

# Etomidate versus propofol for sedation in gastrointestinal endoscopy

### A systematic review and meta-analysis of outcomes

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#### Abstract

**Background:** Propofol is increasingly being used for sedation in gastrointestinal endoscopy; however, owing to its side effects, an alternative drug is needed. We aimed to compare the safety, satisfaction, and efficacy outcomes of etomidate versus propofol in patients undergoing gastrointestinal endoscopy, including advanced endoscopic procedures.

**Methods:** We systematically searched Embase, PubMed, Cochrane Central Register of Controlled Trials, CINAHL (via EBSCO), China National Knowledge Infrastructure, and Web of Science (1946–April 2020) databases for randomized controlled trials of gastrointestinal endoscopy (upper gastrointestinal endoscopy, colonoscopy, and advanced endoscopy) using etomidate or propofol as sedatives. We pooled odds ratios (ORs) for the safety profile and patient and anesthesiologist satisfaction using mixed-effects conditional logistic models and standardized mean differences for efficiency outcomes using random-effects models.

**Results:** Twenty-four studies involving 3875 patients were included. Compared with propofol, etomidate resulted in significantly reduced apnea (OR: 0.22; 95% confidence interval [CI]: 0.13–0.37; P < .001), hypoxemia (OR: 0.43; 95% CI: 0.35–0.54; P < .001), hypotension (OR: 0.20; 95% CI: 0.11–0.36; P < .001), and bradycardia (OR: 0.52; 95% CI: 0.30–0.91; P = .02) but led to increased myoclonus (OR: 8.54; 95% CI: 5.20–14.01; P < .001) and lowered anesthesiologist satisfaction (OR: 0.60; 95% CI: 0.39–0.91; P = .02).

**Conclusion:** Etomidate may be a good alternative to propofol for gastrointestinal endoscopy, especially advanced endoscopy. Etomidate appears to be safe as an inducer for hemodynamically unstable patients or older adult patients undergoing gastrointestinal endoscopy.

**Abbreviations:** CI = confidence interval, OR = odds ratio, RCT = randomized controlled trial, WMD = weighted mean difference. **Keywords:** anesthesia, endoscopy, hemodynamic, intravenous anesthetic agent, respiratory stability

#### 1. Introduction

Sedation is preferred over anesthesia during gastrointestinal endoscopy to minimize patient discomfort and allow examination in a stable state.<sup>[1–3]</sup> To successfully implement therapeutic endoscopy, the selection of an appropriate sedative is crucial for patient safety, patient and physician satisfaction, and maximum efficacy.

Currently, the most commonly used sedatives are midazolam and propofol. In a 2006 survey in the US, midazolam and propofol were used for endoscopy in approximately 75% and 25% of the patients, respectively.<sup>[4]</sup> In a 2016 South Korean survey, propofol was used for gastroscopy in approximately 54% of cases.<sup>[5]</sup> Propofol has amnesic characteristics, the advantage of a short recovery time due to rapid induction of sedation, and high metabolic clearance but also has side effects such as hypotension, respiratory depression, and injection pain.<sup>[6-9]</sup> Additionally, because of the narrow therapeutic window,

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

propofol can induce an unintentional deep sedation state, and there is no antagonist. Especially in high-risk procedures and therapeutic endoscopy requiring a long procedure time, the demand for propofol is inevitably high, causing concerns about dose-dependent side effects.<sup>[10]</sup> Contrarily, etomidate has been used as a relatively stable drug to induce anesthesia in hemodynamically unstable patients and is being considered as an alternative to propofol.

Meta-analyses on the 2 drugs are scarce; most of the studies are from China, and none have included advanced endoscopic procedures. Recently, studies comparing the 2 drugs for diagnostic endoscopy and advanced endoscopic procedures have demonstrated different results. Thus, we conducted a meta-analysis to compare the safety, patient and anesthesiologist satisfaction, and efficacy of propofol and etomidate for optimal sedation in gastrointestinal endoscopy, including advanced endoscopy.

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#### 2. Methods

This systematic review and meta-analysis were conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines.<sup>[11]</sup> The protocol for this systematic review was prospectively registered with PROSPERO (CRD42020184276).

#### 2.1. Literature search and selection

The following databases were systematically searched: Embase, PubMed, the Cochrane Central Register of Controlled Trials, CINAHL (via EBSCO), China National Knowledge Infrastructure, and Web of Science (from 1946 to April 2020). Supplementary data and clinicaltrials.gov for unpublished trials were assessed for potentially eligible studies, including a manual search among conference proceedings between 2001 and 2020.

The keywords used were "colonoscopy" OR "colonoscopies" OR "colonoscopes" OR "endoscopy" OR "diagnostic" OR "procedure" OR "technique" OR "advanced" OR "EUS" OR "ERCP" OR "EMR" OR "ESD" OR "endoscopic submucosal dissection" OR "FNA" OR "endoscopic ultrasound" OR "endoscopic retrograde cholangiopancreatography" OR "endoscopic mucosal resection" OR "fine needle aspiration" OR "endoscopic retrograde cholangiopancreatography" OR "endoscopic mucosal resection" OR "fine needle aspiration" OR "intervention" OR "gastrointestinal" OR "gastroscopy." The results were combined with search terms for the sedatives used ("etomidate" AND "propofol"). Additionally, the reference lists from the retrieved articles were manually searched to identify any missed studies. No language restrictions were applied. For non-English papers, we consulted a professional translator.

Both authors independently reviewed the titles and abstracts of all identified and relevant citations that were aggregated and categorized using EndNote X8 (Thomson Reuters, New York, NY). The inclusion criteria were as follows: prospective randomized controlled trials (RCTs); studies including adults aged ≥18 years who underwent a scheduled elective outpatient gastrointestinal endoscopy; studies comparing a propofol-based sedative regimen with an etomidate-based regimen; and studies assessing the incidence of sedation-related side effects, satisfaction, or efficacy measures as outcomes of interest. We excluded the following studies: non-RCTs, reviews, nonclinical studies, conference abstracts, and case observations; studies with groups that received etomidate plus propofol or propofol plus etomidate; studies reporting the results of a combination of various endoscopic procedures (upper gastrointestinal endoscopy, colonoscopy, and advanced endoscopy); and studies not reporting at least 1 outcome of interest.

#### 2.2. Outcome measures

The primary outcome was the safety profile of etomidate and propofol (hypotension, bradycardia, myoclonus, hypoxemia, and apnea). Secondary outcomes were satisfaction or efficacy (patient satisfaction, anesthesiologist-reported satisfaction, and procedure time) (see Table S1, Supplemental Digital Content, http://links.lww.com/MD/I434).

## 2.3. Data extraction and quality assessment in individual studies

Both authors extracted the following data independently from each study: author names, journal, year of publication, country of origin, study population, sample size, study design, patient characteristics (age, sex), sedative characteristics (sedative regimen, protocol, administrator), and primary and secondary study outcomes (number of adverse events per group, time of measurement, satisfaction). Any disagreements in trial eligibility or data extraction between the 2 authors were resolved via consensus. Data were collected from all studies for the full analysis set.

#### 2.4. Methodological quality appraisal

Both authors independently evaluated the methodological quality of all included trials according to the Cochrane Collaboration's Risk of Bias assessment tool Version 2<sup>[12]</sup> using the following methodological parameters: randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, selection of appropriate reported findings, and overall risk of bias (see Figure S1, Supplemental Digital Content, http://links.lww.com/MD/ I437).

#### 2.5. Quality assessment and risk of bias

Both authors performed this analysis independently using the Cochrane risk-of-bias tool. Disagreements were resolved through discussions. We recorded the method used to generate the randomization schedule and conceal treatment allocation; whether blinding was implemented for participants, personnel, and outcome assessment; and whether there was evidence of incomplete outcome data and selective reporting of outcomes.

#### 2.6. Data synthesis and statistical analyses

Data analyses were performed using Review Manager Version 5.3 (RevMan v 5.3, The Cochrane Collaboration, Oxford, UK) and Comprehensive Meta-Analysis 3.3.070 (Biostat, Englewood, NJ).<sup>[13]</sup> We also performed 2 additional sets of sensitivity analyses: meta-analyses of only older patients and meta-analyses excluding studies with older adults and patients with obesity. A weighted random-effects meta-analysis was performed to compare etomidate with propofol.<sup>[14]</sup> The relative risk of each outcome was used as the primary outcome measure. The results were presented as forest plots.  $I^2$  values were used to evaluate the heterogeneity. An  $I^2$  value > 50% was considered significantly heterogeneous. Publication bias was tested using funnel plots, and P < .05 was considered significant (see Figure S2, Supplemental Digital Content, http:// links.lww.com/MD/I438). In this study, ethical approval was not necessary because the included data were based on previously published articles, and no original clinical data were collected or utilized.

#### 3. Results

#### 3.1. Study and patient characteristics

Figure 1 shows the Preferred Reporting Items for Systematic Reviews and Meta-Analysis flow diagram for the selection process. The initial search strategy identified 16,163 citations. We excluded 11,423 studies by eliminating duplicates and irrelevant studies. After a full-text review of the remaining 64 reports, we identified 24 studies that met the inclusion criteria.[15-38] The characteristics of the included RCTs are presented in Table 1. These studies were published between 2006 and 2020 and investigated a total of 3875 patients: 1913 received etomidate and 1962 received propofol. Twelve studies involved esophagogastroduodenoscopy (2640 patients), 5 involved colonoscopy (534 patients), and 7 involved advanced endoscopy (701 patients). Of the 7 studies involving advanced endoscopy, 4 included endoscopic retrograde cholangiopancreatography (347 patients), 2 included endoscopic ultrasonography (168 patients), and 1 involved a mixture of advanced endoscopy procedures (186 patients).



Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram of assessment procedures.

#### 3.2. Primary outcome (adverse events)

**1.3.2.** *Myoclonus.* Twenty studies (3445 patients) were analyzed. Overall, the etomidate group had a significantly higher proportion of patients with myoclonus than did the propofol group (255/1719 [14.8%] vs 28/1726 [1.6%]; odds ratio [OR]: 8.54; 95% confidence interval [CI]: 5.20–14.01; P < .001; Fig. 2). Subgroup analysis indicated significantly increased myoclonus in the etomidate group compared with the propofol group for each subgroup (upper gastrointestinal endoscopy, colonoscopy, and advanced endoscopy) (Fig. 2).

**2.3.2.** Apnea. Eleven studies (1900 patients) were analyzed. Overall, the etomidate group had a significantly lower side effect of apnea than did the propofol group (25/946 [2.64%] vs 82/954 [8.60%]; OR: 0.22; 95% CI: 0.13–0.37; P < .001; Fig. 2). A low level of heterogeneity across the studies was noted ( $I^2 = 0\%$ ; P = .85). Subgroup analysis indicated significantly decreased apnea with the etomidate group compared with the propofol group for all subgroups.

**3.3.2.** *Hypoxemia.* Sixteen studies (3205 patients) were analyzed. Overall, the etomidate group had a significantly lower hypoxemia side effect than did the propofol group (182/1599 [11.38%] vs 335/1606 [20.86%]; OR: 0.45; 95% CI: 0.36–0.55; P < .001; Fig. 2). A low level of heterogeneity across the studies was noted ( $I^2 = 0\%$ ; P = .83). Subgroup analysis indicated that etomidate provided significantly decreased hypoxemia compared with propofol for advanced endoscopy (OR 0.34; 95% CI 0.16–0.69; P = .003) and upper gastrointestinal endoscopy (OR 0.46; 95% CI 0.36–0.58; P < .001), but no difference was found for colonoscopy (OR 0.44; 95% CI 0.15–1.29; P = .14). The  $I^2$  was 0% both for upper gastrointestinal endoscopy and colonoscopy and 9% for advanced endoscopy.

**4.3.2.** *Hypotension.* Twenty studies (3428 patients) were analyzed. Overall, the etomidate group had a significantly lower hypotension side effect than did the propofol group (92/1711 [5.38%] vs 298/1717 (17.36%); OR: 0.20; 95% CI: 0.11–0.36; P < .001; Fig. 2). A high level of heterogeneity across the studies was noted ( $I^2 = 70\%$ ; P < .001). Subgroup analysis indicated significantly decreased hypotension with the etomidate group compared with the propofol group for all subgroups (upper gastrointestinal endoscopy, colonoscopy, and advanced endoscopy) (Fig. 2). The  $I^2$  was 82%, 55%, and 0% for upper gastrointestinal endoscopy, colonoscopy, and advanced endoscopy, respectively.

**5.3.2.** Bradycardia. Thirteen studies (1521 patients) were analyzed. Overall, the etomidate group had a significantly lower bradycardia side effect than did the propofol group (34/760 [4.47%] vs 70/761 [9.20%]; OR: 0.52; 95% CI: 0.30–0.91; P = .02; Fig. 2). Heterogeneity across the studies was noted ( $I^2 = 23\%$ ; P = .21). However, subgroup analysis indicated no significant difference in bradycardia between the propofol and etomidate groups for each subgroup (upper gastrointestinal endoscopy, colonoscopy, and advanced endoscopy).

#### 3.3. Secondary outcomes (anesthetic performance)

**1.3.3.** Patient satisfaction. Twelve studies (2620 patients) were analyzed. No significant difference was observed in patient satisfaction between the propofol and etomidate groups (OR: 1.071; 95% CI: 0.710–1.614; P = .745; Fig. 3); heterogeneity was observed across the studies ( $I^2 = 43.2\%$ ; P = .062).

**2.3.3.** Anesthesiologist satisfaction. Four studies (1615 patients) were analyzed, all on upper gastrointestinal endoscopy. The etomidate group had a significantly lower physician satisfaction than did the propofol group (688/805 [85.47%] vs 729/810 [90%]; OR: 0.60; 95% CI: 0.39–0.91; P = .02; Fig. 3); heterogeneity was observed across the studies ( $I^2 = 36\%$ ).

**3.3.3. Procedure time.** Seventeen studies (3110 patients) were analyzed. No overall difference in procedure time was observed between propofol and etomidate (weighted mean difference [WMD]: -0.03 min; 95% CI: -0.17-0.12; P = .71; Fig. 3). Heterogeneity across the studies was noted ( $I^2 = 18\%$ ; P = .24). However, subgroup analysis indicated that etomidate had a significantly shorter procedure time than did propofol for advanced endoscopy (WMD: -2.15 min; 95% CI: -4.11--0.19; P = .03; Fig. 3) but a longer procedure time for colonoscopy (WMD: 1.40 min; 95% CI: 0.13-2.68; P = .03; Fig. 3); no difference was found for upper gastrointestinal endoscopy (WMD: 0.00 min; 95% CI: -0.07-0.08; P = .91; Fig. 3).  $I^2$  was 0% for both upper gastrointestinal endoscopy and colonoscopy and 17% for advanced endoscopy.

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Sr.		Country and number of	Sample size		Study			Sex	Body weight			Sex			
ē   -	Shen et al, 2015 <sup>[14]</sup>	Centers China, 1 site	715 (355:360)	Gastrointesti- nal endos-	Elderly patients	Remifentanil + etomidate	<b>Age (yr)</b> 66.3 ± 4.87	200/155	<b>or BMI</b> BMI 21.58±3.45	Remifentanil + propofol	<b>Age (yr)</b> 66.31 ± 6.9	203/157	<b>BW OF BWI</b> BMI 21.86 ± 3.4	a, b, c, d, e, f, g	E: 0.4–0.6 µg/kg remifentanil, etomidate at 0.1–0.15 mg/kg followed by
2	Meng et al, 2016 <sup>(15)</sup>	China, 1 site	100 (50:50)	copy Gastrointesti- nal endos- copy	Elderly patients	Fentanyl + etomidate	69.7 (65–80)	25/25	BW 62.4 (52–82)	Fentanyl + propofol	68.4 (65–78)	24/26	BW 60.7 6 (50–84)	a, d, e, f, g, h	<ul> <li>4-0mg</li> <li>P: 0.4-0.6 µg/kg remifentanil, propofol at 1-2 mg/kg followed by 20-40 mg</li> <li>E: 1.0 µg/kg fentanyl, etomidate at 0.15-0.2 mg/kg followed by 0.4 µg/kg/h</li> <li>P: 1.0 µg/kg fentanvl. propofol at 1.5-</li> </ul>
n	Liu et al, 2017a	China, 1 site	14 5 (72:73)	Gastrointesti- nal endos- copy	Adult patients (aged 18–80 yr)	Fentanyl + etomidate	51.1 ± 14.2	38/34	BW 67.2 ±13.9	Fentanyl + propofol	<b>48.4</b> ± 10.8	34/39	3W 66.6 ±14.3	d, f	<ol> <li>D. Bug/kg, 4.0 mg/kg/h maintenance dose of propofol</li> <li>E: 0.8 mg/kg fentanyl, etomidate induction at 0.3 mg/kg, maintenance influsion of 0.06 mg/kg</li> </ol>
4	Xiao 2018 <sup>[16]</sup>	China, 1 site	300 (150:150)	Gastrointesti- nal endos- copy	Overweight or obese patients	Remifentanil 4 + etomidate	<b>1</b> 4.54 ± 10.02	101/49	BMI 28.53 ±2.21	Remifentanil + propofol	43.67 ± 9.13	103/47	BMI 28.75 ±2.48	a, b, c, d, e, f, g	<ul> <li>T–2mg/kg, 0.50 mg/kg maintenance 1–2mg/kg, 0.50 mg/kg maintenance dose of proportion</li> <li>E: 0.4–0.6 µg/kg followed by at 0.1–0.15 mg/kg followed by</li> <li>P-0.4.0.6 mg/kg comisorianit proportion</li> </ul>
Q	Toklu et al, 2009 <sup>(18]</sup>	Turkey, 1 site	60 (30:30)	Colonoscopy	Adult patients (aged 18–65 yr)	Remifentanil + etomidate	48 ± 11 (28–65)	12/18	BW 72±12 (51–95)	Remifentanil + propofol	51 ± 11 (21-64)	13/17	BW 68±11 (48-87)	c, d, e, g, h	<ul> <li>Cut-Duby/Ng remining proportion at 1–2 mg/kg followed by 20–40 mg E: 0.1 µg/kg/min remifentanil, etomidate at 0.1 mg/kg followed by 0.05 mg/kg</li> <li>P: 0.1 µg/kg/min remifentanil, proporoi</li> </ul>
9 9	3anihashem et al, 2015 <sup>[19]</sup>	Iran, 1 site	90 (43:47)	Colonoscopy	Adult patients (aged 18–55 yr)	Fentanyl + etomidate	$36.6 \pm 9.7$	23/20	NA	Fentanyl + propofol	36.6±11.4	23/24	NA	c, e	at 0.5 mg/kg followed by 0.25 mg/kg E: 1 µg/kg fentanyl, etomidate at 0.1 mg/ kg (15 µg/kg/min) P: 1 µg/kg fentanyl, propofol at 0.5 mg/
~	Lee et al, 2019 <sup>/20]</sup>	South Korea, 1 site	200 (1 00:100)	Colonoscopy	Adult patients	Etomidate + E midazolam	58.17 ± 16.28	54/46	BMI 23.14 ±3.23	Propofol + midazolam	57.14±14.5	50/50	BMI 8 23.83±3.52	a, c, d, f, g, h	kg (25 µg/kg/min) E: 0.05 mg/kg midazolam, etomidate at 0.1 mg/kg followed by 0.05 mg/kg P: 0.05 mg/kg midazolam, propofol at
$\infty$	Lee et al, 2018 <sup>[21]</sup>	South Korea, 1 site	124 (62:62)	Colonoscopy	Elderly patients	Etomidate + midazolam	$71.37 \pm 5.20$	41/21	BMI 23.32 ± 3.02	Propofol + midazolam	71.26±4.53	37/25	BMI 24.84 ±2.97	a, c, d, f, g	<ul> <li>0.5 mg/kg followed by 0.25 mg/kg</li> <li>E: 0.035 mg/kg midazolam, etomidate at 0.07 mg/kg followed by 0.035 mg/kg</li> <li>P: 0.035 mg/kg midazolam, propofol at</li> </ul>
o	Wu et al, 2017 <sup>[22]</sup>	China, 1 site	40 (20:20)	Endoscopic ultraso- nography	Adult patients	Fentanyl + etomidate	51.3±10.7	11/9	BMI 22.4±3.5	Fentanyl + propofol	50.7 ± 11.4	8/12	BMI 22.7 ± 3.6	c, d, f, g	<ul> <li>0.35 mg/kg followed by 0.175 mg/kg</li> <li>E: 0.5 µg/kg fentanyl, etomidate at</li> <li>0.3 mg/kg followed by 0.8–1.0 mg/kg/h</li> <li>P: 0.5 µg/kg fentanyl, propofol at</li> <li>2.0 marka, 4.0–6.0 marka/h</li> </ul>

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Table 1

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(Continued)

Contil	rued)	bue wat					Etomidate	group			Propofol (	group			
Sr. no. St	coun num udy cer	ntry and ther of the second second second	Sample size (E:P)	Operation	Study population	Regimen	Age (yr)	Sex (M/F)	Body weight or BMI	Regimen	Age (yr)	Sex (M/F)	BW or BMI	Outcomes	Protocol
10 Kim 21	et al, South 017 <sup>[23]</sup>	h Korea, 1 site	128 (64:64)	Endoscopic ultraso- nography	Adult patients	Etomidate	54.17±14.47	29/35	BMI 23.42 ± 4.13	Propofol	49.83 ± 16.91	33/31	BMI 23.51 ± 4.31	a, c, d, e, f, g, h	E: etomidate at 0.1 mg/kg followed by 0.05 mg/kg P: propotol at 0.5 mg/kg followed by
11 Sonç 2	j et al, China 015 <sup>[24]</sup>	a, 1 site	80 (40:40)	ERCP	Adult patients	Etomidate + midazolam	55.8±10.6	28/12	BW 62.4±11.4	Propofol + midazolam	52.4±11.4	28/12	BW 63.5±11.8	a, c, d, e, f, g, h	<ul> <li>U.Z.DIIIG/KQ</li> <li>E: 0.5 µg/kg fentanyl, etomidate at 0.3 mg/kg followed by 0.8–1.0 mg/ kg/h</li> <li>P: 0.5 µg/kg fentanyl, propofol at</li> </ul>
12 Park 21	t et al, South 018 <sup>[25]</sup> 1	h Korea, 1 site	127 (64:63)	ERCP	Adult patients	Midazolam + meperidine + etomidate	59.2±17.4	35/29	BMI 24.6±4.2	Midaz- olam + meperidine + nronofol	62.7±17.8	25/38	BMI 24.1 ± 4.0	a, c, d, e, f, g, h	<ol> <li>2.0 mg/kg, 4.0-6.0 mg/kg/h</li> <li>E: 1 μg/kg fentanyl, etomidate at 0.3 μg/mL</li> <li>P: 1 μg/kg fentanyl, propofol at 3 μg/mL</li> </ol>
13 Han 21	et al, South 319 <sup>[26]</sup>	h Korea, 1 site	186 (92:94)	ERCP, ESD, multiple EMR	Adult patients	Midazolam + fentanyl + etomidate	$60.6 \pm 12.84$	61/31	BMI 23.9±2.98	H fentanyl + propofol	63.9 ± 13.06	62/32	BMI 23.0±3.34	a, c, d, f, g, h	<ul> <li>T. E. O.5 µg/kg remifentanil, etomidate at 0.15–0.3 mg/kg followed by 7.5 mg P: 0.5 µg/kg remifentanil, propofol at 1.0–2.0 mo/kg followed hv 15 mg</li> </ul>
14 Jair 2	et al, India 020 <sup>[27]</sup>	a, 1 site	60 (30:30)	ERCP	Adult patients (ASA grade IIII, aged 18–70 yr, weight 45–90 kn)	Dexmede- tomidine + midazolam + butorphanol etomidate	AN	NA	MA	Dexmede- tomidine + midazolam + butorpha- nol propofol	AN	NA	AN	a, d	<ul> <li>E: 50 µg fentaryl, etomidate 6–10 mL</li> <li>E: 50 µg fentaryl, etomidate 6–10 mL</li> <li>(0.2%) followed by 1/3–1/4 of the initial dose</li> <li>P: 50 µg fentaryl, propofol 6–10 mL</li> <li>(1%) followed by 1/3–1/4 of the initial dose</li> </ul>
15 Wan 2	g et al, China 011 <sup>[28]</sup>	a, 1 site	60 (30:30)	Colonoscopy	Adult patients (ASA grade 1–2, aged 18– 70 yr, weight 40–80 km	Fentanyl + etomidate	43±10	14/16	BW 59±12	Fentanyl + propofol	45±9	15/15	BW 62±12	f, g, h	E: 5 mg sufentanil, etomidate at 0.2 mg/ kg P: 5 mg sufentanil, propofol at 0.2 mg/kg
16 2	et al, China 319 <sup>[29]</sup>	a, 1 site	200 (100:100)	Gastrointesti- nal endos- copy	Elderly patients (62–73)	Remifentanil + etomidate	63.8±5.2	NA	BW 77.64±9.04	Remifentanil + propofol	$62.5 \pm 6.8$	NA	BW 78.26±7.91	f, g	E: 0.5 µg/kg fentanyl, etomidate at 0.2 µg/kg P: 0.5 µg/kg fentanyl, propofol at 1.5
17 Xu 2	et al, Ct 015 <sup>[30]</sup> 1	hina, site	200 (100:100)	Gastrointesti- nal endos- copy	Adult patients (ASA grade 1-2, aged 40-60 yr, weight 55-75 kn)	Sufentanil + etomidate	$38.2 \pm 5.8$	47/53	BW 66.5±2.6	Sufentanil + propofol	37.9±6.5	63/37	BW 65.3 ± 3.8	c, d, f	E: 2% lidecaine 2 mL, etomidate at 0.2 mg/kg followed by 5-7 mg P: 2% lidocaine 2 mL, propofol at 1.6 mg/kg
18 (	tuo Cr 017a <sup>[31]</sup> 1	hina, site	120 (60:60)	Gastrointesti- nal endos- copy	Adult patients (ASA grade 1-2, aged 22-85 yr, weight 42-82 kg)	Fentanyl + etomidate	57.20 ± 12.56	28/32	BW 63.65±6.72	Fentanyl + propofol	55.15±12.73	26/34	$BW \\ 61.87 \pm 6.43$	d, e, g, h	E: 0.1 µg/kg sufentanil, etomidate 50 mL/h (0.2%) P: 0.1 µg/kg sufentanil, propofol 50 mL/h (1%)

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<u>c</u> o	ntinued)						Etomidato	4			Dependent				
Sr. Do.	Study	Country and number of centers	Sample size (E:P)	Operation	Study population	Regimen	Age (vr)	Sex (M/F)	Body weight or BMI	Regimen	Age (vr)	Sex (M/F)	BW or BMI	Outcomes	Protocol
19	Guo et al, 2014 <sup>[32]</sup>	China, 1 site	80 (40:40)	Gastrointesti- nal endos- copy	Elderly patients (ASA grade 1-2, aged 65-77 yr, weight	Fentanyl + etomidate	AN	NA NA	MA	Fentanyl + propofol	NA	NA	NA	σ	E: 0.4–0.6 μg/kg remifentanil, etomidate at 0.1–0.15 μg/kg followed by followed by 1/3–1/4 of the initial dose P: 0.4–0.6 μg/kg remifentanil, propolol at 1–2 μg/kg followed by followed by
20	Chen 2017 <sup>[33]</sup>	China, 1 site	120 (60:60)	Gastrointesti- nal endos- copy	40-92.kg) Elderly patients p (ASA grade 1–2, yr, weight 50-80.kn/	Sufentanil + E etomidate	56.25 ± 1.89	31/29	BW 61.07 ± 1.61	Sufentanil + propofol	55.15±2.38	30/30	BW 59.69±1.38	c, d, e, g, h	<ul> <li>1.7–1.14 of the initial doss</li> <li>E: 0.05 mg/kg midazolam, 25 mg im meperidine etomidate at 0.05 mg/kg</li> <li>P: 0.05 mg/kg midazolam, propofol at 0.25 mg/kg</li> </ul>
21	Chun and Zhen 2018 <sup>34]</sup>	China, 1 site	200 (1 00:100)	Gastrointesti- nal endos- copy	Adult patients (ASA grade I–III, aged 18–65 yr, weight 40–90 kg)	Remifentanil 4 + etomidate	5.87±12.43	66/34	BMI 20.89±2.69	Remifentanil + propofol	46.05 ± 11.02	68/32	BMI 21.37 ±3.16	a, b, c, d, f, g, h	<ul> <li>E: Dexmedetomidine 1 µg/kg 2 mg midazolam, 1 mg butorphanol etomidate at 0.3 mg/kg followed by 8–10 µg/kg/min</li> <li>P: dexmedetomidine 1 µg/kg, 2 mg midazolam, 1 mg butorphanol propofol at 1.5 mg/kg followed by</li> </ul>
22	Guo et al, 2017b <sup>l35</sup>	China, 1 site	400 (200:200)	Gastrointesti- nal endos- copy	Elderly patients (ASA grade 1-3, aged 60-80 vr)	Remifentanil 6 + etomidate	37.01 ± 6.92	111/89	BMI 21.83±3.36	Remifentanil + propofol	$66.83 \pm 6.73$	113/87	BMI 21.62 ± 3.25	a, b, c, d, f, ç	100-130 gp/sg/min E: 2-2.5 mg midazolam, 30 µg/kg/min P: 2-2.5 mg midazolam, 0.3 mg/kg/min, P: 2-2.5 mg midazolam, 0.3 mg/kg/min, fallowaed by 0.12-0.18 mg/kg/min,
23	Liu et al, 2020 <sup>[36]</sup>	China, 1 site	80 (40:40)	ERCP	Adult patients (ASA grade I–III, aged 18–65 yr)	Remifentanil + dexmede- tomidine + etomidate	53±10	22/18	BW 65±13 (BMI 23.3±3.2)	Remifentanil + dexmede- tomidine + propofol	49±11	23/17	BW $68 \pm 10$ (BMI: $24.5 \pm 2.5$ )	c, g, h	<ul> <li>E. 2.0 ng/wcu 50 view 2011 view ng/mg/ E. 2.0 ng/mL remifentanil, dexmedetomidine 0.5 µg/kg/h 2min, etomidate at 0.5 µg/mL/</li> <li>P: 2.0 ng/mL remifentanil, dexmedetomidine 0.5 µg/kg/h 2min, pronofol at 2.0 nd/ml</li> </ul>
24	Liu et al, 2017b <sup>i37]</sup>	China, 1 site	60 (30:30)	Gastrointesti- nal endos- copy	Elderly patients (ASA grade 1-2, aged 60 yr)	Fentanyl + etomidate	70.1 ± 8.2	20/10	BW 69.8 ±14.3	Fentanyl + propofol	68.7 ± 5.7	18/12	BW 71.5±18.1	c, d, e, g, h	E: 1 µg/kg fentanyl, etomidate at 0.3 mg/ kg P: 1 µg/kg fentanyl, propofol at 1.5 mg/ kg
Outcc ASA = availa	imes: (a) pati = American S ble, P = prop	ent satisfaction; ( iociety of Anaesth iofol.	b) anesthesiolog iesiology, BMI =	ist satisfaction; (c) body mass index,	procedure time; (d) BW = body weight,	myoclonus; (e) a E = etomidate, E	pnea; (f) hypoxer MR = endoscopi	nia; (g) hyp c mucosal	otension; and (h) bra resection, ERCP = er	tdycardia. ndoscopic retrog	rade cholangiopar	Icreatograp	hy, ESD = endoscop	ic submucosa	dissection, F = female, M = male, NA = not

Table 1

Etomidate Propofol Odds Ratio Study or Subgroup Events Total Events Total Weight M-H Bandom 95% Cl	Odds Ratio	Etomidate Propofol Odds Ratio Odds Ratio Study of Study of Subgroup Events Total Events Total Woln't MA Random 95% C1 MAIA Random 95% C1
Are GO         Central         Central <thcentral< th=""> <thcentral< th=""> <thce< td=""><td></td><td>Bit 600         Charles 1000         Ferrar 10000         Ferrar 10000         Ferrar 10000         Ferrar 10000         Ferrar 10000         Ferrar 10000         Ferrar 100000         Ferrar 100000         Ferrar 100000         Ferrar 1000000         Ferrar 1000000         Ferrar 1000000         Ferrar 1000000         Ferran 100000000         Ferrar 100000000</td></thce<></thcentral<></thcentral<>		Bit 600         Charles 1000         Ferrar 10000         Ferrar 10000         Ferrar 10000         Ferrar 10000         Ferrar 10000         Ferrar 10000         Ferrar 100000         Ferrar 100000         Ferrar 100000         Ferrar 1000000         Ferrar 1000000         Ferrar 1000000         Ferrar 1000000         Ferran 100000000         Ferrar 100000000
Vale 2015 9 130 42 150 7.5% 0.110[0.06,0.35] Subtaint (16% C1) 1196 1174 64.5% 0.17[0.06,0.46] Total events 41 180 feet for overall effect 2 = 3.48 (P = 0.0005) <b>1.22 Colonoscopy</b> <b>1.22 Colonoscopy</b> <b>1.23 Colonoscopy</b> <b>1.23 Colonoscopy</b> <b>1.24 Colonoscopy</b> <b>1.24 Colonoscopy</b> <b>1.25 Colonoscopy</b> <b>1.25 Colonoscopy</b> <b>1.26 Colonoscopy</b> <b>1.26 Colonoscopy</b> <b>1.27 Colonoscopy</b> <b>1.26 Colonoscopy</b> <b>1.28 Colonoscopy</b> <b>1.29 Colonoscopy</b> <b>1.29 Colonoscopy</b> <b>1.29 Colonoscopy</b> <b>1.20 Colonoscopy</b>	•	8.1.2 Colonoscopy         100         1         100         5.1%         3.06 [0.31, 29.95]           Toklu 200         0         30         10         3.3%         0.03 [0.00, 0.58]           Wang 2011         2         30         3         7.1%         0.64 [0.10, 4.15]           Subtocal (#% CI)         160         15.6%         0.46 [0.04, 5.10]         Toll works
ae, JM, 2219         27         100         42         100         7.9%         0.51 (D.28, 0.92)           oku 2009         2         30         16         30         5.2%         0.06 (0.01, 0.31)           warg 2011         2         30         8         30         5.1%         0.20 (D.4, 1.02)           wibboal (MS* C1)         22         222         28.7%         0.31 (D.15, 0.65)         otal events           dotal events         4.61         6.9         etercogenety, Tau* = 0.30, Ch* = 6.4, df = 2 (P = 0.00); P = 55%         se5%		Number         Test for versal filter:         2 - 0.5(1)         - 0.5(1)         - 0.5(1)         - 0.5(1)           8.1.3 Advanced endoscopy         192         3 94         5.1%         0.33 [0.03, 3.26]         - 0.5(1)         -
2.3 Advanced endoscopy         92         4         94         2.7%         0.11 [0.01,2.05]           Iam SJ 2010         0         64         3         64         2.5%         0.11 [0.01,2.05]           Jam SJ 2010         0         64         3         64         2.6%         0.11 [0.01,2.05]           Jam SJ 2010         0         64         2.6%         0.11 [0.01,2.05]         1.00 [1.0,01,121]           Jam SJ 2018         4         64         10         63         6.5%         0.35 [10,0,1.16]           Jam SJ 2018         4         64         10         63         6.5%         0.35 [10,0,1.16]		Song JC 2015         0         40         0         40         Not estimable           Subtolat (95% C)         300         301         41.0%,         0.67 [0.34, 1.32]         •           Table wints         10         25.2         15.2         •         •         •           Total revorant effect 2 = 1.15 (P = 0.55; cff = 3 (P = 0.91); P = 0%         Test for overant effect 2 = 1.15 (P = 0.25)         •         •         •           Total (95%) (C)         760         761         100.0%         0.52 [0.30, 0.91]         ●
Wu 2017         0         20         2         2.5%         0.18 [0.01, 4.01]           Jubichal (19% C)         320         321         19.7%         0.28 [0.11, 0.64]           Chail events         5         26         19.7%         0.28 [0.11, 0.64]           Gradi events         5         26         19.7%         0.28 [0.11, 0.64]           Gradi events         5         26         19.7%         0.28 [0.11, 0.64]           Fast for overall effect Z = 2.5 (0.7 ± 0.05)         19.75 ± 0.05 ± 0.053)         19.75 ± 0.06 ± 0.053 ± 0.053	•	Total events         34         7         102           Heterogeney: Tau' = 0.21; CP = 14.35, df = 11 (P = 0.21); F = 23%         0.001         0.1         10           Test for subgroup differences: Chi* = 0.02)         Favours [etomidate]         Favours [etomidate]         Favours [etomidate]
Total (1954 (1955 k.)) 2111 201 2111 201 2111 10000 0.020 (0.11, 0.36) Heterogenetic (1960 (19	02 0.1 1 10 500 Favours [etomidate] Favours [propofol]	
Etomidate Propofol Odds Ratio Study or Subgroup Events Total Events Total Weight M-H, Random, 95% Cl	Odds Ratio M-H, Random, 95% Cl	Etomidate Propofol Odds Ratio Odds Ratio Study or Subgroup Events Total Events Total Weight M-H, Random, 95% Cl M-H, Random, 95% Cl
transmission         B         00         00         2.4%         19.56 [11:0, 47:6]           Jona 2016         B         100         100         2.6%         10.536 3]           Jua 2014         B         40         0         40         2.6%         2.4% [11:3, 43:55 1]           Jua 2017a         15         60         100         2.6%         2.4% [11:3, 43:55 1]           Jua 2017b         9         200         2         200         7.0%         4.66 [10:0, 21:37]           Jua 2017b         15         00         1         0         4.4%         33:14 [58:275:31]           Jua 2017b         15         00         1         0         4.4%         33:14 [58:275:31]           Jua 2017b         15         00         4.5%         33:14 [58:275:31]         100           Jua 2017b         15         00         4.5%         33:14 [58:275:31]         100         1.5% [10:4]         100 [10:6]           Jua 2017b         15         00         4.5%         33:14 [58:275:31]         100 [10:6]         100 [1:5% [10:4]         100 [10:6]         100 [1:5% [10:4]         100 [10:6]         100 [1:5% [10:4]         100 [10:6]         100 [1:5% [10:4]         100 [10:6]         100 [1:5% [10:6] <td></td> <td>L.7 EGM     Line     Lin</td>		L.7 EGM     Line     Lin
Test for overall effect: Z = 7.89 (P < 0.00001)	 	6.3.2 Codonoscopy         62.3         5         62         1.6%         0.38 [0.07, 2.04]           Lee. MA 2019         2         100         4         100         1.6%         0.49 [0.06, 2.74]           Wang 2011         1         30         2         30         68         0.48 [0.04, 5.63]           Subcload (M%, Cl)         5         192         3.9%         0.44 [0.15, 1.28]         Total events           Total events         ***         0.06, 1/***         0.65, 61/***         0.64 [0.75, 1.28]         Total           Test for overall effect: Z = 1.49 (P, 0.14)         ***         0.06, 1/**         0.06, 1/**         ************************************
test for overails effect: Z = 2.45 (P = 0.01)           3.2.3 Advanced endoscopy           ians J 2019         11         92         0         94         2.7%         26.67 [1.55, 459.61]           taris J 2020         2         30         0         30         2.3%         5.56 [0.25, 116.31]           taris J 2020         2         30         0         30         2.3%         5.56 [0.25, 116.31]           taris J 2019         4         64         12.8%         3.67 [14.49, 0.04]         3.67 [14.49, 0.04]           taris L 2016         4         64         2.65         6.0%         2.30 [0.36, 11.32]           taris L 2016         4         64         0         40         2.1%         3.08 [0.12, 77.80]           taris L 2017         2         0         40         2.2%         2.2.7 [12, 452.26]         1.20, 452.26]           taris L 2016         4         11         2.8.4%         4.22 [2.08, 6.27]         1.20, 452.26]		6.3.3 Advanced endoscopy           Han SJ 2010         92         2         94         0.8%         0.51 [0.05, 5.67]           Kim MG 2017         4         64         20         64         3.5%         0.15 [0.05, 5.67]           Park CH 2018         10         64         16         63         5%         0.54 [0.05, 5.67]           Song JC 2015         0         40         0         40         Not estimable           Wu 2017         0         20         0.4%         0.32 [0.01, 5.28]           Subtocal (8% Ci)         281         0.6%         0.34 [0.16, 6.68]           Total events         92         231.0f = 0.79 = 0.35; P = 9%         Test for overall effect; Z = 2.56 (0.003)
Hetmogeneity, Tau' = 0.00, Chi' = 4.03, df = 5 (P = 0.54), F = 0%           est for overall effect. Z = 3.99 (P = 0.0001)           Total (B5%, CI)         1719           1726         100.0%           8.54 [5.20, 14.01]           Total (B5%, CI)         1719           1726         100.0%           8.54 [5.20, 14.01]           Total (B5%, CI)         1719           1726         100.0%           8.54 [5.20, 14.01]           Total (B5%, CI)         1719           1726         100.0%           8.54 [5.20, 14.01]           Total (B5%, CI)         1719           1726         179           1727         1728 [5.20, 14.01]           100         179           179         1728 [5.20, 15], F = 25%           Tetrorowall effect. 2 = 4.84 [P = 0.0001]         0           0         0		Total (95%, CI)         1599         1606         100,0%         0.45 (0.36, 0.59)           Total vennts         182         335         164 (P = 0.83); P = 0%         0.001         0.1         1         10           Test for subgroup differences:         Ch <sup>2</sup> = 0.00; Ch <sup>2</sup> = 0.0001)         Favours (etomidate)         Favours (etomidate)         Favours (propolo)           Test for subgroup differences:         Ch <sup>2</sup> = 0.86, df = 2 (P = 0.72), № = 0%         Favours (etomidate)         Favours (propolo)
eas to subgroup unierations. One = 4.20, un = 2 ( $r = 0$ , i.e., $r = 02.576$	Favours [etomidate] Favours [propofol]	
tudy or Subgroup Etomidate Propofol Odds Ratio Events Total Events Total Weight M-H, Random, 95% Cl 3.2.1 EGD	Odds Ratio M-H, Random, 95% Cl	
hene 2017         0         60         8         60         115%         0.05 (00.0.91)           uiz 017a         3         60         60         11.7%         0.30 (0.8.0.01)         1           uiz 017b         0         30         8         30         11.4%         0.04 (0.00.078)         1           uiz 017b         0         30         8         30         11.4%         0.04 (0.00.078)         1           may 2016         7         50         150         8.46%         0.22 (10.8.00.078)         1           may 2015         0         355         0         360         Not estimutable         Not estimutable           uibtotal (6% C1)         755         710         95.2%         1.07 (0.56, 0.35]         0.317 (0.66, 0.35]           diate worth         10         45         92.1%         0.5%         0.5%         1.37 (0.56, 0.35]           diate worth         2.12 (2.8.02001)         1.29 (2.9.02001)         1.29 (2.9.02001)         1.29 (2.9.02001)         1.29 (2.9.02001)	•	
$\begin{array}{rrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrr$	•	
Advanced endoscopy         64         1         64         2.0%         0.33 [0.01,8.21]           im MG 2017         0         64         1         64         2.0%         0.33 [0.01,8.21]           win CH 2018         6         04         1         6.3         17.4%         0.34 [0.13, 1.01]           icrop. JC 2015         0         40         0         40         Net estimable           windraft 6% CD         148         167         1.9 KM         0.33 [0.01, 0.66]		



#### 4. Discussion

Our meta-analysis found no significant overall difference in procedure time or patient satisfaction between etomidate and propofol. However, compared with propofol, etomidate resulted

954 100.0% 0.22 [0.13, 0.37]

0.00

0.1

15 (P = 0.95)0%

> in significantly reduced apnea or hypoxemia, hypotension, and bradycardia but increased myoclonus.

> Based on the analysis of endoscopy type, no/low heterogeneity was found for procedure time, apnea, and hypoxemia in

Group	Study		Statisti	cs for ea	ach study		Odds ratio and 95% CI
		Odds ratio	Lower limit	Upper limit	Z-Value	p-Value	
Advanced	Han SJ 2019	0.764	0.453	1.287	-1.011	0.312	-=+
Advanced	Kim MG 2017	1.740	0.925	3.273	1.717	0.086	
Advanced	Park CH 2018	0.492	0.087	2.786	-0.802	0.423	
Advanced	Song 2015	1.000	0.452	2.214	0.000	1.000	
Advanced	Karis h 2020	0.423	0.112	1.596	-1.270	0.204	
Advanced		0.935	0.589	1.486	-0.284	0.777	
Colono	Lee JM 2018	6.536	0.763	55.988	1.713	0.087	
Colono	Lee JM 2019	1.812	0.682	4.811	1.193	0.233	│ │ ┼╋─ │
Colono		2.374	0.851	6.619	1.652	0.098	
EGD	Meng 2016	0.102	0.005	1.952	-1.515	0.130	<b>← </b>
EGD	Xiao 2018	0.331	0.013	8.193	-0.675	0.500	
EGD	Guo 2017b	0.497	0.045	5.531	-0.568	0.570	│
EGD	Chun 2018	3.996	1.080	14.790	2.075	0.038	
EGD		0.715	0.120	4.278	-0.367	0.713	
Overall		1.071	0.710	1.614	0.326	0.745	



#### В

	Experim	ental	Cont	rol		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% CI
Chun 2018	53	100	58	100	31.6%	0.82 [0.47, 1.43]	
Guo 2017b	174	200	188	200	23.5%	0.43 [0.21, 0.87]	
Shen 2015	329	355	339	360	29.5%	0.78 [0.43, 1.42]	
Xiao 2018	132	150	144	150	15.5%	0.31 [0.12, 0.79]	
Total (95% CI)		805		810	100.0%	0.60 [0.39, 0.91]	•
Total events	688		729				
Heterogeneity: Tau <sup>z</sup> =	0.07; Chi	= 4.70	, df = 3 (F	9 = 0.20	); I <sup>z</sup> = 369	%	
Test for overall effect:	Z = 2.39 (	P = 0.0	2)			0.01	Favours [propofol] Favours [etomidate]

#### С

	Ete	omidate	•	Pi	ropofol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
4.2.1 EGD									
Chen 2017	5.2	0.16	60	5.17	0.31	60	37.5%	0.03 [-0.06, 0.12]	•
Chun 2018	4.74	1.55	100	4.64	1.49	100	9.2%	0.10 [-0.32, 0.52]	+
Guo 2017b	4.77	1.6	200	4.85	1.73	200	13.5%	-0.08 [-0.41, 0.25]	1
Liu 2017b	20.1	10.8	30	21.8	9.5	30	0.1%	-1.70 [-6.85, 3.45]	
Shen 2015	4.74	1.71	355	4.86	1.83	360	18.1%	-0.12 [-0.38, 0.14]	1
Xiao 2018	4.8	2.01	150	4.87	1.73	150	9.1%	-0.07 [-0.49, 0.35]	†
Xu 2015	6.5	1.5	100	6.6	1.3	100	10.5%	-0.10 [-0.49, 0.29]	+
Subtotal (95% CI)			995			1000	98.1%	0.00 [-0.07, 0.08]	
Heterogeneity: Tau <sup>z</sup>	= 0.00;	Chi <sup>z</sup> = 2	2.48, d	f = 6 (P	= 0.87	; I <sup>z</sup> = 0	%		
Test for overall effec	t: Z = 0.	12 (P =	0.91)						
4.2.2 Colonoscopy									
Baniheshem 2015	11.43	4.85	43	9.91	2.17	47	0.8%	1.52 [-0.06, 3.10]	<u>––</u>
Lee JM 2018	29.73	12.23	62	29.46	16.04	62	0.1%	0.27 [-4.75, 5.29]	
Lee JM 2019	28.61	11.39	100	27.71	13.88	100	0.2%	0.90 [-2.62, 4.42]	
Tokllu 2009	20.76	7.22	30	18.93	5.72	30	0.2%	1.83 [-1.47, 5.13]	<u>+</u>
Subtotal (95% CI)			235			239	1.3%	1.40 [0.13, 2.68]	◆
Heterogeneity: Tau <sup>z</sup>	= 0.00;	Chi <sup>z</sup> = (	).36, d	f = 3 (P	= 0.95	; I <sup>z</sup> = 0	%		
Test for overall effec	t: Z = 2.	16 (P =	0.03)						
4.2.3 Advanced end	doscop	y							
Han SJ 2019	24.2	15.8	92	28.5	15.38	94	0.1%	-4.30 [-8.78, 0.18]	
Kim MG 2017	12.91	9.32	64	15.56	10.29	64	0.2%	-2.65 [-6.05, 0.75]	
Liu 2020	21.4	14.4	40	21.2	9.1	40	0.1%	0.20 [-5.08, 5.48]	
Park CH 2018	16.8	8.7	64	21.7	13.3	63	0.1%	-4.90 [-8.82, -0.98]	
Song JC 2015	20.9	8.4	40	20.4	9.2	40	0.1%	0.50 [-3.36, 4.36]	
Wu 2017	45.2	11.3	20	44.5	12.4	20	0.0%	0.70 [-6.65, 8.05]	
Subtotal (95% CI)			320			321	0.7%	-2.15 [-4.11, -0.19]	◆
Heterogeneity: Tau <sup>z</sup>	= 1.01;	Chi <sup>z</sup> = 6	6.01, d	f = 5 (P	= 0.31	; I <sup>z</sup> = 1	7%		
Test for overall effec	t: Z = 2.	15 (P =	0.03)						
Total (95% CI)			1550			1560	100.0%	-0.03 [-0.17, -0.12]	
Heterogeneity: Tau <sup>z</sup>	= 0.01;	Chi <sup>z</sup> = '	19.47,	df = 16	(P = 0.2)	24); I <sup>z</sup> =	= 18%		
Test for overall effect	t: Z = 0.	37 (P =	0.71)		-				-10 -5 0 5 10 Favours [stomidate] Favours [propotol]
Test for subgroup dif	fference	s: Chiz	= 9.29.	df = 2	(P = 0.0)	)10), I <sup>z</sup>	= 78.5%		avours [etomicate] Favours [propoioi]

Figure 3. Forest plot of satisfaction or efficacy of etomidate and propofol. (A) Patient-reported satisfaction. (B) Anesthesiologist-reported satisfaction. (C) Procedure time. CI = confidence interval.

all types of endoscopies (esophagogastroduodenoscopy, colonoscopy, and advanced endoscopy); no/low heterogeneity was found for myoclonus and bradycardia only in advanced endoscopy. Importantly, the etomidate group showed safer results than the propofol group for hypotension and apnea in all subgroup analyses of esophagogastroduodenoscopy, colonoscopy, and advanced endoscopy. In esophagogastroduodenoscopy and advanced endoscopy, similar results were found for hypoxemia. In colonoscopy, procedure time increased in the etomidate group. However, the etomidate group showed a decrease in procedure time in advanced endoscopy, with etomidate being safer than propofol for sedation and comparable in efficacy.

To date, only 1 meta-analysis has analyzed 6 studies between 2009 and 2016 comparing etomidate and propofol.<sup>[39]</sup> However, all but 1 study had a relatively small sample size (<100), and both gastroscopy and colonoscopy were analyzed together. The majority of the studies were conducted in China; moreover, inaccessible/unpublished articles and missing data can bias the pooled effect. Therefore, we additionally manually searched extensive databases, including CINAHL and China National Knowledge Infrastructure, through exhaustive and contemporary searches for all possible RCTs. We believe ours is the first meta-analysis to analyze the efficacy and safety of etomidate and propofol by endoscopy type, including advanced endoscopy. Our results were mostly consistent with those of previous meta-analyses (patient satisfaction, apnea, hypoxemia, and myoclonus) but did show a few differing results (hypotension). The different types of endoscopies showed high heterogeneity, except advanced endoscopy, which showed no heterogeneity. In contrast to a previous meta-analysis,<sup>[39]</sup> we found that etomidate caused hypotension less frequently than propofol. This is consistent with other reports.<sup>[6,40–42]</sup>

Because etomidate also had safer results than propofol for apnea, hypoxemia, hypotension, and bradycardia, it is considered safe as an inducer in hemodynamically unstable patients and may be considered an alternative to propofol.<sup>[43,44]</sup> Propofol is preferred for shorter procedures because it is a better inducer than etomidate with fewer side effects, faster action, and faster recovery.<sup>[45-47]</sup> Therefore, we suggest that etomidate be the sedative of choice for advanced endoscopy with long procedure times; its side effects may be reduced with pretreatment agents or by combining it with other sedatives. The combined use of propofol and etomidate in gastroscopy can be effective<sup>[48]</sup>; the use of combination drugs in advanced endoscopy can be considered, yet further research is needed.

Lee et al reported that although patients receiving etomidate did not show a significant difference in procedure time from those receiving propofol, the patients who received etomidate presented with more frequent body movements during the procedure and had more frequent side effects that interfered with the procedure than did those who received propofol, making the procedure more difficult for the assistant/nurse than for the endoscopist.<sup>[22]</sup> In our meta-analyses, similar results were seen in the colonoscopy subgroup analysis of 4 studies.<sup>[19-22]</sup> Contrastingly, in our meta-analyses, the procedure time for etomidate was decreased in advanced endoscopy. Of the 6 studies analyzed, 5 did not show a significant difference,<sup>[23-25,27,37]</sup> and only 1 study (Park et al) showed a significant decrease in the etomidate group.<sup>[26]</sup> When that was excluded as leave-1-out, there was no significant difference between the 2 groups, and heterogeneity was reduced from 17 to 0%. Thus, further research is required, and an appropriate drug should be selected according to the patient's age and general condition and the American Society of Anesthesiology score.

Our study had limitations. First, we excluded the analysis of etomidate and propofol combinations; combined use can reduce individual quantities of propofol and etomidate, thus reducing the side effects of each drug. Therefore, further research is needed for optimal sedation. Second, no analysis of sedation administrators was conducted; anes-thesiologists administered sedation in 6 studies,<sup>[15-17,20,35,37]</sup> nurses - trained and certified in advanced cardiac life support - administered anesthesia in 5 studies, [21,22,24,26,27] and the remainder were insufficiently reported. Administrators of sedation vary - nurses, endoscopists and physicians, and gastroenterologists - and may have different levels of training. Furthermore, different sedation levels may be exhibited depending on the administration method. Therefore, our results need to be interpreted with caution. Third, although etomidate and propofol were being evaluated, other pretreatment agents may cause various side effects. Fourth, although the meta-analysis largely included healthy adults, elderly (>60 years old) and obese individuals were included. The

majority of the results of our sensitivity analyses, excluding the older adult and obese patients and including only older adult patients, did not show any significant difference compared with our overall results (see Table S2, Supplemental Digital Content, http://links.lww.com/MD/I435 and Table S3, Supplemental Digital Content, http://links.lww.com/MD/ I436). Our meta-analysis demonstrated that etomidate was safer than propofol for sedation and comparable in efficacy, even for the older adult population.

In conclusion, etomidate can be a good alternative to the conventional sedative, propofol, for sedation in gastrointestinal endoscopy, especially advanced endoscopy. Further studies on the efficacy and safety of pretreatment agents and combinations of sedatives are needed.

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#### **Author contributions**

Conceptualization: Ji Taek Hong, Sung-Wook Park. Data curation: Ji Taek Hong, Sung-Wook Park. Formal analysis: Ji Taek Hong, Sung-Wook Park. Investigation: Ji Taek Hong. Methodology: Ji Taek Hong, Sung-Wook Park. Software: Ji Taek Hong.

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