SHORT THESIS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY (PHD)

Assesment of pathophysiological characteristics of different ventilatory strategies in thoracic anesthesia

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The Examination takes place at the Library of the Department of Anesthesiology and Intensive Care, Medical and Health Science Center, University of Debrecen,
9th, December, 2013

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INTRODUCTION

Although the risk of intraoperative hypoxia appears to be less than in previous decades, it still remains a dangerous potential complication during OLV. The appropriate tidal volume (TV) during one-lung ventilation (OLV) is still a matter of debate. Based on the work of Katz who compared 7 and 14 mL/kg-1 TV, textbooks and papers recommend using high TV to avoid intraoperative hypoxia and atelectasis. Numerous authors have reported that high TV during OLV might increase the incidence of acute lung injury, due to the large peak inspiratory pressures, end-inspiratory volumes, and shearing forces due to cyclic opening-closing of the alveoli. Low TV during OLV has both advantages (lower risk of postoperative acute lung injury and respiratory distress syndrome, and lower concentrations of circulating inflammatory factors) and disadvantages (worse intraoperative atelectasis, more intrapulmonary shunt, hypoxia, and hypercapnia). There is nonetheless little evidence that the use of low TV during OLV will fail to provide adequate arterial oxygenation or worsen intra-pulmonary shunt. The lower limit for TV is unclear because the extent to which TV influences oxygenation and shunt fraction during OLV remains unknown. Application of external positive end-expiratory pressure can decrease the incidence of atelectasis due to prevention of lung collapse, and minimizes alveolar injury by preventing cyclic openingclosing during OLV. However, the optimal level of PEEP remains unknown. Previous studies reported that the use of high TV with PEEP or the use of low TV without PEEP worsens the oxygenation and is injurious for the lung. It is widely accepted the use of low TV should be accompanied by PEEP whereas high TV can be used safely without PEEP; we thus considered 5 mL/kg TV with 5 cmH_2O PEEP and 10 mL/ kg TV without applied PEEP to be an appropriate comparison.

Physiologically, an approximately 5 to 10 mmHg diff erence exists between end-tidal carbon dioxide (EtCO2) and arterial carbon dioxide (PaCO2) measured during double-lung ventilation (DLV) that may increase during one-lung ventilation (OLV) especially if low tidal volume is applied. There is no evidence that during OLV the EtCO2 or PaCO2 should be kept in the normal range.

In terms of oxygenation as a main outcome measure, one of the most sensitive organs to hypoxemia is the brain, because it makes up approximately 20% of the oxygen demand of the whole body and the oxygen reserve of the brain is sufficient only for 15 seconds during critical decreases of oxygen supply. Two recent reports from the same working group have suggested that administration of lung protective strategy for OLV results in desaturation of the brain parenchyma. The authors of these studies have concluded that further studies are needed to clarify whether this observed desaturation results in long-lasting cognitive consequences. It is known both from animal experiments and from human observations that cerebral blood flow, its metabolic regulation and autoregulation, as well as cerebral blood volume, are largely determined by the alterations of $PaCO_2$ rather than by the partial pressure of oxygen in arterial blood (PaO_2).

As a result, hyper- or hypocapnia during OLV may also have a great impact on the oxygenation of the brain tissue.

The majority of thoracic surgical procedures may require one-lung ventilation (OLV). To achieve this, for the sake of both fast insertion and the proper insertion of the tube, the double-lumen endotracheal tube (DLT) is the first choice. However, there are certain cases when intubation with DLT is not possible, or when the alternate use of a single-lumen tube (SLT) and a DLT during surgery is necessary. In those cases, bronchial blockers (BB) serve as ideal devices. Different BBs are commercially available, among which the EZ-blocker_ (AnaesthIQ, Rotterdam, The Netherlands) is a newly developed device. In the present study we report on our clinical experience with the introduction and intraoperative use of this BB. We also intended to assess how the individual anatomy of the main bronchi influences proper blocking with this type of blocking devices.

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1. OBJECTIVES

1. The purpose of the first study was to compare the effects of low (5 ml/kg) and high (10 ml/kg) TV, without analyzing the independent effect of PEEP, on arterial oxygenation, shunt fraction and ventilatory mechanics during OLV, in patients with open chest, in the lateral position and during surgical manipulation.

2. Aim of our second study was to analyze the effect of end-tidal CO_2-driven or arterial CO_2 driven one-lung ventilation in arterial oxygen tension.

3. In the third study we intended to investigate the influence of the ventilatory strategy with a low (5 ml/kg) TV + 5 cmH_2O along with maintanance of arterial normocapnia during OLV on cerebral blood flow and cerebral oxygen saturation. The most important clinical question related to the study was whether administration of low tidal volume along with maintenance of normocapnia results in cerebral oxygen desaturation and a decrease in cerebral blood flow during one-lung ventilation.

4. In the fourth study we intended to assess how the individual anatomy of the main bronchi influences proper blocking with this type of blocking devices.

2. PATIENTS AND METHODS

3.1 Effects of different tidal volumes for one-lung ventilation on arterial oxygenation

Study population

After approval from the local Ethics Committee (DEOEC RKEB/IKEB 2976-2009; this study was registered at http://www.clinicaltrials.gov, identifier: NCT01513018), written informed consent was obtained from 100 ASA IIII patients scheduled for lung resection surgery.

Preoperatively lung-function tests with wholebody plethysmography, arterial blood gas analysis while breathing room air, ECG, preoperative echocardiography, computerized tomographic lung scan, and bronchoscopy were done. Exclusion criteria were severe cardiovascular disease and severe alteration of the preoperative pulmonary function, with FEV1 <70% and FEV1/FVC ≥70% of the predicted value.

Anesthesia

Patients were premedicated with 5 mg midazolam and 0.5 mg atropine intramuscularly 30 minutes before arrival to the operating room. An epidural catheter was inserted at the midthoracic

level (T5-8); after a successful test dose, an infusion of 0.125% bupivacaine was started at a rate of 0.1 mg/kg/hour and subsequently maintained throughout surgery.

Anaesthesia was induced with a combination of 2 mg/kg propofol, 2 µg/kg fentanyl. Intubation was facilitated by administration of 0.2

mg/kg cis-atracurium. Anaesthesia was maintained with sevoflurane in 100% oxygen. The concentration of sevoflurane was titrated to a target Bispectral Index (BIS) between 40 and 60 (Covidien, Dublin, Ireland) and it was ranged between 0.8-1.2 Vol%. Neuromuscular block was monitored with acceleromyography (TOF Watch Sx, NV Organon, Oss, the Netherlands). The patients' tracheas were intubated with double-lumen endotracheal tubes (DLT) (Broncho-Cath, Mallinckrodt Medical Ltd, Athlone, Ireland). The correct position of the DLT was confirmed by fiber-optic bronchoscopy in both supine and lateral positions. Standard monitoring included five-leads ECG, continuous arterial pressure monitoring *via* a catheter inserted into the radial artery, central venous catheter, NIBP, core temperature at the tympanic membrane, and pulse oximetry. Normothermia was maintained with forced-air (Bair Hugger 750, 3M, Eden Prairie, MN, USA). During two-lung ventilation (TLV) a volume-controlled square-wave flow pattern ventilation with 10 mL/kg TV with a respiratory rate of 10 was used and I:E ratio was kept at 1:2 (Draeger Primus, Draeger Lübeck, Germany). For adjusting the TV the actual body weight was used. After induction of general anaesthesia and intubation, both lungs were ventilated as described above, in supine position for 10 minutes. Thereafter, arterial blood was again sampled for gas analysis and hemodynamic and ventilatory parameters were simultaneously recorded. The patients were then turned into the lateral position and proper insertion of the DLT was confirmed by fiber-optic visualization.

TLV was continued with the same pattern for 10 minutes and all measurements were repeated.

Study protocol

After a recruitment maneuver, following the guidelines described in the literature (holding a constant airway pressure of 40 cmH_2O was applied to the whole lung for 10 s) OLV was started in the lateral position, from the time the thoracic cavity was opened. Considering the fact that a recruitment maneuver under an FiO_2 1.0 may last up to 30 minutes, and the fact that hypoxic pulmonary vasoconstriction becomes maximal after approximately 10-15 minutes, measurements were made every 30 minutes to reach a steady state for PaO_2. Patients were randomly assigned to 30 minutes of ventilation with either a TV of 10 mL/kg TV without external PEEP and respiratory rate of 10 breaths/minute (Group 10, N.=50) or to a TV of 5 mL/kg with 5 cmH_2O PEEP and a respiratory rate of 20 breaths/minute (Group 5, N.=50). According to the rules of crossover design during the subsequent 30 minutes, each patient received the alternative management. Randomization was based on computer-generated codes that were maintained in sequentially numbered sealed opaque envelopes until after induction of anesthesia. During the subsequent 30 minutes of OLV, the alternative ventilatory management was used. Before ventilatory settings were changed, the recruitment maneuver was repeated The I:E ratio, and the FiO_2 were kept constant throughout the study. From the time of closure of thoracic cavity, TLV was started with the pattern described above and FiO_2 of

0.4 oxygen in air was used to avoid absorption. atelectasis in the postoperative period.

Measurements

During OLV, the partial pressure of oxygen in arterial blood (PaO_2), the partial pressure of carbon dioxide in arterial blood ($PaCO_2$), peak inspiratory airway pressure (Ppeak), plateau inspiratory airway pressure (Pplat), hemodynamic parameters were recorded 30 min after each change in the ventilatory setting. Airway pressures were measured by the anesthesia machine. Surgical manipulation on the operated lung was temporarily stopped to allow data collection. After the study period, OLV with the same ventilatory settings was continued to allow the completion of surgery.

Postoperative monitoring and care

All patients were admitted postoperatively to a postanaesthesia care unit for at least a 12-24 hours postoperative monitoring that included serial blood gas analysis measurements and a first-day postoperative chest x-ray. During this period oxygen therapy through nasal cannula was provided as was necessary for proper oxygenation and epidural analgesia was continued to provide appropriate pain control.

Statistical analysis

Intrapulmonary shunt fraction calculations were performed using the nomogram of Benatar *et al*. PaO_2 between 60 and 100 mmHg were considered to be abnormally low. $PaO_2<60$ mmHg or $SaO_2<90\%$

were considered severe hypoxemia. One hundred patients provided an 80% power to detect a two-tailed difference of 50 mmHg in PaO_2 during OLV with an α error of 5% based on an expected standard deviation of 100 mmHg. Distribution normality was determined using the Shapiro-Wilk test. Student's *t* tests were used to for intergroup comparisons of preoperative values and analysis of data obtained during twolung ventilation. Data obtained during one-lung ventilation were analyzed with two-way repeated- measures of ANOVA with "randomization order" and "TV" being considered independent variables. Results are presented as means ± SDs; $P<0.05$ is considered statistically significant. SAS for Windows 9.2. (SAS Institute Inc. Cary, NC USA) was used for statistical analysis.

2.2 Impact of $PaCO_2$ driven and $EtCO_2$ driven one-lung ventilation on arterial oxygenation

Study population

After approval from the local Ethics Committee (DEOEC RKEB/IKEB 2976-2009), written informed consent was obtained from 100 ASA II patients scheduled for lung resection surgery.

Preoperatively lung-function tests with wholebody plethysmography, arterial blood gas analysis while breathing room air, ECG, preoperative echocardiography, computerized tomographic lung scan, and bronchoscopy were done.

Anesthesia

All patients were premedicated with 5 mg of midazolam and 0.5 mg of atropine im prior to arrival in the operating room. Before induction, an epidural catheter was placed at the level of Th V–VIII to ensure appropriate intraoperative and postoperative analgesia. A mixture of 0.1 mg/ml of bupivacaine and 5 mcg/ml of fentanyl was administered at a rate of 0.1 ml/kg/hour throughout the study and in the postoperative period. For the induction of anesthesia, a combination of 2 mg/kg propofol, 2 mcg/ml fentanyl and 0.2 mg/kg cisatracurium was used. Muscle relaxation and depth of anesthesia were monitored by the appropriate monitoring system of the Zeus anesthesia working place (Draeger Medical, Lűbeck, Germany). After the desired level of muscle relaxation was reached, a doublelumen endotracheal tube was inserted using direct laryngoscopy. The position of the tube was always ascertained by fiberoptic bronchoscopy. For maintenance of anesthesia a mixture of sevoflurane in oxygen/air was used. The concentration of sevoflurane was tailored according to the BIS level. Standardised monitoring including five-lead ECG, invasive arterial blood pressure monitoring, core temperature, and pulseoxymeter was used throughout the anesthesia procedure.

Ventilatory strategy during the study and study protocol

Patients were randomly assigned to $EtCO_2$ driven ventilation (Group $EtCO_2$, N.=50) for maintaining $EtCO_2$ in normal range or to a PaCO2 driven ventilation with increased respiratory rate for maintaining arterial normocapnia (Group $PaCO_2$, N.=50). Randomization was based on computer-generated codes that were maintained in sequentially numbered sealed opaque envelopes until after induction of anesthesia.

Measurements

During OLV, the partial pressure of oxygen in arterial blood (PaO_2), the partial pressure of carbon dioxide in arterial blood ($PaCO_2$), end-tidal carbon dioxide (EtCO2), respiratory rate, inspiratory time, peak inspiratory airway pressure (Ppeak), plateau inspiratory airway pressure (Pplat), hemodynamic parameters were recorded in every 15 minutes.

Statistical analysis

Distribution normality was determined using the Kolmogoro-Smirnov test. Student's t tests were used to for intergroup comparisons of preoperative values.Tukey-Kramer tes was uesd for analysis of data obtained during twolung ventilation. Data obtained during one-lung ventilation were analyzed with one-way repeated-measures of ANOVA. Results are presented as means ± SDs; $P<0.05$ is considered statistically significant. SigmaPlot 11. (Systat Software Inc, Chicago, Il, USA) was used for statistical analysis.

3.3 Impact of normocapnic one-lung ventilation on cerebral oxygenation

Study population

Twenty-four patients undergoing lung surgeries were included in the study, which was approved by the local Medical Ethics Committee of the University. All patients gave written and informed consent. There were 20 lobectomies, 2 bilobectomies and 2 video-assisted thoracoscopies.

Anesthetic procedure

All patients were premedicated with 5 mg of midazolam and 0.5 mg of atropine im prior to arrival in the operating room. Before induction, an epidural catheter was placed at the level of Th V–VIII to ensure appropriate intraoperative and postoperative analgesia. A mixture of 0.1 mg/ml of bupivacaine and 5 mcg/ml of fentanyl was administered at a rate of 0.1 ml/kg/hour throughout the study and in the postoperative period. For the induction of anesthesia, a combination of 2 mg/kg propofol, 2 mcg/ml fentanyl and 0.2 mg/kg cisatracurium was used. Muscle relaxation and depth of anesthesia were monitored by the appropriate monitoring system of the Zeus anesthesia working place (Draeger Medical, Lűbeck, Germany). After the desired level of muscle relaxation was reached, a doublelumen endotracheal tube was inserted using direct laryngoscopy. The position of the tube was always ascertained by fiberoptic bronchoscopy. For maintenance of anesthesia a mixture of sevoflurane in oxygen/air was used. The concentration of sevoflurane was tailored according to the BIS level. Standardised monitoring including five-lead ECG, invasive arterial blood pressure monitoring, core temperature, and pulseoxymeter was used throughout the anesthesia procedure.

Ventilatory strategy during the study

end-expiratory pressure (ZEEP). When the patients were turned into lateral decubitus position, this ventilatory mode was maintained for 5 minutes for stabilisation purposes. At the time of skin incision OLV was started with constant squared flow in volume controlled pressure limited mode with a TV of 5 ml/kg and with 5 cmH_2O PEEP. Peak airway pressures were kept below 35 cmH2O, and plateau pressures under 25 cmH_2O. Respiratory frequency was adjusted in order to maintain normocapnia. After closure of the chest, we returned to double-lung ventilation was restarted with 10 ml/kg TV and ZEEP. With the patients back in supine position, a mixture of 50% oxygen in air was used for ventilation, with 10 ml/kg TV and ZEEP.

Monitoring oxygenation and $PaCO_2$

In all patients radial artery catheters were placed in the awake state for continuous monitoring of arterial blood pressure and blood gas sampling. Arterial blood gas samples were taken in the awake state, in the supine position after induction of anesthesia during DLV, in the lateral decubitus position during DLV and every 15 minutes during OLV.

Cerebral oxygen saturation and blood flow monitoring

Before induction of general anesthesia, a cerebral oxymetry probe was placed on the forehead of the patients on the non-dependent side. INVOS 5100C Cerebral Oxymeter System (Somanetics Corporation, Troy, MI, USA) was used to monitor cerebral oxygen saturation (rSO_2). Transcranial Doppler (TCD) measurements were performed using Rimed Digilite Transcranial Doppler sonography (Rimed Ltd, Israel). Temporal window was used for insonation. A fixed probe was used to measure cerebral blood flow velocity in the middle cerebral artery on the non-dependent side. The device permits the assessment of the best available signal of the middle cerebral artery between the depths of 45–55 mm. Systolic, diastolic and mean blood flow velocities were registered, and pulsatility indices were calculated by the device. Both cerebral oxygen saturation and blood flow velocities were continuously monitored from the awake state throughout the study. For the sake of clarity, only those rSO_2 and blood flow velocity values were taken into account in the statistical analysis where simultaneously blood gas analysis was also performed.

Statistical analysis

Before starting the study, a power analysis was performed according to the variance published in a previous study of Hemmerling et al. Power analysis revealed that the predicted population size to be studied in order to obtain a 20% difference in cerebral oxygen saturation during OLV compared to lateral DLV was 20. Twenty-four patients were included in the study.

Statistica for Windows (Tulsa, USA) programme was used for analysis. The normality of distribution was tested by Shapiro–Wilks test. Thereafter, differences were analyzed with the Repeated Measures Analysis of Variance (ANOVA) ($PaCO_2$ introduced as a co-factor, as its variance might have influenced the outcome variable disguising the true relationship) with the Tukey–Kramer Multiple Comparisons Test. The relationship between cerebral oxygen saturation and PaO_2, $PaCO_2$ as well as middle cerebral artery mean blood flow velocity was assessed by linear regression method. Values of $p < 0.05$ were accepted as statistically significant. Data are presented as mean ± SD.

After the patients were intubated in supine position, double-lung ventilation (DLV) was started in volume controlled mode using 1.0 FiO_2 and a tidal volume of 10 ml/kg and a zero

3.4 Clinical experience with a new endobronchial blocker: the EZ-blocker

Subjects and methods

Inclusion of patients started after we had obtained permission from the local medical ethics committee (permission number: DEOEC RKEB/IKEB 3283-2010). All subjects gave written informed consent before surgery.

Description of the EZ-blocker

The main part of the device is a 650 mm long catheter, 7 Fr. in diameter, containing four lumina. Its ending forms a symmetrical, double-stem, 4-cm-long Y-shape. Among the four lumina, two (one on each side) enable the connection between the lumen of the main bronchi and the environment, creating suction and providing oxygen. The other two lumina (one on each side) serve for inflating and deflating the cuff located at the stems of the Y-shaped ending. The extensions are fully symmetrical and are color coded for identification purposes.

Anesthetic procedure

All patients received 5 mg midazolam and 0.5 mg atropine before induction of anesthesia. A thoracic epidural catheter was introduced at thoracic V–VII level, and after the testing dose 0.1 mg/ml bupivacaine plus 5 lg/ml fentanyl was administered at a rate of 0.1 ml/kg/h. Before induction, a radial artery cannula was introduced for continuous blood pressure measurements and for blood gas analysis. During the entire course of anesthesia, relaxometry (TOF Watch SX, NV Organon, Oss, The Netherlands) and BIS monitoring were performed (Aspect Medical Systems, Natick, MA, USA). General anesthesia was induced by fentanyl (2 μg/kg), propofol (2 mg/kg), and cis-atracurium (0.2 mg/kg). After induction, a single-lumen tube (SLT) (Rűschelit, Rűsch, Kernen, Germany) 9 mm in diameter was introduced under direct laryngoscopy. The positioning of the tube was performed and controlled by bronchoscopy; it was desired that the position should allow the opening of the stems of the Y-shaped bronchial blocker in the later course of anesthesia and surgery. After intubation, two-lung ventilation (TLV) was started by a tidal volume of 10 ml/kg and zero positive end-expiratory pressure (ZEEP, with maintenance of the peak airway pressure below 40 cmH_2O until opening the pleural cavity (Draeger Primus anesthesia device; Draeger Lűbeck, Germany). Maintenance of anesthesia was performed by administration of a mixture of sevoflurane and oxygen to maintain an appropriate depth of anesthesia. When the fixation of the single-lumen endotracheal tube was completed, the EZ-blocker was introduced under bronchoscopic control. Until this point, both cuffs of the blocker were deflated. Before opening the pleural cavity, the SLT was disconnected from the anesthesia device. Opening of the pleural cavity resulted in the collapse of the nondependent lung. At this point, the cuff of the bronchial blocker was inflated on the dependent side, and OLV was initiated with 5 ml/kg TV and a PEEP of 5 cmH_2O.

Measurements during the procedure

Assessment of EZ-blocker positioning

After fixation of the SLT, the time necessary for proper positioning of the blocker was recorded. The time required for laryngoscopy and intubation was not included in the time needed for proper positioning of the EZ-blocker. Measurement of insertion time started at the opening of the orifice of the multiport connector for insertion of the

EZ-blocker and was stopped when the correct position was verified by bronchoscopy. Whenever proper positioning of the tube was not successful (two cases), the time necessary for correcting the position was also recorded in seconds.

Assessment of cuff pressures and minimal occlusion volumes

In supine position under closed chest condition, TLV was started with pressure-controlled mode using decelerating flow pattern with 25 cmH_2O of peak and plateau inspiratory pressure. After a stabilization period of 1 min, tidal volume was recorded. The right cuff of the blocker was inflated under manometer control until reaching the pressure necessary to halve the tidal volume as compared to the initial value. This stage was considered proper endobronchial block. At this point, the cuff was deflated by a syringe and the volume that was aspirated from the cuff was measured. The same procedure was repeated with the cuff on the left side. With inflated cuffs we also registered the cuff pressures (in cmH_2O and mmHg). Thus, we gathered information on the amount of air and cuff pressures necessary for proper blocking on the two sides.

Assessment of duration that is necessary for the lung to collapse (lung deflation time)

At open chest in lateral decubitus position with deflated blocker cuffs, the lungs were inflated until the nondependent lung reached the lower border of the rib cage. Duration of lung collapse was determined in different ways.

Collapsing the lung through the stem of the BB

After inflating the nondependent lung, the cuff on the same side was inflated while the cuff on the dependent side was deflated. The nondependent stem was made open to the air, spontaneous deflation of the nondependent lung through the lumen of the BB.

Spontaneous lung collapse through the endotracheal tube

In a second setup, after reinflation of the nondependent lung, the BB cuff on the nondependent side was inflated for a short time, the dependent cuff remained deflated, and OLV was continued. After a short stabilization time, SLT was disconnected from the ventilator and the BB cuff on the nondependent side was deflated. Herewith the duration of spontaneous lung collapse through the lumen of the endotracheal tube was measured.

Facilitated lung collapse through the endotracheal tube

The setup here was the same as for the previous point. Additionally, after disconnecting from the endotracheal tube, a suction system with a force of 20 cmH_2O was attached to the system and the duration of facilitated lung collapse was determined. Proper collapse of the lung was defined by measuring the distance between the upper border of the superior lobe and the rib cage. A distance of 5.5 cm was considered appropriate. Determination of the appropriate distance was based on our previous measurements in which DLTs were used in ten patients. In this study, we asked the thoracic surgeons to determine the ideal collapse of the lung, and we measured the distance between the lung pleural surface and the upper border of the superior rib cage. In this series the distance for appropriate lung collapse was 5.5 cm on average. In the present study, in each case we reached the 5.5-cm lung collapse. The distance was measured with a sterile centimeter scale with open chest condition.

A three-dimensional reconstruction was completed from all preoperative lung CT scans off-line in all patients (eFilm Lite software; MergeeMed, Division of Merge Healthcare, Milwaukee, WI, USA). We could obtain the particular images by utilizing the eFilm Lite software's built-in multiplanar reconstruction function. The MPR function produces three sets of reconstructive images: coronal, sagittal, and transverse scans, by means of the appropriate tool icons. With this function we were able to select the appropriate planes that depict clearly the trachea, the bifurcation, and the origins of both bronchi. The diameters of the two main bronchi were measured perpendicular to the axis of the bronchus at the bifurcation. The angle of the bifurcation is the angle produced by the axes of the left and right bronchi.

Statistical analysis

The Shapiro–Wilk test was used for assessment of data distribution. The Mann–Whitney test was used for comparison of the data. Regression analysis was used to assess the relationship between the diameters of the bronchi and cuff pressures as well as minimal occlusion volumes (MOVs). A P value\0.05 was considered as statistically significant.

3. RESULTS

4.1 Effects of different tidal volumes for one-lung ventilation on arterial oxygenation

Patients characteristics, arterial partial pressures, pulmonary function tests, were similar in both groups of patients.

There were no significant differences in PaO_2, $PaCO_2$, calculated intrapulmonary shunt (Qs/ Qt), ventilatory and hemodynamic values during TLV in the supine and lateral decubitus positions.

There was no significant effect of sequence of randomization on any outcome (PaO_2: P=0.7; $PaCO_2$: P=0,4; Qs/Qt: P=0.3; Ppeak: P=0.3; Pplat: P=0.2); all results are thus presented as afunction of TV. TV during OLV did not significantly alter PaO_2 (10 mL/kg: 218±106 *versus* 5 mL/kg: 211±119 mmHg, P=0.29), or hemodynamic responses. The proportion of patients who demonstrated low PaO_2 during OLV was similar with each TV (TV 10 mL/kg: 7/100 (7%) *versus* TV 5 mL/kg: 9/100 (9%), P=0.6, chi-squared test). No severe hypoxic episodes were noted in either of the patients. The values of $PaCO_2$ during OLV were significantly greater using low TV (10 mL/kg: 39±6 *versus* 5 mL/kg: 44±8 mmHg, P<0.001). The values of TV, Ppeak and Pplat and static compliance (Crs) during OLV were significantly higher using high TV as compared to low TV. All the patients were hemodinamically stable during the surgical procedure.

1.2 Impact of $PaCO_2$ driven and $EtCO_2$ driven one-lung ventilation on arterial oxygenation

Patients characteristics, arterial partial pressures, pulmonary function tests, were similar in both groups of patients There were no significant differences in PaO_2 values between groups during DLV and at the 15th minute of OLV (Group $EtcO_2$: 218±101 mmHg, Group $PaCO_2$:208±107 mmHg). There were significant differences in PaO_2 at the 30th and 45th minutes between groups (30th min Group $EtcO_2$: 152±73 mmHg, Group $PaCO_2$:225±80 mmHg; 45th min Group $EtcO_2$: 154±105 mmHg, Group $PaCO_2$:227±83 mmHg respecively, $p<0.05$). In Group $PaCO_2$ mean airway pressure and RR was higher, and the inspiratory and expiratory time was shorter than in Group $EtCO_2$.

4.3 Impact of normocapnic one-lung ventilation on cerebral oxygenation

Changes in PaO2 and PaCO2 values during the study

PaO2 values significantly increased compared to the resting state when DLV was administered with 1.0 FiO2 in both supine and lateral decubitus positions. After OLV was started, PaO2 values gradually decreased. It is important to note that the average PaO2 remained at 26 kPa throughout the whole study. Partial pressures of CO2 in arterial blood remained relatively stable compared to resting values until introduction of OLV. A gradual increase in PaCO2 was observed during OLV, but due to adjustment of respiratory frequency during mechanical ventilation, average PaCO2 remained within the normocapnic range.

Cerebral oxygen saturation

Cerebral oxygen saturation increased significantly when DLV was started with FiO_2 1.0 and remained relatively stable during the course of the study. When ventilation was changed from DLV to OLV, no significant change was observed. A significant decrease of cerebral oxygen saturation was found compared to the value observed during DLV in lateral decubitus at the time points of 30, 45 and 60 minutes after the start of OLV. It is important to note that even at these time points, average brain oxygen saturation corresponded to the awake value. The relative changes of cerebral oxygen saturation during OLV (in %) were the nexts: Lateral OLV 15 min. –3.8 ± 8.2 (–19.0%–6.9%), Lateral OLV 30 min. –5.6 ± 8.6 (–23.5%–19.2%), Lateral OLV 45 min. –9.22 ± 10.3 (–30.5%–11.0%), Lateral OLV 60 min. –12.6 ± 9.7 (–37.8%–8.9%).

It is obvious that the average decrease in rSO_2 was at all time points of OLV below 20%. A less than 60% oxygen saturation was observed in five cases (out of 24): in case 8 (at 15 min: 58%, at 30 min: 52%, at 45 min: 49% at 60 min: 58%), in case 10 (at 45 min:57%, at 60 min: 51%), in case 11 (at 60 min: 58%), in case 16 (at 30 min: 58%, at 45 min: 53%) and in case 17 (at 15 min: 56%, at 60 min: 52%). Thus, in the majority of the cases only slight decreases of the rSO_2 were observed during OLV.

Mean blood flow velocity of the middle cerebral artery

Middle cerebral artery mean blood flow velocity transiently, slightly increased after starting OLV but returned to the value observed at lateral DLV thereafter and remained relatively stable throughout the course of the thoracic surgical procedure.

The relationship between cerebral oxygen saturation and cerebral blood flow velocity as well as blood gases during OLV

Cerebral oxygen saturation was influenced by both PaO_2 and $PaCO_2$ (r = 0.44 and r = 0,40, $p < 0.001$ in both cases). There was no significant relationship between rSO_2 and cerebral blood flow velocity (r = 0.05, p = 0.51). Cerebral blood flow velocity was independent from PaO_2 (r = 0.1, p = 0.17), while a significant positive correlation was found between $PaCO_2$ and cerebral blood flow velocity.

3.4 Clinical experience with a new endobronchial blocker: the EZ-blocker

Insertion and proper positioning of the EZ-blocker required 71 ± 12 s. Of the ten cases, malposition occurred in two. In both cases the reason for improper first positioning was the too-deep insertion of the endotracheal tube used for guidance of the blocker. With this too-deep positioning, the ending of the single-lumen endotracheal tube was less than 4 cm, making opening and proper positioning of the Y-shaped bronchial blocker impossible. In the case of initial malposition, the correction lasted for 150 and 180 s, respectively.

Comparison of deflation times using different methods

The deflation time of the lung through the lumen of the bronchial blocker was 755 ± 113 s for the left and 676 ± 61.7 s for the right side (P = 0.18). When doing lung deflation with the blocker cuff deflated (with lung collapse thus occurring through the lumen of the singlelumen endotracheal tube), the spontaneous deflation time was 9.4 ± 0.7 s, which could be further decreased by administration of a negative pressure of 20 cmH_2O to 4.1 ± 0.7 s.

Relationship between the morphological properties of tracheal bifurcation and endobronchial block.

When assessing the diameters of the left and right main bronchi, a significant difference was found (13.9 ± 2.6 mm for left side vs. 16.7 ± 2.1 mm for right side; P=0.047). The average angle of the tracheal bifurcation was 73.8° ±15.9°. The amounts of air necessary for proper blocking as well as the corresponding cuff pressures on the two sides were: Amount of air necessary for blocking under airway pressure of 25 cmH_2O (ml) left: 6.7±1.16, right: 8.0±1.1, p= 0.033; Cuff pressure during proper blocking under airway pressure of 25 cmH_2O (mmHg) left: 39.8 ± 4, right: 84.6 ± 5 p<0.001. A greater amount of air was necessary for a proper endobronchial

block on the right side than was necessary on the left side, with a correspondingly higher cuff pressure in the rightside cuff.

In a further analysis, we assessed whether a relationship exists between the ratios of main bronchial diameters and the ratios of

MOV. It was found that a significant positive relationship exists between the two parameters; e.g., the greater the diameter of the main bronchus, the larger the amount of air that was necessary for proper endobronchial block ($r^2 = 0.43$; =0.04).

In contrast to this, no relationship could be detected between the angle of tracheal bifurcation and the MOV values, thus indicating that the angle has no impact on the proper endobronchial block ($r^2=0.06$; P=0.487). Similarly, the bifurcation of the main bronchi did not have any impact on the time that was necessary for proper blocking ($r^2 = 0.26$; P=0.19).

2. DISCUSSION

Our work is a prospective, randomized, crossover design study in humans during thoracic surgery, where the effects of different TVs were investigated during OLV. Our primary result is that arterial oxygenation and shunt fraction are similar with TVs of 5 mL/kg and 10 mL/kg during OLV with open chest in the lateral position, during surgical manipulation in patients with normal lung function. The TV to be used to maintain adequate oxygenation

during OLV remains controversial. Based on the work of Katz, textbooks and reviews recommend using high TV because TV less than 8 mL/kg-1 can lead to atelectasis that may increase the incidence of hypoxemia. However, traditionally OLV has been performed with high TV without added external PEEP because

high TV with external PEEP (5-10 cmH_2O) promotes alveolar hyperinflation which can lead to lung injury.

There is growing evidence that smaller TV during OLV than during two-lung ventilation helps preventing lung injury. As might be expected, low TVs reduced inspiratory airway pressures, which may reduce pressure-related lung injuries that sometimes accompany one-lung ventilation.8 The effect of low TV on oxygenation is controversial. The conclusions of the present study correspond to the findings of Kozian *et al* who compared TVs of 5 and 10 mL/kg for OLV in piglets and evaluated lung density distribution. They found a TV of 5 mL/kg along with PEEP after an alveolar recruitment

maneuver a safe alternative to larger TVs. However, in their study, respiratory rate was different using different TVs, thus minute volume was not identical, the constant level of $PaCO_2$ indicates constant alveolar ventilation. In contrast, in our study the minute ventilation was kept constant with doubling the respiratory rate at low TV. This double respiratory rate produced a reduction in alveolar ventilation and CO_2 retention. Licker *et al* found that use of low TV with PEEP and recruitment maneuvers serves adequate oxygenation during OLV. In our study, we evaluated smaller TVs than commonly clinically used. However our results are different

from the results of Roze *et al* who found that at the same plateau pressure, an increased PEEP with low TV worsened oxygenation. In our study only 5 cmH_2O PEEP was used with low TV, whereas Roze's used 9 cmH_2O PEEP which can lead to compression of alveolar capillaries due to overdistension and has the potential to worsen oxygenation (although clinically not significantly). It has to be noted, that compression of alveolar capillaries due to overdistension would produce an increase in dead space (and an increase in $PaCO_2$) but it would only slightly reduce PaO_2 due to the shunt effect (diversion of blood flow to less ventilated areas). This effect on PaO_2 would only be apparent at low FiO_2. The amount of abnormally low arterial oxygen partial pressure was similar in each of our groups, and neither ventilation strategy produced serious hypoxemia (PaO_2<60 mmHg).

Use of PEEP during ventilation with low TV is also controversial. Application of external positive end-expiratory pressure can decrease the incidence of atelectasis due to prevention lung collapse and minimizes the alveolar injury preventing cyclic opening-closing during OLV. However, the optimal level of PEEP remains unknown. Some studies reported beneficial effects on oxygenation whereas others reported no benefit or worsening of oxygenation. Many now believe that ventilation with low TV without added external PEEP worsens oxygenation and promotes alveolar de-recruitment. Kim *et al* did not found difference in PaO_2/FiO_2 ratio using low TV with and without PEEP. This observation suggests that application of PEEP cannot compensate for hypoxia due to atelectasis caused by low TVs. We thus compared low TV with PEEP and high TV without PEEP as this is probably the safest clinical approach — and one that has been used in many previous studies. The use of a TV of 5 mL/kg was associated with an increased $PaCO_2$, but this increase remained between the limits of normocapnia.

Once low TV is used, the respiratory rate has to be doubled to maintain the constant minute ventilation. This leads to an increased dead-space ventilation and increased $PaCO_2$. There were no significant differences in calculated intrapulmonary shunt values. We note, though, that intrapulmonary shunt fractions were calculated using the nomogram of Benatar *et al.* Better estimates would be available from a pulmonary artery catheter, but invasive monitoring is not routine in our department. A constant FiO_2 of 1.0 during the study was motivated by safety because of the lack of experience in the use of such low TVs in humans. However, the same FiO_2 was used in all patients. This high FiO_2 might accelerate atelectasis after the alveolar recruitment maneuver, but we did not find any differences in PaO_2. Moreover, it seems unlikely that at such a high FiO_2, that an alveolar recruitment maneuver applied 30 minutes before the measures could influence the obtained data. Additonally, administration of higher FiO_2 has also a methodological background: while using high FiO_2, small changes in the shunt fraction may lead to consequently larger changes in PaO_2 and therewith may enhance the comparison of the effects of different ventilatory strategies. After finishing OLV, TLV was continued with FiO_2 of 0.4 in air to avoid the absorption atelectasis in the postoperative period.

There were significantly higher values of static compliance (Crs) using high TV during OLV than using low TV. Higher plateau inspiratory pressures usually reduce compliance. Although, an increased Pplat is logically observed after increasing the TV; however, the increase in TV and the increase of the Pplat are not lineary correlated which may explain the higher compliance using high TV.

We have to mention several limitations to our study. First, only patients with no or minor alterations of the pre-operative pulmonary function were studied. Of course many patients having thoracic surgery present with various degrees of COPD and pulmonary hyperinflation. Some are chronically hypoxic, and others are hypercapnic. We excluded patients with serious cardiac comorbidities and severely abnormal lung function tests, as mentioned in the methods section. The extent to which our results can be generalized to sicker patients remains to be determined.

A second limitation is that our cross-over design may have decreased the intersubject variation and it is widely used in clinical research in investigation of acute effects on oxygenation, because patients served as their own controls. A consequence of our cross-over design is that we were unable to evaluate any long-term effects of this TV management. It thus remains possible that low or high TV is preferable for reasons beyond their acute effects on arterial oxygenation and pulmonary shunt. We did not observe any acute lung injury, ARDS, pulmonary edema, or pneumonia within 72 postoperative hours.

Third, we have studied patients in the lateral position, with open chest and during surgical manipulation. In the lateral position, the eventually gravitational effect on the redistribution of pulmonary blood flow during OLV is already present, so it would have no more influence on the findings of the study. The open chest and surgical manipulation were preferred to reproduce as much as possible the clinical conditions during OLV. Unfortunately, we cannot quantify the amount of blood flow redistribution due to the surgical manipulation, which might influence the results of the present study. However, surgery was temporarily stopped to allow data collection.

The relatively high RR impairs the emptying of alveoli and results in increased functional residual capacity. So the $PaCO_2$ driven lung-protective OLV results in signifi cantly higher PaO_2 $EtCO_2$ driven OLV.

We found that OLV with low (5 ml/kg tidal volume and low PEEP did not result in a significant decrease in cerebral oxygen saturation if normocapnia was maintained. We applied 10 ml/kg TV with ZEEP during DLV in the lateral decubitus position before OLV of the dependent lung was started. Our additional finding was that this respiratory strategy during OLV permitted the maintenance of sufficient level oxygenation and peripheral oxygen saturation without critical decreases of PaO_2. In previous guidelines of OLV, a higher than 13 kPa PaO_2 and a peripheral oxygen saturation above 90% are described as minimal acceptable values. This is the first study to assess both cerebral oxygen saturation and cerebral blood flow with administration of lung protective ventilatory strategy during OLV.

The ideal ventilatory strategy during single lung ventilation is a debated issue.

Based on recent clinical reports and review articles two main sets of respiratory strategies can be drawn: The *traditional approach* uses a fixed higher (10–12 ml/kg) tidal volume and ZEEP both during double-lung and one-lung ventilation. The newer concept of *lung protective strategy* includes low (5–7 ml/kg) TV, low PEEP (5 cmH_2O) and pressure controlled ventilatory mode. Both of these approaches have intra- and postoperative advantages and disadvantages; therefore there are concerns over the ideal approach. A common endpoint of these two approaches is to maintain sufficient oxygenation during OLV. Thus, from this point of view, the ideal approach should be one which permits sufficient oxygenation of the organs with no or minimal intra- and postoperative side effects. The most important side effects of the traditional approach include pulmonary oedema, acute lung injury and dynamic hyperinflation, whereas the lung protective strategy with low tidal volumes might result in lung atelectasis and hypercapnia and low rSO_2.

Weighing up the advantages and disadvantages, we decided to perform our study using the lung protective approach and intended to test whether application of low TV along with low PEEP and maintaining normocapnia resulted in sufficient arterial oxygenation, brain tissue oxygen saturation and cerebral blood flow during OLV. We have found that application of this approach does not significantly affect cerebral oxygen saturation and cerebral blood flow.

Cerebral tissue oxygen saturation as measured by INVOS is determined by several factors, including cerebral blood flow, cerebral blood volume, oxygen saturation and haemoglobin concentration of the arterial blood and cerebral metabolic rate of oxygen. The haematocrit and haemoglobin concentration levels remained constant throughout our study.

Cerebral blood flow and cerebral blood volume are mainly influenced by the cerebral perfusion pressure and the cerebral vascular resistance. The most potent regulatory stimulus of the cerebral arteriolar tone (i.e. the determinant of cerebrovascular resistance) is $PaCO_2$. In cases of hypercapnia a dilation of the cerebral arterioles occurs, leading to increases both in cerebral blood flow and blood volume. By contrast, if hypocapnia is present, a vasoconstriction of the cerebral arterioles occurs, resulting in decreased blood flow and blood volume. Converting these previous physiological observations into our study, maintenance of normocapnia enabled us to keep the metabolic cerebrovascular responses within the physiologic range and therewith cerebral oxygen saturation was independent from changes of cerebral blood flow and blood volume. Although a slight increase of $PaCO_2$ occurred in our study during OLV, the expected increase in cerebral blood flow was probably counteracted by the decrease of cerebral blood flow induced by sevoflurane anesthesia.

The second determinant factor of cerebral tissue oxygen saturation is the peripheral oxygen saturation (SpO_2) of arterial blood. As critical decreases (SpO_2 < 90%) did not occur in our study using lung protective ventilation and the PaO_2 of arterial blood was relatively stable (mean value: 26 kPa) throughout the study, this leads us to think that these factors did not have a significant impact on cerebral oxygen saturation.

The third determinant factor of brain tissue oxygen saturation is cerebral metabolic rate for oxygen ($CMRO_2$). Although we did not assess $CMRO_2$ in our study, it has to be noted that, according to previous reports, the anesthesiological method (sevoflurane-fentanyl based maintenance of anesthesia) used tends to decrease cerebral oxygen metabolic rate. In the present study we intended to assess oxygen saturation in the most sensitive organ to hypoxemia.

Using the lung protective approach we found that it permits sufficient oxygenation of the brain parenchyma. However, we did not assess the potential pulmonary complications of this ventilatory approach, neither do we have information on how the traditional ventilatory approach influences cerebral tissue oxygen saturation and cerebral blood flow. Obviously, there are some differences between the results of the present study and those published by Hemmerling et al. and Kazan et al. For explaining this difference we have different points to mention: First, we used a slightly different ventilatory strategy during OLV, e.g. beside administering low tidal volumes we also intended to maintain normocapnia based on blood gas analysis. This was decided because we were aware of the metabolic regulation of brain circulation as described above. In our study, cerebral oxygenation decreased slightly at 60 minutes, but remained in the normal range and serious cerebral desaturations did not occur throughout the study. We believe this may be explained by maintainance of normocapnia. Second, it could be the different methodology that explains the differences in cerebral oxygen saturation. The third difference to mention is that we also measured cerebral blood flow velocity in the middle cerebral artery. Although it does not measure cerebral blood flow directly, changes in blood flow velocity may reflect changes in cerebral blood flow. Cerebral blood flow is mainly influenced by $PaCO_2$. Thus, maintaining normocapnia may lead to a stable cerebral blood flow during OLV.

In our opinion, the results of the present study and those published by Hemmerling et al. and Kazan et al. are not contradictory, rather serve with complementary information on what is happening within the brain during OLV. Our results speak in favour of maintainance of normocapnia in order to achieve stable brain tissue oxygenation and cerebral blood flow.

Further complex studies focusing on both tissue oxygenation, cerebral blood flow and perioperative pulmonary complications are needed to find out the optimal ventilatory strategy during OLV

During thoracic anesthesia, double-lumen endotracheal tubes (DLT) are widely used in cases where one-lung ventilation is necessary. However, in some cases (such as difficult intubation, tracheostomy, or traumatized patients previously intubated with a SLT), the use of double-lumen tubes or the change from a single-lumen to a double-lumen tube may become difficult or risky. In such cases, endobronchial blockers (BB) may be indicated. Their use is, however, restricted to certain cases because DLTs are characterized by faster lung deflation time, a simpler introduction technique, and easier positioning and bronchial toilet, as well as lower costs.

When taking the insertion and positioning time into consideration, the average insertion time for a bronchial blocker is reported to be as high as 4–6 min. In accordance with the present study, a previous report showed that the EZ-blocker may be positioned more quickly (1–3 min), more safely, and more easily than previously used types of bronchial blockers. The unique design of the EZ-blocker makes proper positioning easier compared with classic BBs. This study does have an important limitation: there were no control groups to compare the EZ-blocker with the other types of BBs. Our aim was to present our experience with this BB and present some technical data that have not been previously reported in the literature. Regarding the other aspect, the rate of malpositions during insertion, in the present study malposition occurred in two cases. The reason for the improper first position was a too-deep initial introduction of the endotracheal tube that served as a guidance for the bronchial blocker. As described in the Methods section, these malpositionings can be avoided by a careful checking of the endotracheal tube position using a bronchoscope. A distance of at least 4 cm from the tracheal bifurcation is necessary to reach the correct position of the BB. Additionally, when the initial insertion of the BB was improper, the correction lasted a maximum of 3 min, which could be handled safely by administering additional oxygenation to the patients before repositioning the BB. One disadvantage of the present blocking tube is the long deflation time of the lung through the lumen of the bronchial blocker. This delay might be tolerable during elective surgeries; however, the deflation time of more than 600 s seems to be too long in emergency surgical procedures and in special cases. For instance, in cases where the surgeon wants to open the chest safely as soon as possible and with minimal possible injury to the lung, or in cases where the two sides of the lung have to be ventilated alternatively during surgery (such as the Nuss procedure), these long deflation times seem to be inappropriate. In such cases, as demonstrated in our study, by deflating the cuff of the BB and opening the endotracheal tube toward the environment (eventually combined with additional suctioning of air through the endotracheal tube), the deflation times may be gradually decreased.

We also intended to assess how individual variations of the tracheobronchial anatomy influence the insertion times and the amount of air necessary for proper inflation of the BB blocker cuffs. It has been demonstrated in previous studies that the diameter of the right main bronchus is larger by 2 mm on average. Recently, it has also been demonstrated that the angle of the bifurcation shows individual variation. Therefore, we hypothesized that anatomical variations possibly do influence proper insertion of and blocking by the EZ-blocker. It has been demonstrated that neither the angle of the bifurcation nor the diameters of the main bronchi influence the time necessary for proper BB insertion. In contrast to this, as the diameter of the right main bronchus was larger on the right side, correspondingly more air was necessary for BB cuff inflation on this side. A significant positive relationship was demonstrated between diameters of the main bronchi and MOV values.

A further critical question regarding endotracheal and blocker tubes is the cuff pressure and the pressure exerted by the cuff on the tracheal wall. In previous tests of the blocker tube cuff pressures, a 25 cmH_2O positive airway pressure was used for testing the proper blocking with tube. In accordance with these tests, we also used this value for predetermination of critical airway pressure while testing the cuff pressures. In a previous study, Roscoe et al. demonstrated that the pressures exerted by the cuffs of DLTs ranged from 16 to 155 mmHg. Pressures exerted by the BB cuffs ranged from 39 to 194 mmHg. At intra-cuff volumes required to create a seal to 25 cmH_2O positive pressure, the pressures exerted by the cuffs of all the devices were less than 30 mmHg. In the present study we found that average cuff pressures were 39.79 ± 4 mmHg on the left side and 84.6 ± 5 mmHg on the right side, respectively. Taking into consideration that pressures exerted by the cuffs on the tracheal wall usually correspond to 10–20% of the cuff pressures, it may be estimated that in our series they correspond to 4–8 and 8.5–16 mmHg, which is far below the critical perfusion pressure of the bronchial wall (30 mmHg). The pressures exerted by the cuffs on the tracheal wall could be affected by the elasticity of cuff materials, and the relationship of the diameters between the cuff and the bronchus; thus, we need some basic research to prove our hypothesis for the EZblocker.

We can suggest that the cuff of the EZ-blocker should be inflated at the minimum volume and at the minimum pressure for the maintenance of one-lung ventilation to prevent bronchial mucosal ischemia. Also, cuff pressure monitoring seems to be essential.

Based on results of our investigation we conclude, that:

A protective ventilator strategy for OLV in humans, during lung surgery, with such a reduced TV as (5 mL/kg) accompanied by 5 cmH_2O PEEP provides a safe arterial oxygenation and reduced inspiratory airway pressures, as compared to higher TVs without PEEP in patients with normal lung function.

Normocapnia-driven lung protective one-lung ventilation provides significantly higher oxygen tension compared to permissive hypercapnia-driven ventilation.

Maintaining normocapnia may lead to a stable cerebral blood flow during OLV.

Proper blocking with the EZ-blocker is not influenced by anatomical variations of the tracheal bifurcation. The EZ-blocker allows for short lung deflation time through the endotracheal tube used for guidance of BB insertion, especially if it is combined with additional suctioning.

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List of publications related to the dissertation

1. **Végh, T.**, Juhász, M., Szatmári, S., Enyedi, Á., Sessler, D.I., Szegedi, L., Fülesdi, B.: Effects of different tidal volumes for one-lung ventilation on oxygenation with open chest condition and surgical manipulation: A randomised cross-over trial.
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   IF:2.818 (2012)

2. **Végh, T.**, Szatmári, S., Juhász, M., László, I., Vaskó, A., Takács, I., Szegedi, L., Fülesdi, B.: One-lung ventilation does not result in cerebral desaturation during application of lung protective strategy if normocapnia is maintained.
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3. **Végh, T.**, Juhász, M., Enyedi, A., Takács, I., Kollár, J., Fülesdi, B.: Clinical experience with a new endobrochial blocker: The EZ-blocker.
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4. **Végh T.**, Szabó-Maák Z., Szatmári S., Hallay J., László I., Takács I., Fülesdi B.: A normokapniás és a permisszív hiperkapniás tüdőprotektív egytüdős lélegeztetés hatása az artériás oxigén tenzióra.
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5. Hallay, J., Oláh, A.V., Fülesdi, B., Kocsor, M., **Végh, T.**, Kovács, G., Takács, I., Sápy, P., Nagy, D., Télessy, I.G.: Hepatobiliary response in postoperative lipid therapy in gastrointestinal surgery. *HepatoGastroenterology. 57* (102-103), 1069-1073, 2010.
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6. Szatmári, S., **Végh, T.**, Csomós, Á., Hallay, J., Takács, I., Molnár, C., Fülesdi, B.: Impaired cerebrovascular reactivity in sepsis-associated encephalopathy studied by acetazolamide test. *Crit. Care. 14* (2), R50, 2010.
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The Candidate's publication data submitted to the Publication Database of the University of Debrecen have been validated by Kenezy Life Sciences Library on the basis of Web of Science, Scopus and Journal Citation Report (Impact Factor) databases.

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