Protocol of a Thesis for Partial Fulfillment of master's degree

in Anesthesiology, Intensive Care and Pain Management

<u>Title of the Protocol</u>: # Single Lung Ventilation versus Two Lung Ventilation in Video Assisted Thoracoscopic Lung Surgeries

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What is already known on this subject? AND
What does this study add?

Single-lung ventilation has been preferred for lung surgeries to provide better surgical field, but its role and drawbacks compared with two-lung ventilation have not been fully evaluated.

This study is designed to evaluate the effectiveness of single lung ventilation and its safety with the best ventilator setting to avoid intraoperative and post-operative hypoxemia versus the conventional two lung ventilation in lung surgeries.

1. INTRODUCTION

Single lung ventilation is a technique commonly used in thoracic anesthesia to make thoracic surgery easier. It is used to create an optimum operative field and to improve surgical exposure. Single lung ventilation can be accomplished using different tools. However, double-lumen tubes are still considered the most popular and reliable choice for single lung ventilation in adult patients **(Brodsky&Lemmens, 2003, Della Rocca et al., 2013).** The use of video-assisted thoracoscopic surgery has become widespread, and the traditional open thoracotomy has been replaced by video-assisted thoracoscopic surgeries due to its minimal invasiveness and associated low morbidity **(Torresini et al., 2001).** No single method of lung isolation can be considered to be the best. The use varies according to the situation and has to be decided on *'as and when'* basis. However, **Alsharani and Eldawlatly** in **2014** described an algorithm for this**.**

Hypoxemia is used to be the primary concern during one lung ventilation. However, hypoxemia has become less frequent due to more effective lung isolation techniques, particularly the routine use of fiberoptic bronchoscopy, and the use of anesthetic agents with little or no detrimental effects on hypoxic pulmonary vasoconstriction. Acute lung injury has replaced hypoxia as the chief concern associated with one lung ventilation **(Lohser, 2008).** Nevertheless, it is not surprising that the rate of hypoxemia during single-lung ventilation is higher than 1.9% which is hypoxemia rate, reported for a general surgical collective **(Morkane et al., 2018)**.

Single lung ventilation creates intrapulmonary shunt that can result in a relevant hypoxemia in up to 10% of the procedures, which could be defined as a decrease in arterial oxygen saturation of the patient blood below 90% while being ventilated with an inspiratory oxygen fraction equal or greater than 0.5 **(Karzai &Schwarzkopf, 2009; Campos &Feider, 2018)**. The treatments of choice are either to re-inflate the operated lung or to raise the inspiratory oxygen fraction of the ventilated lung towards 1.0. However, intra-procedural re-inflation of the operated lung impairs the access for the surgeon to the operational field and may reduce the success of surgery, which is the main drawback of two lung ventilation and that makes the single lung ventilation of choice. Alternative or rather supplemental approaches either intermittent positive airway pressure **(Russell, 2011)** or differential lung ventilation can be applied to the dependent lung **(Kremer et al., 2019)**. Though, excessively the raising of intraoperative inspiratory oxygen fraction with the intention to treat hypoxemia means to replace one evil by another. Oxygen is a powerful vasoconstrictor and the paradoxical situation may arise so that hyperoxia (increased arterial oxygen partial pressure) leads to a reduced oxygen delivery to the vascular beds of various organs, especially of the brain or heart **(Brugniaux et al., 2018)**. The increase of perioperative oxygen stress is furthermore caused by the generation of reactive oxygen species and leads to molecular, cell, and organ damage **(Roberts &Cios, 2019)**. However, it has been argued that reactive oxygen species are not bad as a matter of principle but can be considered beneficial at low to moderate concentrations **(Lavie, 2015)**.

Postoperative pulmonary complications are one of the most serious problems during perioperative period **(Smetana et al., 2006; Canet &Gallart, 2013)**. The incidence of postoperative pulmonary complications depends on patients' co-morbidity, surgical procedures and anesthetic factors **(Smetana et al., 2006;Canet &Mazo, 2010)**. Among these, intraoperative ventilator settings are suggested to be one of the most crucial factors **(Serpa Neto et al., 2012)**. To prevent the occurrence of postoperative pulmonary complications, intraoperative lung protective ventilation (mainly comprised of low tidal volume, slight degree of positive end-expiratory pressure, and limited airway pressure) has been reviewed. This lung protective strategy has been steadily filtering into our ventilation strategy as a standard clinical practice **(Futier et al.,2013, Severgnini et al.,2013).**

In this clinical study, we will investigate the current practice of intraoperative ventilation during single lung ventilation in adult patients undergoing video assisted thoracoscopic lung surgeries versus conventional two lung ventilation. Furthermore, we will test the incidence of post-operative pulmonary complications with certain intraoperative ventilator settings.

2. **AIM/ OBJECTIVES**

The aim of the study is to evaluate single lung ventilation as an alternative to conventional ventilation in video assisted thoracoscopic lung surgeries despite the claimed intra operative and post-operative hypoxemia which could be avoided or even minimized by changing ventilatory setting.

3. METHODOLOGY:

Patients and Methods

- **Type of the study:** Interventional, prospective randomized clinical trial.
- **Study Setting:** The operating theaters of Ain Shams University Hospitals.
- **Study period:** Over four to six months, after the approval of Medical Research Ethical Committee.
- **Study population:**

Inclusion criteria:

- Age group: Adult patients from age of 21 years to 60 years
- Sex: Both sexes
- ASA Classification: patients with ASA classification II, III.
- Elective lung surgeries using video assisted thoracoscopic surgeries.

Exclusion criteria:

- Patients refuse to give informed consent.
- ASA Classification: ASA IV.
- Failure of thoracoscopic surgeries and continue as open thoracotomy
- Patients with ischemic heart diseases, where hypoxemia might be preexisting, or patient be more vulnerable to hypoxemia whatever the technique or time of hypoxia.
- Emergency lung surgeries.
- Patients underwent previous lung surgeries of any cause.
- Patients with pathology to the non-operated side.

Sampling method:

Patients will be randomly allocated by computer generated randomization into two equal groups A and B.

- **Group A:** Patients doing lung surgeries with single lung ventilation using double lumen endotracheal tube.
- **Group B:** Patients doing lung surgeries with two lung ventilation using conventional single lumen endotracheal tube without isolation (two lung ventilation).

Sample size justification:

Using PASS 11 program for sample size calculation setting power at 80% alpha error at 5%, reviewing results from previous study **(Kim et al.,2011)** showed that SaO_2 was higher among two lung ventilation versus one lung ventilation, mean +/- Standard Deviation (99.8 +/- 0.6 Versus 97.8 +/- 1.6). Based on these results a sample size of at least 60 patients (30/group) will be needed.

Ethical considerations:

The study protocol will receive ethical approval from the Medical Research Ethical Committee, Faculty of Medicine, Ain Shams University.

Informed written consent will be obtained from each patient before patients' allocation.

Study Procedures:

Patients will be randomly allocated into two equal groups.

Preoperative setting: Pre-operative assessment will be done by accurate history taking, full physical examination, laboratory and radiological investigations.

Intraoperative setting:

- Standard perioperative monitoring will include pulse oximetry, electrocardiogram, end-tidal CO_2 measurement, inhaled volatile agent concentration, invasive blood pressure measurement, and arterial blood gases measurement.
- Baseline parameters such as oxygen saturation, systolic, diastolic and mean blood pressure, heart rate will be recorded.
- Intravenous line will be inserted.
- Invasive arterial line will be inserted for continuous monitoring of arterial blood pressure and arterial blood gases sampling.
- For all patients, general anesthesia will be induced by intravenous route using midazolam 0.04mg/kg, fentanyl1-2μg/kg, propofol 1-2 mg/kg, atracurium 0.5 mg/kg.
- This will be followed by endotracheal intubation and mechanical ventilation with Maintenance of anesthesia will be achieved by isoflurane 1.5 in oxygen and air (50:50) and atracurium 0.1mg/kg every 20 minutes, so as to maintain end tidal CO_2 between 35 to 45 mm Hg.
- Arterial blood gases will be sampled every hour or if there is any change in oxygen saturation, end tidal CO2, or vital data.

Group A: (the Single lung ventilation)

- After induction of anesthesia, intubation will be done by double lumen endotracheal tube. The operated lung will be deflated on starting the surgical procedure and single lung ventilation will be started.
- The double lumen endotracheal tube used will be left-sided (Mallinckrodt™ endobronchial tube, COVIDIEN™) of the suitable size. The longer lumen (bronchial lumen) is designed to reach the main stem bronchus while the shorter lumen (tracheal) ends in the distal trachea.
- The patient will be placed in the lateral position ready for surgery. Single-lung ventilation of the dependent lung will be initiated by clamping the double-lumen tube connector to the nondependent lung at end expiration.
- If proper positioning of the double lumen endotracheal tube fails, intubation will be done using conventional single lumen tube and the patient will be considered in the group B, unless any complication occurs during intubation so that the patient will be excluded from the study.
- If significant intraoperative hypoxia occurs from single lung ventilation, lung isolation is stopped by removing the clamp of the double lumen connector and two lung ventilation is resumed. Lung recruitment by hyperinflation of both lungs till regain normal bilateral lung inflation and good oxygen saturation. Those patient will be excluded from the study.
- Ventilator settings after intubation are inspiratory oxygen fraction of 1.0, tidal volume of 8 ml/kg, respiratory rate set to maintain an end tidal CO2 between 30 and 35 mmHg, peak inspiratory pressure limit of 35 cm H_2O, and this will be maintained after single lung ventilation initiation with an inspiratory oxygen fraction of 0.5 as long as oxygen saturation is above 96% and no significant hypoxia occurs. Airway management including double lumen endotracheal tube placement will be performed by the anesthesia consultant.

Group B: (the two-lung ventilation)

- After induction of anesthesia, intubation will be done by conventional single lumen endotracheal tube. The two lungs will be inflated together and if lung inflation would interfere with the surgical procedure, both lungs will be deflated for brief time so that no significant hypoxia will occur, then the two lungs will be re-inflated again.
- If lung inflation interferes with the surgical procedure and hinders it, and if the surgery could stop for a while so that single lumen endotracheal tube will be changed by another double lumen endotracheal tube, and the patient will be considered in group A unless any complication occurs during intubation so that the patient will be excluded from the study.

- Same ventilator setting will be applied at the beginning of surgical procedure, inspiratory oxygen fraction of 1.0, tidal volume of 8 ml/kg, respiratory rate set to maintain an end tidal CO2 between 30 and 35 mmHg peak inspiratory pressure limit of 35 cm H2O and this will be maintained after the two lung ventilation initiation with an inspiratory oxygen fraction of 0.5 as long as oxygen saturation is above 96% and no significant hypoxia occurs.

Post-operative setting:

- Common complications in the postoperative period include sputum retention, collapse, consolidation and edema on the operative side. These complications will be recorded and managed accordingly.
- Postoperative pain management in intensive care unit will be intravenous morphine 3mg every 6h in the 1st 24 hours. Adequate pain relief and ability to cough are the most important factors in preventing chest complications.
- Patients will be nursed in intensive care unit for monitoring vital signs, chest drains and for pain relief, physiotherapy, inhaler therapy, and fluid balance.
- Postoperative chest X-ray will be performed in recovery to exclude pneumothorax, hemothorax, misplaced chest drains and collapse.

Measured outcomes:

Primary outcome:

- Incidence of hypoxemia intraoperative and first 24 hours post-operative by monitoring oxygen saturation using pulse oximetry and by serial arterial blood gases (pH, PO_2, SO_2, CO_2, HCO_3).

Secondary outcome:

- Incidence of failure to correct hypoxemia during single lung ventilation by all measures.
- Incidence of failure of two lung ventilation to achieve optimum surgical field so that it is changed to single lung ventilation.
- Occurrence of any complications intra operative and first 24 hours post-operative in intensive care unit.

Statistical analysis:

- Statistical analysis will be carried out using the statistical software SPSS program. Description of quantitative data as mean and standard deviation and qualitative data as number and percentage.

- Comparison between the two groups will be done by using the Chi-square test, independent t-test or Mann–Whitney U-test according to the distribution of data. A p-value less than 0.05 will be considered statistically significant.

End point:

- Persistent hypoxemia despite doing all recommended measures.
- 24 hours post-operative in the intensive care unit.

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