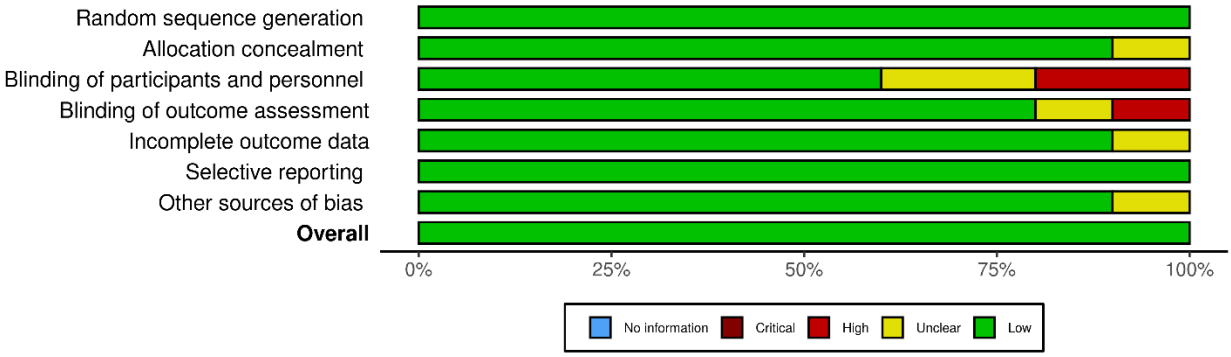
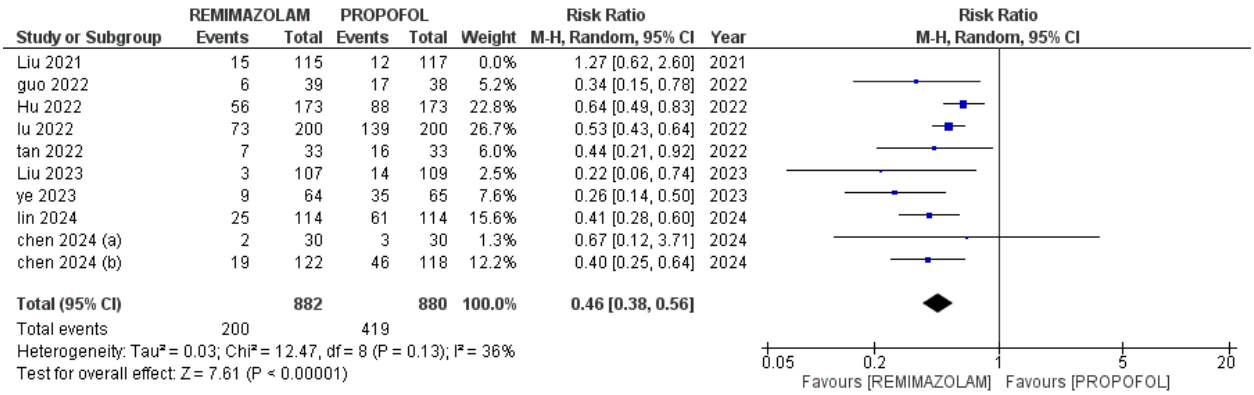
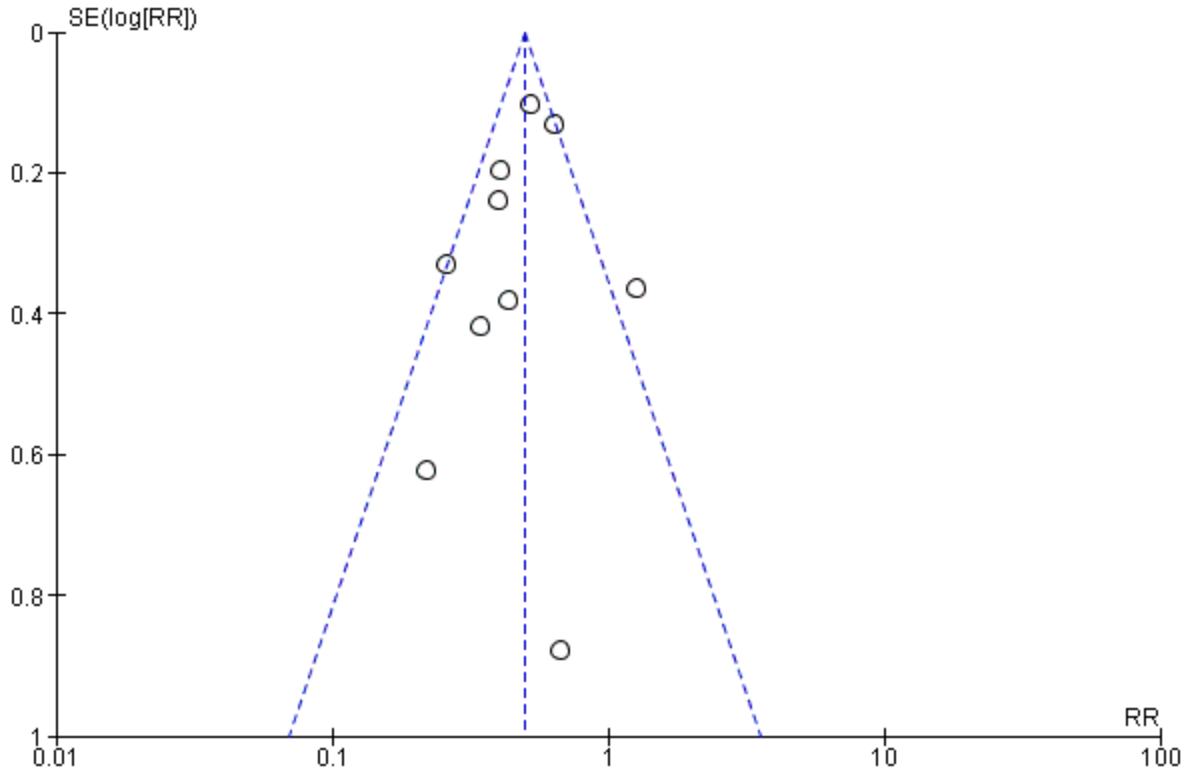
Supplementary Material



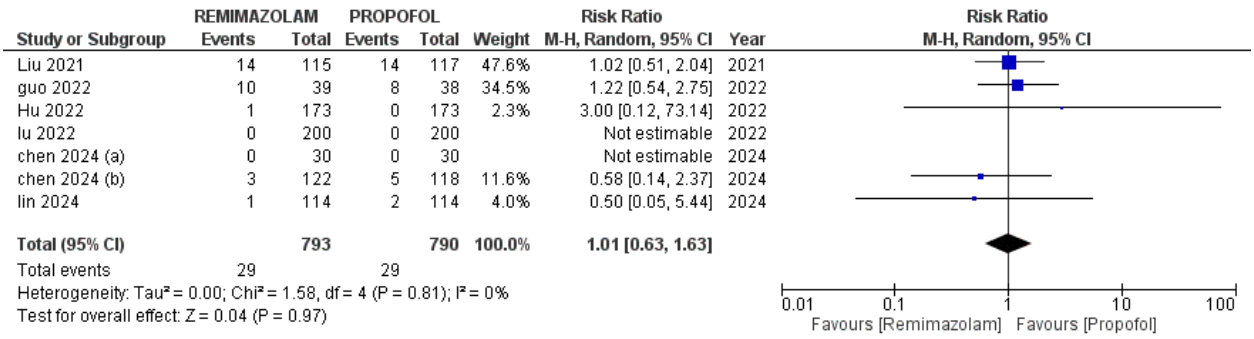
Supplementary Figure 1: Risk of bias graph.



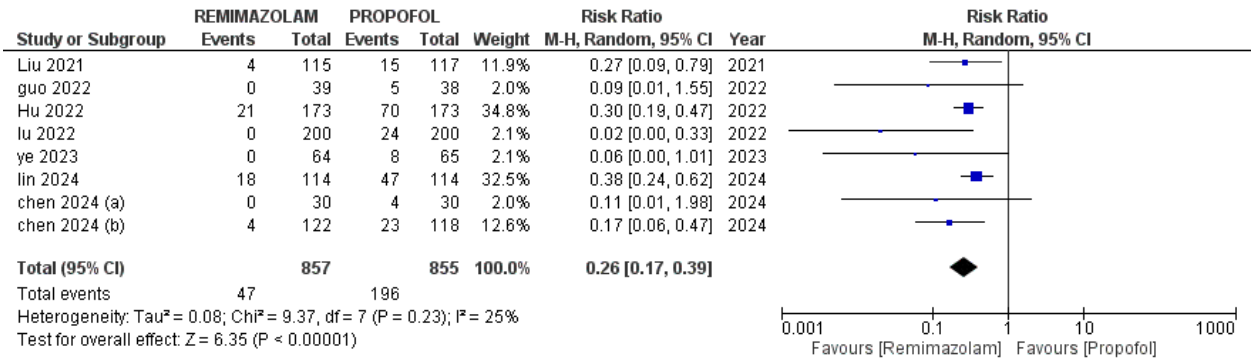
Supplementary Figure 2: Forest plot of leave-one-out analysis of incidence of hypotension in the treatment group.



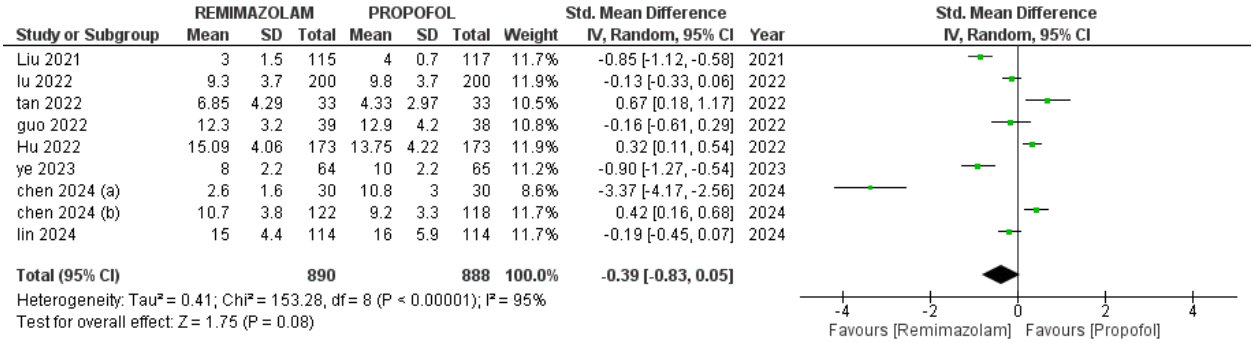
Supplementary Figure 3: Funnel plot of the outcome serious adverse effects in the treatment groups.



Supplementary Figure 4: Forest plot of incidence of nausea and vomiting in the treatment group.



Supplementary Figure 5: Forest plot of the incidence of pain at the injection site in the treatment group.



Supplementary Figure 6: Forest plot of the incidence of time to recovery in the treatment group.

Database	Search strategies
PubMed	(Remimazolam OR "Remimazolam tosylate" OR "Remimazolam tosilate" OR "Remimazolam besylate") AND (Propofol OR "Propofol"[MeSH] OR "2,6-diisopropylphenol" OR Diprivan) AND ("endoscopy, gastrointestinal"[MeSH] OR Endoscop* OR "Gastrointestinal endoscop*" OR "GI endoscop*" OR Colonoscop* OR "Colonic endoscop*" OR "lower GI endoscop*" OR "lower gastrointestinal endoscop*" OR gastroscop* OR "upper GI endoscop*" OR "upper gastrointestinal endoscop*")Filters: Randomized Controlled Trial
Google scholar	(Remimazolam OR "Remimazolam tosylate" OR "Remimazolam tosilate" OR "Remimazolam besylate") AND (Propofol OR "2,6-diisopropylphenol" OR Diprivan) AND (endoscopy OR "gastrointestinal endoscopy" OR "GI endoscopy" OR colonoscopy OR "colonic endoscopy" OR "lower GI endoscopy" OR "lower gastrointestinal endoscopy" OR gastroscopy OR "upper GI endoscopy" OR "upper gastrointestinal endoscopy")
Cochrane Central Register of Controlled Trials	(Remimazolam OR "Remimazolam tosylate" OR "Remimazolam tosilate" OR "Remimazolam besylate") AND (Propofol OR "2,6-diisopropylphenol" OR Diprivan) AND (endoscopy OR "gastrointestinal endoscopy" OR "GI endoscopy" OR colonoscopy OR "colonic endoscopy" OR "lower GI endoscopy" OR "lower gastrointestinal endoscopy" OR gastroscopy OR "upper GI endoscopy" OR "upper gastrointestinal endoscopy") in Title Abstract Keyword - in Trials (Word variations have been searched)

Supplementary Table 1: Search strategies of all databases.

DOI	REASON FOR EXCLUSION
DOI: 10.1111/den.14948	Primary outcome not reported
DOI: 10.2147/DDDT.S454314	Primary outcome not reported
DOI: 10.1111/jgh.15188	Age group is not according to PICO
DOI:10.1016/j.accpm.2024.101377	Population mismatch (hysteroscopic surgery instead of colonoscopy/endoscopy), age limit not mentioned and hypotension not a primary outcome.
DOI: 10.7555/JBR.37.20230110	Population mismatch (Transurethral surgery instead of colonoscopy/endoscopy)
DOI: 10.3389/fphar.2022.900723	Age group is not according to PICO
DOI: 10.21037/atm-22-5133	Age group is not according to PICO
DOI: 10.23736/S0375-9393.21.15517-8	Age group is not according to PICO
DOI: 10.1007/s11096-024-01774-2	Age group is not according to PICO
https://www.cochranelibrary.com/central/doi/10.1002/central/CN-02497472/full	Results of trial not posted
https://www.cochranelibrary.com/central/doi/10.1002/central/CN-02405733/full	Results of trial not posted
DOI: 10.1186/s13063-022-06935-0	Study protocol
https://www.cochranelibrary.com/central/doi/10.1002/central/CN-02797906/full	Results of trial not posted
https://clinicaltrials.gov/study/NCT06169995	Single arm study, also result of trial not posted

Supplementary Table 2: Reasons for exclusion of studies

	Cochrane Risk-of-Bias Tool		
	Bias	Risk of bias	Author judgement
Liu 2023	Random sequence generation (selection bias)	Low Risk	Quote: After recruitment, participants were randomly allocated in a 1:1 ratio to receive either remimazolam tosilate or propofol using a random number table.

	Allocation concealment (selection bias)	Low risk	Quote: The study used a random number table for randomization. Although allocation concealment isn't explicitly stated, the method suggests a low risk of selection bias.
	Blinding of participants and personnel (performance bias)	Unclear Risk	Quote: Participants were blinded, but the anesthetists and data recorders were not. As their influence on sedation or data recording is possible but not clearly addressed, the risk of performance bias is unclear.
	Blinding of outcome assessment (detection bias)	High Risk	Quote: Outcomes were assessed by unblinded personnel, which could introduce detection bias, especially in subjective measures like adverse events, despite some outcomes being objective.
	Incomplete outcome data (attrition bias)	Low Risk	Quote: Although 19 patients were excluded after randomization, the study clearly reported the reasons (e.g., failure of sedation induction, excessive exam time) and retained a balanced final sample in both groups (107 vs. 109). The attrition was minimal and unlikely to bias the results.
	Selective reporting (reporting bias)	Unclear risk	The study does not provide access to a trial protocol or registration, so it is unclear whether all planned outcomes were reported. Without this, we cannot assess if any important outcomes were selectively omitted or modified. Therefore, the risk of reporting bias is unclear.
	Other bias	Low Risk	No specific information suggesting the presence of other biases such as selection, detection, or confounding bias.
Chen 2024 (a)	Random sequence generation (selection bias)	Low Risk	Quote: Participants were randomly assigned using a computer-generated

			algorithm, indicating a proper method of random sequence generation.
	Allocation concealment (selection bias)	Low Risk	Quote: The study used a blinding protocol, ensuring patients, anesthetist assistants, and gastroenterologists were unaware of group assignments, minimizing selection bias. Anesthetist assistants recorded vital signs from an adjacent room, maintaining blinding integrity.
	Blinding of participants and personnel (performance bias)	Low Risk	Quote: Blinding was done for patients, anesthetist assistants, and gastroenterologists. Assistants monitored from another room, reducing performance bias.
	Blinding of outcome assessment (detection bias)	Low Risk	Quote: The blinding protocol was extended to participants and personnel, and outcome assessors were likely blinded to the group assignments.
	Incomplete outcome data (attrition bias)	Low Risk	Quote: No mention of missing data or participant dropouts, so attrition bias is unlikely.
	Selective reporting (reporting bias)	Low Risk	Quote: All primary and secondary outcomes, including recovery times, were reported.
	Other bias	Low Risk	Quote: No other bias was identified from the provided information.
Chen 2024 (b)	Random sequence generation (selection bias)	Low Risk	Quote: The study used a random number table for participant assignment, a reliable method for sequence generation, ensuring randomization was unbiased.
	Allocation concealment (selection bias)	Low Risk	Quote: The study employed a double-blind design, which prevents any bias in the allocation process, as neither participants nor researchers knew the treatment group assignment until after enrollment.
	Blinding of participants and personnel (performance bias)	Low Risk	Quote: The study used a double-blind design for both participants and researchers. This prevents bias from both the patients and the researchers, ensuring that neither group is aware of which

			treatment the participant is receiving during the study.
	Blinding of outcome assessment (detection bias)	Low Risk	Quote: The study clearly mentions that it was a double-blind trial, which means both participants and outcome assessors were blinded to the group allocation. This reduces the potential for detection bias, as outcome assessments would not be influenced by the knowledge of which treatment the participant received.
	Incomplete outcome data (attrition bias)	Low Risk	Quote: “No missing outcome data.”
	Selective reporting (reporting bias)	Low Risk	Quote: The study protocol outlines all primary and secondary outcomes clearly, and no evidence suggests selective reporting.
	Other bias	Low Risk	Quote: The study appears well-structured with appropriate inclusion/exclusion criteria, ethical approval, and clear statistical analysis methods. No additional biases were evident
Lin 2024	Random sequence generation (selection bias)	Low Risk	Quote: The study used permuted block randomization with randomly selected block sizes of 4 or 6, generated by an independent statistician using R version 4.0.5.
	Allocation concealment (selection bias)	Low Risk	Quote: Allocation concealment was ensured by using sequentially numbered, opaque, sealed envelopes and a blinded pharmacist who prepared the study drugs.
	Blinding of participants and personnel (performance bias)	Low Risk	Quote: The study was double-blind, meaning both participants and the personnel administering treatments were blinded to the group assignments.
	Blinding of outcome assessment (detection bias)	Low Risk	Quote: The study blinded outcome assessors, as the research assistant collected data in person and via telephone without knowing the participant’s group allocation
	Incomplete outcome data (attrition bias)	Low Risk	Quote: The study had a low dropout rate with 86% and 88% of participants completing the protocol in the remimazolam and propofol groups,

			respectively. Multiple imputations addressed missing data.
	Selective reporting (reporting bias)	Low Risk	All primary and secondary outcomes were clearly defined in the study protocol and reported as planned, with no evidence of selective reporting.
	Other bias	Low Risk	The study adhered to ethical standards, including informed consent and ethics committee approval. Statistical analysis was clear and appropriate. No other biases were evident.
Ye 2023	Random sequence generation (selection bias)	Low Risk	Quote: The study used a random number table to allocate patients to the remimazolam (R) and propofol (P) groups.
	Allocation concealment (selection bias)	Unclear Risk	Quote: The allocation concealment method was not explicitly mentioned in the study. Although a random number table was used, the description doesn't clarify how the allocation was concealed during the process of assigning participants to groups, which is crucial to prevent selection bias.).
	Blinding of participants and personnel (performance bias)	High Risk	Quote: Anesthetists who performed sedation were unblinded, which could influence the results, especially if any subjective outcomes or treatment-related decisions were involved. However, the blinding of patients, gastroscopists, and outcome recorders reduces bias in assessing the efficacy and safety outcomes.
	Blinding of outcome assessment (detection bias)	Low Risk	Quote: Outcome recorders were explicitly blinded to the group allocation, which minimizes the likelihood of detection bias.
	Incomplete outcome data (attrition bias)	Low Risk	Quote: There is no mention of missing data or a significant number of dropouts. The study clearly states that recruitment stopped after meeting the sample size requirement, suggesting complete data collection.

	Selective reporting (reporting bias)	Low Risk	The study was registered prospectively on the Chinese Clinical Trial Registry (ChiCTR2100046476), and the primary and secondary outcomes reported appear consistent with the study aims (ED95, safety, and efficacy).
	Other bias	Low Risk	The study appears to be free of other sources of bias.
Tan 2022	Random sequence generation (selection bias)	Low Risk	Quote: The study used a computer-generated randomization process, which is considered truly random.
	Allocation concealment (selection bias)	Low Risk	Allocation was concealed using sealed, opaque envelopes, reducing selection bias.
	Blinding of participants and personnel (performance bias)	Low Risk	Quote: Double-blinding was implemented; both participants and personnel were unaware of group allocation, minimizing performance bias.
	Blinding of outcome assessment (detection bias)	Low Risk	Quote: Outcome assessors were blinded, ensuring that measurement of outcomes was not influenced by treatment knowledge.
	Incomplete outcome data (attrition bias)	Low Risk	Quote: Only 3 out of 200 patients were excluded before receiving the intervention, and no missing outcome data impacted the analysis.
	Selective reporting (reporting bias)	Low Risk	The study was registered prospectively with clearly defined outcomes, and all pre-specified outcomes were reported.
	Other bias	Low Risk	No other sources of bias were identified; the study protocol, conduct, and analysis were appropriate and transparent.
Lu 2022	Random sequence generation (selection bias)	Low Risk	Quote: The use of a block design with a centralized randomization service indicates an appropriate and unbiased method of sequence generation.
	Allocation concealment (selection bias)	Low Risk	Quote The use of opaque bags and a centralized randomization service suggests that allocation was concealed from both participants and outcome assessors, reducing the risk of selection bias.

			."
	Blinding of participants and personnel (performance bias)	Low Risk	Quote: Blinding of both participants and outcome assessors was implemented using opaque bags, minimizing the likelihood of performance bias.
	Blinding of outcome assessment (detection bias)	Low Risk	Quote: All outcomes were assessed by an anesthesiologist not otherwise involved in the study.
	Incomplete outcome data (attrition bias)	Low Risk	Quote: Patient flow is clearly reported, and there's no mention of differential dropout or missing data that would impact outcomes. The dropout rate appears low and is accounted for in the sample size calculation.
	Selective reporting (reporting bias)	Low Risk	Outcomes described in the methods are all reported in the results. Trial registration further supports transparency and reduces risk of selective outcome reporting.
	Other bias	Low Risk	There is no apparent source of other bias. Ethics approval, trial registration, and appropriate analysis methods suggest a well-conducted trial.
Guo 2022	Random sequence generation (selection bias)	Low Risk	Quote: The study used a computer-generated random number table to assign participants, which ensures an unpredictable sequence and minimizes selection bias
	Allocation concealment (selection bias)	Low Risk	Allocation was concealed using sealed opaque envelopes, which prevented foreknowledge of group assignment by recruiters
	Blinding of participants and personnel (performance bias)	Unclear Risk	Quote: The trial was single-blinded only participants were blinded, while anesthesiologists were not, which may introduce performance bias, especially in subjective aspects of care.

	Blinding of outcome assessment (detection bias)	Low Risk	Quote: Outcome assessors and statisticians were blinded to group allocation, reducing the risk of bias in outcome measurement and analysis.
	Incomplete outcome data (attrition bias)	Low Risk	Quote: Very few participants were excluded (5 total), with reasons provided and similar distribution across groups, minimizing risk of attrition bias.
	Selective reporting (reporting bias)	Low Risk	All pre-specified primary and secondary outcomes were reported, as registered in the trial protocol, with no evidence of selective omission
	Other bias	Low Risk	No other sources of bias such as baseline imbalances, early stopping, or sponsorship bias were identified in the study.
Hu 2022	Random sequence generation (selection bias)	Low Risk	Quote: The use of SAS software for randomization suggests a proper method for generating random sequences, minimizing the risk of selection bias related to how participants are assigned to groups.
	Allocation concealment (selection bias)	Low Risk	Quote: Use of sealed opaque envelopes indicates proper allocation concealment, reducing risk of selection bias.
	Blinding of participants and personnel (performance bias)	High Risk	Quote: Since the personnel administering drugs knew the allocation, performance bias could be introduced through different care or co-interventions.
	Blinding of outcome assessment (detection bias)	Unclear Risk	Quote: The study is single-blind, and there is no explicit mention of whether outcome assessors were blinded. This raises the possibility of detection bias, especially for subjective outcomes like satisfaction or sedation depth.
	Incomplete outcome data (attrition bias)	Low Risk	Quote: “Minimal loss to follow-up with only 1 participant excluded suggests low risk of attrition bias.
	Selective reporting (reporting bias)	Low Risk	All outcomes mentioned in the methods appear to be reported in the results. No

			evidence of missing or selectively reported outcomes.
	Other bias	Low Risk	No obvious source of other bias like baseline imbalance or financial conflict influencing results.
Liu 2021	Random sequence generation (selection bias)	Low risk	The study used a computer-generated randomization schedule, ensuring unbiased group assignment.
	Allocation concealment (selection bias)	Low risk	Allocation concealment: The allocation was concealed using sequentially numbered, opaque, sealed envelopes. No issues were noted in the randomization process.
	Blinding of participants and personnel (performance bias)	Low risk	Both the patients and healthcare providers were blinded to the treatment allocation, reducing the risk of performance bias.
	Blinding of outcome assessment (detection bias)	Low risk	Outcome assessors were blinded to the treatment allocation, which prevents bias in the assessment of outcomes.
	Incomplete outcome data (attrition bias)		Although no significant differences were observed in dropout rates between groups, the handling of missing data is not explicitly stated.
	Selective reporting (reporting bias)	Unclear risk	All pre-specified outcomes were reported, with no evidence of selective reporting. This is clearly stated in the study's methodology.

	Other bias	Low risk	While no conflicts of interest were declared, the study does not provide detailed information on other potential biases (e.g., funding sources), leaving room for uncertainty.

Supplementary Table 3: Detailed risk of bias assessment according to Cochrane Risk of Bias Tool.

Author	Year	ASA Status	Sample size (n)	Reported Comorbidity frequencies	Major Comorbidities Excluded
Liu 2023 (12)	2023	I-II	216	NR	Cardiac disease (arrhythmia, HF, angina, MI), pulmonary disease (COPD, asthma, PE, lung cancer), hypotension, bradycardia, hypoxemia
Chen 2024 (a) (13)	2024	I-III	60	NR	Severe respiratory disease, uncontrolled hypertension, arrhythmias, psychiatric illness
Chen 2024 (b) (14)	2024	I-II	240	NR	Severe respiratory disease and heart failure (EF <40%)
Lin 2024 (15)	2024	I-III	228	HTN- 96 CAD- 52 DM- 68 COPD- 59	Severe cardiopulmonary, hepatic, or renal dysfunction; psychiatric or neurological disorders; substance/alcohol abuse; obesity (BMI ≥30 kg/m²); cognitive impairment.
Ye 2023 (16)	2023	I-II	129	NR	Severe cardiac dysfunction (NYHA III–IV), recent myocardial/cerebral infarction, arrhythmia, severe renal dysfunction, severe hepatic dysfunction (Child–Pugh C), epilepsy, mental illness.
Tan 2022 (17)	2022	I-II	66	HTN- 26 DM- 12	Cardiorespiratory, renal, hepatic, neurologic, and psychiatric disease; substance abuse; cognitive impairment.
Lu 2022 (18)	2022	I-III	400	HTN- 130 DM- 30	Severe HTN, severe arrhythmia, psychiatric disorders, substance abuse.
Guo 2022 (19)	2022	I-II	77	HTN- 32 DM- 9 CHD- 9 COPD- 10 Surgical History- 38	Uncontrolled hypertension, sleep apnea syndrome, hepatic or renal dysfunction, and substance/opioid abuse.
Hu 2022 (20)	2022	I-III	346	HTN- 118 DM- 55 CHD- 16 COPD- 36	Cardiorespiratory disease, obstructive sleep apnea, renal or hepatic dysfunction, neurologic or psychiatric disorders, and substance/alcohol abuse.
Liu 2021 (21)	2021	I-II	232	HTN- 80 DM- 46 CHD- 15	Liver dysfunction, adrenocortical insufficiency, porphyria, sleep apnea, and substance/alcohol abuse

				HYPERLIPIDEMIA- 24	

Supplementary Table 4: Summary of major comorbidities and sedation risk factors in included studies. (Abbreviations: NR= Not Reported, DM= Diabetes Mellitus, HTN= Hypertension, CHD= Coronary Heart Disease, COPD= Chronic Obstructive Pulmonary Disease, PE= Pulmonary Embolism, HF= Heart Failure)

STUDY	Hypotension Definition	Bradycardia Definition	Respiratory Depression Definition	
Liu 2023 (12)	SBP < 80 mmHg	HR < 40 beats/min	85<SpO2<90%	Deep (MOA
Chen 2024 (a) (13)	MBP <60 mmHg OR SBP <90 mmHg	HR <50 beats/min	SpO2 <90%	Deep (OAA
Chen 2024 (b) (14)	≥30% decrease in BP from baseline;	N/A	SpO2 <90%	Deep (MOA
Lin 2024 (15)	MAP < 65 mmHg or ≥30% decrease in BP from baseline;	HR <50 beats/min	SpO2 <90%	Deep (MOA
Ye 2023 (16)	30% decrease in MAP	HR dropped by > 20%	SpO2 <90%	Deep (MOA
Tan 2022 (17)	N/A	N/A	SpO2 <90%	Deep (MOA
Lu 2022 (18)	SBP < 90 mmHg	HR <50 beats/min	SpO2 <90%	Deep (MOA
Guo 2022 (19)	≥20% decrease in MAP	HR dropped by > 20%	SpO2 <90%	Deep (MOA
Hu 2022 (20)	SBP decrease > 20% or SBP < 80mmHg	HR <50 beats/min	SpO2 <90%	Deep (MOA
Liu 2021 (21)	SBP < 90 mmHg, DBP < 50mmHg	HR <50 beats/min	SpO2 <90%	Prolonged (

Supplementary Table 5: Operative definitions of outcomes in individual studies included.