

# Effect of Inhaled Oxygen Concentration before Extubation on the Recovery Period of Patients Undergoing Laparoscopic Cholecystectomy

Song Junli<sup>1,a</sup>, Zeng Jingzheng<sup>1</sup>, Shi Qin<sup>1</sup>, Gong Gu<sup>1,b,\*</sup>

<sup>1</sup>Department of Anesthesiology, The General Hospital of Western Theater Command, Chengdu, Sichuan, China

<sup>a</sup>744243839@qq.com, <sup>b</sup>gonggu68@163.com

\*Corresponding author

**Abstract:** This study aimed to evaluate the effect of the fraction of inspired oxygen (FiO<sub>2</sub>) before extubation on the washout time of sevoflurane, recovery quality, and the incidence of early postoperative hypoxemia in patients undergoing laparoscopic cholecystectomy, in order to assess the effectiveness of preoxygenation prior to extubation. Sixty patients classified as American Society of Anesthesiologists physical status I–II, aged 18–60 years and with a body mass index of 18–30 kg/m<sup>2</sup>, scheduled for laparoscopic cholecystectomy, were randomly assigned to two groups according to the inhaled oxygen concentration: 50% (Group A, n = 30) and 100% (Group B, n = 30). The time for end-tidal sevoflurane concentration to decrease from 0.8 to 0.2 minimum alveolar concentration (MAC), time to eye opening, time to extubation, Steward scores immediately after extubation (T<sub>1</sub>), at 3 minutes (T<sub>2</sub>), and at 5 minutes (T<sub>3</sub>) after extubation, the incidence of postoperative hypoxemia, and patient satisfaction assessed using the Likert scale were recorded. Compared with Group B, patients in Group A exhibited a significantly shorter sevoflurane washout time ( $P < 0.05$ ) and higher Steward scores at T<sub>1</sub> and T<sub>2</sub> ( $P < 0.05$ ). No significant differences were observed between the two groups in terms of time to eye opening, time to extubation, Steward score at T<sub>3</sub>, incidence of postoperative hypoxemia, or patient satisfaction. These results suggest that a lower FiO<sub>2</sub> (50%) prior to extubation shortens sevoflurane washout time and improves early recovery quality without increasing the risk of postoperative hypoxemia.

**Keywords:** Inhaled Oxygen Concentration; Recovery Period; Laparoscopic Cholecystectomy; Hypoxemia

## 1. Introduction

Approximately 310 million surgical procedures are performed worldwide each year <sup>[1]</sup>, and approximately 15% of hospitalized patients receive supplemental oxygen therapy <sup>[2]</sup>, particularly during general anesthesia with muscle relaxants. Perioperative oxygen therapy offers numerous advantages, including hyperoxia preconditioning to enhance myocardial tolerance to ischemia <sup>[3]</sup>, reducing postoperative wound infection rates, and minimizing gas microemboli generated during extracorporeal circulation <sup>[4]</sup>. It also increases tolerance to apnea and respiratory dysfunction to prevent intraoperative hypoxia and improves hypoxemia caused by ventilation-perfusion mismatch <sup>[5]</sup>.

Short-term high-concentration oxygen therapy enhances patient safety during anesthesia induction, such as by preoxygenation, which increases alveolar oxygen partial pressure by raising FiO<sub>2</sub>, reduces nitrogen content, and boosts the body's oxygen content by nearly threefold, thereby delaying the time it takes for blood oxygen saturation to drop below 90% during apnea or hypoventilation, extending this period to about 10 minutes. In the early stages of extubation, residual effects of anesthetic drugs and incomplete reversal of neuromuscular blockade can lead to hypoventilation. Factors such as supine position, loss of airway patency, and reduced responsiveness of peripheral chemoreceptors to hypoxic stimuli often contribute to postoperative hypoxemia <sup>[6]</sup>. After tracheal tube removal, patients typically maintain spontaneous breathing during transport from the operating room to the post-anesthesia care unit (PACU), without supplemental oxygen or oxygenation monitoring, resulting in a postoperative hypoxemia incidence of 4.6% to 32% <sup>[7,8]</sup>. Studies have shown that a brief decrease in oxygen saturation following tracheal tube removal in the operating room is also associated with higher adverse risks. Therefore, it is recommended to maximize the body's oxygen reserves by administering pure oxygen before tube removal <sup>[9]</sup>. Due to differences in physiological status between the post-tube removal phase

and the general anesthesia induction phase: following general anesthesia induction, the use of general anesthetics weakens or eliminates respiratory movements. During apnea, oxygen in the alveoli and blood is continuously absorbed and released to supply tissue cells. Adequate oxygen content in the body prolongs the duration of oxygen saturation decline, benefiting from preoxygenation. However, unlike general anesthesia where ventilation function is lost, by the time the ventilator is removed after surgery, most drugs have been metabolized or excreted from the patient's body. Mental awareness and neuromuscular junction function have effectively recovered. Respiratory secretions are cleared through procedures such as suctioning. These conditions eliminate factors causing airway obstruction and restore spontaneous breathing function. Therefore, under conditions where the risk factors for hypoxemia have been eliminated, whether the use of high-concentration oxygen prior to extubation reduces the incidence of postoperative hypoxemia remains unclear, as there is currently a lack of relevant research.

During general anesthesia, compression of thoracic lung tissue, diaphragmatic elevation, and reduced tidal volume lead to decreased closed-volumetric capacity, reduced pulmonary surfactant levels, and factors such as surgery and patient conditions result in atelectasis in 90% of patients under general anesthesia [10]. The extent of atelectasis increases in a dose-dependent manner with increasing  $\text{FiO}_2$ . Five minutes of pure oxygen ventilation results in a significantly larger area of atelectasis compared to low-oxygen concentration ventilation strategies [11]. Additionally, high  $\text{FiO}_2$  produces a large amount of oxygen free radicals, triggering inflammatory responses and alveolar cell damage [12]. These factors may affect the elimination phase of inhaled anesthetics, slowing the rate of reduction in sevoflurane concentration in the alveoli, thereby impacting the quality of recovery in patients undergoing general anesthesia. As is well known, 95% of the inhaled anesthetic sevoflurane is exhaled through the lungs, primarily influenced by fresh gas flow (FGF). Additionally, minute ventilation and cardiac output also affect its elimination. Most existing studies have focused on the effect of FGF on the washout phase of volatile inhalation anesthetics, with elimination time shortening as FGF increases, reaching a plateau at 4–6 L/min [13]. However, there is currently a lack of research on the impact of pre-extubation  $\text{FiO}_2$  on the elimination phase of inhalation anesthetics, which is the primary objective of this study. Remifentanyl, as a selective  $\mu$ -opioid receptor agonist, is easily metabolized by lung-specific esterases without requiring hepatic or renal metabolism. Additionally, remifentanyl has a very short half-life of approximately 3 minutes, which is independent of dosage and administration time. When combined with sevoflurane for combined anesthesia, it can facilitate rapid recovery from anesthesia. Additionally, remifentanyl typically enhances the efficacy of inhaled anesthetics and reduces the minimum alveolar concentration (MAC) of inhaled sevoflurane [14]. Previous studies have shown that when the end-tidal concentration of the inhaled anesthetic sevoflurane exceeds 1.5%, adverse events such as intraoperative movement, auditory perception, and the formation of conscious memory can be avoided [15]. It is recommended to maintain sevoflurane peak end concentrations within the range of 0.7 to 1.3 MAC during surgery [16]. Subsequent studies confirmed that maintaining a sevoflurane concentration of 0.8 MAC during general anaesthesia resulted in fewer body movements and shorter recovery times [17]. Based on this, the present study employed remifentanyl combined with sevoflurane for general anaesthesia maintenance, targeting a sevoflurane end-tidal concentration of 0.8 MAC.

Against the backdrop of inhaling high  $\text{FiO}_2$  to prevent post-extubation hypoxaemia, this study aims to investigate the effects of  $\text{FiO}_2$  on the clearance process of inhaled anaesthetics, patient recovery time and quality, and the incidence of postoperative hypoxaemia. It further evaluates the efficacy of pre-extubation oxygenation measures to enhance the quality and safety of emergence from general anaesthesia.

## 2. Methods

### 2.1 Patients and Methods

A total of 60 patients who underwent laparoscopic cholecystectomy at the Western Theater Command General Hospital from March to June 2021 were enrolled in this study. The patients were aged 18–60 years, with a body mass index (BMI) of 18–30  $\text{kg/m}^2$ , and had an American Society of Anesthesiologists (ASA) physical status classification of I–II. They had no severe organic diseases of the heart, brain, lungs, liver, kidneys, or blood system. The exclusion criteria were as follows: (1) Patients unwilling to cooperate or unable to complete the trial; (2) Pregnant women; (3) Patients with or suspected of having malignant hyperthermia; (4) Inhalation equilibrium time <30 minutes; (5) Patients who do not meet the study protocol criteria.

## 2.2 Experimental procedures

All patients were continuously monitored with non-invasive blood pressure, electrocardiogram, pulse oxygen saturation (SpO<sub>2</sub>), end-tidal carbon dioxide (PETCO<sub>2</sub>), and tetradotoxin (TOF). Intravenous induction of anesthesia was induced with 5 mg dexamethasone, 0.01 mg/kg propofol, 0.04 mg/kg midazolam, 0.4–0.5 µg/kg sufentanil, 0.2–0.4 mg/kg etomidate, 0.15–0.25 mg/kg rocuronium bromide, and then a laryngeal mask was placed. Intraoperative anesthesia was maintained through inhaled sevoflurane and continuous infusion of remifentanyl (4–12 µg/kg/h). The concentration of sevoflurane was titrated to maintain an end-tidal sevoflurane concentration at 0.8 MAC, rocuronium and remifentanyl were administered as needed. Hemodynamic stability was maintained by ensuring that the patient's heart rate and blood pressure did not deviate by more than 20% from baseline values through positional adjustment, fluid resuscitation, and administration of cardiovascular drugs. The mechanical ventilation mode was pressure-controlled volume-guaranteed ventilation (PCV-VG), with a tidal volume of 8 mL/kg, an inspiratory-to-expiratory (I: E) ratio of 1:2, PEEP of 0 cmH<sub>2</sub>O, and a mixture of oxygen and air with FiO<sub>2</sub> of 50–60%. The respiratory rate was adjusted to maintain PETCO<sub>2</sub> between 35 and 45 mmHg. Half an hour before the end of the surgery, 0.25 mg of palopressin hydrochloride injection was administered intravenously to prevent postoperative nausea and vomiting. Five minutes before the completion of skin suturing, 1 mg of neostigmine and 0.5 mg of atropine were administered intravenously based on the TOF value to antagonize residual muscle relaxant effects. Subsequently, remifentanyl and sevoflurane were discontinued, and the fresh gas flow rate was adjusted to 2 L/min. The respiratory rate and tidal volume resulted in a minute ventilation of 6 L/min. FiO<sub>2</sub> was adjusted to 50% or 100% according to the group until the laryngeal mask was removed. During the recovery period, the patient's name was called every minute until they opened their eyes. No additional oxygen was administered after laryngeal mask removal unless the patient experienced a decrease in oxygen saturation (hypoxemia was defined as SpO<sub>2</sub> ≤ 90% on room air or SpO<sub>2</sub> ≤ 97% on oxygen via a face mask). After the patient was transferred to the PACU and completed the study procedures, intravenous analgesia was administered according to the patient's needs.

## 2.3 Observation indicators

The primary indicator is the time taken for the end-tidal sevoflurane concentration to decrease from 0.8 MAC to 0.2 MAC. Secondary indicators include time to eye opening and time to extubation. The Steward Assessment Scale is used at T1, T2, and T3 using the Steward Assessment Scale, and the occurrence of hypoxemia from the time of laryngeal mask removal to admission to the recovery room, as well as the Likert Scale assessment.

## 2.4 Statistical Analysis

Data analysis was performed using SPSS 26.0 software, and graphs were created using GraphPad Prism 8.0. The normality test was the Shapiro-Wilk test, and the homogeneity of variance test was the Levene's test. For normally distributed continuous data, the mean ± standard deviation ( $\bar{x} \pm s$ ) was used; for non-normally distributed continuous data, the median (interquartile range) [M(Q)] was used. For normally distributed, homoscedastic quantitative data, an independent samples t-test was used; otherwise, the Mann-Whitney U test was used for intergroup comparisons. For normally distributed quantitative data, repeated measures analysis of variance was used; otherwise, the Friedman test was used. Count data were expressed as frequency (percentage). The  $\chi^2$  test or Fisher's exact test was used for comparisons. The significance level was set at  $\alpha = 0.05$  for two-tailed tests, and a significant p-value was set at  $<0.05$ .

## 3. Results

A total of 104 cases were screened in this study. Among them, 32 patients did not meet the trial requirements, and 8 patients had incomplete data. Ultimately, 64 patients were included in the statistical analysis.

### 3.1 General Information

The groups showed similar patient characteristics, and there was no statistically significant difference between the two groups in terms of age, gender, BMI, ASA, pulse oximetry, blood pressure, anesthesia duration, balancing time, and operation duration were shown in Table 1.

*Table 1 Demographic and intraoperative characteristics.*

Variable	ALL	Group A	Group B	P value
Age (years)	42.00(18.00)	43.50(19.50)	41.00(18.25)	0.99 <sup>a</sup>
Gender				
Male	19(30)	9(26)	10(33)	0.46 <sup>b</sup>
Female	45(70)	25(74)	20(67)	
BMI (kg/m <sup>2</sup> )	23.34±2.84	23.23±2.89	23.48±2.83	0.73 <sup>c</sup>
ASA physical status				
I	51(80)	27(80)	24(80)	0.94 <sup>b</sup>
II	13(20)	7(20)	6(20)	
Pulse oximetry	99.00(1.75)	99.00(1.25)	99.00(2.00)	0.88 <sup>a</sup>
Blood pressure (mmHg)	90.03±10.03	90.62±9.04	89.37±11.17	0.17 <sup>c</sup>
Anesthesia duration (min)	65.09±18.02	66.06±18.94	64.00±17.18	0.65 <sup>c</sup>
Balancing time (min)	43.50(24.75)	49.00(27.00)	41.00(14.00)	0.19 <sup>a</sup>
Operation duration (min)	61.23±18.66	62.76±20.12	59.50±17.04	0.49 <sup>c</sup>

<sup>a</sup> Mann-Whitney *U* test, <sup>b</sup>  $\chi^2$  test, <sup>c</sup> independent samples t-test.

BMI: body mass index; ASA: American Society of Anesthesiologists; Balancing time: The time for maintaining the end-tidal concentration of sevoflurane at 0.8 MAC.

### 3.2 Primary and secondary outcomes

#### 3.2.1 Exhalation time of sevoflurane

The Exhalation time of sevoflurane was 427.00(70.00) s in Group A and 450.00(196.25) s in Group B, and the difference between the two groups was statistically significant ( $P < 0.05$ ), as shown in Table 2.

*Table 2 Comparison of recovery times between the two groups of patients.*

Outcome	ALL	Group A	Group B	P value
Exhalation time of sev (s)	440.00(95.00)	427.00(70.00)	450.00(196.25)*	0.04 <sup>a</sup>

<sup>a</sup> Mann-Whitney *U* test.

Exhalation time of sev: The time taken for the end-tidal sevoflurane concentration to decrease from 0.8 MAC to 0.2 MAC.

#### 3.2.2 Comparison of recovery time

The average eye-opening time was 841.44±171.87 s in Group A and 885.53±126.46 s in Group B. No significant difference in eye-opening time was observed between the groups ( $p = 0.25$ ). The extubation time was 865.06±190.01 s in Group A and 898.60±132.16 s in Group B, which was not statistically significant ( $p = 0.42$ ). (See Table 3.)

*Table 3 Comparison of emergence time during the awakening period between the two groups of patients.*

Outcome	ALL	Group A	Group B	P value
Eye-opening time (s)	862.11±152.73	841.44±171.87	885.53±126.46	0.25 <sup>c</sup>
Extubation time (s)	880.78±165.04	865.06±190.01	898.60±132.16	0.42 <sup>c</sup>

<sup>c</sup> independent samples t-test.

Eye-opening time: The time from discontinuation of sevoflurane to eye-opening. Extubation time: The time from discontinuation of sevoflurane to tracheal extubation.

#### 3.2.3 Comparison of Steward Scores

Steward scores were statistically analyzed across three time points (T1, T2, and T3) using the Friedman test. The results showed there were statistically significant differences in Steward scores at T1 and T2 ( $P < 0.05$ ). As the duration of awakening increased, patients had higher Steward scores. At 5 minutes post-extubation, Steward scores were similar between the two groups ( $P = 0.29$ ). The differences in Steward scores between the different FiO<sub>2</sub> groups were statistically significant ( $P < 0.05$ ), with the low FiO<sub>2</sub> group having higher Steward scores than the pure oxygen group. (See Table 4.)

*Table 4 Comparison of Steward Scores during the Awakening Period between the Two Groups of Patients.*

Outcome	ALL	Group A	Group B	P value
Steward T1	6.00(1.75)	6.00(1.00)	5.00(2.25)*	0.04 <sup>a</sup>
Steward T2	6.00(0.00)	6.00(0.00)	6.00(1.00)*	0.01 <sup>a</sup>
Steward T3	6.00(0.00)	6.00(0.00)	6.00(0.00)	0.29 <sup>a</sup>

<sup>a</sup> Mann-Whitney *U* test.

### 3.2.4 Incidence of hypoxemia and satisfaction scores

There was no statistically significant difference in the incidence of hypoxemia and satisfaction scores between the two groups ( $P > 0.05$ ), and inhaling pure oxygen before extubation did not significantly reduce the incidence of postoperative hypoxemia. (See Table 5.)

*Table 5 Comparison of indicators related to the recovery period between the two groups.*

Outcome	ALL	Group A	Group B	P value
Hypoxemia (%)	17.2	14.7	20.0	0.58 <sup>b</sup>
Likert satisfaction score	5.00(0)	5.00(0)	5.00(0)	0.86 <sup>a</sup>

<sup>a</sup> Mann-Whitney *U* test, <sup>b</sup>  $\chi^2$  test.

## 4. Discussion

As our understanding and application of perioperative knowledge continue to evolve, numerous intervening factors can influence the quality of a patient's recovery period. This study compared the effects of pre-extubation FiO<sub>2</sub> on sevoflurane clearance and recovery quality in patients undergoing laparoscopic cholecystectomy. The results of this study indicate that during the low FGF phase of sevoflurane elimination, the low FiO<sub>2</sub> group had a shorter sevoflurane elimination time compared to the pure oxygen group, higher Steward scores within 3 minutes postoperatively, and the incidence of postoperative hypoxemia did not decrease with reduced FiO<sub>2</sub>, but it did not affect patients' eye-opening time, extubation time, or patient satisfaction.

The time for sevoflurane to decrease from 0.8 MAC to 0.2 MAC at the end of the tidal volume increased with rising inspired oxygen concentration, a mechanism potentially similar to the second gas effect [18]. High-concentration oxygen is rapidly absorbed, leading to increased concentrations of volatile anesthetics in the alveoli, reducing the partial pressure difference between pulmonary capillaries and alveoli. Additionally, the inflammatory response, alveolar cell damage, and atelectasis caused by inhaling pure oxygen reduce effective alveolar exchange. These factors synergistically reduce the diffusion rate of inhaled anesthetics. As the diffusion of sevoflurane from pulmonary capillary to alveoli slows down, it also slows down the washout rate of inhaled anesthetics from the effect chamber, thereby affecting the recovery of consciousness [19]. This is supported by the statistically significant difference in Steward scores between the two groups within 3 minutes after removal of the laryngeal mask. However, overall, FiO<sub>2</sub> does not affect the time to eye opening or extubation. At an FGF of 2 L/min, the time to eye opening is approximately 14 minutes. The results can be interpreted as follows: the patients included in this study were relatively healthy, and good lung ventilation, gas exchange function, and cardiac pumping function reduced the impact of FiO<sub>2</sub> on sevoflurane clearance, or the inhibitory concentration range of sevoflurane on the brain was within the difference in sevoflurane concentrations in the brains of the two groups of patients. Therefore, the clinical application of the results of this study has certain limitations and expandability. First, the patients included in this study had no significant impairment of cardiopulmonary function, but in clinical practice, most patients have cardiopulmonary insufficiency, which limits the generalizability of these findings to a broader patient population. On the other hand, while this study demonstrated certain differences in patients with normal cardiopulmonary function, it raises the question of whether such differences would be more pronounced in patients with cardiopulmonary insufficiency.

Therefore, further investigation is needed to explore these differences in such patient populations. Finally, in clinical practice, most patients can maintain adequate oxygenation with 50% oxygen concentration. Higher oxygen concentrations increase the dissolved oxygen content and partial pressure of oxygen in the blood, which may alleviate the stimulatory effect of peripheral oxygen partial pressure on respiration [20]. The benefit of preoxygenation lies in delaying the decline in partial pressure of oxygen during apnea, which depends on achieving maximum preoxygenation before apnea, maintaining airway patency, and a high functional residual capacity-to-body weight ratio. Most patients regain consciousness after extubation [21], and the risk factors for hypoxemia have been resolved. Therefore, there is no

statistically significant difference in the incidence of postoperative hypoxemia between the two groups. The incidence of hypoxemia after extubation in this study was similar to previous studies, approximately 20%, and a larger sample size is needed to test the difference in the effect of  $\text{FiO}_2$  on the incidence of hypoxemia after extubation. The results of this study indicate that in combined inhalation and intravenous balanced anesthesia, the MAC-awake of sevoflurane is below 0.3 MAC [22]. Due to the different protocols between pure inhalation general anesthesia and combined inhalation and intravenous balanced anesthesia, other general anesthetic agents may synergize with sevoflurane anesthesia, thereby reducing the MACawake value of sevoflurane. Based on this, more large-scale, multi-center, high-quality randomized controlled studies are needed, along with comparisons of different fresh gas flow rates to explore their effects on the patient's recovery period, identify the optimal sevoflurane elimination protocol, and improve the quality of patient recovery.

Additionally, the findings of this study offer the following insights for clinical anesthesia practice: The use of high-concentration oxygen for preoxygenation before extubation does indeed delay the time it takes for  $\text{SpO}_2$  to decrease when patients experience respiratory dysfunction; however, it does not significantly reduce the incidence of postoperative hypoxemia. This may give anesthesiologists the false impression that the patient's respiratory function is still adequate, leading to their discharge from the operating room. During the process of removing vital signs monitoring and transferring the patient to the PACU, the patient may experience a decrease in  $\text{SpO}_2$  due to respiratory failure and oxygen depletion, which may go unnoticed and untreated due to the lack of monitoring, often resulting in severe hypoxia or threatening the patient's safety. Therefore, in clinical practice, efforts should be made to avoid hypoxia in patients without monitoring or intervention measures. Greater emphasis should be placed on monitoring anesthesia depth, neuromuscular junction function, and end-tidal anesthetic concentration, combined with procedures such as suctioning, positioning, and placement of auxiliary ventilation devices to eliminate airway obstruction risk factors, ensuring that the patient's consciousness and respiratory function are fully restored after extubation. If the patient experiences a decrease in  $\text{SpO}_2$ , additional oxygen should be administered promptly, and the underlying causes of hypoxia should be actively addressed. Furthermore, in the absence of robust clinical evidence substantiating its benefits, the administration of high  $\text{FiO}_2$  during the perioperative period may exacerbate inflammatory responses and oxidative stress, potentially leading to significant adverse effects on pulmonary function, microcirculatory perfusion, coronary artery dynamics, and cerebral hemodynamics [23]. Therefore, the necessity of this measure requires reevaluation [24].

Finally, the primary sources of systematic error in this study include the following: (1) Errors in the gas analyzer, which may be related to the calibration method and algorithms used; (2) The true differences between the two groups were very small and fell within the sampling error range, particularly for eye-opening and extubation times. For example, an excessively long interval between calling for the patient to open their eyes may explain the lack of statistical significance in eye-opening and extubation times between the two groups; (3) Other mid- and short-acting drugs were used during and after surgery, which may have weakened the effect of the difference in sevoflurane concentration between the two groups, resulting in no statistically significant difference in patient eye-opening time and extubation time; (4) The trial design requires further refinement. In this study, cardiac output was not collected or analyzed, and the influence of cardiac output on the elimination of inhaled anesthetics was not excluded [25]. These findings suggest that these aspects should be avoided in future studies.

## 5. Conclusions

The results of this study showed that there was no statistically significant difference in the incidence of postoperative hypoxemia between the  $\text{FiO}_2$  50% group and the pure oxygen group before extubation, indicating that inhaling pure oxygen before extubation does not have a positive effect on reducing postoperative hypoxemia. Additionally, inhaling the anesthetic sevoflurane at an  $\text{FiO}_2$  of 50% resulted in faster elimination and higher quality of recovery after extubation, but  $\text{FiO}_2$  did not affect overall patient satisfaction.

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