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Choice of sedation in endoscopic retrograde cholangiopancreatography: is monitored anesthesia care as safe as general anesthesia? A systematic review and meta-analysis

Amaninder Dhaliwal[a], Banreet Singh Dhindsa[b], Syed Mohsin Saghir[c], Daryl Ramai[d], Saurabh Chandan[e], Harmeet Mashiana[f], Neil Bhogal[g], Harlan Sayles[h], Ishfaq Bhat[f], Shailender Singh[f], Aamir Dam[a], Pushpak Taunk[i], Rene Gomez Esquivel[i], Jason Klapman[a], Stephanie McDonough[j], Douglas G. Adler[j]

Moffitt Cancer Center, Tampa, FL; University of Nebraska Medical Center, Omaha, NE; University of Nevada Las Vegas School of Medicine, Las Vegas; The Brooklyn Hospital Center, Brooklyn, NY; Creighton University School of Medicine, Omaha, NE; University of South Florida Morsani College of Medicine, Tampa, FL; University of Utah School of Medicine, Salt Lake City, UT, USA

Abstract

Background Monitored anesthesia care (MAC) and general anesthesia (GA) are the 2 most common methods of sedation used for endoscopic retrograde cholangiopancreatography (ERCP). We performed a systematic review and meta-analysis to compare the overall safety between MAC vs. GA in ERCP.

Methods We conducted a comprehensive search of electronic databases to identify studies reporting the use of MAC or GA as a choice of sedation for ERCP. The primary outcome was to compare the overall rate of sedation-related adverse events in MAC vs. GA groups. The secondary endpoint was to investigate the total duration of the procedure, recovery time, ERCP cannulation rates, and conversion rate of MAC to GA. The meta-analysis was performed using a Der Simonian and Laird random-effects model.

Results A total of 21 studies reporting on 11,592 patients were included. The overall sedation-related side-effects were similar in the GA (12.76%, 95% confidence interval [CI] 5.80-21.73; I^2=95%) and MAC (12.08%, 95%CI 5.38-20.89; I^2=99%) groups (P=0.956). Hypoxia, arrhythmias, hypotension, aspiration and other sedation-related side-effects were similar between the 2 groups. The mean duration of the procedure was longer in the MAC group, but the mean recovery time was shorter. Significant heterogeneity was noted in our meta-analysis.

Conclusions In our meta-analysis, the overall sedation-related side-effects were similar between the MAC and GA groups. MAC could be used as a safer alternative to GA when performing ERCP. However, large multicenter randomized control trials are needed to further validate our findings.

Keywords Sedation, ERCP, anesthesia, adverse events, meta-analysis

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Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) is the treatment of choice in pancreaticobiliary diseases [1]. The 2 types of anesthesia used for ERCP at most institutions are monitored anesthesia care (MAC) or general anesthesia (GA). MAC involves an additional anesthesia provider employed to control the level of patients' sedation, pain and anxiety, while preserving their spontaneous breathing and intact airway reflexes. Patients should be able to respond to verbal commands, maintain their airway, and spontaneously ventilate. Often a combination of sedatives is employed to achieve a rapid onset, high clearance of drugs and minimal side effects [2,3]. GA is similar to MAC in that it also utilizes multiple sedatives to control patients' sedation, pain and anxiety, while also dampening their autonomic nervous system and paralyzing their skeletal muscles. Patients are unarousable to stimulation, are in deep sedation, and are unable to maintain a patent airway or their own ventilation independently. Patients undergoing ERCP via GA also have

Conflict of Interest: None

Correspondence to: Douglas G. Adler, MD, FACG, AGAF, FASGE, Professor of Medicine, Director of Therapeutic endoscopy, Director, GI fellowship program, Gastroenterology and Hepatology, University of Utah School of Medicine, Huntsman Cancer Center, 30 N 1900 E, Room 4R118, Salt Lake City, Utah 84132, USA,
e-mail: dougraham2001@gmail.com

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their airway accessed and protected via an endotracheal tube [4]. There remains an ongoing debate regarding the relative merits and risks of MAC vs. GA for patients undergoing ERCP.

This systematic review and meta-analysis compares the overall safety of MAC vs. GA for patients undergoing ERCP. The primary endpoint is to compare the adverse events of both types of anesthesia used in ERCP procedures. The secondary endpoint is to investigate the total duration of the procedure, recovery time, ERCP cannulation rates, and conversion rate of MAC to GA.

Materials and methods

Search strategy

We conducted a comprehensive search of multiple databases and conference proceedings, including PubMed, EMBASE, Google-Scholar, LILACS, Scopus, and Web of Science (inception to 3/2020). The "Preferred Reporting Items for Systematic reviews and Meta-Analyses" (PRISMA) guidelines were used to identify studies reporting on outcomes among patients undergoing ERCP with sedation via MAC and/or GA [5]. The literature search was performed by an experienced medical librarian using inputs from the study authors.

Key words used in the literature search included a combination of "ERCP, "MAC, "general", "anesthesia, "sedation", "monitored", "adverse events", "hypoxia" and "cannulation rates". The search was restricted to studies in human subjects published in the English language in peer-reviewed journals. Two authors (BD, JS) independently reviewed the titles and abstracts of studies identified in the primary search and excluded studies that did not address the research question, based on pre-specified exclusion and inclusion criteria. The full text of remaining articles was reviewed to determine whether they contained relevant information. Any discrepancy in article selection was resolved by consensus, and in discussion with a co-author. The bibliographic section of the selected articles was manually searched for additional relevant articles, as well as systematic and narrative articles on the topic.

[a]Division of Gastroenterology and Hepatology, Moffitt Cancer Center, Tampa, FL (Amaninder Dhaliwal, Aamir Dam, Jason Klapman); [b]Department of Internal Medicine, Division of Gastroenterology and Hepatology, University of Nebraska Medical Center, Omaha, NE (Banreet Singh Dhindsa); [c]Department of Internal Medicine, University of Nevada Las Vegas School of Medicine, Las Vegas (Syed Mohsin Saghir); [d]Department of Internal Medicine, The Brooklyn Hospital Center, Brooklyn, New York (Daryl Ramai); [e]Division of Gastroenterology and Hepatology, Creighton University School of Medicine, Omaha, NE (Saurabh Chandan); [f]Division of Gastroenterology and Hepatology, University of Nebraska Medical Center, Omaha, NE (Harmeet Mashiana, Ishfaq Bhat, Shailender Singh); [g]Division of Gastroenterology and Hepatology, University of Nebraska Medical Center, Omaha, NE (Neil Bhogal); [h]Department of Biostatistics, University of Nebraska Medical Center, Omaha, NE (Harlan Sayles); [i]Division of Digestive Diseases and Nutrition, University of South Florida Morsani College of Medicine, Tampa, FL (Pushpak Taunk, Rene Gomez Esquivel); [j]Division of Gastroenterology and Hepatology, University of Utah School of Medicine, Salt Lake City, UT (Stephanie McDonough, Douglas G. Adler), USA

Study selection

In this meta-analysis, we included studies that evaluated the safety of GA and MAC for patients undergoing ERCP. Studies were included irrespectively of inpatient/outpatient setting, geography, abstract/manuscript status, as long as they provided relevant data for the analysis.

The following were our exclusion criteria: (1) studies with sample size <10 patients; (2) studies performed in a pediatric population (age <18 years); (3) MAC/GA for procedures other than ERCP; and (4) studies not published in the English language. In cases of multiple publications from the same cohort and/or overlapping cohorts, data from the most recent and/or most appropriate comprehensive report were included.

Data abstraction and quality assessment

Data on study-related outcomes in the individual studies were abstracted onto a standardized form by at least 3 authors (BD, AD, JS), and 2 authors (BD, AD) did the quality scoring independently.

For randomized trials and case-control studies, the data collected were recorded as number of reported events (n) of total number of patients (N) from each study. The collected data were treated as in single-group cohort studies, and we used the Newcastle-Ottawa scale for cohort and case-control studies to assess the quality of studies [6]. This quality score consisted of 8 questions, the details of which are provided in Table 1.

Quality assessment for randomized controlled trials was performed using the Jadad (Oxford) scale (Table 1). A maximum of 5 points could be awarded to a study on the basis of randomization, blinding and withdrawals from the study. A score of ≤3 was defined as a poor quality study [7].

Outcomes assessed

The collected data were matched between the groups (general and MAC) before statistical analysis. This model of comparison is indirect, but the approach is comparable to a retrospective case-control study with matched groups.

The primary outcome was to compare the overall rate of adverse events of GA vs. MAC in patients undergoing ERCP. Comparisons between the 2 groups were also performed to evaluate the rate of individual side effects, including, but not limited to, hypoxia, arrhythmias, hypotension, aspiration and other sedation-related adverse events (the data were extracted directly, as reported by the study). The secondary outcome was to compare the total duration of the procedure, recovery time, ERCP cannulation rates, and the rate of conversion of MAC to GA. A subgroup analysis was performed for randomized controlled trials (RCT) and observational studies in the MAC group.

Table 1 Quality assessment of the study with Newcastle-Ottawa and Jadad (Oxford) scales

Author [Ref.]	Year	Type of study	Quality	Newcastle-Ottawa scale		
				Selection	Comparability	Outcome
Patel [29]	2018	case control	high	***	*	***
Jokelainen [11]	2018	case control	high	***	**	**
Kamani [26]	2018	cohort	high	***	*	***
El-Sherif [23]	2018	cohort	high	***	*	***
Antoury [20]	2017	case control	high	***	*	***
Yang [32]	2016	cohort	medium	**	*	***
Yuen [33]	2016	cohort	high	***	*	**
Joshi [25]	2015	cohort	high	***	*	***
Khoi [27]	2015	cohort	medium	**	*	***
Patel [28]	2014	cohort	medium	**	*	**
Sorser [29]	2014	case control	high	***	**	***
Barnett [21]	2013	case control	high	***	**	***
Goudra [24]	2013	cohort	medium	**	*	***
Amornyotin [19]	2004	case control	high	***	*	***
Fanti [9]	2004	cohort	high	***	*	***
Raymonodos [30]	2002	case control	high	***	*	***
Cocking [22]	2000	cohort	medium	**	*	**
				Jadad scale		
				Randomization	Blinding	Attrition
Smith [10]	2019	RCT	high	2	0	1
Amornyotin [34]	2011	RCT	low	1	0	1
Jung [12]	2000	RCT	low	1	0	1
Wehrmann [8]	1999	RCT	high	2	0	1

RCT, randomized controlled trial

Technical success was defined as successful cannulation in ERCP. The duration of the procedure was defined in only one study, as the time interval from insertion to final withdrawal of the endoscope [8]. Five studies defined the recovery time using different scoring systems: Aldrete score [9,10], Schultz score [11], post-anesthesia recovery score [8], and Seward score [12]. The other studies did not define recovery time.

Statistical analysis

We used meta-analysis techniques to calculate the pooled estimates in each case, following the methods suggested by DerSimonian and Laird using the random-effects model [13]. When the incidence of an outcome was zero in a study, a continuity correction of 0.5 was added to the number of incident cases before statistical analysis [14]. We assessed heterogeneity between study-specific estimates using the Cochran Q statistical test for heterogeneity and the I^2 statistic [15,16], for which values of <30%, 30-60%, 61-75% and >75% were suggestive of low, moderate, substantial and considerable heterogeneity, respectively [17]. Publication bias was ascertained, qualitatively, by visual inspection of a funnel plot, and quantitatively, by the Egger test [18]. All analyses were performed using STATA v16.1 software (StataCorp, LLC College Station, TX).

Results

Search results and population characteristics

From an initial pool of 457 studies, 21 studies reported on the use of GA and MAC in patients undergoing ERCP [8-12,19-34]. Overall, 10 studies provided data on ERCP with GA [10,19-

23,29-31,33], and 17 studies on ERCP with MAC for our analysis [9-12,20,21,24-34]. Six studies were included in both the ERCP and MAC groups [10,20,21,29,31,33]. The schematic diagram of study selection as per PRISMA guidelines is illustrated in Fig. 1.

The mean patient age was 60.4 and 58.92 years in the GA and MAC groups, respectively, with a predominantly male population in the GA group (51.9% reported in 9 studies). Patient demographic characteristics are described in Table 2.

Characteristics and quality of included studies

Eleven studies were prospective and the rest were retrospective in nature. One study was multicenter and the rest were single-center. None were population-based. All studies reported adequately on the clinical outcomes, assessments, and factors of interest. Overall, 14 studies were considered of high quality, 5 were of medium quality, and 2 were low-quality studies. The detailed assessment of study quality is shown in Table 1.

Meta-analysis outcomes

A total of 11,592 patients were included in the analysis. ERCP was performed under GA and MAC in 3062 and 8530 patients, respectively. The overall adverse event rates among patients undergoing ERCP with GA vs. MAC were similar: 12.76%, 95% confidence interval [CI] 5.80-21.73; I^2=95% vs. 12.08%, 95%CI 5.38-20.89; I^2=99%, respectively (P=0.956). Adverse events are described in Table 3 (Fig. 2).

Hypoxia was more prevalent in the MAC group (1.88%, 95%CI=0.04-5.48; I^2=99.11% vs. 0.01%, 95%CI 0.00-0.55; I^2=58.87%; P=0.067) whereas hypotension was more prevalent in the GA group (7.01%, 95%CI 1.62-15.19; I^2=99.25% vs. 4.74%, 95%CI 2.18-8.11; I^2=97.84%; P=0.309). The P-value was not statistically significant for either hypoxia or hypotension. Overall pooled rates of arrhythmias were similar between GA (0.09%, 95%CI 0.00-0.84; I^2=60.13%) and MAC (0.08%, 95%CI 0.00-0.36; I^2=75.17%) groups with P=0.40. Overall pooled rates for aspiration pneumonia, post-ERCP pancreatitis (PEP) and other sedation-related adverse events were similar between the 2 groups, with non-significant P-values. Forest plots for overall

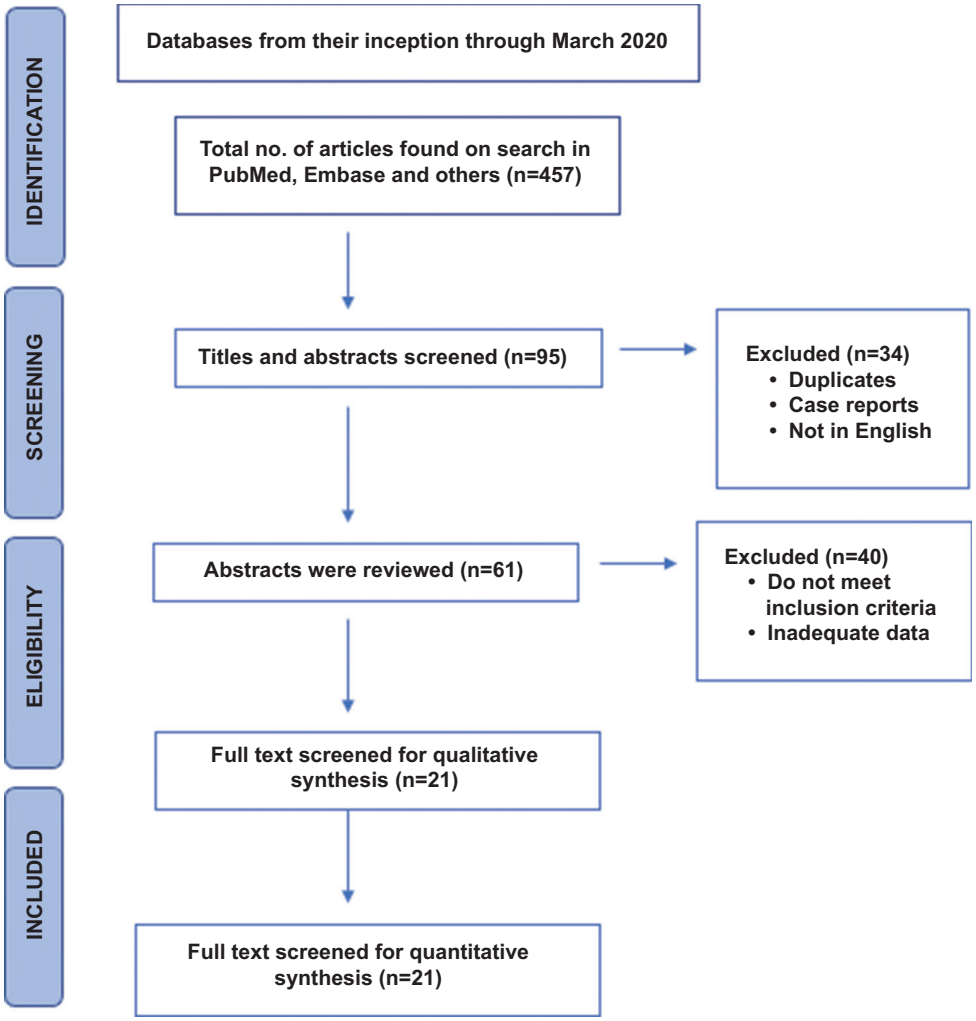

Figure 1 Study selection process in accordance with preferred reporting items for systematic reviews and meta-analysis statement

Table 2 Description of 21 studies used in the final analysis

Author [Ref.]	Study year	Study type	Single-center or multicenter	Abstract or Manuscript	No. of patients	Mean age	Male	Female
Monitored anesthesia care								
Smith [10]	2019	Prospective	single	manuscript	99	61.3	57	42
Patel [29]	2018	Prospective	single	abstract	366	60.5	218	148
Jokelainen [11]	2018	Prospective	single	manuscript	133	58	77	56
Kamani [26]	2018	Retrospective	single	manuscript	550	50.85	197	353
Antoury [20]	2017	Retrospective	single	abstract	50	62	11	39
Yang [32]	2016	Retrospective	single	manuscript	3041	58.2	1399	1642
Yuen [33]	2016	Retrospective	single	manuscript	185	57.3	106	79
Khoi [27]	2015	Retrospective	single	manuscript	552	60	283	269
Joshi [25]	2015	Prospective	single	manuscript	744	63	333	296
Patel [28]	2014	RetWrospective	single	abstract	829	45.1	249	580
Sorser [31]	2014	Retrospective	multi	manuscript	367	-	-	-
Barnett [21]	2013	Prospective	single	manuscript	393	63.4	183	210
Goudra [24]	2013	Retrospective	single	manuscript	653	60.5	420	233
Amornyotin [34]	2011	Prospective	single	manuscript	86	58.2	41	45
Fanti [9]	2004	Prospective	single	manuscript	205	63	97	108
Jung [12]	2000	Prospective	single	manuscript	80	62.5	32	48
Wehrmann [8]	1999	Prospective	single	manuscript	197	-	-	-
General anesthesia								
Smith [10]	2019	Prospective	single	manuscript	101	60.9	64	37
Patel [29]	2018	Prospective	single	abstract	136	52.3	71	65
El-Sherif [23]	2018	Prospective	single	manuscript	67	55.8	27	37
Antoury [20]	2017	Retrospective	single	abstract	50	70	14	36
Yuen [33]	2016	Retrospective	single	manuscript	21	55.7	12	9
Sorser [31]	2014	Retrospective	multi	manuscript	283	-	-	-
Barnett [21]	2013	Prospective	single	manuscript	45	65.9	25	20
Amornyotin [19]	2004	Retrospective	single	manuscript	2144	57.2	1106	1108
Raymonodos [30]	2002	Retrospective	single	manuscript	190	42	118	72
Cocking [22]	2000	Prospective	single	manuscript	25	84.2	8	17

adverse events and individual adverse events are provided in Supplementary Figs. 1-5.

The secondary outcome was to compare the total duration of the procedure, recovery time, ERCP cannulation rates, and the need to convert from MAC to GA. Technical success was comparable between MAC (97.17%, 95%CI 95.25-98.65; I^2=78.6%) and GA (95.29%, 95%CI 90.76-98.51; I^2=73.04%) groups (P=0.232) (Supplementary Fig. 6). The recovery time and duration of the procedure were reported in 8 and 11 studies, respectively. Although, the mean duration of the procedure was longer in the MAC group (47 vs. 33 min) mean recovery time was shorter when compared to the GA group (47 vs. 59 min). A total of 1.7% of patients in MAC group were converted to GA, with a range varying from 0.4-10.1%.

On subgroup analysis of the MAC studies, RCT (n=4) had similar rates of adverse events (12.93%, 95%CI 4.25-25.28; I^2=99.36%) compared to observational studies (12.69%, 95%CI 2.39-29.02; I^2=97.92%), with a P-value of 0.989. Technical success was also similar in RCT as compared to observational studies (97.98%, 95%CI 95.09-99.71; I^2=82.12% vs. 96.41%, 95%CI 93.25-98.67; I^2=75.85%; P=0.385). Individual adverse events were also comparable. No subgroup analysis was possible for the GA studies as there were insufficient RCTs in this group.

Validation of meta-analysis results

Sensitivity analysis

To assess whether any one study had a dominant effect on the meta-analysis, we excluded one study at a time and analyzed its effect on the main summary estimate. On this analysis, no single study significantly affected the outcome or the heterogeneity.

Heterogeneity

We assessed the dispersion of the calculated rates using I^2 percentage values. The I^2 tells us what proportion of the dispersion is true vs. chance [15]. Overall pooled rates for sedation-related adverse events, individual adverse events and technical success showed substantial to considerable heterogeneity.

Publication bias

Based on visual inspection of the funnel plot, there seemed to be greater possible publication bias in the MAC compared to the GA group. Based on quantitative analysis via the Egger regression test, the statistical 2-tailed P-value was 0.004

Table 3 Adverse events in monitored anesthesia care and general anesthesia

Author [Ref.]	Study year	Total adverse effects	Hypotension	Hypoxia	Arrhythmia	Aspiration pneumonia	PEP	Others
Monitored anesthesia care								
Smith [10]	2019	51	9	19	0	0	1	23
Patel [29]	2018	9	0	0	0	0	10	9
Jokelainen [11]	2018	17	15	1	1	0	0	0
Kamani [26]	2018	2	0	0	0	0	0	2
Antoury [20]	2017	14	10	2	2	0	0	0
Yang [32]	2016	872	20	843	0	6	0	3
Yuen [33]	2016	93	38	15	0	0	0	40
Khoi [27]	2015	166	165	1	0	0	0	0
Joshi [25]	2015	8	3	2	1	1	0	2
Patel [28]	2014	1	0	1	0	0	0	0
Sorser [31]	2014	55	0	17	5	0	19	23
Barnett [21]	2013	85	16	59	10	0	0	0
Goudra [24]	2013	3	0	3	0	0	0	0
Amornyotin [34]	2011	26	18	1	5	0	0	2
Fanti [9]	2004	4	0	4	0	0	0	0
Jung [12]	2000	3	1	2	0	0	0	0
Wehrmann [8]	1999	26	9	10	0	0	13	7
General anesthesia								
Smith [10]	2019	10	10	0	0	0	0	0
Patel [29]	2018	7	0	0	0	0	7	7
El-Sherif [23]	2018	0	0	0	0	0	0	0
Antoury [20]	2017	28	22	1	5	0	0	0
Yuen [33]	2016	17	10	0	0	0	0	7
Sorser [31]	2014	9	0	1	0	0	0	8
Barnett [21]	2013	13	8	3	2	0	0	0
Amornyotin [19]	2004	194	171	0	8	0	0	15
Raymonodos [30]	2002	1	0	0	0	0	0	1
Cocking [22]	2000	0	0	0	0	0	0	0

PEP, post-endoscopic retrograde cholangiopancreatography pancreatitis

for the MAC group and 0.605 for the GA group. Refer to Supplementary Figs. 7 and 8 for the funnel plots.

Discussion

The choice between MAC and GA as a means of sedation for patients undergoing ERCP depends upon many factors, including the patient's acuity, operator experience, institutional practices, and the preferences and experience of the endoscopists and the anesthesiologist [35].

High-risk features that may result in sedation-related adverse events include having an American Society of Anesthesiologists (ASA) class greater than 3, obstructive sleep apnea, male sex, body mass index (BMI) greater than 30 kg/m^2, presence of abdominal ascites prior to ERCP, Mallampati class 4, Cotton grade greater than 3, and heavy alcohol use (>3 drinks for men and >2 drinks for women) [9,10,12,19,21,25,27,32,35,36]. The overall adverse event rate was comparable between MAC and GA (P=0.956). The subgroup analysis of the individual adverse events showed hypoxia was more common with MAC than GA, but the difference was not statistically significant (P=0.067). Fanti *et al* reported a similar rate (1.9%) of hypoxia-related adverse events. Yang *et al* reported hypoxia in 28% of their patients when MAC was utilized for ERCP, but it resolved with airway manipulation. Of these, only 0.1% of cases were terminated because of refractory laryngospasm [32]. On the other hand, Goudra *et al* did not describe a significant number of hypoxia-related events with MAC, and this was attributed to the low threshold of desaturation (<95% oxygen saturation) compared to <90% oxygen saturation in other studies. The threshold of <95% allowed earlier supplementation of oxygen through airway conduits to avoid episodes of hypoxia [24].

Hypotension was more prevalent among patients undergoing GA vs. MAC, but the difference was not statistically significant (P=0.309). Amorynotin *et al* reported hypotension in 8.8% of their patients with GA, mostly seen after rapid propofol injection, and it was corrected with fluids and vasopressors [19]. Khoi *et al* reported that 29.9% of their 552 patients experienced hypotension with MAC, and this was attributed to older age (67.7 years) and a longer duration of anesthesia [27]. The overall pooled rates of arrhythmias were low and comparable in GA vs. MAC with a nonsignificant P-value of 0.40.

The pooled rates for aspiration pneumonia (P=0.172), PEP (P=0.867), and other sedation-related adverse events (P=0.79) in our study were similar between the 2 groups. No cases of aspiration pneumonia were reported in the GA group, but 7 were reported in the MAC group [25,32]. Yang *et al* reported that 6 of their 7 cases of aspiration pneumonia were in the MAC group. This was seen

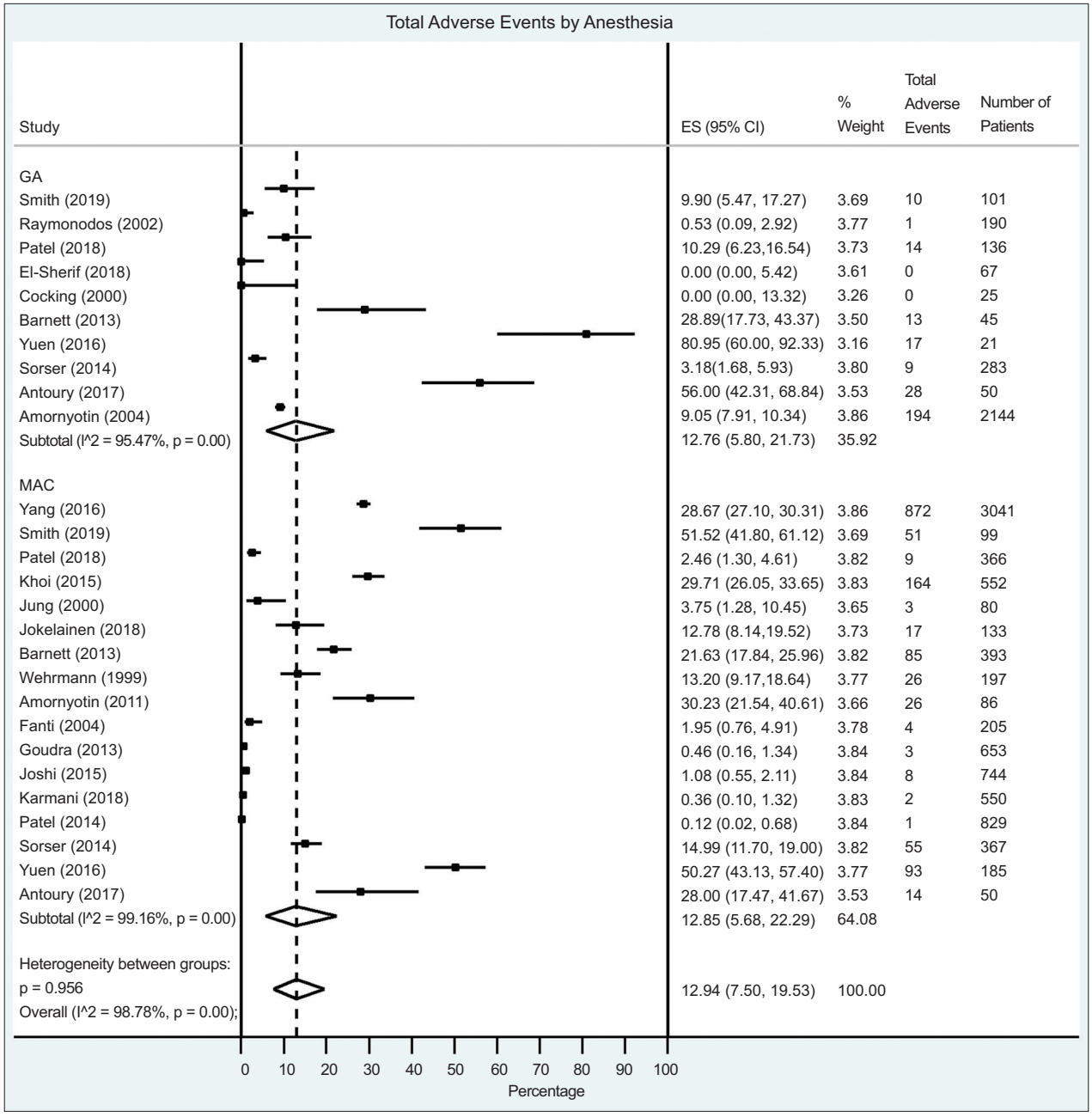

Figure 2 Forest plot showing overall adverse events of endoscopic retrograde cholangiopancreatography under MAC and GA
MAC, monitored anesthesia care; GA, general anesthesia; ES, effect size; CI, confidence interval

in individuals converted to GA as a measure to prevent aspiration, since there were gastric contents seen on endoscopy [32].

Conversion from MAC to GA occurred in 1.7% of patients, ranging from 0.4-10.1%. Yang *et al* reported that 1.6% of patients underwent conversion [32]. In our meta-analysis, the highest conversion rate (10.1%) was seen in the study by Smith *et al*. This was the first prospective RCT to compare GA vs. MAC. The reasons for conversion in our meta-analysis are multifactorial and include visualization of gastric contents during endoscopy (aspiration prophylaxis), ASA class >3, respiratory compromise refractory to airway maneuvers, chronic obstructive pulmonary disease, BMI >30 kg/m^2, and agitation/restlessness despite maximum sedation [10,21,24,26,32,35].

ERCP cannulation rates were comparable between MAC and GA at 97.17% (95%CI 95.25-98.65) vs. 95.29% (95%CI 90.76-98.51), respectively (P=0.232). In a study by Raymondos *et al*, MAC was associated with more unsuccessful ERCP procedures as compared to GA (14% vs. 7%; P=0.012) [30]. This was attributed to the endoscopist's level of experience, as the ERCP procedures under GA were performed by more experienced endoscopists, whereas ERCP with MAC was performed by a less experienced endoscopist [30].

The mean procedural duration was longer in the MAC group (47 vs. 33 min), but the mean recovery time was shorter when compared to the GA group (47 vs. 59 min). Fanti *et al* attributed a long procedure time with MAC to the complexity of the ERCPs [9]. The shorter recovery times in the MAC group were associated with propofol utilization, as the GA group utilized several anesthetic agents including paralytics, benzodiazepines, opiates and/or propofol [8,9,20,29,30,33,34]. It has been reported that shorter recovery times are associated with propofol utilization compared to benzodiazepines/opiates [9,23,33,35].

There are several limitations in our study. Heterogeneity was considerable to substantial in our meta-analysis in regard to the overall pooled rates for sedation-related adverse events, individual adverse events and technical success. This may be due to the indications for the procedure, choice of sedation, anesthesia provider, endoscopist, patient population, or endoscopy technique. A definition of procedure time was only provided in one study. Defining the procedure time as patient in room to scope out vs. scope in to scope out, may factor in the time it takes to intubate and could provide a useful measure. Many of our studies were retrospective and did not undergo randomization, which introduces selection bias. Most studies were conducted at single tertiary referral centers, so results may be difficult to generalize. The results from a high-volume endoscopy center may not be generalizable to a low-volume endoscopy center. Another limitation was the presence of publication bias, as measured by the Eggers regression test. Lastly, the studies included did not compare the healthcare costs associated with either of the methods for sedation.

The results of our meta-analysis show that overall adverse events, individual adverse events, and technical success were comparable between the 2 groups. Although not statistically significant, MAC had higher rates of hypoxia, lower rates of hypotension, longer procedure times, and a shorter recovery period as compared to GA.

Summary Box

What is already known:

- Endoscopic retrograde cholangiopancreatography (ERCP) is the treatment of choice in pancreaticobiliary diseases
- There is ongoing debate regarding the relative merits and risks of monitored anesthesia care (MAC) vs. general anesthesia (GA) for patients undergoing ERCP

What the new findings are:

- Sedation-related side effects were similar in the GA and MAC groups
- Although not statistically significant, MAC had higher rates of hypoxia, lower rates of hypotension, longer procedure times, and a shorter recovery period compared to GA

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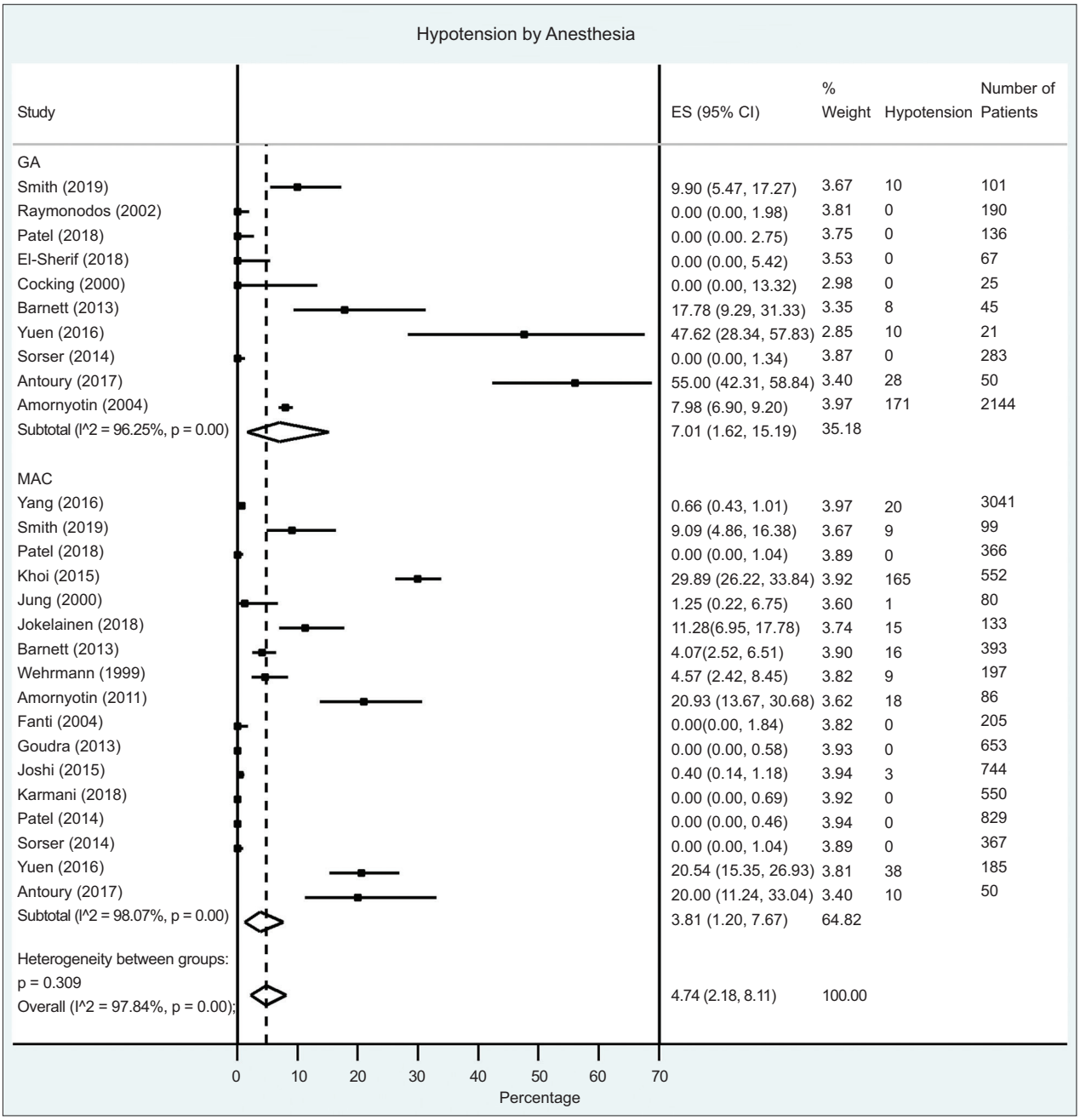
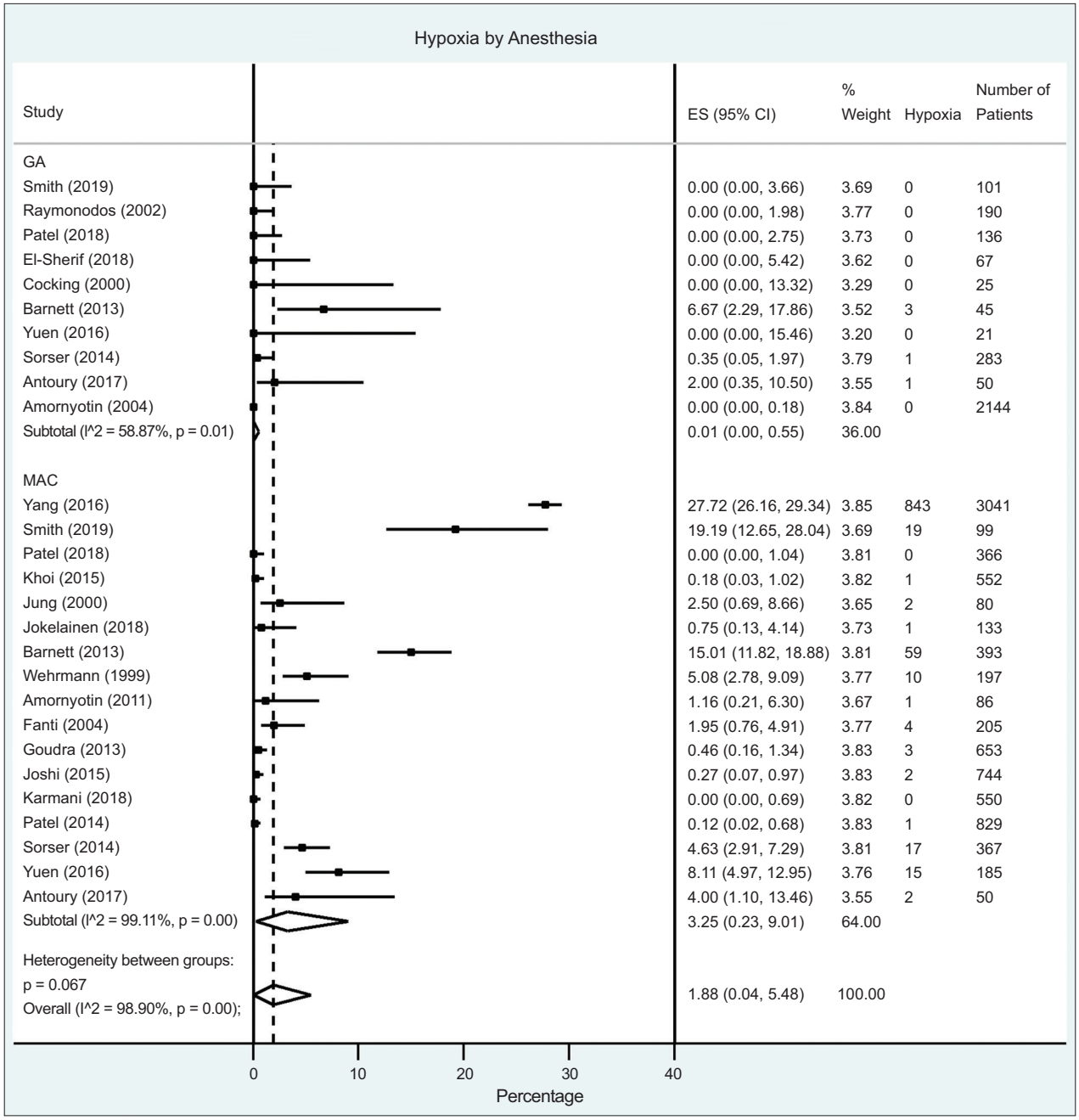
Supplementary material



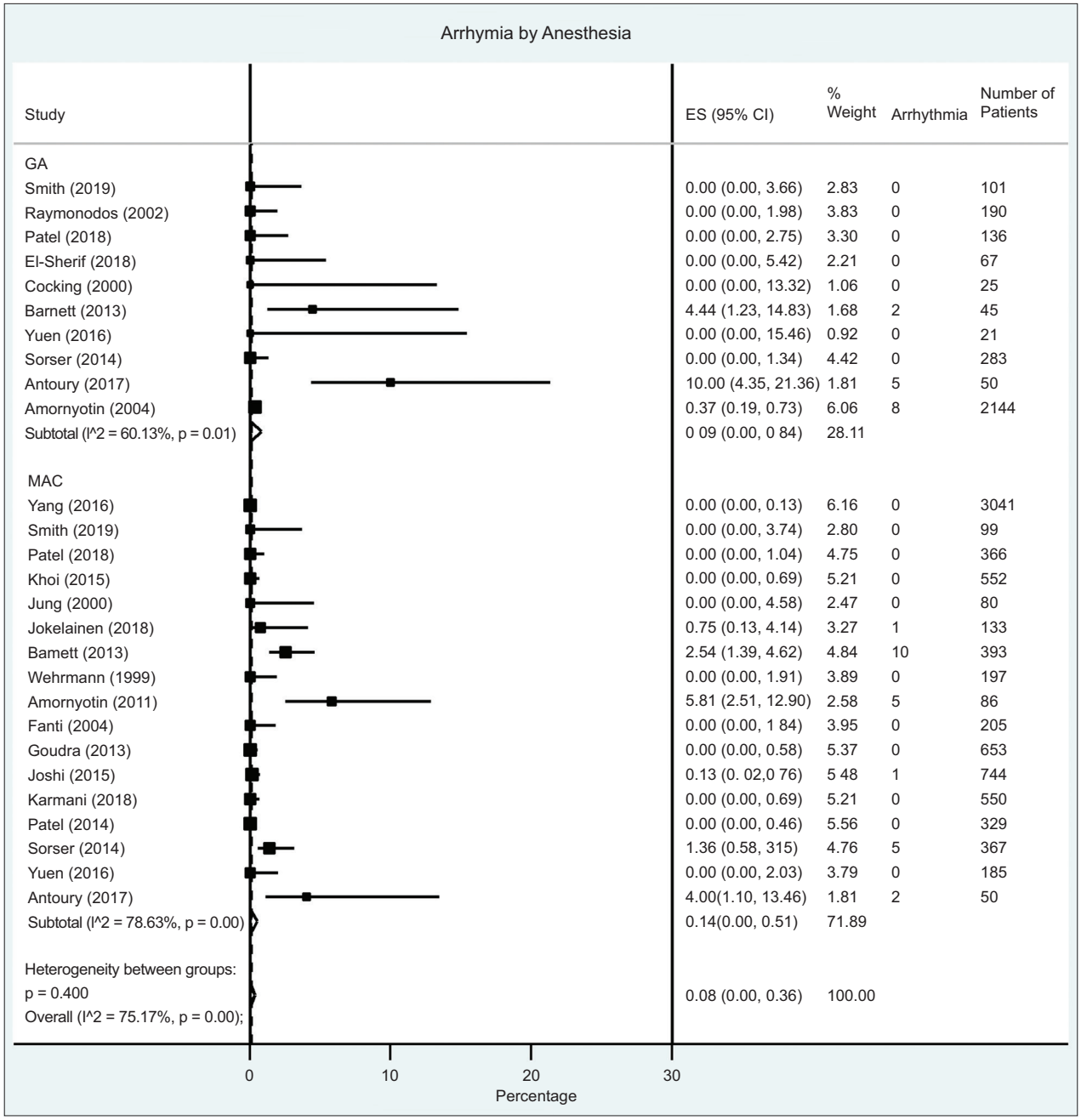
Supplementary Figure 1 Forest plot showing hypotension rates in patients undergoing endoscopic retrograde cholangiopancreatography under MAC and GA

MAC, monitored anesthesia care; GA, general anesthesia; ES, effect size; CI, confidence interval



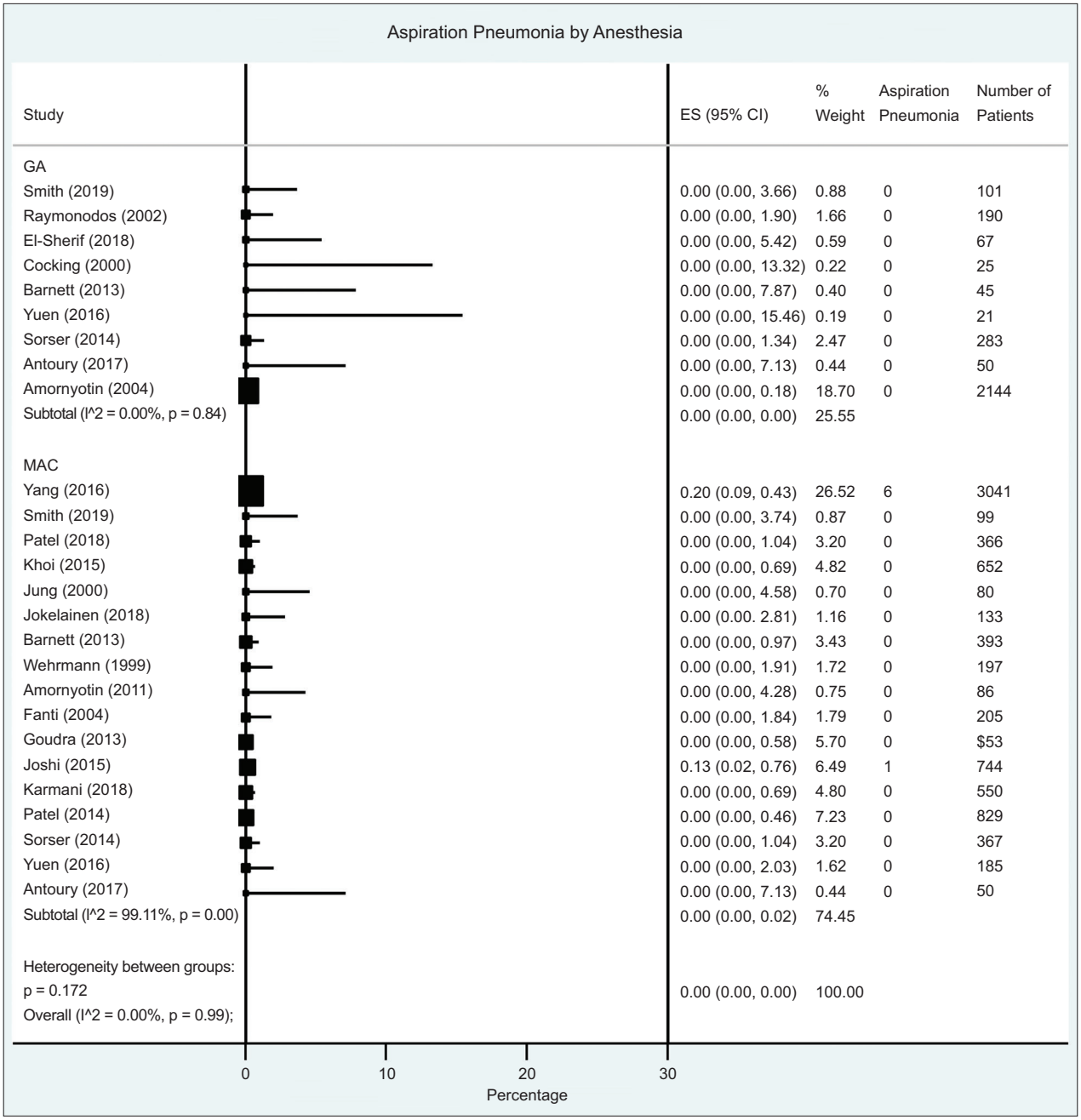
Supplementary Figure 2 Forest plot showing hypoxia rates in patients undergoing endoscopic retrograde cholangiopancreatography under MAC and GA

MAC, monitored anesthesia care; GA, general anesthesia; ES, effect size; CI, confidence interval



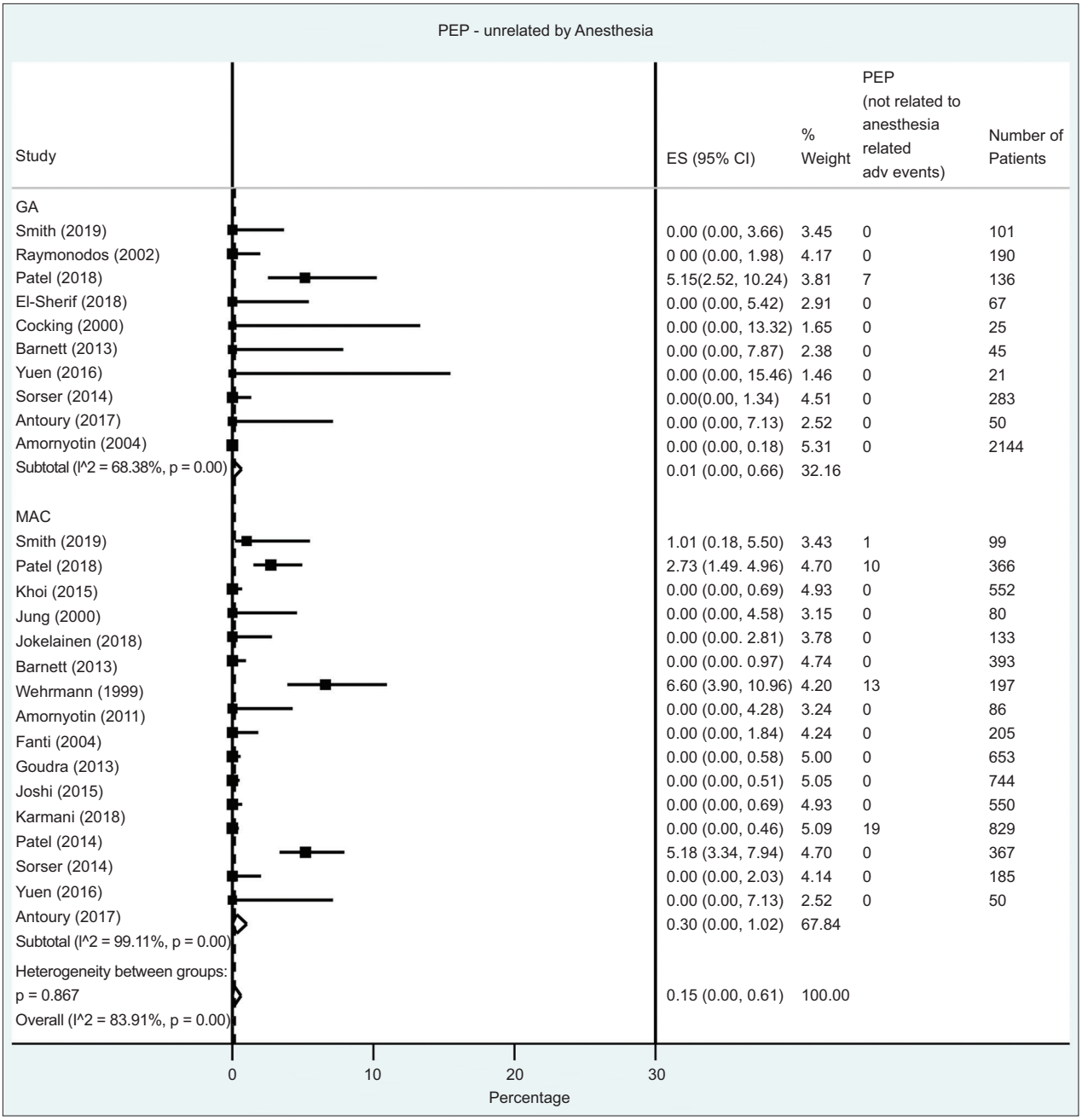
Supplementary Figure 3 Forest plot showing arrhythmia rates in patients undergoing endoscopic retrograde cholangiopancreatography under MAC and GA

MAC, monitored anesthesia care; GA, general anesthesia; ES, effect size; CI, confidence interval



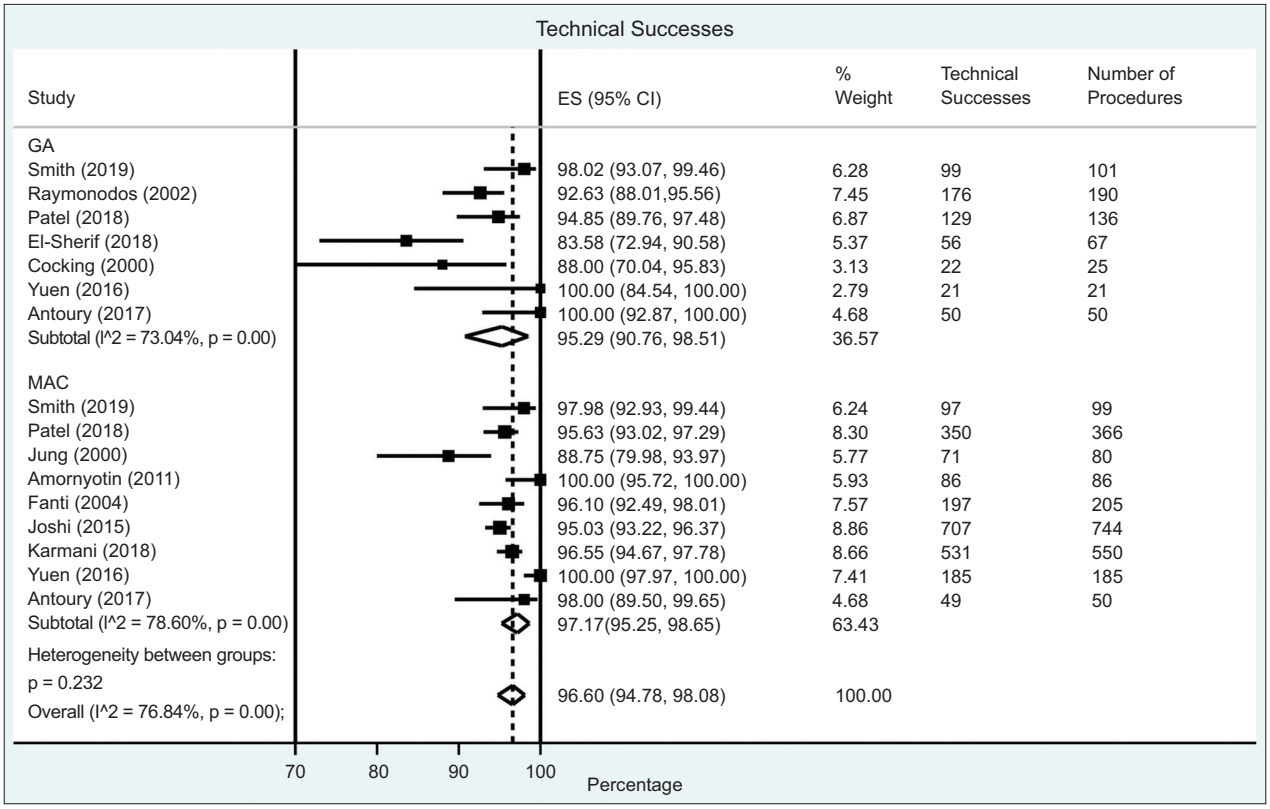
Supplementary Figure 4 Forest plot showing aspiration pneumonia rates in patients undergoing endoscopic retrograde cholangiopancreatography under MAC and GA

MAC, monitored anesthesia care; GA, general anesthesia; ES, effect size; CI, confidence interval



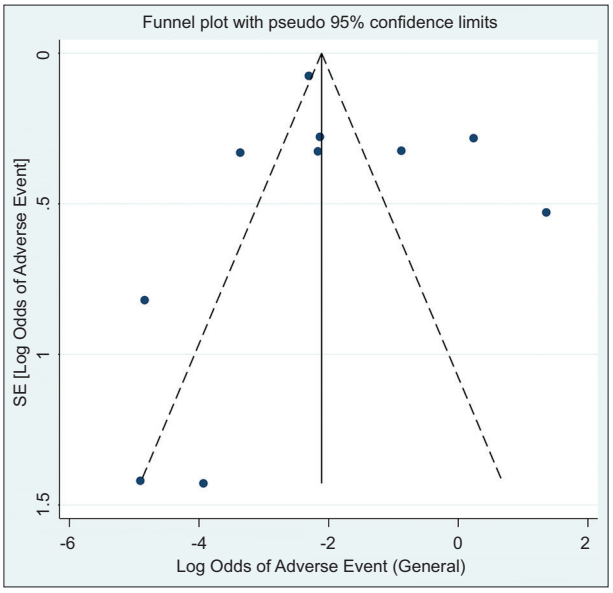
Supplementary Figure 5 Forest plot showing PEP rates in patients undergoing post-endoscopic retrograde cholangiopancreatography under MAC and GA

PEP, pancreatitis; MAC, monitored anesthesia care; GA, general anesthesia; ES, effect size; CI, confidence interval

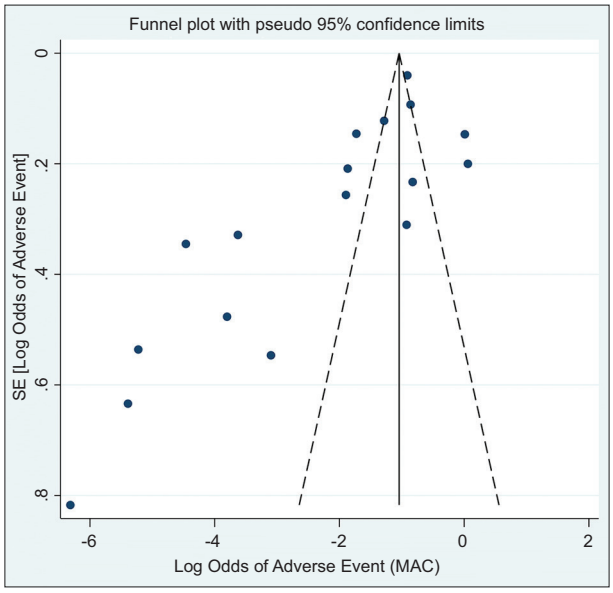


Supplementary Figure 6 Forest plot showing technical success in patients undergoing endoscopic retrograde cholangiopancreatography under MAC and GA

MAC, monitored anesthesia care; GA, general anesthesia; ES, effect size; CI, confidence interval



Supplementary Figure 7 Funnel plot for general anesthesia in endoscopic retrograde cholangiopancreatography



Supplementary Figure 8 Funnel plot for MAC in endoscopic retrograde cholangiopancreatography

MAC, monitored anesthesia care