

Official Title: Adherence rate to lung protective mechanical ventilation in patients admitted to surgical intensive care units and associated clinical outcomes

Brief Title: Adherence to LPV in SICU and Associated Clinical Outcomes

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Introduction

Mechanical ventilation (MV) is one of the one organ support most frequently applied to patients admitted to intensive care units (ICUs). Despite considering as a life-saving intervention, MV may have detrimental effects, namely ventilator-induced lung injury (VILI)⁽¹⁾. A mechanical breath with positive airway pressure may overstretch alveoli, especially in the non-dependent part of the lungs, and subsequently result in barotrauma and volutrauma. While cyclic opening and closing of alveoli during mechanical breath due to alveolar collapse at the end of expiration can cause atelectrauma or cyclic atelectasis. All of these can lead to the activation of respiratory and systemic inflammatory response, so-called biotrauma. To minimize the effects of MV on VILI, the lung protective mechanical ventilation (LPV) strategy have been proposed and now generally accepted as a standard practice in mechanically ventilated patients⁽¹⁻³⁾. The LPV strategy is basically consisted of ventilation with low tidal volume of 6-8 mL/kg of predicted body weight (PBW) with limited plateau pressure of less than 30 cm H₂O plus applying sufficient amount of positive end-expiratory pressure (PEEP) to prevent atelectasis⁽¹⁻³⁾. The LPV strategy has been clearly demonstrated benefits not only in patients with acute respiratory distress syndrome (ARDS)^(4, 5) but also in

those with normal lungs^(1, 6, 7) including lessened respiratory and systemic inflammatory response and injured lungs, decreased duration of MV and length of stay (LOS), improved organ failure, and decreased pulmonary and other complications as well as mortality. Nevertheless, the adherence rate to the LPV strategy reported in the literatures is only approximately 40% in mechanically ventilated patients⁽⁸⁾ and patients with ARDS⁽⁹⁻¹¹⁾. For surgical patients, approximately 65% of those admitted to ICU require MV support either following operation or during their stay in ICU⁽¹²⁾. To date, there is limited data regarding MV management in surgical patients who required MV support perioperatively. Similarly, the difference in perioperative MV practices and their associated clinical outcomes has been not well determined in this setting. Therefore, the aim of this study is to explore the current practice of MV according to the LPV strategy applied to surgical patient admitted to surgical ICU (SICU) and their associated clinical outcome.

Methods

Study design and patient population. This is a prospective observational cohort study conducted in two SICUs at Siriraj Hospital. Generally, patients undergoing vascular, abdominal, urological, head and neck, orthopedic, plastic, otorhinolaryngologic, gynecologic, obstetric, and ophthalmologic surgeries who require perioperative care in ICU are admitted to these two SICUs and are eligible for inclusion. Patients undergoing cardiothoracic, neurological, trauma surgery and pediatric patients are admitted to other specific ICUs and are not included in this study. All patients whose age of 18 years old or more admitted to these two SICU and requiring MV support, either at SICU admission or during stay in SICU, via either endotracheal or tracheostomy tube with anticipated duration of 12 hours or more are included. Patients not requiring MV support during SICU stay, those requiring MV support for less than 12 hours in SICU, those requiring MV support for more than 24 hours prior to SICU admission, those included in this study once and re-admitted to the SICU, those requiring non-invasive MV support, moribund or terminal cases, and those who refuse to participate in the study are excluded from this study. Writing informed consents are obtained from all included patients or their relatives prior to inclusion or as soon as possible.

Study procedure. The inclusion is started on the day of the initiation of MV support, which is labeled as the index day. All included patients receive all medical care including resuscitation, medication, and MV support based on the

discretion of the primary care team. They are daily evaluated for 7 consecutive days following the index day or until they are discharged from the SICU or are deceased, whichever comes first. Ventilator parameters are recorded on the index day and then once a day between 06:00 and 09:00 in the morning for 3 consecutive days following the index day or until MV is liberated or patients are discharged from the SICU or are deceased, whichever comes first. The day of the liberation from MV is recorded. Pulmonary and other complications occurred during 7 days of the observation, SICU and hospital discharge status as well as status at 90 days following the index day are also documented. At 90 days following the index day, patients are followed up in the hospital if they are still admitted or by phone call if they have been discharged from the hospital.

Data collection. Demographic and baseline data recorded on the index day include age, gender, weight, height, comorbidities, smoking status and alcohol use (either never, stopped, current, or unknown), diagnosis at SICU admission, operation, type (either elective or emergency), site (thoracoabdominal, upper abdominal, lower abdominal, vascular, urological, head and neck, orthopedic, gynecologic and obstetric), and duration of surgery, intraoperative fluid balance, reasons for SICU admission (either planned SICU admission following elective or emergency surgery, unplanned SICU admission following elective or emergency surgery, or admission due to medical condition), reasons for MV support (after general anesthesia for surgery, respiratory failure, hemodynamic instability, or post-cardiac arrest), laboratory values, arterial blood gas, chest

radiograph, requirement of inotrope/vasopressor, presence of sepsis, ARDS, and acute kidney injury (AKI), Acute Physiology and Chronic Health Evaluation (APACHE) II score, Sequential Organ Failure Assessment (SOFA) score, predictive score for postoperative pulmonary complications (PCCs)⁽¹³⁾, and lung injury prediction score (LIPS)⁽¹⁴⁾. Daily evaluations include hemodynamic and clinical parameters, SOFA score, and fluid balance. Ventilator parameters include modes of MV, expired tidal volume, level of PEEP, measured respiratory rate, peak and plateau pressure or maximal airway pressure, fraction of inspired oxygen (FiO₂), inspiration to expiration ratio (I:E), minute ventilation, use of neuromuscular blocking agents, and arterial blood gas corresponding to the setting of MV. Pulmonary complications include pneumonia, ARDS, atelectasis, restoration of MV support after liberation from MV, pleural effusion, cardiogenic pulmonary edema, pneumothorax and new pulmonary infiltration. Other complications include stroke, myocardial ischemia/infarction, arrhythmias, AKI, sepsis, new infection other than pneumonia, and re-admission to the SICU. Duration of MV support, LOS in SICU and in hospital, SICU and hospital discharge status and status at 90 days either alive or death as well as activities of daily living measured by the Thai version of the Barthel index⁽¹⁵⁾ are also collected.

Study outcomes and sample size calculation. The primary outcome of this study is to determine the adherence rate to the LPV strategy at the initiation of MV support in mechanically ventilated patients in SICU. The LVP strategy in

this study is defined as ventilation with tidal volume of <8 mL/kg of PBW plus applying PEEP of at least 5 cm H₂O. Based on the previously reported adherence rate to the LPV strategy in mechanically ventilated patients of approximately 40%⁽⁸⁻¹¹⁾ with 80% power and 95% confidence interval, a sample size of 213 subjects is required. After 10% inflation for possible missing data, 235 subjects are planned to include. The secondary outcomes are factors associated with the adherence to the LPV strategy, incidences of pulmonary and other complications, LOS in SICU and in hospital, SICU and hospital discharge status, and status at 28 and 90 days following the initiation of MV support.

Statistical analysis. Data are expressed as mean with standard deviation, median with interquartile range (IQR) or number with percentage as appropriate. Student's t-test or Mann-Whitney U test is used to compare continuous variables, and chi-squared test or Fisher's exact test is used for categorical variables as appropriate. Univariate analyses are performed to identify potential factors associated with the adherence to the LPV strategy. A multivariate logistic regression model is used to identify the independent factors using stepwise approach to enter new variables with *p*-value of less than 0.2 into the model. Time-to-event variables are analyzed using Cox regression and are visualized by Kaplan–Meier curve. All statistical analyses are 2-tailed and *p*-value of less than 0.05 is considered as statistical significance. Data are prepared and analyzed using PASW Statistics 18 (SPSS Inc., Chicago, IL, USA).

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Siriraj Institutional Review Board
Certificate of Approval

COA no. Si 184/2018

Protocol Title(English) : Adherence rate to lung protective mechanical ventilation in patients admitted to surgical intensive care units and associated clinical outcomes

Protocol Title(Thai) : อัตราการตั้งเครื่องช่วยหายใจตามหลักการตั้งเครื่องช่วยหายใจแบบป้องกันการบาดเจ็บต่อปอดในผู้ป่วยที่เข้ารับการรักษานในหออภิบาลศัลยกรรมและผลลัพธ์ทางคลินิกที่เกี่ยวข้องกับการใช้เครื่องช่วยหายใจ

Protocol number : 077/2561(EC4)

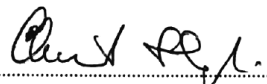
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Research site : Faculty of Medicine Siriraj Hospital

Approval date : March 23, 2018

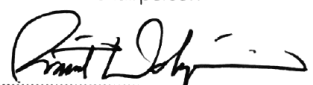
Expired date : March 22, 2019

This is to certify that Siriraj Institutional Review Board is in full compliance with international guidelines for human research protection such as the Declaration of Helsinki, the Belmont Report, CIOMS Guidelines and the International Conference on Harmonization in Good Clinical Practice (ICH-GCP)


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(Prof. Chairat Shayakul, M.D.)
Chairperson

30 MAR 2018

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date


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(Prof. Dr. Prasit Watanapa, M.D., Ph.D.)
Dean of Faculty of Medicine Siriraj Hospital

- 2 APR 2018

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date

Approval includes :

1. SIRB Submission form date March 14, 2018
2. Participant information sheet date March 13, 2018
3. Informed consent form date March 13, 2018
4. Telephone script
5. Case record form
6. Curriculum Vitae

All Siriraj Institutional Review Board (SIRB) Approved Investigators must comply with the following:

1. Conduct the research as approved by the SIRB and will not make any changes in the research without prior SIRB review and approval, except when necessary to eliminate apparent immediate hazards to participants.
2. Use only the forms bearing the 'SIRB APPROVED STAMP' in the research.
3. Conduct the informed consent process without coercion or undue influence, and give sufficient opportunity to consider participation. One copy of the consent and/or assent form must be given to the subject after it is signed.
4. Promptly report to the SIRB of any new information that may affect the safety and well-being of the subjects.
5. Report to the SIRB all serious adverse events, unanticipated problems, protocol deviation and/or violation in accordance with the SIRB policy and operating procedures.
6. Provide the progress report to the SIRB as a Continuing Review 30 days prior to the COA expiration for at least once a year from the approval date unless otherwise indicated. The Continuing Review must be used to renew approval prior to the expired date.
7. Provide the Final Report as a close-out within 30 days after the research is complete.

Non-compliance may result in the suspension or termination of the study.