

Meta-analysis of the effects of dexmedetomidine vs esmolol for used controlled hypotension during surgery

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Abstract

Background: At present, the anesthetist usually uses controlled hypotension technique to reduce blood loss and improve the surgical field. Dexmedetomidine and esmolol have been proved effective for controlled hypotension. This meta-analysis aimed to evaluate the effects of dexmedetomidine versus esmolol on the controlled hypotension during surgery.

Methods: All articles were retrieved from PubMed, Embase, Cochrane Library up to January 2020. JL and HD independently screened, extracted and evaluated the literature that meet the inclusion and exclusion criteria, and used RevMan 5.3 for statistical analysis.

Results: Eight randomised trials, including 418 patients were selected in this meta-analysis. And its results showed: 1) The dexmedetomidine group was more favorable in reducing blood loss (MD 49.48 with 95% CI [-5.44,104.40], $P = 0.08$); 2) Compared with the esmolol group, HR (MD 3.30 with 95% CI [2.11,4.50], $P < 0.00001$), requiring of fentanyl (SMD 5.96 with 95% CI [3.43,8.48], $P < 0.00001$) were considerably lower in the dexmedetomidine group, while emergence time (MD -6.69 with 95% CI [-9.61,-3.76], $P < 0.0001$) was more longer in the dexmedetomidine group. 3) Compared with the esmolol group, duration of surgery (MD -0.12 with 95% CI [-6.24,6.01], $P = 0.97$), MAP (MD 2.29 with 95% CI [-2.02,6.60], $P = 0.30$), the recovery period (MD -0.52 with 95% CI [-3.07,2.04], $P = 0.69$) were not statistically significant differences in the dexmedetomidine group.

Conclusion: Two drugs were effective for controlled hypotension, but compared with esmolol, dexmedetomidine is more better in reducing blood loss, and less requiring of fentanyl. But attention should be paid to the long emergence time and bradycardia.

Background

Controlled hypotension is the effective method to reduce intraoperative bleeding. Nevertheless, both procedure and patients pathology can increase arterial blood pressure that give rise to excessive blood loss and adverse outcomes[1]. Intra-operative bleeding is associated with poor surgical field visibility, and increased surgical time for various surgery. Many drugs have been developed to limit blood loss during surgery. But these interventions are reported some adverse effects. Therefore, we remain to determine an ideal intervention to provide controlled hypotension.

Dexmedetomidine (a potent and highly selective α_2 -adrenergic agonist) has many effects: sedation, analgesia, anesthesia, and sympatholytic properties. α_2 -adrenergic agonists can reduce sympathetic tone that results in a lower HR, blood pressure, and hemodynamic response. That drop of blood pressure are caused by the inhibited outflow of central sympathetic or the decreased norepinephrine release of presynaptic[2]. Esmolol (a short-acting β -blocker) can effectively lower heart rate and blood pressure, resulting in controlled perioperative stress response. The fall of blood pressure are because the reduced cardiac output due to negative chronotropic or the inotropic effects of β -

adrenergic was blocked. Esmolol can win a stable controlled hypotension ,and beneficial for surgery and blood conservation[3].

Although many studies have confirmed that the above two drugs have significant clinical effects on intraoperative controlled hypotension[4, 5], no systematic study has been founded to compare the efficacy of the two drugs. Therefore, this literature systematically reviews the available evidence and compares the two drugs in the control of hypotension.

Methods

Search strategy

Two reviewers (JL, HD) independently searched and retrieved relevant studies from PubMed, EMBASE, and the Cochrane Library up to January, 2020. No language or publication status restrictions were applied, and the study was limited to human. Noteexpress 3.0 was used to merge and remove duplicate documents.

Inclusion and exclusion criteria

Patients. Adult patients who have received general anesthesia and used dexmedetomidine or esmolol as hypotensive drug were required in this study.

Experiment and control. Trial groups: dexmedetomidine; control groups: esmolol

Outcome indicators. Anticipated indicators included blood loss, Mean arterial pressure (MAP), Heart rate (HR), duration of surgery, requiring of fentanyl, and the recovery period (The time required to reach Aldrete score > 9)[6] and emergence time[7](the interval between discontinuation of the anesthetics to response of eye opening to the verbal command).

Studies. The literature eligible for inclusion in this study should be randomized controlled trial. animal studies, reviews, case reports, or protocols were eliminated.

Data Extraction and Quality Assessment

J. Li and H. Deng separate review these studys for data that meet the inclusion and exclusion criteria. After scanned, two reviewers cross-checked the data. and resolved disagreements through discussion or the third author. The Cochrane Handbook for Systematic Reviews of Interventions was used to scan each study for methodological quality. Evaluation contents included: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other bias. These categories include : low risk of bias, unclear of bias and high risk of bias.

Statistical Analysis

We choose RevMan 5.3 for this meta-analysis. The mean difference (MD) or standard error of the mean (SEM) and 95% confidence interval (CI) were described for the continuous data, and the risk ratio (RR), 95% confidence interval (CI) for the numerical data. Follow the Cochrane guidelines, I^2 test was used for quantitative heterogeneity, and $I^2 \geq 50\%$ means significant heterogeneity. When the results had no significant heterogeneity, the fixed effect model was applied for this system review. Otherwise the random effect model was used. And $p < 0.05$ was specified as significance level.

Result

The flowchart (Fig. 1) show the process of literature search and selection. A total of 115 articles were retrieved from three databases After excluded duplicating, The remaining 75 articles were identified for further assessment. In the end, eight RCTs were included [8–15].

Study Characteristics

Table 1 displayed the Characteristics of eight RCTS

Quality Assessment

Figures 2 and 3 shown risk of bias of all the included study. As shown in the figure, the included RCTs showed good quality in risk of bias.

Meta-Analysis Results

Bleeding loss

A total of there RCTs were included in the study, involving 110 patients, which compared intraoperative blood loss of dexmedetomidine and esmolol. The random effects model was used because of the high heterogeneity ($I^2 = 92\%$). The results indicated that there was no significant difference between the two group in reducing intraoperative blood loss (MD 49.48 with 95% CI [-5.44, 104.40], $P = 0.08$). The result is shown in Fig. 4

HR

A total of four RCTs were included in the study, involving 230 patients, which compared HR of dexmedetomidine and esmolol. The fixed effects model was applied because of significant heterogeneity ($I^2 = 34\%$). The results indicated that there was significant difference between the two group in HR. (MD 3.30 with 95% CI [2.11, 4.50], $P < 0.00001$, $I^2 = 34\%$). The result is shown in Fig. 5

MAP

A total of four RCTs were included in the study, involving 230 patients, which compared HR of dexmedetomidine and esmolol. The random effects model was applied because of higher

heterogeneity ($I^2 = 95\%$). The results showed that there was no significant difference between the two group in MAP. (MD 2.29 with 95% CI [-2.02,6.60], $I^2 = 95\%$, $P = 0.30$). The result is shown in Fig. 6.

Duration of surgery

All seven RCTs involving 338 patients was included. The heterogeneity test ($I^2 = 56\%$) indicates that heterogeneity was existence between the selected literatures in this study, and the random effect was applied for meta analysis. The results indicated that there was no significant difference in duration of surgery between the esmolol group and the dexmedetomidine group (MD -0.12 with 95% CI [-6.24,6.01], $P = 0.97$). The result is shown in Fig. 7

Requiring of fentanyl

All five RCTS involving 278 patients were included. The heterogeneity test ($I^2 = 96\%$) indicates that heterogeneity was existence between the selected literatures in this study, and the random effect was selected for meta analysis. The results indicated that the dexmedetomidine group required less fentanyl than the esmolol group. (SMD 5.96 with 95% CI [3.43,8.48], $P < 0.00001$). The result is shown in Fig. 8

Recovery period

Three RCTs involving 148 patients were included. The heterogeneity test ($I^2 = 87\%$) indicates that heterogeneity was existence between the selected literatures in this study, and the random effect was selected for meta analysis. The results of meta analysis indicated that the difference in the recovery period was not significant in two group. (MD -0.52 with 95% CI [-3.07,2.04], $P = 0.69$, $I^2 = 87\%$). The results are shown in Fig. 9.

Emergence time

Three RCTs involving 188 patients was included. The heterogeneity test ($I^2 = 95\%$) indicates that heterogeneity was existence between the selected literatures in this study, and the random effect was selected for meta analysis. The results of meta analysis indicated that the interval between discontinuation of the anesthetics to response of eye opening to the verbal command in the esmolol group was more shorter than dexmedetomidine group. (MD -6.69 with 95% CI [-9.61,-3.76], $P < 0.0001$), $I^2 = 95\%$). The results are shown in Fig. 10.

Discussion

Deliberate hypotension is an important method to reduce intraoperative bleeding and maintain the perfusion of vital organs. The reduction of bleeding at the surgical site improves the quality of surgical field, reduces the number of operations and the occurrence of adverse reactions, and shorten the operation time [16, 17]. This is the underlying concept for controlled hypotensive anesthesia [18], which is

frequently used in neurosurgery, orthopaedic surgery, lumbar spine surgeries and middle ear and nose surgery[19, 20]. A variety of hypotensive drugs included sodium nitroprusside, volatile anaesthetics, nitroglycerin, adenosine, sympathetic antagonists, hydralazine, trimethaphan, fenoldopam and α_2 agonists have been applied to achieve controlled hypotension. These drugs have adverse effects [21] such as resistance to vasodilators, a longer post-sensory recovery period, cyanide toxicity, and the possibility of myocardial inhibition, which often limited the use in controlled hypotension.

The result of dexmedetomidine and esmolol in reducing blood loss of surgical site indicated the difference between two groups in reducing blood loss was not significant, but the outcomes indicated that dexmedetomidine group showed better reduction of bleeding. It may be resulted from two main reason: on the one hand, previous studies demonstrated that hemodynamic control and peripheral vasoconstriction of dexmedetomidine can reduce intraoperative bleeding and improve the operative field of vision; On the other hand, relevant studies[5] have shown that reduced the HR can significantly improve the field of vision in the operative area, rather than reduced the MAP to a dangerously low level and affected the perfusion of vital organs. In our study, compared with esmolol, HR was lower in the dexmedetomidine group, while MAP was not significant difference. The results were consistent with our study description of the advantages of dexmedetomidine in reducing blood loss.

The effect of the two drugs on the duration of surgery showed no significant difference between the two groups. In addition, this study has found dexmedetomidine can decrease the necessity of fentanyl administration during operation. This can be due to sedative, analgesic and anaesthetic sparing effects, and sympatholytic properties of dexmedetomidine[22].

In our study, we used two approach to assess objectively the quality of postoperative recovery, including recovery period and emergence time. The recovery period of patients were reported in all three studies, and the outcome from analysis indicated the recovery condition was not significant in two group. But from the result of emergence time, it was observed that patients receiveing dexmedetomidine needed longer time to response of eye opening to the verbal command. It could be explained that dexmedetomidine selectively binds to alpha-2adrenergic receptor with greater affinity, and it need to take longer time to restoration when the drug diffuses out of its receptors.

Finally, the limitations of this study need to be taken into account. Although we conduct a comprehensive retrieval from the two aspects of retrieval strategy and retrieval database to the greatest extent, the sample size of this study was still insufficient. In addition, we did not conduct further subgroup analysis of surgical types to avoid heterogeneity in our meta-analysis. The next work is to further compare the adverse effects of two drugs in the perioperative period. To sum up, in order to ensure the reliability of the research conclusion, large sample size and more high-quality evidence is needed in the following work.

Conclusion

Both esmolol and dexmedetomidine was effective for controlled hypotension, but compared with esmolol, dexmedetomidine is more better in reducing blood loss, and less requiring of fentanyl. But

attention should be paid to the long emergence time and bradycardia.

Abbreviations

MD: Mean difference; SEM: standard error of the mean ;RR: Relative risk; CI: Confidence interval; MAP: Mean arterial pressure; HR: Heart rate; RCT: Randomized controlled trials; ASA: American Society of Anesthesiologists

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Competing interests

The authors declare that they have no competing interests.

Funding

Not applicable.

Authors' contributions

JL and HD participated in the design, collected the data, performed statistical analyses, and drafted the manuscript. ZZ acted as critical revision of manuscript. All authors read and approved the final manuscript.

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Tables

Table 1: Baseline characteristics of included studies.

Study baseline characteristics	Year	ASA	Surgery	Gender (F/M)		Age (yr)		Intervention	
				Esmolol	Dexmedetomidine	Esmolol	Dexmedetomidine	Esmolol	Dexmedetomidine
Rumani Ruku	2019	I-II	Spine Surgery	NR	NR	41.6±12.07	44.2±15.34	500 µg/kg followed by 1 min-1	50-300 µg/kg-1 µg/kg followed by 0.2-0.7 ug/kg/h
Ovais Nazir	2016	I-II	Spine Surgery	3/12	3/12	58.58± 6.12	51.15 ± 8.88	500 µg/kg followed by 1 min-1	10-200 µg/kg- 1 µg/kg followed by 0.4-0.7 ug/kg/h
Das A	2016	I-II	Functional endoscopic sinus	5/25	7/23	34.06±7.86	38.68±9.72	1 mg/kg followed by 0.5 mg/kg/h	1 µg/kg followed by 0.5
Bajwa SJ	2016	I-II	Functional endoscopic sinus	12/38	31/19	34.3±5.6	31.6±5.2	1 mg/kg followed by 0.5 -1mg/kg/h	1 µg/kg followed by 0.5-1ug/kg/h
Erbesler ZA	2013	I-II	middle-ear Surgery	15/10	11/14	31.72±10.26	35.20±12.20	1 mg/kg followed by 10-200 µg kg(-1) min(-1)	1 µg/kg followed by 0.2-0.7ug/kg/h
Shams T	2013	I-II	functional endoscopic sinus	NR	NR	36.1±8.8	34.8±9.4	1 mg/kg followed by 0.4-0.8 mg/kg/h	1 µg/kg followed by 0.4-0.8ug/kg/h
Kol IO	2009	I-II	tympanoplasty Surgery	16/8	17/7	38.4±10.5	35.5 ±14.7	1 mg/kg followed by 0.4-0.8 mg/kg/h	1 µg/kg followed by 0.4-0.8ug/kg/h
Khaled M	2014	I-II	Shoulder arthroscopy	14/11	12/13	36.9 ± 12	41.1 ± 10.3	0.5 mg/kg followed by 0.05-0.3 mg/kg/h	1 µg/kg followed by 0.4-0.6ug/kg/h

Figures

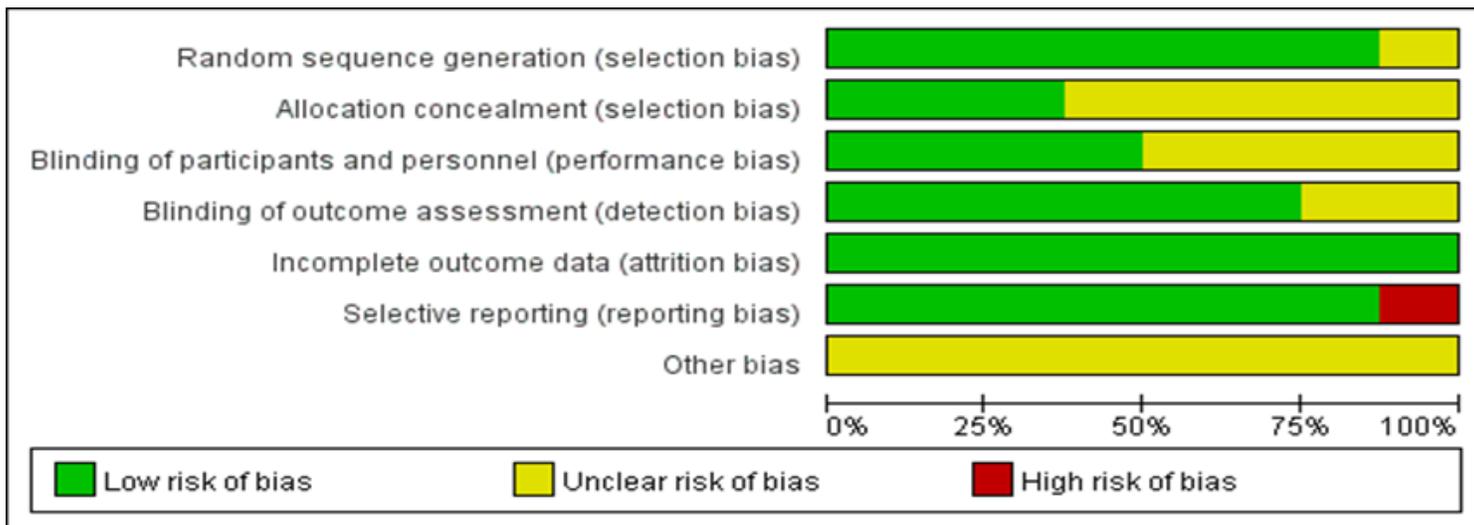


Figure 1

The risk of bias assessment of the included trials.

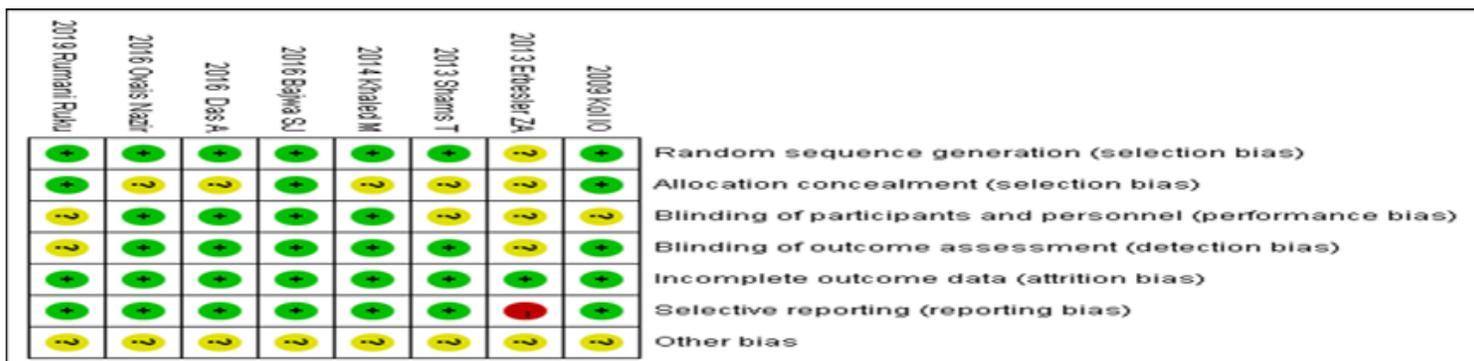


Figure 2

The risk of bias summary of the included trials.

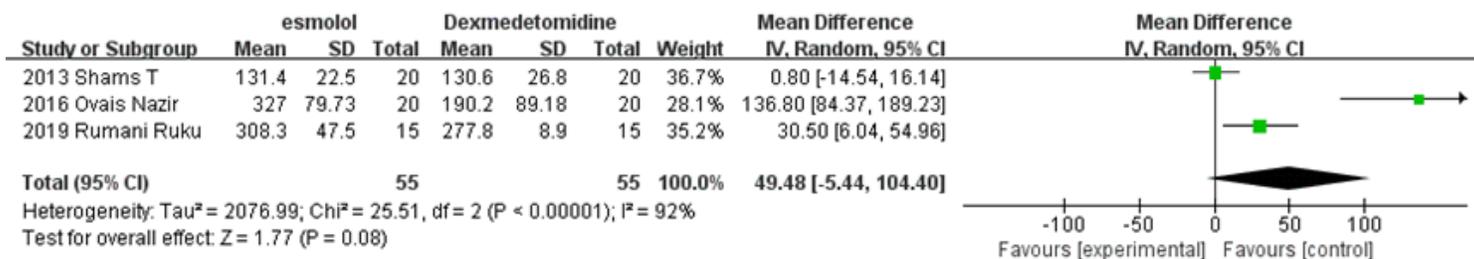


Figure 3

The effects of dexmedetomidine and esmolol in bleeding loss

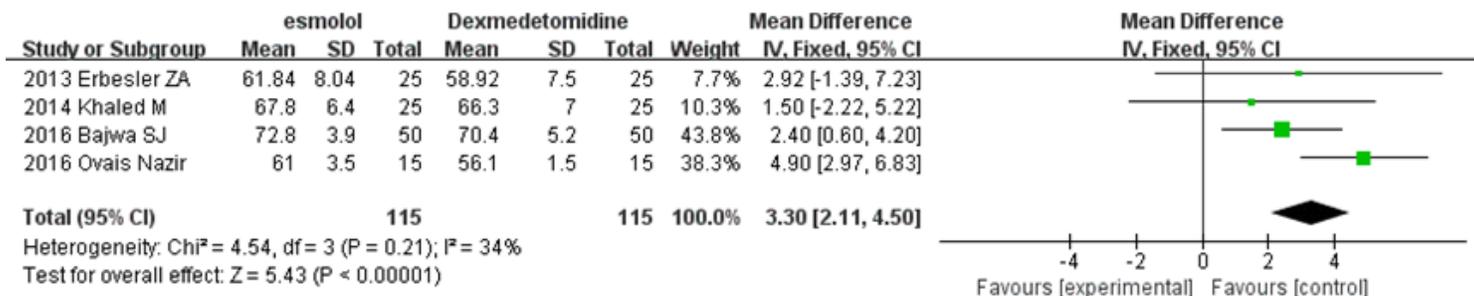


Figure 4

The effects of dexmedetomidine and esmolol in HR

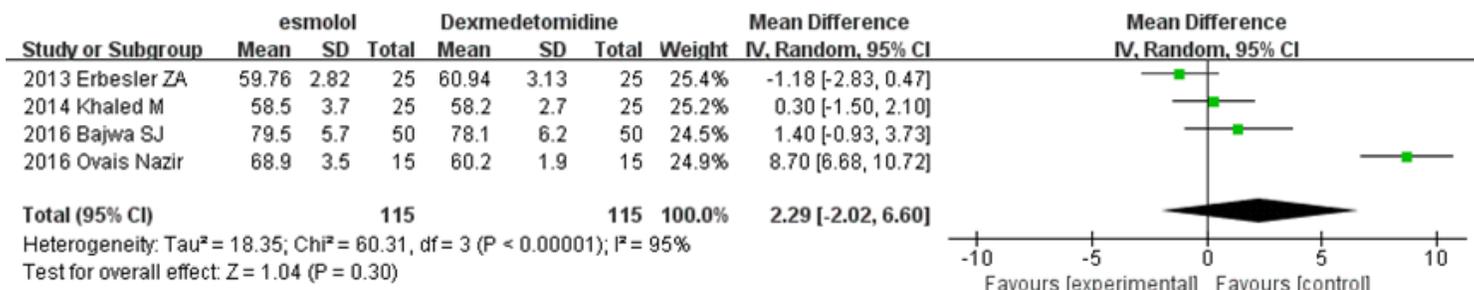


Figure 5

The effects of dexmedetomidine and esmolol in MAP

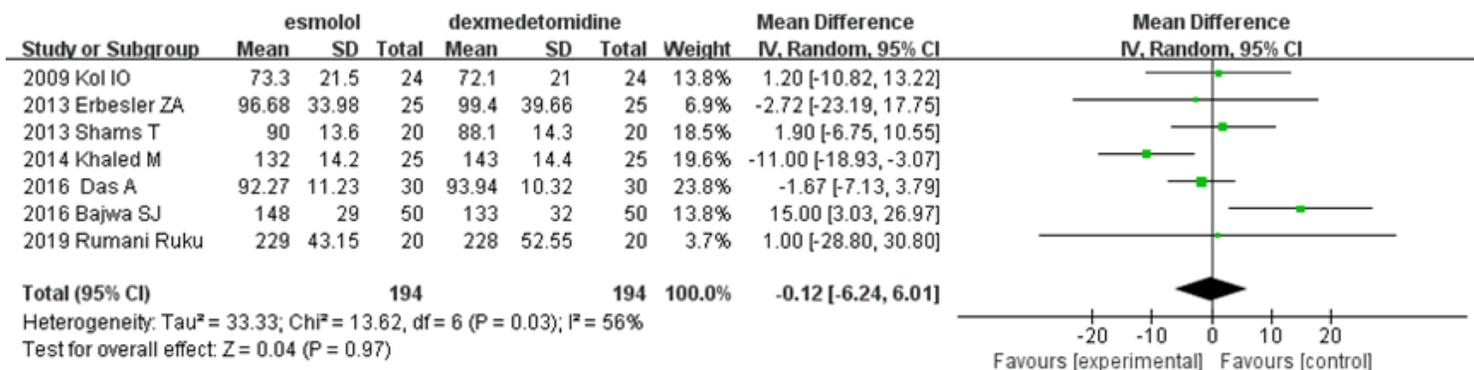


Figure 6

The effects of dexmedetomidine and esmolol in duration of surgery

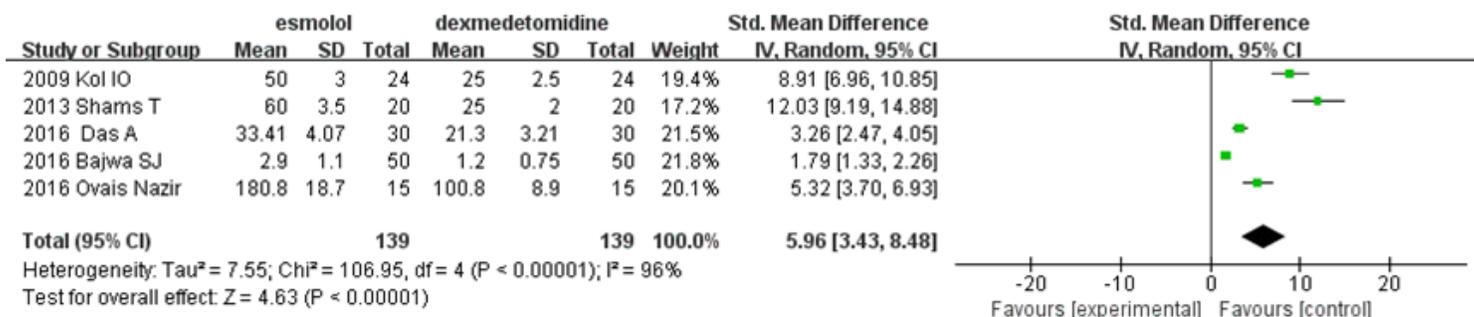


Figure 7

The effects of dexmedetomidine and esmolol in requiring of fentanyl

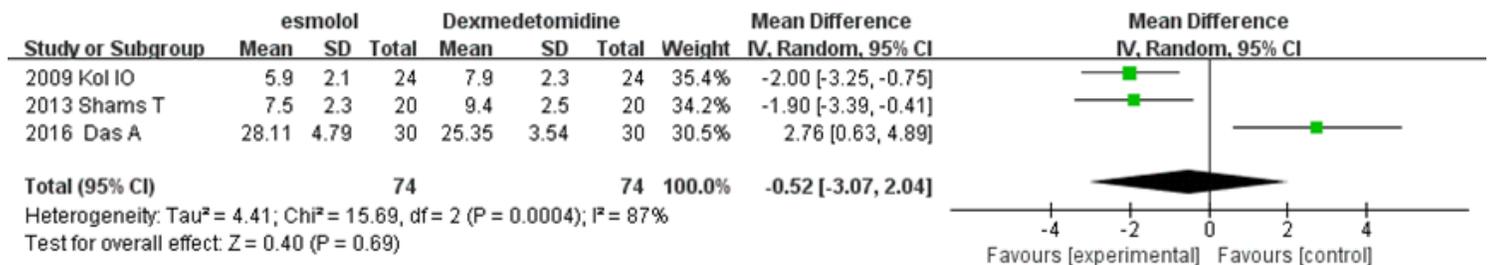


Figure 8

The effects of dexmedetomidine and esmolol in the recovery period

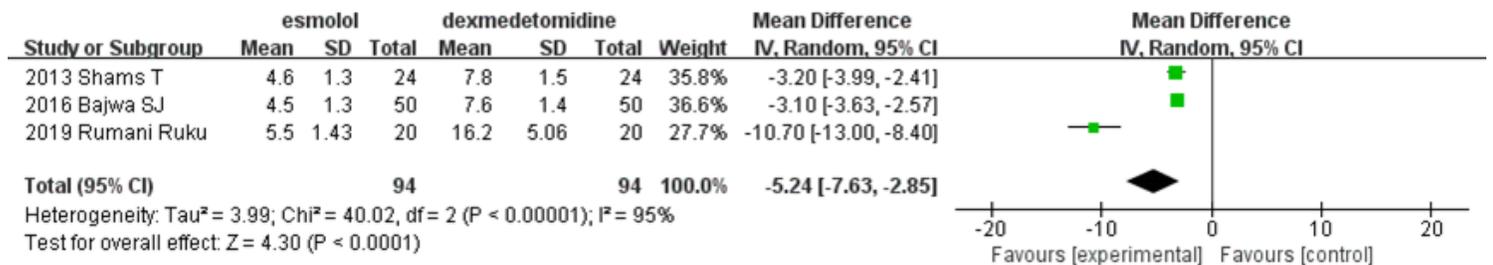


Figure 9

The effects of dexmedetomidine and esmolol in emergence time

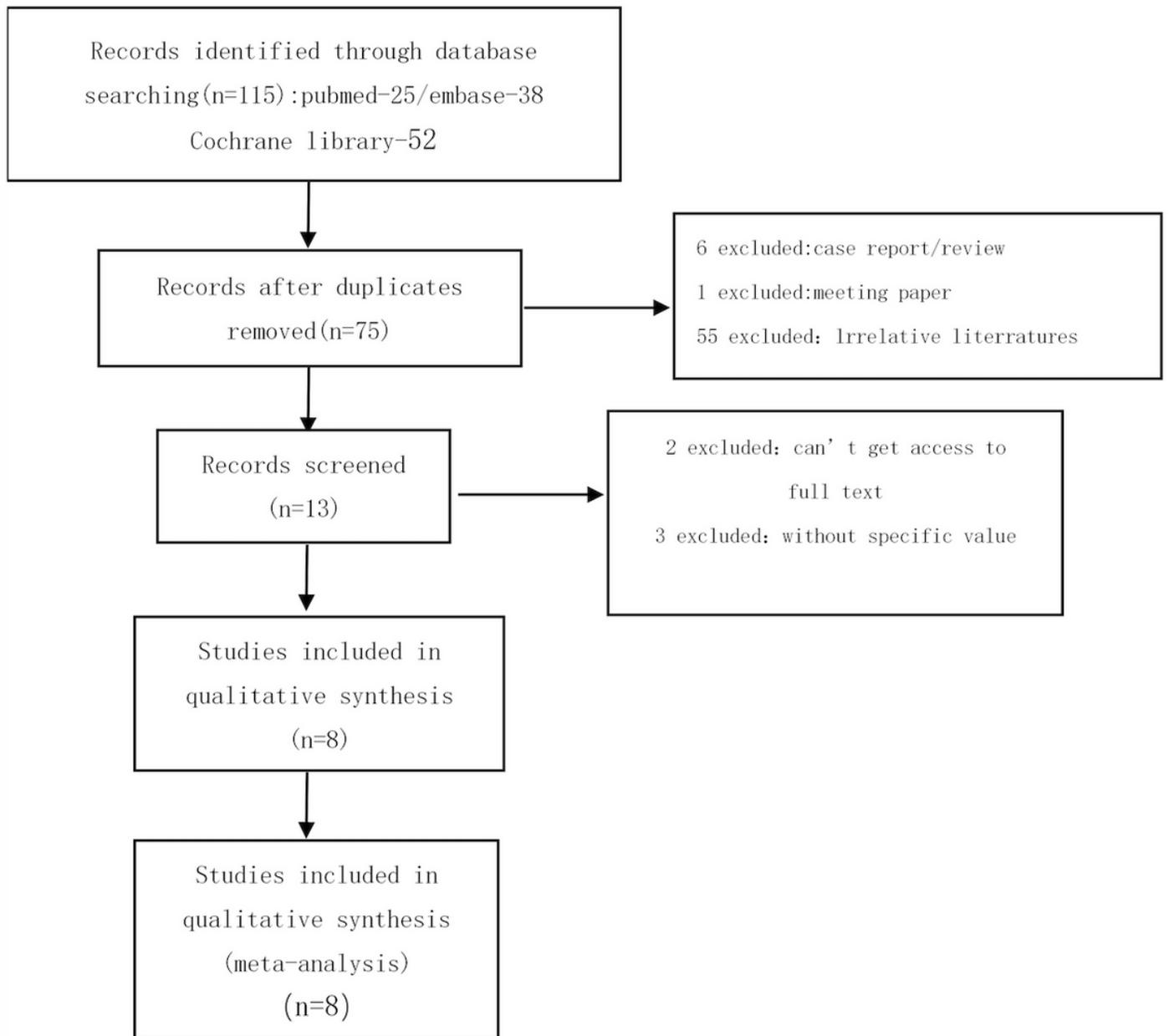


Figure 10

The flow chart of trial selection in the meta-analysis

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