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Original Article

Meta-analysis of the sedative effects of midazolam and dexmedetomidine in patients undergoing bronchoscopy

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Abstract: Objective: To perform a meta-analysis on the sedative effects of midazolam and dexmedetomidine in patients undergoing bronchoscopy. Methods: Relevant literature on the sedative effects of midazolam and dexmedetomidine in patients undergoing bronchoscopy was searched in both Chinese and English databases. Results: A total of 19 studies published between 2012 and 2024 were included, involving 38 groups and 2,339 patients. Meta-analysis of continuous variables from fifteen studies reported no statistically significant difference in systolic blood pressure between the study group and the control group (MD = -0.27, 95% CI: -2.16 to 1.61, Z = -0.28, P = 0.78). Similarly, eight studies showed no significant difference in heart rate between the study group and the control group (MD = -0.62, 95% CI: -2.67 to 1.43, Z = -0.59, P = 0.55). Twelve studies demonstrated significantly higher oxygen saturation (SaO2) levels in the study group compared to the control group (MD = 1.88, 95% CI: 0.56 to 3.20, Z = 2.79, P = 0.01). Nine studies indicated that sedation satisfaction was significantly higher in the study group than in the control group (MD = 2.93, 95% CI: 1.16 to 4.70, Z = 3.25, P < 0.01). Ten studies assessed sedation scores, showing no statistically significant difference between groups (MD = 0.32, 95% CI: -0.02 to 0.67, Z = 1.82, P = 0.07). Awakening time, reported in eight studies, also showed no significant difference (MD = -2.70, 95% CI: -5.50 to 0.09, Z = -1.89, P = 0.06). Six studies reported VAS (Visual Analogue Scale) scores, showing a statistically significant difference (MD = -0.46, 95% CI: -0.83 to -0.08, Z = -2.39, P = 0.02). Meta-analysis of dichotomous variables from fourteen studies showed no significant difference in the incidence of adverse events between the groups (OR = -0.10, 95% CI: -0.49 to 0.29, Z = -0.49, P = 0.62). Meta-regression analysis suggested that heterogeneity mainly originated from differences in study type and methodology (P < 0.05). Conclusion: Both midazolam and dexmedetomidine demonstrate good sedative effects during bronchoscopy, and their use should be tailored to individual patient conditions.

Keywords: Midazolam, dexmedetomidine, bronchoscopy, sedative effect, meta-analysis

Introduction

A bronchoscope is a commonly used medical instrument for examining pulmonary diseases, hemoptysis, airway stenosis, bronchial foreign bodies, and other conditions [1]. It not only enables sampling, lesion imaging and observation, and dynamic recording, but also assists physicians in performing airway polypectomy procedures, thereby achieving precise localization and early treatment of respiratory diseases [2]. However, bronchoscopy is an invasive procedure that requires the use of sedatives during diagnosis or treatment to minimize irritation to the respiratory mucosa and reduce patient discomfort, thereby ensuring procedural safety and optimal visualization [3, 4]. Midazolam, a short-acting benzodiazepine widely used in diagnostic examinations and therapeutic procedures, has significant sedative, muscle relaxant, anticonvulsant, and anxiolytic effects [5]. Particularly in flexible bronchoscopy, the safety of midazolam combined with other local anesthetics is significantly higher than that of propofol [6].

Dexmedetomidine is commonly used for sedation during tracheal intubation and mechanical ventilation due to its strong affinity for α2-adrenergic receptors. It not only effectively lowers blood pressure but also alleviates patient anxiety [7]. However, Lima A et al. [8] point-

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ed out that as interventional pulmonologists increasingly use both flexible and rigid bronchoscopies for advanced diagnostic and therapeutic purposes, complications related to anesthetic combinations, airway management, and ventilation techniques have also been rising. Additionally, the ASRA practice guidelines [9] highlight that while there are numerous sedative agents, each with its advantages, improper sedation duration or dosage during respiratory disease examinations or treatments can lead to neurotoxicity or even respiratory depression. Therefore, this study conducts a meta-analysis to evaluate the sedative effects of midazolam and dexmedetomidine in bronchoscopy, aiming to provide clear guidance for optimizing the safety and efficacy of bronchoscopy procedures.

Materials and methods

Data sources

Relevant literature on "the sedative effects of midazolam and dexmedetomidine in patients undergoing bronchoscopy" was retrieved from Chinese and English databases, covering the period from 2000 to 2024. In Chinese databases, including VIP Database, Wanfang Medical, China National Knowledge Infrastructure (CNKI), and X-MOL academic platform, the search terms used were "Midazolam", "Dexmedetomidine", "Bronchoscopy", "Bronchoscopy Examination", and "Sedation" For English databases, including Wiley InterScience, PubMed, Web of Science, Cochrane Library, and Springer Link, the search terms applied were "Midazolam", "Fentanyl-Midazolam Combination", "Dexmedetomidine", "Bronchoscopy", "Bronchoscopy Examination", and "Sedation".

Literature selection

Inclusion criteria: The inclusion criteria were as follows: (1) Studies published between 2000 and 2024; (2) Study subjects requiring bronchoscopy based on medical history, clinical symptoms and signs, and laboratory examinations; (3) Studies involving only bronchoscopy and its associated systems, without the use of other endoscopic procedures; (4) Study methods were closely related to the sedative effects of midazolam and/or dexmedetomidine during bronchoscopy; (5) Study subjects had no systemic tumors, severe psychiatric disorders, hepatic or renal dysfunction, respiratory diseases, severe cardiovascular or cerebrovascular diseases, or surgical history; (6) Study subjects had no history of sedation or hypnotic drug abuse.

Exclusion criteria: The exclusion criteria were as follows: (1) Studies that were systematic reviews, quantitative analyses, network pharmacology analyses, descriptive studies, case studies, animal experiments, or other meta-analyses; (2) Unpublished studies or those with academic copyright disputes; (3) Studies with incomplete or unclear information, such as vague research content, inaccessible full texts, unclear treatment methods, or unknown authors; (4) Redundant publications of the same study; (5) Studies with significant statistical errors or flawed research designs.

Literature screening and data extraction

First, relevant literature was retrieved from Chinese and English databases using the selected keywords. The titles of the retrieved studies were then imported into the "NoteExpress 3.2 Literature Retrieval and Management" system for duplicate removal. After deduplication, the titles and abstracts were carefully reviewed to exclude studies of poor quality or low relevance. Subsequently, two researchers independently screened the literature based on inclusion and exclusion criteria, extracting and summarizing study information. In case of disagreements, a third party with higher clinical experience and professional qualifications was consulted for judgment. Extracted information included: (1) Basic details such as the first author, publication year, journal, and country; (2) Study population characteristics, including source, gender, age, number of cases, and disease type; (3) Study type, grouping or setup method, research contents and objectives, outcome/observation indicators, etc.; (4) Key factors influencing the risk of bias assessment.

Risk of bias assessment

The quality of the included studies was assessed using the "Risk of Bias Assessment Tool" in the Cochrane web-based Review Manager 5.4. The assessment covered the following aspects: (1) Grouping methods, such as random sequence allocation, grouping by disease type, admission time, or treatment method, which may introduce selection bias; (2) Whether

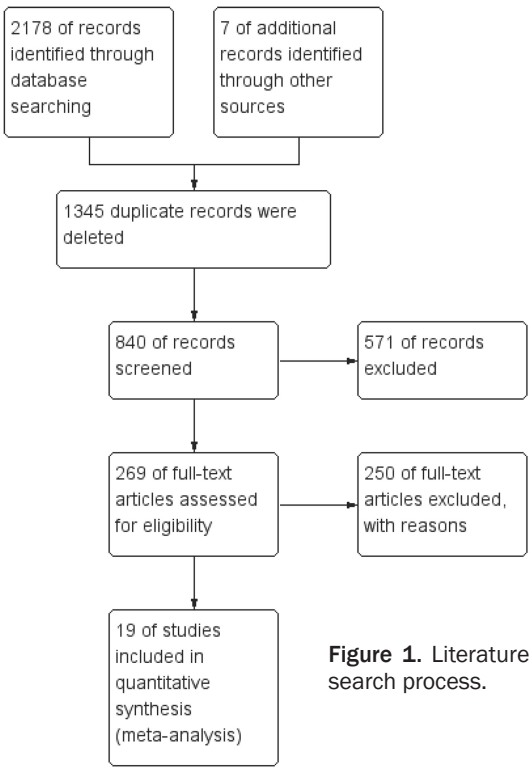

Figure 1. Literature search process.

allocation concealment was implemented, which may also cause selection bias; (3) Whether blinding was applied, including blinding of patients and researchers, which may result in performance bias; (4) Whether outcome assessors were blinded, which may lead to detection bias; (5) Data completeness, which may introduce attrition bias; (6) Selective reporting of study results, which may cause reporting bias; (7) Other potential sources of bias, such as unreliable study data, studies targeting a specific population, or declared research misconduct. The risk of bias for these seven domains was categorized as "low risk", "high risk", or "uncertain risk". After evaluation, the results were summarized, and the risk of bias was visualized using the built-in "figure" function in Review Manager 5.4.

Statistical analysis

The data analysis was conducted using the meta-analysis module in Stata 18.0. For dichotomous variables, the effect measure was expressed as the odds ratio (OR) with a 95% confidence interval (CI). For continuous variables, the effect measure was represented by the mean difference (MD) with a 95% CI. If the units of continuous variables differed across studies, the standardized mean difference (SMD) with a 95% CI was used instead. Heterogeneity was assessed using the Q-test and quantitatively evaluated with the I^2 statistic. If no significant heterogeneity was detected among the study results ($P > 0.1$, $I^2 \leq 50\%$), a fixed-effects model was applied to calculate the pooled OR and 95% CI. If significant heterogeneity was present ($P \leq 0.1$, $I^2 > 50\%$), a random-effects model was used instead, and a forest plot was generated. Additionally, funnel plot analysis was performed on the two most extensive combined outcomes to assess potential publication bias. Finally, the pooled OR and 95% CI were subjected to a Z-test, with $P < 0.05$ indicating statistical significance in the combined results across multiple studies.

Results

Literature search and selection process

After searching databases using Chinese and English keywords, a total of 2,178 relevant studies on "the sedative effects of midazolam and dexmedetomidine in patients undergoing bronchoscopy" were identified, with an additional 7 studies retrieved from other sources, yielding a total of 2,185 studies. The study titles were imported into the "NoteExpress 3.2 Literature Retrieval and Management" system for duplicate removal, eliminating 1,345 studies and leaving 840. After screening titles and abstracts, 571 studies with low relevance or poor quality were excluded, leaving 269. Based on inclusion and exclusion criteria, another 250 studies were removed, resulting in a final inclusion of 19 studies. The literature selection process is shown in **Figure 1**.

Basic information of included studies

The final included 19 articles [10-28], published between 2012 and 2024, comprising 38 groups and 2,339 patients. Among these, 13 articles [11, 12, 16, 17, 19, 21-28] were RCTs, and 6 articles [10, 13-15, 18, 20] were Non-RCTs. All 19 articles were in English, as detailed in **Table 1**.

Assessment of risk of bias in the literature

Among the 19 included studies, twelve studies [12, 14, 17, 19, 21-28] used random number tables or computer-generated random num-

Table 1. Basic information of included studies

author	year	n	type	Study group	Control group	Research measure	Control measure	Observation index
Prabhudev AM et al. [10]	2017	121	Non RCT	62	59	Midazolam + Fentanyl	Midazolam	①, ②, ③, ④, ⑤
Yan Q et al. [11]	2023	200	RCT	100	100	Midazolam + Fentanyl	Midazolam + Fentanyl	①, ②, ③, ④, ⑥, ⑦, ⑧, ⑨, ⑩
Luo ZM et al. [12]	2018	132	RCT	66	66	Midazolam + Fentanyl	Lidocaine	①, ④
Lee H et al. [13]	2019	186	Non RCT	75	111	Midazolam + Propofol	Remifentanil	①, ④, ⑧, ⑨
Zhang Q et al. [14]	2021	433	Non RCT	222	211	Midazolam + Dexmedetomidine	Midazolam + Fentanyl	⑨, ⑪
Katsurada M et al. [15]	2022	96	Non RCT	47	49	Midazolam + Pethidine	Midazolam	①, ⑥, ⑨, ⑪
Ishiwata T et al. [16]	2018	185	RCT	94	91	Midazolam + Fentanyl	Midazolam	④, ⑨
Magazine R et al. [17]	2020	54	RCT	27	27	Midazolam	Dexmedetomidine	①, ④, ⑥, ⑪
Öztaa S et al. [18]	2017	274	Non RCT	122	152	Midazolam	Midazolam + Propofol	⑥, ⑦, ⑨
Sumi T et al. [19]	2021	74	RCT	37	37	Midazolam + Fentanyl	Midazolam + Pethidine	①, ②, ⑨, ⑪
Wu SH et al. [20]	2020	68	Non RCT	35	33	Dexmedetomidine + Propofol + Fentanyl	Midazolam + Propofol + Fentanyl	⑤, ⑧, ⑨
Apostolos F et al. [21]	2024	50	RCT	25	25	Dexmedetomidine + Ketamine	Midazolam + Fentanyl	①, ⑤, ⑥, ⑧, ⑨
Chun EH et al. [22]	2016	56	RCT	28	28	Dexmedetomidine + Midazolam + Fentanyl	Dexmedetomidine + Ketamine	①, ④, ⑤, ⑥, ⑧, ⑨, ⑪
Magazine R et al. [23]	2021	45	RCT	24	21	Dexmedetomidine	Midazolam	①, ②, ③, ⑤, ⑥, ⑨, ⑪
Pertzov B et al. [24]	2022	63	RCT	30	33	Dexmedetomidine	Propofol	①, ④, ⑤, ⑨
Ibrahim E et al. [25]	2019	70	RCT	35	35	Dexmedetomidine + Pregabalin	Dexmedetomidine	①, ②, ③, ④, ⑤, ⑥
Ryu JH et al. [26]	2012	72	RCT	36	36	Dexmedetomidin + Propofol	Remifentanil + Propofol	①, ②, ④, ⑤, ⑥, ⑧, ⑨
Paul M et al. [27]	2021	40	RCT	20	20	Dexmedetomidine + Propofol	Propofol	①, ②, ④, ⑥, ⑧
Xu H et al. [28]	2024	120	RCT	60	60	Dexmedetomidine	Remimazolam	①, ②, ④, ⑤, ⑧, ⑨

Note: ① blood pressure, ② heart rate, ③ respiratory rate, ④ oxygen saturation of blood (SaO2), ⑤ sedation satisfaction, ⑥ sedation score, ⑦ RSS agitation scale, ⑧ awakening time, ⑨ adverse events, ⑩ anesthesia effect, and ⑪ visual analogue scale (VAS).

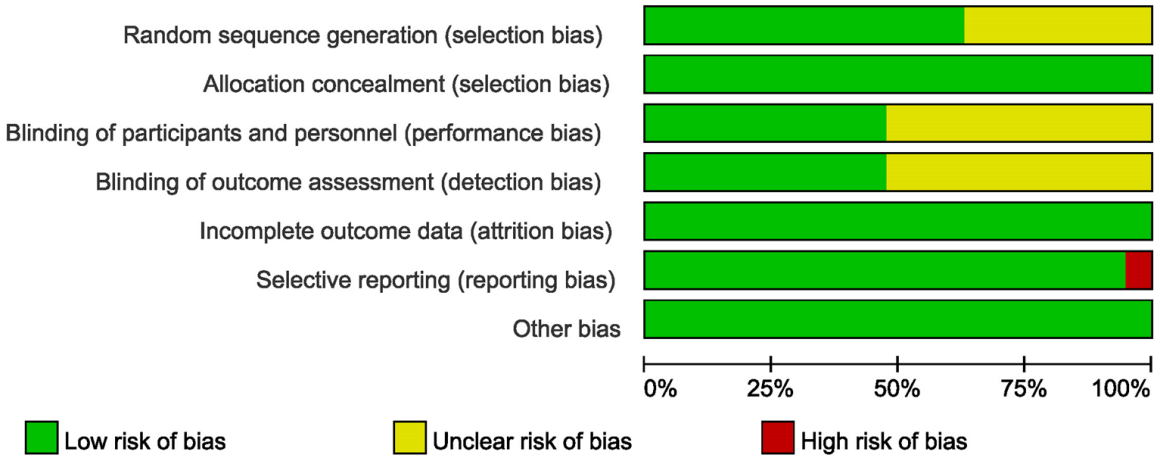

Figure 2. Risk of bias assessment of studies.

bers for group allocation and were all rated as "low risk". Seven studies [10, 11, 13, 15, 16, 18, 20] were grouped based on treatment methods and were evaluated as "uncertain risk". Nine studies [10, 15, 17, 21, 23, 25-28] used allocation concealment and blinding, all of which were evaluated as "low risk". Ten studies [11-14, 16, 18-20, 22, 24] did not describe allocation concealment, blinding, or outcome assessor blinding, and were all rated as "uncertain risk". All 19 studies had complete research data. Eighteen studies [10-24, 26-28] showed no selective reporting, reporting bias, or other biases and were evaluated as "low risk". One study [25] exhibited selective reporting and was rated as "high risk", as shown in **Figure 2**.

Meta-analysis of primary outcomes

Meta-analysis of blood pressure: Fifteen studies [10-13, 15, 17, 19, 21-28] reported blood pressure, including 30 groups and 1,379 patients. Systolic blood pressure was used as a continuous variable for meta-analysis. Significant heterogeneity was observed among the study results ($P \leq 0.1$, $I^2 > 50\%$), so a random-effects model was applied. The meta-analysis confirmed no statistically significant difference in systolic blood pressure between the study and control groups (MD = -0.27, 95% CI: -2.16-1.61, Z = -0.28, P = 0.78). The "Dexmedetomidine + Pregabalin" group showed significantly higher systolic blood pressure compared to the control group, while the "Midazolam + Pethidine" group exhibited significantly lower systolic blood pressure ($P < 0.05$ for both). No statistically significant differences were found in the remaining 7 subgroups ($P > 0.05$ for all), as shown in **Figure 3**.

Meta-analysis of heart rate: Eight studies [10, 11, 19, 23, 25-28] reported heart rate, comprising 16 groups and 742 patients. Heart rate was used as a continuous variable for meta-analysis. Given the significant heterogeneity among the study results ($P \leq 0.1$, $I^2 > 50\%$), a random-effects model was used. The analysis indicated no statistically significant difference in heart rate between the study and control groups (MD = -0.62, 95% CI: -2.67-1.43, Z = -0.59, P = 0.55). Subgroup analysis showed that the heart rate was significantly higher in the "Dexmedetomidine + Pregabalin" group and significantly lower in the "Midazolam + Fentanyl" group compared to the control group ($P < 0.05$ for both). No statistically significant differences were found in the remaining 2 subgroups ($P > 0.05$ for both), as shown in **Figure 4**.

Meta-analysis of SaO2: Twelve studies [10-13, 16, 17, 22, 24-28] reported SaO2, involving 24 groups and 1,299 patients. SaO2 was used as a continuous variable for meta-analysis. Due to substantial heterogeneity among the study results ($P \leq 0.1$, $I^2 > 50\%$), a random-effects model was adopted. The results confirmed that SaO2 in the study group was significantly higher than in the control group (MD = 1.88, 95% CI: 0.56-3.20, Z = 2.79, P = 0.01). Subgroup analysis demonstrated that SaO2 levels in the "Dexmedetomidine + Pregabalin", "Midazolam

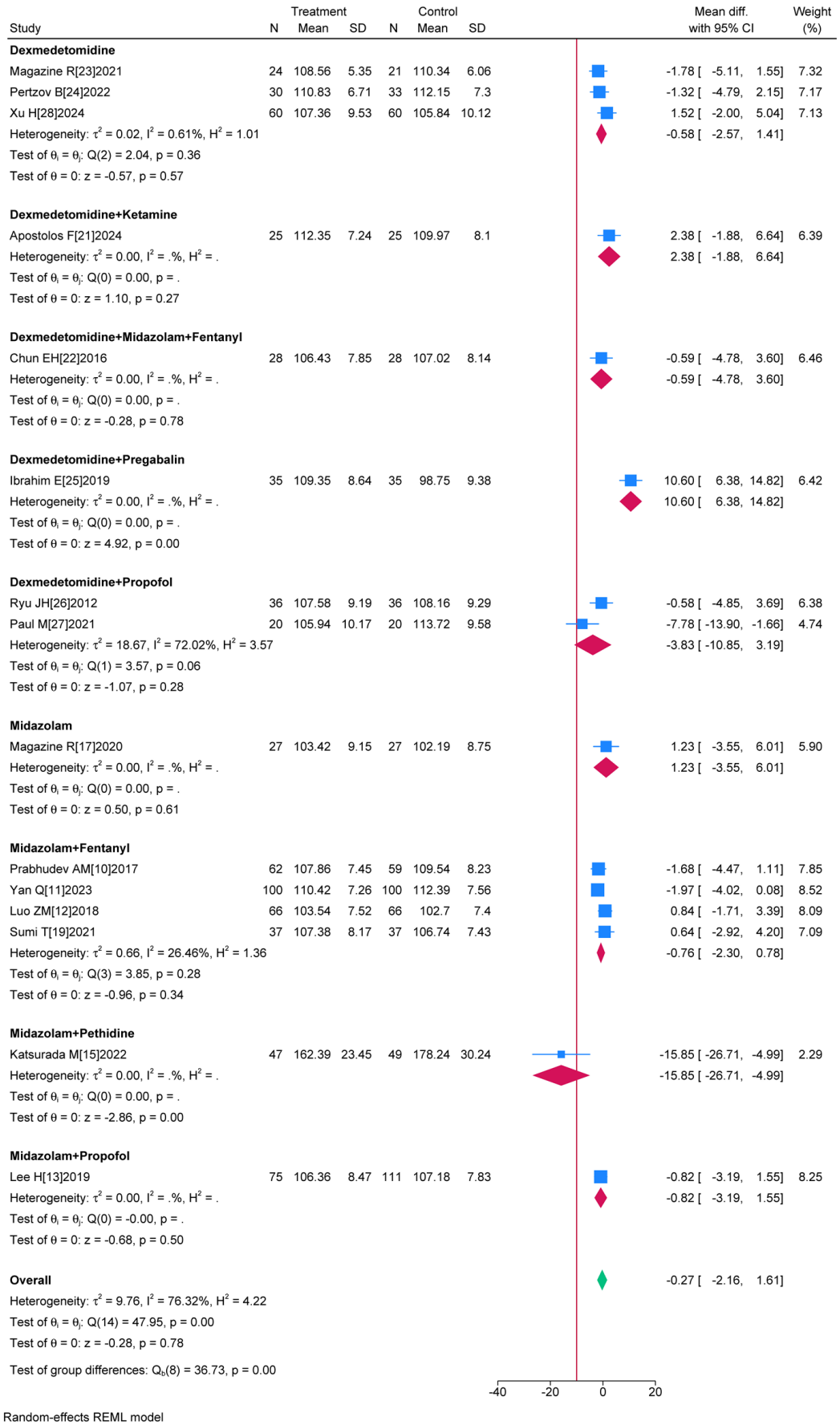
Study
Treatment N Mean SD
Control N Mean SD
Mean diff. with 95% CI
Weight (%)
Dexmedetomidine
Magazine R[23]2021 24 108.56 5.35 21 110.34 6.06 -1.78 [-5.11, 1.55] 7.32
Pertzov B[24]2022 30 110.83 6.71 33 112.15 7.3 -1.32 [-4.79, 2.15] 7.17
Xu H[28]2024 60 107.36 9.53 60 105.84 10.12 1.52 [-2.00, 5.04] 7.13
Heterogeneity: τ² = 0.02, I² = 0.61%, H² = 1.01 -0.58 [-2.57, 1.41]
Test of θi = θj: Q(2) = 2.04, p = 0.36
Test of θ = 0: z = -0.57, p = 0.57
Dexmedetomidine+Ketamine
Apostolos F[21]2024 25 112.35 7.24 25 109.97 8.1 2.38 [-1.88, 6.64] 6.39
Heterogeneity: τ² = 0.00, I² = .%, H² = . 2.38 [-1.88, 6.64]
Test of θi = θj: Q(0) = 0.00, p = .
Test of θ = 0: z = 1.10, p = 0.27
Dexmedetomidine+Midazolam+Fentanyl
Chun EH[22]2016 28 106.43 7.85 28 107.02 8.14 -0.59 [-4.78, 3.60] 6.46
Heterogeneity: τ² = 0.00, I² = .%, H² = . -0.59 [-4.78, 3.60]
Test of θi = θj: Q(0) = 0.00, p = .
Test of θ = 0: z = -0.28, p = 0.78
Dexmedetomidine+Pregabalin
Ibrahim E[25]2019 35 109.35 8.64 35 98.75 9.38 10.60 [6.38, 14.82] 6.42
Heterogeneity: τ² = 0.00, I² = .%, H² = . 10.60 [6.38, 14.82]
Test of θi = θj: Q(0) = 0.00, p = .
Test of θ = 0: z = 4.92, p = 0.00
Dexmedetomidine+Propofol
Ryu JH[26]2012 36 107.58 9.19 36 108.16 9.29 -0.58 [-4.85, 3.69] 6.38
Paul M[27]2021 20 105.94 10.17 20 113.72 9.58 -7.78 [-13.90, -1.66] 4.74
Heterogeneity: τ² = 18.67, I² = 72.02%, H² = 3.57 -3.83 [-10.85, 3.19]
Test of θi = θj: Q(1) = 3.57, p = 0.06
Test of θ = 0: z = -1.07, p = 0.28
Midazolam
Magazine R[17]2020 27 103.42 9.15 27 102.19 8.75 1.23 [-3.55, 6.01] 5.90
Heterogeneity: τ² = 0.00, I² = .%, H² = . 1.23 [-3.55, 6.01]
Test of θi = θj: Q(0) = 0.00, p = .
Test of θ = 0: z = 0.50, p = 0.61
Midazolam+Fentanyl
Prabhudev AM[10]2017 62 107.86 7.45 59 109.54 8.23 -1.68 [-4.47, 1.11] 7.85
Yan Q[11]2023 100 110.42 7.26 100 112.39 7.56 -1.97 [-4.02, 0.08] 8.52
Luo ZM[12]2018 66 103.54 7.52 66 102.7 7.4 0.84 [-1.71, 3.39] 8.09
Sumi T[19]2021 37 107.38 8.17 37 106.74 7.43 0.64 [-2.92, 4.20] 7.09
Heterogeneity: τ² = 0.66, I² = 26.46%, H² = 1.36 -0.76 [-2.30, 0.78]
Test of θi = θj: Q(3) = 3.85, p = 0.28
Test of θ = 0: z = -0.96, p = 0.34
Midazolam+Pethidine
Katsurada M[15]2022 47 162.39 23.45 49 178.24 30.24 -15.85 [-26.71, -4.99] 2.29
Heterogeneity: τ² = 0.00, I² = .%, H² = . -15.85 [-26.71, -4.99]
Test of θi = θj: Q(0) = 0.00, p = .
Test of θ = 0: z = -2.86, p = 0.00
Midazolam+Propofol
Lee H[13]2019 75 106.36 8.47 111 107.18 7.83 -0.82 [-3.19, 1.55] 8.25
Heterogeneity: τ² = 0.00, I² = .%, H² = . -0.82 [-3.19, 1.55]
Test of θi = θj: Q(0) = -0.00, p = .
Test of θ = 0: z = -0.68, p = 0.50
Overall -0.27 [-2.16, 1.61]
Heterogeneity: τ² = 9.76, I² = 76.32%, H² = 4.22
Test of θi = θj: Q(14) = 47.95, p = 0.00
Test of θ = 0: z = -0.28, p = 0.78
Test of group differences: Qb(8) = 36.73, p = 0.00
-40
-20
0
20
Random-effects REML model

Figure 3. Meta-analysis of blood pressure.

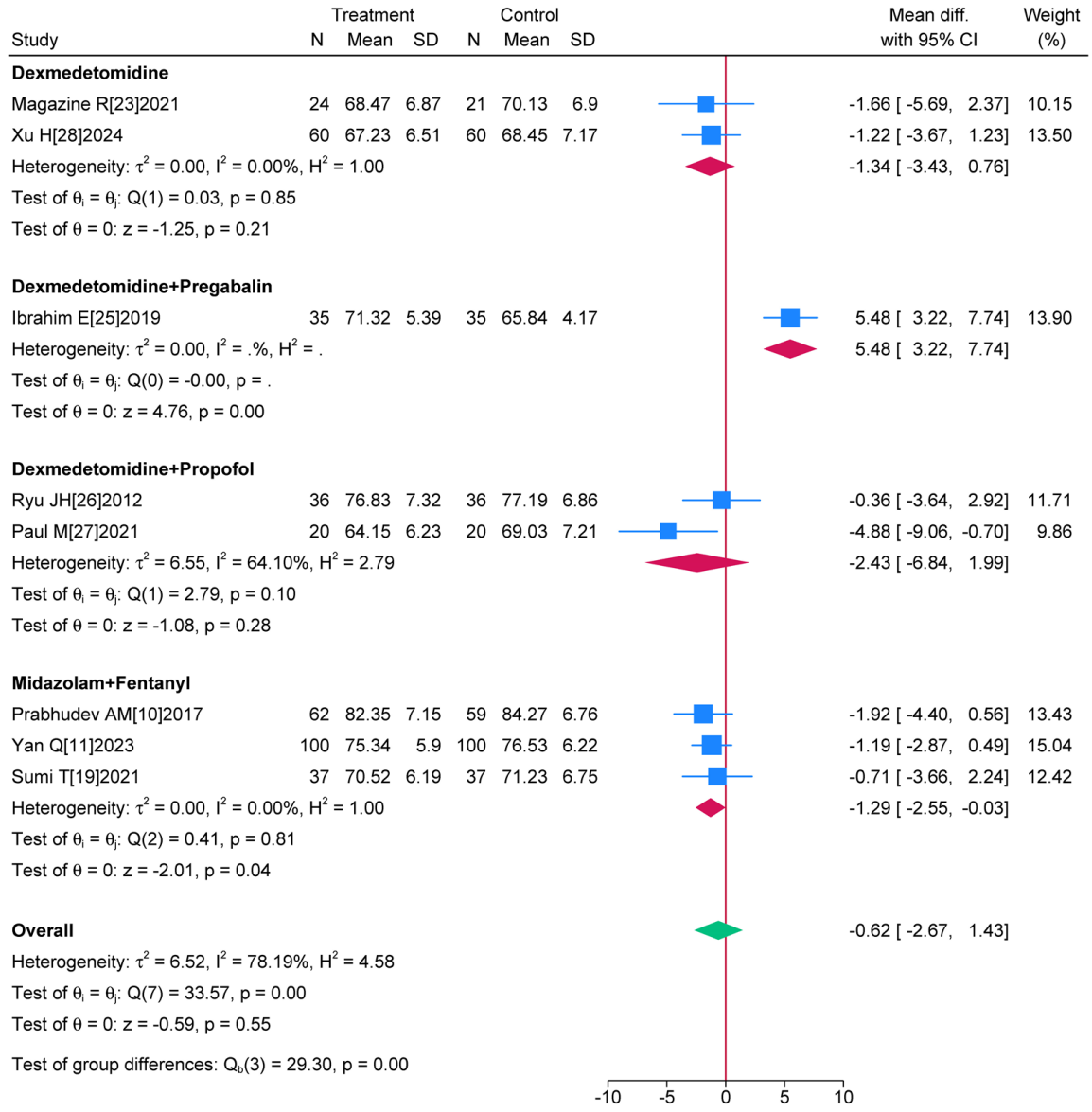

Figure 4. Meta-analysis of heart rate.

+ Fentanyl" and "Midazolam + Propofol" groups were significantly higher than in the control group ($P < 0.05$ for all). No statistically significant differences were found in the other 5 subgroups ($P > 0.05$ for all), as shown in **Figure 5**.

Meta-analysis of sedation satisfaction: Nine studies [10, 20-26, 28] reported sedation satisfaction, including 18 groups and 665 patients. Sedation satisfaction was used as a continuous variable for meta-analysis. Given the significant heterogeneity among the study results ($P \leq 0.1$, $I^2 > 50\%$), a random-effects model was applied. The results confirmed that the sedation satisfaction in the study group was significantly higher than in the control group (MD = 2.93, 95% CI: 1.16-4.70, Z = 3.25, $P < 0.01$). The sedation satisfaction was significantly higher in the "Dexmedetomidine + Midazolam + Fentanyl", "Dexmedetomidine + Pregabalin",

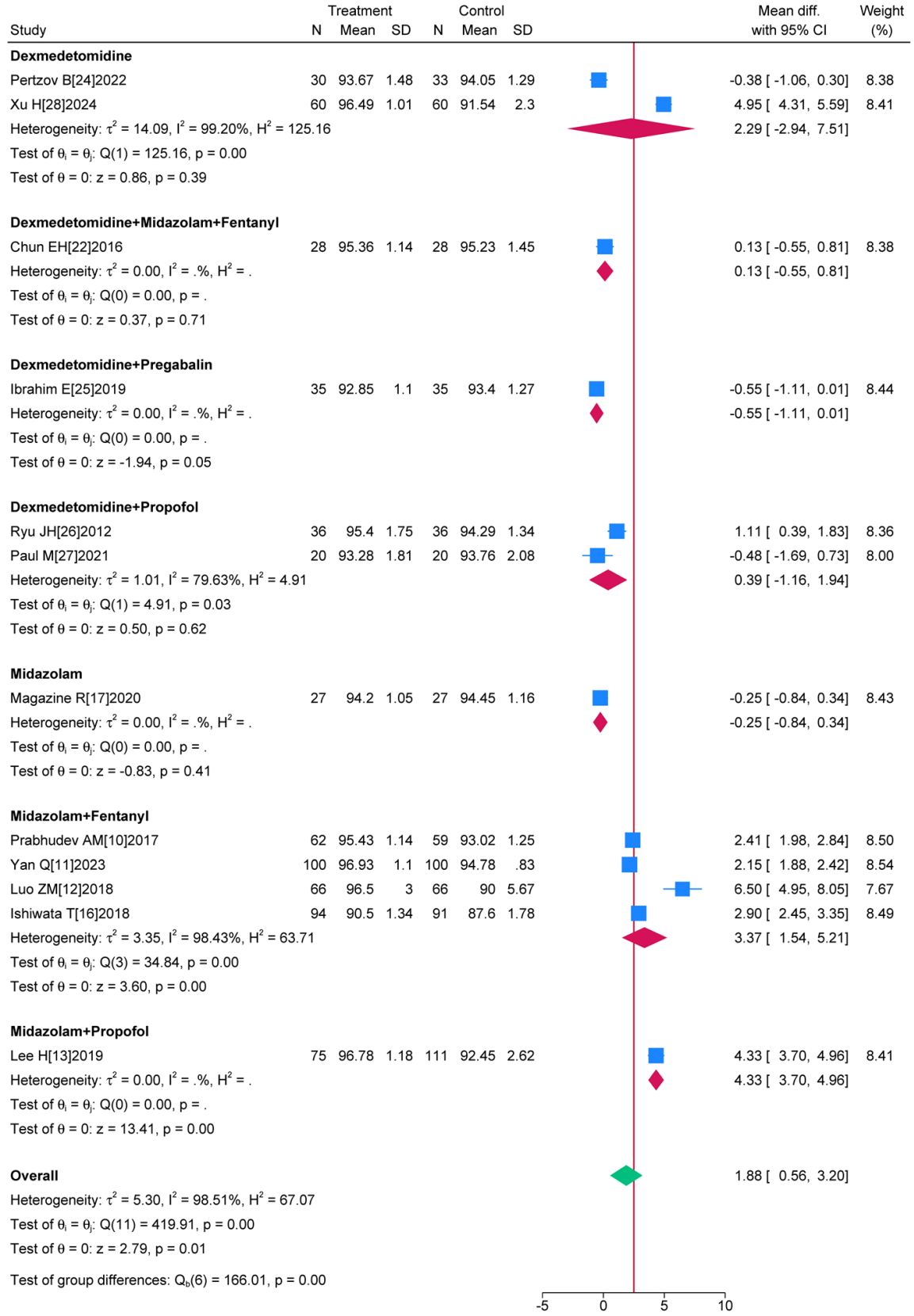

Figure 5. Meta-analysis of SaO2.

"Dexmedetomidine + Propofol + Fentanyl", and "Midazolam + Fentanyl" groups than in the control group (P < 0.01 for all). No statistically significant differences were found in the other 3 subgroups (P > 0.05 for all), as shown in **Figure 6**.

Meta-analysis of sedation scores: Ten studies [11, 15, 17, 18, 21-23, 25-27] reported sedation scores, comprising 20 groups and 957 patients. Sedation score was used as a continuous variable for meta-analysis. There was significant heterogeneity among the study results (P ≤ 0.1, I^2 > 50%), so a random-effects model was applied. The results confirmed that there was no statistically significant difference in sedation scores between the study and control groups (MD = 0.32, 95% CI: -0.02-0.67, Z = 1.82, P = 0.07). The sedation scores were significantly higher in the "Dexmedetomidine + Ketamine", "Dexmedetomidine + Midazolam + Fentanyl", "Dexmedetomidine + Pregabalin", and "Midazolam + Fentanyl" groups compared to the control group, while the sedation score in the "Midazolam + Pethidine" group was significantly lower than in the control group (P < 0.05 for all). No statistically significant differences were found in the remaining 3 subgroups (P > 0.05 for all), as shown in **Figure 7**.

Meta-analysis of recovery time: Eight studies [11, 13, 20-22, 26-28] reported awakening time, encompassing 16 groups and 792 patients. Awakening time was used as a continuous variable for meta-analysis. Due to significant heterogeneity among the study results (P ≤ 0.1, I^2 > 50%), a random-effects model was applied. The results confirmed that there was no statistically significant difference in awakening time between the study and control groups (MD = -2.70, 95% CI: -5.50-0.09, Z = -1.89, P = 0.06). The awakening time was significantly shorter in the "Dexmedetomidine", "Dexmedetomidine + Propofol + Fentanyl", "Midazolam + Fentanyl", and "Midazolam + Propofol" groups than in the control group (P < 0.05 for all). No statistically significant differences were found in the other 3 subgroups (P > 0.05 for all), as shown in **Figure 8**.

Meta-analysis of adverse events: Fourteen studies [11, 13-16, 18-24, 26, 28] reported adverse events, involving 28 groups and 1,922 patients. Adverse events were treated as dichotomous variables for meta-analysis. Significant heterogeneity was observed among the study results (P ≤ 0.1, I^2 > 50%), so a random-effects model was employed. The results showed no statistically significant difference in the incidence of adverse events between the study and control groups (OR = -0.10, 95% CI: -0.49 to 0.29, Z = -0.49, P = 0.62). Subgroup analysis revealed that the incidence of adverse events was significantly higher in the "Midazolam + Dexmedetomidine" group and significantly lower in the "Midazolam + Fentanyl" group compared to the control group (P < 0.05 for both). No statistically significant difference were observed in the remaining 8 subgroups (P > 0.05 for all), as shown in **Figure 9**.

Meta-analysis of VAS: Six studies [14, 15, 17, 19, 22, 23] reported VAS scores, including 12 groups and 758 patients. VAS was used as a continuous variable for meta-analysis. Given the significant heterogeneity among the study results (P ≤ 0.1, I^2 > 50%), a random-effects model was applied. The results confirmed no statistically significant difference in VAS scores between the study and control groups (MD = -0.46, 95% CI: -0.83-0.08, Z = -2.39, P = 0.02). Subgroup analysis showed that VAS scores were significantly lower in the "Dexmedetomidine", "Midazolam + Fentanyl", and "Midazolam + Pethidine" groups than in the control group (P < 0.05 for all). No statistically significant differences were found in the other 3 subgroups (P > 0.05 for all), as shown in **Figure 10**.

Meta-regression analysis

Meta-regression analysis was conducted on 19 studies. The sources of heterogeneity were primarily related to study type and methodology (P < 0.05), as shown in **Table 2**.

Publication bias analysis

In the funnel plots for systolic blood pressure and adverse events, the combined effect sizes showed an asymmetric distribution, with several studies falling outside the 95% confidence interval, indicating the presence of publication bias. This may be related to factors such as the observation period for the indicators, the types of drugs used, and their administration methods, as shown in **Figures 11** and **12**.

Discussion

With the widespread use of interventional procedures in gastroenterology and respiratory

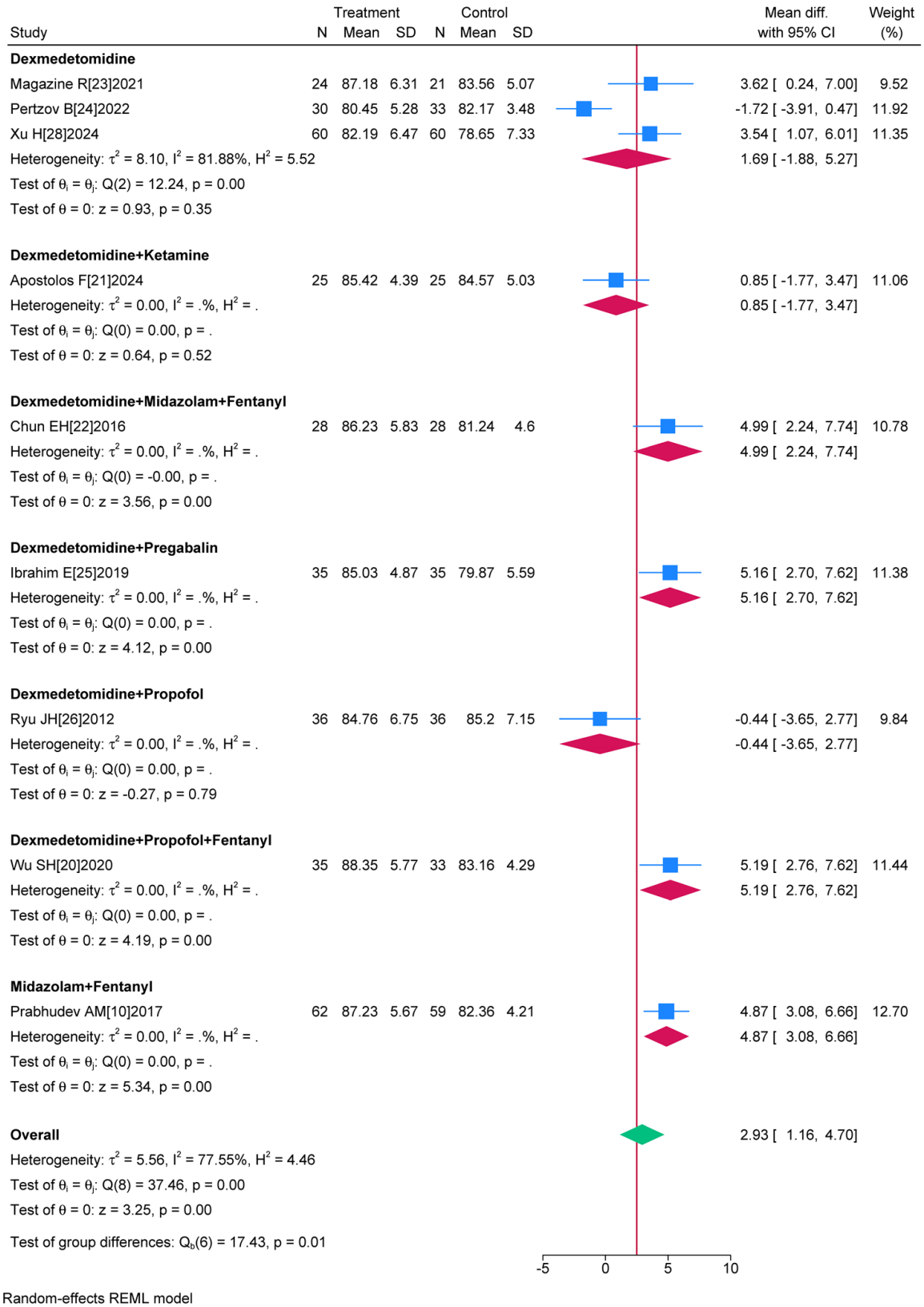

Figure 6. Meta-analysis of sedation satisfaction.

Meta analysis of sedative effects in patients undergoing bronchoscopy examination

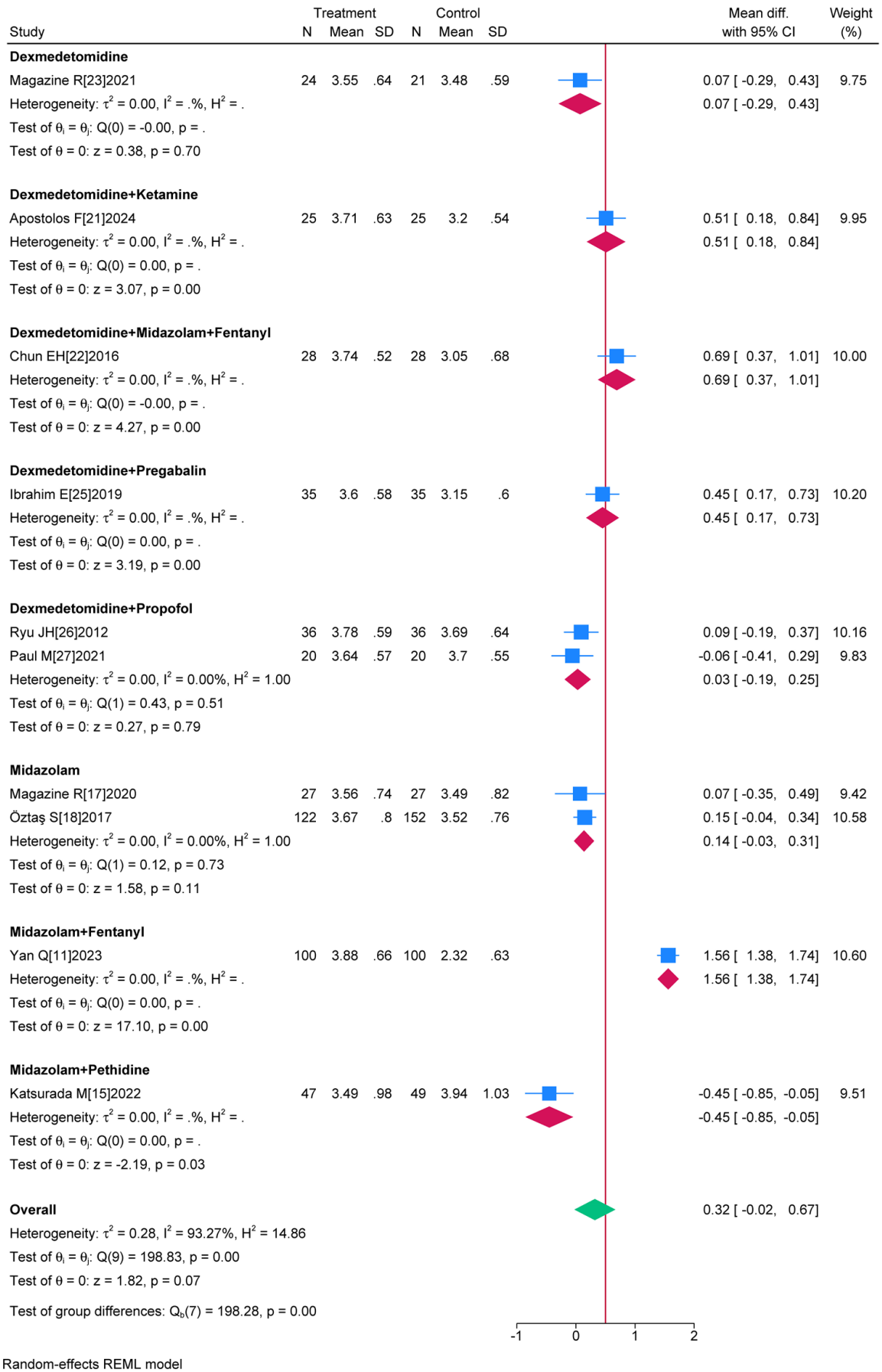

Figure 7. Meta-analysis of sedation scores.

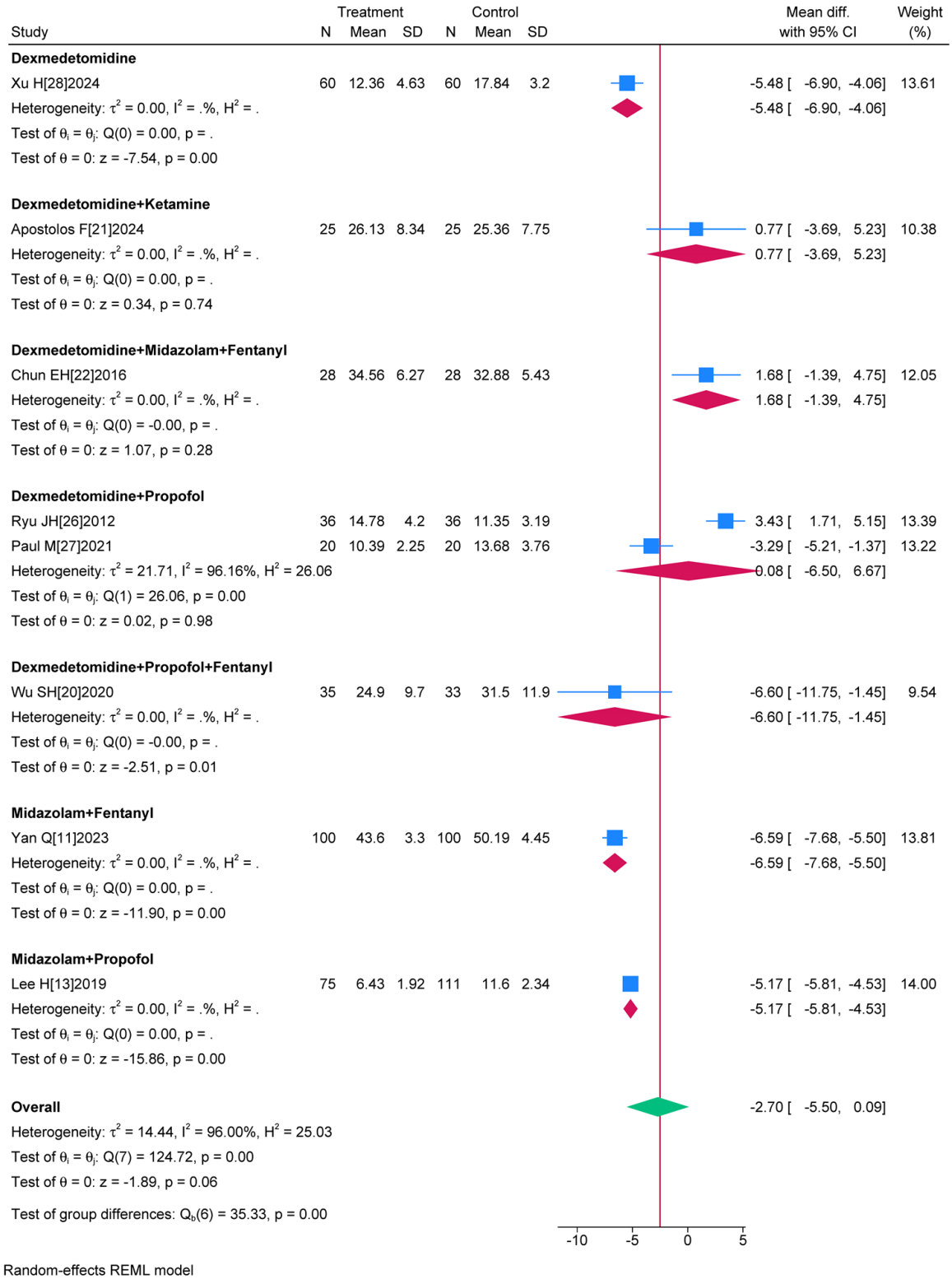

Figure 8. Meta-analysis of awakening time.

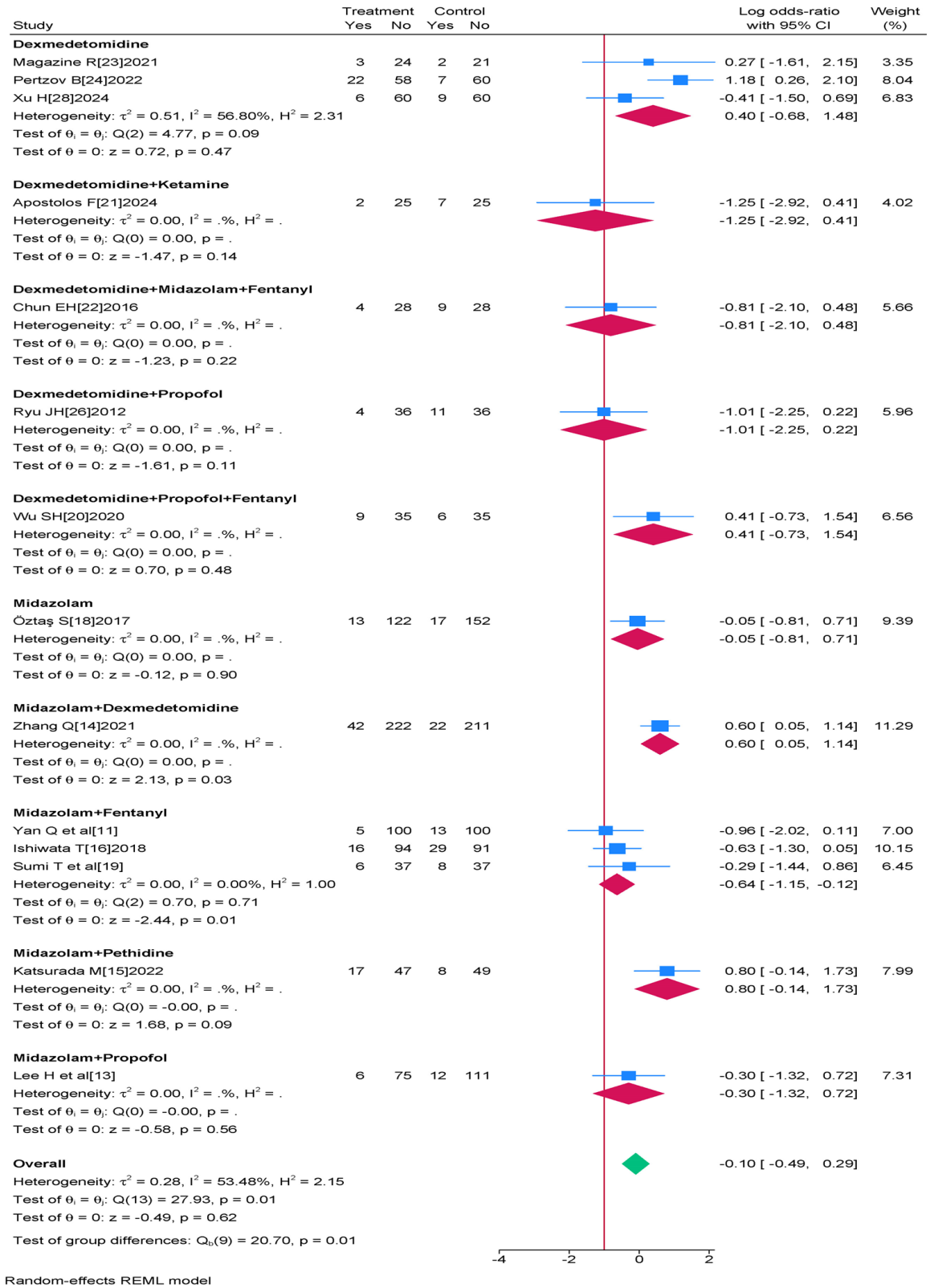

Figure 9. Meta-analysis of adverse events.

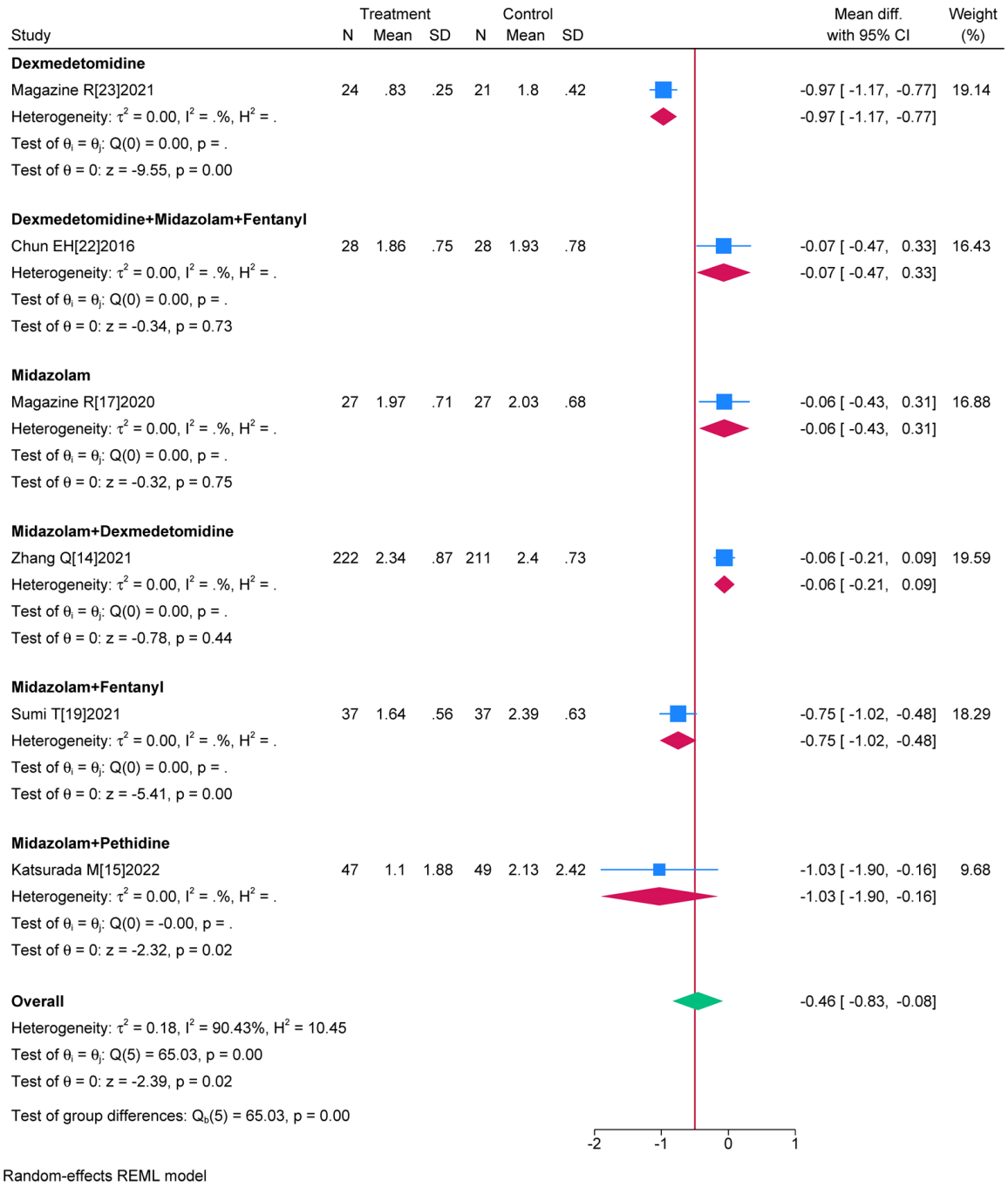

Figure 10. Meta-analysis of VAS.

Table 2. Meta-regression analysis

variable	*β*	*SE*	*P*	DOR	95% CI
year	-0.121	0.420	0.772	-0.29	-0.944-0.701
n	0.084	0.137	0.542	0.61	-0.185-0.352
type	4.994	2.479	0.044	2.01	0.136-9.853
measure	5.715	2.851	0.032	3.14	0.553-11.783
Observation index	-0.123	0.376	0.641	-0.31	-0.978-0.654

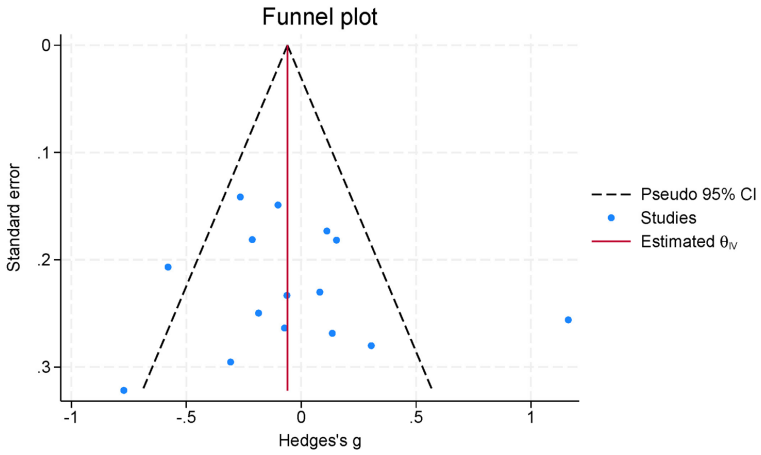

Figure 11. Funnel plot of systolic blood pressure.

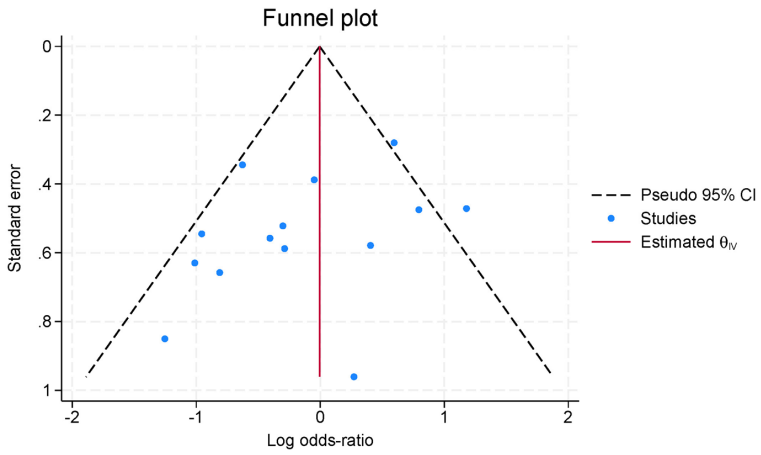

Figure 12. Funnel plot of adverse events.

medicine, the clinical demands for the sedative effects and safety of anesthetic drugs have been continuously increasing [29]. Bronchoscopy not only allows for direct observation of lesions in the lower respiratory tract (such as lobes, segments, and subsegments of the bronchi) but is also one of the commonly used minimally invasive treatment methods [30]. However, improper use of anesthetic drugs has always been a major factor affecting the sedative effect of bronchoscopy, and the resulting adverse events have significantly impacted the accuracy of the procedure and the development of sedation techniques. According to the meta-analysis of continuous variables for blood pressure, there were no significant differences in systolic blood pressure and heart rate between the two groups. This suggests that both midazolam and dexmedetomidine effectively stabilize the patient's hemodynamics, adequately meeting the sedation needs of different patients. For example, in the "Dexmedetomidine + Pregabalin" subgroup, systolic blood pressure was significantly higher than that of the control group, which is because "Dexmedetomidine + Pregabalin" can modulate sympathetic nervous function, relieve anxiety and depression, and prevent hypotension [31]. In contrast, the "Midazolam + Pethidine" subgroup showed significantly lower systolic blood pressure compared to the control group, which may be due to its ability to prevent hypertension and improve the patient's comfort during bronchoscopy. Additionally, international studies [32, 33] also suggest that the combination of midazolam and opioids (such as fentanyl, pethidine, etc.) can significantly improve patients' tolerance to bronchoscopy, thus improving the procedural conditions for the physician and ensuring the effectiveness and rapid onset of sedation.

However, study 15 compared the maximum blood pressure after anesthesia, while other studies evaluated the average blood pressure during the entire interventional or surgical procedure. This discrepancy in observation periods leads to variations in the results. Therefore, in clinical practice, it is essential to compare blood pressure or blood pressure variability within the same period for each patient to more accurately assess the sedation effects and prevent safety risks. In this study, a total of 12 studies reported SaO2, and the meta-analysis confirmed that the SaO2 levels in the study group were significantly higher than those in the control group. Notably, the subgroups "Midazolam + Fentanyl" and "Midazolam + Propofol" showed the most significant advantages. This indicates that midazolam-based combination regimens can effectively maintain blood oxygen homeostasis in patients undergoing bronchoscopy. However,

conflicting findings have been reported. One study [34] noted that while midazolam combined with fentanyl provided satisfactory sedation, about half of the patients experienced respiratory depression lasting more than 30 seconds, accompanied by a decline in blood oxygen saturation. This is related to the mechanism of action of midazolam. Midazolam is a short-acting sedative with minimal side effects, and its onset time is closely related to dose and patient age [35]. Especially for patients with low behavioral scores, its sedative effect tends to be weaker compared to those with higher behavioral scores in the same population [36]. Studies by Kim SH [37] and Wu Q [38] even suggest that for elderly patients undergoing bronchoscopy, midazolam offers inferior sedative effect and safety compared to remimazolam. Therefore, the application range of midazolam is still relatively limited, and for patients with poor compliance or advanced age, sedative regimens should be selected with caution.

In the studies reporting sedation satisfaction and sedation scores, the subgroups "Dexmedetomidine + Midazolam + Fentanyl" and "Dexmedetomidine + Pregabalin" showed significantly higher sedation satisfaction and sedation scores compared to the control group. This is because dexmedetomidine rapidly suppresses central nervous system activity, reduces the excitability of the sympathetic nervous system, and decreases the transmission or release of pain signals, inflammatory mediators, and other neurotransmitters, thereby reducing neural sensitivity and optimizing the sedative effect [39]. A systematic literature review by Barends CR et al. [40] indicated that compared to midazolam, dexmedetomidine provides greater intraoperative comfort for patients, thereby improving physician satisfaction with the procedure. On the other hand, dexmedetomidine can also provides an appropriate depth of anesthesia and ideal conditions for rigid bronchoscopy in airway foreign body removal, thus avoiding respiratory depression or hemodynamic instability caused by improper sedation [41]. Moreover, a study by Zhang X et al. [42] showed that for patients requiring mechanical ventilation after bronchial foreign body removal, the extubation success rate was significantly higher with dexmedetomidine than with remifentanil-propofol. A single-center randomized study [43] confirmed that compared to remifentanil, dexmedetomidine provides more stable hemodynamics during catheter ablation, with a lower incidence of safety events such as respiratory depression and hypotension.

It is important to note that when the dosage of dexmedetomidine is too high, it can simultaneously act on both α1- and α2-adrenergic receptors, leading to excessive vasodilation and a higher incidence of adverse events such as hypotension, bradycardia, and arrhythmias [44]. This aligns with the findings of a meta-analysis by Guo Q et al. [45]. In addition, study 20 compared the sedative effects of dexmedetomidine and midazolam, each combined with propofol-fentanyl, and found that although the overall incidence of adverse events between the two groups showed no statistical difference, the incidence of bradycardia in the dexmedetomidine group was significantly higher than in the midazolam group. Study 26 also pointed out that because dexmedetomidine has a relatively short duration of action, repeated dosing or dose escalation is often required, which may prolong the recovery or awakening time. This suggests that compared to midazolam, dexmedetomidine sedation during bronchoscopy is more likely to cause bradycardia [46, 47]. Therefore, it is speculated that for patients with impaired cardiac function or during prologned procedures, the total dosage of dexmedetomidine should be minimized while ensuring effective sedation. Furthermore, aside from sedation during bronchoscopy, the post-procedure period is also a high-risk phase for adverse events. Thus, reducing awakening time and minimizing agitation during recovery could potentially reduce the occurrence of adverse events to some extent.

Conclusion

In summary, both midazolam and dexmedetomidine provide good sedative effects during bronchoscopy, with each having its own advantages and limitations. The choice of the appropriate sedative drug and regimen should be made flexibly based on the clinical circumstances. Moreover, the sedative effect during bronchoscopy is often influenced by factors such as the type of instruments used, the patient's age, mental state, weight, and other variables, but this article has not analyzed these aspects, and the research depth remains

insufficient. In future clinical practice, more scientific reports and objective indicators should be referenced to further expand the research depth and scope.

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Disclosure of conflict of interest

None.

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References

[1] Panda CK, R Karim HM and Neema PK. Bronchoscopy examination of a patient with tracheobronchial injury having intractable cough: role of sevoflurane sedation and paraoxygenation. Ann Card Anaesth 2021; 24: 121-123.

[2] Uluç K, Öngel EA, İlkaya NK, Devran Ö and Özçelik HK. Indication, complication, and prognosis of fiberoptic bronchoscopy guided percutaneous dilatation tracheostomy opening in respiratory intensive care unit: a retrospective study. Eur Rev Med Pharmacol Sci 2023; 27: 11771-11779.

[3] Goussard P, Eber E, Venkatakrishna S, Frigati L, Greybe L, Janson J, Schubert P and Andronikou S. Interventional bronchoscopy in pediatric pulmonary tuberculosis. Expert Rev Respir Med 2023; 17: 1159-1175.

[4] Goussard P, Andronikou S, Fourie B, Janson JT and Schubert PT. Tuberculous bronchial stenosis: diagnosis and role of interventional bronchoscopy. Pediatr Pulmonol 2022; 57: 2445-2454.

[5] Pastis NJ, Yarmus LB, Schippers F, Ostroff R, Chen A, Akulian J, Wahidi M, Shojaee S, Tanner NT, Callahan SP, Feldman G, Lorch DG Jr, Ndukwu I, Pritchett MA and Silvestri GA; PAION Investigators. Safety and efficacy of remimazolam compared with placebo and midazolam for moderate sedation during bronchoscopy. Chest 2019; 155: 137-146.

[6] Yuan Y, Zhang J, Yue HL, Wang J, Pei YH, Qiu XJ, Wang YL and Wang T. A preliminary study of different methods of anesthesia for painless bronchoscopy. Zhonghua Jie He He Hu Xi Za Zhi 2019; 42: 106-113.

[7] Abdelmalak BB and Doyle DJ. Updates and controversies in anesthesia for advanced interventional pulmonology procedures. Curr Opin Anaesthesiol 2021; 34: 455-463.

[8] Lima A, Kheir F, Majid A and Pawlowski J. Anesthesia for interventional pulmonology procedures: a review of advanced diagnostic and therapeutic bronchoscopy. Can J Anaesth 2018; 65: 822-836.

[9] Neal JM, Neal EJ and Weinberg GL. American Society of Regional Anesthesia and pain medicine local anesthetic systemic toxicity checklist: 2020 version. Reg Anesth Pain Med 2021; 46: 81-82.

[10] Prabhudev AM, Chogtu B and Magazine R. Comparison of midazolam with fentanyl-midazolam combination during flexible bronchoscopy: a randomized, double-blind, placebo-controlled study. Indian J Pharmacol 2017; 49: 304-311.

[11] Yan Q, Sheng B, Huang X, Lin K, Lin J and Ye X. Effect of different doses of midazolam combined with fentanyl during painless bronchoscopy in adults. Am J Transl Res 2023; 15: 563-572.

[12] Luo ZM, Xiao H and Yuan J. Effectiveness and safety in bronchoscopy under anesthesia with fentanyl combined with midazolam. Zhonghua Jie He He Hu Xi Za Zhi 2018; 41: 47-50.

[13] Lee H, Choe YH and Park S. Analgosedation during flexible fiberoptic bronchoscopy: comparing the clinical effectiveness and safety of remifentanil versus midazolam/propofol. BMC Pulm Med 2019; 19: 240.

[14] Zhang Q, Zhou J, He Q, Guan S, Qiu H, Xu X, Xu Q, Dai P, Dong D, Wang X and Zhang S. Dexmedetomidine combined with midazolam infusion guided by bispectral index during bronchoscopy. Clin Respir J 2021; 15: 929-936.

[15] Katsurada M, Tachihara M, Katsurada N, Takata N, Sato H, Mimura C, Yoshioka J, Furukawa K, Yumura M, Otoshi T, Yasuda Y, Kiriu T, Hazama D, Nagano T, Yamamoto M, Nishimura Y and Kobayashi K. Randomized single-blind comparative study of the midazolam/pethidine combination and midazolam alone during bronchoscopy. BMC Cancer 2022; 22: 539.

[16] Ishiwata T, Tsushima K, Terada J, Fujie M, Abe M, Ikari J, Kawata N, Tada Y and Tatsumi K. Efficacy of end-tidal capnography monitoring during flexible bronchoscopy in nonintubated patients under sedation: a randomized controlled study. Respiration 2018; 96: 355-362.

[17] Magazine R, Venkatachala SK, Goneppanavar U, Surendra VU, Guddattu V and Chogtu B. Comparison of midazolam and low-dose dexmedetomidine in flexible bronchoscopy: a pro-

spective, randomized, double-blinded study. Indian J Pharmacol 2020; 52: 23-30.
[18] Öztaş S, Aka Aktürk Ü, Alpay LA, Meydan B, Ogün H, Taylan M, Yalçınsoy M, Çalışır HC, Görgüner AM and Ernam D. A comparison of propofol-midazolam and midazolam alone for sedation in endobronchial ultrasound-guided transbronchial needle aspiration: a retrospective cohort study. Clin Respir J 2017; 11: 935-941.
[19] Sumi T, Kamada K, Sawai T, Shijubou N, Yamada Y, Nakata H, Mori Y and Chiba H. Sedation with fentanyl and midazolam without oropharyngeal anesthesia compared with sedation with pethidine and midazolam with oropharyngeal anesthesia in ultrathin bronchoscopy for peripheral lung lesions. Respir Investig 2021; 59: 228-234.
[20] Wu SH, Lu DV, Hsu CD and Lu IC. The effectiveness of low-dose dexmedetomidine infusion in sedative flexible bronchoscopy: a retrospective analysis. Medicina (Kaunas) 2020; 56: 193.
[21] Apostolos F, Nikolaos Z, Charalampos M, Kyriakos K, Sotirios F and Gregorios V. Dexmedetomidine-ketamine combination versus fentanyl-midazolam for patient sedation during flexible bronchoscopy: a prospective, single-blind, randomized controlled trial. BMC Pulm Med 2024; 24: 301.
[22] Chun EH, Han MJ, Baik HJ, Park HS, Chung RK, Han JI, Lee HJ and Kim JH. Dexmedetomidine-ketamine versus Dexmedetomidine-midazolam-fentanyl for monitored anesthesia care during chemoport insertion: a prospective randomized study. BMC Anesthesiol 2016; 16: 49.
[23] Magazine R, Antony T, Chogtu B, Prabhudev AM, Surendra VU and Guddattu V. Clinical usefulness of intermediate-dose dexmedetomidine (0.75 μg/kg) in flexible bronchoscopy - A prospective, randomized, double-blinded study. Indian J Pharmacol 2021; 53: 440-447.
[24] Pertzov B, Krasulya B, Azem K, Shostak Y, Izhakian S, Rosengarten D, Kharchenko S and Kramer MR. Dexmedetomidine versus propofol sedation in flexible bronchoscopy: a randomized controlled trial. BMC Pulm Med 2022; 22: 87.
[25] Ibrahim E, Sultan W, Helal S, Abo-Elwafa H and Abdelaziz A. Pregabalin and dexmedetomidine conscious sedation for flexible bronchoscopy: a randomized double-blind controlled study. Minerva Anestesiol 2019; 85: 487-493.
[26] Ryu JH, Lee SW, Lee JH, Lee EH, Do SH and Kim CS. Randomized double-blind study of remifentanil and dexmedetomidine for flexible bronchoscopy. Br J Anaesth 2012; 108: 503-11.
[27] Paul M, Rastogi A, Chatterje A, Agarwal A, Mishra P and Khan A. Comparative evaluation of propofol and combination of propofol-dexmedetomidine in adjunct with topical airway anesthesia for rigid bronchoscopy: a randomized double-blinded prospective study. Ann Card Anaesth 2021; 24: 49-55.
[28] Xu H, Wang L, Zhu W, Ren C, Liu G and Liu Y. Comparison of the safety and efficacy of remimazolam besylate versus dexmedetomidine for patients undergoing fiberoptic bronchoscopy: a prospective, randomized controlled trial. Drug Des Devel Ther 2024; 18: 2317-2327.
[29] Ulutas H, Ucar M, Celik MR, Agar M and Gulcek I. Sedation with propofol and propofol-ketamine (Ketofol) in flexible bronchoscopy: a randomized, double-blind, prospective study. Niger J Clin Pract 2023; 26: 1817-1823.
[30] Gao S, Wang T, Cao L, Li L and Yang S. Clinical effects of remimazolam alone or in combination with dexmedetomidine in patients receiving bronchoscopy and influences on postoperative cognitive function: a randomized-controlled trial. Int J Clin Pharm 2023; 45: 137-145.
[31] Jain A, Sinha R, Pandey S and Sahu V. Comparative evaluation of dexmedetomidine and pregabalin as premedication agent to attenuate adverse hemodynamic and stress response in patients undergoing laparoscopic cholecystectomy. Anesth Essays Res 2019; 13: 608-614.
[32] Minami D and Takigawa N. Safe sedation during diagnostic and therapeutic flexible bronchoscopy in Japan: a review of the literature. Respir Investig 2023; 61: 52-57.
[33] Matsumoto T, Kaneko A, Fujiki T, Kusakabe Y, Nakayama E, Tanaka A, Yamamoto N, Aihara K, Yamaoka S and Mishima M. Impact of adding pethidine on disinhibition during bronchoscopy with midazolam: a propensity score matching analysis. Respir Investig 2023; 61: 409-417.
[34] Minami D, Murakami E, Shibata Y, Nakamura K, Kishino T, Takigawa N, Onishi K, Takigawa Y, Shimonishi A, Kudo K, Sato A, Sato K, Fujiwara K and Shibayama T. End-tidal capnographic monitoring during flexible bronchoscopy under fentanyl and midazolam sedation. Ann Palliat Med 2021; 10: 8665-8671.
[35] Monteiro ANB, Petri BSS, Furuya H, Milanelo L, Scognamillo MVR and Hayashi AM. Sedative effect of Ketamin-Midazolam administered at acupoint GV20 compared to intramuscular route in Blue-Fronted Amazon (Amazona aestiva): a pilot study. J Acupunct Meridian Stud 2022; 15: 314-321.

[36] Vasakova J, Duskova J, Lunackova J, Drapalova K, Zuzankova L, Starka L, Duskova M and Broukal Z. Midazolam and its effect on vital signs and behavior in children under conscious sedation in dentistry. Physiol Res 2020; 69 Suppl 2: S305-S314.

[37] Kim SH, Cho JY, Kim M, Chung JM, Yang J, Seong C, Kim EG, Seok JW, Shin YM, Lee KM, Choe KH, Han JH and Yang B. Safety and efficacy of remimazolam compared with midazolam during bronchoscopy: a single-center, randomized controlled study. Sci Rep 2023; 13: 20498.

[38] Wu Q, Xu R, Zhou X, Wang L, Sheng C, Ding M and Cao Y. Bolus administration of remimazolam was superior to midazolam for deep sedation in elderly patients undergoing diagnostic bronchoscopy: a randomized, double-blind, controlled trial. Medicine (Baltimore) 2024; 103: e37215.

[39] Magazine R, Elenjickal VM, Padukone AM, Bhat A and Chogtu B. Comparison between dexmedetomidine and midazolam-fentanyl combination in flexible bronchoscopy: a prospective, randomized, double-blinded study. J Bronchology Interv Pulmonol 2024; 31: e0985.

[40] Barends CR, Absalom A, van Minnen B, Vissink A and Visser A. Dexmedetomidine versus midazolam in procedural sedation. A systematic review of efficacy and safety. PLoS One 2017; 12: e0169525.

[41] Cai Y, Li W and Chen K. Efficacy and safety of spontaneous ventilation technique using dexmedetomidine for rigid bronchoscopic airway foreign body removal in children. Paediatr Anaesth 2013; 23: 1048-53.

[42] Zhang X, Wu J, Wang L and Li W. Dexmedetomidine facilitates extubation in children who require intubation and respiratory support after airway foreign body retrieval: a case-cohort analysis of 57 cases. J Anesth 2018; 32: 592-598.

[43] Hassan R, Mutalib AA, Shang CY, Sachdev NS, Rahman FA and Ling ESL. Randomized single-blinded study comparing sedation effectiveness and hemodynamic stability of remifentanil vs dexmedetomidine infusion for electrophysiology procedures in patients of National Heart Institute cathlab. J Interv Card Electrophysiol 2024; 67: 1735-1743.

[44] Grégoire C, De Kock M, Henrie J, Cren R, Lavand'homme P, Penaloza A and Verschuren F. Procedural sedation with dexmedetomidine in combination with ketamine in the emergency department. J Emerg Med 2022; 63: 283-289.

[45] Guo Q, An Q, Zhao L, Wu M, Wang Y and Guo Z. Safety and efficacy of dexmedetomidine for bronchoscopy: a systematic review and meta-analysis. J Clin Med 2023; 12: 1607.

[46] Goudra B, Sundararaman L, Chandar P and Green M. Anesthesia for bronchoscopy-an update. J Clin Med 2024; 13: 6471.

[47] Müller T, Thümmel K, Cornelissen CG, Krüger S and Dreher M. Analogosedation during flexible bronchoscopy using a combination of midazolam, propofol and fentanyl - A retrospective analysis. PLoS One 2017; 12: e0175394.