Comparison of Pulmonary Gas Exchange According to Intraoperative Ventilation Modes for Mitral Valve Repair Surgery via Thoracotomy With One-Lung Ventilation: A Randomized Controlled Trial

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Objective: **Impaired pulmonary gas exchange after cardiac surgeries with cardiopulmonary bypass (CPB) often occurs, and the selection of mechanical ventilation mode, pressure-controlled ventilation (PCV) or volume-controlled ventilation (VCV), may be important for preventing hypoxia and improving oxygenation. The authors hypothesized that patients with PCV would show better oxygenation, compared with VCV, during one-lung ventilation (OLV) for mitral valve repair surgery (MVP) via thoracotomy.**

Design: **Randomized controlled trial.**

Setting: **University teaching hospital.**

Participants: **Sixty patients in each group.**

Interventions: **MVP was performed using thoracotomy with OLV by PCV or VCV.**

Measurements and Main Results: **Arterial partial pressure of oxygen (PaO_2) and fraction of inspired oxygen (F_IO_2) were measured before anesthesia induction (T0), at skin incision (T1), after administration of heparin (T2), at 30 minutes after CPB weaning (T3), just before departure from the operating room to the intensive care unit (ICU) (T4), and 1 hour after ICU admission (T5), and PaO_2/F_IO_2 ratio was calculated. Peak inspiratory pressure (PIP) and mean inspiratory pressure (P_{mean}) were recorded at T1, T2, T3, and T4. No significant difference was noted in the PaO_2/F_IO_2 ratio between the groups at any measured point. PIP in the PCV group at all measured points was lower than that in the VCV group (T1, $p < 0.001$; T2, $p < 0.001$; T3, $p < 0.001$; T4, $p = 0.025$, respectively). P_{mean} was not different between the two groups at any measured point.**

Conclusions: **PCV during OLV in patients undergoing MVP via a thoracotomy with OLV showed lower PIP compared with VCV, but this did not improve pulmonary gas exchange.**

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KEY WORDS: cardiac anesthesia, one-lung ventilation, pressure-controlled ventilation, volume-controlled ventilation

AMONG VARIOUS MECHANICAL VENTILATION modes, pressure-controlled ventilation (PCV) is thought to provide a more homogenous distribution of the ventilated gas, improve ventilation/perfusion mismatch, and contribute to better oxygenation.[1–4] These data and conclusions have been derived from observational/randomized studies in patients with respiratory failure or decreased functional residual capacity and in patients undergoing thoracic surgical procedures or coronary artery bypass surgery without cardiopulmonary bypass (CPB).

A median sternotomy is the traditional approach for cardiac surgery, but thoracotomy increasingly has been used for various reasons.[5–8] For thoracotomy, one-lung ventilation (OLV) is necessary and thought to lead to more deterioration of lung function, compared with two-lung ventilation (TLV), because of the increase in ventilation/perfusion mismatch and shunt, ischemia/reperfusion injury, and the inflammatory reaction from re-expansion of the collapsed lung.[9–11] However, mitral valve repair surgery under thoracotomy with OLV did not increase the adverse effects on perioperative pulmonary function.[12]

Pulmonary gas exchange often becomes impaired after cardiac surgery with CPB because of inflammatory reactions and ischemic tissue damage.[13–15] Thus, the selection of intraoperative mechanical ventilation mode may play an important role in preventing hypoxia and improving oxygenation, but it has not been well established.

The aim of the present study was to evaluate the effects of different intraoperative mechanical ventilation modes on pulmonary gas exchange in patients undergoing cardiac surgery with CPB.

The authors hypothesized that patients with PCV would show better oxygenation compared with volume-controlled ventilation (VCV) in cardiac surgeries with CPB under thoracotomy with OLV. This study compared pulmonary gas exchange during mitral valve repair surgery under thoracotomy with OLV between PCV and VCV.

METHODS

The authors obtained approval (KUH1160022, June 2011) from the Institutional Review Board of Konkuk University Medical Center, Seoul, Korea. The study was registered at http://cris.nih.go.kr (KCT0000184). Written informed consent was obtained from the patients undergoing mitral valve repair surgery.

Patients were studied prospectively at a university teaching hospital from June 2011 to February 2013. Exclusion criteria were (1) urgent or emergency surgery, (2) other concurrent cardiac valvular surgery, (3) age < 16 years, (4) left or right ventricular functional reduction (ejection fraction < 40%), (5) severe pulmonary hypertension aggravated by OLV, (6) preexisting respiratory disease, (7) arterial partial pressure of oxygen (PaO_2)/fraction of inspired oxygen (F_IO_2) ratio < 300 mmHg before anesthesia induction, (8) preoperative arrhythmia, (9) intracardiac shunt disease, (10) severe renal disease, (11) severe hepatic disease, (12) hematocrit (Hct) < 30% at preoperative evaluation, or (13) reoperation for cardiac valvular disease. The surgical approach was decided by the surgical team and patients before arrival at the operating room and confirmed by anesthesiologists at anesthesia induction. The trial design of the study was parallel and the

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patients were allocated randomly (allocation ratio = 1:1) to undergo either PCV or VCV using sealed envelopes opened before anesthesia induction.

Mitral valve repair surgeries were performed by a single surgical team, and CPB was performed by a single perfusionist. The anesthesiologists, surgeons, nurses, and perfusionists were blinded to the study.

The primary outcome variable was the PaO_2/F_IO_2 ratio immediately before departure from the operating room to the intensive care unit (ICU). A PaO_2/F_IO_2 ratio of 285.4 ± 88.8 mmHg was determined from 10 patients undergoing mitral valve repair surgery under thoracotomy with OLV using VCV. For the PaO_2/F_IO_2 ratio, a minimum 20% difference (PCV group with a PaO_2/F_IO_2 ratio > 300 mmHg) between the 2 groups was considered to be clinically significant. A sample size of 52 in each group was determined to be appropriate to achieve a power of 0.9 and an α value of 0.05. Secondary outcome variables were the intubation time and length of ICU stay. Using the same method to determine sample sizes for the intubation time (615 ± 205 minutes) and length of ICU stay (2312 ± 634 minutes), sample sizes of 60 and 41, respectively, were determined.

Anesthesiologists were asked to anesthetize the patient using the following standardized protocols. After achieving invasive arterial blood pressure monitoring and other noninvasive patient monitoring, including pulse oximetry, electrocardiography, cerebral oximetry, and bispectral index, anesthesia induction and maintenance were conducted using target-controlled infusion of remifentanil and propofol. During anesthesia, the plasma concentration of remifentanil was fixed at 10 ng/mL and the effect-site concentration of propofol was adjusted to maintain a bispectral index of 40 to 60. Muscle relaxation was achieved by administering rocuronium with peripheral neuromuscular transmission monitoring. All patients were intubated with a double-lumen endotracheal tube (DLT; Silbroncho, Fuji Systems Corporation, Tokyo, Japan) for OLV. In the PCV group, the ventilator (ADU, Datex-Ohmeda, Helsinki, Finland) settings during TLV were as follows: A fresh gas flow of 4 L/min (F_IO_2 0.4); a peak inspiratory pressure (PIP) adjusted to achieve the tidal volume, calculated as ideal body weight (50 [female: 45.5] + 0.91 · [height: 152.4]) × 7 mL; a respiratory rate adjusted according to the end-tidal carbon dioxide pressure ($EtCO_2$) at 35 to 40 mmHg measured by capnography (S/5 Compact Anesthesia Monitor, Datex-Ohmeda, Helsinki, Finland) with an inspiratory/expiratory ratio of 1:2; and no application of positive end-expiratory pressure (PEEP). In the VCV group, the same ventilator settings were used except that the prescribed tidal volume was applied, calculated using the same method as that for the PCV group, instead of adjusting PIP. The ventilator settings for OLV in both groups followed the same settings except that an F_IO_2 value of 1.0 was used. Pulmonary artery catheterization and transesophageal echocardiography probe insertion for perioperative cardiac functional monitoring were performed after anesthesia induction.

The adequate position and bronchial balloon volume of the DLT were confirmed by fiberoptic bronchoscopic examination before and after the patients' position change from the supine to the lateral position. OLV was initiated before the splitting of the right fourth intercostal space and completed at the time of thorax closure. After aortic cross-clamp (ACC) application with CPB, OLV was stopped and the bronchial balloon of the DLT was decompressed. When the ACC was released, OLV was restarted. Immediately before switching from OLV to TLV, the lung recruitment maneuver (breath holding with a TLV of PIP 25 cmH_2O for 10 seconds 3 to 4 times) was applied. The OLV duration was defined as the sum of the period from OLV initiation to CPB start and the period from CPB weaning to TLV initiation because the oxygenation was determined by CPB during OLV with CPB.

Mitral valve repair procedures were conducted via thoracotomy with surgical incisions of 10-cm length in the fourth intercostal space with the patient's right back elevated up to 30 degrees. Cases requiring TLV because of low oxygen concentration (<90%), even with PEEP application to the dependent lung and continuous positive airway pressure (CPAP) to the nondependent lung or PIP > 30 cmH_2O during OLV, were excluded from the analysis.

During the entire anesthesia period, except during CPB, the mean systemic blood pressure and cardiac index were maintained above 60 mmHg and above 2.0 L/min/m^2, respectively, with medications or fluid administration according to the variations of the stroke volume index and echocardiographic findings. Milrinone was administered when the mean pulmonary artery pressure was higher than 30 mmHg. Administration of crystalloid solution was performed to compensate for the maintenance fluid requirements, fluid redistribution, and evaporative surgical fluid losses based on the body weight (4 mL/kg). The estimated blood that was lost was replaced with colloid solution until laboratory values reached the predetermined indications of transfusion. Red blood cells (RBCs) were transfused when the Hct was less than 20% during CPB and 30% after CPB. Other blood products were not used.

After arrival at the ICU, a different mechanical ventilator (Puritan Bennett 840 Ventilator System; Puritan-Bennett Corporation, Pleasanton, CA, USA) and strategy were applied to the patients according to the standard protocol of this institution.

After a bolus injection of 300 units/kg of heparin, arterial and venous cannulations for CPB were conducted when the activated coagulation time (ACT) was greater than 450 seconds. In both groups, arterial cannulation was performed using the right femoral artery and venous cannulation was performed using the superior vena cava and right femoral vein. During CPB, ACT was maintained at greater than 450 seconds. CPB consisted of a reservoir, a membrane oxygenator, a roller pump, and a heat exchanger. The priming solution comprised normal saline, $NaHCO_3$, 20% albumin, 20% mannitol, antibiotics, heparin, and calcium gluconate. The initial flow of the CPB was 60 mL/kg/min, which was adjusted according to the level of hemodilution and temperature. Retrograde cold blood cardioplegic solution (20 mL/kg) was infused via the coronary sinus for myocardial protection after ACC application. Blood cardioplegic solution (1 L) contained the following: 6.43 g NaCl, 1.193 g KCl, 0.176 g $CaCl_2$, and 3.253 g $MgCl_2$ (pH 7.4; temperature, 4-8°C).

F_IO_2 and PaO_2 were measured before anesthesia induction (T0), at skin incision (T1), after administration of heparin (T2), at 30 minutes after CPB weaning (T3), just before departure from the operating room to ICU (T4), and 1 hour after ICU admission (T5), and the PaO_2/F_IO_2 ratio was determined. PIP and the mean inspiratory pressure (P_{mean}) were also measured at the same time, except at T5, using a different mechanical ventilator and strategy.

The amounts of medications (inotropes and vasopressors), fluid administration, transfusion requirements, and urine output (UO) were recorded intraoperatively. Postoperative hemoglobin (Hb), Hct, and serum creatinine (Cr) were measured at T4. OLV duration, CPB time, intubation time, and ICU stay were recorded. All the data of the present study were collected by anesthesiologists who were blinded to the study.

The extubation process was initiated when the patients' status and the following criteria were met[16]: Stable hemodynamic status, UO ≥ 0.5 mL/kg/h, temperature > 36°C, and chest tube drainage < 100 mL/h. At that time (approximately 45 minutes before extubation), morphine, 0.2 mg/kg, was administered to all patients for pain management, and the patients' hemodynamic parameters and pain and sedation scales were assessed repeatedly. If the patients complained about pain, an additional 5 mg of morphine were administered.

Extubation was performed when the patients' status and the following criteria were met: Proper response to verbal commands;

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