

Procedural sedation in emergency departments: Efficacy and adverse outcomes from a systematic review and meta-analysis

ZhiJun Qu^{1,A}, Chengshi Xu^{1,B}, Zhijie Qu^{2,C}, Haofeng Liang^{3,D–F}

¹ Department of Anesthesiology, Beijing Jishuitan Hospital, Capital Medical University, China

² Department of Emergency Medicine, Qingdao Eighth People's Hospital, China

³ Department of Anesthesiology, The Fourth People's Hospital of Nanning, China

A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation;

D – writing the article; E – critical revision of the article; F – final approval of the article

Advances in Clinical and Experimental Medicine, ISSN 1899–5276 (print), ISSN 2451–2680 (online)

Adv Clin Exp Med. 2026;35(3):419–436

Address for correspondence

Haofeng Liang

E-mail: lianghaofeng2023@outlook.com

Funding sources

None declared

Conflict of interest

None declared

Received on January 2, 2025

Reviewed on January 26, 2025

Accepted on May 27, 2025

Published online on February 16, 2026

Abstract

Background. Procedural sedation reduces pain, anxiety, and discomfort during emergency department (ED) procedures. Analgesics, sedatives and anxiolytics ensure patient comfort but can cause respiratory, cardiovascular, neurological, and gastrointestinal (GI) side effects.

Objectives. To synthesize data on adverse events and procedural efficacy from randomized controlled trials (RCTs) involving the use of different drugs/drug combinations used for procedural sedation.

Materials and methods. A systematic literature review was conducted using MEDLINE and CENTRAL databases for RCTs that involved adult patients who were administered drugs for procedural sedation in the ED. Outcomes such as hypoxia, hypotension, apnea, agitation, GI disturbances (nausea, vomiting), and bradycardia/dysrhythmia were extracted from the trials. A meta-analysis was performed using OpenMeta (Analyst) software to determine the pooled incidence of each adverse outcome and procedural success for the different drugs and drug combinations.

Results. A total of 50 RCTs were included in the meta-analysis with information from 5,398 patients. Meta-analysis of the data showed a pooled incidence of 136 events/1,000 sedations (95% confidence interval (95% CI): 112–160) for hypoxia, 23 events/1,000 sedations (95% CI: 15–31) for hypotension, 143 events/1,000 sedations (95% CI: 110–177) for agitation, 51 events/1,000 sedations (95% CI: 38–64) for apnea, 45 events/1,000 sedations (95% CI: 30–60) for GI disturbances, and 30 events/1,000 sedations (95% CI: 19–41) for bradycardia/dysrhythmia. The procedural success rate was 921 events/1,000 sedations (95% CI: 896–946).

Conclusions. The results of this meta-analysis shed light on the adverse effects of various procedural sedation agents used for different procedures in the ED. Ketamine–propofol combinations were associated with less hemodynamic instability, whereas propofol caused hypotension and respiratory events and GI disturbances were associated with the administration of fentanyl and ketamine. Thus, individual patient factors such as age and comorbidities and the risk profile of different agents should be considered during procedural sedation protocols. This meta-analysis summarizes the side effects of several drugs to help physicians administer them safely.

Key words: ketamine, emergency department, propofol, midazolam, procedural sedation

Cite as

Qu ZJ, Xu C, Qu Z, Liang H. Procedural sedation in emergency departments: Efficacy and adverse outcomes from a systematic review and meta-analysis.

Adv Clin Exp Med. 2026;35(3):419–436.

doi:10.17219/acem/205615

DOI

10.17219/acem/205615

Copyright

Copyright by Author(s)

This is an article distributed under the terms of the Creative Commons Attribution 3.0 Unported (CC BY 3.0)

(<https://creativecommons.org/licenses/by/3.0/>)

Highlights

- In the emergency department, procedural sedation and analgesia are used to reduce anxiety, discomfort, and pain during complex procedures, ensuring patient comfort and safety.
- Procedural sedation and analgesia may cause adverse effects involving the respiratory, cardiovascular, neurological, and gastrointestinal systems.
- This study aimed to synthesize data on adverse events and procedural efficacy from randomized controlled trials evaluating different drugs and drug combinations for procedural sedation.
- Midazolam and ketofol were associated with fewer cardiovascular adverse events; however, ketamine was linked to a higher incidence of agitation, while propofol was associated with respiratory depression and a higher incidence of hypotension.

Introduction

Procedural sedation, also referred to as procedural sedation and analgesia (PSA), is a cornerstone practice in the emergency department (ED) to relieve anxiety, discomfort, and pain during painful procedures, thus ensuring patient comfort and safety. The American College of Emergency Physicians (ACEP) defines procedural sedation as “a technique of administering sedatives or dissociative agents with or without analgesics to induce a state that allows patients to tolerate unpleasant procedures while maintaining cardiorespiratory function. PSA is intended to result in a depressed level of consciousness that allows the patient to maintain oxygenation and airway control independently.”^{1,2} Therefore, it is important that the medications that are administered alleviate the pain of performing procedures as well as preserve vital physiological functions.³ Common procedures for which PSA is used in the ED include orthopedic manipulations (closed reduction of fractures or dislocations), laceration repairs, burn debridement and wound care, chest tube insertions, and cardioversions for arrhythmias.

Single drugs, or more often multiple drug combinations, are used to achieve suitable levels of sedation, analgesia, and anxiolysis, and their application is guided based on patient characteristics (age, comorbidities), type of procedure, and safety considerations. Sedatives such as short-acting benzodiazepines (midazolam), diazepam, and propofol are often used along with opioid analgesics (fentanyl, morphine and remifentanyl), and dissociative agents (ketamine) are commonly administered.^{4,5} Despite careful consideration of patient characteristics prior to the administration of medications for procedural sedation, trained emergency medicine personnel, and policies in place to monitor patients and report adverse events, individual responses to procedural sedation drugs are variable. Jones et al. have reported the occurrence of several respiratory adverse events such as hypoxemia, over-sedation, and apnea, which are related to age and comorbidities.⁶ Therefore, despite advances in monitoring and vigilance

protocols, and titration of drug/drug combinations, adverse events are common and should be analyzed to determine the safety of different drugs and drug combinations.

Studies conducted to determine the safety and efficacy of procedural sedation agents have been single-center randomized controlled trials (RCTs), observational studies, and most often studies with smaller sample sizes (<100 patients), making it difficult to draw conclusions on the safety of these agents. Meta-analysis is necessary to synthesize the data from various trials, thereby providing a more robust knowledge base regarding the safety of drugs and drug combinations used for procedural sedation.

Objectives

The objective of this work is to synthesize and analyze the available literature and evaluate the efficacy and safety of procedural sedation in adult patients in the ED, with a focus on adverse effects of various drugs and drug combinations.

Materials and methods

Search strategy

A systematic literature search was conducted of MEDLINE (PubMed) and the Cochrane Register of Controlled Trials (CENTRAL) in December 2024, covering the period from 1990 to 2024. The following search terms were used in various combinations: “procedural sedation”, “conscious sedation”, “emergency department”, “hypoxia”, “adverse events”, “midazolam”, “fentanyl”, “propofol”, “ketamine”, “etomidate”, and “lidocaine”. Additionally, a comprehensive list of search terms, including Medical Subject Headings (MeSH) terms, was applied. The titles and abstracts of potentially relevant studies were scanned, and the full-text versions of the appropriate articles were read. Additional studies were identified by cross-checking the reference lists of the relevant studies.

Study selection

We included RCTs that included patients undergoing different types of procedures and undergoing procedural sedation and analgesia. Adult patients (≥ 18 years) in the ED given all types of medication for procedural sedation were included in our analysis. Exclusion criteria included non-randomized studies and prospective and retrospective study designs.

Data extraction and quality assessment

Following identification of articles that met the inclusion criteria, data were extracted using a predefined data extraction form that included the following items: authors, year, study design, intervention (drug and drug combinations), and type of procedure. Outcomes such as procedural success and adverse events (hypoxia, hypotension, agitation, apnea, gastrointestinal (GI) disturbances, and bradycardia or dysrhythmia) were analyzed. One reviewer checked the articles and extracted the required information. The Cochrane Collaboration's risk of bias tool (RoB 2)⁷ was used to assess the methodological quality of the included studies. This tool includes the following criteria: randomization, allocation concealment, blinding, and completeness of follow-up. The risk of bias for each item was graded as high, low, or unclear risk.

Quantitative data synthesis

Meta-analysis and statistical calculations were performed using OpenMeta (Analyst) software (<https://www.cebm.brown.edu/openmeta>) and a random-effects model (DerSimonian–Laird) to calculate the pooled proportion of patients experiencing various adverse effects and procedural success related to the use of procedural sedation medications. The studies included in this single-arm meta-analysis are comparable, as they all evaluate the safety profile of [intervention name] in [patient population], sharing similar study designs, population demographics, and outcome measures. The data from different studies were pooled together to provide pooled estimates for each adverse event based on similarities such as adult patients, ED procedures, and definition of outcomes. Heterogeneity in the included studies was evaluated using the I^2 statistic, with small heterogeneity for I^2 values $< 25\%$, moderate heterogeneity for I^2 values of $25\text{--}50\%$, and high heterogeneity for I^2 values $> 50\%$. Forest plots were constructed and $p < 0.05$ was statistically significant. Publication bias was assessed with Egger's test and a funnel plot, in which the log odds ratio (OR) for each study was plotted against its standard error (SE) for the hypoxia outcome.

Results

Identification of studies

A total of 1,640 records were identified by database searching, of which 549 were screened by title and abstract. Duplicates and irrelevant records were removed ($n = 375$), and 174 RCTs were assessed for eligibility. However, 124 RCTs were excluded due to reasons such as incorrect study design, inappropriate outcome, setting, and population. The process of selection is shown in Fig. 1.

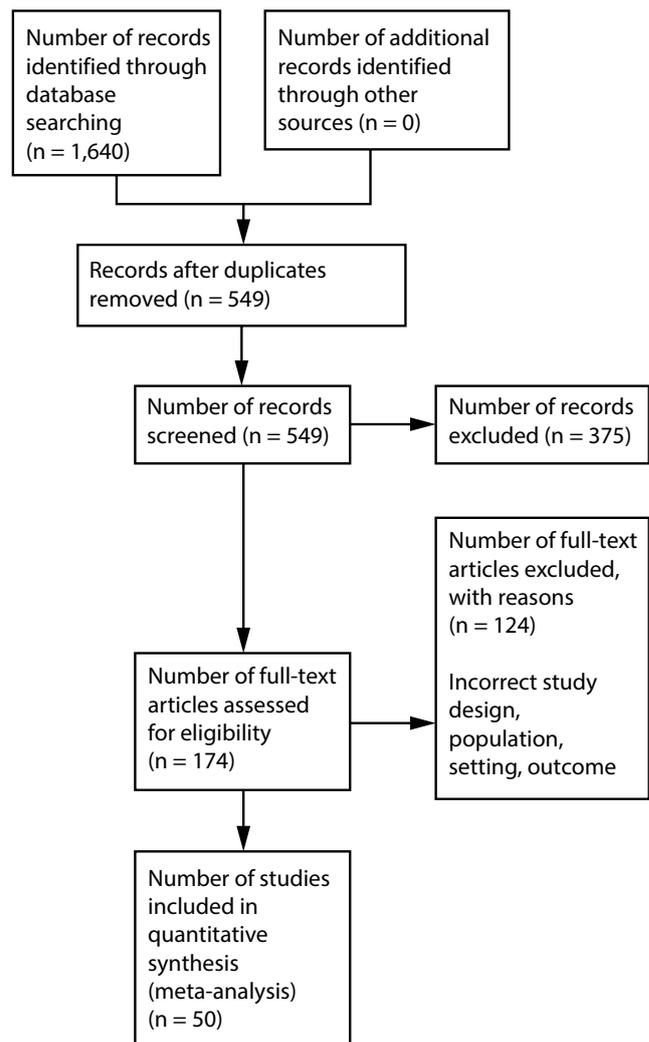


Fig. 1. Flowchart for identification and inclusion of studies in the meta-analysis according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)

Study characteristics

In total, 50 RCTs totaling 5,398 participants met the inclusion criteria for the meta-analysis. Ketamine, midazolam, propofol, and fentanyl and their combinations were the most frequently used medications for sedation, and some studies also included the use of etomidate, lidocaine, and diazepam. Most procedures for which procedural sedation and

analgesia were used were fracture and dislocation reductions, and in some cases cardioversion and abscess incision and drainage. Table 1 shows the details of the various

drugs/drug combinations included in each study, along with the procedures that were conducted in the ED for which procedural sedation was used.^{8–58}

Table 1. Characteristics of the included studies

Study reference	Drug/drug combination 1	Drug/drug combination 2	Drug/drug combination 3	Procedure
Abdolrazaghnejad and Banaie, 2017 ⁸	midazolam–ketamine	midazolam–fentanyl	–	fracture and dislocation reduction
Akhlaghi et al., 2019 ⁹	midazolam	haloperidol	–	fracture and dislocation reduction
Amini et al., 2018 ¹⁰	fentanyl–propofol–midazolam–ketamine	propofol–fentanyl	–	limb and soft tissue injury
Andolfatto et al., 2012 ¹¹	propofol–ketamine	propofol	–	fracture and dislocation reduction, I&D, cardioversion
Arhami et al., 2018 ¹²	dexmedetomidine–fentanyl	midazolam–fentanyl	–	distal radial fracture reduction
Bahreini et al., 2020 ¹³	sodium thiopental–fentanyl	propofol–ketamine	–	fracture and dislocation reduction, chest tube placement, lumbar puncture
Blaivas et al., 2011 ¹⁴	etomidate	–	–	dislocation reduction
Burton et al., 2002 ¹⁵	etomidate	midazolam	–	anterior shoulder dislocation reduction
Cevik et al., 2013 ¹⁶	midazolam–ketamine	midazolam–fentanyl	–	extremity injury closed reduction
Chan and Ho, 2008 ¹⁷	midazolam	etomidate	–	fracture and dislocation reduction
Coll-Vinet et al., 2003 ¹⁸	etomidate	propofol	midazolam	cardioversion
Deitch et al., 2010 ¹⁹	propofol	–	–	fracture and joint reduction
Deitch et al., 2011 ²⁰	propofol + high-flow oxygen	propofol + compressed air	–	fracture and joint reduction
Dolatabandi et al., 2018 ²¹	midazolam–fentanyl–placebo	midazolam–fentanyl–lidocaine	–	shoulder dislocation reduction
Dunn et al., 2010 ²²	morphine–midazolam	remifentanyl–propofol	–	shoulder dislocation reduction
Fathi et al., 2014 ²³	midazolam–fentanyl	–	–	distal radial fracture reduction
Ferguson et al., 2016 ²⁴	propofol–ketamine	propofol	–	fracture and joint reduction, I&D, cardioversion
Genzlinger et al., 2012 ²⁵	etomidate	ketamine	–	dislocation reduction
Gharavifard et al., 2016 ²⁶	midazolam–fentanyl	remifentanyl	–	anterior shoulder dislocation reduction
Hatamabadi et al., 2015 ²⁷	propofol	midazolam	–	anterior shoulder dislocation reduction
Holger et al., 2005 ²⁸	midazolam	propofol	–	orthopedic reductions, I&D
Hunt et al., 2005 ²⁹	etomidate	midazolam	–	fracture and joint reduction
Jamal et al., 2011 ³⁰	midazolam–fentanyl	ketamine	–	fracture and dislocation reduction
Kasmaee et al., 2019 ³¹	remifentanyl	propofol–fentanyl	–	anterior shoulder dislocation reduction
Lemoel et al., 2017 ³²	propofol–ketamine	ketamine	–	fracture and dislocation reduction
Mahshidfar et al., 2011 ³³	midazolam–fentanyl	–	–	anterior shoulder dislocation reduction
Massaeli et al., 2022 ³⁴	ketamine	propofol–ketamine	propofol–fentanyl	anterior shoulder dislocation reduction
Messenger et al., 2008 ³⁵	ketamine	fentanyl	–	fracture and dislocation reduction, I&D
Miner et al., 2003 ³⁶	propofol	remifentanyl	–	fracture and dislocation reduction
Miner et al., 2005 ³⁷	etomidate	propofol	–	fracture and dislocation reduction, cardioversions, tube placements
Miner et al., 2007 ³⁸	etomidate	propofol	–	fracture and dislocation reduction, cardioversions, tube placements, I&D
Miner et al., 2009 ³⁹	propofol	propofol–alfentanil	–	fracture and dislocation reduction, cardioversions, tube placements, I&D
Miner et al., 2010 ⁴⁰	propofol	ketamine	–	fracture and dislocation reduction, cardioversions, tube placements, I&D
Miner et al., 2013 ⁴¹	propofol	propofol–alfentanil	–	fracture and dislocation reduction
Miner et al., 2015 ⁴²	propofol	propofol–ketamine (1:1)	propofol–ketamine (4:1)	fracture and dislocation reduction, cardioversions, tube placements, I&D
Miner et al., 2017 ⁴³	propofol	alfentanil	–	fracture and dislocation reduction, I&D

Table 1. Characteristics of the included studies – cont.

Study reference	Drug/drug combination 1	Drug/drug combination 2	Drug/drug combination 3	Procedure
Nashibi et al., 2017 ⁴⁴	propofol–ketamine	midazolam–fentanyl	–	fracture reduction
Nejati et al., 2011 ⁴⁵	midazolam–ketamine	midazolam–fentanyl	–	fracture reduction, laceration repair
Ozturk et al., 2014 ⁴⁶	propofol	midazolam	–	anterior shoulder dislocation reduction
Parlak et al., 2006 ⁴⁷	propofol	midazolam	–	cardioversion
Phillips et al., 2010 ⁴⁸	propofol–ketamine	propofol	–	fracture and joint dislocation reduction
Salen et al., 2016 ⁴⁹	etomidate	ketamine	–	joint dislocation reduction
Sawas et al., 2013 ⁵⁰	propofol–ketamine	propofol	–	fracture and dislocation reduction, cardioversion, I&D, burn debridement, tube placement
Sener et al., 2011 ⁵¹	midazolam–ketamine	ketamine	–	fracture and dislocation reduction, burn wound care, I&D, laceration repair, lumbar puncture
Soysal et al., 2004 ⁵²	fentanyl	thiopental	–	fracture and dislocation reduction
Stronati et al., 2020 ⁵³	propofol	midazolam	–	cardioversion
Tajoddini and Motaghi, 2020 ⁵⁴	propofol–ketamine	propofol–fentanyl	–	joint reduction, chest tube placement
Taylor et al., 2005 ⁵⁵	propofol	midazolam–fentanyl	–	anterior shoulder dislocation reduction
Tezel et al., 2004 ⁵⁶	ketamine	–	–	shoulder dislocation reduction
Vahidi et al., 2018 ⁵⁷	midazolam	thiopental	–	shoulder dislocation reduction
Wright et al., 1993 ⁵⁸	midazolam	propofol	–	fracture and joint reduction, burn debridement, tube insertion, lumbar puncture, suturing, and soft tissue repair

I&D – incision and drainage; GI – gastrointestinal; RCT – randomized controlled trial; ED – emergency department.

Characteristics of participants

All participants in the studies were ≥18 years of age and were trauma patients admitted to the ED for various reasons, of which orthopedic manipulations and abscess incision and drainage procedures were the most common. To be included in the analysis, all procedures were required to be performed by emergency physicians and personnel in the ED

and drugs or drug combinations for sedation were administered parenterally.

Bias assessment

The results of the risk of bias evaluation are shown in Fig. 2. It was seen that the risk was low to unclear across most fields but a relatively high risk (>20%) was observed

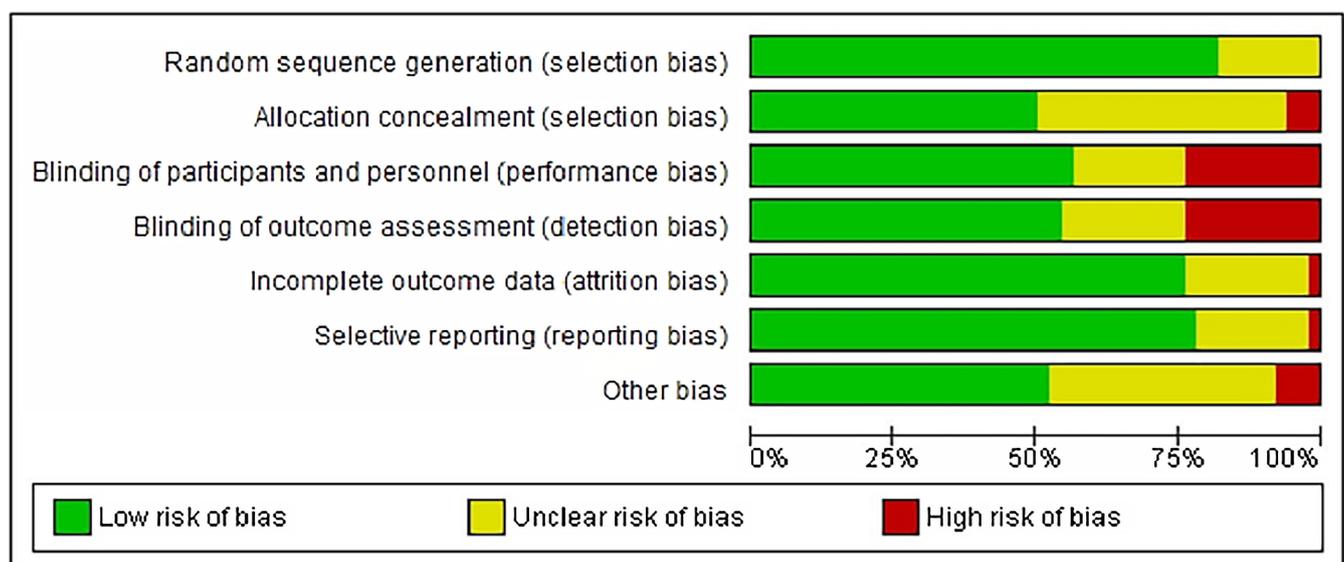


Fig. 2. Risk of bias summary for studies included in the meta-analysis

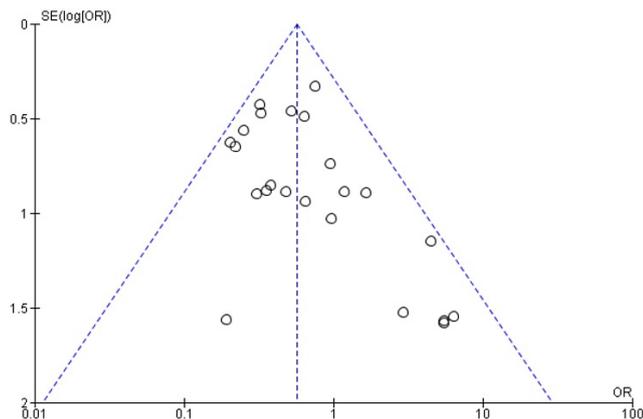


Fig. 3. Funnel plot to assess publication bias in meta-analysis (hypoxia outcome)

in the categories of blinding of personnel, participants, and outcome assessment. Difficulties in completely masking the medication administered, and side effects associated with the use of certain drugs that physicians and other healthcare personnel involved in the ED are well-versed in, make it difficult to perform blinding.

The funnel plot was not symmetrical (Fig. 3) for the hypoxia outcome for the use of different drugs and drug combinations, indicating the risk of publication bias.

Meta-analysis results

A total of 50 RCTs comprising 5,398 patients were included in the meta-analysis. The studies spanned from 1993 to 2022, with sample sizes ranging from 20 to 591. The studies evaluated the effects of procedural sedation in adult populations undergoing orthopedic manipulations, cardioversions, abscess incision, drainage procedures, and chest tube placements. Various drugs were used as a single entity such as midazolam ($n = 10$), propofol ($n = 18$), ketamine ($n = 5$), etomidate ($n = 9$), fentanyl ($n = 2$), alfentanil ($n = 10$), methohexital ($n = 1$), remifentanyl ($n = 3$), meperidine ($n = 1$), thiopental ($n = 2$), and diazepam ($n = 1$). Drug combinations that were used included propofol–fentanyl ($n = 4$), midazolam–ketamine ($n = 5$), midazolam–fentanyl ($n = 12$), propofol–ketamine ($n = 11$), propofol–alfentanil ($n = 2$), and remifentanyl–propofol ($n = 1$).

The most reported adverse events that were included in the studies and that were analyzed to determine the pooled proportion (Table 2) are discussed below.

Hypoxia: Of the included studies, 30 reported hypoxia as an adverse outcome. The incidence of hypoxia was 136 per 100 events (95% confidence interval (95% CI): 112–160). Patients receiving midazolam and fentanyl and their combinations showed the highest incidence of hypoxia. The high I^2 value of 91.31% was caused by pooling of studies with different drugs/drug combinations and procedures for which sedation was used, along with heterogeneous patient populations in terms of age and

previous medications received (Fig. 4A). The funnel plot (Fig. 4B) exhibited pronounced symmetry across various control treatments, indicating a minimal risk of publication bias. This observation was further validated using Egger's test, which yielded statistically insignificant p -values ($p = 0.217 > 0.05$).

Hypotension: This adverse effect was reported in 21 studies, and its incidence was 23 per 1,000 sedations (95% CI: 15–31). Propofol and its combinations were associated with the highest incidence of hypotension events, and moderate heterogeneity of 50.18% was associated with heterogeneous patient characteristics, drug/drug combinations, and procedures (Fig. 5A). The funnel plot (Fig. 5B) displayed notable symmetry across different control treatments, suggesting a low likelihood of publication bias. This finding was corroborated with Egger's test, which produced a non-significant p -value ($p = 0.178$), exceeding the conventional significance threshold of 0.05.

Agitation: This adverse outcome was seen in 18 studies and had an incidence of 143 events per 1,000 sedations (95% CI: 110–177). Patients receiving propofol and propofol–ketamine were seen to report high incidences of agitation, and the heterogeneity was high at 96.41% due to pooling of different studies (Fig. 6A). The funnel plot (Fig. 6B) showed symmetry, indicating minimal publication bias risk, confirmed using Egger's test, which yielded a nonsignificant p -value ($p = 0.135 > 0.05$).

Apnea: 24 studies reported apnea as an adverse outcome with an incidence of 51 per 1,000 sedations (95% CI: 38–64). Midazolam administration was related to a relatively high incidence of apnea, and a high heterogeneity of 70.68% was also seen as studies with different drugs were pooled together (Fig. 7A). The funnel plot (Fig. 7B) revealed a symmetrical pattern across various control treatments, implying a low risk of publication bias. Egger's test reinforced this conclusion, yielding $p = 0.165$, which falls above the standard significance level of 0.05.

Gastrointestinal disturbances: Nausea and vomiting were the most reported GI disturbances in 19 studies. The pooled incidence was 45 events per 1,000 sedations (95% CI: 30–60). The highest incidence of GI disturbances was seen in patients receiving ketamine, and a high heterogeneity of 67.73% was attributed to combining differing studies (Fig. 8A). The symmetry observed in the funnel plot (Fig. 8B) suggests that publication bias is unlikely to be a significant concern. This assessment was supported by Egger's test, which returned a $p = 0.298$, indicating no statistically significant evidence of bias.

Cardiovascular disturbances: Bradycardia and dysrhythmias were reported in 11 studies in the meta-analysis, with an incidence of 30 per 1,000 sedations (95% CI: 19–41). Propofol and propofol combinations and midazolam caused cardiovascular symptoms. Moderate heterogeneity of 31.38% indicated some homogeneity between the studies chosen (Fig. 9A). The funnel plot (Fig. 9B) demonstrated symmetry, indicating a low risk of publication bias.

Table 2. Adverse events in the included studies

Study reference	Hypoxia	Hypotension	Agitation	Apnea	Gastrointestinal (GI) disturbances	Bradycardia/dysrhythmia
Abdolrazaghnejad and Banaie, 2017 ⁸	✓		✓		✓	
Akhlaghi et al., 2019 ⁹	✓		✓	✓	✓	
Amini et al., 2018 ¹⁰					✓	
Andolfatto et al., 2012 ¹¹		✓	✓	✓		
Arhami et al., 2018 ¹²						✓
Bahreini et al., 2020 ¹³	✓	✓	✓	✓	✓	✓
Blaivas et al., 2011 ¹⁴	✓	✓				
Burton et al., 2002 ¹⁵	✓	✓		✓	✓	✓
Cevik et al., 2013 ¹⁶	✓		✓		✓	
Chan and Ho, 2008 ¹⁷		✓			✓	
Coll-Vinet et al., 2003 ¹⁸	✓			✓		
Deitch et al., 2010 ¹⁹	✓					
Deitch et al., 2011 ²⁰	✓					
Dolatabandi et al., 2018 ²¹	✓			✓		✓
Fathi et al., 2014 ²³		✓		✓	✓	
Ferguson et al., 2016 ²⁴	✓	✓	✓	✓		✓
Gharavifard et al., 2016 ²⁶			✓		✓	
Hatamabadi et al., 2015 ²⁷				✓		✓
Holger et al., 2005 ²⁸					✓	
Hunt et al., 2005 ²⁹	✓	✓	✓	✓		
Jamal et al., 2011 ³⁰	✓					
Kasmaee et al., 2019 ³¹			✓	✓		
Lemoel et al., 2017 ³²	✓	✓		✓	✓	
Mahshidfar et al., 2011 ³³				✓		
Massaeli et al., 2022 ³⁴	✓	✓	✓	✓	✓	
Messenger et al., 2008 ³⁵	✓	✓			✓	✓
Miner et al., 2003 ³⁶	✓					
Miner et al., 2005 ³⁷	✓	✓				
Miner et al., 2007 ³⁸	✓	✓				
Miner et al., 2009 ³⁹		✓	✓			
Miner et al., 2010 ⁴⁰		✓	✓			
Miner et al., 2013 ⁴¹	✓		✓	✓		
Miner et al., 2015 ⁴²	✓			✓		
Nashibi et al., 2017 ⁴⁴				✓		
Nejati et al., 2011 ⁴⁵	✓		✓	✓		✓
Ozturk et al., 2014 ⁴⁶	✓			✓		
Parlak et al., 2006 ⁴⁷	✓			✓		
Salen et al., 2016 ⁴⁹	✓	✓	✓		✓	
Sawas et al., 2013 ⁵⁰	✓					
Sener et al., 2011 ⁵¹	✓		✓	✓	✓	
Soysal et al., 2004 ⁵²		✓		✓		✓
Stronati et al., 2020 ⁵³	✓	✓				✓
Tajoddini and Motaghi, 2020 ⁵⁴		✓	✓			✓
Taylor et al., 2005 ⁵⁵	✓	✓			✓	
Tezel et al., 2004 ⁵⁶	✓		✓		✓	
Vahidi et al., 2018 ⁵⁷				✓	✓	
Wright et al., 1993 ⁵⁸		✓		✓	✓	

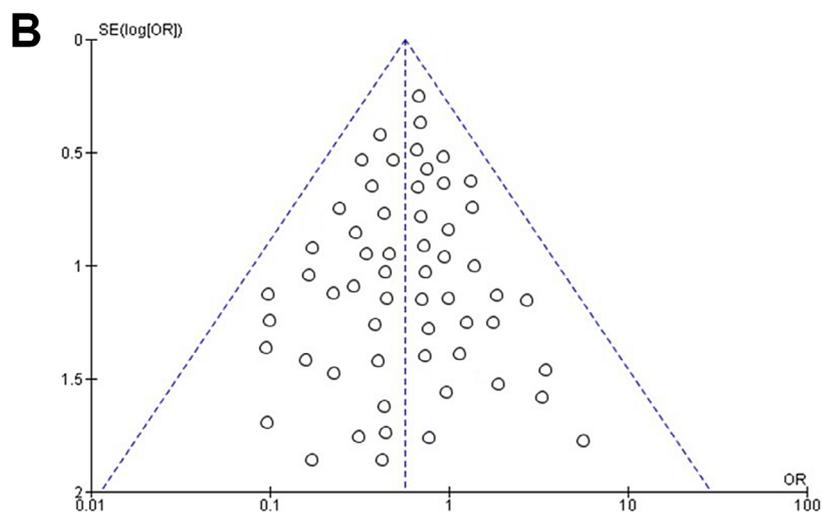
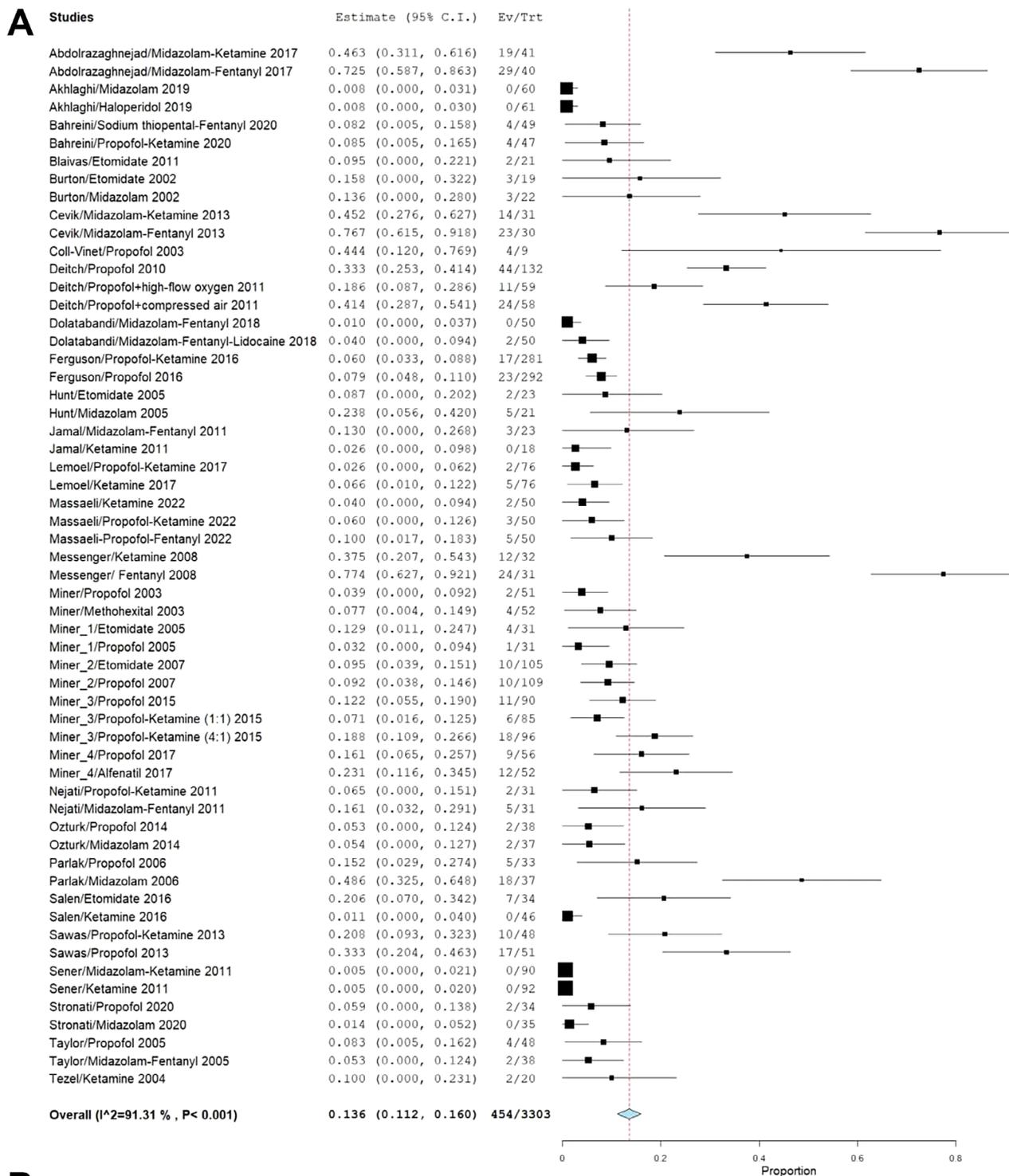


Fig. 4. Hypoxia outcomes in patients undergoing procedural sedation with various drugs/drug combinations. A. Forest plot of the pooled incidence: proportions and 95% confidence intervals (95% CIs); B. Funnel plot for publication bias

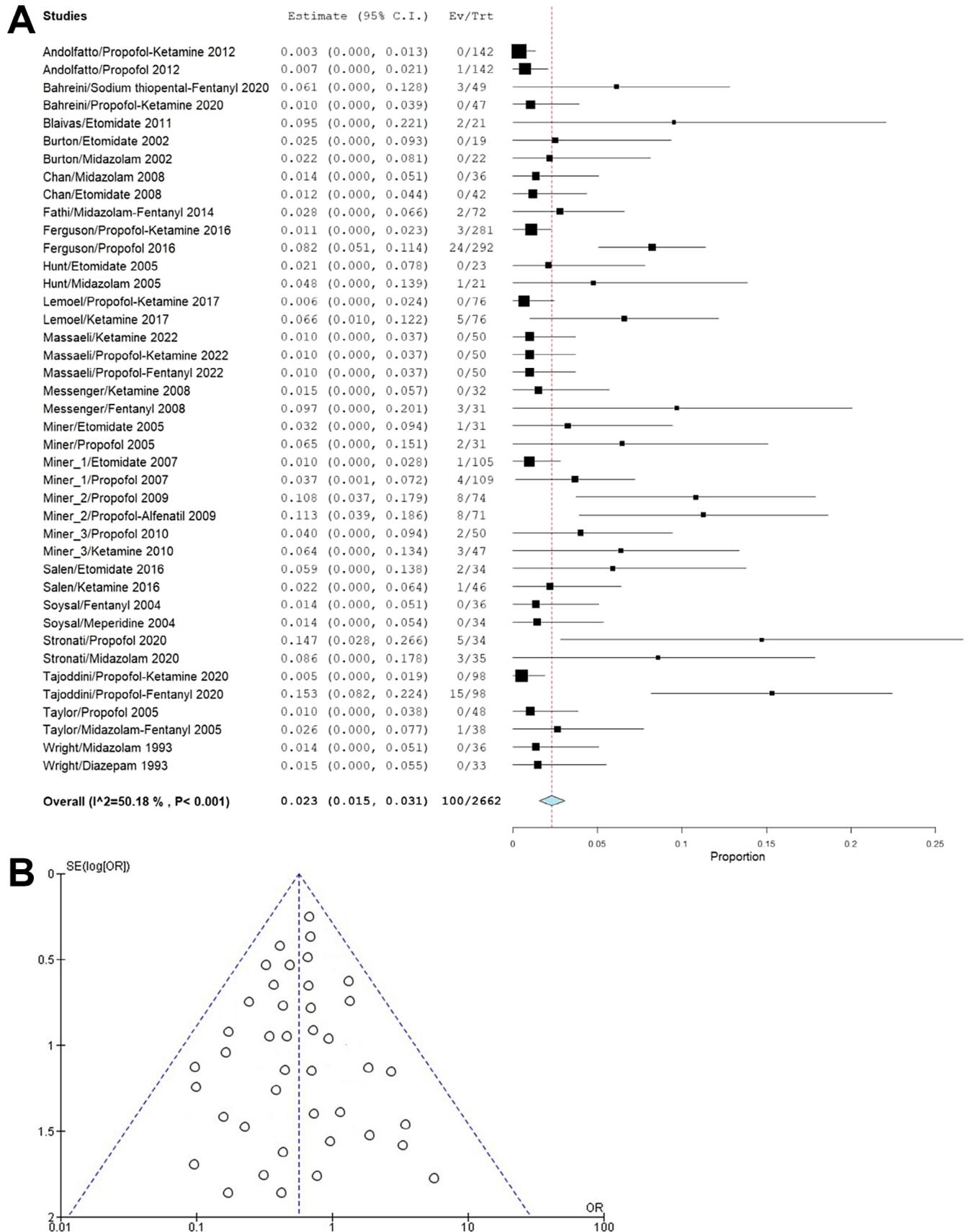


Fig. 5. Hypotension outcomes in patients undergoing procedural sedation with various drugs/drug combinations. A. Forest plot of the pooled incidence: proportions and 95% confidence intervals (95% CIs); B. Funnel plot for publication bias

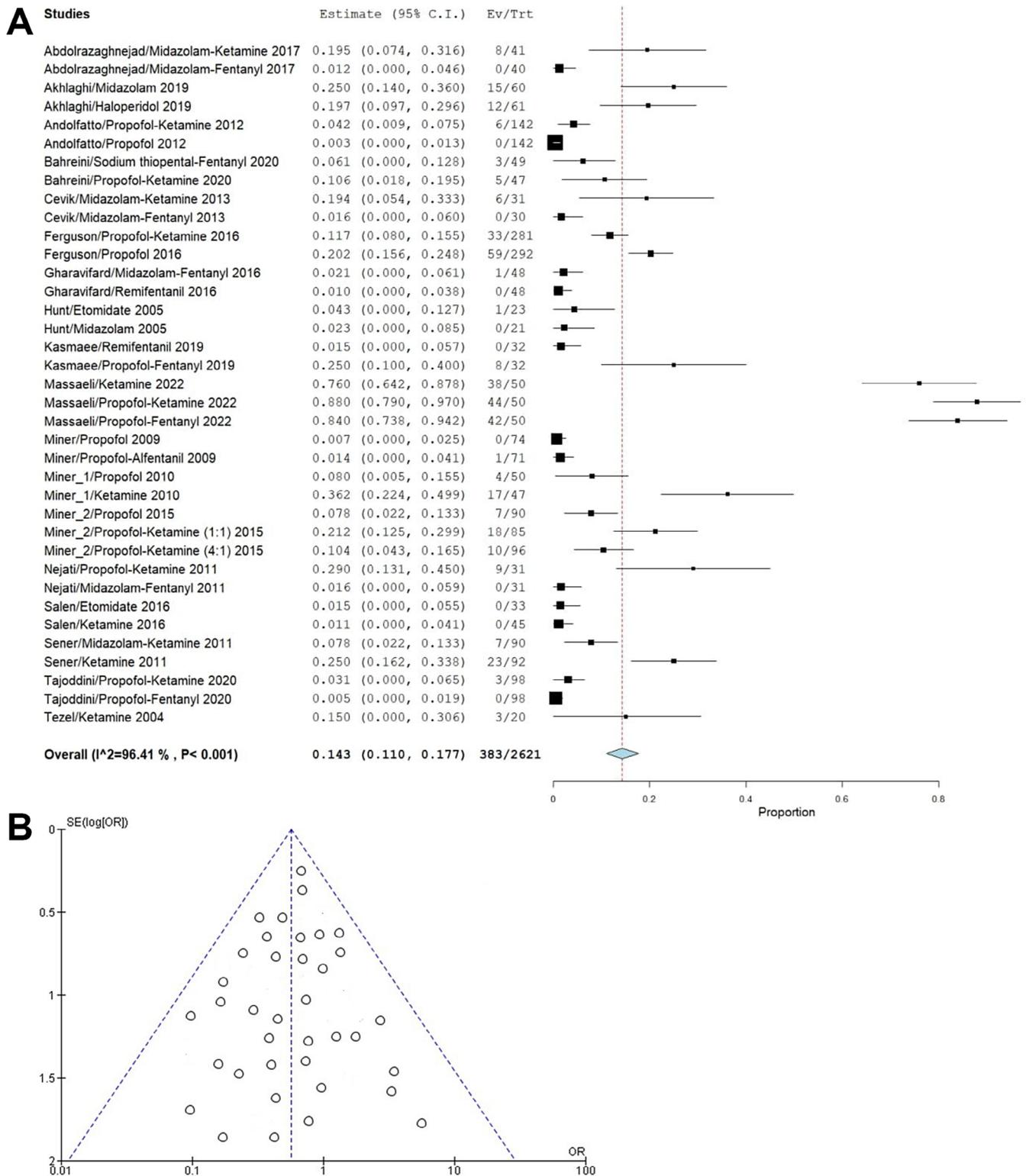


Fig. 6. Agitation outcomes in patients undergoing procedural sedation with various drugs/drug combinations. A. Forest plot of the pooled incidence: proportions and 95% confidence intervals (95% CIs); B. Funnel plot for publication bias

The results of Egger’s test ($p = 0.251$) further substantiated this finding, suggesting that the observed effects are unlikely to be influenced by publication bias.

Procedural success: The outcome of procedural success, which can be related to the efficacy of the medications,

had a pooled incidence of 921 events per 1,000 sedations (95% CI: 896–946), with only midazolam, fentanyl, and nitrous oxide (Entonox) showing a lower success rate than the pooled incidence estimate (Fig. 10A). The symmetrical shape of the funnel plot (Fig. 10B)

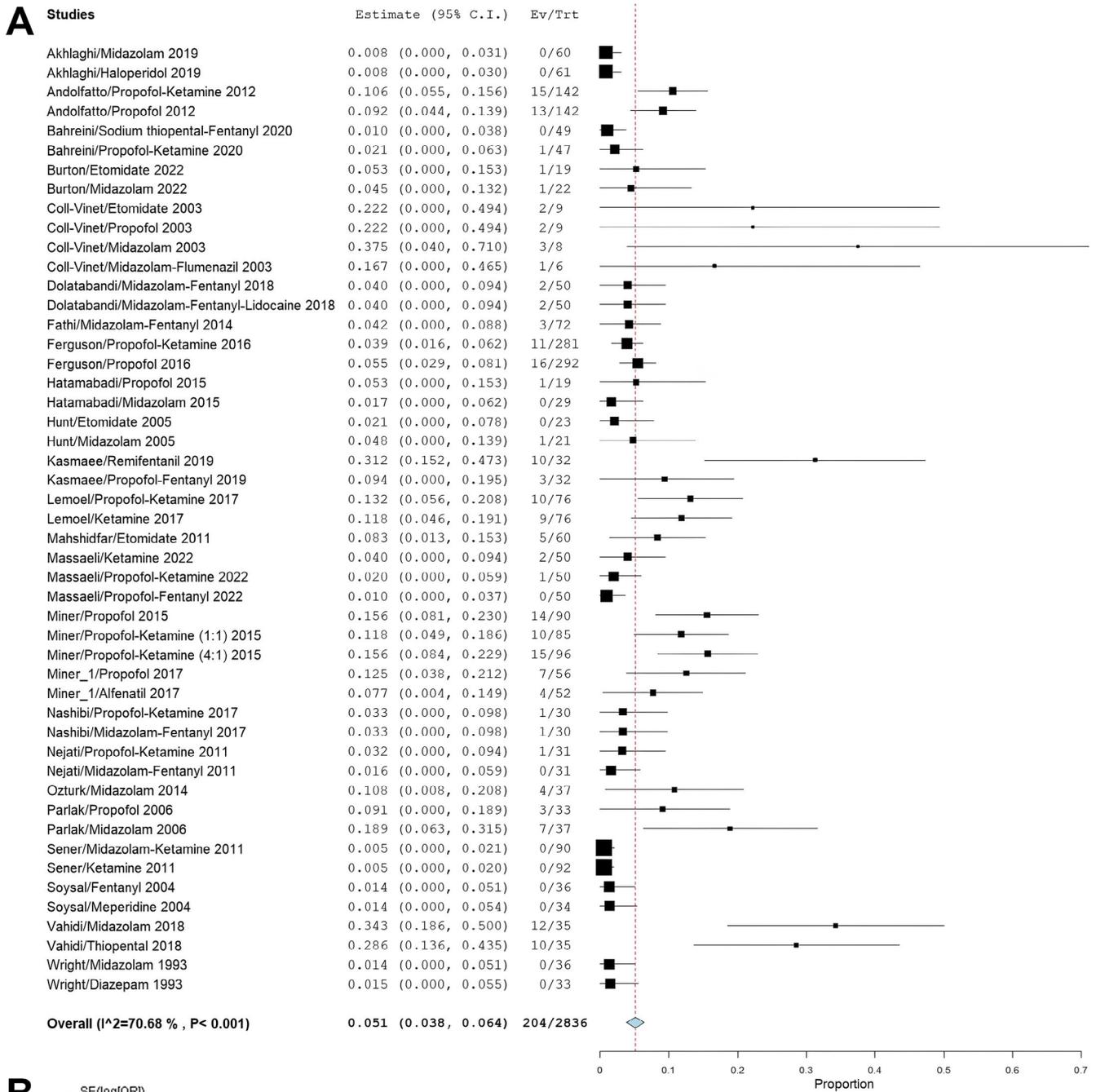


Fig. 7. Apnea outcomes in patients undergoing procedural sedation with various drugs/drug combinations. A. Forest plot of the pooled incidence: proportions and 95% confidence intervals (95% CIs); B. Funnel plot for publication bias

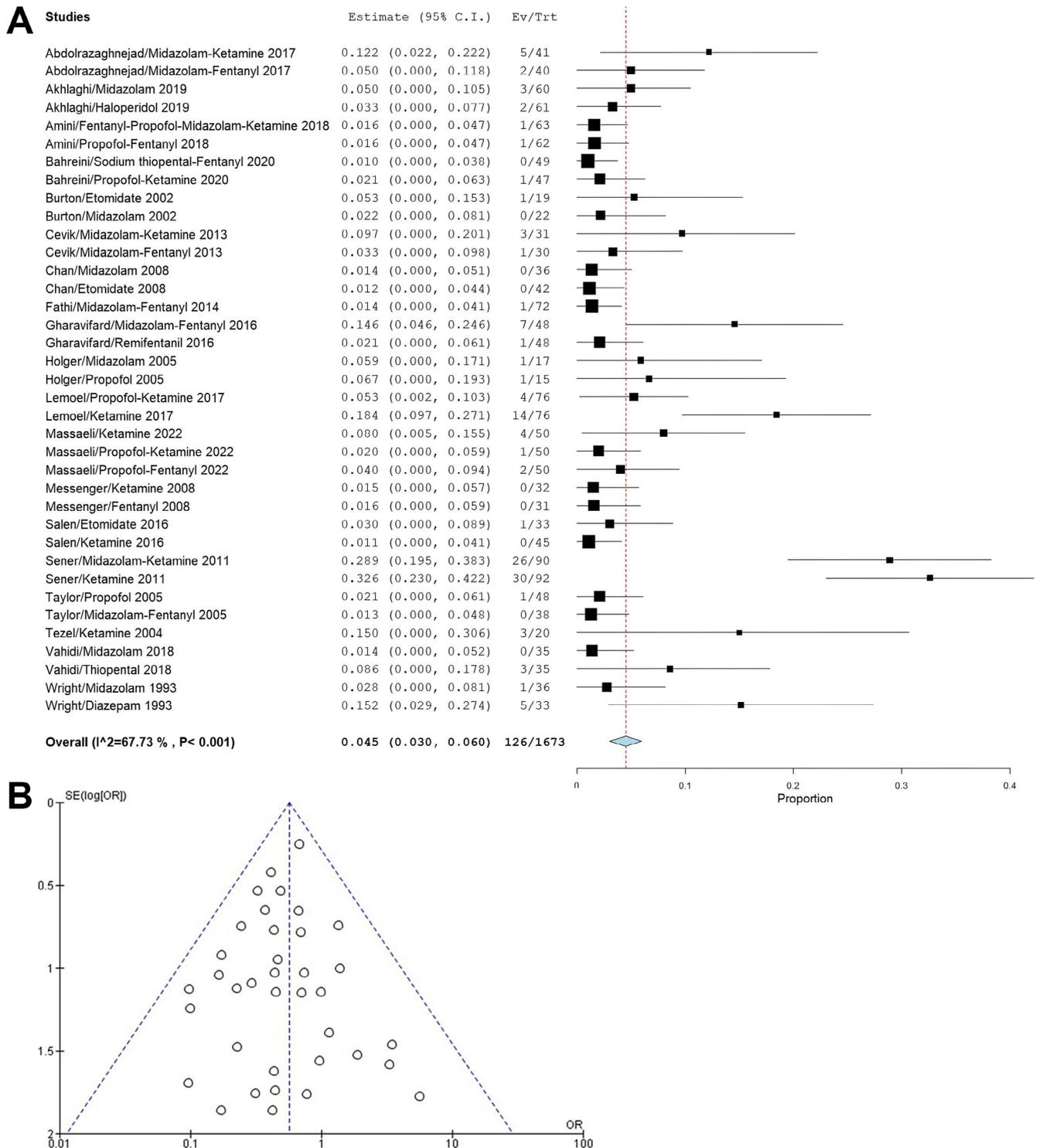


Fig. 8. Gastrointestinal disturbances (nausea, vomiting) outcomes in patients undergoing procedural sedation with various drugs/drug combinations. A. Forest plot of the pooled incidence: proportions and 95% confidence intervals (95% CIs); B. Funnel plot for publication bias

provides evidence against publication bias. This conclusion is reinforced by the nonsignificant result of Egger’s test ($p = 0.178$), which suggests that the results are robust and unbiased. The p -value for the pooled incidences of all adverse events and procedural success was <0.001 , indicating statistically significant pooled

incidence estimates for all outcomes (except cardiac disturbances; $p = 0.081$). Table 3 summarizes the results of the meta-analysis across all outcomes. Supplementary Table 1 demonstrates that the studies incorporated in the meta-analysis included the effect size (incidence rate) of the outcomes.

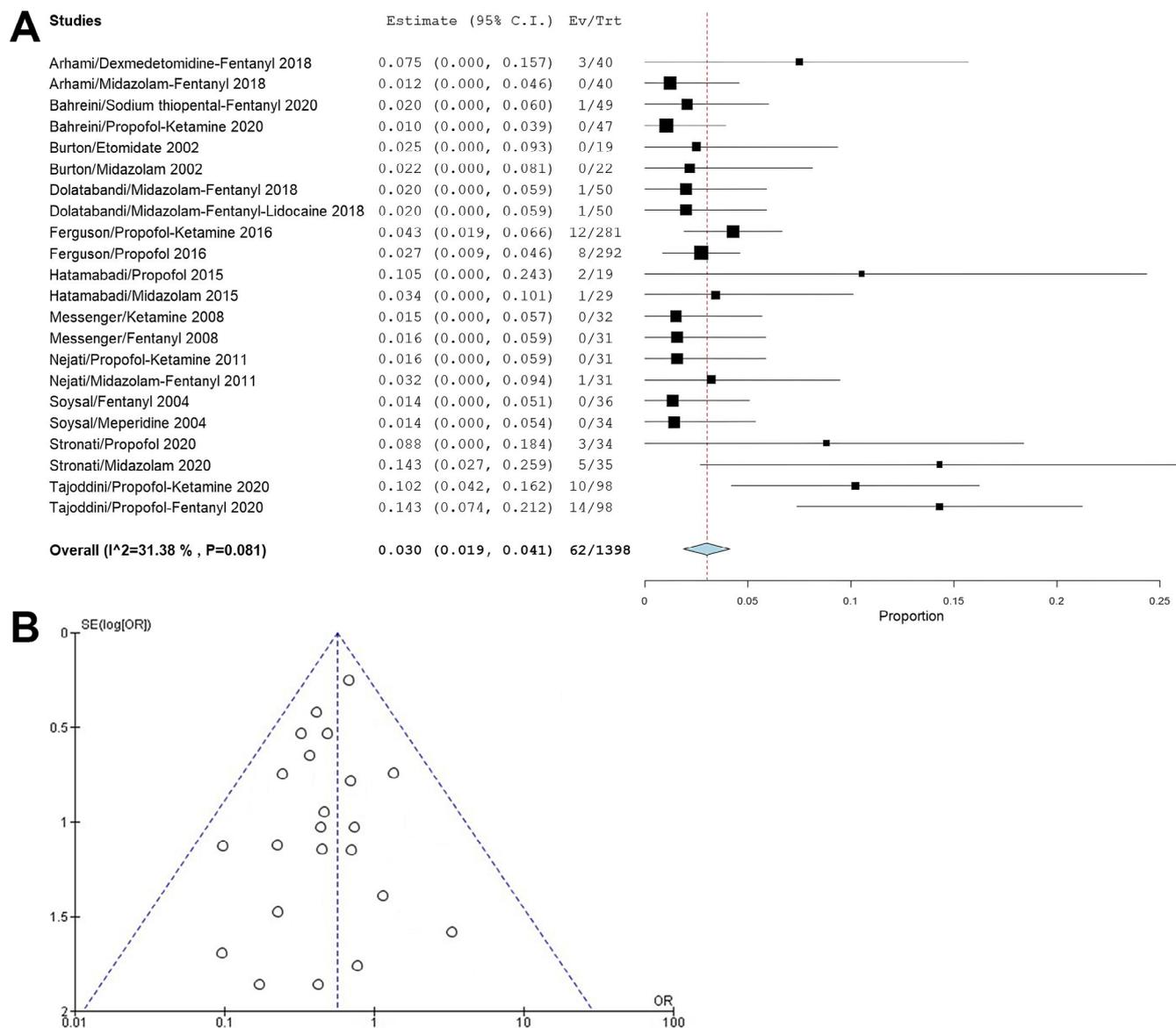


Fig. 9. Cardiac disturbances (bradycardia/dysrhythmia) outcomes in patients undergoing procedural sedation with various drugs/drug combinations. A. Forest plot of the pooled incidence: proportions and 95% confidence intervals (95% CIs); B. Funnel plot for publication bias

Table 3. Incidence of adverse events from meta-analysis of included studies

Adverse event	Events/sedation	Estimate/1000	95% CI	I ² (%)
Hypoxia	454/3303	136	112–160	91.31
Hypotension	100/2662	23	15–31	50.18
Agitation	383/2621	143	110–177	96.41
Apnea	204/2836	51	38–64	70.68
GI disturbances	126/1673	45	30–60	67.73
Bradycardia/dysrhythmia	62/1398	30	19–41	31.38

95% CI – 95% confidence interval; GI – gastrointestinal.

Discussion

This meta-analysis provides a comprehensive and up-to-date review of the adverse outcomes associated with the use of several drugs and drug combinations administered for

procedural sedation in the ED. Most of the procedures included in the analysis were orthopedic manipulations, mainly fracture and joint dislocation reductions. We included 40 randomized controlled trials comparing different drugs, all of which were administered by trained emergency medicine

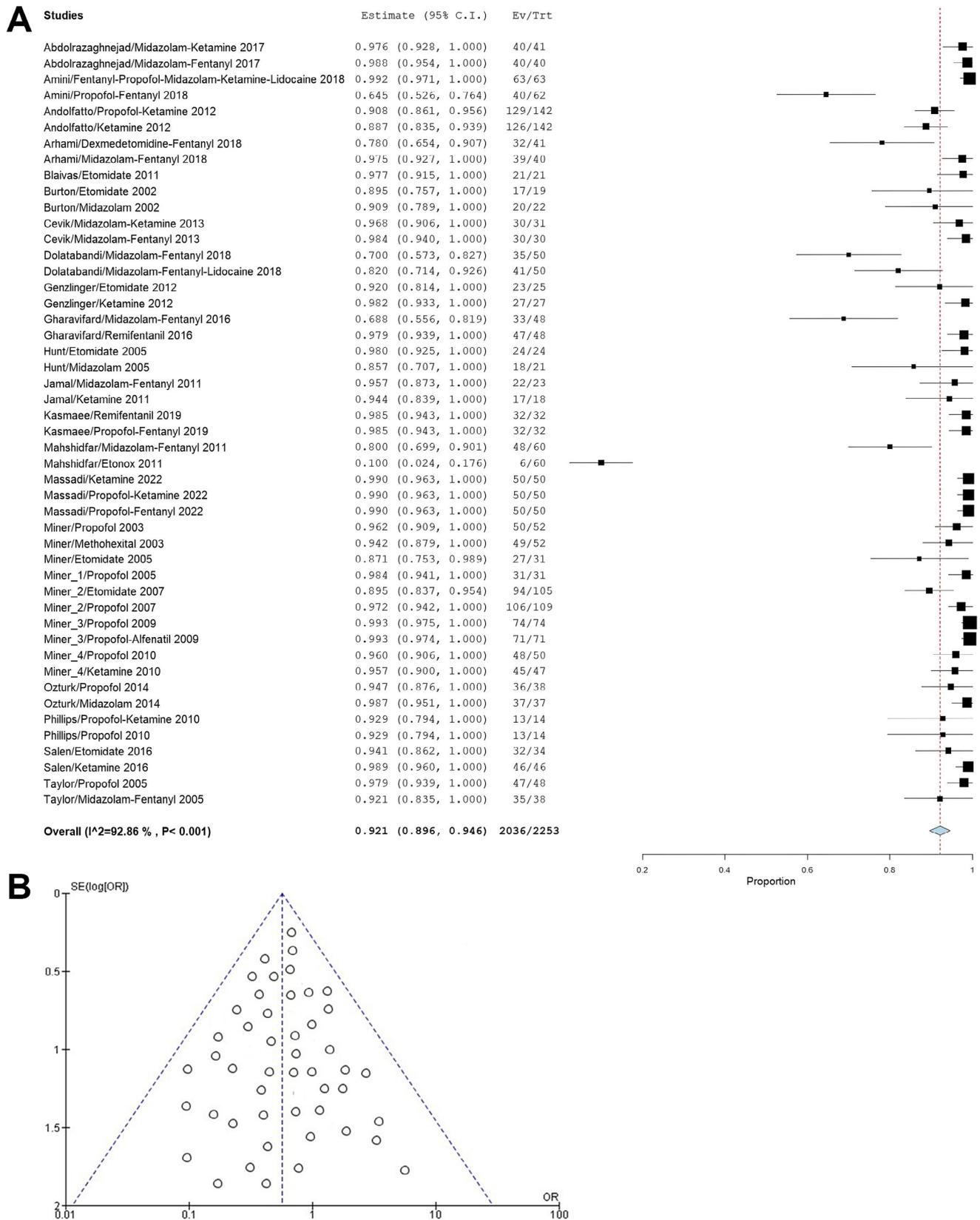


Fig. 10. Procedural success outcomes in patients undergoing procedural sedation with various drugs/drug combinations. A. Forest plot of the pooled incidence: proportions and 95% confidence intervals (95% CIs); B. Funnel plot for publication bias

physicians in ED. Since this meta-analysis aimed to determine the pooled incidence of adverse events in patients receiving different drugs, a single-arm meta-analysis was used with

the application of a random-effects model to account for differences in studies regarding patient characteristics, settings, and interventions.

The administration of procedural sedation involves a delicate balance of the benefit–risk profile, as analgesics and sedatives are meant to ease procedural comfort but can cause respiratory side effects such as hypoxia and hypoxemia, apnea, hypoventilation, and more serious side effects such as airway obstructions and laryngospasm. Thus, individual patient characteristics need to be considered heavily prior to deciding on a choice of any drug or drug combination to induce sedation. In line with previous meta-analyses, the incidence of respiratory adverse outcomes such as apnea and hypoxia was relatively frequent, with propofol, midazolam and their combinations with fentanyl showing higher incidences of these side effects. Respiratory depression is due to their action on gamma-aminobutyric acid (GABA) receptors, leading to inhibitory neurotransmission.⁵⁹ Although ketamine is expected to be a relatively safe option for minimizing the incidence of respiratory events, our study showed mixed results, with ketamine and its combinations with other drugs causing a low incidence of hypoxia and apnea in some cases, whereas propofol–ketamine combinations caused a higher incidence than the pooled effect size.

Hypotension and bradycardia are the most common cardiovascular disturbances observed during procedural sedation, and their occurrence is dependent on patient factors such as pre-existing cardiovascular diseases, elderly patients, diabetic neuropathy, and dehydration. Etomidate, midazolam and midazolam–opioid combinations are considered, as they have a neutral cardiovascular profile with minimal hemodynamic effects. These agents and their combinations were associated with a low incidence of hypotension and bradycardia/dysrhythmia in our study. In contrast, propofol was associated with a high risk of cardiovascular adverse effects caused by its cardiac depressant activity that leads to a decrease in cardiac output and arterial pressure.^{60,61} To overcome the negative effects of propofol on cardiovascular outcomes, combinations of ketamine–propofol, known as ‘ketofol’, are commonly used. This combination includes the analgesic effect of ketamine and the sedative effect of propofol, and the drugs balance each other out in terms of each one’s adverse effects, thereby resulting in a better safety profile. A RCT has shown that ketofol has better hemodynamic stability than propofol during the first 30 min of general anesthesia.⁶² Similarly, our meta-analysis also showed that the incidences of hypotension were higher than the pooled incidence of this adverse outcome in patients receiving propofol alone compared to the ketofol combination.

Gastrointestinal side effects such as nausea and vomiting are commonly associated with procedural sedation agents such as ketamine and opioids such as fentanyl. However, ketofol and combinations of opioids with propofol or midazolam resulted in fewer GI disturbances. Neurological adverse events caused by procedural sedation include dizziness, confusion, seizures, and agitation. Ketamine

and its combinations were seen to cause high incidences of agitation in our meta-analysis, which is in line with previous studies.⁶³

Procedural success rates were high in our study with all sedation agents irrespective of the adverse outcomes in each trial, highlighting the importance of procedural sedation in emergency procedures. Other meta-analyses on adverse outcomes associated with procedural sedation have included similar events as our study, such as agitation, bradycardia, hypotension, hypoxia, intubation, and aspiration, and concluded that these events were relatively rare and PSA could be used safely.⁶⁴

Through this meta-analysis, it is clear that the choice of drug that is used for procedural sedation should be dictated by specific clinical scenarios and patient needs. It is important to consider comorbidities, use continuous monitoring and vigilance strategies to prevent serious adverse outcomes, and have emergency equipment, medications and resuscitation agents available in case of respiratory distress. Furthermore, recovery times are also a crucial factor that should be taken into account when using a particular agent for specific patient populations and procedure types.

Limitations of the study

Although our meta-analysis includes the most recent trials and information on procedural sedation, it is not without certain limitations. We included all studies that had the adverse event outcomes that we had defined a priori in our study, regardless of the sample size and bias. Additionally, we did not perform subgroup analyses as per the procedure and drug type or combination due to the limited amount of data for each, which may not have been statistically robust. However, pooling data across all studies resulted in high statistical heterogeneity, which was seen in our study. Adverse outcomes such as agitation, hypotension, and hypoxia were not consistently defined across all the studies, which also could contribute to heterogeneity. Since some studies included only a few patients (<50) in most cases, the confidence intervals were wide, decreasing the confidence in the results. Small single-center studies and publication bias could have also influenced the quality and reliability of the data.

To allow for the use of data on procedural sedation agents in emergency medicine scenarios, it is necessary to have results available from larger, multicenter RCTs with a standardized definition of adverse events.

Conclusions

This paper provides a current meta-analysis on trials using procedural sedation agents in the ED and the adverse outcomes and efficacy associated with the use of these agents. Meta-analysis results for each adverse event show

that certain agents are safer than others in specific patients and procedures. Whilst midazolam and ketofol administration cause fewer cardiovascular events, ketamine was associated with a high incidence of agitation, and propofol caused respiratory depression and a high incidence of hypotension. Thus, tailoring the choice of the sedative and analgesic agent to patient needs is of prime importance and must be guided by data from clinical trials, and should not be a one-size-fits-all approach.

Supplementary data

The supplementary materials are available at <https://doi.org/10.5281/zenodo.14884141>. The package contains the following files:

Supplementary Table 1. Effect size (incidence rate) of outcomes for studies included in this meta-analysis.

Data Availability Statement

The datasets supporting the findings of the current study are openly available in Zenodo at <https://doi.org/10.5281/zenodo.15757978>.

Consent for publication

Not applicable.

Use of AI and AI-assisted technologies

Not applicable.

ORCID iDs

ZhiJun Qu  <https://orcid.org/0009-0007-0196-4257>
 Chengshi Xu  <https://orcid.org/0009-0005-5051-5058>
 Zhijie Qu  <https://orcid.org/0009-0006-3065-3530>
 Haofeng Liang  <https://orcid.org/0009-0008-1247-332X>

References

- Godwin SA, Caro DA, Wolf SJ, et al. Clinical policy: Procedural sedation and analgesia in the emergency department. *Ann Emerg Med.* 2005;45(2):177–196. doi:10.1016/j.annemergmed.2004.11.002
- Cappellini I, Bavestrello Piccini G, Campagnola L, et al. Procedural sedation in emergency department: A narrative review. *Emerg Care Med.* 2024;1(2):103–136. doi:10.3390/ecm1020014
- Molina JAD, Lobo CA, Goh HK, Seow E, Heng BH. Review of studies and guidelines on fasting and procedural sedation at the emergency department: Fasting and procedural sedation. *Int J Evid Based Healthc.* 2010;8(2):75–78. doi:10.1111/j.1744-1609.2010.00163.x
- Peña BMG, Krauss B. Adverse events of procedural sedation and analgesia in a pediatric emergency department. *Ann Emerg Med.* 1999; 34(4):483–491. doi:10.1016/S0196-0644(99)80050-X
- Jagoda AS, Campbell M, Karas S, et al. Clinical policy for procedural sedation and analgesia in the emergency department. *Ann Emerg Med.* 1998;31(5):663–677. doi:10.1016/S0196-0644(98)70216-1
- Jones MR, Karamnov S, Urman RD. Characteristics of reported adverse events during moderate procedural sedation: An update. *Jt Comm J Qual Patient Saf.* 2018;44(11):651–662. doi:10.1016/j.jcjq.2018.03.011
- Crocker TF, Lam N, Jordão M, et al. Risk-of-bias assessment using Cochrane's revised tool for randomized trials (RoB 2) was useful but challenging and resource-intensive: Observations from a systematic review. *J Clin Epidemiol.* 2023;161:39–45. doi:10.1016/j.jclinepi.2023.06.015
- Abdolrazaghejad A, Banaie M. Fentanyl-midazolam vs midazolam-ketamine regarding patient sedation analgesia for emergency orthopedic procedures. *Bangladesh J Pharmacol.* 2017;12(2):180–185. doi:10.3329/bjpp.v12i2.30381
- Akhlaghi N, Payandemehr P, Yaseri M, Akhlaghi AA, Abdolrazaghejad A. Premedication with midazolam or haloperidol to prevent recovery agitation in adults undergoing procedural sedation with ketamine: A randomized double-blind clinical trial. *Ann Emerg Med.* 2019;73(5):462–469. doi:10.1016/j.annemergmed.2018.11.016
- Amini A, Arhami Dolatabadi A, Kariman H, et al. Low-dose fentanyl, propofol, midazolam, ketamine and lidocaine combination vs regular dose propofol and fentanyl combination for deep sedation induction: A randomized clinical trial. *Emergency (Tehran).* 2018;6(1):e57. PMID:30584573. PMCID:PMC6289150.
- Andolfatto G, Abu-Laban RB, Zed PJ, et al. Ketamine-propofol combination (ketofol) versus propofol alone for emergency department procedural sedation and analgesia: A randomized double-blind trial. *Ann Emerg Med.* 2012;59(6):504–512.e2. doi:10.1016/j.annemergmed.2012.01.017
- Arhami Dolatabadi A, Memary E, Shojaee M, Kamalifard H. Dexmedetomidine-fentanyl versus midazolam-fentanyl in pain management of distal radius fractures reduction: A randomized clinical trial. *Emerg (Tehran).* 2018;6(1):e10. PMID:29503835. PMCID:PMC5827042.
- Bahreini M, Talebi Garekani M, Sotoodehnia M, Rasooli F. Comparison of the efficacy of ketamine-propofol versus sodium thiopental-fentanyl in sedation: A randomised clinical trial. *Emerg Med J.* 2021;38(3):211–216. doi:10.1136/emermed-2020-209542
- Blaivas M, Adhikari S, Lander L. A prospective comparison of procedural sedation and ultrasound-guided interscalene nerve block for shoulder reduction in the emergency department. *Acad Emerg Med.* 2011;18(9):922–927. doi:10.1111/j.1553-2712.2011.01140.x
- Burton JH, Bock AJ, Strout TD, Marcolini EG. Etomidate and midazolam for reduction of anterior shoulder dislocation: A randomized, controlled trial. *Ann Emerg Med.* 2002;40(5):496–504. doi:10.1067/mem.2002.126607
- Sterne JAC, Savović J, Page MJ, et al. RoB 2: A revised tool for assessing risk of bias in randomised trials. *BMJ.* 2019;366:14898. doi:10.1136/bmj.l4898.
- Chan K, Ho H. Etomidate and midazolam for procedural sedation in the emergency department of Queen Elizabeth Hospital: A randomised controlled trial. *Hong Kong J Emerg Med.* 2008;15(2):75–87. doi:10.1177/102490790801500203
- Coll-Vinent B, Sala X, Fernández C, et al. Sedation for cardioversion in the emergency department. *Ann Emerg Med.* 2003;42(6):767–772. doi:10.1016/S0196-0644(03)00510-9
- Deitch K, Miner J, Chudnofsky CR, Dominici P, Latta D. Does end tidal CO₂ monitoring during emergency department procedural sedation and analgesia with propofol decrease the incidence of hypoxic events? A randomized controlled trial. *Ann Emerg Med.* 2010;55(3): 258–264. doi:10.1016/j.annemergmed.2009.07.030
- Deitch K, Chudnofsky CR, Dominici P, Latta D, Salamanca Y. The utility of high-flow oxygen during emergency department procedural sedation and analgesia with propofol: A randomized controlled trial. *Ann Emerg Med.* 2011;58(4):360–364.e3. doi:10.1016/j.annemergmed.2011.05.018
- Arhami Dolatabadi A, Mohammadian A, Kariman H. Lidocaine-midazolam-fentanyl combination in controlling pain for reduction of anterior shoulder dislocation: A randomized clinical trial. *Emergency (Tehran).* 2018;6(1):e24. PMID:30009226. PMCID:PMC6036533.
- Dunn MJG, Mitchell R, DeSouza CLB, Drummond GB, Waite A. Recovery from sedation with remifentanyl and propofol, compared with morphine and midazolam, for reduction in anterior shoulder dislocation. *Emerg Med J.* 2011;28(1):6–10. doi:10.1136/emj.2008.067652
- Fathi M, Moezzi M, Abbasi S, Farsi D, Zare MA, Hafezimoghadam P. Ultrasound-guided hematoma block in distal radial fracture reduction: A randomised clinical trial. *Emerg Med J.* 2015;32(6):474–477. doi:10.1136/emermed-2013-202485
- Ferguson I, Bell A, Treston G, New L, Ding M, Holdgate A. Propofol or ketofol for procedural sedation and analgesia in emergency medicine: The POKER Study. A randomized double-blind clinical trial. *Ann Emerg Med.* 2016;68(5):574–582.e1. doi:10.1016/j.annemergmed.2016.05.024

25. Genzlinger MA, Salen P, Grossman M, Stehly C, Stoltzfus J. 145 “Put Me Out Doc”: Ketamine versus etomidate for the reduction of orthopedic dislocations. *Ann Emerg Med.* 2012;60(4 Suppl):S52–S53. doi:10.1016/j.annemergmed.2012.06.122
26. Gharavifard M, Tafakori A, Zamani Moghadam H. Remifentanyl versus fentanyl/midazolam in painless reduction of anterior shoulder dislocation: A randomized clinical trial. *Emergency (Tehran).* 2016;4(2):92–96. PMID:27274520. PMCID:PMC4893758.
27. Hatamabadi HR, Arhami Dolatabadi A, Derakhshanfar H, Younesian S, Ghaffari Shad E. Propofol versus midazolam for procedural sedation of anterior shoulder dislocation in emergency department. *Trauma Mon.* 2015;20(2):e13530. doi:10.5812/traumamon.13530
28. Holger JS, Satterlee PA, Haugen S. Nursing use between 2 methods of procedural sedation: Midazolam versus propofol. *Am J Emerg Med.* 2005;23(3):248–252. doi:10.1016/j.ajem.2005.01.001
29. Hunt GS, Spencer MT, Hays DP. Etomidate and midazolam for procedural sedation: Prospective, randomized trial. *Am J Emerg Med.* 2005;23(3):299–303. doi:10.1016/j.ajem.2005.02.042
30. Jamal SM, Fathil SM, Nidzwani MM, Ismail AK, Yatim FM. Intravenous ketamine is as effective as midazolam/fentanyl for procedural sedation and analgesia in the emergency department. *Med J Malaysia.* 2011;66(3):231–233. PMID:22111446.
31. Monsef Kasmaee V, Zia Zibari SM, Aghajani Nargesi M. Remifentanyl versus propofol/fentanyl combination in procedural sedation for dislocated shoulder reduction: A clinical trial. *Arch Acad Emerg Med.* 2019;7(1):e10. PMID:30847445. PMCID:PMC6377222.
32. Lemoel F, Contenti J, Giolito D, et al. Adverse events with ketamine versus ketofol for procedural sedation on adults: A double-blind, randomized controlled trial. *Acad Emerg Med.* 2017;24(12):1441–1449. doi:10.1111/acem.13226
33. Mahshidfar B, Asgari-Darian A, Ghafouri HB, Ersoy G, Yasinzadeh MR. Reduction of anterior shoulder dislocation in emergency department: Is Entonox® effective? *Bioimpacts.* 2011;1(4):237–240. PMID:23678434
34. Massaeli M, Nasouhi S, Bahrani H, et al. Comparison of sedatives for the reduction of shoulder dislocation based on bispectral index system in emergency department: A randomized, three-group, double-blinded clinical trial. *J Adv Med Biomed Res.* 2022;30(142):407–416. doi:10.30699/jamb.30.142.3
35. Messenger DW, Murray HE, Dungey PE, Van Vlymen J, Sivilotti MLA. Subdissociative-dose ketamine versus fentanyl for analgesia during propofol procedural sedation: A randomized clinical trial. *Acad Emerg Med.* 2008;15(10):877–886. doi:10.1111/j.1553-2712.2008.00219.x
36. Miner JR, Biros M, Krieg S, Johnson C, Heegaard W, Plummer D. Randomized clinical trial of propofol versus methohexital for procedural sedation during fracture and dislocation reduction in the emergency department. *Acad Emerg Med.* 2003;10(9):931–937. doi:10.1197/S1069-6563(03)00310-5
37. Miner JR, Biros MH, Seigel T, Ross K. The utility of the bispectral index in procedural sedation with propofol in the emergency department. *Acad Emerg Med.* 2005;12(3):190–196. doi:10.1197/j.aem.2004.10.004
38. Miner JR, Danahy M, Moch A, Biros M. Randomized clinical trial of etomidate versus propofol for procedural sedation in the emergency department. *Ann Emerg Med.* 2007;49(1):15–22. doi:10.1016/j.annemergmed.2006.06.042
39. Miner JR, Gray RO, Stephens D, Biros MH. Randomized clinical trial of propofol with and without alfentanil for deep procedural sedation in the emergency department. *Acad Emerg Med.* 2009;16(9):825–834. doi:10.1111/j.1553-2712.2009.00487.x
40. Miner JR, Gray RO, Bahr J, Patel R, McGill JW. Randomized clinical trial of propofol versus ketamine for procedural sedation in the emergency department. *Acad Emerg Med.* 2010;17(6):604–611. doi:10.1111/j.1553-2712.2010.00776.x
41. Miner JR, Moore JC, Plummer D, Gray RO, Patel S, Ho JD. Randomized clinical trial of the effect of supplemental opioids in procedural sedation with propofol on serum catecholamines. *Acad Emerg Med.* 2013;20(4):330–337. doi:10.1111/acem.12110
42. Miner JR, Moore JC, Austad EJ, Plummer D, Hubbard L, Gray RO. Randomized, double-blinded, clinical trial of propofol, 1:1 propofol/ketamine, and 4:1 propofol/ketamine for deep procedural sedation in the emergency department. *Ann Emerg Med.* 2015;65(5):479–488.e2. doi:10.1016/j.annemergmed.2014.08.046
43. Miner JR, Driver BE, Moore JC, et al. Randomized clinical trial of propofol versus alfentanil for moderate procedural sedation in the emergency department. *Am J Emerg Med.* 2017;35(10):1451–1456. doi:10.1016/j.ajem.2017.04.041
44. Nashibi M, Mottaghi K, Faraji M, Delavari A, Taghipour H, Amiri M. Comparison of analgesic and sedative effects of ketamine-propofol (ketofol) and fentanyl-midazolam (fentazolam) combinations in outpatient orthopedic procedures. *Trauma Mon.* 2017;22(5):e41315. doi:10.5812/traumamon.41315
45. Nejati A, Moharari RS, Ashraf H, Labaf A, Golshani K. Ketamine/propofol versus midazolam/fentanyl for procedural sedation and analgesia in the emergency department: A randomized, prospective, double-blind trial. *Acad Emerg Med.* 2011;18(8):800–806. doi:10.1111/j.1553-2712.2011.01133.x
46. Ozturk TC, Guneysele O, Akoglu H. Anterior shoulder dislocation reduction either with midazolam or propofol in combination with fentanyl. *Hong Kong J Emerg Med.* 2014;21(6):346–353. doi:10.1177/102490791402100602
47. Parlak M, Parlak I, Erdur B, Ergin A, Sagiroglu E. Age effect on efficacy and side effects of two sedation and analgesia protocols on patients going through cardioversion: A randomized clinical trial. *Acad Emerg Med.* 2006;13(5):493–499. doi:10.1197/j.aem.2005.12.013
48. Phillips W, Anderson A, Rosengreen M, Johnson J, Halpin J. Propofol versus propofol/ketamine for brief painful procedures in the emergency department: Clinical and bispectral index scale comparison. *J Pain Palliat Care Pharmacother.* 2010;24(4):349–355. doi:10.3109/15360288.2010.506503
49. Salen P, Grossman M, Grossman M, Milazzo A, Stoltzfus J. A comparison of ketamine versus etomidate for procedural sedation for the reduction of large joint dislocations. *Int J Crit Illn Inj Sci.* 2016;6(2):79. doi:10.4103/2229-5151.183022
50. Sawas A, Youngquist ST, Madsen TE, Davis VW. Combined ketamine and propofol sedation versus propofol sedation for emergency department procedures: A prospective randomized trial. *Ann Emerg Med.* 2013;62(4 Suppl):S76–S77. doi:10.1016/j.annemergmed.2013.07.029
51. Sener S, Eken C, Schultz CH, Serinken M, Ozsarac M. Ketamine with and without midazolam for emergency department sedation in adults: A randomized controlled trial. *Ann Emerg Med.* 2011;57(2):109–114.e2. doi:10.1016/j.annemergmed.2010.09.010
52. Soysal S, Karcioglu O, Demircan A, et al. Comparison of meperidine plus midazolam and fentanyl plus midazolam in procedural sedation: A double-blind, randomized controlled trial. *Adv Ther.* 2004;21(5):312–321. doi:10.1007/BF02850035
53. Stronati G, Capucci A, Dello Russo A, et al. Procedural sedation for direct current cardioversion: A feasibility study between two management strategies in the emergency department. *BMC Cardiovasc Disord.* 2020;20(1):388. doi:10.1186/s12872-020-01664-1
54. Tajoddini S, Motaghi M. Sedative and analgesic effects of propofol–ketamine versus propofol–fentanyl for emergency department procedures. *Hong Kong J Emerg Med.* 2022;29(4):212–219. doi:10.1177/1024907919893466
55. Taylor DM, O’Brien D, Ritchie P, Pasco J, Cameron PA. Propofol versus midazolam/fentanyl for reduction of anterior shoulder dislocation. *Acad Emerg Med.* 2005;12(1):13–19. doi:10.1197/j.aem.2004.08.039
56. Tezel O, Kaldirim U, Bilgic S, et al. A comparison of suprascapular nerve block and procedural sedation analgesia in shoulder dislocation reduction. *Am J Emerg Med.* 2014;32(6):549–552. doi:10.1016/j.ajem.2014.02.014
57. Vahidi E, Hemati R, Momeni M, Jahanshir A, Saeedi M. Comparison of sedative effectiveness of thiopental versus midazolam in reduction of shoulder dislocation. *World J Emerg Med.* 2018;9(2):125. doi:10.5847/wjem.j.1920-8642.2018.02.007
58. Wright SW, Chudnofsky CR, Dronen SC, et al. Comparison of midazolam and diazepam for conscious sedation in the emergency department. *Ann Emerg Med.* 1993;22(2):201–205. doi:10.1016/S0196-0644(05)80203-3
59. Brown TB, Lovato LM, Parker D. Procedural sedation in the acute care setting. *Am Fam Physician.* 2005;71(1):85–90. PMID:15663030.
60. Goodchild CS, Serrao JM. Propofol-induced cardiovascular depression: Science and art. *Br J Anaesth.* 2015;115(4):641–642. doi:10.1093/bja/aeV320

61. Bilotta F, Fiorani L, La Rosa I, Spinelli F, Rosa G. Cardiovascular effects of intravenous propofol administered at two infusion rates: A trans-thoracic echocardiographic study. *Anaesthesia*. 2001;56(3):266–271. doi:10.1046/j.1365-2044.2001.01717-5.x
62. Hailu S, Getachew H, Hailu S, et al. Effectiveness of ketofol versus propofol induction on hemodynamic profiles in adult elective surgical patients: A randomized controlled trial. *Int J Surg Open*. 2021; 37:100392. doi:10.1016/j.ijso.2021.100392
63. Bellolio MF, Gilani WI, Barrionuevo P, et al. Incidence of adverse events in adults undergoing procedural sedation in the emergency department: A systematic review and meta-analysis. *Acad Emerg Med*. 2016;23(2):119–134. doi:10.1111/acem.12875
64. Alqassab EH, Alzanitan AI, Alghamdi SB, et al. Adverse events rate in adults having procedural sedation in the emergency department: A systematic review and meta-analysis. *Ann Med Health Sci Res*. 2020;10:970–979. <https://www.amhsr.org/articles/adverse-events-rate-in-adults-having-procedural-sedation-in-the-emergency-department-a-systematic-reviewand-metaanalysis-6435.html>.