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Original Article

Safety and efficacy of remifentanil-propofol combination on "muscle relaxant-free" general anesthesia for therapeutic endoscopic retrograde cholangiopancreatography: a randomized controlled trial

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Abstract: Objective: To prospectively evaluate the safety and efficacy of a "muscle relaxant-free" general anesthesia using a combination of remifentanil and propofol, compared to propofol-based monitored anesthesia care and conventional general anesthesia during therapeutic endoscopic retrograde cholangiopancreatography (ERCP). Methods: From September to December 2019, 360 patients scheduled for elective ERCP at the Endoscopy Center of the First Affiliated Hospital of Nanjing Medical University were randomly assigned to three different groups: Group *MAC* (propofol-based monitored anesthesia care, n=120), Group GA_1 (general anesthesia with neuromuscular blocking agents, n=120), or Group GA_2 (remifentanil-propofol combination-based muscle relaxant-free general anesthesia, n=120). Results: The results showed that there was a significant difference in intraprocedural cardiopulmonary adverse events among the three groups (Group *MAC*, 37.5%; Group GA_1, 19.2%; Group GA_2, 17.5%; $P < 0.001$). Total time (from patient entry into the Endoscopy Center to departure) and room time (from patient entry into the endoscopy suit to departure) were shorter in Group GA_2 and Group *MAC* compared to Group GA_1 ($P < 0.001$). Additionally, endoscopist satisfaction levels were significantly higher in Group GA_1 and Group GA_2 compared to Group *MAC* ($P < 0.001$). Conclusion: The study found that administering propofol-remifentanil combination for "muscle relaxant-free" general anesthesia during therapeutic ERCP was safe and effective. This approach offered greater safety and endoscopist satisfaction than propofol-based monitored anesthesia care, as well as shorter total time and room time than conventional general anesthesia.

Keywords: Endoscopic retrograde cholangiopancreatography, propofol, remifentanil, monitored anesthesia care, general anesthesia

Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) is an important procedure for diagnosing and treating biliary and pancreatic problems. It is also identified as one of the most invasive endoscopic procedures. The procedure can be divided into two categories: diagnostic ERCP and therapeutic ERCP [1]. Diagnostic ERCP is used to diagnose conditions, while therapeutic ERCP is used to treat conditions. Sedation appears to be effective for diagnostic ERCP. However, therapeutic ERCP is more complex, time-consuming, and requires a greater depth of sedation, making the optimal anesthetic strategies for this procedure still unknown and a controversial topic [2]. Propofol-based monitored anesthesia care (MAC) is widely used in many medical centers [3-6], due to its high safety profile and pharmacokinetic and pharmacodynamic features that allow for rapid onset of action and recovery. However, the use of MAC during endoscopy procedures and its impact on endoscopy unit efficiency remain controversial. Some studies suggest that ERCP performed under MAC can enhance endoscopy unit efficiency compared to general anesthesia (GA), particularly in tertiary-care, high-volume endoscopy units [7]. Yet others have found no significant positive effect of MAC on the efficiency [8]. It is worth noting that propofol may also cause dose-dependent adverse events, such as respiratory depression and hemodynamic compromise. Moreover, with

the increasing elderly population, many ERCP patients are older, sicker, and have multiple comorbidities [9, 10]. Sedation-related adverse events are the most common ERCP-related events [11, 12]. Administering and overseeing MAC for ERCP can be anxiety-provoking for the anesthesiologist, thus a subset of patients will require urgent conversion from MAC to GA [13]. Alternatively, GA provides a protective upper airway, prevents, or at least limits, aspiration, and enables the patient to tolerate this invasive and painful procedure. GA may be preferred in certain cases where the patient has a higher risk of complications or requires a longer procedure time. However, GA also has several limitations, including prolonged duration of emergence, potential complications, such as cardiovascular, respiratory, neurologic, and renal complications, drug reactions, postoperative nausea and vomiting, and sore throat [14]. Serious complications may contribute to perioperative morbidity and mortality. Furthermore, in general, the overall cost of the procedure may be higher when using GA compared to MAC and may require additional staffing and resources. Therefore, finding an ideal anesthetic strategy for ERCP that ensures patient safety and comfort while increasing endoscopy unit efficiency is of great significance.

Previous studies have demonstrated that endotracheal intubation is feasible without a muscle relaxant. Propofol, when combined with short-acting opioids and local anesthetic agents, can create suitable conditions for intubation without the need for muscle relaxation [15-18]. This technique has potential use in cases where intubation is necessary but neuromuscular blockade is not required to facilitate surgical access. However, there are no worldwide studies on the use of "muscle relaxant-free" general anesthesia as a new anesthetic technique for ERCP. This prospective study aimed to compare the safety and feasibility of remifentanil-propofol combination for "muscle relaxant-free" GA with two traditional anesthetics in patients undergoing ERCP.

Materials and methods

Study design

This prospective study was approved by the Ethics Committee of the First Affiliated Hospital of Nanjing Medical University (ID: 2019-SR-205) and was registered at ClinicalTrials.gov (NCT04087668). The study was conducted in accordance with the Consolidated Standards of Reporting Trials (CONSORT) statement, and the Helsinki Declaration. Written informed consent was obtained from each patient prior to study commencement. Patients referred for an elective therapeutic ERCP at the Endoscopy Center were enrolled in this study.

The inclusion criteria: (1) patients with an age of 18-70 years old, (2) patients with grade I and III according to the American Society of Anesthesiologists physical status (ASA PS) classification, (3) patients with coagulation function tests in the normal range.

The exclusion criteria: (1) patients with potentially difficult airways, (2) patients with administration of sedative or narcotic drugs in the previous 24 hours, (3) patients with severe renal or hepatic impairment, (4) patients with severe cardiopulmonary comorbidities (defined as American Society of Anesthesiologists physical status IV or greater), (5) patients with contraindications to nasotracheal intubation, (6) patients with coagulopathy, (7) patients with a history of frequent episodes of epistaxis, (8) patients with emergency ERCP, (9) patients at risk of regurgitation and aspiration (such as gastroesophageal reflux disease, cardia achalasia, history of digestive tract reconstruction).

Study intervention

A meticulous pre-anesthetic visit was conducted one day before the ERCP. Prior to the commencement of the study, patients were randomly assigned to three different groups: Group *MAC* (propofol-based monitored anesthesia care), Group GA_1 (standard GA with neuromuscular blocking agents), or Group GA_2 (muscle relaxant-free GA) using a research randomizer program available at http://www.randomizer.org/.

Subjects were monitored with three-lead electrocardiography (ECG), end-tidal CO_2 partial pressure ($P_{ET}CO_2$), respiration rate (RR), pulse oximetry (SpO_2), and blood pressure (Bp), all of which were measured using a Mindray T6 monitor (Mindray Inc., Shenzhen, China). After cannulation of a large forearm vein, lactated Ringer's solution was administered, and patients were preoxygenated with 100% O_2 via a face

mask for 3 min. Anesthesia was then induced in each of the three groups.

Group *MAC*: Monitored anesthesia care (MAC) was induced and maintained via the continuous infusion of propofol using a target-controlled infusion (TCI) pump. The appropriate level of sedation was 45 to 60 points on the BIS. When involuntary body movements appeared, a bolus of 50 mg of propofol was administered.

Group GA_1: Induction was done with propofol (2 mg kg^{-1}), cis-atracurium (0.15 mg kg^{-1}), and fentanyl (3 μg kg^{-1}). Intubation was performed with the video laryngoscope using endotracheal tubes (Shiley™; Covidien, Mansfield, MA, USA) with appropriate internal diameters. After orotracheal intubation, GA was maintained with sevoflurane (1%-1.5%), propofol (3 mg/kg/h), remifentanil (0.05-0.2 ug/kg/min), and repetitive doses of 0.02 mg cis-atracurium per kilogram. The BIS was 45 to 60 points. Volume-controlled ventilation (VCV) was used. After excluding contraindications, neostigmine mixed with atropine was used as a reversal agent for the muscle relaxant at the end of the case.

Group GA_2: Anesthesia was induced with propofol (2 mg kg^{-1}), remifentanil (3 ug kg^{-1}), and 2% lidocaine (1 mg kg^{-1}). Remifentanil was administered as a slow bolus infusion over 1 minute. 2% lidocaine (3 ml) was applied with a spray tip attached to a syringe and injected into the larynx (1 ml) and trachea (2 ml) under direct vision with the video laryngoscope. Intubation was attempted 60 seconds after the administration. Nasotracheal intubation was performed using endotracheal tubes (Shiley™; Covidien, Mansfield, MA, USA) with appropriate internal diameters. Before insertion, the tube was well-lubricated with lidocaine jelly. The nasotracheal intubation procedure was as follows: 1) passage through the nose into the pharynx, 2) video laryngoscope-guided passage into the glottic inlet, and 3) video laryngoscope-guided passage into the trachea [19]. After intubation, GA was sevoflurane (1%-1.5%), propofol (3 mg/kg/h), remifentanil (0.05-0.2 ug/kg/min). Synchronous intermittent mandatory ventilation (SIMV) mode was used. After the procedure was completed, the patient was extubated when the recovery from anesthesia was confirmed. The BIS was 45 to 60 points. Patients who could not be intubated were given cis-atracurium (0.15 mg kg^{-1}) and intubation was accomplished.

The anesthesia team had discretion over the use of adjunctive sedatives, such as fentanyl and midazolam. Ten minutes before the end of ERCP, each patient was administered 50 mg of intravenous flurbiprofen for postoperative analgesia and 12.5 mg of intravenous dolasetron mesilate for the prevention of postoperative nausea and vomiting. Following completion of the procedure, patients were resuscitated in the endoscopy unit until they either spontaneously opened their eyes (Group *MAC*) or the anesthesiologist assessed the safety of extubation (Group GA_1 and Group GA_2). Subsequently, patients were transferred to the post-anesthetic care unit (PACU) and monitored by nurses until they reached a modified Aldrete score of 9 or 10 points.

The therapeutic ERCP procedure was performed with patients in the semi-prone position using a video duodenoscope with standard accessories by a highly experienced endoscopist. The endoscopist selected endoscopic sphincterotomy, endoscopic balloon dilatation, endoscopic stenting, and other therapeutic options based on the patient's condition and the endoscopist's judgment.

Outcome assessment

The instrument was filled by the procedure and recovery room nurses. The primary outcome was the overall intraprocedural cardiopulmonary adverse events that occurred among the three groups. Cardiopulmonary adverse events recorded in the anesthesia record were assessed based on previous literature [5, 8, 20] and established criteria by the American Society of Gastrointestinal Endoscopy [21]. Pulmonary events were recorded as follows: hypoxia (SpO_2 < 90%), the use of airway maneuvers, regurgitation and aspiration, laryngospasm, bronchospasm, and chest wall rigidity. Cardiac events were recorded as follows: hypertension (a mean artery pressure (MAP) increase > 40% and a MAP > 110 mmHg); hypotension (a MAP decrease > 40% and a MAP < 70 mmHg; or a MAP < 60 mmHg); new-onset arrhythmia or worsening of a pre-existing arrhythmia; and a major adverse cardiac event.

Total time, room time, and endoscopist and patient anesthetic satisfaction were included

Table 1. Intubating condition score

Variable Assessed	Clinically Acceptable		Not Clinically Acceptable
	Excellent	Good	Poor
Mask ventilation	Easy	Difficult	Impossible
Laryngoscopy	Easy	Fair	Difficult
Vocal cord position	Abducted	Intermediate/moving	Closed
Diaphragmatic movement/coughing	None	Slight[#]	Vigorous/sustained[‡]

[#]1 to 2 weak contractions or movement for less than 5 s, Vigorous; [‡]More than two contractions and/or movement for longer than 5 s.

as secondary outcome variables. Total time was defined from the moment the patient entry into the Endoscopy Center to patient departure. Room time was defined from the moment the patient entry into the endoscopy suit to patient departure from the endoscopy suit. Procedure time was defined as the time from insertion of the endoscope until withdrawal of the endoscope. Cannulation time was defined as the time from starting cannulation to the time when the catheter had been introduced deeply inside the common bile duct so that therapeutic procedures could be performed as needed. The time from the end of the procedure, until the patient was awake (Group MAC) or extubated (Group GA_1 and Group GA_2), was included in the awake/extubating time. PACU time was measured from entry to exit PACU. Patient and endoscopist satisfaction surveys were conducted on a scale of 0-10 (0= not at all satisfied, 10= the most satisfied). The occurrences of specific events (anesthesia conversion, early procedure termination, transient interruption, and procedural success) were also recorded.

The intubating conditions were assessed and scored for four variables: mask ventilation, laryngoscopy, vocal cord position, and diaphragmatic movement/coughing as reported [22] (**Table 1**). Variables were assessed as excellent, good, or poor. Patients who could not be intubated after receiving the assigned induction drugs were noted and given cis-atracurium (0.15 mg kg^{-1}).

Statistical analysis

Based on a previous study, the incidence of adverse events in MAC was reported at 51% [8]. To detect a significant difference of 15% in total rate among the three groups with a power of 0.9 at the 5% level of significance, 94 patients were needed in each group. To allow for dropouts, we increased the sample size to 120 patients per group.

All analyses were carried out using the statistical software SPSS version 23 (SPSS Inc., Chicago, USA). Continuous variables were presented as the mean ± standard deviation and analyzed using One-way ANOVA (Post-hoc test/Bonferroni test). Categorical variables were expressed as number of patients (n, %) and assessed using Pearson's chi-squared test or Fisher's exact test. $P < 0.05$ was deemed significant.

Results

A total of 405 signed informed consents were involved in this study. After excluding 45 patients, a total of 360 patients completed the study and were included in the final analysis (**Figure 1**). The patient demographic and baseline data are outlined in **Table 2**. There were no significant differences in patient and case characteristics among the groups.

There was a significant difference in the overall intraprocedural pulmonary and cardiac adverse events among the three groups [45/120 (37.5%) in Group *MAC*, 23/120 (19.2%) in Group GA_1, 21/120 (17.5%) in Group GA_2; $P < 0.001$] (**Table 3**). The incidence of cardiac adverse events was not significantly different among the three groups (P=0.911). All patients with cardiac adverse events were treated as needed and discharged without issues. No major adverse cardiac events occurred. However, the incidence of pulmonary complications was significantly higher in Group *MAC* ($P < 0.001$). During the procedure, 25 (20.8%) patients in Group *MAC* experienced episodes of SpO_2 < 90%. Airway maneuvers were used alone or in combination with other techniques, but only one technique that ultimately worked was counted in the results.

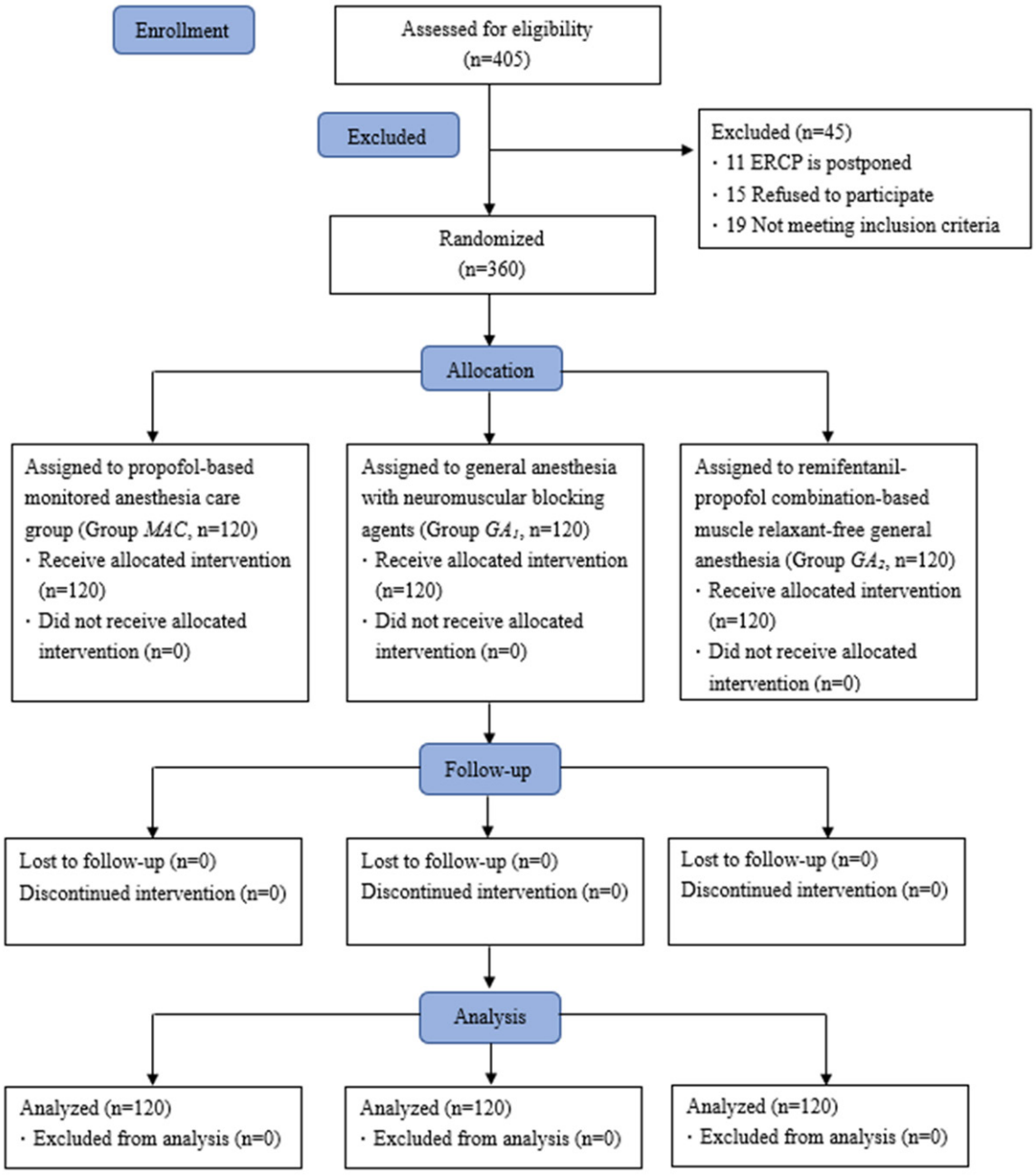

Figure 1. Consort flow diagram of the trial design.

Fifteen of the 360 patients were excluded from the analysis, because they were terminated prematurely due to endoscopy-related causes. There was no significant difference in cannulation time and procedure time (**Table 4**). Group GA_2 and Group *MAC* had a similarly shorter total time compared to Group GA_1 (67.3±13.9 min in Group *MAC*, 83.5±15.7 min in Group GA_1, 69.8±12.8 min in Group GA_2; $P < 0.001$). Room times were also similarly shorter in Group GA_2 and Group *MAC* than in Group GA_1 (56.8±13.3 min in Group *MAC*, 68.4±14.6 min in Group GA_1, 58.5±12.0 min in Group GA_2; $P < 0.001$).

The patient satisfaction score was not significantly different among groups (**Figure 2**). Both Group GA_1 and Group GA_2 endoscopist satisfaction scores were significantly higher than Group *MAC* (8.7±1.7 in Group *MAC*, 9.4±0.9 in Group GA_1, 9.4±0.8 in Group GA_2; $P < 0.001$).

Table 2. Characteristics of patients, and indications of ERCP procedures

	Group *MAC* (n=120)	Group GA_1 (n=120)	Group GA_2 (n=120)	Statistical significance
Demographics				
Age (years) (mean ± SD)	53.3±10.5	54.8±11.4	55.7±9.5	0.215
Gender (Male/Female)	68/52	62/58	60/60	0.560
Height (cm) (mean ± SD)	164.6±6.8	166.9±7.9	165.1±8.5	0.063
Weight (kg) (mean ± SD)	63.2±8.9	65.0±9.5	62.7±8.7	0.120
BMI (kg/m^2) (mean ± SD)	23.3±3.1	23.3±2.9	23.0±2.8	0.594
ASA Classification and Comorbidities				
ASA (I/II/III)	28/65/27	32/55/33	29/57/34	0.707
Hypertension	70 (58.3%)	63 (52.5%)	68 (56.7%)	0.644
Ischemic heart disease	24 (20.0%)	21 (17.5%)	17 (14.2%)	0.486
Diabetes mellitus	23 (19.2%)	28 (23.3%)	25 (20.8%)	0.728
Chronic Obstructive Pulmonary Disease	14 (11.7%)	16 (13.3%)	11 (9.2%)	0.593
Cerebral ischemia	16 (13.3%)	13 (10.8%)	12 (10.0%)	0.699
ERCP indications				
Stones	61 (50.8%)	66 (55.0%)	74 (61.7%)	0.234
Strictures	10 (8.3%)	14 (11.7%)	7 (5.8%)	0.271
Tumor or malignancy	26 (21.7%)	19 (15.8%)	19 (15.8%)	0.394
Acute Pancreatitis	9 (7.5%)	6 (5.0%)	5 (4.2%)	0.502
Chronic Pancreatitis	4 (3.3%)	6 (5.0%)	8 (6.7%)	0.496
Others	10 (8.3%)	9 (7.5%)	7 (5.8%)	0.748

Abbreviation: BMI, Body Mass Index; ASA, American Society of Anesthesiologists; ERCP, Endoscopic Retrograde Cholangiopancreatography. Data presented as mean ± SD or n (%) of patients. Continuous data were compared using the one-way ANOVA. Categorical data were compared using Pearson's chi-squared test or Fisher's exact test.

There was no significant difference in procedure success. Both Group GA_1 and Group GA_2 had no anesthesia conversion. The conversion rate from MAC to GA during the ERCP procedure was 5.8% (n=7) (**Table 5**). Four cases were due to respiratory depression, two were due to unstable hemodynamics, and one was due to prominently retained gastrointestinal material owing to concerns about regurgitation and aspiration. Premature termination associated with endoscopy-related causes was similar in the three groups. Group *MAC* had a significantly higher rate of transient procedure interruption ($P < 0.001$). More than half of the cases were interrupted due to pulmonary adverse events.

In Group GA_2, intubation was completed in all patients. Mask ventilation and laryngoscopy were easy in all patients 100% after anesthesia induction. The vocal cords were abducted in 107 (89.2%) patients. The patient reaction following intubation and inflation of the endotracheal tube cuff was rated excellent, with 101 (84.2%) patients reporting no coughing. No patient manifested signs of remifentanil-induced muscular rigidity.

Discussion

To the best of our knowledge, this is the first prospective, randomized trial to evaluate the clinical safety and efficacy of this remifentanil-propofol combination "muscle relaxant-free" GA in patients undergoing therapeutic ERCP, in comparison to two conventional anesthetic techniques. Our findings demonstrate that this "muscle relaxant-free" GA can be safely administered to patients undergoing therapeutic ERCP, with no serious cardiopulmonary adverse events. Furthermore, it proved to be superior to propofol-based MAC in terms of safety and ensuring an uninterrupted procedure, and outperformed conventional GA in terms of overall shorter total time.

The results of this prospective trial demonstrated that propofol-based MAC was associated with a higher frequency of intraprocedural hypoxemia compared to GA. In contrast, no cases of hypoxia occurred in the GA group. Multiple previous studies have reported a higher incidence of hypoxia in patients undergoing propofol-based sedation for ERCP, ranging from

Table 3. Intraprocedural pulmonary and cardiac adverse events

	Group *MAC* (n=120)	Group GA_1 (n=120)	Group GA_2 (n=120)	Statistical significance
Overall complication (n, %)	45 (37.5%)	23 (19.2%)	21 (17.5%)	< 0.001
Pulmonary events (n, %)	25 (20.8%)	0	0	< 0.001
Hypoxemia	25 (20.8%)	0	0	< 0.001
The use of airway maneuvers	25 (20.8%)	0	0	< 0.001
Jaw thrust	10 (7.5%)	0	0	< 0.001
Nasal airway	4 (3.3%)	0	0	0.036
Bag mask ventilation	6 (4.2%)	0	0	0.004
Endotracheal intubation	5 (1.7%)	0	0	0.012
Regurgitation	0	0	0	N/A
Aspiration	0	0	0	N/A
Laryngospasm	0	0	0	N/A
Bronchospasm	0	0	0	N/A
Chest wall rigidity	0	0	0	N/A
Cardiac Events (n, %)	20 (16.7%)	23 (19.2%)	21 (17.5%)	0.911
Hypertension	4 (3.3%)	0	0	0.036
Hypotension	8 (6.7%)	11 (9.2%)	9 (7.5%)	0.829
New-onset arrhythmia or worsening of pre-existed arrhythmia	8 (6.7%)	12 (10.0%)	12 (10.0%)	0.605
Premature atrial contractions	2 (1.7%)	5 (4.2%)	4 (3.3%)	0.639
Premature ventricular contractions	2 (1.7%)	2 (1.7%)	0	0.552
Bradycardia	4 (3.3%)	5 (4.2%)	8 (6.7%)	0.548
Tachycardia	0	0	0	N/A
ST-segment changes	0	0	0	N/A
Major adverse cardiac events	0	0	0	N/A
Cardiac arrest	0	0	0	N/A
Shock	0	0	0	N/A
Acute coronary syndrome	0	0	0	N/A

Defined criteria: Hypoxemia (SpO_2 < 90%); hypertension (MAP increase > 40% and a MAP > 110 mmHg); hypotension, systolic pressure < 90 mmHg or mean pressure < 60 mmHg; tachycardia, heart rate > 120 beats/min; bradycardia, heart rate < 55 beats/min. Data presented as n (%) of patients. Categorical data were compared using Pearson's chi-squared test or Fisher's exact test. MAP, Mean artery pressure.

Table 4. Efficiency metrics for ERCP procedures

Time (min)	Group *MAC* (n=116)	Group GA_1 (n=114)	Group GA_2 (n=115)	Statistical significance
Total time	67.3±13.9	83.5±15.7	69.8±12.8	< 0.001
Room time	56.8±13.3	68.4±14.6	58.55±12.0	< 0.001
Procedure time	38.0±11.1	40.3±14.1	37.2±12.3	0.166
Cannulation time	9.2±3.3	8.9±2.9	9.2±3.1	0.756
Awake/Extubating time	8.7±3.3	15.2±4.4	9.6±3.1	< 0.001
PACU time	10.3±3.1	15.0±3.8	10.6±2.7	< 0.001

Abbreviation: PACU, post-anesthesia care unit. Data presented as mean ± SD. Continuous data were compared using the one-way ANOVA.

15.4 to 36.8% [8, 23, 24]. Cote et al. identified male sex, higher body mass index (BMI), and an ASA physical classification of III or higher as independent predictors of airway modifications [3]. Factors such as obesity, high ASA classification, and chronic obstructive pulmonary disease (COPD) are linked to a higher likelihood of cardiovascular events and are also important

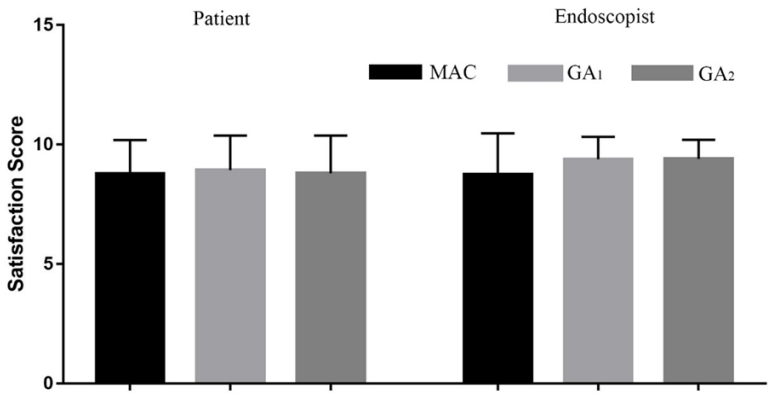

Figure 2. Differences in patient and endoscopist satisfaction scores. Patient and endoscopist satisfaction surveys on a scale of 0-10 were conducted (0= not at all satisfied, 10= the most satisfied). Data are expressed as the mean ± SD. Data were compared using the Kruskal-Wallis test.

factors in converted anesthesia [5, 6, 25]. Age was also found to be an independent predictor of sedation-related outcomes [6], which may be due to the higher number of comorbidities and higher ASA grades associated with older age. While the convenience of sedation is preferred in some cases, the risk of an unprotected airway is a major concern. In contrast, endotracheal intubation protects the airway and minimizes the risk of aspiration while ensuring adequate oxygenation. Regardless of whether muscle relaxants were used, GA was not associated with any intraprocedural pulmonary problems in our current investigation, suggesting that GA is safe in this aspect. It is also known that GA may be associated with an increased incidence of hypotension and arrhythmia [5]. However, this study showed no difference in the frequency of cardiac events, while a slightly higher proportion of hypotension requiring vasopressor was observed in GA patients without significant difference. Post-induction hypotension is a common occurrence in clinical practice and is associated with several factors, including older age, pre-induction hypotension, high ASA PS scores, preoperative renin-angiotensin blockade, a high revised cardiac risk index, propofol induction, or increasing fentanyl induction dosage [26-28]. However, hemodynamic parameters can be titrated as needed, and various vasoactive drugs are available to correct transient post-induction hypotension, suggesting the safety of the protocol.

Perbtani et al. showed that the procedure time was significantly prolonged under GA, which decreased endoscopy unit efficiency [7]. Carriere et al. suggested that MAC was implicitly optimized to maximize efficiency [29], while Smith et al. reported no significant difference in various efficiency metrics between GA and MAC [8]. Our data show that Group GA_2 and Group *MAC* had similar shorter total time and room time, compared to Group GA_1, excluding cases that ended prematurely. All patients under GA were extubated in the endoscopy suit, with awake/extubating time significantly shorter in Group *MAC* and Group GA_2 than in Group GA_1. The rapid elimination of propofol and remifentanil allowed for fast recovery of consciousness, autonomous respiration, and the upper airway reflex in Group GA_2 without concern for postoperative residual curarization. Compared with conventional GA, "muscle relaxant-free" GA can improve efficiency.

The procedure success rate was similar in all three groups and none of the ERCP procedures had to be prematurely terminated due to anesthesia-related complications. However, ERCP was transiently interrupted in 21.7% of patients when MAC was used, mostly due to anesthesia conversion, hypoxia, and body movements. These interruptions can be inconvenient for endoscopists. Body movements during the procedure may result in decreased image quality and increased radiation exposure. Anesthesia nurses may be less satisfied with respiratory management, and intraprocedural radiation is another noteworthy issue. Anesthesia care providers are particularly vulnerable to radiation exposure during this therapeutic procedure, especially under MAC. Without a protective airway, the anesthesiologist must always be vigilant. Since a proportion of patients may require urgent conversion from MAC to GA, administering and supervising MAC for ERCP can be stressful for the anesthesiologist. During the procedure, GA provides a more stable pulmonary function and cardiovascular state, and anesthesiologists can monitor changes from outside via a monitor screen, reducing prolonged radiation exposure. The use of GA

Table 5. The success of ERCP, anesthesia conversion, and transient interruption of ERCP

	Group *MAC* (n=120)	Group GA_1 (n=120)	Group GA_2 (n=120)	Statistical significance
Success of ERCP	116 (96.7%)	114 (95.0%)	115 (95.8%)	0.945
The success of ERCP with planned anesthesia	109 (90.8%)	114 (95.0%)	115 (95.8%)	0.233
Early termination of ERCP	4 (3.3%)	6 (5.0%)	5 (4.2%)	0.945
Anesthesia causes	0	0	0	N/A
Endoscopy-related causes	4 (3.3%)	6 (5.0%)	5 (4.2%)	0.945
Anesthesia conversion	7 (8.3%)	0	0	0.001
Respiratory depression	4 (3.3%)	0	0	0.036
Unstable hemodynamics	2 (1.7%)	0	0	0.331
Retained gastrointestinal content	1 (0.8%)	0	0	1.000
Transient interruption	26 (21.7%)	0	0	< 0.001
Body movements	5 (4.2%)	0	0	< 0.001
Pulmonary adverse events	14 (11.7%)	0	0	< 0.001
Anesthesia conversion	7 (5.8%)	0	0	< 0.001

Abbreviation: ERCP, Endoscopic Retrograde Cholangiopancreatography. Data presented as n (%) of patients. Categorical data were compared using Pearson's chi-squared test or Fisher's exact test.

appears to be a reasonable and appealing option, with significantly higher satisfaction and increased security. We tend to provide GA for ERCP, especially for more complex or time-consuming procedures. When prior attempts using sedation have exposed patients to the risk of cardiopulmonary complications, regurgitation, and aspiration, we should immediately switch to GA. "Muscle relaxant-free" GA, like standard GA, prevents movements during the ERCP procedure.

The feasibility of "muscle relaxant-free" GA using a remifentanil-propofol combination is based on the assumption that propofol has a depressant effect on upper airway reflexes [30] and that opioids improve conditions by attenuating the hemodynamic response to laryngoscopy and intubation, thus eliminating the risk of residual postoperative paralysis. However, the main concern is the intubation condition. Our results show that the conditions for nasotracheal intubation were clinically acceptable. In Group GA_2, all patients could be easily ventilated via facemask after induction, and we achieved a 100% success rate in nasotracheal intubations. Topical lidocaine spray applied to the vocal cords and airway is an effective method [31], and intravenous lidocaine may also be a useful adjunct [32]. Studies of nasotracheal intubation without muscle relaxants are very limited [15, 33]. Although nasotracheal intubation may be more challenging than orotracheal intubation, anesthesiologists can develop the necessary skills through training. Nasal tubes are thought to be better tolerated than oral tubes [34], although the mechanism of which remains unclear. One theory is that the nasal mucosa is less sensitive to irritation than the oral mucosa. Another theory is that the angle at which the tracheal tube enters the trachea is shallower with a nasotracheal tube than with an orotracheal tube, resulting in a smaller contact area and stress on the epiglottis laryngeal surface. This may lead to a reduced cough reflex and better tolerance.

However, there is still controversy surrounding the safety and efficacy of intubating patients without a difficult airway using a muscle relaxant-free approach. The intubation conditions may not be optimal, and there is a risk of airway reactivity, including glottis closure and laryngospasm during intubation, which may compromise ventilation. Additionally, this approach may be associated with airway injury, leading to post-intubation symptoms such as hoarseness or a sore throat. Research has shown that using a smaller endotracheal size can significantly reduce the incidence and severity of these symptoms [35]. Nasotracheal tubes with a smaller diameter are also better at reducing the chance of sore throats and hoarseness [36]. The use of muscle relaxant-free intubation remains a topic of debate, although the availability of the drug Sugammadex has provided

patients undergoing ERCP with a rapid and predictable recovery. However, the high cost of Sugammadex prevents it from being used as a standard neuromuscular reversal drug. This muscle relaxant-free intubation technique may be useful in some surgical procedures where intubation is necessary, but neuromuscular block is not needed to facilitate the procedure. This approach is appropriate for ERCP, for example. There are other surgical procedures where paralysis is not desirable, such as orthopedic and neurosurgical procedures, as well as thyroid and parathyroid surgeries that require intraoperative neuromonitoring. Patients with neuromuscular diseases such as myasthenia gravis have been shown to be sensitive to non-depolarizing agents, which further complicates the use of muscle relaxants in these cases [37, 38].

This study has a few limitations. First, this study was conducted at a single center with a limited number of cases, so further research involving larger, multicenter cohorts is therefore needed. Additionally, the age range of patients in this study was 18-70, and the ASA grades were between I and III. However, many patients who require ERCP are older, sicker, and have multiple comorbidities, so it is important to determine the safety and feasibility of remifentanil-propofol combination-based "muscle relaxant-free" GA in this population. Ongoing research will evaluate the use of this technique in older patients or those with an ASA IV score. Finally, the study did not collect data on postoperative complications, outcomes, or cost, which would be valuable for comparing the benefits and risks of different anesthetic techniques.

Conclusion

The use of remifentanil-propofol combination-based "muscle relaxant-free" general anesthesia for ERCP is both safe and efficient for patients. In comparison to propofol-based monitored anesthesia care, this technique has been found to result in greater satisfaction among endoscopists, less interruption during the procedure, and fewer cardiopulmonary adverse events. Additionally, it has a shorter total time and room time than traditional general anesthesia. Therefore, we suggest that remifentanil-propofol combination-based "muscle relaxant-free" general anesthesia may be a valuable option for advanced endoscopic procedures, including ERCP.

Disclosure of conflict of interest

None.

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