease the incidence of postoperative AF [32]. Besides, compared with other cardiac surgery, the incidence of AF after heart transplantation is relatively lower [33]. Inflammation promotes the occurrence of AF as well. The relationship between AF and inflammatory response was first proposed by Bruins et al. [34] They found that the peak of postoperative AF in patients undergoing coronary artery bypass grafting is generally 2–3 days after surgery, and C reactive protein also reached its peak at the same time. Korantzopoulos et al. [35] found that the white blood cell level of patients with AF gradually decreased after cardioversion and considered that the occurrence of AF was closely related to the white blood cell count. Weymann et al. [36] found that white blood cell count was related to the recurrence of AF and emphasized that the percentage of

neutrophils to lymphocytes and the ratio between them were more predictive than white blood cells for the recurrence of AF. Oxidative stress also plays an essential role in the occurrence and maintenance of AF. During cardiac surgery, injured myocardial cells produce many reactive oxygen species, which leads to atrial structural and electrical remodeling, imbalance of redox gene expression, and oxidative damage to mitochondrial DNA [37]. The mechanism of postoperative malignant ventricular arrhythmia is similar to that of AF, which is related to many factors, such as atrioventricular hypertrophy, myocardial ischemia and hypoxia, acid-base imbalance, and electrolyte disorder, pain, drainage tube stimulation, and drug effect.

DEX was first approved by U.S. Food and Drug Administration for sedation in ICU. However, with the in-depth understanding of DEX's pharmacological effects and a series of clinical observations, DEX's protective effects on essential organs such as the heart, brain, lung, and kidney have been gradually confirmed. DEX is a highly selective α_2 adrenergic receptor agonist, mainly including, α_2B , and α_2C , which has specific effects on α_2 receptors in the brain, spinal cord, and periphery. Among them, α_2A excitement can regulate autonomic nervous tension, regulate the release of endogenous catecholamines, and produce sedative, analgesic and anti-anxiety effects. The stimulation of α_2B can constrict blood vessels, maintain hemodynamic stability, and produce an analgesic effect by inhibiting the transmission of pain signals and reducing substance P release. The antiarrhythmic effect of DEX may be related to regulating the autonomic nervous system, inhibition of inflammatory response, and oxidative stress response. DEX can inhibit the sympathetic nerve, excite the vagus nerve, reduce catecholamine concentration, and inhibit epinephrine's arrhythmogenic effect [13, 38]. Animal experiments showed that DEX could reduce calcium influx, inhibit early and late depolarization, and significantly reduce the incidence of VF in rabbits with acquired long QT syndrome [39]. Yu et al. [40] found that DEX can induce myocardial autophagy, improve inflammatory state and inhibit cardiomyocyte apoptosis in rats through the animal model of sepsis induced by cecal ligation and puncture. Besides, DEX can inhibit apoptosis induced by reactive oxygen species and thus has a myocardial protective effect on rat cardiomyocytes [41]. Given the above myocardial protective effects of DEX, our meta-analysis showed consistent results. As for the effect of DEX on VF, we did not get a positive result. The reason was no more than the following two factors. First of all, with the in-depth understanding of patients' pathophysiology with heart disease, the improvement of surgical skills, and the increase of anesthesia, cardiopulmonary bypass, and postoperative nursing team level, the incidence of VF after cardiac surgery is gradually decreasing. Secondly, our meta-analysis research's primary indicator is AF, so collecting information on the incidence of VF is imperfect.

Previous systematic reviews and meta-analysis [20, 42] found that DEX did not affect AF incidence after cardiac surgery. However, Liu et al. [43] indicated that DEX could reduce the incidence of AF and VT after cardiac surgery but has no effect on VF incidence (this result was consistent with our research results). By comparison, we found that the literature as mentioned earlier has uniform inclusion criteria, and the types of surgery were CABG or valve replacement surgery, and the language of publication was English. Six of the included randomized controlled trials were different. The reason lay in the different retrieval times and comprehensiveness of the author. The inclusion indicators of our study have slightly changed. The type of surgery included all cardiac operations. The occurrence time of the analysis results was limited after the operation, and there was no restriction on the language of publication. A total of 18 studies involving 3171 patients were included. The number of patients included in the meta-analysis was twice as large as that in the previous meta-analysis, including a 5-year multicenter large-scale randomized controlled study conducted by Turan and his colleagues [29] in 2020. In conclusion, the reliability of our results is significantly increased.

Our study also performed a pooled analysis of MI and mortality, and found that DEX did not affect these indicators, which was consistent with the results of other meta-analyses [43, 44], but it still needs further study to confirm. Besides, our study showed that DEX could shorten the time of patients in ICU. However, the studies' heterogeneity is

high, which may be related to different surgery types, different critical conditions, different ICU transport standards in the different centers, and whether to use fast-track anesthesia. No positive results were found in this study on the influence of MV time and hospitalization time. However, Lin et al. [45] believe that DEX can lead to early extubation of patients after CABG. Compared with CABG patients, patients with valve disease, patients undergoing combined cardiac surgery, and patients undergoing large vessel surgery usually have higher postoperative complications and need more prolonged mechanical ventilation and hospitalization time. There are no restrictions on the types of adult cardiac surgery in our study, which may be one reason for not getting positive results.

There are some limitations in our study. First, it is not clear how long the antiarrhythmic effect of DEX can last, and most of the observation time included in the studies is no more than five days after surgery. Second, some studies have potential bias risks, such as open-label design and pharmaceutical industry funds. Third, this study did not further analyze the effects of DEX dosage and timing on the results. Not all the included studies used load capacity. The maintenance dose of DEX ranged from 0.04 to 1.5 ug/kg/h; the timing of intervention varies from study to study, including before, during, and even after surgery. The optimal time and dose of DEX intervention are unknown. Future large-sample clinical trials should focus on the above two points to maximize the antiarrhythmic effects of DEX.

5. Conclusions

Perioperative use of DEX can reduce the incidence of AF, SVT, VT and ICU stay. However, it has no effect on the incidence of VF, MI, and mortality, and has no effect on MV duration and hospital stay. Our research supports the application of DEX in the perioperative period of adult cardiac surgery, which provides a new way of thinking for the prevention and treatment of arrhythmia after adult cardiac surgery.

Abbreviations

AF: atrial fibrillation; CABG: coronary artery bypass grafting; CI: confidence interval; DEX: dexmedetomidine; ECG: electrocardiogram; ICU: intensive care unit; M-H: Mantel-Haenszel; MI: myocardial infarction; MV: mechanical ventilation; RCT: randomized controlled trial; SVT: supraventricular tachycardia; VF: ventricular fibrillation; VT: ventricular tachycardia.

Declarations

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Authors' contributions:

WZW and JL conducted the primary data search, analyzed data and wrote the manuscript. HBY conducted the data analysis and helped in manuscript preparation. MSW solved the classification discrepancies in data collection designing the study and in the primary search and substantially contributed in manuscript preparation and data interpretation. TW designed the study, and drafted the manuscript. All the authors approved the final version of the paper and agree to be accountable for all aspects of the work, thereby ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All authors read and approved the final manuscript.

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Tables

Table 1: Characteristics of included studies

Study	Number of patients		Type of Surgery	Dexmedetomidine dose	Control	Endpoints	Follow-up time
	DEX	Control					
Balkanay 2015[21]	60	28	CABG	0.04-0.5 µg/kg/h	Placebo	AF; MV duration; ICU stay; hospital stay	5 days postoperative
Corbett 2005[22]	43	46	CABG	Loading dose: 1 µg/kg over 15mins; Infusion rate: 0.4 µg/kg/h	Propofol	AF; VF; Mortality; MV duration; ICU stay	Time in ICU
Cui 2018[12]	30	30	Valve replacement surgery	0.7 µg/kg/h at 20:00 every day 3 days before surgery, and stop infusion at 06:00 the next day	Meperidine and promethazine	AF	3 days in ICU
Djaiani 2016[23]	91	92	Complex cardiac surgery	Loading dose: 0.4 µg/kg over 10-20 mins; Infusion rate: 0.2-0.7 µg/kg/h for 24 h	Propofol	AF; Mortality; MV duration; ICU stay; hospital stay	5 days postoperative
Göksedef 2013[15]	49	37	CABG	0.04-0.5 µg/kg/h	Placebo	AF; MV duration; ICU stay; hospital stay	5 days postoperative
Herr 2003[16]	148	147	CABG	Loading dose: 1.0 µg/kg over 20 minutes; Infusion rate: 0.2-0.7 µg/kg/h	Propofol	AF; VT; Myocardial infarction; MV duration	24 h in ICU
Jalonen 1997[17]	40	40	CABG	Loading dose: 50 ng/kg/min for 30 min; Infusion rate: 7 ng/kg/min	Saline	AF; VT; Myocardial infarction; Mortality	6 days postoperative
Karaman 2015[24]	31	33	CABG	0.2-1.0 µg/kg/h	Propofol	AF; MV duration	6h after surgery
Li 2017[25]	142	143	CABG and/or valve replacement surgery	Loading dose: 0.6 µg/kg over 10mins; Infusion rate: 0.4 µg/kg/h until end of surgery, and then 0.1 µg/kg/h until the end of mechanical ventilation.	Saline	AF; MV duration; ICU stay	6 days postoperative
Liu	44	44	Elective	≤1.5 µg/kg/h	Propofol	AF;	96h after

2016[11]			cardiac surgery with CPB			Mortality; MV duration; ICU stay; hospital stay	surgery
Liu 2016-CTVA[26]	29	32	Elective valve surgery	0.2-1.5 µg/kg/h	Propofol	AF; MV duration	Time in ICU
Park 2014[27]	67	75	On-pump cardiac surgery	Loading dose: 0.5 µg/kg; Infusion rate: 0.2-0.8 µg/kg/h	Remifentanyl	AF; MV duration; ICU stay; hospital stay	3 days postoperative
Ren 2013[13]	81	81	On-pump CABG	0.2-0.5 µg/kg/h	Saline	AF; SVT; VT; Mortality	3 days postoperative
Shehabi 2009[28]	152	147	On-pump cardiac surgery	0.1-0.7 µg/kg/h	Morphine	AF; SVT; VT; VF; Mortality; MV duration; ICU stay; hospital stay	12 days postoperative
Shi 2019[18]	84	80	Cardiac surgery	0.4-0.6 µg/kg/h during the surgery	Placebo	AF; MV duration; ICU stay; hospital stay	Time in ICU
Turan 2020[29]	398	396	On-pump cardiac surgery	During the operation: 0.1-0.4 µg/kg/h; ICU: 0.4 µg/kg/h until 24 h after the infusion began	Saline	AF; Myocardial infarction; Mortality; ICU stay	5 days postoperative or discharge
Yu 2019[14]	52	56	On-pump cardiac surgery	≤1.5 µg/kg/h	Propofol	AF; ICU stay; hospital stay	4 days postoperative

AF, atrial fibrillation; CABG, coronary artery bypass grafting; DEX, dexmedetomidine; ICU, intensive care unit; MV, mechanical Ventilation; SVT, supraventricular tachycardia; VF, ventricular fibrillation; VT, ventricular tachycardia.

Figures

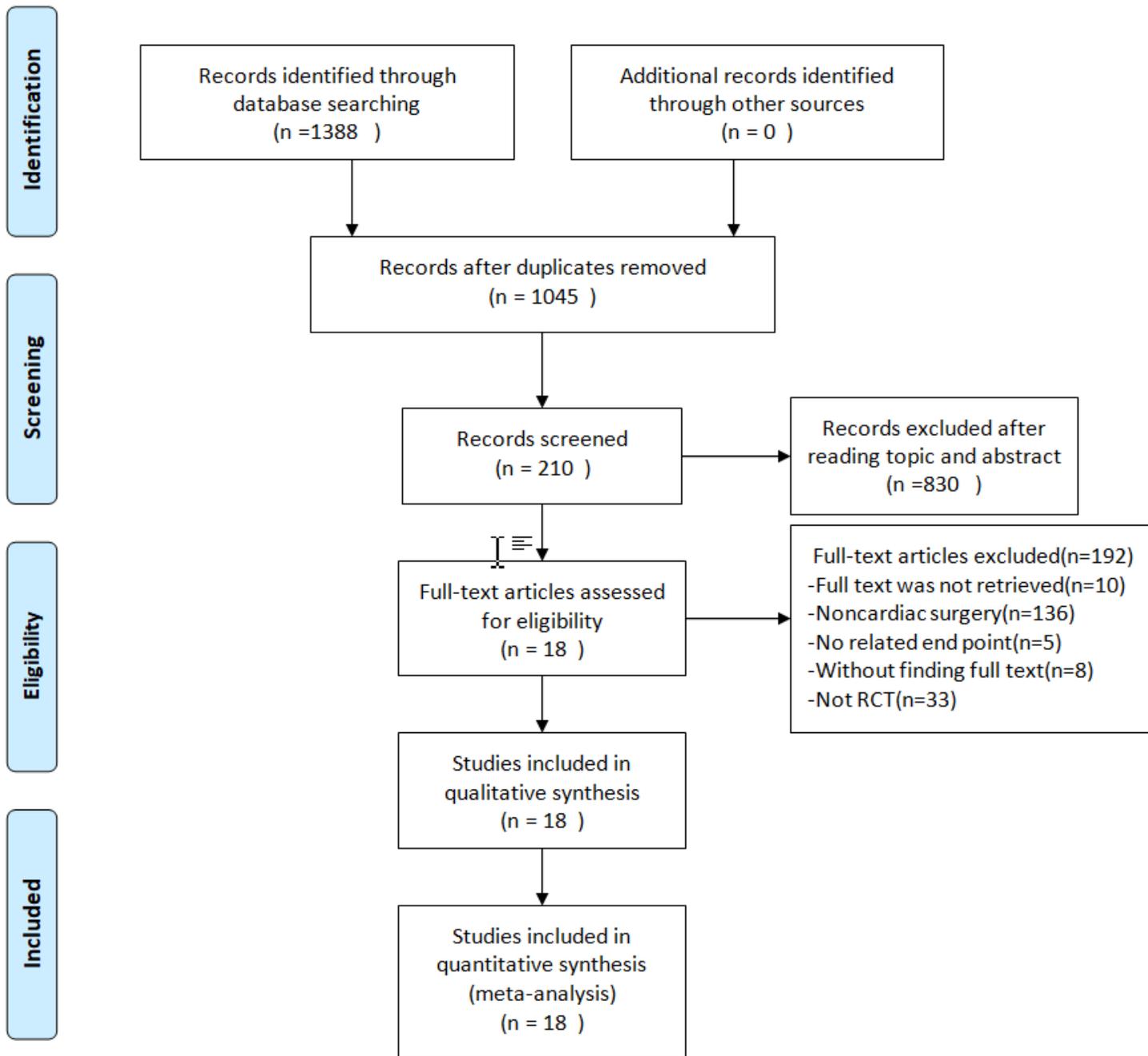


Figure 1

Study flow diagram

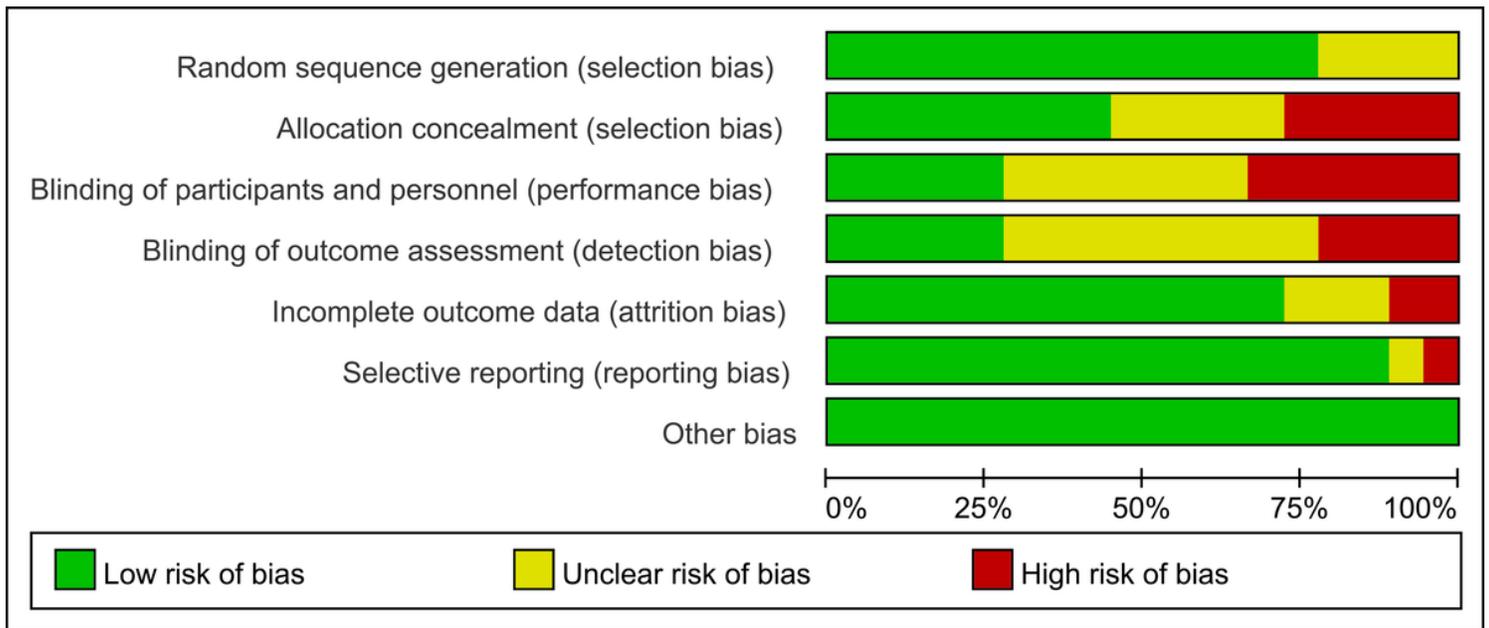


Figure 2

Risk of bias graph

	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
Balkanay 2015	?	+	+	+	+	+	+
Corbett 2005	+	+	+	+	+	+	+
Cui 2018	+	+	?	?	?	+	+
Djaiani 2016	+	+	+	?	+	+	+
Göksedef 2013	+	?	?	?	+	+	+
Herr 2003	+	+	+	+	+	+	+
Jalonen 1997	+	?	?	?	?	+	+
Karaman 2015	?	+	?	?	+	+	+
Li 2017	+	+	+	?	?	+	+
Liu 2016	+	+	+	+	+	+	+
Liu 2016-CTVA	+	+	?	?	+	+	+
Park 2014	?	?	+	+	+	?	+
Ren 2013	?	?	+	+	+	+	+
Shehabi 2009	+	+	+	+	+	+	+
Shi 2019	+	?	?	?	+	+	+
Turan 2020	+	+	+	+	+	+	+
Yu 2019	+	+	?	?	+	+	+
Zi 2020	+	+	+	+	+	+	+

Figure 3

Risk of bias summary

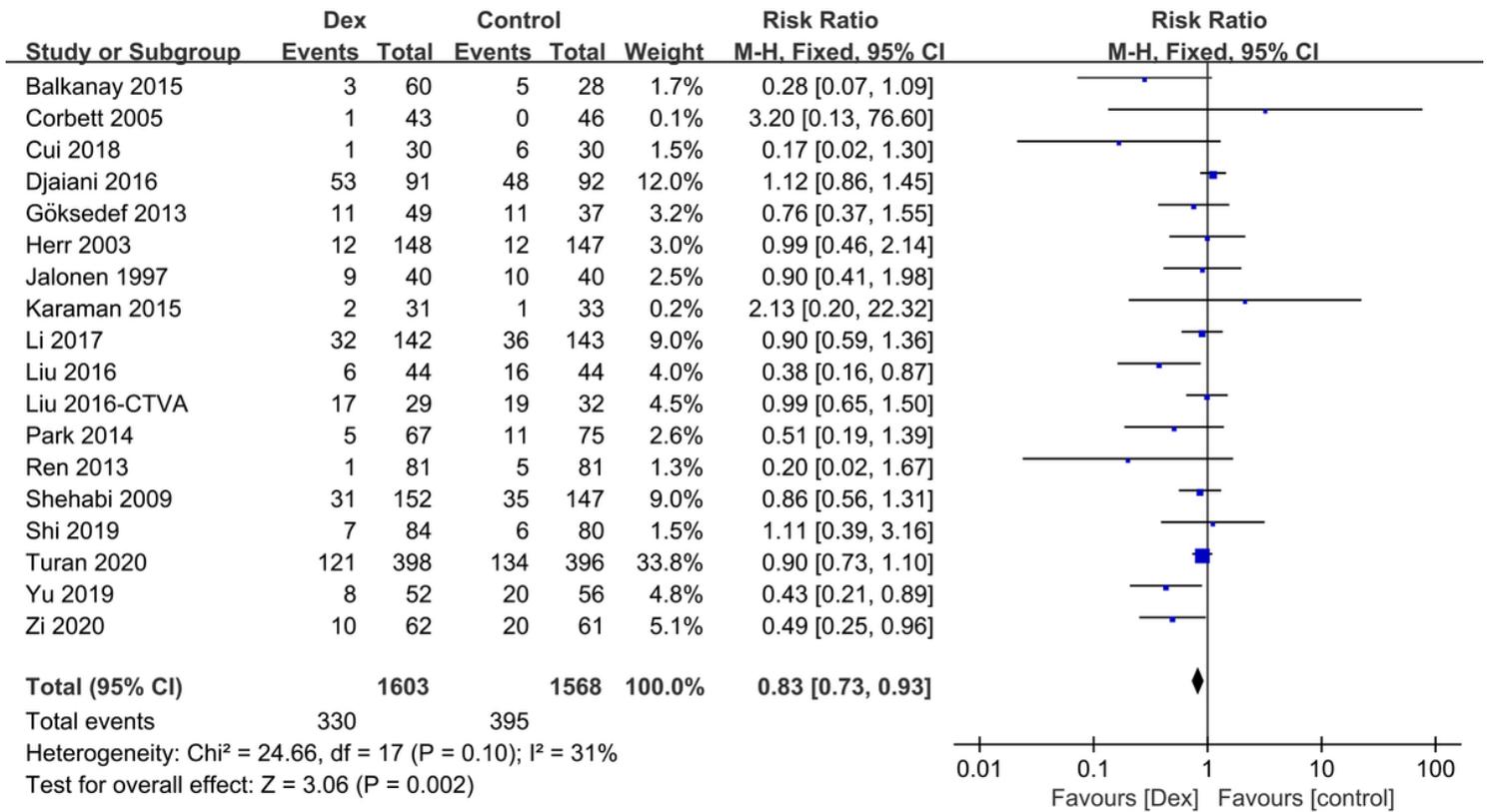


Figure 4

Forest plot of a trial fibrillation

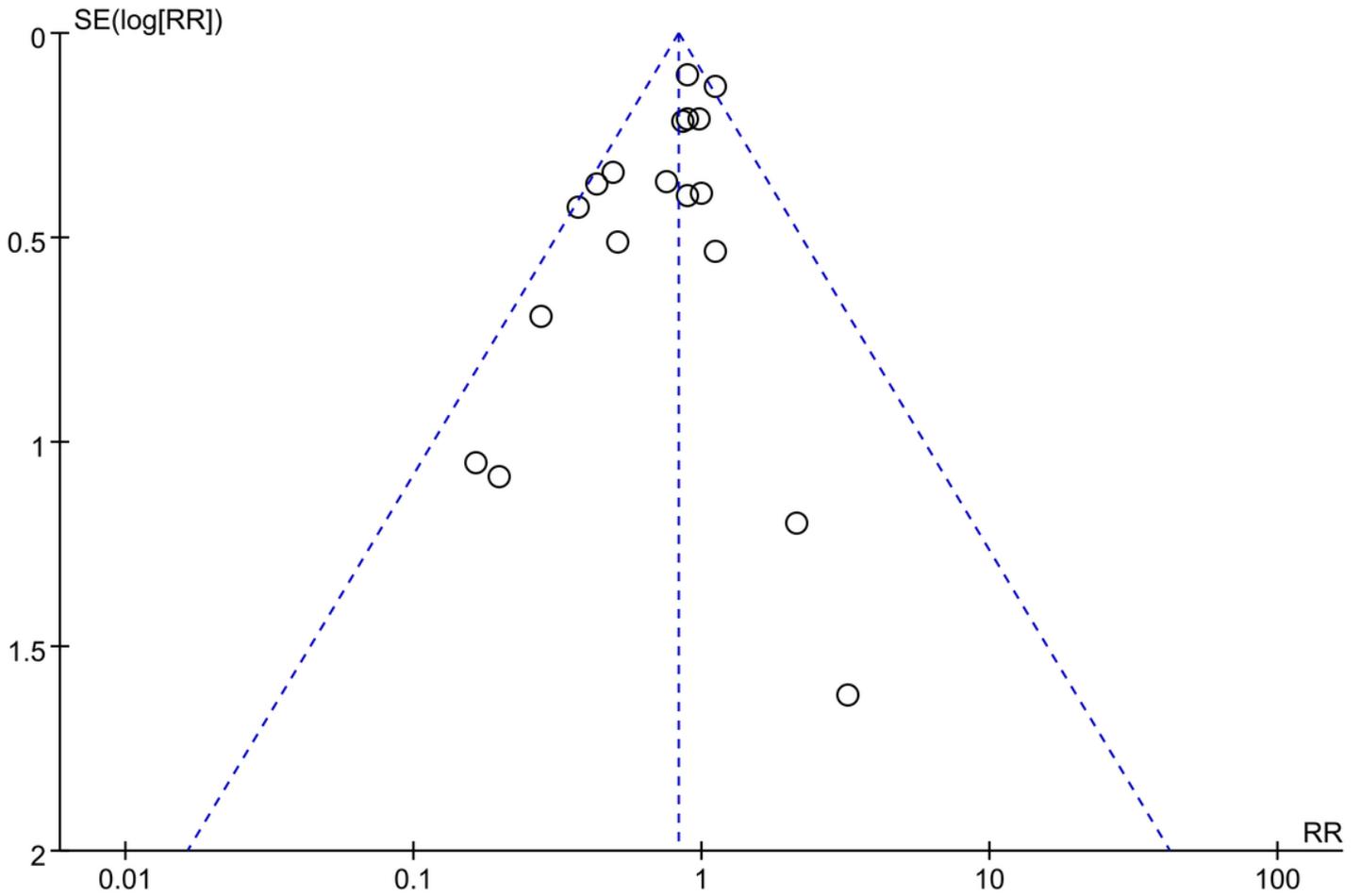


Figure 5

Funnel plot of a trial fibrillation



Figure 6

Forest plot of supraventricular tachycardia

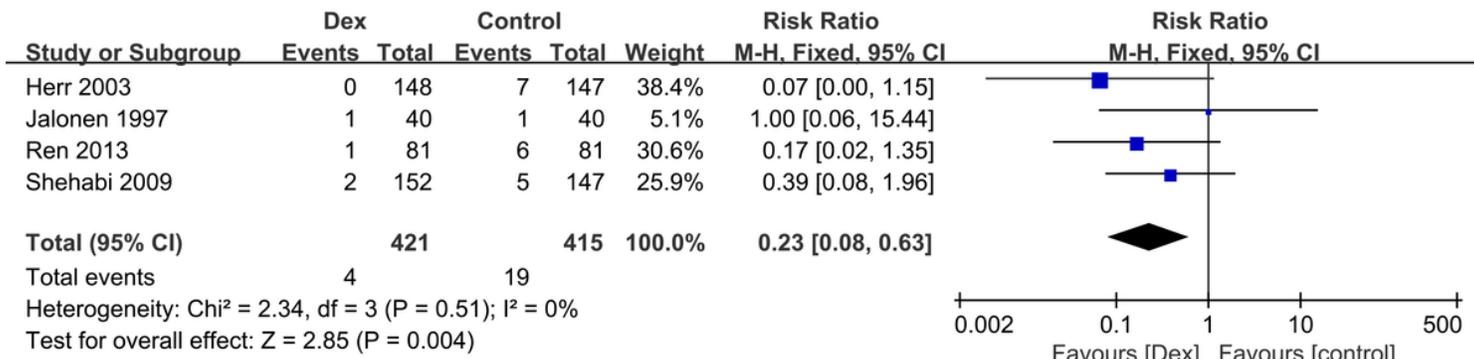


Figure 7

Forest plot of ventricular tachycardia

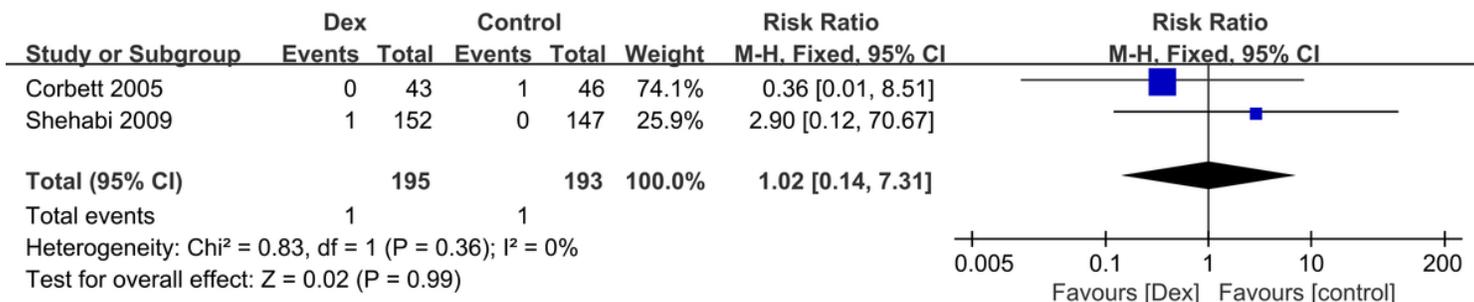


Figure 8

Forest plot of ventricular fibrillation

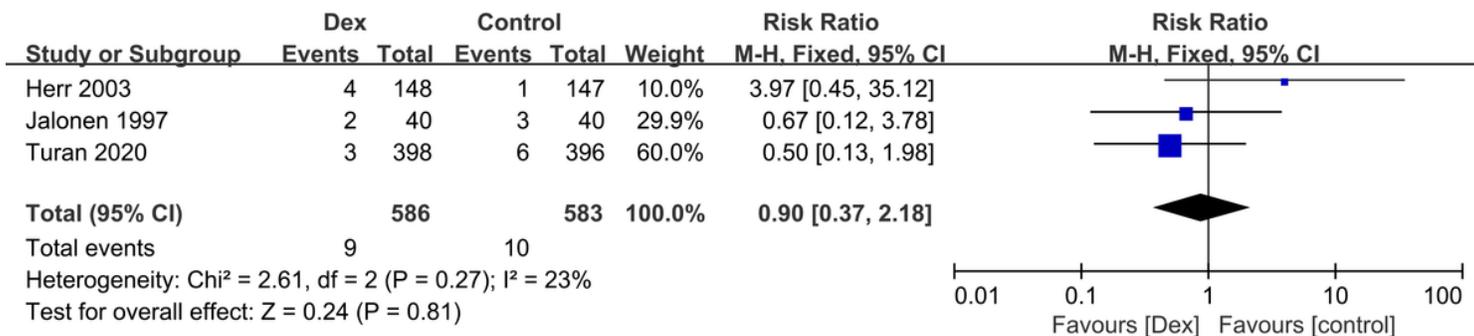


Figure 9

Forest plot of myocardial infarction

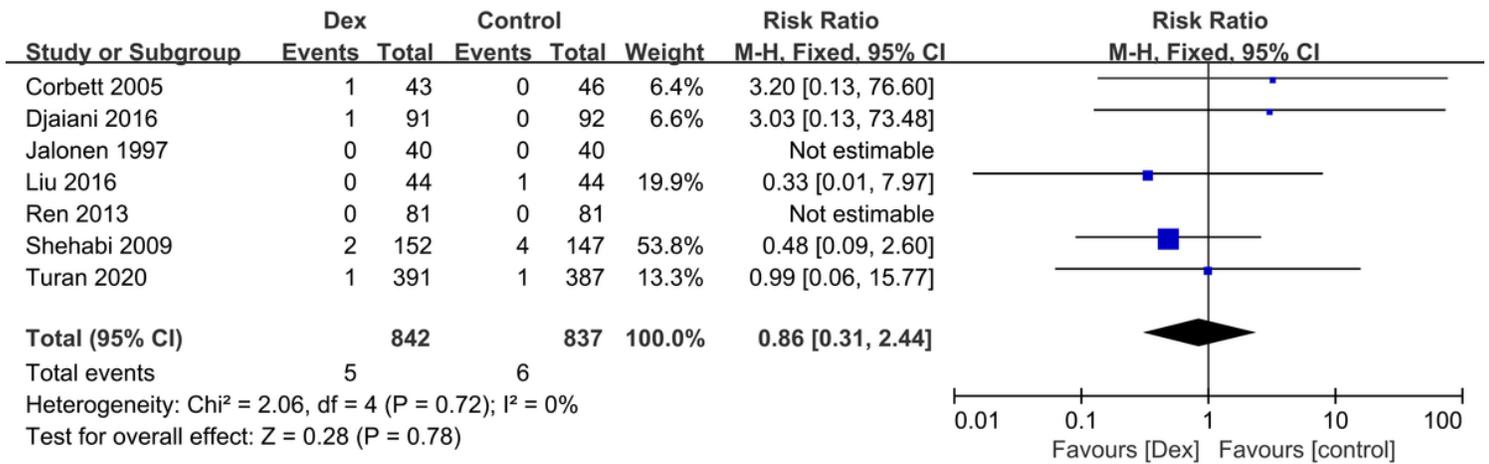


Figure 10

Forest plot of mortality

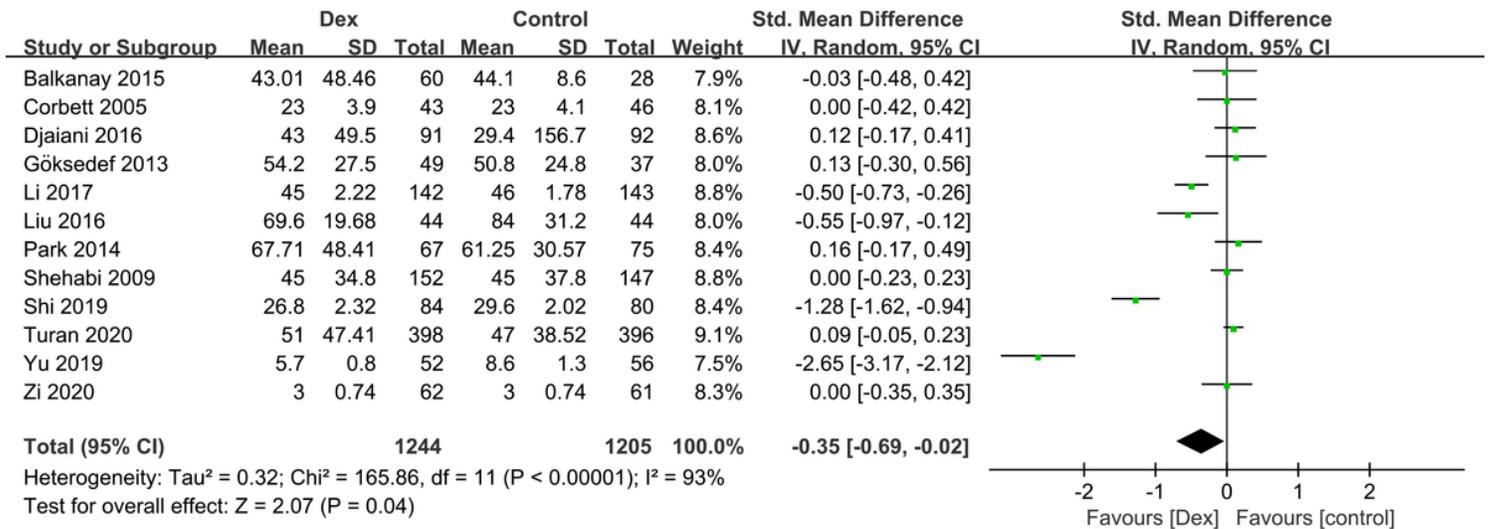


Figure 11

Forest plot of ICU stay

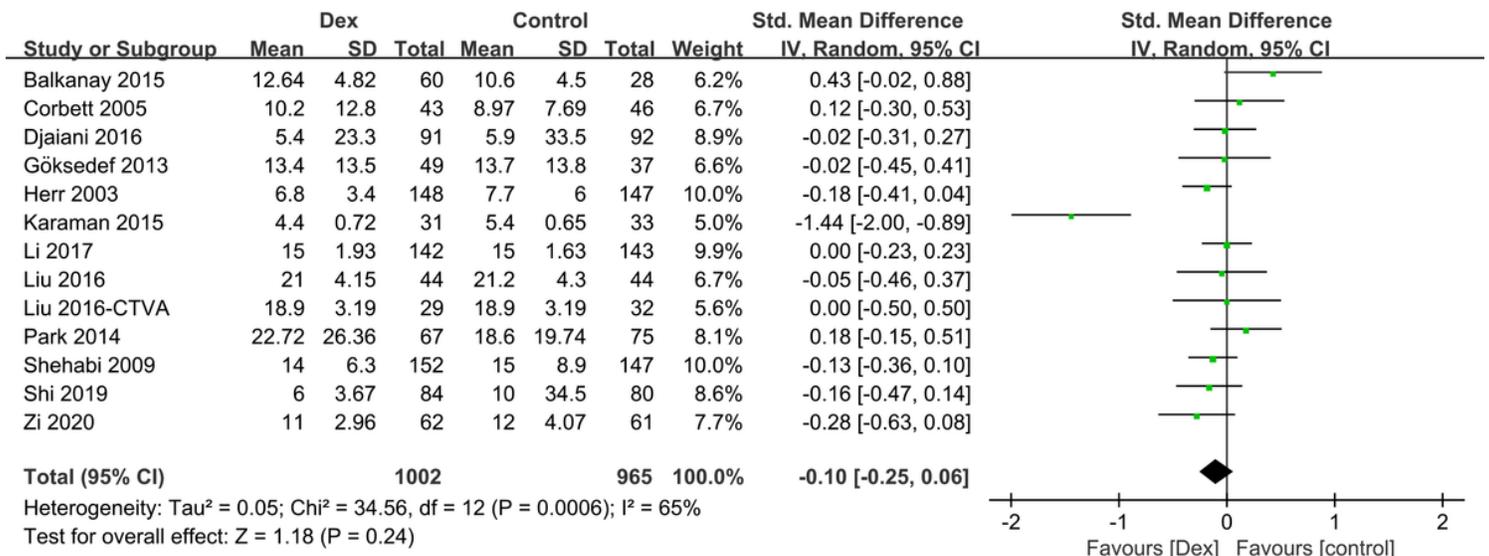


Figure 12

Forest plot of mechanical ventilation time

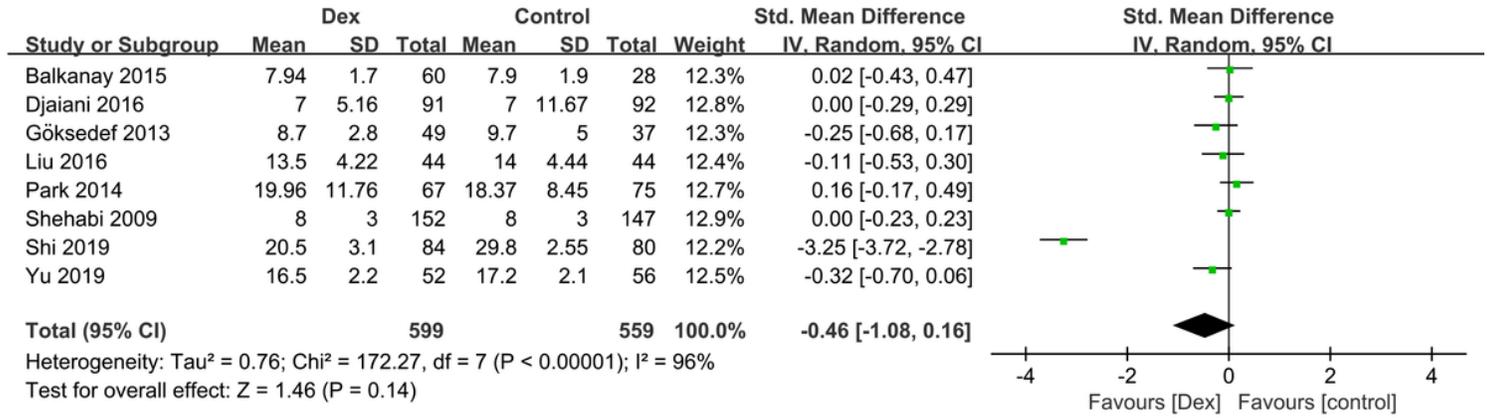


Figure 13

Forest plot of hospital stay

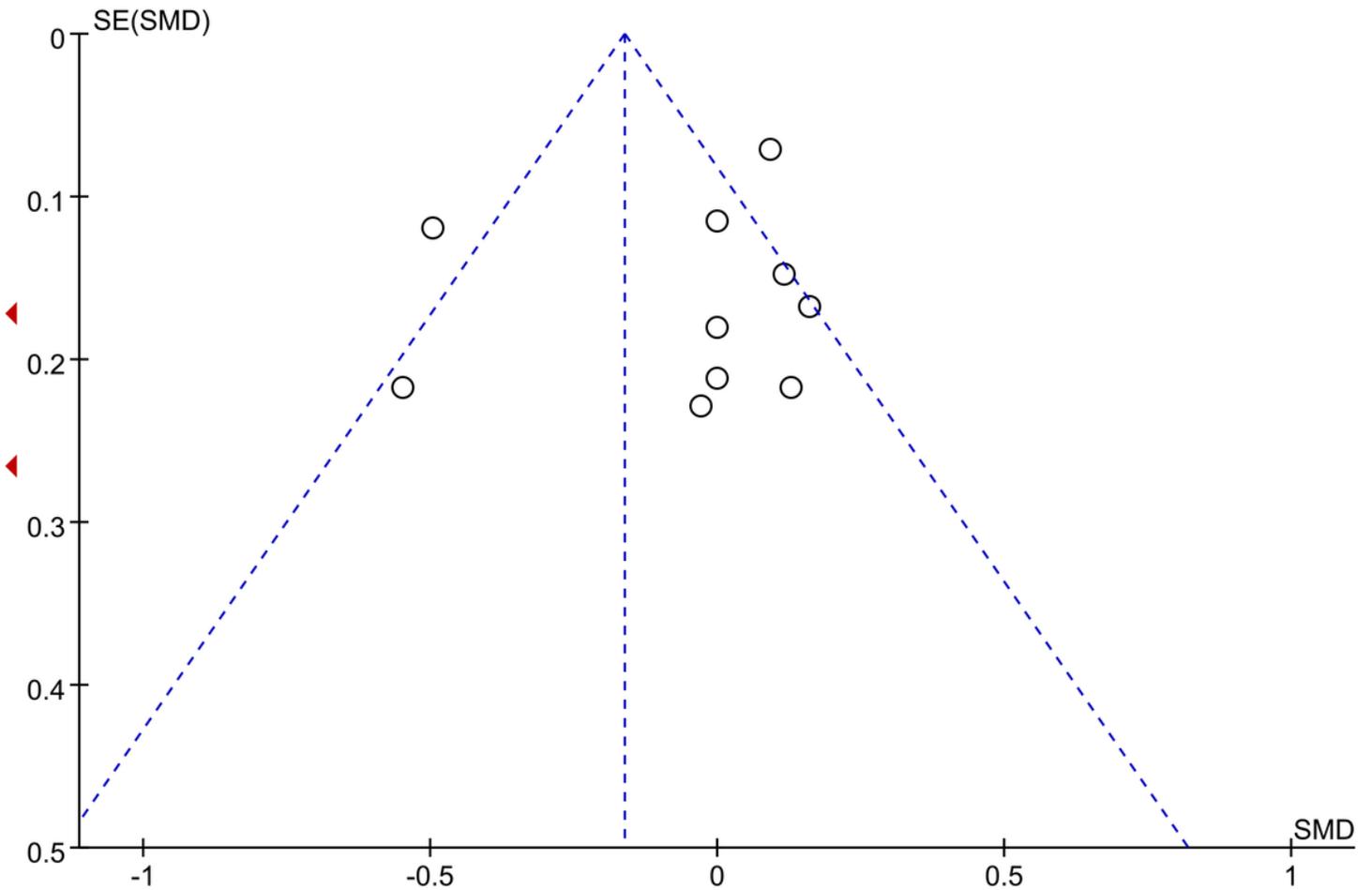


Figure 14

Funnel plot of ICU stay

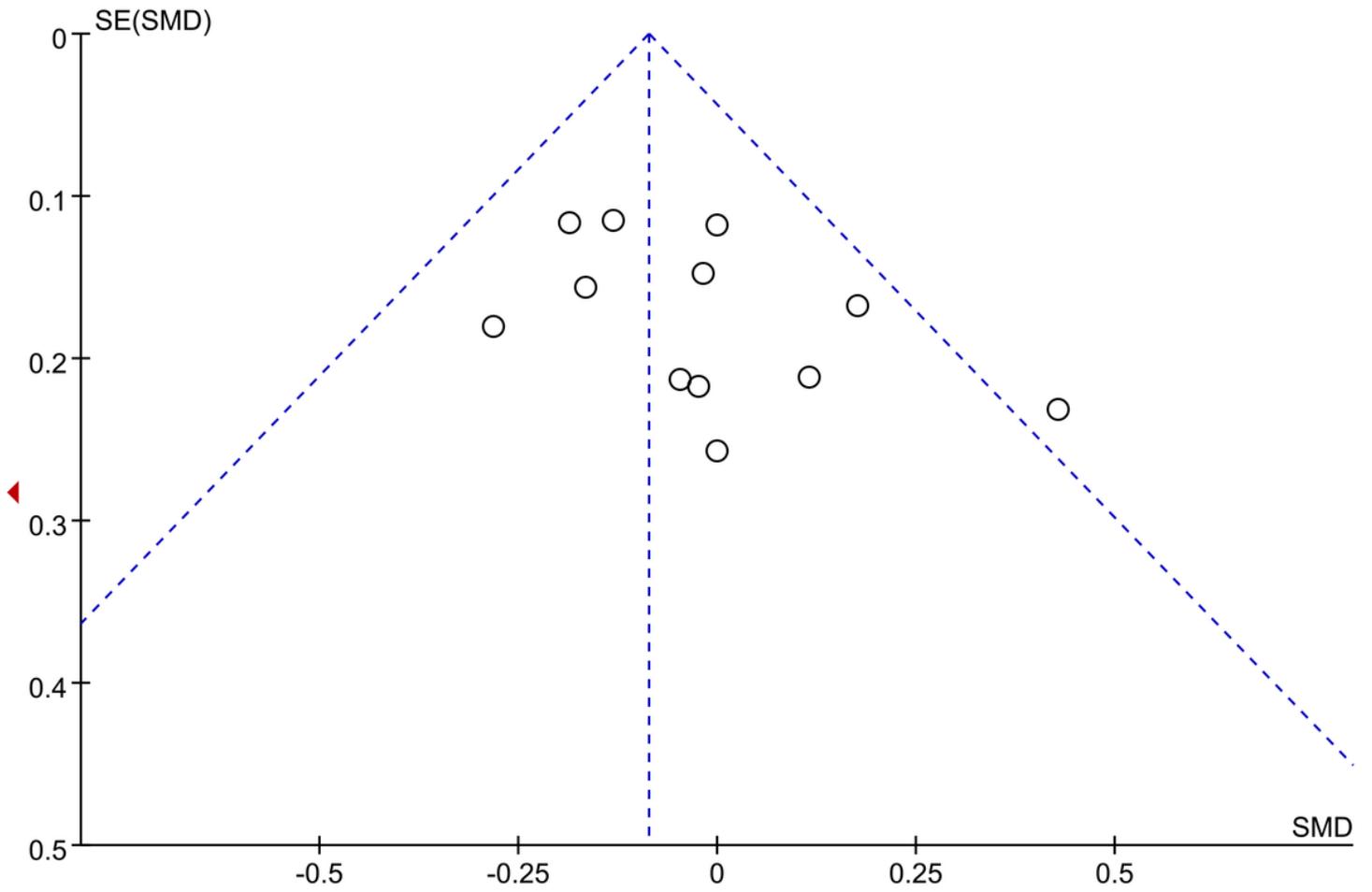


Figure 15

Funnel plot of mechanical ventilation time