

Effect of Dexmedetomidine on Maintaining Perioperative Hemodynamic Stability in Elderly Patients: A Systematic Review and Meta-analysis

Li-Juan Tian^{1*}, Yun-Tai Yao¹, Su Yuan¹, Zheng Dai²

¹Department of Anesthesiology, Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing 100037, China

²Department of Anesthesiology, Yunnan Fuwai Cardiovascular Hospital, Kunming 650102, China

ABSTRACT

Objective Dexmedetomidine is a highly selective alpha-2 adrenergic receptor agonist with sedative and analgesic properties but without respiratory depression effect and has been widely used in perioperative anesthesia. Here we performed a systematic review and meta-analysis to evaluate the effect of dexmedetomidine on maintaining perioperative hemodynamic stability in elderly patients.

Methods PubMed, Web of Science, the Cochrane Library, China National Knowledge Infrastructure (CNKI), and Wanfang Data were searched for randomized-controlled trials (RCTs) on the application of dexmedetomidine in maintaining perioperative hemodynamic stability in elderly patients from their inception to September, 2021. The standardized mean differences (SMD) with 95% confidence interval (CI) were employed to analyze the data. The random-effect model was used for the potential clinical inconsistency.

Results A total of 12 RCTs with 833 elderly patients (dexmedetomidine group, 546 patients; control group, 287 patients) were included. There was no significant increase in perioperative heart rate (HR), mean arterial pressure (MAP), and diastolic blood pressure (DBP) in the dexmedetomidine group before and during the operation. In addition, the variations of hemodynamic indexes including HR, MAP, SBP (systolic blood pressure), and DBP were significantly lower in the dexmedetomidine group compared with the control group (HR: SMD = -0.87, 95% CI: -1.13 to -0.62; MAP: SMD = -1.12, 95% CI: -1.60 to -0.63; SBP: SMD = -1.27, 95% CI: -2.26 to -0.27; DBP: SMD = -0.96, 95% CI: -1.33 to -0.59). Subgroup analysis found that with the prolongation of 1.0 µg/kg dexmedetomidine infusion, the patient's heart rate declined in a time-dependent way.

Conclusion Dexmedetomidine provides more stable hemodynamics during perioperative period in elderly patients. However, further well-conducted trials are required to assess the effective and safer doses of dexmedetomidine in elderly patients.

Key words: dexmedetomidine; elderly patient; hemodynamics; perioperative period

INTRODUCTION

Dexmedetomidine is widely used in perioperative

anesthesia as it has sedative, anti-anxiety, and analgesic effects and can avoid respiratory depression caused by over-sedation^[1-3]. With a high alpha-2/alpha-1 receptor activity ratio, dexmedetomidine is a highly specific and selective alpha-2 adrenergic receptor agonist^[4-6]. Alpha-2 adrenergic receptors are present in presynaptic and postsynaptic membranes. The activation of alpha-2 adrenergic receptors in presynaptic membrane can reduce the release of norepinephrine and epinephrine, while the activation of alpha-2 adrenergic receptors in postsynaptic membrane can lead to neuronal membrane

Received March 21, 2022; accepted July 27, 2022; published online September 19, 2022.

*Corresponding author: Li-Juan Tian, e-mail: tljuan1982@163.com.

© The authors 2023. Published by Chinese Academy of Medical Sciences. This is an open access article attributed under the CC BY-NC license (<http://creativecommons.org/licenses/by-nc/4.0>).

hyperpolarization. Therefore, the stimulation of alpha-2 adrenergic receptors by dexmedetomidine can attenuate the sympathetic responses, maintain hemodynamic stability, and exert sedative and analgesic effects^[7]. Notably, loading or rapid dose-escalation of dexmedetomidine leads to transient hypertension followed by hypotension, which is due to the activation of postsynaptic alpha-2 adrenergic receptors in vascular smooth muscle cells, resulting in increased peripheral vascular resistance and elevated blood pressure. Furthermore, dexmedetomidine may directly inhibit cardiac myocytes by affecting sodium and calcium channels to decrease the frequency of spontaneous action potentials and prolong the duration of action potentials^[8].

Intubation, extubation, and surgical resection during the perioperative period can lead to increase in blood pressure, heart rate, and plasma catecholamine concentration^[9, 10]. Due to the decline in the cardiovascular and cerebrovascular functions, drug absorption, distribution, metabolism, and elimination in elderly people are worse than those in young people. Hepatic metabolism of drugs is affected by aging due to a decrease in hepatic blood flow in elderly patients. The age-related decrease in liver parenchyma reduces hepatic microsomal enzymes and extends the half-life of drugs. Decreased renal function is manifested as a progressive reduction in creatinine clearance and glomerular filtration rate. Furthermore, reduction in the renal clearance prolongs the plasma half-life of renally excreted drugs and increases the steady-state concentration^[11]. Therefore, elderly patients are prone to have a significant increase in blood flow fluctuations due to surgical operations during the perioperative period, and a higher rate of hypotension and bradycardia after the loading or rapid dose of dexmedetomidine, which increases the occurrence of complications^[12]. Therefore, it is very important for anesthesiologists to reduce the sympathetic adrenal response in elderly patients during the perioperative period.

The purpose of this study was to provide a more comprehensive description of the effect of dexmedetomidine on maintaining perioperative hemodynamic stability in elderly patients based on the currently available studies.

METHODS

Search strategy

This study followed the methodology outlined in the *Cochrane Handbook for Systematic Reviews of Interventions*

version 6.1^[13]. We performed it in accordance with the *Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols* (PRISMA) statement^[14].

PubMed, Web of Science, the Cochrane Library databases, China National Knowledge Infrastructure (CNKI), and China Wanfang databases were searched for articles published from their inception to September, 2021. Randomized-controlled trials (RCTs) evaluating the application of dexmedetomidine in maintaining perioperative hemodynamic stability in elderly patients were considered. The relevant ongoing or completed studies on ClinicalTrials.gov were also searched, and references of the retrieved studies were also reviewed to identify further relevant studies. The search formula was as follows: ((Dexmedetomidine) OR (Dexmedetomidine [MeSH Terms])) AND ((Elderly) OR (Elderly [MeSH Terms])) AND ((Cardiovascular) OR (Cardiovascular [MeSH Terms]) OR (Hemodynamic) OR (Hemodynamic [MeSH Terms])) AND ((Randomized-controlled trials) OR (Randomized-controlled trials [MeSH Terms])). In addition, we manually searched the references of the identified studies. There was no language restriction.

Inclusion and exclusion criteria

Two researchers (LJT and SY) independently reviewed the titles and abstracts of all the retrieved studies to evaluate whether the articles could be included in the analysis. When the two researchers disagreed, they would consult a third researcher (ZD). According to *Participants, Interventions, Comparisons, Outcomes, and Study design* (PICOS) protocol, the following inclusion criteria were applied: a) Patients: The elderly patients in perioperative period or the study population were older than or equal to 60 years. b) Intervention and comparison: Each study contained at least two groups of subjects, one receiving dexmedetomidine and the other receiving control treatment (blank or saline). c) Outcomes: The hemodynamic parameters included heart rate (HR), mean arterial pressure (MAP), systolic blood pressure (SBP), and diastolic blood pressure (DBP). And d) study design: Only RCTs were included to ensure that the combined results were of good quality; in addition, studies that could not provide effective analysis data were excluded.

Data extraction and quality assessment

Two researchers independently extracted the following data: article title, author's name, year of publication, journal name, research area (hospital or research insti-

tute), total number of patients, number of patients in each group, type of surgical procedure, hemodynamic parameter, and dexmedetomidine dosage and administration. After data extraction was completed, a third researcher checked the consistency of the data extracted.

The two researchers evaluated the quality of included studies in accordance with the quality assessment section of *Cochrane Handbook for Systematic Reviews of Interventions* (version 6.1). They also assessed selection bias, blinding bias, incomplete outcome data bias, selective reporting bias, and other biases for each included study. Disagreements were resolved by discussion during data abstraction. The bias of the study was categorized as low-risk, medium-risk, or high-risk accordingly. In addition, the baseline characteristics and co-morbidities were compared between intervention and control groups in each study as these factors might have significant impacts on the conclusions.

Statistical analysis

The results of the meta-analysis were analyzed by Review Manager 5.4 (Cochrane Collaboration, Oxford, UK) and Stata 12.0 (Stata Corporation, College Station, TX, USA)^[15,16]. The standardized mean differences (SMD) with 95% confidence interval (CI) were estimated for continuous data. The random-effect model was used to pool the data for the consideration of methodological and clinical heterogeneities. Q test ($P < 0.1$ denoted statistically significant heterogeneity) and I^2 statistics ($I^2 > 50\%$ was considered the presence of significant heterogeneity) were used to evaluate the

heterogeneities of the studies.

If more than 6 studies are included in the meta-analysis, the results were shown with a forest graph. Publication bias was evaluated with the Egger's test, and Duval and Tweedie's trim and fill test was used to evaluate the sensitivity of the results^[17,18]. Unless the P was less than 0.001, we would give an accurate P value, except for $P < 0.05$ in Egger's test, which was considered statistically significant. Other $P < 0.05$ could be considered statistically significant.

RESULTS

Literature search, study characteristics, and quality assessment

A total of 955 and 13 articles, respectively, were retrieved through database system retrieval and manual retrieval. After 108 duplicate papers were removed, the titles and abstracts of the remaining papers were screened. Additionally, 834 articles that did not meet the inclusion criteria were excluded. Ten trials were terminated without hemodynamic data. Finally, 12 studies were included in the meta-analysis (**Fig. 1**). The screening included 833 elderly patients during perioperative period for meta-analysis, including 546 dexmedetomidine patients and 287 control patients (blank or saline). The basic characteristics of the 12 studies included in the meta-analysis are presented in **Table 1**^[19-30].

Based on the quality assessment part of Cochrane handbook, a systematic evaluation was conducted to

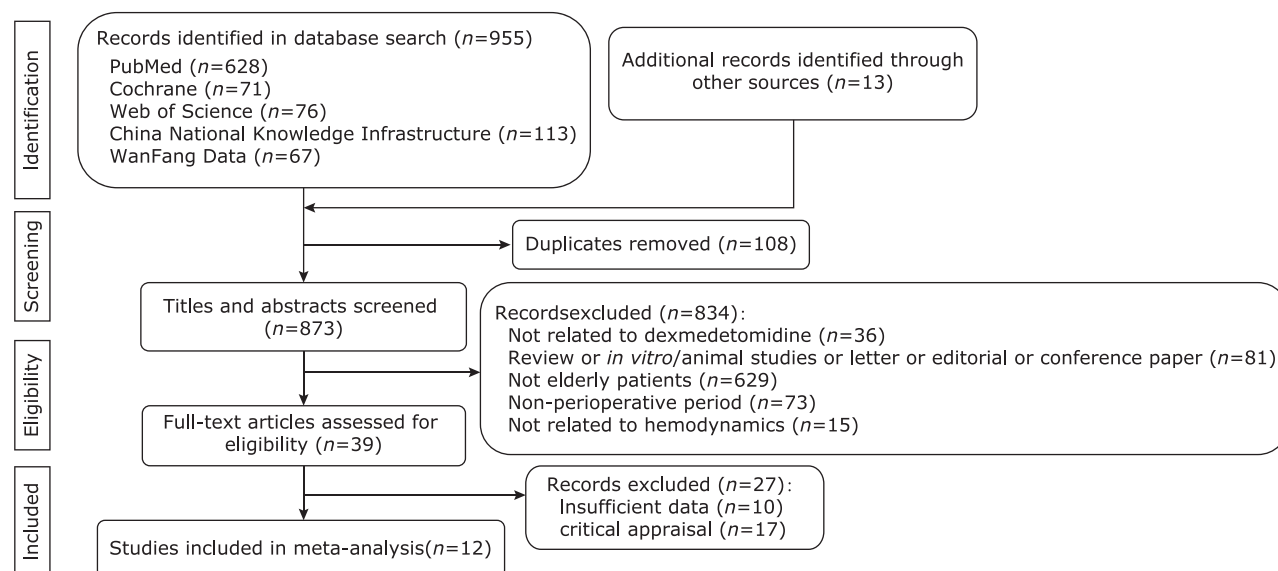


Figure 1. Flowchart of the literature search and selection process.

Table 1. Baseline characteristics of included studies for meta-analysis

| Author, year | Sample size | | Dexmedetomidine dose/administration | Control group | Surgery |
|-----------------------------|-------------|-----|---|---------------|--|
| | Dex | Con | | | |
| Qiao, 2020 ^[19] | 50 | 50 | 0.40 µg/kg loading | Blank | Undergoing laparoscopic cholecystectomy |
| Li, 2015 ^[20] | 20 | 20 | 1.00 µg/kg loading | Blank | ERCP |
| Song, 2017 ^[21] | 30 | 30 | 1.00 µg/kg loading | Blank | Undergoing tracheal intubation under general anesthesia |
| Chen, 2019 ^[22] | 90 | 30 | 0.20, 0.40, 0.60 µg/kg/h infusion | Saline | Colorectal cancer surgery |
| Lin, 2017 ^[23] | 44 | 22 | 0.50, 1.00 µg/kg loading; 0.50 µg/kg/h infusion | Blank | Radical resection of esophageal carcinoma under thoracoscopy surgery |
| Su, 2014 ^[24] | 25 | 25 | 0.50 µg/kg loading; 0.40 µg/kg/h infusion | Saline | Thoracolumbar surgery |
| Zhang, 2018 ^[25] | 30 | 30 | 0.50 µg/kg loading | Saline | Abdominal operation |
| Cao, 2018 ^[26] | 90 | 0 | 0.30, 0.50, 0.70 µg/kg loading | Blank | Radical resection of colorectal cancer |
| Guan, 2015 ^[27] | 60 | 20 | 0.25, 0.50, 1.00 µg/kg loading; constant speed infusion in 10mins | Saline | Abdominal surgery |
| Lee, 2017 ^[28] | 20 | 20 | 0.50 µg/kg loading; constant speed infusion in 10 min | Saline | Hypertension patients with noncardiac surgery |
| Ko, 2015 ^[29] | 47 | 0 | 0.10, 0.30, 0.50, 0.70, 1.00 µg/kg loading | Blank | Orthopedic or urologic surgery |
| Du, 2019 ^[30] | 40 | 40 | 0.60 µg/kg/h infusion | Saline | Laparoscopic cholecystectomy surgery |

Dex: dexmedetomidine; Con: control; ERCP: endoscopic retrograde cholangiopancreatography.

assess the bias risk of all included articles, including selection bias, selective reporting bias, incomplete reporting bias, and publication bias. According to the above manual, the quality of the literature was defined as low, moderate, and high. Except that some studies did not describe the RCTs proposal in detail and were not clear about the selective reporting bias, almost all the included RCTs were assessed as low bias risk, indicating that they were of good quality (Fig. 2). Moreover, patients with severe co-morbidity were excluded from RCTs, and the basic characteristics and co-morbidities were not significantly different between intervention group and control group.

Hemodynamic indexes

Comparison between before and after operation

Ten RCT articles provided HR of elderly patients before and after operation with dexmedetomidine treatment. The merged results of 10 RCT articles showed that the increase of HR was not statistically significant (SMD = 0.13, 95%CI: -0.44 to 0.70; Fig. 3A and Table 2)^[19-22,24,25,26,27,28,30]. Sensitivity analysis revealed that the sources of heterogeneity might be related to Qiao *et al.* 2020^[19], Zhang *et al.* 2017^[25], and Du *et al.* 2019^[30].

A meta-analysis of 8 articles on MAP before and after operation found that there was no statistical sig-

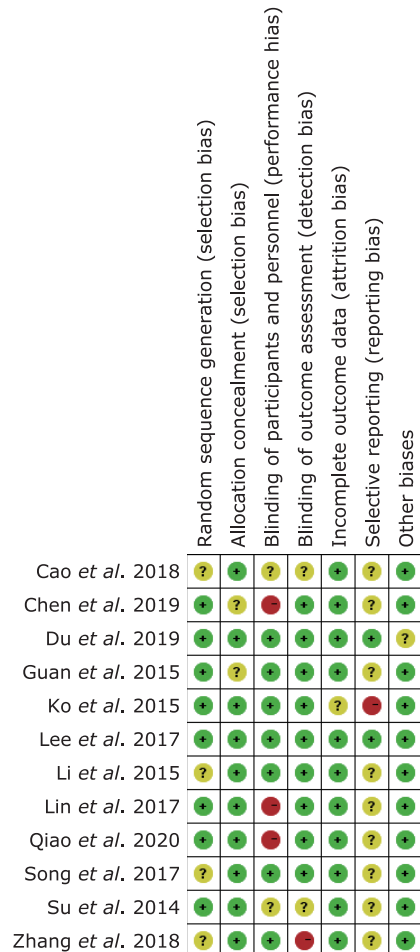


Figure 2. Bias risk of all included articles

Table 2. Summary of included studies

| Indexes | No. of studies | Sample size | SMD (95% CI) | Heterogeneity | |
|--|----------------|-------------|----------------------|---------------|----------------|
| | | | | I^2 (%) | <i>P</i> value |
| Comparison between before and after operation | | | | | |
| MAP | 8 | 450 | 0.12 (-0.54, 0.79) | 93.1 | <0.001 |
| HR | 10 | 550 | 0.13 (-0.44, 0.70) | 91.7 | <0.001 |
| SBP | 4 | 200 | 1.38 (0.11, 2.64) | 93.5 | <0.001 |
| DBP | 4 | 200 | 1.11 (-0.25, 2.46) | 94.5 | <0.001 |
| Comparison between dexmedetomidine and control | | | | | |
| MAP | 8 | 440 | -1.12 (-1.60, -0.63) | 81.6 | <0.001 |
| HR | 10 | 540 | -0.87 (-1.13, -0.62) | 50.8 | 0.032 |
| SBP | 4 | 200 | -1.27 (-2.26, -0.27) | 90.0 | <0.001 |
| DBP | 4 | 200 | -0.96 (-1.33, -0.59) | 34.9 | 0.203 |
| Time effect of SBP and HR with 0.5 µg/kg and 1.0 µg/kg dexmedetomidine, respectively | | | | | |
| SBP _(0.5, 0) | 3 | 112 | -1.17 (-3.36, 1.02) | 96.0 | <0.001 |
| SBP _(0.5, 10) | 3 | 112 | -0.07 (-0.43, 0.28) | 0.0 | 0.686 |
| SBP _(0.5, 20) | 2 | 62 | -0.59 (-1.10, -0.08) | 0.0 | 0.320 |
| SBP _(1, 0) | 2 | 64 | -0.24 (-0.73, 0.25) | 0.0 | 0.889 |
| SBP _(1, 10) | 2 | 64 | -0.86 (-1.95, 0.22) | 74.5 | 0.048 |
| SBP _(1, 20) | 2 | 64 | -0.24 (-0.73, 0.25) | 0.0 | 0.889 |
| HR _(0.5, 0) | 5 | 212 | -0.41 (-0.95, 0.13) | 72.4 | 0.006 |
| HR _(0.5, 10) | 5 | 212 | -0.73 (-1.51, 0.04) | 85.7 | <0.001 |
| HR _(0.5, 20) | 3 | 102 | -1.48 (-2.30, -0.66) | 68.5 | 0.042 |
| HR _(1, 0) | 2 | 64 | -0.14 (-0.63, 0.35) | 0.0 | 0.340 |
| HR _(1, 10) | 2 | 64 | -1.53 (-2.09, -0.97) | 0.0 | 0.709 |
| HR _(1, 20) | 2 | 64 | -1.96 (-2.56, -1.36) | 0.0 | 0.944 |

MAP: mean arterial pressure; HR: heart rate; SBP: systolic blood pressure; DBP: diastolic blood pressure; SMD: standardized mean difference; CI: confidence interval; SBP_(0.5, 0): systolic blood pressure measured at the beginning of infusing 0.5 µg/kg dexmedetomidine; SBP_(0.5, 10): systolic blood pressure measured after 10 minutes of infusing 0.5 µg/kg dexmedetomidine; SBP_(0.5, 20): systolic blood pressure measured after 20 minutes of infusing 0.5 µg/kg dexmedetomidine; SBP_(1, 0): systolic blood pressure measured at the beginning of infusing 1 µg/kg dexmedetomidine; SBP_(1, 10): systolic blood pressure measured after 10 minutes of infusing 1 µg/kg dexmedetomidine; SBP_(1, 20): systolic blood pressure measured after 20 minutes of infusing 1 µg/kg dexmedetomidine; HR_(0.5, 0), HR_(0.5, 10), HR_(0.5, 20), HR_(1, 0), HR_(1, 10) and HR_(1, 20) were similar to SBP_(0.5, 0), SBP_(0.5, 10), SBP_(0.5, 20), SBP_(1, 0), SBP_(1, 10) and SBP_(1, 20).

nificance in the increase of MAP before and after operation in patients treated with dexmedetomidine anesthesia (SMD = 0.12, 95%CI: -0.54 to 0.79; **Fig. 3B** and **Table 2**)^[19-22,24,26,28,30]. We used sensitivity analysis to study the source of heterogeneity and found that it might be related to the two studies including Qiao *et al.*^[19] and Du *et al.*^[30].

Four RCTs^[21,25,27,28] reported two hemodynamic indexes of SBP and DBP before and after operation. Similar to MAP and HR, SBP and DBP also increased accordingly, but only the increase in SBP was statistically significant (SBP: SMD = 1.38, 95%CI: 0.11 to 2.64; DBP: SMD = 1.11, 95%CI: -0.25 to 2.46; Table

2). SBP and DBP had strong heterogeneity, and both of them were related to two articles including Song *et al.*^[21] and Lee *et al.*^[28].

Comparison between dexmedetomidine group and control group

The differences in the increase of MAP, HR, SBP, and DBP before and after intubation, extubation, and surgical resection in the dexmedetomidine group were significantly lower than those in the control group (MAP: SMD = -1.12, 95%CI: -1.60 to -0.63; HR: SMD = -0.87, 95%CI: -1.13 to -0.62; SBP: SMD = -1.27, 95%CI: -2.26 to -0.27; DBP: SMD = -0.96, 95%CI: -1.33 to

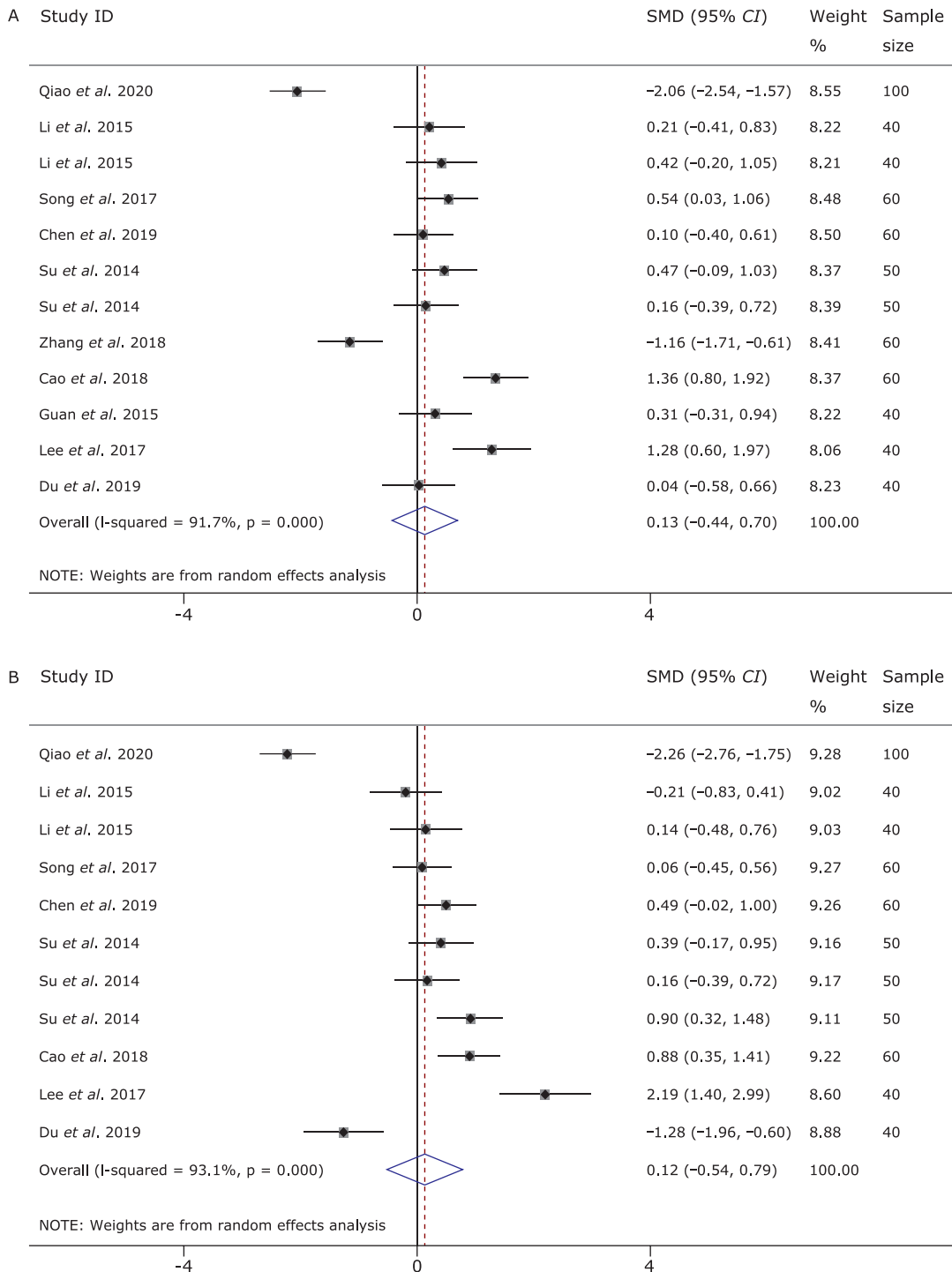


Figure 3. Forest plot of comparison between before and after operation in elderly patients during perioperative period. (A) Heart rate; (B) mean arterial pressure.

-0.59; **Fig. 4A, Fig. 4B, and Table 2**)^[19-22,24,25,26-28,30]. There was strong heterogeneity in the hemodynamic indexes of MAP and SBP, but the SMD of 8 RCTs related to MAP and 4 RCTs related to SBP were less than 0. These results indicated that the merged effect

obtained in this study reflected that the four hemodynamic indexes including MAP, HR, SBP, and DBP in the dexmedetomidine group were more stable before and after intubation, extubation, and surgical resection, compared with the control group.

By comparing the immediate, 10 min, and 20 min later changes of SBP and HR after dexmedetomidine 0.5 µg/kg and dexmedetomidine 1.0 µg/kg treatment, there was no continuous decrease of SBP and HR in patients treated with dexmedetomidine 0.5 µg/kg. However, the HR of patients treated with dexmedetomidine 1.0 µg/kg showed a progressive decline over time

[HR(1, 0): SMD = -0.14, 95%CI: -0.63 to 0.35; HR(1, 10): SMD = -1.53, 95%CI -2.09 to -0.97; HR(1, 20): SMD = -1.96, 95%CI -2.56 to -1.36; **Table 2**]^[23,29].

Publication bias assessment and sensitivity analysis

Results of publication bias analysis which was based

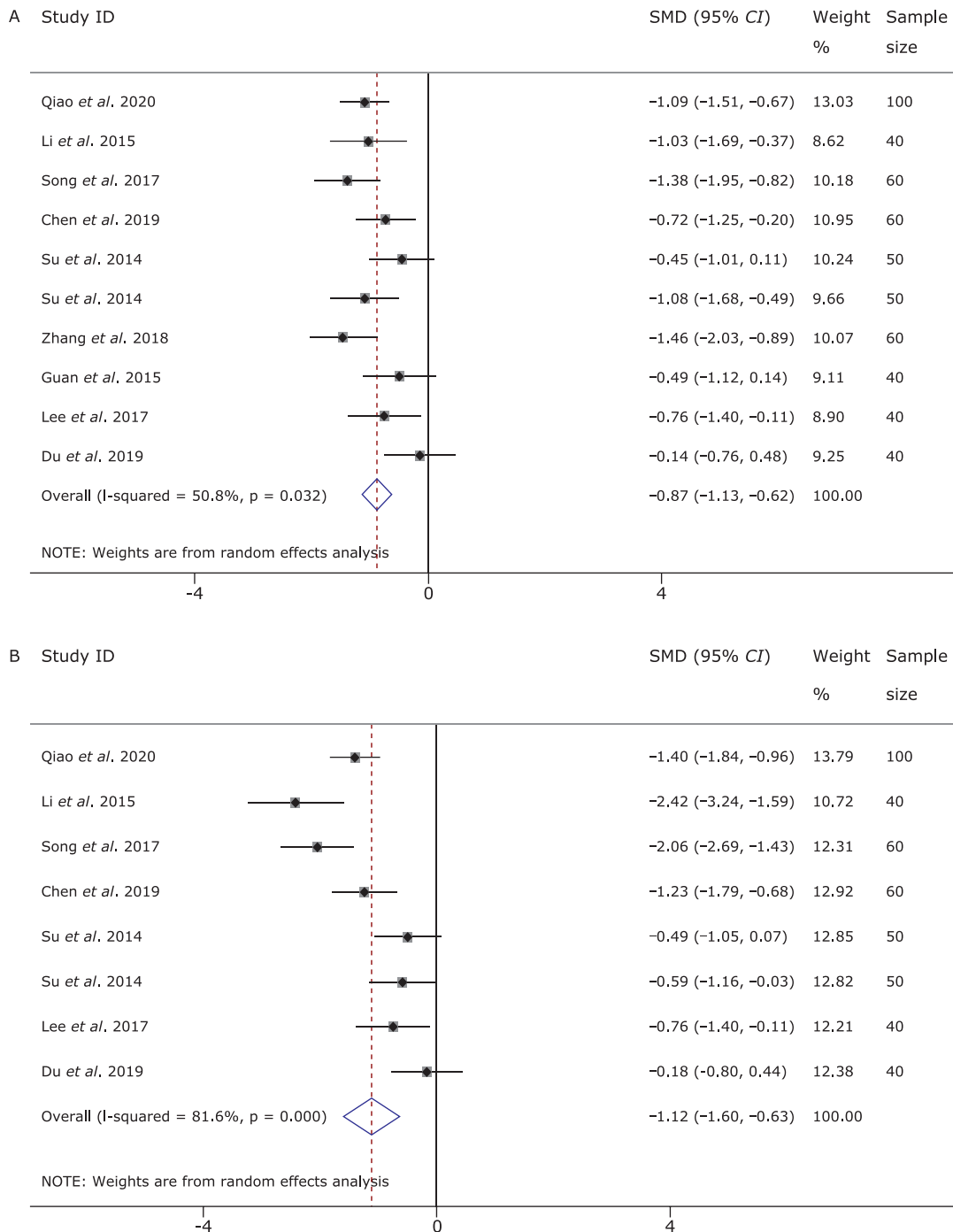


Figure 4. Forest plot of comparison between dexmedetomidine and control in elderly patients during perioperative period. (A) Heart rate; (B) mean arterial pressure.

on Egger's test. There was no obvious publication bias in MAP and HR (**Table 3**). The Duval and Tweedie's trim and fill test of MAP and HR found that the effect amount obtained by the two indexes was stable.

DISCUSSION

The present meta-analysis suggested that treatment with dexmedetomidine might effectively decrease the variations of perioperative hemodynamic indexes including MAP, HR, SBP, and DBP in surgical elderly patients and provided more stable and safer hemodynamics compared with blank or saline. According to literature, compared with blank or saline, dexmedetomidine had a better inhibitory effect on the increase of MAP, HR, SBP, and DBP caused by perioperative intubation, extubation, or surgical resection in elderly patients. HR and MAP of patients in surgical intensive care unit after major abdominal surgery were significantly lower in the dexmedetomidine group than in the propofol group^[32]. During robot-assisted laparoscopic prostatectomy, the HR of dexmedetomidine group was significantly lower than that of saline group^[33]. Among conscious patients undergoing carotid endarterectomy, the intraoperative HR, SBP, and DBP in dexmedetomidine group were lower than those in metoprolol and labetalol groups^[34]. Among patients undergoing endoscopic retrograde cholangiopancreatography, the lowest SBP and minimum HR in dexmedetomidine group were significantly lower than those in midazolam group, and there was no severe acute heart failure or arrhythmia^[35].

Our meta-regression analysis showed that HR progressively decreased over time after the application of dexmedetomidine in perioperative elderly patients. Dexmedetomidine reduced sympathetic activity and

the excitability of the sinus node, thus slowing down patient's heart rate^[36]. In many RCTs, adverse clinical outcomes of bradycardia were rarely reported in the dexmedetomidine group. However, during total knee arthroplasty in elderly patients, the median effective dose of dexmedetomidine in the younger group (65 - 74 years old) was significantly higher than that in the older group (75 - 85 years old), suggesting more studies are needed on the safe application of dexmedetomidine in elderly patients during the perioperative period^[37]. Zhong *et al.* provided a meta-analysis highlighting an elevated risk of bradycardia with dexmedetomidine but no difference in risk of hypotension in critically ill patients^[38]. Specific patient characteristics such as preexisting low blood pressure and history of coronary artery disease have been considered as risk factors for hypotension and bradycardia. More research is needed to identify patient characteristics that may indicate higher risks for dexmedetomidine-associated bradycardia and the different administration modalities of dexmedetomidine (*e.g.*, agent, dose, route, and timing), so as to maintain perioperative hemodynamic stability in elderly patients.

The indexes including MAP, HR, SBP and DBP in this meta-analysis had high heterogeneity, which we believe may be related to different surgical procedures, individual patient differences, and various dexmedetomidine regimens (*e.g.*, dosage, route, time of administration). Duval and Tweedie's trim and fill test showed that the conclusion of this meta-analysis was not affected by such a high heterogeneity. After the article-influenced heterogeneity was excluded, the conclusion of our analysis remained stable.

Inevitably, this meta-analysis had several limitations. First, there was heterogeneity in the administration protocols of dexmedetomidine (*e.g.*, agent, dose, route, and timing), along with varied surgical operation

Table 3. Evaluation of publication bias and sensitivity analysis

| Index | Egger's regression | | Duval and Tweedie's trim and fill | | |
|--|--------------------|---------|-----------------------------------|-----------------|----------------------|
| | Intercept | P value | Original OR | Studies trimmed | Adjusted OR |
| Comparison between before and after operation | | | | | |
| MAP | 9.392 | 0.334 | 0.12 (-0.54, 0.79) | 2 | -0.18 (-0.84, 0.49) |
| HR | 18.491 | 0.067 | 0.13 (-0.44, 0.71) | 3 | -0.21 (-0.78, 0.36) |
| Comparison between dexmedetomidine and control (blank or saline) | | | | | |
| MAP | -2.395 | 0.669 | -1.12 (-1.61, -0.63) | 0 | -1.12 (-1.61, -0.63) |
| HR | 2.967 | 0.408 | -0.87 (-1.13, -0.62) | 0 | -0.87 (-1.13, -0.62) |

Evaluation of publication bias for the meta-analyses containing at least six studies. MAP: mean arterial pressure; HR: heart rate; OR: odds ratio.

types and different clinical practices among the included studies, and the possible biases might also limit the certainty of the findings of our meta-analysis. Second, only 12 RCTs were included in this meta-analysis. Third, the administration of dexmedetomidine in different studies was inconsistent, and the control drugs used by the included studies were heterogeneous. Therefore, more high-quality RCTs are needed to explore the effect of dexmedetomidine in maintaining perioperative hemodynamic stability in elderly patients.

In conclusion, dexmedetomidine can effectively maintain perioperative hemodynamic stability in elderly patients. Yet, more research is needed to determine the effective and safe dose of dexmedetomidine in elderly patients during perioperative period.

Conflict of interest

None disclosed.

Authors' contributions

Tian LJ and Yao YT critically revised the manuscript; Tian LJ, Yao YT, Dai Z, and Yuan S made substantial contribution to the conception and design of the work and manuscript drafting; Tian LJ, Yao YT, Dai Z, and Yuan S acquired, analyzed, and interpreted the data. All authors have read and approved the final manuscript.

Funding

Supported by National High Level Hospital Clinical Research Funding (2022 GSP-QN-16) and Yunnan Provincial Cardiovascular Disease Clinical Medical Center Project (FZX2019-06-01).

REFERENCES

1. Chattopadhyay U, Mallik S, Ghosh S, et al. Comparison between propofol and dexmedetomidine on depth of anaesthesia: A prospective randomized trial. *J Anaesthesiol Clin Pharmacol* 2014;30(4):550-4. doi:10.4103/0970-9185.142857.
2. Venn RM, Hell J, Grounds RM. Respiratory effects of dexmedetomidine in the surgical patient requiring intensive care. *Crit Care* 2000;4(5):302-8. doi:10.1186/cc712.
3. Hwang W, Lee J, Park J, et al. Dexmedetomidine versus remifentanyl in postoperative pain control after spinal surgery: a randomized controlled study. *BMC Anaesthesiol* 2015;15:21. doi:10.1186/s12871-015-0004-1.
4. Talke P, Chen R, Thomas B, et al. The hemodynamic and adrenergic effects of perioperative dexmedetomidine infusion after vascular surgery. *Anesth Analg* 2000; 90(4):834-9. doi:10.1097/0000539-200004000-00011.
5. Keniya VM, Ladi S, Naphade R. Dexmedetomidine attenuates sympathoadrenal response to tracheal intubation and reduces perioperative anaesthetic requirement. *Indian J Anaesth* 2011;55(4):352-7. doi:10.4103/0019-5049.84846.
6. Virtanen R, Savola JM, Saano V, et al. Characterisation of selectivity, specificity and potency of medetomidine as an α_2 -receptor agonist. *Eur J Pharmacol* 1988;150(1-2):9-14. doi:10.1016/0014-2999(88)90744-3.
7. Hall JE, Uhrich TD, Barney JA, et al. Sedative, amnestic, and analgesic properties of small-dose Dexmedetomidine infusions. *Anesth Analg* 2000;90:699-705. doi:10.1097/0000539-200003000-00035.
8. Yang L, Gong Y, Tan Y, et al. Dexmedetomidine exhibits antiarrhythmic effects on human-induced pluripotent stem cell-derived cardiomyocytes through a Na/Ca channel-mediated mechanism. *Ann Transl Med* 2021;9(5):399. doi:10.21037/atm-20-5898.
9. Shribman AJ, Smith G, Achola KJ. Cardiovascular and catecholamine responses to laryngoscopy with and without tracheal intubation. *Br J Anesth* 1987;59(3):295-9. doi:10.1093/bja/59.3.295.
10. Tsujikawa S, Ikeshita K. Low-dose dexmedetomidine provides hemodynamics stabilization during emergence and recovery from general anesthesia in patients undergoing carotid endarterectomy: a randomized double-blind, placebo-controlled trial. *J Anesth* 2019;33(2):266-72. doi:10.1007/s00540-019-02612-w.
11. Andres TM, McGrane T, McEvoy MD, et al. Geriatric Pharmacology: An Update. *Anesthesiol Clin* 2019;37(3):475-92. doi:10.1016/j.anclin.2019.04.007.
12. Bloor BC, Ward DS, Belleville JP, et al. Effects of intravenous dexmedetomidine in humans, II : hemodynamic changes. *Anesthesiology* 2000; 77(3): 1134-42. doi:10.1097/0000542-199212000-00014.
13. Higgins JPT, Thomas J, Chandler J, et al. *Cochrane Handbook for Systematic Reviews of Interventions* version 6.1. (updated September 2020). Cochrane 2020. Available from www.training.cochrane.org/handbook.
14. Moher D, Shamseer L, Clarke M, et al. Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015 statement. *Syst Rev* 2015;4(1):1. doi:10.1186/2046-4053-4-1.
15. Borenstein M, Hedges LV, Higgins JP, et al. A basic introduction to fixed-effect and random-effects models for meta-analysis. *Res Synth Methods* 2010;1(2):97-111. doi:10.1002/jrsm.12.
16. Nyaga VN, Arbyn M, Aerts M. Metaprop: a Stata command to perform meta-analysis of binomial data. *Arch Public Health* 2014;72(1):39. doi:10.1186/2049-3258-72-39.
17. Egger M, Davey Smith G, Schneider M, et al. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997;315(7109):629-34. doi:10.1136/bmj.315.7109.629.
18. Duval S, Tweedie R. Trim and fill: A simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. *Biometrics* 2000;56(2):455-63. doi:10.1111/j.0006-341x.2000.00455.x.
19. Qiao KK, Li X. Effects of dexmedetomidine on anesthesia and cognitive function in elderly patients undergoing laparoscopic cholecystectomy. *Chin J Pharmacovigilance* 2020;17(2):81-6.
20. Li SM, Dong TL. The observation on the anesthetic effect of dexmedetomidine for the elder ERCP. *Chin J Geriatr Care* 2015;13(2):68-70.
21. Song TX, Hu WS. Cardiovascular effects of pre prescribed dexmedetomidine on elderly patients undergoing tracheal intubation under general anesthesia. *Chin Med Pharm* 2017;7(17):180-2,198.
22. Chen SY, Li XL, Zhou DX, et al. Effects of different doses of dexmedetomidine on the extubation reaction of elderly patients after general anesthesia colorectal cancer surgery. *Chin Anti-tumor Pharmacy* 2019;9(3):451-5.
23. Lin YB, Shu HH, Ye F, et al. The effects of dexmedetomidine of two different dose infusion on myocardial oxygen supply and hemodynamics in patients with radical resection of esophageal carcinoma under thoracoscopy surgery. *Chin Progress in Modern Biomedicine* 2017;17(4):692-5.
24. Su XJ, Li P, Guo ZG, et al. Clinical observation of continuous infusion of dexmedetomidine in elderly patients undergoing spinal surgery. *Chin J Med Res* 2014;43(4):108-11.
25. Zhang XH, Tian XT, Zhou Z. Effect of dexmedetomidine on recovery period of elderly patients under intravenous inhalation combined with general anesthesia. *Chin J Laboratory Diagn* 2018;22(6):946-9.

26. Cao BF, Hu HZ, Zhang SJ, et al. The effect of dexmedetomidine on cardiovascular response during extubation in older patients undergoing laparoscopic radical resection of colorectal cancer. *Chin J Colorect Anal Surg* 2018;24(1):77-80.
27. Guan ZY, Wang CM, Tang S, et al. Comparison of effects of different doses dexmedetomidine on inhibiting tracheal intubation-evoked haemodynamic response in the elderly patients. *J Clin Diagn Res* 2015;9(9):UC10-3. doi:10.7860/JCDR/2015/14624.6455.
28. Lee CW, Kim MW. Effects of preanesthetic dexmedetomidine on hemodynamic responses to endotracheal intubation in elderly patients undergoing treatment for hypertension: a randomized, double-blinded trial. *Korean J Anesthesiol* 2017;70(1):39-45. doi:10.4097/kjae.2017.70.1.39.
29. Ko KH, Jun IJ, Lee SS, et al. Effective dose of dexmedetomidine to induce adequate sedation in elderly patients under spinal anesthesia. *Korean J Anesthesiol* 2015;68(6):575-80. doi:10.4097/kjae.2015.68.6.575.
30. Du XX, Song F, Zhang XQ, et al. Protective efficacy of combined use of parecoxib and dexmedetomidine on postoperative hyperalgesia and early cognitive dysfunction after laparoscopic cholecystectomy for elderly patients. *Acta Cir Bras* 2019;34(9): e201900905. doi:10.1590/s0102-865020190090000005.
31. Yun SH, Park JC, Kim SR, et al. Effects of dexmedetomidine on serum interleukin-6, hemodynamic stability, and postoperative pain relief in elderly patients under spinal anesthesia. *Acta Med Okayama* 2016;70(1):37-43. doi:10.18926/AMO/54002.
32. Chang YF, Chao A, Shih PY, et al. Comparison of dexmedetomidine versus propofol on hemodynamics in surgical critically ill patients. *J Surg Res* 2018;228:194-200. doi:10.1016/j.jss.2018.03.040.
33. Yu J, Park JY, Kim DH, et al. Dexmedetomidine attenuates the increase of ultrasonographic optic nerve sheath diameter as a surrogate for intracranial pressure in patients undergoing robot-assisted laparoscopic prostatectomy: A randomized double-blind controlled trial. *Medicine (Baltimore)* 2019;98(33):e16772. doi:10.1097/MD.00000000000016772.
34. Bekker AY, Basile J, Gold M, et al. Dexmedetomidine for awake carotid endarterectomy: efficacy, hemodynamic profile, and side effects. *J Neurosurg Anesthesiol* 2004;16(2):126-35. doi:10.1097/00008506-200404000-00004.
35. Inatomi O, Imai T, Fujimoto T, et al. Dexmedetomidine is safe and reduces the additional dose of midazolam for sedation during endoscopic retrograde cholangiopancreatography in very elderly patients. *BMC Gastroenterol* 2018;18(1):166. doi:10.1186/s12876-018-0897-5.
36. Ueki M, Kawasaki T, Habe K, et al. The effects of dexmedetomidine on inflammatory mediators after cardiopulmonary bypass. *Anaesthesia* 2014;69:693-700. doi:10.1111/anae.12636.
37. Wang C, Zhang H, Fu Q, et al. Effective dose of dexmedetomidine as an adjuvant sedative to peripheral nerve blockade in elderly patients. *Acta Anaesthesiol Scand* 2018;62(6):848-56. doi:10.1111/aas.13087.
38. Zhong Q, Kumar A, Deshmukh A, et al. Dexmedetomidine Reduces Incidences of Ventricular Arrhythmias in Adult Patients: A Meta-Analysis. *Cardiol Res Pract* 2022;2022:5158362. doi:10.1155/2022/5158362.

(Edited by Liang-Jun Gu)

论著

右美托咪定对老年患者围术期血流动力学稳定性影响的系统评价与 Meta 分析

田丽娟¹, 姚允泰¹, 袁素¹, 戴峥²

1 中国医学科学院北京协和医学院 国家心血管病中心 阜外医院 麻醉科, 北京市 100037, 中国
2 云南省阜外心血管病医院 麻醉科, 昆明市 650102, 中国

摘要

目的 右美托咪定 (dexmedetomidine) 作为一种高选择性 α_2 肾上腺素受体激动剂, 具有镇静、镇痛、无呼吸抑制作用, 广泛用于围手术期麻醉。本研究采用 Meta 分析方法评估右美托咪定对老年患者围手术期血流动力学稳定性的影响。

方法 利用 PubMed、EMBASE、Ovid、Cochrane 图书馆、中国知网和万方数据库检索截至 2021 年 9 月关于右美托咪定对老年患者围手术期血流动力学稳定性影响随机对照试验的相关文献。采用标准加权均数差 (standardized mean differences, SMD) 作为效应量, 以各效应量及其 95% 可信区间 (confidence interval, CI) 进行结果分析。由于各研究间存在异质性, 采用随机效应模型分析。

结果 共纳入 12 项随机对照试验研究, 共 833 例老年患者 (右美托咪定组患者 546 例; 对照组患者 287 例)。Meta 分析结果显示, 与术前比较, 右美托咪定组老年患者术中心率 (heart rate, HR)、平均动脉压 (mean arterial pressure, MAP) 和舒张压 (diastolic blood pressure, DBP) 均无明显升高。与对照组比, 右美托咪定组老年患者的 HR、MAP、收缩压 (systolic blood pressure, SBP) 和 DBP 等血流动力学指标的变化显著降低 (HR: SMD = -0.87, 95% CI: -1.13 ~ -0.62; MAP: SMD = -1.12, 95% CI: -1.60 ~ -0.63; SBP: SMD = -1.27, 95% CI: -2.26 ~ -0.27; DBP: SMD = -0.96, 95% CI: -1.33 ~ -0.59)。亚组分析表明给予 1.0 $\mu\text{g}/\text{kg}$ 右美托咪定治疗, 患者心率呈现时间相关性下降。

结论 右美托咪定可维持老年患者围手术期血流动力学更稳定。然而, 关于右美托咪定在老年患者应用的有效性和安全剂量尚需开展高质量研究予以验证。

关键词: 右美托咪定; 老年患者; 血流动力学; 围手术期

通讯作者: 田丽娟, 邮箱: tlijuan1982@163.com