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ORIGINAL RESEARCH

Effect of volume-controlled and pressure-controlled ventilation modes on cerebral oximetry in laparoscopic cholecystectomy: a randomized controlled trial

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Abstract

This study aimed to compare the effect of volume-controlled ventilation (VCV) and pressure-controlled ventilation (PCV) modes on cerebral oximetry during laparoscopic cholecystectomy using near-infrared spectroscopy (NIRS). Seventy patients who underwent elective laparoscopic cholecystectomy were randomized to receive either VCV (group V) or PCV (group P). Demographic and operative data (anesthesia, surgery and insufflation durations) were recorded. The primary outcome was the NIRS value, while the secondary outcomes were peripheral oxygen saturation (SpO_2), blood gas parameters and peak and plateau pressures in mechanical ventilation. Measurements were conducted at the start of anesthesia (T0), end of intubation (T1), 5 min after insufflation (T2), just before desufflation (T3), and 5 min after desufflation (T4). Both groups were comparable in terms of age, sex, body mass index, intraoperative time, anesthesia and insufflation durations. The average NIRS right T1–T2–T3 and left T2–T3 values were significantly higher in group P than in group V (p = 0.030, p = 0.001, p = 0.001, p = 0.006 and p = 0.002 respectively). In contrast, the mean peak and mean plateau pressures in group P at T1, T2 and T4 were significantly lower than those in group V (p = 0.003, p = 0.001, $p < 0.001$, p = 0.011, p = 0.001 and $p < 0.001$ respectively).The PCV mode allows better cerebral oxygenation than VCV while maintaining lower peak pressure and plateau pressures.

Keywords

Laparoscopic cholecystectomy; Mechanical ventilation; Near-infrared spectroscopy

1. Introduction

Laparoscopic cholecystectomy has become the gold standard for cholelithiasis surgery ever since the introduction of laparoscopic surgery [1]. For any laparoscopic surgery, carbon dioxide (CO_2) insufflation is used to increase intra-abdominal pressure; however, this technique affects arterial oxygenation, functional residual capacity and lung compliance which may result in adverse cardiovascular events [2, 3].

Volume-controlled ventilation (VCV) and pressure-controlled ventilation (PCV) are the two mechanical ventilation modes used which offer several advantages and disadvantages [3]. VCV requires a predetermined tidal volume (TV) with the primary concern being the risk of lung damage. In contrast, while PCV avoids excess respiratory tract pressure to the lungs, the resultant TV may become unstable. Previous studies have compared both techniques to determine which one provides lower respiratory work and better tissue oxygenation. A study indicated that PCV is better for arterial and tissue oxygenation [4].

Certain studies have reported using near-infrared spectroscopy (NIRS) in addition to arterial blood gas results to evaluate the tissue-level oxygenation changes in the prefrontal cortex [5]. Although NIRS has been used in different surgeries, there is a paucity of literature on its use in laparoscopic abdominal surgery [6, 7]. Furthermore, to the best of our knowledge, no study has determined the effectiveness of different perioperative ventilation modes using the NIRS method. Therefore, this study aimed to compare the effects of two ventilation modes, VCV and PCV, on cerebral oximetry in patients undergoing laparoscopic cholecystectomy.

2. Materials and methods

This prospective randomized controlled trial was conducted between February and July 2021 in Sisli Hamidiye Etfal Research and Training Hospital. The study was registered with the Clinical Trials Registry (ClinicalTrials.gov; trial number: NCT04723043; dated 25 January 2021).

2.1 Sample size calculation and randomization

The sample size was calculated using the G*Power (Version 3.1.9.7, Heinrich Heine University, Dusseldorf, Germany) program. Assuming a higher peak airway pressure in VCV than in PCV, we estimated a mean difference of 2 $\pm$ 2 cmH_2O between the two groups at a 1:1 allocation ratio [8, 9]. Based on these data, to obtain an effect size of 0.8 with 90% power and 0.05 alpha error probability, a sample size of 68 was calculated which was increased to 70 to account for follow-up losses. Randomization was conducted with a computer-generated program.

2.2 Inclusion and exclusion criteria

Patients who were planned to undergo elective laparoscopic cholecystectomy during the study period were screened for inclusion in the study. Those aged 18–65 years with an American Society of Anesthesiology (ASA) score of 1 and 2 and a body mass index (BMI) of $<$30 kg/m^2, were included in the study. After enrollment, patients ventilated with PCV mode constituted group "P" and those ventilated with the VCV mode were categorized as group "V" (control group).

Patients who had undergone previous thoracic/abdominal surgery or emergency laparoscopic cholecystectomy, had an ASA score $\geq$3, hematocrit $\leq$30 and BMI $>$30 kg/m^2, or refused to provide consent were excluded. Additionally, those with a history of cardiac, neuromuscular, hepatorenal, endocrine or major pulmonary disease (a decrease in the capacity or flow rates $<$70% in pulmonary function tests), patients converted to open laparotomy for surgical reasons (such as perioperative hemodynamic instability) after starting laparoscopically, patients using respiratory mechanics outside the study protocol, and having a positive Allen's test were excluded from the study.

2.3 Primary-secondary outcomes

The primary outcome of the study was cerebral oxygenation measured with NIRS. As secondary outcomes, we measured peak pressures (P_{peak}), plateau pressures ($P_{plateau}$), peripheric oxygen saturation (SpO_2), pH, partial pressure of oxygen (PO_2), partial pressure of carbon dioxide (PCO_2), and bicarbonate levels in blood gases.

2.4 Preoperative care

All patients underwent standard pre-anesthetic evaluation for the procedure. As premedication, 0.07 mg/kg midazolam was administered intravenously.

2.5 Intraoperative care

After the patient was taken to the operating room, they were monitored using standard methods, such as electrocardiogram, pulse oximetry, non-invasive blood pressure cuff, end tidal carbon dioxide ($EtCO_2$), and thermometer. Allen test was performed on all patients. Since it is an invasive procedure, patients were asked about the time of intra-arterial cannulation. In some patients, arterial pressures were monitored by placing a cannula in the radial artery before induction of anesthesia, while it was done after induction in other patients. Hence, pre-anesthesia blood gas analysis results were not included in the study.

NIRS monitoring was performed using a Masimo (Masimo RDS7A, Masimo Corporation, Irvine, CA, USA) device. NIRS cerebral probes were placed in the right and left frontal regions. General anesthesia was induced with propofol (3 mg/kg), fentanyl (2 mcg/kg) and rocuronium (0.6 mg/kg), and maintained with 0.5–1 minumum alveolar concentration (MAC) sevoflurane in a mixture of 50% oxygen and 50% air. During the operation, an additional 0.1 mg/kg rocuronium was administered intermittently at 30-minute intervals with 0.3 mcg/kg/min remifentanil infusion. During anesthesia, mechanical ventilation was applied with a anesthesia machine (Drager Primus, Drager Medical AG&Co KG, Luberck, Germany).

In all patients, the mechanical ventilation settings were adjusted according to the ideal body weight. In group P, the inspiratory pressure (P_{insp}) was set to obtain a tidal volume (TV) of 8 mL/kg in a PCV mode, whereas, in group V, the TV was set to 8 mL/kg in the volume-controlled mode. In both groups, the initial respiratory frequency was set to 12 breaths/min, the inspiration-expiration time ratio at 1:2, and the positive end-expiratory pressure at 5 cmH_2O. During mechanical ventilation, the $EtCO_2$ was kept between 33 and 35 mmHg; if the $EtCO_2$ was $>$35 mmHg, the respiratory frequency was increased by two units every 5 min in both groups. With this increase, a frequency of 18 breaths/min was accepted as the upper limit. If the $EtCO_2$ did not decrease to $<$35 mmHg at the 5th minute after reaching 18 breaths per minute, the P_{insp} value of group P was increased by 2 cmH_2O every 5 min as needed; in group V, the volume settings were incremented by 1 mL/kg every 5 min as needed. The upper limit was set as 30 cmH_2O for group P and 10 mL/kg for group V. Patients whose $EtCO_2$ level did not fall $<$35 mmHg despite mechanical ventilation settings were excluded from the final analysis. If $EtCO_2$ values remained $<$33 mmHg in both groups, it was first reduced to 10 breaths/minute; if there was no increase and the TV was decreased by 1 mL/kg in group V. However, the TV was not allowed to fall below 6 mL/kg in either group.

Demographic (sex, age, height, weight and ASA score) and intraoperative (anesthesia, operation and insufflation duration) data were recorded in both groups. Measuring times were defined as T0: before anesthesia, T1: after intubation, T2: 5 min after insufflation, T3: just before desufflation; and T4: 5 min after desufflation. NIRS (bilaterally) and SpO_2 values were recorded at all time points. Additionally, peak pressure (P_{peak}), plateau pressure ($P_{plateau}$), and blood gas parameters were recorded in T1, T2, T3 and T4.

2.6 Statistical analysis

All analyses were conducted using SPSS Statistics for Windows (version 15.0; SPSS Inc., Chicago, IL, USA). Categorical variables were described as frequency and percentages and numerical variables as mean $\pm$ standard deviation and range. Numerical variables in two independent groups were compared using the Student's t-test (when normally distributed) and Mann-Whitney U test (non-normally distributed). Different rates in the two groups were compared using the Chi-square test. An alpha level of 5% ($p < 0.05$) was considered to determine statistical significance.

3. Results

A total of 84 patients were enrolled in the study between February and July 2020. After excluding 11 patients before randomization and three patients after randomization, a total of 70 patients were included in the study. The CONSORT flowchart for the study participants is presented in Fig. 1. The two groups were statistically comparable in terms of age, BMI, operative time, anesthesia duration and insufflation duration (Table 1).

The mean NIRS values at T1–T2–T3 on the right side and T2–T3 on the left side were significantly higher in group P than in group V (p = 0.030, p = 0.001, p = 0.001, p = 0.006 and p = 0.002, respectively) (Table 2). In both groups, no significant differences were found in the right and left averages of the T0 and T4 NIRS measurements (Table 2).

SpO_2 levels were significantly lower in group P at T1 (p = 0.006) (Table 3); no other significant difference was noted between the two groups at all time points (Table 3).

For ventilation parameters, P_{peak} and $P_{plateau}$ values at T1, T2 and T4 were significantly lower in group P than in group V (group P: p = 0.003, p = 0.001 and $p < 0.001$; group V: p = 0.011, p = 0.001 and $p < 0.001$, respectively) (Table 4).

4. Discussion

Using a randomized controlled study design, we observed that cerebral oxygenation was better in patients with the PCV mode due to higher NIRS. Also, the P group patients had lower P_{peak} and $P_{plateau}$ values with the PCV mode. Laparoscopic surgery allows superior postoperative quality of life by avoiding abdominal incisions, extensive dissection and related

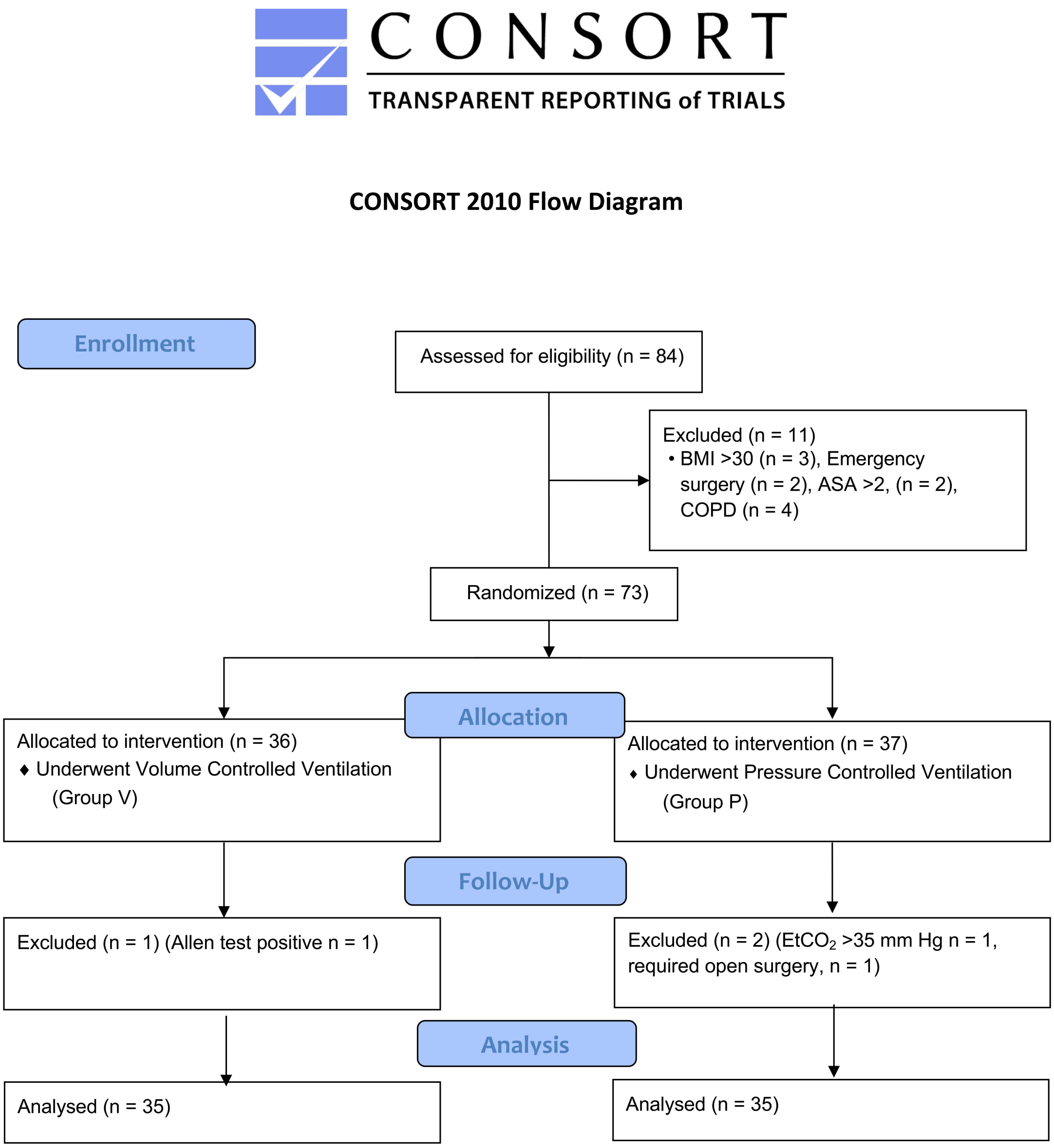

FIGURE 1. CONSORT 2010 flow diagram. BMI: body mass index; ASA: American Society of Anesthesiology; COPD: chronic obstructive pulmonary disease; $EtCO_2$: end tidal carbon dioxide.

TABLE 1. Comparison of demographic characteristics, operative time, and anesthesia duration of the patients that underwent volume-controlled/pressure-controlled ventilation in laparoscopic cholecystectomy.

	Group V	Group P	
	n = 35 (%)	n = 35 (%)	*p*
Gender			
Male	7 (20.0)	11 (31.4)	[b]0.274
Female	28 (80.0)	24 (68.6)	
	Mean ± SD (Min–Max)	Mean ± SD (Min–Max)	*p*
Age	48.8 ± 11.1 (27–65)	48.0 ± 10.1 (23–65)	[a]0.753
BMI	27.1 ± 2.3 (20–30)	26.7 ± 3.0 (20–30)	[c]0.882
Operative time	76.0 ± 16.8 (50–110)	77.3 ± 19.9 (50–130)	[c]0.990
Anesthesia duration	86.0 ± 16.8 (60–120)	87.6 ± 20.2 (60–140)	[c]0.952
İnsufflation duration	41.4 ± 9.4 (30–70)	40.0 ± 11.8 (30–90)	[c]0.297

[a]Student-t Test; [b]Pearson Chi-Square Test; [c]Mann Whitney U Test; BMI: Body Mass Index; SD: Standard Deviation.

TABLE 2. Comparison of NIRS of patients that underwent volume-controlled/pressure-controlled ventilation in laparoscopic cholecystectomy.

	Group V		Group P		
	Mean ± SD	Median (Min–Max)	Mean ± SD	Median (Min–Max)	*p*
NIRS–Right					
T0	65.5 ± 4.8	65 (54–75)	67.7 ± 5.0	68 (57–79)	[a]0.060
T1	67.1 ± 6.5	67 (52–80)	70.5 ± 6.1	71 (58–80)	[a]0.030*
T2	64.8 ± 5.9	65 (54–75)	70.1 ± 6.4	72 (56–81)	[a]0.001*
T3	67.4 ± 5.0	68 (58–77)	71.7 ± 4.9	73 (62–82)	[a]0.001*
T4	68.1 ± 4.5	69 (59–77)	70.1 ± 5.0	70 (62–83)	[a]0.081
NIRS–Left					
T0	65.0 ± 4.6	65 (57–77)	66.5 ± 5.5	66 (55–80)	[a]0.208
T1	66.2 ± 6.7	66 (54–85)	68.7 ± 6.6	68 (55–81)	[a]0.122
T2	64.1 ± 6.5	63 (53–77)	68.4 ± 6.1	69 (53–79)	[a]0.006*
T3	65.9 ± 5.2	67 (55–74)	70.2 ± 6.0	71 (56–81)	[a]0.002*
T4	66.7 ± 4.9	68 (56–77)	68.7 ± 5.6	69 (57–80)	[c]0.137

*[a]Student-t Test; [c]Mann Whitney U Test; NIRS: Near infrared spectroscopy; *$p < 0.05$; SD: Standard Deviation.*

comorbidities [1]. However, the pneumoperitoneum involved in laparoscopic surgery increases intra-abdominal pressure, which indirectly decreases lung volumes, functional residual capacity and pulmonary compliance. This increase in airway resistance may result in atelectasis in the basal parts of the lung, resulting in ventilation-perfusion mismatch [1, 3]. The VCV mode increases P_{peak} and $P_{plateau}$ values, which are directly related to lung damage. Jo *et al.* [10] conducted a randomized controlled trial to compare VCV and PCV on 50 patients who underwent laparoscopic cholecystectomy and reported higher P_{peak} values in patients who underwent VCV after pneumoperitoneum. Likewise, Nethra *et al.* [11] compared VCV and PCV on 60 patients undergoing laparoscopic cholecystectomy and indicated that PCV resulted in lower P_{mean} and P_{peak} values. We observed concurring findings that are in favor of using PCV in laparoscopic cholecystectomy.

It is noteworthy that the P_{peak} and $P_{plateau}$ values in our study were significantly higher in group V, especially after insufflation. The existing literature also suggests that in laparoscopic surgeries, the VCV mode may decrease the safety index by increasing the risk of volutrauma and barotrauma. To stop this increase in P_{peak} and avert lung injury, techniques, such as changing the respiratory rate and TV or switching to the PCV mode, are performed [12]. Although the PCV mode is a good alternative for managing elevated P_{peak} values, its effects on ventilation dynamics and hemodynamic parameters are yet to be determined.

The high P_{peak} values observed with the VCV mode may also result in decreased PO_2 pressure. However, the effects of the VCV and PCV modes on tissue oxygenation are contradictory. Balick-Weber *et al.* [13] examined the respiratory effects of laparoscopic surgery on 21 patients and did not find changes in the PO_2 pressures after insufflation. Hans *et al.* [14] also reported no significant difference between PO_2 pressures in 40 patients with obesity who underwent laparoscopic bypass surgery. However, in two other studies conducted on obese

TABLE 3. Blood gas parameters and SpO_2 of the patients that underwent volume-controlled/pressure-controlled ventilation in laparoscopic cholecystectomy.

	Group V		Group P		
	Mean ± SD	Median (Min–Max)	Mean ± SD	Median (Min–Max)	*p*
pH					
T1	7.45 ± 0.04	7.45 (7.38–7.52)	7.43 ± 0.04	7.43 (7.33–7.49)	^{a}0.118
T2	7.41 ± 0.04	7.41 (7.33–7.49)	7.40 ± 0.04	7.41 (7.30–7.46)	^{a}0.273
T3	7.40 ± 0.04	7.40 (7.33–7.50)	7.41 ± 0.04	7.42 (7.30–7.49)	^{c}0.285
T4	7.39 ± 0.04	7.38 (7.31–7.47)	7.40 ± 0.04	7.41 (7.30–7.49)	^{a}0.161
PaO_2					
T1	157.2 ± 26.6	150 (118–220)	159.7 ± 32.9	160 (90–220)	^{a}0.730
T2	140.3 ± 27.4	138 (95–190)	144.9 ± 30.5	140 (95–200)	^{c}0.510
T3	142.4 ± 34.0	140 (90–263)	151.7 ± 25.3	150 (109–210)	^{a}0.195
T4	163.2 ± 44.2	150 (107–355)	161.0 ± 30.5	150 (115–260)	^{c}0.750
PCO_2					
T1	35.1 ± 2.9	35 (30.0–40)	35.8 ± 2.1	36 (32–41)	^{c}0.280
T2	37.7 ± 2.8	38 (32.0–43)	38.2 ± 1.9	38 (34–41)	^{a}0.503
T3	38.3 ± 2.9	38 (32.6–43)	37.3 ± 2.5	38 (30–43)	^{c}0.166
T4	38.9 ± 4.1	38 (34.0–53)	37.1 ± 2.4	37 (32–42)	^{c}0.116
HCO_3					
T1	24.9 ± 1.8	25.5 (20–27.6)	24.3 ± 1.7	25 (18–26.6)	^{c}0.111
T2	24.3 ± 2.0	25.0 (20–27.5)	23.9 ± 1.6	24 (20–26.8)	^{c}0.124
T3	24.1 ± 1.9	25.0 (20–27.0)	23.6 ± 1.8	24 (20–27.4)	^{c}0.083
T4	24.0 ± 1.6	24.0 (21–26.2)	23.6 ± 1.8	24 (20–26.9)	^{c}0.284
SpO_2					
T0	98.5 ± 1.3	99 (95–100)	98.7 ± 1.3	99 (96–100)	^{c}0.456
T1	99.1 ± 0.9	99 (97–100)	98.4 ± 1.0	98 (96–100)	^{c}0.006*
T2	98.4 ± 2.6	99 (85–100)	98.3 ± 1.5	98 (93–100)	^{c}0.314
T3	98.8 ± 1.1	99 (97–100)	98.7 ± 1.2	99 (96–100)	^{c}0.710
T4	99.2 ± 0.9	99 (97–100)	98.7 ± 1.1	99 (96–100)	^{c}0.113

^{a}*Student-t Test;* ^{c}*Mann Whitney U Test; *$p < 0.05$; SD: Standard Deviation; pH: potential of hydrogen;* PaO_2*: partial oxygen pressure;* PCO_2*: partial carbon dioxide pressure;* HCO_3*: bicarbonate;* SpO_2*: oxygen saturation.*

TABLE 4. Ventilation parameters that underwent volume-controlled/pressure-controlled ventilation in laparoscopic cholecystectomy.

	Group V		Group P		
	Mean ± SD	Median (Min–Max)	Mean ± SD	Median (Min–Max)	p
P_{peak}					
T1	16.9 ± 2.9	17 (13–26)	15.0 ± 2.1	15 (11–19)	^{c}0.003*
T2	23.1 ± 3.8	24 (16–33)	20.3 ± 2.7	21 (15–25)	^{a}0.001*
T3	21.6 ± 3.7	21 (15–31)	20.0 ± 3.2	20 (14–25)	^{a}0.053
T4	18.8 ± 2.7	19 (14–27)	15.3 ± 2.1	16 (11–20)	^{c}<0.001**
$P_{plateau}$					
T1	16.3 ± 2.6	16 (12–24)	14.8 ± 2.0	15 (11–19)	^{a}0.011*
T2	22.5 ± 3.6	23 (16–30)	19.9 ± 2.5	20 (15–25)	^{a}0.001*
T3	20.8 ± 3.7	20 (15–30)	19.5 ± 3.1	20 (14–25)	^{c}0.129
T4	17.8 ± 2.5	18 (14–25)	15.0 ± 2.2	15 (11–20)	^{a} <0.001*

^{a}*Student-t Test;* ^{c}*Mann Whitney U Test; *$p < 0.05$, **$p < 0.01$. SD: Standard Deviation.*

patients, PO_2 pressure was higher in patients ventilated with the PCV mode [15, 16]. In the present study, the PO_2 values were higher with the PCV mode; however, no significant difference was found in blood gas parameters between the groups.

In recent years, tissue oxygenation measurements have been frequently used in perioperative patient management. Different methods, such as bispectral index electroencephalography or auditory evoked potentials, have been used to measure anesthetic depth. The NIRS was used for evaluating the oxygenation change at the tissue level in the prefrontal cortex [5]. Although NIRS has been used in different surgeries, only one study has evaluated cerebral oxygenation with NIRS in laparoscopic surgery [15]. Green *et al.* [7] analyzed 46 patients who underwent major abdominal surgery and detected low tissue oxygenation using NIRS, which could not be detected by conventional monitoring methods. Furthermore, Gipson *et al.* [17] compared NIRS values before and after insufflation in 70 patients who had undergone laparoscopic abdominal surgery and found that NIRS values decreased significantly after insufflation. In the present study, although no significant difference was found between SpO_2 and PaO_2 pressures, the NIRS values of patients with the PCV mode were significantly higher than those with the VCV mode during pneumoperitoneum. This corroborates the presumed oxygenation disorder occurring at the tissue level, although the resulting oxygenation change was not reflected in conventional monitoring parameters and arterial blood gas analysis.

Kurukahvecioglu *et al.* [18] evaluated 60 patients who had undergone laparoscopic abdominal surgery and showed that insufflation pressure caused blood to pool in the lower extremities, which decreased cerebral NIRS values. This decrease is a direct mechanical result of the high abdominal pressure created by insufflation. This mechanical distension is also seen in the thorax with a high P_{peak} created by the VCV mode as demonstrated in the present study. Although we did not measure the cardiac output of our patients, presumably, the high P_{peak} values in group V may have indirectly increased the intrathoracic pressure and decreased the cardiac output, contributing to the low NIRS values in group V.

The study had certain limitations. First, we used P_{peak} and $P_{plateau}$ values instead of transpulmonary pressure to evaluate the safety of controlled mechanical ventilation modes. The transpulmonary pressure is the most objective parameter for evaluating ventilator-induced lung injuries. However, it was not preferred because it is measured by invasive methods. Second, neuromuscular monitoring could not be performed because there was only one ToF (Train of Four) device in our hospital.

5. Conclusions

Intraoperative cerebral oxygenation is higher in patients using the PCV mode as compared to the VCV mode during laparoscopic cholecystectomy. These results indicate that ventilation with the PCV mode provides statistically better tissue oxygenation with lower P_{peak} and $P_{plateau}$ values as compared to using the VCV mode. Although this result is statistically significant, it does not clinically indicate that the VCV mode is riskier for lung barotrauma and volutrauma than the PCV mode. Since insufficient neuromuscular blockade causes high ventilation pressures and indirectly high peritoneal insufflation pressures, neuromuscular monitoring is mandatory to provide deep neuromuscular blockade in laparoscopic surgeries. Therefore, when looking at the results, it should be kept in mind that neuromuscular monitoring was not performed in the study.

AVAILABILITY OF DATA AND MATERIALS

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

AUTHOR CONTRIBUTIONS

EB, MA, ASÇ, TY and LT—study conception and design; data collection; analysis and interpretation of results; draft manuscript preparation; critical revision of the article; other (study supervision, fundings, materials, *etc.*). All authors (EB, MA, ASÇ, TY and LT) reviewed the results and approved the final version of the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This prospective randomized controlled trial was conducted between February and July 2021 after obtaining approval from the Sisli Hamidiye Etfal Research and Training Hospital Ethical Committee (approval no.: 1496). All procedures were performed in accordance with the ethical standards of the Helsinki Declaration (2008); informed consent for participation was obtained from all patients.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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