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The Ventilatory Influence on Cerebral Oxygenation in Patients Undergoing Video Assisted Thoracoscopic Surgery

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Abstract

Background: During One lung ventilation (OLV) in video assisted thoracoscopic surgery (VATS); many physiological factors may increase the risk of hypoxemia such as positioning and intrapulmonary shunt thus compromising cerebral blood flow and oxygenation, resulting in postoperative neurocognitive dysfunctions. The authors hypothesized that increasing ($EtCO_2$) is a convenient and powerful method for the management of cerebral desaturation and postoperative cognitive function.

Methods: Mechanical ventilation was adjusted to maintain an $EtCO_2$ of 32-38 mmHg in group I and an $EtCO_2$ of 39–45 mmHg in group II. Regional cerebral oxygenation was monitored using near-infrared spectroscopy (O3™, Masimo, Irvine, CA) placed on the patient's forehead. The primary outcomes were the change in regional cerebral oxygen saturation from baseline (rSO_2%) of both sides to the end of surgery and the postoperative cognitive function measured by MMSE. Secondary outcomes included intraoperative (mABP) and (HR) changes and postoperative length of stay (LOS) in hospital.

Results: The (%ΔrSO2) from baseline of both sides differs significantly between both groups with (P value < 0.05). No significant difference between the two groups in LOS in hospital.

Conclusion: Adjusting the ventilator parameters to develop $EtCO_2$ of 39-45 mm Hg improved cerebral oxygenation more than $EtCO_2$ of 32-38 mm Hg that play a protective role in the brain causing significant impact on the early postoperative cognitive function in patients with OLV undergoing VATS.

Keywords: VATS; OLV; Cerebral oxygen saturation; Postoperative cognitive dysfunction

Abbreviations: OLV: One lung ventilation; TLV: Two lung ventilation; VATS: Video assisted thoracoscopic surgery; $EtCO_2$: End-tidal carbon dioxide; Et Sevo: End tidal sevoflurane concentration; $rSpO_2$: Regional cerebral oxygen saturation; %ΔrSO_2: Percentage change in regional cerebral oxygen saturation from the base line; IABP: Invasive arterial blood pressure; HR: Heart rate; Mabp: Mean arterial blood; LOS: Length of stay in hospital; NIRS: Near-infrared spectroscopy; FiO_2: Fraction of inspired oxygen; I:E: Inspiratory: expiratory ratio; PSI: Patient State Index; EEG: Electroencephalogram; SpO_2: Peripheral oxygen saturation; ABG: Arterial blood gas; Hb: Haemoglobin concentration; Pmean: Mean airway pressure; PIP: Peak inspiratory pressure; Pplat: Plateau airway pressure; PEEPtot: Total PEEP; DLT: Double-lumen tube; PACU: Post anesthesia care unit; MMSE: Mini-Mental State Exam; POCD: Postoperative cognitive dysfunction; ASA: American Society of Anesthesiologists; BMI: Body mass index; FEV1: Forced expired volume in 1 second; FVC: Forced vital capacity.

Introduction

Cerebral oximetry is a noninvasive device depends on the property of near-infrared light and used to measure changes in concentration of oxyhaemoglobin and deoxyhaemoglobin in the entire tissue bed [1]. The risk of intraoperative cerebral ischemia due to an imbalance between oxygen supply and demand can be immediately detected with this technology [2].

Most thoracic surgeries require one lung ventilation (OLV). However, OLV is associated with important physiological disturbances such as hypoxic pulmonary vasoconstriction (HPV) in the non-ventilated lung, pulmonary arteriovenous shunt of the deoxygenated blood, decrease in oxygen partial pressure [3], changes in alveolar–arterial oxygen tension, activation of inflammatory processes, or changes in cardiac output and pulmonary/systemic pressures. Moreover, prolonged OLV is associated with severe oxidative stress [3]. Postoperative neurocognitive dysfunction may be correlated with cerebral oxygen desaturation so intraoperative monitoring and proper controlling of these episodes is necessary [4].

CO_2 is a major contributing factor affecting cerebral vascular tone. There is strong evidence that hypopnea causes cerebral vasoconstriction, a decrease in CBF and an increased risk of cerebral ischemia, while hypercapnea causes cerebral vasodilation and an increase in CBF [4]. Cerebral perfusion and oxygen transport widely affect cerebral oxygenation , increasing systemic arterial pressure with vasopressors, increasing end-tidal carbon dioxide ($EtCO_2$) with ventilatory adjustment and increasing fraction of inspired oxygen (FiO2) used for prevention and treatment of intraoperative cerebral desaturation [5-7]. Brain tissue is highly affected by hypoxia, and cerebral oxygen saturation is an important predictor of short- and long-term clinical outcomes. Cerebral hypoxia could be linked to neurological problems [8], stroke [9], organ dysfunctions [10,11], and increased LOS [12]. The aim of this study was to evaluate the effect of two different ventilatory strategies that affect the ($EtCO_2$) on ($rSpO_2$) from baseline of both sides measured by (O3™, Masimo, Irvine, CA) and the effect of postoperative cognitive function in patients undergoing VATS.

Patients and Methods

This study was conducted between September 2021 and September 2022 at The King Fahd General Hospital Jeddah after ethics committee approval and has clinical trial registry ID: NCT05033353. An informed consent was signed from all patients before surgery. Data was collected from 72 patients 18-65 years old ASA I and II and with body mass index (BMI) 21-29 kg/m^2 who were admitted for elective VATS requiring OLV for not more than 1-1.5h including intrathoracic cavity, diagnosis or biopsy of any intrathoracic structure, diagnosis and drainage of pleural effusions, lungs wedge resection, segmentectomy, lobectomy, closure of persistent/recurrent pneumothorax, identification of broncho-pleural fistula, pleurolysis of adhesions, decortication, thymectomy, pericardectomy, thoracic sympathectomy, assess injury and evacuation of clot.

All patients were operated on by the same surgical team. Patients with severe bronchial asthma, chronic obstructive pulmonary disease, severe renal insufficiency, severe liver dysfunction, cerebrovascular disease, coagulopathy, uncontrolled diabetes mellitus, uncontrolled hypertension or cardiovascular disease, or patients with surgical bleeding > 500 ml were excluded. Patients were assessed on the day of surgery by a single trained interviewer, blinded to randomization and proficient and trained in MMSE score, in the preoperative area prior to administration of premedication to establish a baseline. Assessment was repeated twice 3 and 24 hours after surgery respectiely. The Mini-Mental State Exam (MMSE) is a simple and reliable test for evaluation of neurocognitive functions, incuding orientation, registration, attention, calculation, recall, and language [13]. The MMSE scale ranges from 0 to 30, higher scores indicate better cognitive function, and MMSE score ≤ 23 is considered abnormal. A decrease in MMSE score 2 points from baseline was defined as POCD [14].

A 16 or 18-gauge peripheral venous cannula and a 20-gauge radial artery were inserted to all patients preoperatively. Randomization was done by sealed envelope method and the patients were divided into two groups: group I (targeted $EtCO_2$ 32-38 mmHg) and group II (targeted $EtCO_2$ 39-45 mmHg). Each patient envelops had been opened just before starting OLV.

In the operating room, Patients were monitored by 5 lead electrocardiogram, invasive arterial blood pressure (IABP) through the arterial catheter and (Masimo®, Irvine, CA) which provides non-invasive continuous technologies for monitoring and measuring many physiological variables such as arterial oxygen saturation (SpO_2), heart rate (HR) and hemoglobin concentration (Hb%) from the (RD Rainbow® SET Pulse Co-Oximeter), end tidal CO2 by capnometer (Nomoline sampling line Masimo ®, CA), noninvasive blood pressure, body temperature, (O3 ®, Masimo, Irvine, CA) attached to the patient to provide continuous monitoring of regional cerebral oxygen saturation (rSO_2) of the two hemispheres by a near-infrared spectroscopy sensors connected to regional oximetry system. The sensors were placed bilaterally on patient's forehead after the skin of the forehead had been wiped with an alcohol swab and allowed to dry as recommended by the manufacturer (photos 1 and 2), and (SedLine ®, Masimo, CA) brain function monitoring by Patient State Index (PSI) which is a processed EEG parameter affected by the anesthetic agents (photo 3).

After preoxygenation for 2 minutes, anesthesia was induced in all patients with propofol 1.5-2 mg /kg, fentanyl 3-5 micg/ kg, and rocuronium 0.6-0.8 mg/ kg. A left-sided double-lumen tube (DLT) (39F for males and 37F for females) (Broncho-Cath; Mallinckrodt Medical Ltd, Athlone, Ireland) was used for endotracheal intubation and checked by fibreoptic bronchoscope (Olympus company, Tokyo, Japan) and auscultation. The patient was then positioned in left or right lateral decubitus position according to the surgical side and the DLT was rechecked again. Maintenance anesthesia was provided by Sevoflurane to keep a patient state index (Psi) measured by (SedLine, Masimo®, CA) level between 25-50. Additional doses of fentanyl to a total of 7-15 micg/kg and rocuronium boluses were given to control the depth of anesthesia and to maintain stable neuromuscular block.

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Photo 1: A patient in supine position.

Photo 2: A patient in lateral position.
Photo (1 and 2): (O3 ®, Masimo, Irvine, CA) and (SedLine ®, Masimo, CA) electrodes were attached to the patient forehead.

Photo 3: An intraoperative screenshot of Masimo®.

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Initially, all patients were applied with two-lung ventilation using a constant-flow, volume-controlled ventilation mode with a tidal volume 8 mL/kg of the actual body weight, an inspiratory to expiratory (I:E) ratio of 1:2, a respiratory rate of 12 breaths/min, oxygen flow rate of 1.5 L/min, and FiO_2 (fraction of inspiratory oxygen) of 1.0 without PEEP. OLV was initiated with skin incision, and the tube lumen of the dependent non ventilated lung was opened to room air. During OLV, tidal volume was reduced to 7 mL/kg, respiratory rate of 12-15 breaths/min, PEEP of 5 cm H_2O, FiO_2 of 1.0, oxygen flow rate of 1.5 L/min, I:E 1:2. Then patients were assigned a ventilation strategy designed to achieve an $EtCO_2$ of 32-38mm Hg or of 39-45mmHg in group I or II respectively throughout the intraoperative period by (MAQUET FLOW i anesthesia delivery system). This could be achieved by changing the respiratory rate and inspiratory: expiratory (I:E) ratio. rSO_2 values obtained and after achieving and maintaining the target $EtCO_2$ for 3 minutes baseline $\%\Delta rSO_2$ was considerd and recorded every 10 minutes till the end of surgery. The data were available to the anesthetist. Peak inspiratory pressure (PIP) was monitored using a side stream spirometry device (MAQUET FLOW-i). If PIP >30 cm H_2O, the volume-controlled ventilation mode was changed to a pressure-controlled mode to achieve a targeted tidal volume. Intraoperative fluid replacement by Lactated Ringer's solution or Hydroxyethyl starch solution was infused at rate of 8-10 ml/kg/h. $rSPO_2$, PSi, SpO_2, mean BP, and HR were recorded before anesthesia, 5 minutes after intubation, 5 minutes after putting the patient in lateral position, after initiating OLV, after achieving and maintaining this target $EtCO_2$ for 3 minutes, and every 10 min till the end of surgery . Hypotension (defined as more than 20% drop in mean ABP from baseline values obtained on admission to the operating room) was treated with ephedrine in 4 mg increments. We used ephedrine rather than phenylephrine as a previous study showed that cerebral oxygen saturation decreases after phenylephrine but remains unaffected after ephedrine in anaesthetized patients [13].

ABG analysis by (ABL 800, Radiometer, Copenhagen, Denmark. PaO_2, $PaCO_2$, pH, serum lactate, HCO_3 concentration, haemoglobin concentration (Hb) ,and sodium and potassium ion concentrations. ABG was performed before anesthesia, after induction of anesthesia when the patient was in supine position, after positioning in the lateral decubitus position during two lung ventilation (TLV), 15 minutes after one lung ventilation (OLV) and every 15 minutes till the end of surgery. All the patients were in lateral position with head down 10º during surgery. If SpO_2 decreased below 92% and lasted 30 seconds during OLV, surgery was temporarily interrupted and two-lung ventilation was resumed. At the end of surgery patient turned supine and neuromuscular block was antagonized with sugamadex 2mg/kg. At the time of closure of thoracic cavity, two-lung ventilation was started and both lungs were re-expanded by hand bagging in all patients. Aldrete scores were recorded by post anesthesia care unit (PACU) nurses blinded to group assignment on arrival to the PACU and then every 15 min thereafter until discharge from PACU. Patients were followed up for any complications of lung during their hospital stays.

Statistics

Sample size of 35 patients for each group was calculated for 90% power, $\alpha = 0.05$, $\beta = 0.1$, and anticipated effect size = 0.40 using sample size software (G*Power version 3.00.10, Germany). All statistical analyses were performed using SPSS [15] for windows. Continuous variables were tested for normal distribution by the Kolmogorov-Smirnov test. Parametric data were comparedusing analysis of variance (ANOVA). Between-group comparisons at different time intervals were assessed by using paired t-test. All categorical data were compared by using x2 test. A sample size of 35 patients in each group was needed to detect an intergroup difference of at least 20% (= 0.01, two-sided, power = 95%) with two sample t-test. Data were collected by a blinded observer and presented as mean SD or N (%). A p-value of < 0.05 was considered as statistically significant. And a p-value of < 0.05 was considered as statistically highly significant.

Results

72 patients were enrolled in this study. Flow diagram for the study is presented in (Figure 1). Two patients were excluded; a patient with surgical bleeding more than 500 ml in the first group and a patient with the duration of OLV exceeded 1.5 hour in the second group. Statistical analysis was therefore conducted on 70 patients: 35 in each group. The two groups were comparable in terms of preoperative patient characteristics: including age, sex, BMI, baseline hemoglobin values, ASA group, preoperative arterial blood gases and preoperative spirometric tests (Table 1). There were no significant differences observed between the two groups as regards to operative side, total anesthetic and surgical times, duration of OLV, blood loss, total intraoperative fluid, fentanyl or rocuronium. While the mean of Aldrete scores were significantly higher in the second group on patients' arrival at the PACU and after 15 minutes after patients' arrival at the PACU, then the scores became comparable between the two groups 30 minutes after patients' arrival at the PACU till discharge from it. In both groups the patients had a baseline MMSE value of 27- 30 points, with mean value and SD (28.8, 1.023) and (28.85, 1.033067) in group I and II respectively and no significant difference between the two groups p value = 0.817, 3 hours after surgery the MMSE value decreased with high significant difference p value < 0.001 with mean value and SD (25.11, 1.1) and (26, 1.03) in group I and II respectively. On repeating the test 24 hours after surgery, the MMSE value increased with no significant difference between the two groups p value = 0.503 with mean value and SD (28.69, 1.18) and (28.89, 1. 3) in group I and II respectively (Table 2).

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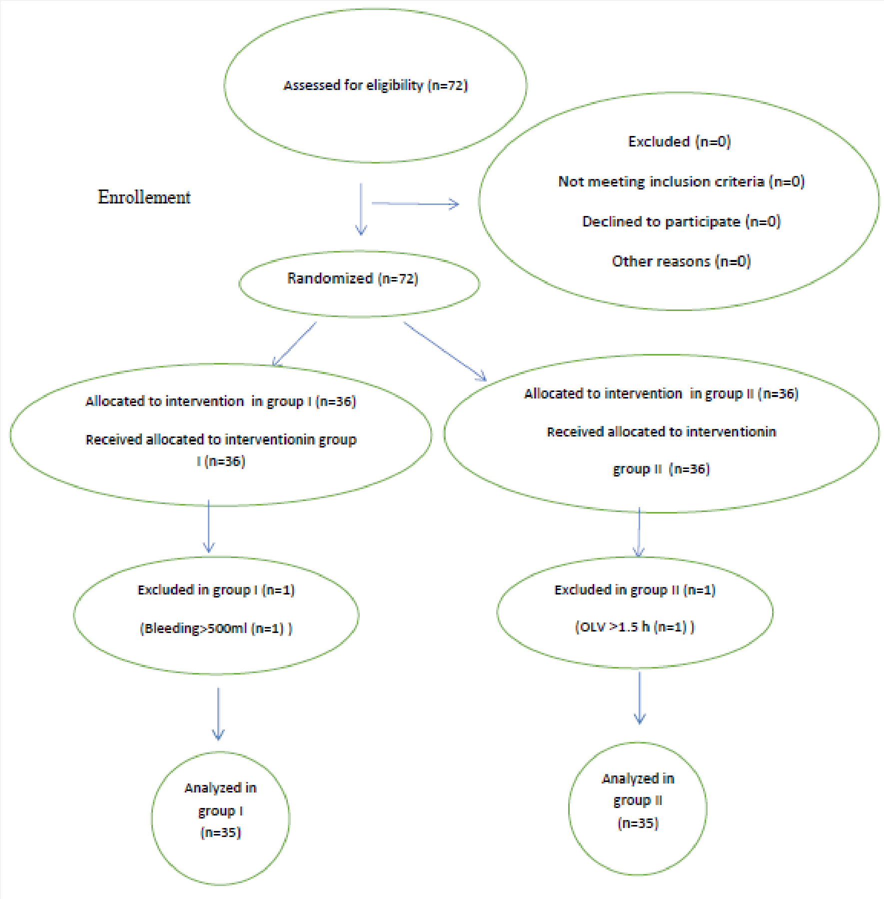

Figure 1: Flow chart of participants.

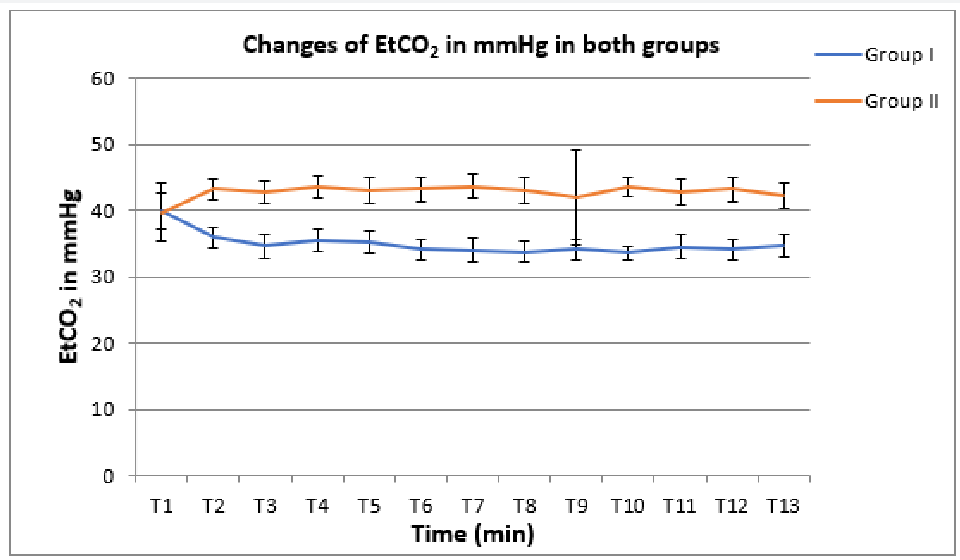

Figure 2: $EtCO_2$ in mmHg in both groups.
The data are presented as mean (SD).
At T1 P value = 0.871 while at T2-13 P value < 0.001.

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Table 1: Patients characteristics.

	Group I	Group II	P value
Demographic Data			
Age (years)	40.54 ± 12.48	41.34 ± 13.07	0.794
Sex (M/F)	27-Aug	25-Oct	
BMI (kg/m-2)	25.43 ± 1.94	25.08 ± 4.35	0.67
ASA I/II (n)	Sep-26	Jul-28	
Hb (g/dl)	12.67 ± 0.91	12.97 ± 0.86	0.162
Preoperative Arterial Blood Gases			
PH	7.39 ± 0.04	7.4 ± 0.05	0.385
PaO_2	67.3 ± 7.1	67.1 ± 7.3	0.647
$PaCO_2$	39.7 ± 3.5	40.2 ± 3.9	0.611
HCO_3	22.8 ± 2.48	23 ± 2.74	0.75
Preoperative Spirometric Tests			
FEV1 (% of predicted value)	78.42 ± 4.16	78.17 ± 5	0.817
FVC (% of predicted value)	81 ± 4.45	80.2 ± 5.5	0.553
FEV1/FVC (%)	80.74 ± 5.39	80 ± 60.27	0.597

Values are number or mean ± S.D.
* P value < 0.05 statistically significant.

Table 2: Perioperative data.

	Group I	Group II	P-value
Operative side(Rt/LT)	15/20	Dec-23	
Duration of anesthesia (min)	142.23 ±10.48	141.31 ±10.18	0.712
Duration of surgery (min)	99.51 ± 10.46	101.46 ± 11.42	0.46
Duration of OLV (min)	65.69 ± 4.58	66.91 ± 4.62	0.267
Blood loss (ml)	245.71 ± 82.53	244.29 ± 81.14	0.942
IV fluid (ml)	1005.71± 59.13	997.14 ± 61.77	0.555
IV fentanyl (microgram)	360 ± 41.66	370 ± 42.36	0.322
IV rocuronium (mg)	72 ± 4.57	71.57 ± 4.82	0.7
Aldrete Scores (PACU)			
At arrival	6.71 ± 0.95	6.82 ± 1.2	0.013*
After 15 min	8.3 ± 0.9	8.8 ± 0.93	0.03*
After 30 min	9.14 ± 0.77	9.31 ± 0.63	0.313
After 45 min	9.57 ± 0.65	9.51 ± 0.61	0.707
After 60 min	9.71 ± 0.57	9.62 ± 0.54	0.524
On discharge	9.85 ± 0.42	9.74 ± 0.5	0.311
MMSE			
Baseline MMSE	28.8 ± 1.02	28.86 ± 1.03	0.338
MMSE 3 h postop.	25.11 ± 1.11	26 ± 1.03	0.0009 **
MMSE 24 h postop.	28. 69 ± 1.18	28.89 ± 1.3	0.5

.Values are means ± SD. Number (percentage). (*) denotes P value < 0.05 and (**) denotes P value < 0.001.

ABG and ventilatory changes of the cases were summarized in (Table 3) which shows highly significant differences of the pH in group I compared to group II 15 minutes after OLV, 60 minutes after OLV and 15 minutes after TLV (P value < 0.001), $PaCO_2$ showed highly significant differences 15 minutes after OLV and 60 minutes after OLV, HCO_3 concentration was significantly

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higher 15 minutes after TLV (P value < 0.001) this is attributed to the $PaCO_2$ and $EtCO_2$ changes induced by the anesthetist and maintained within the $EtCO_2$ goals established in the protocol throughout the intraoperative period. Significant difference of the HCO_3 concentration and the serum lactate appeared only 15 minutes after TLV (P = 0.013), 60 minutes after OLV (P = 0.022) respectively. Hemoglobin concentration and serum sodium PIP and Pplat didn't differ between the two groups overall the surgery, while serum potassium showed highly significant difference 60 minutes after OLV (P = 0.0017). Changes in $EtCO_2$ is accompanied by direct relation with right and left rSPO2% overtime which is shown in (Figures 2, 3 and 4). HR did not change significantly from baseline measures within either group, and there were no statistically significant differences between the groups at any time (Figure 5), while some differences were recorded between the two groups at T2-T5 as regards to the mean arterial blood pressure as shown in (Figure 6).

Table 3: ABG and the ventilatory summery of the cases.

	T1		T2		T3		T4	
	Group I	Group II	Group I	Group II	Group I	Group II	Group I	Group II
pH	7.39 ± 0.48	7.4 ± 0.05	7.41 ± 0.05	7.3 ± 0.036	7.41 ± 0.05	7.3 ± 0.037	7.39 ± 0.042	7.31± 0.04
	P = 0.386		P < 0.001 **		P < 0.001 **		P < 0.001 **	
$PaCO_2$	41.8 ± 3	40.9 ± 4.1	37.17 ± 2.2	47.85 ± 2.2	36.8 ± 2.3	48.9 ± 1.9	36.7 ± 1.3	36.4 ±1.6
	P =0.32		P < 0.001 **		P < 0.001 **		P = 0.509	
HCO_3 concentration	22.9 ± 2.5	23.1 ± 2.7	22 ± 2.7	.21.5 ± 2.9	20.7 ± 2.7	20 ± 3.2	21.3 ± 2.7	19.6 ± 2.9
	P = 0.75		P = 0.446		P = 0.296		P = 0.013 *	
Serum lactate	1.3 ± 0.3	1.33 ± 0.33	1.7 ± 0.53	1.6 ± 0.44	1.9 ± 0.57	2.26 ± 0.55	1.9 ± 0.5	2.07 ± 0.88
	P = 0.731		P = 0.406		P = 0.022 *		P = 0.275	
Hb%	12.67 ± 0.91	12.88 ± 0.87	12.61 ± 0.92	12.88 ± 0.87	12.46 ± 0.93	12.62 ± 0.92	12.42 ± 0.95	12.59 ± 0.88
	P = 0.163		P = 0.223		P = 0.479		P = 0.46	
Na ion concentrations	137.6 ± 2.4	137.5 ± 2.7	137.9 ± 2.4	138.3 ± 2.6	138.1 ± 2.4	138.6 ± 2.6	136.9 ± 2.8	137.4 ± 2.7
	P = 0.889		P = 0.449		P = 0.418		P = 0.462	
K ion concentrations	3.8 ± 0.43	3.9 ± 0.43	4 ± 0.45	3.8 ± 0.37	4.1 ± 0.45	3.8 ± 0.44	4.1 ± 0.4	3.82 ± 0.4
	P = 0.229		P = 0.066		P = 0.0017 *		P = 0.0035 *	
PIP	19.66 ± 2.95	18.71 ± 2.64	23.37 ± 3.78	22.4 ± 3.56	20.74 ± 3.28	19.91 ± 3.18	18.2 ± 4.69	18.06 ± 3.32
	P = 0.164		P = 0.275		P = 0.286		P = 0.884	
Pplat	14.86 ± 1.96	14.69 ± 2.08	17 ± 2.11	17.4 ± 2.09	18.57 ± 2.06	19.46 ± 2.15	15 ± 1.8	15.43 ± 1.82
	P = 0.724		P = 0.429		P = 0.828		P = 0.325	

Values are presented in mean ± standard deviation. (*) denotes P value < 0.05 and (**) denotes P value < 0.001.

In **Table (3):** T1: Baseline T2: 15 min. after OLV. T3: 60 min. after OLV. T4: 15 min. after TLV.

Discussion

This is a prospective, single-blinded, randomized controlled trial. The authors believed that NIRS-based cerebral oximetry is a non-invasive and practical method of real time continuous monitoring rSO_2, can be added to the routine monitoring variables, that is in agreement with other researches [16-18].

Changing intraoperative ventilatory parameters in order to raise $EtCO_2$ values is a relatively simple method that potentially increasing CBF and rSpO2 values [17]. To the authors knowledge this is the first study evaluating the effects of two different $EtCO_2$32–38mm Hg and 39-45mmHg in group I and group II respectively on rSO_2 values measured noninvasively by near infrared cerebral oximetry (Masimo®, Irvine, CA) in patients undergoing VATS.

Although few previous studies used (Masimo®, Irvine, CA) [16,20] , we preferred using it as it can display several clinical measurements on the same time such as HR, BP, temperature, SpO_2, $EtCO_2$, Psi and rSO_2, moreover Redford et al investigated the accuracy of the Masimo O3 regional oximetry, measurement error was reported to be approximately 4% when compared with reference blood samples taken from the radial artery and internal jugular venous bulb [16]. Patients underwent VATS with expected OLV not more than 120 min done by the same surgeon were selected in this study to enable a fair comparison of data across the two groups.

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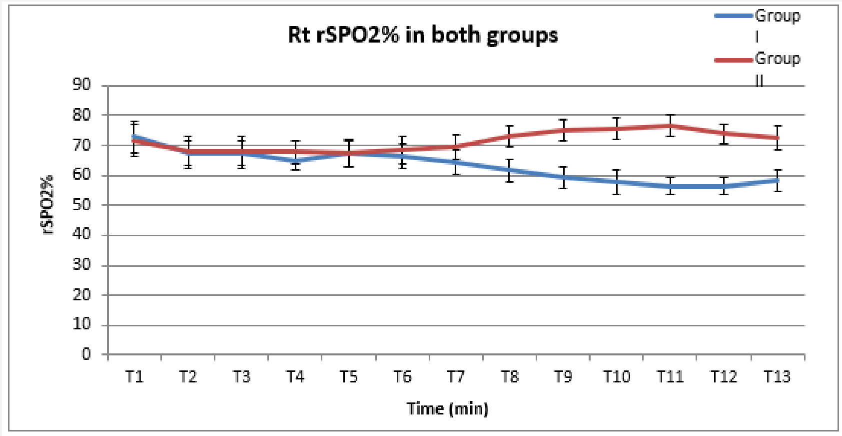

Figure 3: Rt rSPO$_2$% in both groups. The data are presented as mean (SD).
The data are presented as mean (SD).
P values: At T1 = 0.406, T2= 0.835, T3 = 0.816, T4 = 0.0012 and T4-13 < 0.001.

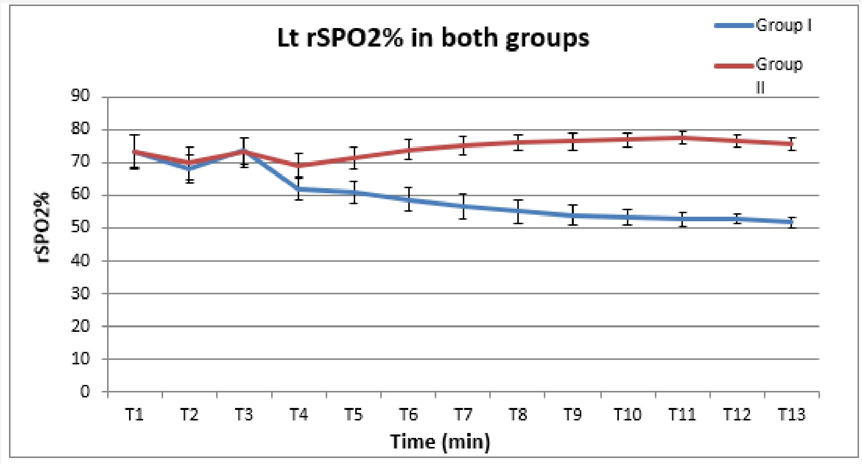

Figure 4: Lt rSPO$_2$% in both groups.
The data are presented as mean (SD).
P values: At T1 = 0.794, T2 = 0.09 and T3-13 < 0.001.

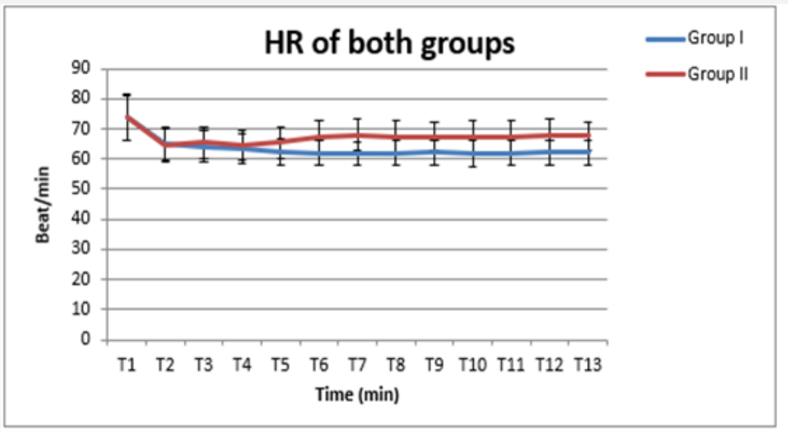

Figure 5: HR in both groups.
The data are presented as mean (SD).
P values: At T1 = 0.899, T2 = 0.634, T3 = 0.358, T4 = 0.262, T5 = 0.008 and T6-T13 < 0.001.

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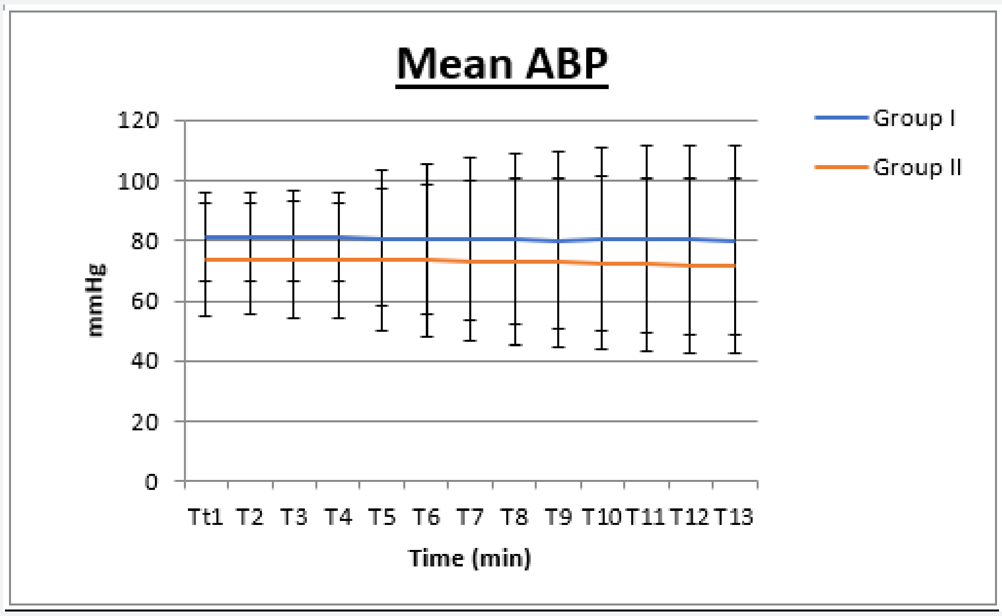

Figure 6: Mean ABP in both groups.
The data are presented as mean (SD).
P values: At T1 = 0.032, T2 < 0.001, T3 = 0.008, T4 < 0.001, T5= 0.004, T6 = 0.212, T7= 0.4, T8 = 0.281, T9 = 0.313, T10 = 0.383, T11 = 0.297, T12 =0.326 and T13 = 0.5.

Results showed increase in both left and right rSO_2 from the baseline values with the passage of time. This is consistent with a previous prospective, controlled study on unshunted patients undergoing carotid endarterectomy under general anesthesia which showed that changing the $EtCO_2$ from 40 -45 to 30-35 mm Hg leads to a 5-6% decrease in regional cerebral oxygen saturation [21]. Also in healthy elective surgical patients, ventilatory adjustment to change the $EtCO_2$ from 45 mm Hg to $EtCO_2$ of 25 mm Hg resulted in a 4.3% drop in cerebral oxygen saturation [22]. In a prospective double cross-over physiological study done on postcardiac arrest patients Eastwood et al compared rSO2 values at the end of alternating hypercapnic and normocapnic periods, they found that mild hypercapnia resulted in higher rSO2 [23]. Murphy et al. concluded that cerebral oxygenation was higher during beach chair shoulder surgery in patients ventilated to attain an $EtCO_2$ of 40-42 mm Hg compared with those with $EtCO_2$ of 30-32 mm Hg [5]. Wong C et al. has one of the few randomized controlled trials investigated rSO2 change over time in patients undergoing major surgery, they found that a stable increase in rSO2 from the baseline in the targeted mild hypercapnic group and a stable decrease in rSO_2 from the baseline in the targeted normocapnic group [24]. Deschamps A et al. had a multicenter prospective randomized study found that use of a physiologic algorithmic approach to adjust the intraoperative rSO_2 during high-risk patients undergoing cardiac surgery decreases the incidence of cerebral desaturation in the ICU [25].

Elevated $PaCO_2$ and $EtCO_2$ strongly affects cerebral blood flow (CBF) but further investigations should be done to clearly explain the relationship between hypercapnia and higher rSO_2 [26]. Although rSO_2 is affected by many factors such as cardiac output, haemoglobin concentration and cerebral autoregulation [5,27] but there is a direct relationship between $PaCO_2$ and CBF within a normal physiological range of $PaCO_2$ [28]. These findings may explain our results which showed that higher intraoperative rSO_2 was associated with a lower incidence of delirium in the first 24 hours postoperatively; as the other variables in the current study affecting rSO_2 such as MAP, PaO_2 , Hb concentration and intraoperative position, were similar between the two groups.

On the other hand, LOS remained similar between the groups. Some studies showed similar cognitive outcomes between groups with or without NIRS-based rSO2 optimization [26,30] Casati et al also reported shorter LOS with and improved cognitive function in elderly patients after major abdominal surgery [30], Schoen et al used regional cerebral oxygen saturations which were measured preoperatively as an indicator of delirium after the on-pump cardiac surgery patients in a prospective observational trial and found that patients who developed delirium had a greater intraoperative drop in rSO2 which is consistent with our results [31]. Previous research has recorded that decreases in $SctO_2$ were associated with adverse events, such as fainting [32], symptoms of cerebral insufficiency in patients undergoing carotid endarterectomy [33], postoperative cognitive dysfunction following hip and cardiac surgery [34], and longer PACU and hospital stay after abdominal surgery [35]. The current research results showed that adjusting the intraoperative ventilatory parameters to achieve $EtCO_2$ (39-45) can be delivered reliably during VATS with OLV, and its

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effects on rSO_2 can be monitored with NIRS. Its delivery is reliably associated with increased levels of intraoperative rSO_2.

Limitation

Due to the nature of the intervention this study has a limitation that the attending anesthetist was not blinded as the measurements were taken directly from the (Masimo®, Irvine, CA) machine. Also, wide range of the patients' age makes it difficult to assess the differences of the changes of the postoperative cognitive function.

Conclusion

Patients received OLV during VATS with higher intraoperative $EtCO_2$ values 39-45 mmHg had better intraoperative cerebral oxygen saturation and early postoperative cognitive function than those with lower intraoperative $EtCO_2$ values 32-38mm Hg.

Conflict of interest

Nil

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Recommendation

The authors recommend future study on special age group to assess the effect on the postoperative cognitive function.

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