ORIGINAL RESEARCH **HEPATOBILIARY ANESTHESIA**

Comparative risk of pulmonary microaspiration in intubated versus sedated patients undergoing ERCP

Mohamed A. Maher [1], Hend F. Hassan [2], Ahmed I. Refaat [3], Moshira S. Amer [4]

Author affiliations:

1. Mohamed Ahmed Maher, MD, Assistant Professor of Anesthesia at Theodor Bilharz Research Institute. Giza, Egypt; E-mail: dmohmaher@gmail.com.
2. Hend Fayed Hassan, MD, Lecturer of Anesthesia at Theodor Bilharz Research Institute. Giza, Egypt; E-mail: Hend10_fayed@hotmail.com {ORCID ID: 0000-0002-1469-0597}
3. Ahmed Ibrahim Refaat, MD, Assistant Professor of Anesthesia at Theodor Bilharz Research Institute. Giza, Egypt.
4. Moshira Sayed Amer, MD, Lecturer of Anesthesia at Theodor Bilharz Research Institute. Giza, Egypt; E-mail:.

Correspondence: Moshira Sayed Amer, MD; **E-mail:** moshira.amer83@gmail.com; **ORCID:** {0000-0003-3867-568X}

ABSTRACT

Introduction: Endoscopic retrograde cholangio-pancreatography (ERCP) is by far considered the cornerstone in the diagnosis and treatment of biliary and pancreatic diseases. The optimal anesthetic choice for ERCP remains under debate. While general anesthesia offers certain benefits, some drawbacks limit its routine use in ERCP. Monitored anesthesia care (MAC) or deep sedation offers a viable alternative in remote locations, avoiding these drawbacks. Pulmonary aspiration may lead to a serious complication or even death. Potential microasprition during ERCP is an underreported complication and data about it is scarce. We assessed the comparative risk of pulmonary micro aspiration in intubated versus sedated patients undergoing ERCP

Methodology: 130 ASA I-III patients were enrolled in the study and divided into two groups: general anesthesia with endotracheal intubation (Group-I) and deep sedation (Group-S). Each group had 65 patients. All patients were monitored for hypoxic episodes in the HDU unit for 48 HRs after ERCP. Also, they were subjected to Computed Tomography (CT) chest after 48 HRs to detect acute pulmonary infiltrates of micro aspiration.

Results: The incidence of positive postoperative CT findings for micro aspiration was statistically significantly higher in the Group-S (24.62%) than Group-I (4.62%) with P-value: of 0.002. The incidence of postoperative hypoxic episodes was higher in the Group-S 27.69% versus 6.15% in Group-I but there was no statistically significant difference between both groups. Also, it was found that the incidence of postoperative micro aspiration was statistically significantly higher in patients of ≥ 65 years (52%) than < 65 years (7.5%) of the Group-S with P = 0.014. Incidence of postoperative fever, cough, tachypnea, and the need for O_2 supplementation were comparable in both groups.

Conclusion: The incidence of positive postoperative CT findings for microaspiration was higher in the sedation group. It was also higher in patients aged ≥ 65 years in the sedation group. Despite these findings, none of the patients developed clear signs of postoperative chest infection.

Abbreviations: CT - Computed Tomography; ERCP - Endoscopic retrograde cholangio-pancreatography; ETT-endotracheal intubation; MAC - Monitored anesthesia care

Keywords: ERCP, MAC, GA with ETT, pulmonary micro aspiration.

Citation: Maher MA, Hassan HF, Refaat AI, Amer MS. Comparative risk of pulmonary microaspiration in intubated versus sedated patients undergoing ERCP. Anaesth. pain intensive care 2024;28(6):1029-1034; **DOI:**10.35975/apic.v28i6.2611

Received: August 02, 2024; **Reviewed:** September 06, 2024; **Accepted:** September 18, 2024

1. INTRODUCTION

Endoscopic retrograde cholangiopancreatography (ERCP) is by far considered the cornerstone in the diagnosis and treatment of biliary and pancreatic diseases. The extensive use of ERCP has facilitated the management of many critical patients, for whom conventional surgical procedures were deemed to be high-risk interventions. [1]

However, ERCP is considered a complex procedure compared to other endoscopic interventions, often requiring longer duration and carrying a substantially higher complication rate like aspiration, hypoxemia, and hypotension.[2] Moreover, Patients planned for ERCP often have additional comorbidities that make them high-risk candidates. So, optimizing anesthetic techniques is crucial for successful outcomes without compromising patient safety.[3, 4]

Selecting the appropriate anesthetic approach for ERCP presents a significant challenge. A spectrum of anesthetic techniques exists, ranging from conscious sedation to general anesthesia (GA).[5]

The optimal anesthetic choice for ERCP remains under debate. While general anesthesia offers certain benefits, some drawbacks limit its routine use in ERCP. These include prolonged induction and recovery times, which can impact patient turnover, the risk of residual neuromuscular blockade, and increased cost. Additionally, ERCP is typically a day-case procedure, favoring sedation techniques.[6] Monitored anesthesia care (MAC) or deep sedation offers a viable alternative in remote locations, avoiding these drawbacks.[7] However deep sedation may lead to some complications, the most dangerous of which are regurgitation and pulmonary aspiration in addition to hypoxia, bradycardia, and airway obstruction.

Pulmonary aspiration may lead to a serious complication or even death.[8] Apparent aspiration is a notable adverse event during gastrointestinal endoscopy especially in prolonged or difficult procedures, but on the other hand, potential microasprition during ERCP is an underreported complication and data about it is scarce.[9]

Since pulmonary microaspiration associated with ERCP has not been evaluated and there is no conclusive data to support or oppose the need for endotracheal intubation (ETT) to avoid microaspiration; therefore, we aim to evaluate both techniques of anesthesia concerning microaspiration risk.[10]

Aim of the study

We aimed to compare the incidence of pulmonary microaspiration in deep sedation versus GA with ETT in patients undergoing ERCP.

2. METHODOLOGY

The study was designed to be a prospective, randomized, single-blinded study that was conducted in the Department of Gastrointestinal Endoscopy unit of Theodor Bilharz Research Institute after approval by the research ethics committee (PT: 485), and patients informed consents were signed. The trial was registered in clinical trials.gov: NCT04831489. 130 patients were enrolled in the study and divided into two groups: general anesthesia with endotracheal intubation (Group-I) and deep sedation (Group-S). (Figure 1) Each group had 65 patients. Randomization was done by computerized generated numbers and allocation was done as 1:1 of scheduled cases per day. The patient as well as the radiologist responsible for evaluating the CT chest were blinded to group assignment.

2.1. Sample size estimation

Dunham et al.[10] indicated that the perioperative pulmonary aspiration rate in the intubated patients under general anesthesia was 4.8% while we are expecting the microaspiration rate under deep sedation to be 24%. Based on this; a minimum sample size of 61 cases per group (total 122 cases) is required with a power of 80% and alpha error of 0.05. The sample size was estimated using PS (Power and Sample Size Program) Version 3.1.2.

2.2. Inclusion criteria

Inclusion criteria included ASA I-III, age ≥ 18 years old, and BMI < 35 Kg/m^2. Preoperative pulmonary stability criteria defined as a respiratory rate of 12–24 breaths per minute, $SpO_2 \geq 94\%$ on room air, and normal CT chest.

2.3. Exclusion criteria

Exclusion criteria included Pregnancy; fasting ≤ 8 hours for solid and clear liquids. A pre-existing lung condition in patients requiring mechanical ventilation, supplemental oxygen, inhalational bronchodilator, or systemic bronchodilator or steroid. Tracheostomized patients. Patients having swallowing disorders. Bowel obstruction. And anticipated difficult intubation.

2.4. Anesthesia Technique

A preoperative assessment, including a history, physical examination, review of laboratory data, and computed tomography (CT) chest was done. Anesthesia and procedural consent were obtained. Upon arrival at the endoscopy unit, the following monitors were applied to all patients: five lead ECG, non-invasive blood pressure monitor (NIBP) every 10 minutes, pulse oximetry, and end-tidal capnography ($EtCO_2$) in mechanically ventilated patients. Then monitoring was continued intraoperatively. Anesthesia was induced as follows:

2.4.1. GA with ETT (Group-I):

Pre-oxygenation was done. GA was induced with 2 mg/kg propofol, 1 µg/kg fentanyl and 0.5 mg/kg atracurium followed by endotracheal intubation. Anesthesia was maintained with 1 MAC with sevoflurane. Mechanical ventilation was adjusted with fresh gas flow oxygen in air 30-40% at a rate of 2 L/min to maintain end-tidal carbon dioxide of 35-40 mm Hg. Reversal of neuromuscular blockade was achieved by intravenous administration of neostigmine 0.05 mg/kg and atropine 0.02 mg/kg.

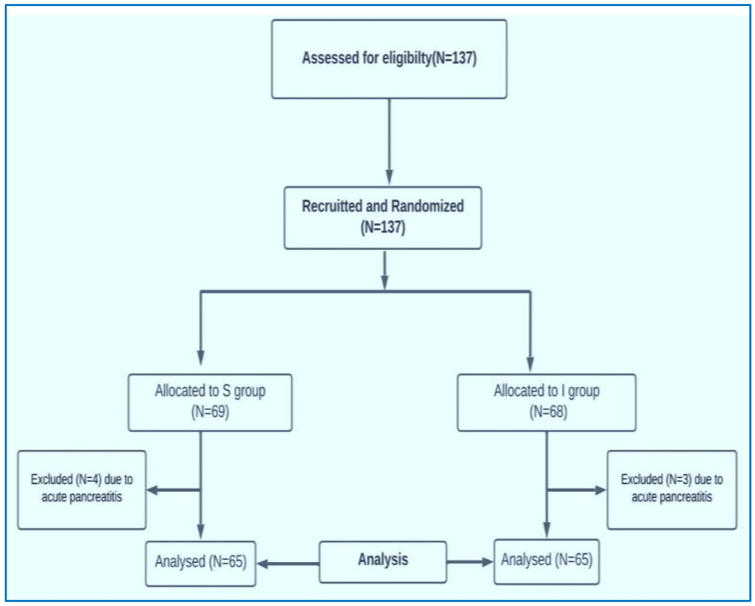

Figure 1: flow chart.

2.4.2. Deep sedation (Group S):

Anesthesia was induced using titrated IV doses of propofol (1-1.5 mg/kg) and fentanyl (25-50 µg) to maintain spontaneous breathing and airway patency. Once adequate jaw relaxation was achieved, the endoscopy probe was inserted. Maintenance of sedation was carried out using propofol infusion between 80-120 µg/kg/min. An additional dose of 25-50 mg propofol was given to the patient if spontaneous movement occurred.

2.5. Positioning in both groups

Patients were put into the prone position with the head turned to the right on the fluoroscopy table. In this position, a pillow was placed under the upper chest which raised the head and neck. This position made the airway more accessible for suctioning and airway manipulations and allowed pressure relief from the abdomen. In patients receiving a GA, positioning was done after securing the airway by ETT in the supine position. In deeply sedated patients, positioning was done before sedation.

Intraoperative hemodynamic changes were managed as follows; intraoperative hypotension defined as MAP < 20% of the baseline was managed by IV ephedrine 5-10 mg. Intraoperative bradycardia was managed by IV 0.4 mg atropine. Intraoperative hypoxic episodes defined as $SpO_2 < 95\%$ were managed as follows in the sedation group; increasing O_2 flow, applying chin left and jaw thrust, and suctioning excessive secretions from the airway. If persistent desaturation was below 90% and declining, 1.5 mg/kg succinylcholine was administered and ETT intubation was done. Patients who required ETT in the sedation group were excluded from the study.

2.6. Detection of microaspiration

Postoperative CT chest was done for all patients 48 hours after the procedure. Pulmonary micro-aspiration was defined as the presence of a new pulmonary infiltrate on the CT chest within the 48 hours following ERCP.

During the first postoperative 48 hours following ERCP, all patients were monitored in a high dependency unit (HDU) for postoperative hypoxic episodes, any hypoxic episode in the first 2 hours after transfer to the HDU was excluded to eliminate any confounding factor of hypoxia; residual anesthetics and residual muscle relaxants. Also signs of postoperative chest infection (fever, cough, tachypnea, and need for O_2 supplementation if $SpO_2 < 90\%$), and signs of pancreatitis: persistent abdominal pain, elevated serum levels of pancreatic enzymes and positive abdomen CT findings were monitored. Patients who developed acute pancreatitis were transferred to the intensive care unit (ICU) to be managed according to the clinical signs and were excluded from the study.

2.7. Outcomes

Pulmonary micro aspiration was defined as the presence of an acute pulmonary infiltrate on the CT chest within the 48 hours following ERCP. Secondary outcomes were number of intra-operative hypoxic episodes defined as SpO_2 < 94%; number of intra-operative hypotensive episodes; and postoperative fever, cough, tachypnea, and requiring oxygen supplementation during the first 48 hours post ERCP.

2.8. Statistical analysis

Statistical analysis was done by SPSS v27 (IBM©, Armonk, NY, USA). Shapiro-Wilks test and histograms were used to evaluate the normality of the distribution of data. Quantitative parametric data were presented as mean and standard deviation (SD) and were analyzed by unpaired student t-test. Qualitative variables were presented as frequency and percentage (%) and analyzed using the Chi-square test or Fisher's exact test when appropriate. A two-tailed P value < 0.05 was considered statistically significant.

3. RESULTS

The demographic data of both groups including age, sex, BMI, and ASA classification showed no statistically significant difference between both groups (Table 1).

Regarding the intraoperative events in both groups: the incidence of hypoxic episodes was significantly higher in the Group-S than Group-I (P< 0.001) but none of them required endotracheal intubation. There was no significant difference between the incidence of hypotensive and bradycardic episodes between both groups. There was no recorded incidence of intraoperative vomiting in both groups (Table 2).

Postoperative events in both groups showed the following:

The incidence of postoperative hypoxic episodes was higher in the Group-S 27.69% versus 6.15% in Group-I but there was no statistically significant difference between both groups. The incidence of positive postoperative CT findings for microaspiration was statistically significantly higher in the Group-S (24.62%) than Group-I (4.62%) with P-value: of 0.002. Incidence of postoperative fever, cough, tachypnea, and the need for O2 supplementation were comparable in both groups (Table 3).

Concerning the association between the age ≥ 65 years and the incidence of positive postoperative CT findings for micro aspiration. It was found that the incidence of postoperative microaspiration was statistically significantly higher in patients age ≥ 65 years (52%) than in patients aged < 65 years (7.5%) of the Group-S with a p-value: of 0.014. In Group-I, there was no statistically significant difference between the incidences of postoperative microaspiration in the 2 age groups (Table 4).

Table 1: Demographic data of the studied groups

Parameter		Group S (N = 65)	Group I (N = 65)	P-value
Age (Years)		58.48 ± 10.02	59.17 ± 8.01	0.664
Sex	Male	34 (52.31)	32 (49.23)	0.726
	Female	31 (47.69)	33 (50.77)	
BMI (kg/m^2)		27.28 ± 2.93	27.49 ± 2.18	0.648
ASA	I	9 (13.85)	3 (4.62)	0.185
	II	33 (50.77)	38 (58.46)	
	III	23 (35.38)	24 (36.92)	

Significant P value ≤ 0.05. Data are presented as frequency (%) or mean ± SD; BMI: Body mass index

4. DISCUSSION

Deep sedation is the most used anesthetic technique for ERCP as it is thought to have the same safety profile with more simplicity than GA with ETT in a large spectrum of patients. There is limited data in the literature comparing the pulmonary risks of conducting ERCP under monitored anesthesia care versus general anesthesia with ETT. The current study raises concerns about an unnoticed possible complication of anesthesia for ERCP, which is pulmonary microaspiration.

This study showed that there is a higher incidence of postoperative pulmonary microaspiration in the deep sedation group (24.62%) versus the ETT group (4.62%) evidenced by CT chest. Even though this led to a higher incidence of postoperative hypoxic episodes noticed in Group-S (27.68%) than Group-I (6.15%) 2 patients only in Group-I needed O_2 supplementation as their oxygen saturation fell below 90% and the event resolved without further management. Moreover, no pneumonia or any serious respiratory complication that affected postoperative clinical course was noticed in either group.

The incidence of hypoxic episodes in Group-S (33.85%) was higher than Group-I (0%) which is due to the tight airway protection and ventilation control offered by the endotracheal intubation and mechanical ventilation. However, all hypoxic episodes were managed by simple maneuvers such as head tilt, jaw elevation, oro-pharyngeal suctioning, or increasing fraction of inspired

Table 2: Intraoperative events of the studied groups

	Group S (N = 65)	Group I (N = 65)	P value
Incidence of hypoxic episodes	22 (33.85)	0 (0)	**< 0.001***
Incidence of hypotensive episodes	7 (10.77)	3 (4.62)	0.324
Incidence of bradycardic episodes	7(10.77)	2 (3.08)	0.164
Vomiting	0 (0)	0 (0)	-----

**: Significant as P value ≤0.05. Data are presented as frequency (%).*

Table 3: Postoperative events of both groups

Postoperative event	Group S (N = 65)	Group I (N = 65)	P value
Incidence of hypoxic episodes	18 (27.69)	4 (6.15)	0.842
Post-operative CT findings	16 (24.62)	3 (4.62)	0.002*
Fever	1 (1.54)	0 (0)	1
Cough	1 (1.54)	0 (0)	1
Tachypnea	2 (3.08)	1 (1.54)	1
O_2 supplementation	2 (3.08)	0 (0)	0.496

**: Significant as P value ≤ 0.05. Data are presented as frequency (%).*

Table 4: Association between postoperative CT findings and age in both groups

Postoperative CT findings	Age < 65 years	Age ≥ 65 years	P value
Group S (N = 65)	3 (7.5)	13 (52)	0.014*
Group I (N = 65)	0 (0)	3 (13.04)	0.244

**: Significant as P ≤ 05. Data are presented as frequency (%).*

oxygen (FiO_2) without further need to convert any patient to GA with ETT.

Concerning hemodynamics, the incidence of intraoperative hypotensive and bradycardic episodes was higher in the Group-S than Group-I, yet there was no significant difference between them. This is consistent with Zachary et al. 2019 who studied the incidence of sedation-related adverse events in high-risk patients scheduled for ERCP under MAC or GA with ETT. They stated that there was no difference in the incidence of hypotension and cardiac dysthymia between both techniques of anesthesia.[11]

Most studies exploring perioperative pulmonary complications of both anesthetic techniques focused on studying the incidence of gross aspiration, and intra and postoperative hypoxia, but none of them explored micro aspiration up to the knowledge of the authors.

In the current study, we are the first study, up to the knowledge of the authors, who used CT chest to compare both techniques. This is due to its known accuracy in detecting pulmonary microaspiration rather than hypoxia as an indicator of pulmonary complications as hypoxia may be affected by other factors not related to anesthetic technique i.e. Distension, pain, and pulmonary embolism. This was evident in our study as hypoxic episodes were higher than CT findings in both groups.

The relative safety of Intubation over Sedation revealed by our study agrees with Zachary et al. 2019 who depended on the hypoxic episodes and the need for airway maneuvers to compare the incidence of sedation-related adverse events in Anesthesia with intubation versus Deep sedation in high-risk patients undergoing ERCP. He found them to be (19%) in the sedation group slightly lower than our findings in the same group (33.85 % intraoperative and 27.68% postoperative). This difference may be attributed to the difference in the definition of hypoxia limit. Their study defined hypoxia when O_2 saturation fell below 90% while our study chose a higher limit < 95%. We chose this hypoxia limit because this is the

acceptable safe limit during the postoperative period, which is the primary concern of our study. Also, this is the safe limit in patients with limited cardiopulmonary reserve.[11]

Moreover, Ahmad et al. (2019) found that intra and postoperative hypoxic episodes in ERCP patients receiving deep sedation were 23.7%, lower than noted in our study. They defined hypoxia < 90% in his study.[12]

Another finding in our study is that there was a significant association between age ≥ 65 years and the incidence of aspiration in patients of the deep sedation group (52%) yet none of these patients developed clinical signs of pneumonia. This comes in consistence with the Consensus guidelines of the BJA (2023), which stated that patient age and ASA physical status are not considered independent determinants of choosing between monitored anesthesia care and general anesthesia. Meanwhile, the frailty index is the more accurate method for predicting perioperative morbidity and mortality and hence can be used for the proper selection of the anesthetic technique. Subsequently, it can be suggested that if the patient is aged≥ 65 years and has another potential risk factor, this may increase the risk of postoperative pulmonary complications.[13]

5. CONCLUSION

In conclusion; we assume that the MAC in ERCP had a higher incidence of pulmonary microaspiration especially in patients aged more than 65 years. Also, this was accompanied by a higher incidence of postoperative hypoxic episodes. Yet there was no incidence of clear signs of chest infection. So it can be wisely recommended that patients above the age of 65 years should be anesthetized with GA and ETT.

7. Ethical considerations

All participants were fully informed about the conduct of the study and written informed consent obtained.

8. Acknowledgments

The authors would like to thank the staff of the diabetic and endocrine center in Al-Sadder Teaching Hospital for their efforts which made this study possible. Our special thanks are to Alia Maghney for her collaborative efforts in the data collection and entry.

9. Authors contribution

MAM: manuscript writing and editing
HFH: concept and writing of the manuscript.
AIR: manuscript editing and revision.
MSA: Conduction of the study work and data entry

10. REFERENCES

1. Shah SK, Mutignani M, Costamagna G. Therapeutic biliary endoscopy. Endoscopy 2002; 34:43-53.
2. Davinder Garewal and PallaviWaikar. Propofol Sedation for ERCP Procedures: A Dilemna? Observations from an Anesthesia Perspective , Diagnostic and Therapeutic Endoscopy ,Volume 2012,
3. Youssef Motiaa, Mustapha Bensghir, Abdelhamid Jaafari, Anesthesia for endoscopic retrograde cholangiopancreatography: target-controlled infusion versus standard volatile anesthesia. Annals of Gastroenterology (2016); 29, 530-535
4. Garewal D, Vele L, Waikar P. Anesthetic considerations for endoscopic retrograde cholangiopancreatography procedures. Curr Opin Anaesthesiol 2013; 26: 475-480.
5. Mazanikov M, Udd M, Kylänpää L, et al. Patient-controlled sedation with propofol and remifentanil for ERCP: a randomized, controlled study. Gastrointest Endosc 2011; 73:260-266. 8
6. Sorser SA, Fan DS, Tommolino EE, et al. Complications of ERCP in patients undergoing general anesthesia versus MAC. Dig Dis Sci, 2014; 59:696-697.
7. Sheila Ryan, Tyler Berzin, Sirish Sanaka , et al. Deep Sedation Without Intubation for ERCP Is Appropriate in Healthier, Non-obese Patients, *Dig Dis Sci* (2013) 58:3287–3292
8. C Michael Dunham, Barbara M Hileman, Amy E Hutchinson, et al. Perioperative hypoxemia is common with horizontal positioning during general anesthesia and is associated with major adverse outcomes: a retrospective study of consecutive patients. BMC Anesthesiology, 2014, 14:43
9. Christopher M Kollmann, Wolff Schmiegel and Thorsten Brechmann. Gastrointestinal endoscopy under sedation is associated with pneumonia in older inpatients. United European Gastroenterology Journal; 2018, Vol. 6(3) 382–390.
10. Dunham CM, Hileman BM, Hutchinson AE, Chance EA, Huang GS. Perioperative hypoxemia is common with horizontal positioning during general anesthesia and is associated with major adverse outcomes: a retrospective study of consecutive patients. BMC Anesthesiol. 2014 Jun 9; 14:43.
11. Zachary L. Smith, DO, Daniel K. Mullady, Gabriel D. Lang, et al. A randomized controlled trial evaluating general endotracheal anesthesia versus monitored anesthesia care and the incidence of sedation-related adverse events during ERCP in high-risk patients. Gastrointestinal Endoscopy. 2019; 89: 855-862.
12. Ahmad Hormati, Reza Aminnejad, Mohammad Saeidi, et al. Prevalence of Anesthetic and Gastrointestinal Complications of Endoscopic Retrograde Cholangiopancreatography. Anesth Pain Med. 2019: 1-6.
13. Omid Azimaraghi, Mohammad Bilal, Somchai Amornyotin, et al. Consensus guidelines for the perioperative management of patients undergoing endoscopic retrograde cholangiopancreatography. British Journal of Anesthesia. 2023; 130: 763e77

