

Intraoperative Oxygen Concentration and Postoperative Delirium After Laparoscopic Gastric and Colorectal Malignancies Surgery: A Randomized, Double-Blind, Controlled Trial

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Purpose: Postoperative delirium (POD) is common in elderly patients undergoing laparoscopic surgery for gastric and colorectal malignancies. POD may be affected by different fraction of inspired oxygen (FiO₂). The purpose of this study was to compare the effects of different FiO₂ on POD.

Patients and Methods: A randomized, double-blind controlled trial was performed in Qingdao Municipal Hospital Affiliated to Qingdao University. A total of 662 patients aged 65 to 85 years old underwent isolated laparoscopic radical gastrectomy, radical resection of colon cancer, or radical resection of rectal cancer only. A random number table method was used to divide the patients into two groups: 40% FiO₂ (group A) and 80% FiO₂ (group B). The primary endpoint was the incidence of POD, which was assessed by the Confusion Assessment Method (CAM) twice daily during the first 7 postoperative days, and POD severity was measured by the Memorial Delirium Assessment Scale (MDAS). The secondary endpoints were the intraoperative regional cerebral oxygen saturation (rSO₂), Bispectral (BIS) index, invasive arterial blood pressure (IABP), oxygen saturation (SpO₂), end-tidal carbon dioxide partial pressure (P_{ET}CO₂), the number of atelectasis cases and visual analogue scale (VAS) scores on days 1–7 after surgery.

Results: The incidence of POD was 19.37% (122/630), including 20.38% (64/314) in group A and 18.35% (58/316) in group B. No statistical significance was found in the incidence of POD between the two groups ($P > 0.05$); compared with group B, SpO₂, rSO₂ and PaO₂ decreased at T₂ to T₄ time point ($P < 0.01$), and the incidence of postoperative atelectasis decreased ($P < 0.05$) in group A.

Conclusion: The incidence of POD was not significantly affected by different FiO₂ and the incidence of postoperative atelectasis was decreased at low FiO₂.

Keywords: intraoperative oxygen concentration, postoperative delirium, malignancy

Introduction

Postoperative delirium (POD), as an acute central nervous system dysfunction, has a high incidence of up to 50% during laparoscopic abdominal surgery.¹ The occurrence of POD is associated with worse outcomes, including prolonged length of hospital stay, increased morbidity and mortality, impaired long-term cognitive function and physical ability, and increased medical care costs.^{2–5}

The causes of POD are multifactorial, including predisposing and precipitating factors.⁶ The study has shown that intraoperative hypoxia is an important factor for

postoperative cognitive dysfunction,⁷ while the hyperoxia does not increase neurological complications.⁸ It is well known that perioperative hypoxia or hyperoxia can be regulated by the fraction of inspired oxygen (FiO_2), which is the main factor affecting regional cerebral oxygen saturation (rSO_2), and has a high correlation with rSO_2 .⁹ Moreover, the rSO_2 is a non-invasive method for assessing the adequacy of the oxygen supply-demand balance in the fronto parietal brain areas at any position during surgery.¹⁰ The rSO_2 value is a very sensitive indicator of cerebral hypoxia, which can cause cerebral hypoperfusion, resulting in POD.^{11,12} At present, there is no unified standards for the optimal FiO_2 in operation, which is 30% ~ 100% in clinical operation. However, for elderly patients undergoing laparoscopic abdominal surgery, no unified conclusion has been reached on the effects of different FiO_2 on POD.

In this study, FiO_2 was controlled at 40% and 80%, to compare the incidence of POD after laparoscopic abdominal surgery in two groups of elderly patients. The primary outcome was the incidence of POD every 1–7 days post-operatively. We hypothesized that 80% FiO_2 would reduce the incidence of POD, which is associated with increased rSO_2 .

Patients and Methods

Participants

Patients, in this study, who underwent laparoscopic surgery for gastric and colorectal malignancies had an American Society of Anesthesiologists (ASA) physical status I, II or III and a New York Heart Association Functional Classification (NYHA) class I or II. Their age was between 65 and 85 at the time of the study. Those who were excluded from this study met any of the following criteria: preoperative Mini Mental State Scale (MMSE) scores of 23 or less; history of severe mental or nervous system; history of drug or psychotropic substance abuse, long-term use of steroids and steroids; preoperative complicated with III or IV hepatic encephalopathy; severe visual and hearing impairment; preoperative asthma, chronic obstructive pulmonary disease, or pulmonary function test showing moderate or severe ventilation dysfunction; low hemoglobin ($\text{HB} < 100\text{g/L}$) and hypoproteinemia; operation time $< 2\text{ h}$ or $> 5\text{ h}$; preoperative radiotherapy or chemotherapy; intraoperative blood loss $> 200\text{ mL}$; patients were admitted to intensive care unit after operation with blood oxygen saturation (SpO_2) $< 95\%$

(Based on the results of our preliminary trial) or anesthesia complications occurred. Patients in this study were randomly divided into two groups according to the level of FiO_2 : Group A with 40% FiO_2 and Group B with FiO_2 80%.

Ethics Approval and Consent to Participate

This prospective, randomized, double-blind controlled trial was performed from February 2018 to February 2020 in accordance with the Declaration of Helsinki principles. This study was approved by the Ethics Committee for Clinical Trials of the Qingdao Municipal Hospital Affiliated to Qingdao University, China [approval no: 2018 PRO FORMA Y number 003]. The trial was registered in the Chinese Clinical Trial Registry prior to patient enrollment (ChiCTR1800014972). All patients submitted written informed consent.

Management of General Anesthesia and Analgesia

None of the enrolled patients received any sedative or analgesic treatment prior to induction of anesthesia. Routine venous access was established after patients entered the operating room. Vital parameters, including oxygen saturation (SpO_2), invasive radial arterial pressure, non-invasive arterial blood pressure (NABP), heart rate (HR), electrocardiogram (ECG), and end-tidal carbon dioxide partial pressure (P_{ETCO_2}), were monitored using a Drager monitor (model: Primus, Qingdao unity medical co.). Two near-infrared spectral sensors spectroscopy (model: EGOS-600B, Jiangsu Aiqin Bio-Medical Electronics Co.) were pasted on the left and right sides of each patient's forehead for measuring the rSO_2 value. The rSO_2 baseline data were collected before induction of anesthetic while patients breathing room air. For the BIS monitor (the Germany, Philips, M1034A Co.), a disposable BIS sensor was applied to the patient's forehead after the skin was wiped with an alcohol swab. Provide 100% oxygen to the mask before intubation. Sufentanil $0.5\text{ }\mu\text{g}\cdot\text{kg}^{-1}$ and etomidate $0.2\text{ mg}\cdot\text{kg}^{-1}$ were used for induction of general anesthesia, and cisatracurium $0.2\text{ mg}\cdot\text{kg}^{-1}$ was used for muscle relaxation. For tracheal intubation, the mechanical ventilation was set to the target of P_{ETCO_2} in the 35 to 45 mmHg range and $\text{SpO}_2 \geq 95\%$. Radial artery and central venous catheterization were performed to monitor invasive arterial pressure and central

venous pressure (CVP). Maintaining perioperative blood pressure and HR at $\pm 20\%$ of baseline value is often the ideal control goal. The two groups of FiO_2 were set to 40% and 80%, respectively. Anesthesia was kept with propofol ($6\text{--}8 \text{ mg}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$), remifentanyl ($0.1\text{--}0.3 \text{ }\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$), sevoflurane (1–2%), and cisatracurium ($0.1\text{--}0.2 \text{ mg}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$). The (Bispectral) BIS index was held in the 40 to 60 range. The patient's body temperature, monitored by an ear thermometer (Jiangsu, Jiruida, Xingsheng co.), was maintained at 36.0°C and 37.0°C . Cisatracurium besylate infusion and sevoflurane inhalation were terminated about 40 minutes and 20 minutes before the end of surgery, respectively. Oxycodone was administered with 10 mg to provide the analgesia postoperatively, meanwhile propofol and remifentanyl were discontinued. However, glucocorticoid drugs, dexmedetomidine nonsteroidal analgesics, and midazolam were avoided during surgery. Early recovery was managed in a post-anesthesia care unit (PACU) after surgery, while patients were returned to the ward and headed by an anesthesiologist, with a Steward resuscitation score of above 6.¹³ All patients were treated with patient-controlled intravenous analgesia (PCIA) for 48 hours after surgery. The PCIA opioid composed of $2.5 \text{ }\mu\text{g}\cdot\text{kg}^{-1}$ sufentanil and 5 mg tropisetron (total volume of 100 mL, including 0.9% normal saline, bolus 2 mL, basal rate 2 mL/h, and lockout time 15 mins). Pulmonary ultrasound (the Germany, SIEMENS, ACUSON SC2000) was performed 24 hours after surgery to assess and record the incidence of atelectasis.

Outcome Measures

The primary endpoint was the incidence of POD on every 7 days postoperatively, which was evaluated twice daily at 8 a.m. and 2 p.m. by an anesthesiologist who was blinded to group assignment. POD was defined by the Confusion Assessment Method (CAM), and the severity of POD was measured by the Memorial Delirium Assessment Scale (MDAS).^{14,15} The CAM and MDAS in the Chinese research have been proven to have high reliability and validity in the Chinese elderly population.^{16,17} In addition to the baseline, mean arterial pressure (MAP), rSO_2 , BIS, HR, SpO_2 and arterial blood gas (PH value, PaO_2 , PaCO_2) were also recorded at the following endpoints, which were continuously measured and recorded before anesthesia induction (T_1); (T_2) after 45 minutes; (T_3) after 90 minutes; 10 min before the end of the operation (T_4). Additionally, preoperative hemoglobin, operation time, anesthetic time, type of surgery, estimated blood loss, postoperative the highest

MDAS and visual analogue scale (VAS) score, length of PACU stay,¹⁸ length of hospital stays, and 6 months post-operative mortality were recorded.

Randomization and Blinding

A study statistician at the leading center generated random numbers without restriction (simple randomization) by a computerized system. The random numbers were sealed in sequentially numbered envelopes and sent to a research coordinator of our research team the day before surgery by a research nurse. The coordinator communicated the group assignment to an anesthesiologist, and upon consent, assigned participants to study groups according to the random numbers. An allocated random number was used to perform block randomization in a 301:301 ratio. The anesthesiologist was not blind to trials, who should know the FiO_2 target for each assigned participant and make proper adjustment to achieve the target FiO_2 level. The outcome assessment and statistical analyses were conducted by researchers independently. Outcome assessors and the surgical team were blind to the distribution of participants in the study.

Sample Size Estimation

In this study, PASS 11.0 (NCSS, LLC, Kaysville, Utah, USA) software was used to estimate the required sample size, with a sensitivity of 0.9, a sensitivity tolerance of 0.05, a specificity tolerance of 0.05, $\alpha = 0.05$, $1-\beta = 0.8$, a bilateral, and a 10% dropout rate. The sample size was 662.

Statistical Analyses

SPSS version 20.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. The Shapiro–Wilk test was used to assess the normality of continuous data. Normally distributed continuous data were presented as mean \pm standard deviation, and abnormal distributions were expressed as median (25–75% percentile). Categorical variables were expressed by numbers (%), and tested by χ^2 test. Differences in continuous variables were measured by independent sample *t*-test or Kruskal–Wallis rank-sum test as appropriate, and the intra-group comparisons were performed by repeated measurement design. $P < 0.05$ was statistically significant.

Results

Participants' Demographic Characteristics

The present study enrolled 662 participants, including 10 people refused to participate. Six hundred and

fifty-two participants were randomly divided into two groups: 40% FiO₂ maintenance (group A), 80% FiO₂ maintenance (group B). Twenty-two participants were excluded. The criteria are shown in Figure 1. Finally, 314 participants in group A and 316 participants in group B were included in the analysis. All patients underwent isolated laparoscopic radical gastrectomy, radical resection of colon cancer or radical resection of rectal cancer only.

Participants' Characteristics and Operative Data

No significant differences in gender, age, years of education, BMI, dependence on smoking, alcohol abuse, types of surgery, comorbidity, ASA class, preoperative Hb, time of anesthesia, time of surgery, BIS value, estimated blood loss, postoperative the highest VAS score, length of PACU stay, length of stay in hospital and mortality in 6 months were observed among two groups in Table 1.

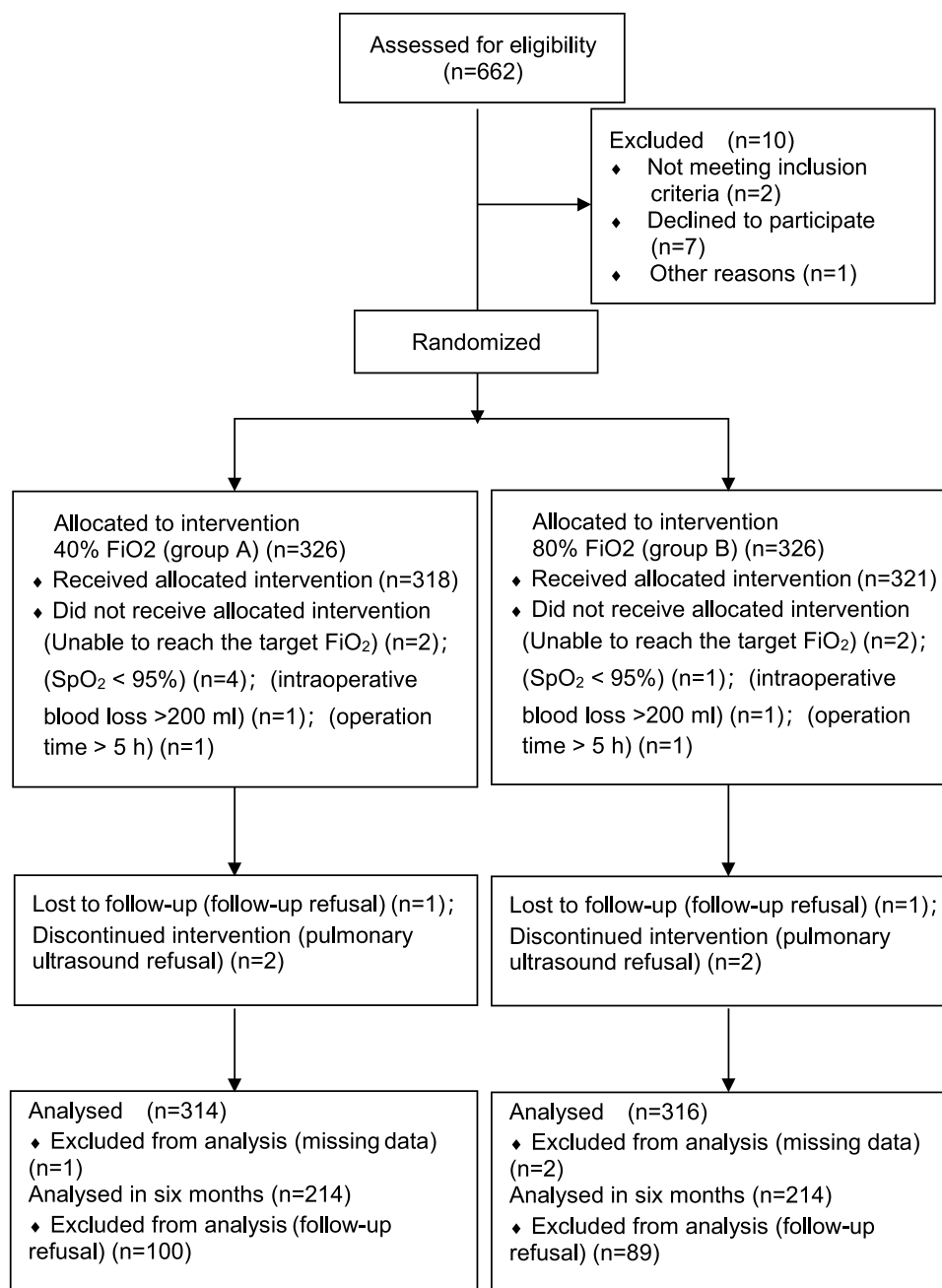


Figure 1 Flow chart of the trial.

Abbreviations: FiO₂, fraction of inspired oxygen; SpO₂, oxygen saturation; h, hour.

Table I Characteristics of Participants

Characteristics	Group A	Group B	P value
Age (year), mean \pm SD	71.39 \pm 2.80	71.45 \pm 3.85	0.805
Gender, n (%)	144 (45.85%)	149 (47.15%)	0.752
Years of education (year), n (%)			
0, n (%)	2 (0.64%)	2 (0.63%)	1.001
1 to 9, n (%)	31 (9.87%)	33 (10.44%)	0.816
10 to 13, n (%)	104 (33.12%)	104 (32.91%)	0.965
14 to 17, n (%)	93 (29.62%)	94 (29.75%)	0.978
>17, n (%)	15 (4.78%)	18 (5.70%)	0.612
Height (cm), mean \pm SD	170.13 \pm 3.02	170.41 \pm 3.05	0.257
Body weight (kg), mean \pm SD	68.87 \pm 2.32	68.71 \pm 2.19	0.374
BMI (kg/m ²), mean \pm SD	22.75 \pm 1.25	22.76 \pm 1.31	0.864
Dependence on smoking (n), n (%)	74 (23.57%)	73 (23.10%)	0.893
Alcohol abuse, n (%)	17 (5.41%)	20 (6.32%)	0.637
Coronary heart disease, n (%)	37 (11.78%)	39 (12.34%)	0.832
Hypertension, n (%)	123 (39.17%)	108 (34.18%)	0.195
Diabetes, n (%)	63 (20.06%)	72 (22.78%)	0.412
Radical gastrectomy for gastric cancer, n (%)	68 (21.66%)	74 (23.42%)	0.603
Radical resection of colon cancer, n (%)	127 (40.45%)	131 (41.46%)	0.802
Radical resection of rectal cancer, n (%)	119 (37.90%)	111 (35.13%)	0.472
Preoperative Hb (g/L), median and 25–75 percentile	124 (120–130)	124 (119–134)	0.440
ASA			
ASA class I, n (%)	182 (57.96%)	186 (58.86%)	0.962
ASA class II, n (%)	94 (29.94%)	94 (29.75%)	0.814
ASA class III, n (%)	31 (9.87%)	33 (10.44%)	0.891
Time of anesthesia (min), mean \pm SD	224.32 \pm 5.21	224.38 \pm 4.96	0.586
Time of surgery (min), mean \pm SD	188.71 \pm 8.56	188.23 \pm 12.67	0.582
BIS value	48 \pm 4	47 \pm 3	0.972
Estimated blood loss (mL), mean \pm SD	119.11 \pm 13.40	117.09 \pm 13.55	0.863
VAS score, median and 25–75 percentile	2 (1–3)	2 (1–3)	0.170
Length of PACU stay (min), median and 25–75 percentile	35 (33.75–37.56)	35 (33.37–38.15)	0.592
Length of hospital stay (days)	14.35 \pm 1.06	14.30 \pm 1.08	0.563
Mortality in 6 months, n (%)	20 (9.35%)	10 (4.67%)	0.421

Note: The values are presented as means \pm SD, median (interquartile range), or n (%) depending on type and distribution.

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; Hb, hemoglobin; PACU, post anesthesia care unit; VAS, visual analogue scale.

Primary Outcomes

The incidence of POD in the Group B was 18.35% (58/316) compared to 20.38% (64/314) in Group A ($P = 0.402$) in [Table 2](#).

Secondary Outcomes

The incidence of postoperative atelectasis in Group A (19.11%) was lower than that in Group B (41.77%) ($P = 0.026$). However, the incidence of adverse events

Table 2 Postoperative Characteristics of Participants

Characteristics	Group A	Group B	P value
Pneumonia, n (%)	20 (6.36%)	30 (9.49%)	0.552
Wound infection, n (%)	30 (9.55%)	40 (12.65%)	0.741
Cerebral hemorrhage, n (%)	0	0	
Cerebral infarction, n (%)	0	0	
Myocardial infarction, n (%)	1 (0.32%)	0	
Pulmonary embolism, n (%)	0	1 (0.32%)	
Reoperation, n (%)	0	1 (0.32%)	
Postoperative atelectasis, n (%)	60 (19.11%)	132 (41.77%)	0.026
Incidence of POD, n (%)	64 (20.38%)	58 (18.35%)	0.402

Note: The values are presented as n (%) depending on variable type.

Abbreviation: POD, postoperative delirium.

including wound infection, cerebral hemorrhage and cerebral infarction, myocardial infarction, pulmonary embolism, pneumonia and reoperation was not statistically significantly different between two groups in Table 2.

Oxygen Administration and Protocol Adherence

The included participants were subjected to the following protocol immediately after intubation. FiO₂ was maintained 40% (group A) and 80% (group B) by a Drager

monitor (model: Primus, Qingdao unity medical co.). There was no statistical significance of PaO₂, SpO₂ and rSO₂ at T₁ time point in the two groups included, so we primarily analyzed at T₂₋₄ time points. Thus, compared with Group B, PaO₂, SpO₂ and rSO₂ of Group A at T₂₋₄ time points decreased significantly. The difference was statistically significant ($P < 0.01$) in Figure 2A–C.

Preoperative MMSE Score and Postoperative MDAS Score

The preoperative MMSE score (25.16 ± 1.02) in the Group B compared to (25.10 ± 0.93) in Group A ($P = 0.40$); postoperative MDAS score (7.03 ± 2.08) in the Group B compared to (6.75 ± 1.86) in Group A ($P = 0.09$) in Figure 3.

Discussion

This prospective, randomized, double-blind controlled trial assessed the effects of different FiO₂ on POD, and measured CAM and MDAS scores in elderly patients undergoing laparoscopic surgery for isolated gastric and colorectal malignancies. In this study, the incidence of POD in Group B was 18.35% compared to 20.38% in Group A ($P = 0.402$). At the same time, the POD and its severity mainly diagnosed on the first and second days postoperatively by CAM and MDAS scores, which was the same as the previous study.¹⁹

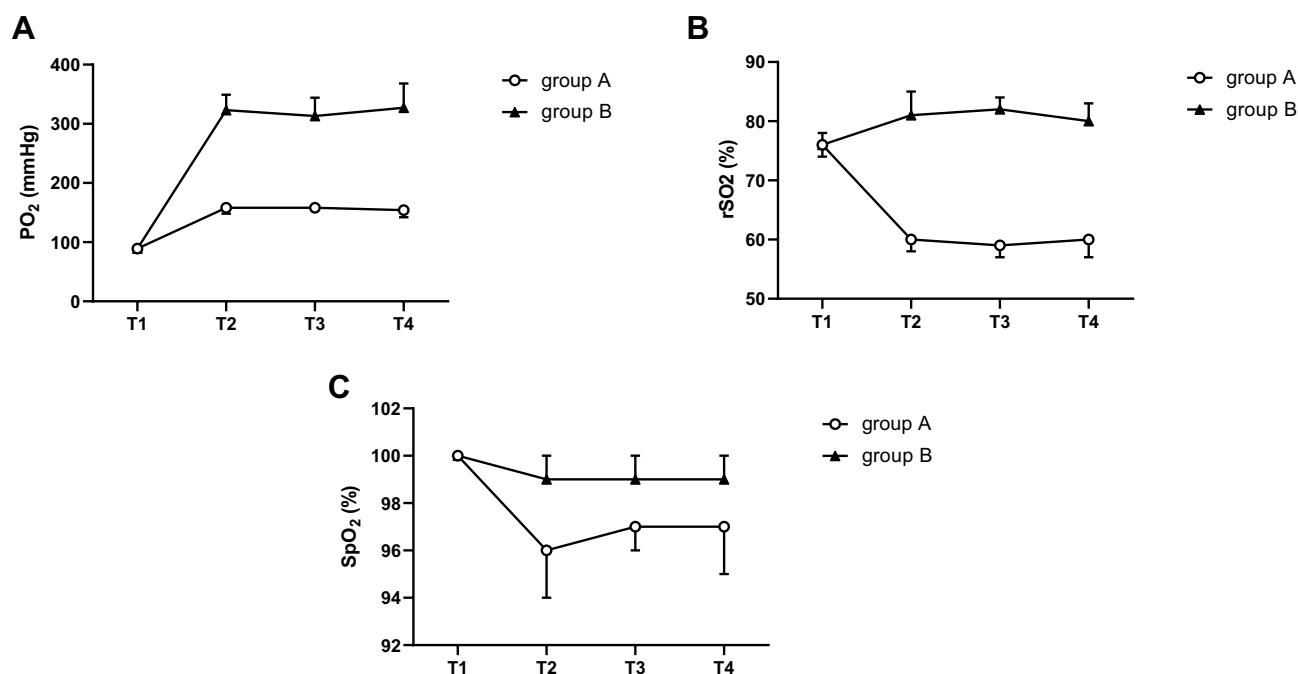


Figure 2 (A) Comparison of intraoperative PaO₂ at T₁₋₄ time points in the two groups included. (B) Comparison of intraoperative rSO₂ at T₁₋₄ time points in the two groups included. (C) Comparison of intraoperative SpO₂ at T₁₋₄ time points in the two groups included.

Abbreviations: PaO₂, oxygen partial pressure; rSO₂, regional cerebral oxygen saturation; SpO₂, oxygen saturation.

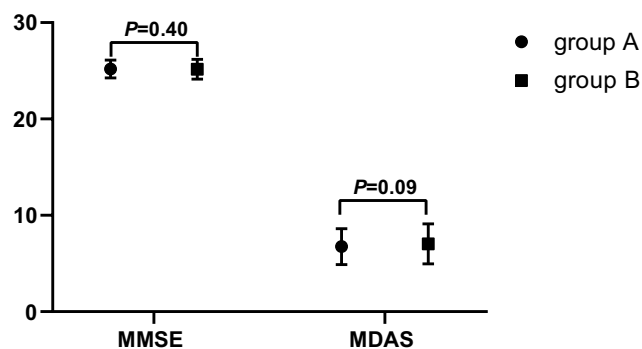


Figure 3 Preoperative MMSE and postoperative MDAS score for the study period are presented over time. Values are reported for 40% FiO₂ (circles) and 80% FiO₂ (squares) randomization groups individually.

Abbreviations: MMSE, Mini Mental State Scale; MDAS, Memorial Delirium Assessment Scale.

Different FiO₂ had no significant effect on the incidence of POD in 1 to 7 days postoperative between two groups. Although low FiO₂ did not impact the length of PACU and hospital stay, nor patient mortality, it indeed reduced the incidence of postoperative atelectasis. All the above results benefited from the strict exclusion criteria in this study, such as anemia, hypoalbuminemia, massive intraoperative bleeding and prolonged surgery, which could have influence on the development of POD.²

Currently, the optimal interoperative FiO₂ is still controversial. “Miller Anesthesiology” points out that whether spontaneous inhalation or mechanical ventilation following muscle relaxation, anesthesia would lead to lung function damage, because most of the blood oxygenation function of the subjects after anesthesia has been damaged. Therefore, it is recommended to add air to the inhaled gas to maintain the FiO₂ at 30% to 40%. The oxygen-departure curve shows that when SpO₂ is 99% to 100%, PaO₂ is about 160 mmHg by. It is well known that the oxygenation index of normal lung is 400 to 500, while the oxygenation index is equal to PaO₂/FiO₂, so the FiO₂ is 32% to 40%. Although the evidence regarding the exact association between lower FiO₂ and clinically outcomes intraoperatively is weak, a FiO₂ of ≤0.4 was recommended in the latest consensus.²⁰ However, the included patients were treated with FiO₂ 32% to 40% and SpO₂ nearly less than 95%, while the use of FiO₂ 40% improved SpO₂ in the preliminary trial. In the meantime, World Health Organization (Geneva, Switzerland) recommended that FiO₂ should be less than or equal to 80% in patients with tracheal intubation under general anesthesia to reduce complications such as postoperative atelectasis.²¹

Therefore, 40% and 80% of FiO₂ were selected for this study.

Nevertheless, the results of this study did not clarify the optimal FiO₂ for POD patients undergoing isolated laparoscopic radical gastrectomy, radical resection of colon cancer or radical resection of rectal cancer only. Other randomized controlled trials also demonstrated that the titration of intraoperative oxygenation resulted in no significant differences in postoperative cognition after cardiac surgery,²² potentially because both high and low levels of FiO₂ can be monitored with rSO₂ to ensure changes in cerebral oxygen supply and consumption. As we known, rSO₂ is the weighted average of the regional cerebral oxygenation, and near-infrared spectroscopy is the only way to continuously and noninvasively monitor rSO₂.²³ Additionally, FiO₂ is the main factor affecting rSO₂, which has a high correlation with FiO₂.⁹ In this study, compared with high FiO₂, rSO₂ and PaO₂ decreased at low FiO₂; however, SpO₂ remained at 95% to 100% intraoperatively, so low FiO₂ could meet the balance of oxygen supply and consumption in the brain during operation. And yet, atelectasis occurred more frequently, which might be related to the damage of lung function caused by high FiO₂.²⁴

The results of this study show that different levels of FiO₂ lead to different rSO₂, but there is no significant difference in the incidence of POD. Although previous studies have shown that decreased intraoperative rSO₂ is associated with an increased incidence of POD,²⁵ the latest research results do not support the correlation between the intraoperative reduction of rSO₂ and the incidence of POD.²⁶

At present, the relationship between the optimal perioperative FiO₂ and POD is still under discussion. The lack of a consensus definition of hypoxia and hyperoxia makes clinical work and studies difficult to carry out effectively. Nowadays, both of the World Health Organization (Geneva, Switzerland) and the Centers for Disease Control and Prevention (Atlanta, Georgia) recommend high FiO₂ to reduce surgical site infection.^{20,27} These recommendations are controversial because of the potential damage of hyperoxia, such as postoperative atelectasis.^{28–30} Our results confirm that low levels of FiO₂ can reduce the incidence of postoperative atelectasis. In our study, low FiO₂ may still provide adequate tissue oxygenation during the perioperative surgery without affecting the incidence of POD and survival after six months, even in patients with malignant tumors included.

In fact, apart from postoperative atelectasis, our study did not find any significant differences in postoperative complications with low levels of FiO₂, although these results must be interpreted carefully to support the safety of low FiO₂. Therefore, it should be continuously concerned about the relationship between intraoperative low FiO₂ and POD, and their severity scores and postoperative survival rate in patients with malignant tumors, so as to improve the quality of life of these patients.

This study has several limitations. First, since it is a single-center study, more multi-center studies are needed to confirm the results of this study. Second, only 40% and 80% of FiO₂ were studied, and our team will continue to study other levels of FiO₂ to further explore the optimal interoperative FiO₂ associated with perioperative neurocognitive disorder. Third, we did not assess neurocognitive function for the follow up six months of survival time. By including patients with malignant tumors, we sought to reduce the rate of loss, lessen possible missed data, and improve the assessment of 6-month survival after surgery. Unfortunately, only about 68% of patients could be contacted, which may affect the evaluation of the 6-month survival rates of intraoperative FiO₂ in elderly patients with malignant tumors.

Conclusion

In conclusion, although there was no significant effect of FiO₂ on postoperative delirium in elderly patients after laparoscopic gastric and colorectal malignancies surgery, low FiO₂ was beneficial to decrease postoperative atelectasis, suggesting that low FiO₂ may be safely employed without postoperative delirium.

Abbreviations

POD, postoperative delirium; FiO₂, fraction of inspired oxygen; rSO₂, regional cerebral oxygen saturation; BIS, Bispectral; IABP, invasive arterial blood pressure; SpO₂, oxygen saturation; P_{ET}CO₂, end-tidal carbon dioxide partial pressure; ASA, American Society of Anesthesiologists; NYHA, New York Heart Association Functional Classification; MMSE, Mini-mental State Examination; PACU, post-anesthesia care unit; NABP, non-invasive arterial blood pressure; MAP, mean arterial pressure; HR, heart rate; ECG, electrocardiogram; CVP, central venous pressure; PCIA, Patient-controlled intravenous analgesia; VAS, visual analogue scale; CAM, Confusion Assessment Method; MDAS, Memorial

Delirium Assessment Scale; SD, standard deviation; BMI, body mass index.

Data Sharing Statement

All data generated or analyzed during this study are included in this published article.

Ethics Approval and Informed Consent

The study was approved by the Research Ethics Committee of Qingdao Municipal Hospital Affiliated to Qingdao University and registered at ClinicalTrials.gov (ChiCTR1800014972). Written informed consent was obtained from each participant.

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Disclosure

Xu Lin and Bin Wang are co-first authors for this study. The authors have no conflicts of interest to report.

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