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*Original Article*

# Comparison of etomidate and propofol-mediated anesthesia induction followed by intubation and sevoflurane maintenance during ERCP in obese patients

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**Abstract:** Objective: In this study, we focused on obese patients (Body Mass Index (BMI) ≥30 kg/m$^2$) and compared the efficacy and safety of etomidate or propofol-mediated anesthesia induction followed by intubation and sevoflurane maintenance during endoscopic retrograde cholangiopancreatography (ERCP). Methods: A total of 180 patients were computer-randomized into a propofol group or an etomidate group, with 90 cases in each group. Patients received anesthesia induction by etomidate or propofol followed by intubation and sevoflurane maintenance during ERCP. Baseline characteristics, information about procedure-related time and satisfaction, and adverse events were collected and compared between the etomidate group and propofol group. Results: Baseline characteristics of both groups were similar. The propofol group had a longer time of intraoperative $SpO_2$ <95% (etomidate group vs propofol group, 0.07±0.47 min vs 0.24±0.87 min, *P*-value = 0.019), higher frequency of $SpO_2$ <95% for any period of time (etomidate group vs propofol group, 2.22% vs 11.11%, *P*-value = 0.032), and higher frequency of transient hypotension (etomidate group vs propofol group, 1.11% vs 8.89%, *P*-value = 0.034). The etomidate group had longer induction time and recovery time than the propofol group with *P*-values of 0.019 and 0.004, respectively. Conclusion: In obese patients who underwent ERCP and needed intubation, etomidate appears better than propofol for anesthesia induction followed by anesthesia maintenance of sevoflurane.

**Keywords:** Endoscopic retrograde cholangiopancreatography (ERCP), obese patients, etomidate, propofol, sevoflurane

## Introduction

Since the first endoscopic retrograde cholangiopancreatography (ERCP) performed by McCune in 1968, ERCP has opened up a new area in pancreaticobiliary diagnosis and is widely used in many diseases, including acute cholangitis, pancreatic cancer, benign biliary stenosis, cholangiocarcinoma, chronic pancreatitis, and pancreas divisum [1-6]. ERCP is an invasive endoscopic procedure that needs anesthesia throughout the procedure. Nowadays, anesthesia without intubation is preferred since intubation may induce stress responses and increase the risk of hypertension and respiratory tract damage [7-9]. However, for patients with high risk of breathing problems, such as people with obesity, intubation is needed to keep an unobstructed respiratory tract and facilitate oxygen supply [10, 11].

Sevoflurane is a new type of inhaled general anesthetic. It has a low blood-gas distribution coefficient, which makes it an anesthetic with efficiency, fast awakening speed, and easy control of the depth of anesthesia [12-14]. Sevoflurane smells aromatic and causes no irritation to the respiratory tract [15]. It also has little effect on hemodynamics and spontaneous breathing [16, 17]. However, sevoflurane may be inadequate for anesthesia induction in anesthesia with intubation due to its complex operation, longer induction time, and diverse efficiency [18, 19]. Therefore, propofol and etomidate are commonly used for anesthesia induction. Etomidate is a common intravenous anesthetic with a rapid hypnotic effect in clinical practice [20]. Etomidate induces a sleeping situation in the cerebral cortex and does not affect the sympathetic and autonomic nervous systems [21]. Propofol is a non-barbiturate

anesthetic [22]. It is found that etomidate can easily increase the heart load during anesthesia [23], and propofol may cause hypotension and respiratory depression [24]. Nevertheless, the efficacy and safety of etomidate or propofol-mediated anesthesia induction followed by sevoflurane maintenance is uncertain. In this study, we focused on obese patients (Body Mass Index (BMI) ≥30 kg/m$^2$) and compared the efficacy and safety of etomidate or propofol-mediated anesthesia induction followed by intubation and sevoflurane maintenance during ERCP.

## Materials and methods

### *Patients*

This study was conducted from August 2018 to December 2020 in Hanchuan People's Hospital. 180 patients who underwent ERCP with American Society of Anesthesiologists (ASA) grade I-III, 18-65 years old, BMI ≥30 kg/m$^2$ were selected. Patients with one of the following characteristics were excluded: left ventricular ejection fraction <30%, valvular disease affecting hemodynamics, pacemakers, long-term alcohol or drug abusers, BMI <30 kg/m$^2$, Mallampati grade 3 or 4, severe kidney disease or blood creatinine >1,290 mmol/L, severe liver disease, Alzheimer's disease, and epilepsy. The patients were computer-randomized into the propofol group or the etomidate group, with 90 cases in each group.

Human samples involved in this study were managed using protocols approved by the Ethical Committee of the Hanchuan People's Hospital (E2018010). Informed consent was obtained from all patients.

### *Anesthesia protocols*

Before surgery, both groups of patients were requested to fast and water-deprived for 8 hours. Large-bore intravenous lines were placed, and they were given regular injections of 10 mL/(kg·h) Ringer's lactate solution. Both groups were given an intravenous injection of 2 mg midazolam, 3 μg/kg sufentanil, and 0.15 mg/kg injectable atracurium cisbesilate. The etomidate group was given 0.3 mg/kg etomidate and the propofol group was given 1 mg/kg propofol. 30 seconds after full muscle relaxation, all patients underwent tracheal intubation. Sevoflurane was administered with 50% oxygen at a 2% concentration. When the bispectral index (BIS) reached 60, the surgery was started. During the surgery, BIS was used to monitor the depth of anesthesia in both groups. The medication was stopped immediately after the surgery.

During ERCP, if the mean arterial pressure (MAP) was less than 60 mmHg (1 mmHg = 0.133 kPa), an appropriate amount of metahydroxylamine was given; if the heart rate was less than 50 beats/min, an appropriate amount of atropine was given. If the MAP was higher than 120 mmHg, an appropriate amount of nitroglycerin was given; if the heart rate was higher than 120 beats/min, an appropriate amount of esmolol was given. If oxygen saturation ($SpO_2$) was lower than 0.95, oxygen flow was increased and sevoflurane dose was reduced by 50%; if the $SpO_2$ was lower than 0.90, the operation was stopped, and the patients were supported with assisted ventilation until $SpO_2$ was restored. Each ERCP operation was performed by two experienced gastroenterologists. After ERCP, clinical symptoms of adrenal suppression, such as hypotension and arrhythmia, were closely observed because etomidate may cause temporary adrenal suppression. If necessary, 200 to 300 mg/dose hydrocortisone may be given.

### *Outcome measures*

Baseline characteristics, procedure-related time (induction time, duration time, and recovery time), satisfaction (patient's satisfaction and gastroenterologist's satisfaction), cardiovascular-related adverse events (tachycardia, bradycardia, transient hypotension, and transient hypertension), respiratory-related adverse events (intraoperative $SpO_2$ <90%, intraoperative $SpO_2$ <95%, $SpO_2$ <95% for any period, and $SpO_2$ <95% for >3 min), and some other adverse events (nausea-vomiting, myoclonus, injection site pain, pancreatitis, cholangitis, sepsis, and adrenal crisis) were collected and compared between the etomidate group and the propofol group.

Induction time refers to the time from the start of anesthesia to BIS = 60. Duration of ERCP refers to the time from scope intubation to scope withdrawal. Recovery time refers to the time from stopping the drugs to full recovery (modified Aldrete score = 10). Patient satisfac-

**Table 1.** Baseline characteristics of patients

| | Etomidate group (n = 90) | Propofol group (n = 90) | *P*-value | Significance |
|---|---|---|---|---|
| Age, years | 50.2±10.7 | 52.7±9.3 | 0.867 | n.s. |
| Sex, n (%) | | | 0.650 | n.s. |
| Male | 51 (56.67) | 54 (60.00) | | |
| Female | 39 (43.33) | 36 (40.00) | | |
| Body mass index, kg/m$^2$ | 34.3±2.6 | 33.7±3.0 | 0.238 | n.s. |
| ASA grade, n (%) | | | 0.881 | n.s. |
| I | 29 (32.22) | 32 (35.56) | | |
| II | 53 (58.89) | 51 (56.67) | | |
| III | 8 (8.89) | 7 (7.78) | | |

n.s.: no significance.

**Table 2.** Clinical characteristics of procedure-related time and satisfaction

| | Etomidate group (n = 90) | Propofol group (n = 90) | *P*-value | Significance |
|---|---|---|---|---|
| Induction time, min | 7.74±2.51 | 6.42±2.63 | 0.019 | * |
| Duration of ERCP, min | 22.73±10.87 | 21.91±13.51 | 0.843 | n.s. |
| Recovery time, min | 15.35±3.67 | 12.63±2.52 | 0.004 | |
| Patient satisfaction | 3.65±0.46 | 3.57±0.45 | 0.531 | |
| Gastroenterologist satisfaction | 3.85±0.41 | 3.81±0.43 | 0.937 | |

n.s.: no significance; *P<0.05.

tion about ERCP was interrogated 60 min after ERCP and the scoring scheme was as follows: (1) represented unacceptable; (2) extremely uncomfortable; (3) slightly uncomfortable; (4) no discomfort. Gastroenterologist satisfaction about ERCP was interrogated immediately after ERCP and the scoring scheme was as follows: (1) represented poor; (2) fair; (3) good; (4) excellent.

Tachycardia refers to a heart rate (HR) of more than 100 beats/min and bradycardia refers to a HR less than 50 beats/min. Transient hypotension refers to an MBP that fell below 65 mmHg or decreased by more than 20% from baseline and recovered without any intervention. Transient hypertension refers to an MBP that went above 120 mmHg or increased by more than 20% from baseline and recovered without any intervention.

*Statistical analysis*

Continuous variables are presented as mean ± SD and categorical variables are presented as number (present). Statistical analysis was performed using SPSS18.0 software. Comparisons of continuous variables between different groups were performed using a 2-tailed Student t-test. Comparisons of categorical variables between different groups were performed using the $\chi^2$ test or Fisher's exact test. *P*-values less than 0.05 were considered significant.

## Results

*Baseline characteristics of patients*

No significant clinical complication was observed in this study. No significant difference was observed between the baseline characteristics (age, sex, BMI, and ASA grade) of both groups (**Table 1**).

The mean age of the patients was about 50 years old. There were more male patients than female patients. The majority of patients (58.89% in the etomidate group and 56.67% in the propofol group) were of ASA II grade.

*Clinical characteristics of procedure-related time and satisfaction*

Detailed information about the clinical characteristics of procedure-related time and satisfaction are listed in **Table 2**.

There was no significant difference between the ERCP duration of both groups (22.73± 10.87 min in the etomidate group and 21.91±

**Table 3.** Clinical characteristics of respiratory-related adverse events

| | Etomidate group (n = 90) | Propofol group (n = 90) | *P*-value | Significance |
|---|---|---|---|---|
| Intraoperative $SpO_2$ <90%, min | 0.00±0.00 | 0.00±0.00 | NA | n.s. |
| Intraoperative $SpO_2$ <95%, min | 0.07±0.47 | 0.24±0.87 | 0.019 | * |
| $SpO_2$ <95% for any period, n (%) | 2 (2.22) | 10 (11.11) | 0.032 | * |

n.s.: no significance; *P<0.05.

**Table 4.** Clinical characteristics of cardiovascular-related adverse events

| | Etomidate group (n = 90) | Propofol group (n = 90) | *P*-value | Significance |
|---|---|---|---|---|
| Tachycardia, n (%) | 0 (0.00) | 0 (0.00) | NA | n.s. |
| Transient hypertension, n (%) | 6 (6.67) | 1 (1.11) | 0.118 | n.s. |
| Bradycardia, n (%) | 2 (2.22) | 4 (4.44) | 0.682 | n.s. |
| Transient hypotension, n (%) | 1 (1.11) | 8 (8.89) | 0.034 | * |

n.s.: no significance; *P<0.05.

**Table 5.** Clinical characteristics of other adverse events

| | | Etomidate group (n = 90) | Propofol group (n = 90) | *P*-value | Significance |
|---|---|---|---|---|---|
| During ERCP | Nausea-vomiting, n (%) | 2 (2.22) | 3 (3.33) | 1.000 | n.s. |
| | Myoclonus, n (%) | 2 (2.22) | 1 (1.11) | 1.000 | n.s. |
| | Injection site pain, n (%) | 0 (0.00) | 6 (6.67) | 0.029 | * |
| After ERCP | Pancreatitis, n (%) | 1 (1.11) | 1 (1.11) | 1.000 | n.s. |
| | Cholangitis, n (%) | 3 (3.33) | 4 (4.44) | 1.000 | n.s. |

n.s.: no significance; *P<0.05.

13.51 min in the propofol group) (*P*-value = 0.843). However, the etomidate group had statistically longer induction time and recovery time than the propofol group (*P*-values of 0.019 and 0.004, respectively). For the induction time, etomidate group vs propofol group was 7.74±2.51 min vs 6.42±2.63 min; for recovery time, etomidate group vs propofol group was 15.35±3.67 min vs 12.63±2.52 min.

Patient satisfaction and gastroenterologist satisfaction had no significant difference between both groups.

*Clinical characteristics of adverse events*

The detailed information about the clinical characteristics of respiratory-related adverse events is listed in **Table 3**. No $SpO_2$ <90% was observed in both groups. However, the propofol group had a worse oxygen maintenance than the etomidate group, since it had a longer time of intraoperative $SpO_2$ <95% (etomidate group vs propofol group, 0.07±0.47 min vs 0.24±0.87 min, *P*-value = 0.019) and higher frequency of $SpO_2$ <95% for any period (etomidate group vs propofol group, 2 (2.22%) vs 10 (11.11%), *P*-value = 0.032).

Detailed information about the clinical characteristics of cardiovascular-related adverse events is listed in **Table 4**. No tachycardia was observed in both groups and no significant difference of bradycardia was detected between both groups. The propofol group had a significantly higher frequency of transient hypotension than the etomidate group (1.11% in the etomidate group and 8.89% in the propofol group) (*P*-value = 0.034). However, even though there was no statistical significance (*P*-value = 0.118), it seemed that the etomidate group had a higher frequency of transient hypertension (6.67% in the etomidate group and 1.11% in the propofol group).

Detailed information about the clinical characteristics of other adverse events is listed in **Table 5**. There was no significant difference in the rates of nausea-vomiting, myoclonus, pancreatitis, and cholangitis between both groups, while the propofol group had a significantly

higher frequency of injection site pain than the etomidate group (0% in the etomidate group and 6.67% in the propofol group) (*P*-value = 0.029).

## Discussion

As a complex diagnostic and therapeutic endoscopic operation, ERCP requires a high degree of patient cooperation. Regularly, ERCP surgery requires sedation and anesthesia. In this study, we compared the efficacy and safety of etomidate or propofol-mediated anesthesia induction followed by intubation and sevoflurane maintenance during ERCP in obese patients and found that the propofol induction more readily caused hypoxia and transient hypotension and the etomidate induction might cause a longer induction time and recovery time.

The majority of previous studies about anesthesia during ERCP used anesthesia without intubation for the patients in these studies had commonly lower risk of breathing problems with no more than 65 years old and normal BMI [25-27]. Sevoflurane, a kind of inhaled anesthetic, is inappropriate for the maintenance of these patients, and intravenous infusion is regularly adopted. However, for patients with obesity (BMI ≥30 kg/m$^2$), intubation is beneficial to keep an unobstructed respiratory. During anesthesia maintenance, sevoflurane is a better choice compared to etomidate and propofol according to previous studies [28, 29]. Therefore, we chose sevoflurane for anesthesia maintenance.

The efficacy and safety of etomidate and propofol have been studied extensively for anesthesia without intubation during ERCP. Park et al. reported that there was no significant difference in the induction time and recovery time between the etomidate group and the propofol group [30]. In this study, we found that the etomidate group had a significantly longer induction time and recovery time compared to the propofol group. These contrary results may be induced by the combination of etomidate, sufentanil, and atracurium cisbesilate in our anesthesia procedure because the interaction between different anesthetics could influence their effect [31]. Park et al. reported that the propofol group had a higher frequency of transient hypotension and the etomidate group had a higher frequency of tachycardia. However, they did not analyze the frequency of transient hypertension [30]. Song et al. reported that there was no significant difference in tachycardia, bradycardia, transient hypotension, and transient hypertension between both groups [32]. In Song's study, transient hypotension was defined as MBP <60 mmHg or decreased more than 25% from the baseline while in Park's study, transient hypotension was defined as MBP <65 mmHg or decreased by more than 20% from baseline. Tachycardia was defined as HR >120 beats/min in Song's study while it was defined as HR >100 beats/min in Park's study [30, 32]. The rigorous evaluative criteria in Song's study may have led to their different results; however, Song et al. uncovered that etomidate caused a more stable MBP curve. Our evaluative criteria were the same as Park's and our results were similar to Park's. Nevertheless, in our study, the frequency of transient hypotension was lower than that of Park's, and we did not observe tachycardia, indicating an advantage of sevoflurane in anesthesia maintenance. It is worth noting that even though there was no significant difference in the frequency of transient hypertension, it was higher in the etomidate group, indicating that evaluation and monitoring of hypertension may be beneficial for the use of etomidate. A larger study size may be needed.

The propofol group tended to have injection site pain, and this might have influenced patient satisfaction. The mean value of patient satisfaction in the propofol group was indeed lower than that of the etomidate group, but there was no significant difference. We have noticed that the patient satisfaction was lower than the gastroenterologist satisfaction. This may be because of the intubation.

In conclusion, we found that in obese patients who underwent ERCP and needed intubation, etomidate may be better than propofol for anesthesia induction, followed by anesthesia maintenance with sevoflurane. However, several limitations exist in this study. First, in this study, only patients less than 65 years old were enrolled, so the conclusions might not be appropriate for the elderly. Secondly, the patients in this study were of ASA I to III grades, therefore the data on ASA IV patients are lacking. In-depth work is needed in the future.

## Disclosure of conflict of interest

None.

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