

# Comparison of effects of low-flow and normal-flow anesthesia on cerebral oxygenation and bispectral index in morbidly obese patients undergoing laparoscopic sleeve gastrectomy: a prospective, randomized clinical trial

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## Abstract

**Introduction:** The effects of low-flow anesthesia on cerebral oxygenation in high-risk, morbidly obese patients are not well known.

**Aim:** In this prospective randomized study, we compared the effects of low-flow (0.75 l/min) and normal-flow (1.5 l/min) anesthesia on regional cerebral oxygen saturation (rSO<sub>2</sub>) and the bispectral index (BIS) in morbidly obese patients undergoing laparoscopic bariatric surgery.

**Material and methods:** Fifty-two morbidly obese patients undergoing laparoscopic bariatric surgery (sleeve gastrectomy) were enrolled in this study. Patients were randomly allocated to two study groups: low-flow and normal-flow anesthesia groups. Heart rate, mean arterial pressure, peripheral oxygen saturation, end-tidal carbon dioxide, BIS, left and right rSO<sub>2</sub>, and duration of anesthesia and surgery were recorded.

**Results:** The groups were similar with respect to age, gender, height, weight, body mass index, American Society of Anesthesiology physical status, heart rate, duration of anesthesia, and procedure. Mean arterial pressure and end-tidal carbon dioxide, both before and after insufflation of carbon dioxide and after the reverse Trendelenburg position, were significantly higher in the low-flow group. BIS values and left and right rSO<sub>2</sub> during the preoperative and intraoperative periods were similar. Although the difference in right rSO<sub>2</sub> between the two groups after awakening from anesthesia was statistically significant, the results of both groups remained within the normal range and were not clinically meaningful.

**Conclusions:** Low-flow anesthesia is safe regarding hemodynamic and respiratory characteristics, depth of anesthesia, and regional cerebral oxygen saturation in morbidly obese patients undergoing laparoscopic bariatric surgery.

**Key words:** morbid obesity, bispectral index, bariatric/metabolic surgery, anesthesia management, low flow anesthesia, regional cerebral oximetry.

## Introduction

Obesity is a chronic disease that negatively affects the quality and duration of life [1]. Severe obesity is a highly prevalent chronic disease, which leads to substantial morbidity, premature mortality,

impaired quality of life, and excess healthcare expenditures [2].

Laparoscopic bariatric surgery is the most effective long-term treatment for severe obesity and obesity-related comorbidities [3]. Insufflation of the

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abdominal cavity with carbon dioxide (CO<sub>2</sub>) is necessary for good surgical visibility and proper surgical manipulation [4]. The level of carbon dioxide is the most potent regulatory stimulus for cerebrovascular resistance [5, 6].

Cerebral oximetry is therefore used to estimate regional tissue oxygenation using near-infrared spectroscopy (NIRS), which is a noninvasive and continuous measurement technique used to assess the adequacy of cerebral perfusion [7, 8]. On the other hand, BIS is the most effective method for assessing depth of anesthesia and sedation. BIS monitoring reduces the number of intraoperative wake-ups in patients [9].

Low-flow anesthesia has several potential benefits. It improves the flow dynamics of the inhaled air, increases mucociliary clearance, maintains body temperature, reduces fluid loss, results in savings of up to 75% and reduces greenhouse gas emissions and treatment costs [10–13]. However, it is necessary to examine whether the reduction of fresh gas flow affects the quality and safety of anesthesia management, especially during high-risk operations such as laparoscopic bariatric surgery.

## Aim

Low-flow anesthesia has been used for years with positive results, but its effects on cerebral oxygenation are not known in high-risk morbidly obese patients who are prone to pulmonary dysfunction related to the obesity. Therefore, our prospective randomized study compared the effects of low-flow (0.75 l/min) and normal-flow (1.5 l/min) anesthesia on regional cerebral oxygen saturation (rSO<sub>2</sub>) and the bispectral index (BIS) in morbidly obese patients undergoing laparoscopic bariatric surgery.

## Material and methods

### Protocol

This trial was approved by the Local Ethic Committee of Inonu University (Protocol no: 2017/113) and registered at the US National Institutes of Health (ClinicalTrials.gov) # NCT03438734. We conducted a prospective, randomized controlled clinical trial with 52 adult morbidly obese patients who were undergoing laparoscopic bariatric surgery in the period from June 2017 to February 2018 at a university hospital. This study was prepared in accordance

with the Consolidated Standards of Reporting Trials (CONSORT) guidelines [14].

### Study participants

Morbidly obese patients with American Society of Anesthesiologists (ASA) scores of III–IV, who were aged 18–65 years old, and had a BMI > 40 kg/m<sup>2</sup> were included in our study. Patients were interviewed before surgery to obtain informed consent. Patients were excluded if they were pregnant or had uncontrolled diabetes mellitus, cardiovascular disease, pulmonary disease, cerebrovascular disease, or drug and alcohol addiction. Patients who refused informed consent were also excluded.

### Preoperative procedures

Patients were taken to the operating room without premedication. Standard monitoring procedures were used, including heart rate (HR), noninvasive blood pressure (NIBP), electrocardiogram (ECG), peripheral oxygen saturation (SpO<sub>2</sub>), and body temperature monitoring by esophageal probe. In addition, regional cerebral oxygen saturation (rSO<sub>2</sub>) monitoring was conducted with all individuals using near-infrared spectroscopy (NIRS; INVOS 4100 Cerebral Oximeter, Software Version 7.2.5.0, Somanetics Corporation, Minneapolis, USA) and depth of anesthesia was monitored with the bispectral index (BIS; VISTA Monitoring System, Massachusetts, USA) monitoring. Two cerebral NIRS and BIS sensors were placed in the right and left frontal areas under the hairline and covered with tape to prevent exposure to light.

### General anesthesia

A standardized general anesthesia protocol was administered in all patients by an experienced anesthesiologist. After preoxygenation (100% 4 l/min O<sub>2</sub> for 3 min), propofol (1–2 mg/kg), rocuronium (0.8 mg/kg) and fentanyl (0.1 µg/kg) were administered during the induction of anesthesia via the intravenous (IV) route at doses calculated according to ideal body weights. End-tidal carbon dioxide (EtCO<sub>2</sub>) was continuously monitored after intubation. Tidal volume and ventilation rate were adjusted to maintain EtCO<sub>2</sub> partial pressure of arterial blood at 35–45 mm Hg. Rocuronium was intermittently injected according to need based on train of four (TOF; Dräger AG, Lübeck, Germany) values. Train of four

responses were assessed by ulnar nerve stimulation and adductor muscle response. 0.1–0.2 µg/kg of fentanyl was titrated for analgesia, as needed, if HR and/or mean arterial pressure (MAP) increased by 20% above baseline during surgery. Anesthesia was maintained in both groups at desflurane inhalation in a 0.5 O<sub>2</sub> oxygen-air mixture. Desflurane was discontinued with the beginning of the skin sutures and the fresh gas flow was changed to 4 l/min of oxygen for both groups. In patients who did not experience complications during the surgery, sugammadex (IV, 2–4 mg/kg, Bridion, MSD, Greenville, USA) was then administered to reverse residual muscle relaxation at the end of surgery.

### Randomization

This study was planned as a randomized prospective trial. Randomization was performed with the MedCalc for Windows (medcalc.com.tr.), version 16 statistical software. Fifty-two patients were randomly allocated to two study groups: a low-flow group (group L,  $n = 26$ ) and a normal-flow group (group N,  $n = 26$ ). Patients in group L received a fresh gas flow of 4 l/min for the first 10 min and were then maintained with a fresh gas flow of 0.75 l/min. Patients in group N received the same initial fresh gas flow of 4 l/min for the first 10 min but were then maintained with a fresh gas flow of 1.5 l/min. All patients were mechanically ventilated with a tidal volume of 8 ml/kg based on ideal body weight and a frequency of 12–14 breaths/min using a Dräger Primus ventilator (Dräger AG, Lübeck, Germany). Age-related minimum alveolar concentration values were determined and expressed as a percentage of volume. All patients received the standard surgical procedures determined by the same team of surgeons with experience in gastroenterology surgery. Pneumoperitoneum pressure ranged between 10 and 12 mm Hg. Also the pneumoperitoneum level was 30–45°. Surgical management of sleeve gastrectomy was not changed in any way.

### Postoperative management

Patients were transferred to the post-anesthesia care unit (PACU) after surgery. Patients were transferred to the general surgery intensive care unit when they achieved a score of 9 or higher on the Modified Aldrete score (range: 0–12; scores of 9 and above indicate that the patient can be discharged from the PACU) [15]. In all patients, postoperative

analgesia was achieved with IV analgesic medication using appropriate doses of tramadol (0.5–1 mg/kg, IV) and paracetamol (1 g, IV) at the time of beginning skin sutures [16].

### Outcome measures

HR, SpO<sub>2</sub>, EtCO<sub>2</sub>, MAP, BIS values, left rSO<sub>2</sub> (LrSO<sub>2</sub>) and right rSO<sub>2</sub> (RrSO<sub>2</sub>) were recorded before anesthesia ( $T_0$ ), 10 min after intubation ( $T_1$ ), 5 min before insufflation of CO<sub>2</sub> ( $T_2$ ), 5 min after insufflation of CO<sub>2</sub> ( $T_3$ ), 5 min after the reverse Trendelenburg position was applied ( $T_4$ ), 5 min after the supine position was applied ( $T_5$ ), 5 min after desufflation of CO<sub>2</sub> ( $T_6$ ), and 15 min after awakening from anesthesia ( $T_7$ ). In addition to anesthesia and surgery times, perioperative and postoperative complications were recorded.

### Statistical analysis

On the basis of Kemerci's *et al.* [17] study and the assumption that a difference of 10 U on cerebral oximetry is clinically relevant, using the power calculation method (OpenEpi, Version 3), assuming an  $\alpha$  of 0.05 and a  $\beta$  of 0.80, we calculated that 19 patients per group should be included in this study. Data were analyzed using the SPSS (Statistical Package for Social Sciences Statistics for Windows, Version 22.0 Software. Armonk, NY: IBM Corp). As some pre- and anesthetic characteristics of patients were distributed abnormally, nonparametric statistics was used. Quantitative data are presented as mean or standard deviation and categorical data are shown as numbers or percentages. Continuous variables were compared between the groups using the Mann-Whitney *U*-test. Categorical variables were summarized using frequencies and percentages (%) and compared between the groups using the  $\chi^2$  test. The results were evaluated at a 95% confidence interval at a significance level of  $p < 0.05$ .

### Results

The two groups were similar with respect to age, gender, height, weight, body mass index (BMI), ideal body weight (IBW), ASA physical status, fentanyl consumption and duration of pneumoperitoneum. The mean duration of anesthesia was also similar in both groups (161.15 ±41.17 min in group L and 184.69 ±46.41 min in group N), as was the mean duration of surgery (144.23 ±40.36 min in group L and 166.92

±42.59 min in group N). Desflurane consumption was significantly lower in group L than group N ( $p < 0.001$ ). Demographic and procedural data are presented in Table I.

The HRs were similar in both groups ( $p > 0.05$  for all time points). MAPs at  $T_2$ ,  $T_3$ , and  $T_4$  were sig-

nificantly higher in group L than group N ( $p = 0.041$ ,  $p = 0.008$  and  $p = 0.019$ , respectively). EtCO<sub>2</sub> values at the same time points ( $T_2$ ,  $T_3$ , and  $T_4$ ) were also significantly higher in group L than group N ( $p = 0.016$ ,  $p = 0.001$  and  $p = 0.002$ , respectively). MAP and EtCO<sub>2</sub> values between the two groups were not

**Table I.** Demographic and procedure data

Parameter	Group L (n = 26)		Group N (n = 26)		P-value
	Range	Mean ± SD	Range	Mean ± SD	
Age [years]	18–64	35.69 ±13.02	19–60	35.42 ±10.54	0.935
Gender, male/female	7/19	–	6/20	–	0.751
Height [cm]	149–185	164.42 ±10.31	102–193	163.61 ±16.52	0.833
Weight [kg]	98–180	126.24 ±20.98	102–198	129.07 ±27.40	0.678
BMI [kg/m <sup>2</sup> ]	36–63	46.60 ±6.46	38–59	45.75 ±5.91	0.622
IBW	42–79	57.80 ±10.49	44–86	58.79 ±11.35	0.746
ASA, III/IV	26/0	–	26/0	–	0.508
Sleeve gastrectomy, n	26	–	26	–	–
Desflurane consumption [ml]	23–145	70.46 ±29.49	59–202	120.57 ±39.25	< 0.001*
Fentanyl consumption [µg]	100–200	127.88 ±30.27	90–200	140.96 ±24.16	0.091
Duration of pneumoperitoneum [min]	67–186	117.26 ±36.78	79–194	136.65 ±35.36	0.058
Duration of surgery [min]	90–230	144.23 ±40.36	100–240	166.92 ±42.59	0.054
Duration of anesthesia [min]	100–255	161.15 ±41.17	110–260	184.69 ±46.41	0.059

ASA – American Society of Anesthesiologists, BMI – body mass index, Group L – low flow group, Group N – normal flow group, IBW – ideal body weight, n – number, SD – standard deviation.

**Table II.** Heart rate (HR), mean arterial pressure (MAP), peripheral oxygen saturation (SpO<sub>2</sub>), End-tidal carbon dioxide (EtCO<sub>2</sub>) and minimum alveolar concentration (MAC) of desflurane values

Time	Group L (n = 26)					Group N (n = 26)				
	HR [1/min]	MAP [mm Hg]	SpO <sub>2</sub>	EtCO <sub>2</sub>	MAC	HR [1/min]	MAP [mm Hg]	SpO <sub>2</sub>	EtCO <sub>2</sub>	MAC
T <sub>0</sub>	86.42	105.03	95.53	–	–	84.34	105.34	96.69	–	–
T <sub>1</sub>	96.69	85.46	98.50	36.19	0.94	90.61	82.80	97.92	34.07	1.39
T <sub>2</sub>	84.30	80.61*	97.88	33.38*	0.97	82.80	72.03*	98.03	30.65*	1.02
T <sub>3</sub>	86.76	95.23*	97.23	37.23*	1.01	85.65	82.73*	97.61	32.65*	1.02
T <sub>4</sub>	85.84	85.69*	97.84	36.73*	0.99	85.53	73.50*	96.96	33.30*	1.05
T <sub>5</sub>	84.61	85.19	97.96	36.69	0.93	85.69	87.34	97.80	37.65	1.00
T <sub>6</sub>	89.50	88.57	98.19	37.23	0.90	85.30	89.34	98.11	36.96	0.94
T <sub>7</sub>	99.96	108.80	94.69	–	–	94.80	106.15	95.42	–	–

Group L – low flow group, Group N – normal flow group. T<sub>0</sub> – before anesthesia, T<sub>1</sub> – 10 min after intubation, T<sub>2</sub> – 5 min before insufflation of CO<sub>2</sub>, T<sub>3</sub> – 5 min after insufflation of CO<sub>2</sub>, T<sub>4</sub> – 5 min after reverse Trendelenburg position, T<sub>5</sub> – 5 min after supine position, T<sub>6</sub> – 5 min after desufflation of CO<sub>2</sub>, T<sub>7</sub> – 15 min after awakening from anesthesia. \*When compared with each one ( $p < 0.05$ ).

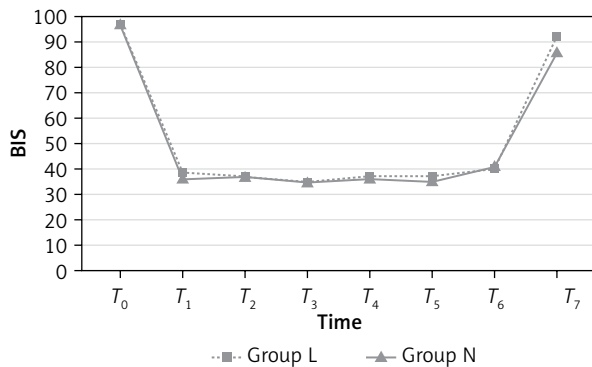


Figure 1. Bispectral index (BIS) values

significantly different at other time points. SpO<sub>2</sub> and MAC values were similar in both groups ( $p > 0.05$  for all time points). HR, MAP, SpO<sub>2</sub>, EtCO<sub>2</sub> and MAC data are presented in Table II.

The BIS values, representing sedation level, were similar in both groups during the preoperative (T<sub>0</sub>) and intraoperative (T<sub>1</sub>, T<sub>2</sub>, T<sub>3</sub>, T<sub>4</sub>, T<sub>5</sub> and T<sub>6</sub>) periods ( $p > 0.05$ ; Figure 1); however, the BIS values at T<sub>7</sub> were significantly higher in group L than group N ( $p = 0.001$ ). BIS values are presented in Table III.

LrSO<sub>2</sub> measurements were similar in both groups ( $p > 0.05$ ; Figure 2) at all time points. However, RrSO<sub>2</sub> measurements at T<sub>7</sub> were significantly higher in group N than group L ( $p = 0.018$ ; Figure 3). Mean values (%) for rSO<sub>2</sub> are presented in Table IV.

## Discussion

We did not observe significant differences between low-flow and normal-flow groups with respect to HR and SpO<sub>2</sub>. Similarly, Kupisiak *et al.* reported no significant differences between patients

Table III. Bispectral index (BIS) values

Time	Group L (n = 26)	Group N (n = 26)	P-value
T <sub>0</sub>	97.61	97.30	0.513
T <sub>1</sub>	39.73	36.57	0.167
T <sub>2</sub>	37.92	37.11	0.690
T <sub>3</sub>	35.73	35.96	0.889
T <sub>4</sub>	37.61	36.38	0.556
T <sub>5</sub>	37.61	35.19	0.257
T <sub>6</sub>	40.61	41.15	0.873
T <sub>7</sub>	92.50*	86.65*	0.001*

Group L – low flow group, Group N – normal flow group. T<sub>0</sub> – before anesthesia, T<sub>1</sub> – 10 min after intubation, T<sub>2</sub> – 5 min before insufflation of CO<sub>2</sub>, T<sub>3</sub> – 5 min after insufflation of CO<sub>2</sub>, T<sub>4</sub> – 5 min after reverse Trendelenburg position, T<sub>5</sub> – 5 min after supine position, T<sub>6</sub> – 5 min after desufflation of CO<sub>2</sub>, T<sub>7</sub> – 15 min after awakening from anesthesia. \*When compared with each one ( $p < 0.05$ ).

who received low-flow and high-flow anesthesia during laparoscopic cholecystectomy with respect to HR, MAP, EtCO<sub>2</sub>, and SpO<sub>2</sub>; patients also did not have a high risk of awakening from anesthesia [9]. Although we found that the MAPs of the low-flow group were significantly higher than the normal-flow group at T<sub>2</sub>, T<sub>3</sub>, and T<sub>4</sub>, the higher MAPs were considered clinically negligible because the MAPs did not increase by 20% above baseline during surgery. These results are similar to those obtained by Kupisiak *et al.* [9], even though patients in our study underwent a higher-risk surgical procedure and were morbidly obese.

Fassoulaki *et al.* reported that BIS was equally effective for depth of anesthesia with sevoflurane and desflurane [18]. In our study, anesthesia was maintained by desflurane because it has a shorter recov-

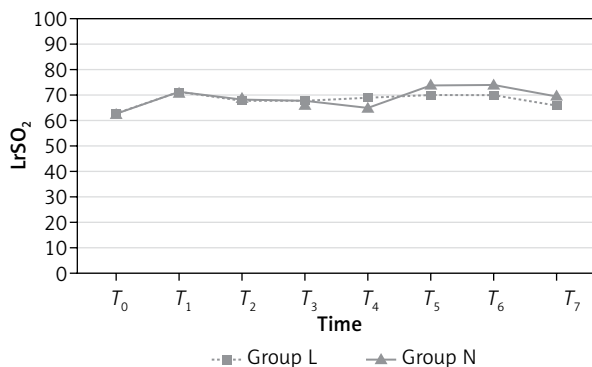


Figure 2. Left regional cerebral oxygen saturation (LrSO<sub>2</sub>)

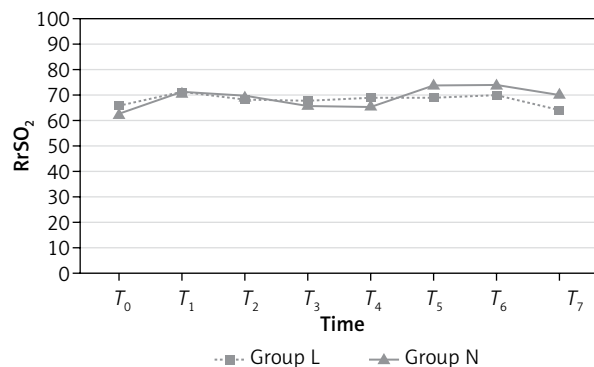


Figure 3. Right regional cerebral oxygen saturation (RrSO<sub>2</sub>)

**Table IV.** Mean values of regional cerebral oxygen saturation (%) for left and right cerebral hemisphere

Time	Group L Left	Group N Left	P-value	Group L Right	Group N Right	P-value
T <sub>0</sub>	63.76	63.34	0.854	66.15	62.38	0.117
T <sub>1</sub>	71.92	71.96	0.988	71.00	71.23	0.943
T <sub>2</sub>	68.84	69.15	0.918	69.26	70.00	0.813
T <sub>3</sub>	68.19	66.69	0.629	68.00	66.96	0.730
T <sub>4</sub>	69.00	65.61	0.292	69.73	66.03	0.235
T <sub>5</sub>	70.30	74.57	0.208	69.65	74.65	0.107
T <sub>6</sub>	70.30	74.15	0.254	70.80	74.46	0.201
T <sub>7</sub>	66.46	70.46	0.169	64.69*	71.65*	0.018*

Group L – low flow group, Group N – normal flow group. T<sub>0</sub> – before anesthesia, T<sub>1</sub> – 10 min after intubation, T<sub>2</sub> – 5 min before insufflation of CO<sub>2</sub>, T<sub>3</sub> – 5 min after insufflation of CO<sub>2</sub>, T<sub>4</sub> – 5 min after reverse Trendelenburg position, T<sub>5</sub> – 5 min after supine position, T<sub>6</sub> – 5 min after desufflation of CO<sub>2</sub>, T<sub>7</sub> – 15 min after awakening from anesthesia. \*When compared with each one ( $p < 0.05$ ).

ery time. We observed that BIS values in both groups were similar at all time points during the intraoperative period. Although BIS values at T<sub>7</sub> were significantly higher in the low-flow group (mean BIS value at T<sub>7</sub>: 92.50) than the normal-flow group (mean BIS value at T<sub>7</sub>: 86.65), these results were considered clinically negligible because there were no anesthesia complications during the postoperative period, based on intensive care unit records.

All patients in our study met the threshold criteria for morbid obesity with a BMI of 40 or more. The mean duration of anesthesia (nearly 160 min) was longer than those. Despite this, patients in our study experienced no cerebrovascular events during the postoperative period, according to intensive care unit records.

Identification and prevention of risk factors for reductions in cerebral oxygenation are crucial tasks for all anesthetists [19]. Keeping regional cerebral saturation at safe levels during surgery may reduce perioperative complications and shorten the length of stay in the hospital [20]. We did not observe any reduction of the cerebral oxygenation compared to the baseline. Although the fresh gas flow rate was different, we provided oxygenation using the appropriate oxygen concentration.

Higher BMI scores are associated with reduced functional residual capacity and oxygenation index, increasing respiratory system resistance and workload. A BMI score over 40 kg/m<sup>2</sup> becomes an important predictor for lung volumes, respiratory mechanics, and oxygenation in patients undergoing general anesthesia [21].

Laparoscopic bariatric surgery has many benefits compared to conventional open surgery, such as less postoperative pain, shorter hospital stays, and faster recovery times [22]. However, changes in body position are required in laparoscopic bariatric surgery which can cause significant hemodynamic and respiratory changes that can reduce brain perfusion and oxygenation [23]. Specifically, laparoscopic bariatric surgery requires that patients be placed in a reverse Trendelenburg position with long-duration pneumoperitoneum for good surgical visibility and proper surgical manipulation. In addition, insufflation of the abdominal cavity with CO<sub>2</sub> during laparoscopy results in increased intra-abdominal pressure, hypercapnia, and systemic vascular resistance, and decreased functional residual capacity and pulmonary compliance. Similarly, elevated thoracoabdominal pressure disturbs cerebral venous drainage, and CO<sub>2</sub> absorption dilates the cerebral vessels and increases cerebral blood volume. This can lead to significant changes in cerebral homeostasis, which in turn can lead to cognitive dysfunction [24, 25]. Gipson *et al.* found significant decreases in cerebral oxygenation associated with neurocognitive changes after 10–12 mm Hg pneumoperitoneum [26]. It is therefore crucially important to monitor cerebral oxygenation levels during laparoscopic bariatric surgery. However, it can be difficult to predict cerebral hypoxia when patients are in the Trendelenburg position required by laparoscopic bariatric surgery, due to the reduced intracranial pressure and cerebral blood flow [4].

Yi Jo *et al.* also reported that cerebral oxygen and EtCO<sub>2</sub> values were significantly increased after pneumoperitoneum during laparoscopic bariatric surgery, but that there was no change of cerebral oxygen saturation in any of their patients [27]. In our study, we observed that no significant changes in cerebral oxygen saturations during the entire intraoperative ( $T_1$ ,  $T_2$ ,  $T_3$ ,  $T_4$ ,  $T_5$  and  $T_6$ ) period. Although there was a statistically significant difference between the low-flow and normal flow groups for RrSO<sub>2</sub> at  $T_7$  (64.69 and 71.65, respectively), this difference was considered clinically unimportant, and neither group had a clinically superior outcome in terms of cerebral oxygenation.

Our study did not include the use of transcranial colored Doppler and jugular bulb oxygen saturation, which can help monitor cerebral function. We also did not include cognitive function assessments during the postoperative period, which could give more reliable results. Further research should make use of these measures of cerebral functioning.

## Conclusions

Our study examined the effects of low-flow vs normal-flow anesthesia on hemodynamic and respiratory characteristics, depth of anesthesia, and cerebral oxygen saturation in morbidly obese patients during laparoscopic bariatric surgery. No significant perioperative or postoperative complications were recorded among our sample. While a few differences between the two groups reached statistical significance, all results were within normal ranges and none of the differences suggested any meaningful clinical differences. We therefore conclude that low-flow anesthesia can be used safely with morbidly obese patients during laparoscopic bariatric surgery.

## Conflict of interest

The authors declare no conflict of interest.

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