Int J Clin Exp Med 2015;8(8):13099-13108
www.ijcem.com /ISSN:1940-5901/IJCEM0011234

*Original Article*

# Echocardiographic evaluation of pulmonary venous blood flow and cardiac function changes during one-lung ventilation

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Received June 9, 2015; Accepted August 1, 2015; Epub August 15, 2015; Published August 30, 2015

**Abstract:** Objectives: The intra-pulmonary shunt induced by one-lung ventilation (OLV), is alleviated by increased pulmonary blood flow by gravitational redistribution and hypoxic pulmonary vasoconstriction. We investigated the changes of pulmonary venous blood flow (PVBF) and biventricular function during OLV with echocardiography. And the correlation between PVBF and intra-pulmonary shunt fraction (Qs/Qt) was evaluated. Methods: PVBF of the left upper pulmonary vein and cardiac function were measured with echocardiography in twenty-five patients who underwent elective thoracic surgery in left lateral decubitus. Qs/Qt and $PaO_2$ were measured with blood gas analysis. Data was obtained at 10 min after two-lung ventilation in supine (TLV-S) and lateral decubitus position (TLV-L), and at 10, 20 and 30 min after OLV in lateral decubitus position (OLV-10, -20 and -30). Results: There were significant changes in PVBF among TLV-S, TLV-L and OLV-10 (959.5±280.8, 1416.9±489.7 and 1999.9±670.5 ml/min; $P<0.05$, respectively). There were not differences in PVBF, Qs/Qt and $PaO_2$ among OLV-10, -20 and -30. There were an inverse correlation between percent change of PVBF and change of Qs/Qt ($r^2 = 0.5$; $P<0.0001$) and positive correlations between the percent change of PVBF and change of $PaO_2$ ($r^2 = 0.4$; $P<0.0001$) during OLV over TLV-L. No significant changes in biventricular systolic and diastolic function were observed during positional change and OLV. Conclusions: A remarkable change of PVBF relevant to gravitational distribution and hypoxic pulmonary vasoconstriction was proved by echocardiography. And PVBF changes could represent the changes of Qs/Qt and $PaO_2$ during OLV. However, biventricular function was not impaired during OLV.

**Keywords:** One-lung ventilation, pulmonary venous blood flow, intra-pulmonary shunt, arterial oxygenation, hypoxic pulmonary vasoconstriction, echocardiography, cardiac function

## Introduction

One-lung ventilation (OLV) is required in thoracic surgery, but because the other lung is not ventilated, a ventilation/perfusion mismatch may result from the sustained pulmonary perfusion in the non-ventilated lung. Intraoperative hypoxemia during OLV is a common with an incidence as 4-10% [1-3], posing a great challenge to anesthesiologists. Fortunately, gravitational redistribution of the pulmonary blood flow [4, 5] and hypoxic pulmonary vasoconstriction (HPV) acts as a protective mechanism to alleviate the intra-pulmonary shunt during OLV [6].

Since intra-pulmonary shunt was demonstrated to correlate with pulmonary blood flow [7], the importance of pulmonary blood flow distribution resulting from the pulmonary vasculature of the pulmonary vessel has gained attention. To date, intra-pulmonary shunt has been evaluated by using single-photon emission computed tomography (SPECT) or blood gas analysis. Previous studies measured pulmonary blood flow by using radioactive-labeled microspheres or single-photon emission computed tomography [7, 8]. However, only few studies have closely identified the effect of patients' positional changes and OLV on pulmonary blood flow during thoracic surgery. As the heart and lungs are adjacent to each other, a close interaction exists between them, which is called cardiopulmonary interaction. Several studies have examined the postoperative cardiac function after lung surgery [9-11], but the changes

in cardiac function during lung isolation for surgery have not been systematically evaluated.

Echocardiography has been proven to be relatively noninvasive, widely applicable in intraoperative evaluations and clinically useful [12]. Recently, transesophageal echocardiography (TEE) can effectively visualize the pulmonary vein, with higher sensitivity and specificity than other imaging modalities for measuring pulmonary venous blood flow (PVBF) [13-15]. Accordingly, its application has recently expanded to include atrial fibrillation ablation procedures and lung transplantation [14-16]. We investigated the changes of PVBF assessed by echocardiography could represent pulmonary blood flow redistribution relevant to gravitational effect and HPV. We evaluated the correlation between the changes of PVBF and changes in intra-pulmonary shunt and arterial oxygenation during thoracic surgery with OLV. We also observed the change in cardiac performance using echocardiography in patients undergoing thoracic surgery with OLV in lateral decubitus position.

## Materials and methods

This study was approval by the institutional review board of Severance Hospital, Yonsei University Health System, Seoul, South Korea (Ref. 4-2014-0486) and registered at Clinical Trials.gov (NCT 02365311). All of the participants provided written informed consent before participation.

### *Patients' characteristics*

We included twenty-five patients with isolated right lung cancer who were scheduled to undergo video-assisted thoracoscopic surgery in left lateral decubitus position. The inclusion criteria were healthy patients (classified by the American Society of Anesthesiologists physical status class II and III) above 20 years of age. The exclusion criteria were cardiovascular disease, arrhythmia, severe functional liver or kidney disease, chronic obstructive or restrictive pulmonary disease and obesity (body mass index >30 $kg/m^2$).

### *General anesthetic management*

Standard monitoring devices were attached to the patients as they arrived at the operating room. Anesthesia was induced by administering 1.5 mg/kg propofol and 1.0 μg/kg remifentanil. Tracheal intubation with 37- or 39-Fr left-sided double-lumen tube (Broncho-Cath®; Mallinckrodt Medical Inc., Athlone, Ireland) was facilitated with 0.9 mg/kg rocuronium. The position of the left side double-lumen tube was confirmed by fiberoptic bronchoscopy. After the induction of anesthesia, a 20 G radial artery catheter was inserted. A 7-Fr central venous catheter (Arrow International®; Reading, PA, USA) was inserted in the right internal jugular vein. The length of the central venous catheter was calculated by using a height-based formula for placement for the constant placement near the right atrium [17]. Placement of the catheter tip was confirmed by portable chest radiography. Anesthesia was maintained with 1.0-3.0% sevoflurane, 0.1-0.4 μg/kg/min remifentanil and 4.0-8.0 μg/kg/min rocuronium. An autoflow pressure-controlled ventilation mode (Primus i® ventilator; Dräger™ Medical, Lübeck, Germany) was used for ventilation in all of the patients. Tidal volume was set to units of 6 ml/kg and inspiratory to expiratory ratio of 1:2. Fractional ratio of inspiratory oxygen ($FiO_2$) was set at 1.0 until completion of the study.

### *Respiratory and hemodynamic measurements*

The respiratory rate was adjusted to maintain an end-tidal carbon dioxide tension of 34-42 mmHg. Hemodynamic variables, respiratory variables and arterial and central venous blood gas analysis parameters were recorded at five time points as follows: 10 min after two-lung ventilation (TLV) in supine position (TLV-S), 10 min after TLV in left lateral decubitus position (TLV-L), 10 min (OLV-10), 20 min (OLV-20) and 30 min after OLV in left lateral decubitus position (OLV-30). The hemodynamic parameters measured included heart rate (HR), mean arterial pressure (MAP) and central venous pressure (CVP), while the respiratory variables included, peak airway pressure ($AP_{Peak}$), mean airway pressure ($AP_{Mean}$) and dynamic compliance ($C_{dyn}$). Intra-pulmonary shunt fraction (Qs/Qt) was also calculated. The oxygen content ($CxO_2$) in arterial and central venous blood was calculated using the following equation: $CxO_2 = (1.34 \times Hb \times SxO_2) + (0.0031 \times PxO_2)$, in which Hb = hemoglobin concentration (g/dl) and $SxO_2$ = oxygen saturation. Qs/Qt was determined using the following formula: Qs/Qt =

**Table 1.** Patient characteristic and Intraoperative variables

| Characteristic | (n=25) |
|---|---|
| Age (yr) | 63.7±10.8 |
| Male/Female ratio | 12:13 |
| Height (cm) | 161.5±6.3 |
| Weight (kg) | 60.3±8.3 |
| Body mass index (kg/m$^2$) | 27.4±4.2 |
| Preoperative PFT | |
| FVC (l) | 3.1±0.8 |
| FVC (% predicted) | 95.1±13.6 |
| $FEV_1$ (l) | 2.4±0.5 |
| $FEV_1$ (% predicted) | 104.0±12.3 |
| $FEV_1$/FVC (% predicted) | 77.7±7.7 |
| $DL_{CO}$ (ml/mmHg/min) | 17.4±4.2 |
| Intraoperative data | |
| Duration of surgery (min) | 147.2±57.4 |
| Duration of anesthesia (min) | 161.8±62.6 |
| Time of OLV (min) | 133.2±54.2 |
| Intake fluid (ml) | 504.4±40.3 |
| Urine output (ml) | 200.2±118.8 |
| Estimated blood loss (ml) | 85.6±6.7 |
| Total ephedrine dose (mg) | 4.2±6.6 |

Values are mean ± SD or number. PFT = pulmonary function test; FVC = forced vital capacity; $FEV_1$ = forced expiratory volume in 1 sec; $DL_{CO}$ = diffusion capacity of lung for carbon monoxide; OLV = one-lung ventilation.

$(CcO_2\text{-}CaO_2)/(CcO_2\text{-}CvO_2)$, where the central venous oxygen saturation ($ScvO_2$) is considered to be equal to the mixed venous oxygen saturation ($SvO_2$). $CcO_2$, $CaO_2$, $CvO_2$ are $O_2$ contents in pulmonary capillary, systemic arterial, and mixed venous blood, respectively. If MAP decreased by >20% compared to its post induction value in this study, vasoactive drugs such as ephedrine were administered. If $SpO_2$ as measured by pulse oximetry decreased to <90% during OLV, TLV was performed to terminate the study.

*Echocardiographic measurement*

The anesthetists inserted a 4 to 7 MHz multiplane TEE probe (6Tc; General Electric, Horten, Norway) via the esophagus and connected it to a cardiac ultrasonographic system (Vivid E9; General Electric, Horten, Norway). Standard mid-esophageal four-chamber and transgastric short-axis TEE views were obtained. Echocardiographic measurement values were recorded at five time points as follows: 10 min after TLV in supine position (TLV-S), 10 min after TLV in left lateral decubitus position (TLV-L) and 10 min (OLV-10), 20 min (OLV-20) and 30 min (OLV-30) after OLV in left lateral decubitus position. The left upper pulmonary vein was located just lateral to the left atrial appendage, after withdrawal of the probe from the two-chamber view with a slight turn to the left. It was possible to calculate the pulsed-wave Doppler velocity flow of the left upper pulmonary vein when the sector was rotated 30 to 60° or even up to 90°. Color and pulsed-wave Doppler measurements were performed. Doppler sample volume was placed as parallel as possible to the flow, 4 mm away from left upper pulmonary vein junction and the left atrium. The largest diameter obtained at any place was used for left upper pulmonary vein ostial diameter. Doppler sample blood flow of the left upper pulmonary vein was assessed by using the velocity time integral (VTI) obtained by pulsed-wave Doppler measurements and the cross-sectional area (CSA) of the left upper pulmonary vein. The PVBF (PVBF) was calculated by using the following formula: PVBF = VTI × CSA × HR. Assuming a circular shape, the CSA of the LUPV was calculated as follows: $CSA = \pi \times (D/2)^2$, where D is the pulmonary vein internal diameter. To identify the left ventricular (LV) systolic function and dimension, LV end-diastolic area (LVEDA), LV end-systolic area (LVESA) and ejection fraction (EF) were measured in the mid-esophageal four-chamber view. Fractional area change (FAC) was calculated in the mid-esophageal four-chamber view by using the following formula: FAC = ([EDA-ESA]/EDA) × 100. RV end-diastolic area (RVEDA), RV end-systolic area (RVESA), RV EF and RV FAC for RV systolic function were measured in the mid-esophageal four-chamber view. Tricuspid annular plane systolic excursion (TAPSE) was used to assess RV systolic function [10]. To assess LV and RV diastolic function, pulsed-wave Doppler ultrasonography was used to measure the transmitral and transtricuspid flow. The peak early (E) transmitral filling and transtricuspid inflow velocities and deceleration time (DT) of the E wave were measured. Mitral annulus velocities (e', s') were measured at the septal annulus by tissue Doppler imaging. Tricuspid annulus velocities (e', s') were also measured at the lateral annulus by tissue Doppler imaging. E/e' was calculated by using the above results. Cardiac output (CO) was assessed based on

**Table 2.** Respiratory and hemodynamic variables

| | TLV-S | TLV-L | OLV-10 | OLV-20 | OLV-30 |
|---|---|---|---|---|---|
| $PaO_2$ (mmHg) | 381.4±90.9 | 354.2±72.1 | 232.0±82.5*,† | 203.0±67.1*,† | 214.5±95.6*,† |
| $PaCO_2$ (mmHg) | 37.3±3.7 | 38.9±4.8 | 39.8±2.6 | 39.5±4.1 | 39.2±3.9 |
| Qs/Qt (%) | 25.4±7.9 | 28.0±10.5 | 35.5±7.9*,† | 38.3±7.0*,† | 35.2±6.9*,† |
| $SvO_2$ (%) | 89.8±4.1 | 92.2±4.5 | 87.16±5.0 | 87.2±5.0 | 85.9±5.0 |
| $AP_{peak}$ ($cmH_2O$) | 12.6±3.1 | 13.8±3.8 | 18.4±2.5*,† | 19.0±2.3*,† | 18.7±2.3*,† |
| $AP_{mean}$ ($cmH_2O$) | 4.3±1.3 | 4.7±1.5 | 5.9±1.2*,† | 6.4±1.4*,† | 6.3±1.4*,† |
| $C_{dyn}$ ($ml/cmH_2O$) | 37.9±7.7 | 35.2±7.5 | 23.2±4.7*,† | 22.4±4.1*,† | 22.5±3.9*,† |
| MAP (mmHg) | 89.4±12.6 | 87.4±11.4 | 94.6±13.8 | 87.1±10.1 | 85.9±11.3 |
| HR (beats/min) | 78.8±12.6 | 78.5±11.9 | 81.9±13.7 | 83.7±12.7 | 79.4±17.9 |
| CVP (mmHg) | 7.9±2.2 | 8.0±2.1 | 10.2±2.1*,† | 9.8±3.2*,† | 9.8±2.4*,† |

*$P$<0.05 compared to TLV-S. †$P$<0.05 compared to TLV-L. $PaO_2$ = arterial oxygen tension; $PaCO_2$ = arterial carbon dioxide tension; $SvO_2$ = central venous oxygen saturation; $AP_{peak}$ = peak airway pressure; $AP_{mean}$ = mean airway pressure; $C_{dyn}$ = dynamic compliance; MAP = mean arterial pressure; HR = heart rate; CVP = central venous pressure. TLV-S = 10 min after two-lung ventilation in supine position; TLV-L = 10 min after two-lung ventilation in left lateral decubitus position; OLV-10, OLV-20 and OLV-30 = 10 min, 20 min and 30 min after one-lung ventilation in left lateral decubitus position, respectively.

**Table 3.** Left ventricular function

| | TLV-S | TLV-L | OLV-10 | OLV-20 | OLV-30 |
|---|---|---|---|---|---|
| LVEDA ($cm^2$) | 22.3±5.5 | 24.9±5.4 | 25.6±5.8 | 23.0±5.4 | 23.0±4.9 |
| LVESA ($cm^2$) | 14.5±5.5 | 17.6±5.4 | 15.8±4.9 | 16.3±10.6 | 13.8±4.8 |
| LV EF (%) | 48.5±16.4 | 48.6±12.9 | 51.3±11.4 | 51.4±10.6 | 54.4±13.5 |
| LV FAC (%) | 38.6±14.3 | 37.8±12.2 | 37.6±10.7 | 39.0±11.0 | 40.9±12.8 |
| CO (l/min) | 4.8±1.4 | 5.2±1.0 | 5.2±1.0 | 5.2±1.0 | 5.0±1.0 |
| MV e' (cm/s) | 5.1±2.2 | 5.2±2.4 | 5.5±2.6 | 6.4±2.4 | 6.2±1.7 |
| MV s' (cm/s) | 4.3±1.4 | 4.6±1.8 | 4.7±1.5 | 5.3±1.5 | 5.2±1.3 |
| MV DT (ms) | 143.3±64.6 | 156.1±71.4 | 148.3±45.2 | 142.1±49.5 | 143.4±44.4 |
| MV E/e' | 11.1±7.0 | 12.2±5.7 | 12.1±4.9 | 12.1±4.8 | 11.1±5.3 |

LVEDA = left ventricular end-diastolic area; LVESA = left ventricular end-systolic area; EF = ejection fraction; FAC = fractional area change; CO = cardiac output; MV = mitral valve; MV e' = peak early diastolic mitral annular velocity; MV s' = peak systolic mitral annulus velocity; DT = deceleration time; MV E = transmitral flow E (early diastolic) wave; TLV-S = 10 min after two-lung ventilation in supine position; TLV-L = 10 min after two-lung ventilation in left lateral decubitus position; OLV-10, OLV-20 and OLV-30 = 10 min, 20 min and 30 min after one-lung ventilation in left lateral decubitus position, respectively.

**Table 4.** Right ventricular function

| | TLV-S | TLV-L | OLV-10 | OLV-20 | OLV-30 |
|---|---|---|---|---|---|
| RVEDA ($cm^2$) | 17.0±4.9 | 18.1±4.7 | 18.1±4.0 | 18.1±4.4 | 17.7±3.4 |
| RVESA ($cm^2$) | 8.6±3.2 | 9.6±3.2 | 9.1±2.5 | 9.8±3.0 | 9.0±3.3 |
| TAPSE (mm) | 18.8±4.7 | 19.8±5.5 | 19.8±6.2 | 18.4±4.2 | 17.8±4.8 |
| RV EF (%) | 59.9±13.1 | 61.2±10.5 | 62.2±15.1 | 62.6±9.9 | 62.6±14.2 |
| RV FAC (%) | 45.9±11.8 | 49.1±10.2 | 48.5±13.4 | 49.2±9.8 | 49.6±13.0 |
| TV e' (cm/s) | 4.8±1.7 | 4.1±1.7 | 4.2±1.8 | 4.7±1.2 | 4.6±1.3 |
| TV s' (cm/s) | 2.4±1.3 | 2.6±1.2 | 2.4±0.8 | 2.2±0.9 | 2.8±0.7 |
| TV DT (ms) | 151.1±50.7 | 139.3±50.4 | 178.9±42.2† | 154.2±45.8 | 154.7±40.9 |
| TV E/e' | 8.1±3.9 | 7.4±4.0 | 7.4±3.0 | 7.0±2.2 | 8.2±3.6 |

†$P$<0.05 compared to TLV-L. RVEDA = right ventricular end-diastolic area; RVESA = right ventricular end-systolic area; TAPSE = tricuspid annular plane systolic excursion; EF = ejection fraction; FAC = fractional area change; TV = tricuspid valve; TV e' = peak early diastolic tricuspid annular velocity; TV s' = peak systolic tricuspid annulus velocity; DT = deceleration time; TV E = transtricuspid flow E (early diastolic) wave; TLV-S = 10 min after two-lung ventilation in supine position; TLV-L = 10 min after two-lung ventilation in left lateral decubitus position; OLV-10, OLV-20 and OLV-30 = 10 min, 20 min and 30 min after one-lung ventilation in left lateral decubitus position, respectively.

**Table 5.** Intra- and inter-observer variability of echocardiographic parameters

| | Intra-observer variability (%) | Inter-observer variability (%) |
|---|---|---|
| LVEDA | 3.8 (2.9-4.2) | 4.6 (4.7-6.1) |
| LV FAC | 3.3 (2.7-3.9) | 4.5 (2.9-5.1) |
| MV e' | 1.0 (0.9-1.7) | 1.2 (0.8-2.7) |
| MV DT | 6.5 (4.7-7.6) | 7.2 (4.8-8.1) |
| TAPSE | 2.3 (1.6-3.4) | 2.5 (1.5-3.5) |
| RVEDA | 2.1 (1.6-2.7) | 3.7 (1.9-4.2) |
| VTI | 6.9 (5.3-8.5) | 8.6 (7.2-11.7) |

Values are proportion (95% CI). LVEDA = left ventricular end-diastolic area; FAC = fractional area change; MV = mitral valve; MV e' = peak early diastolic mitral annulus velocity; DT = deceleration time; TAPSE = tricuspid annular plane systolic excursion; RVEDA = right ventricular end-diastolic area; VTI = velocity-time integral.

stroke volume (SV) by using pulsed-wave Doppler measurements from the LV outflow tract. CO was calculated by using the following equation: CO = SV × HR. The means of all the variables were measured over three cardiac cycles of end-expiration. All of the studies were performed by a single operator. Analysis of the echocardiographic data was performed by two anesthesiologists to determine intra-observer and inter-observer variability (**Table 5**). A random sample of 25% of the cycles was submitted twice to the first investigator (SH Lee) and once to a second investigator (NM Kim). The variabilities were calculated as the mean absolute differences between the two readings divided by their means. The values expressed as percentages and 95% confidence intervals (CIs).

*Statistical analysis*

In the data from a previous study, the mean (SD) of velocity-time integral (VTI) tracking of left pulmonary venous blood flow was 24.2 (9.2)% [18]. A sample size of 21 patients was required to detect about 30% increase (7 cm) in the VTI of left pulmonary venous blood flow at a power of 90% and two-sided significance level of 0.05. To compensate for possible dropouts, we included 25 patients per group. The power Analysis and Sample Size 2008 software (NCSS, LLC; Kaysville, UT, USA) was used to calculate the number of required patients.

Continuous and discontinuous variables in every result were expressed as mean (SD) and number (%), respectively. Continuous variables at each time point were compared by using the one-way analysis of variance with Bonferroni post hoc test. To confirm the hypothesis that PVBF change induced by HPV can predict intrapulmonary shunt and oxygenation during OLV, PVBF volume was estimated as the percent (%) change in PVBF at OLV-10, -20 and -30 over TLV-L, while changes in Qs/Qt and $PaO_2$ assessed by blood gas analysis were determined in a same fashion. The Pearson correlation test was used to analyze the correlation between % change of PVBF and change of Qs/Qt or $PaO_2$ assessed by blood gas analysis during OLV. A *P* value less than 0.05 was considered statistically significant. SPSS version 20.0 (SPSS Inc., Chicago, IL, USA) was used for all of the statistical analyses.

## Results

*Patients' characteristics*

Twenty-five enrolled patients completed the study successfully. **Table 1** presents their characteristics, details of pulmonary function and intraoperative data.

*Respiratory and hemodynamic variables*

$PaO_2$ and $C_{dyn}$ were significantly decreased, but Qs/Qt, $AP_{Peak}$, $AP_{Mean}$ and CVP were significantly increased at OLV-10, -20 and -30 compared with TLV-S and TLV-L ($P<0.05$). There were no differences in respiratory and hemodynamic variables between TLV-S and TLV-L as well as among OLV-10, -20 and -30 (**Table 2**).

*Changes in pulmonary venous blood flow and intra-pulmonary shunt*

PVBF showed a significant increase at TLV-L compared with TLV-S (1416.9±489.7 to 959.5±280.8 ml/min; $P<0.05$, respectively), whereas no change was observed in Qs/Qt. The PVBF significantly increased after conversion from TLV-L to OLV, as did Qs/Qt at OLV-10, -20 and -30 (1999.9±670.5, 2072.6±605.7 and 2006.1±615.9 ml/min; $P<0.05$, respectively). **Figures 1** and **2** present that the change of PVBF and pulsed-wave Doppler of left upper pulmonary blood flow velocity. No significant differences in PVBF and Qs/Qt occurred among OLV-10, -20 and -30. **Figure 3** shows the correlation between PVBF and intra-pulmonary

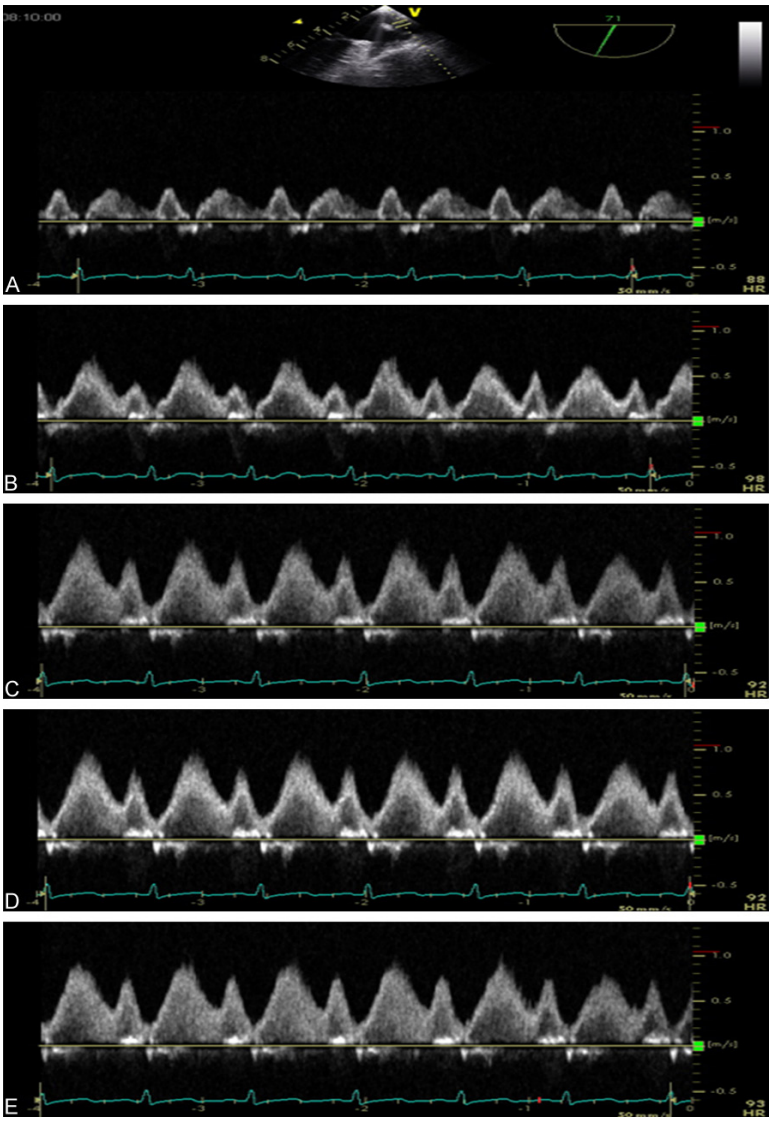


**Figure 1.** Pulsed-wave Doppler of left upper pulmonary venous blood flow velocity. A. 10 min after two lung ventilation in supine position. B. 10 min after two lung ventilation in lateral decubitus position. C. 10 min after one-lung ventilation in left lateral decubitus position. D. 20 min after one-lung ventilation in lateral decubitus position. E. 30 min after one-lung ventilation in left lateral decubitus position.

shunt. There was an inverse correlation between percent change of PVBF and change of Qs/Qt ($r^2$ = 0.5; $P$<0.0001) and a positive correlations between the percent change of PVBF and change of $PaO_2$ ($r^2$ =0.4; $P$<0.0001).

*Changes in biventricular systolic and diastolic function*

Echocardiographic measurement and calculation are reported in **Tables 3** and **4**. A significant prolongation in RV DT was observed at OLV-10 compared with TLV-L, but it was within the normal range, RV e' or E/e' remained unchanged. No significant changes occurred in the systolic indices such as biventricular EF, FAC and s' or RV TAPSE. The results of the intra-observer and inter-observer variabilities in echocardiographic examinations were similar (**Table 5**).

## Discussion

This study demonstrated that OLV in the lateral decubitus position induced a dynamic change of PVBF relevant to gravitational effect and HPV. In addition, changes in blood flow of the left upper pulmonary vein, assessed by using echocardiography, represented intra-pulmonary shunt and oxygenation obtained by blood gas analysis during lung isolation. However, cardiac performance during OLV remained unchanged.

The traditional estimation of pulmonary blood flow was based on older techniques, such as the technique that utilizes fluorescence, radioactive-labeled microspheres or SPECT [8, 19-21]. However, those modalities were hardly applicable during the surgery, thus the intra-pulmonary shunt which is closely associated with oxygenation during OLV, has been measured via blood gas analysis in most previous studies. Our study demonstrated the existing hypothesis that gravity is a physiologically independent determinant of pulmonary blood flow distribution. The lateral decubitus position itself increased the pulmonary blood flow to the dependent lung by as much as 33%, which seems to be owing to redistribution by the gravitational effect. Mure et al [8] insisted that pulmonary blood flow was not redistributed in dogs by the positional changes. However, this is a species variation

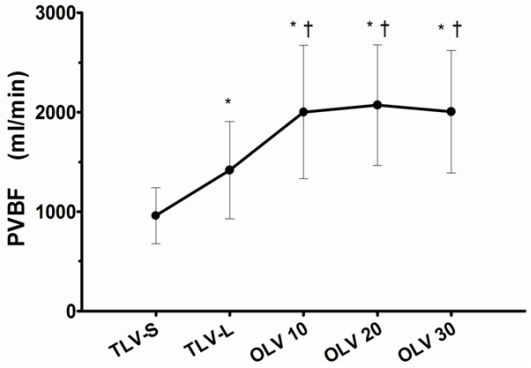


**Figure 2.** The change of left upper pulmonary venous blood flow. *$P$<0.05 compared to TLV-S. †$P$<0.05 compared to TLV-L. PVBF = pulmonary venous blood flow; TLV-S = 10 min after two-lung ventilation in supine position; TLV-L = 10 min after two-lung ventilation in lateral decubitus position; OLV-10 = 10 min after one lung ventilation in left lateral decubitus position; OLV-20 = 20 min after one lung ventilation in lateral decubitus position; OLV-30 = 30 min after one lung ventilation in left lateral decubitus position.

attributed to geometric differences between humans (greater lateral dimension) and animals (greater dorsal-ventral dimensions). The interesting finding of present study was that HPV was established at early phase of OLV. Since there was about 66% increase of PVBF at 10 min of OLV than TLV in lateral decubitus position, without change until the 30 min after OLV. That is, similar to the arguments of Domino et al [22, 23] the maximal response of HPV seems to occur after 10-15 min of OLV. The increase in PVBF to the ventilated lung during OLV can be interpreted as pulmonary vasoconstriction at the hypoxic lesion due to HPV. HPV is a protective autoregulatory mechanism that is activated when a ventilation-perfusion mismatch occurs [6, 24]. The HPV which acts as a homeostatic mechanism at hypoxic lesion improved oxygenation and reduced intra-pulmonary shunt during OLV.

Szegedi et al [4] suggested that oxygenation during OLV is determined more so based on gravity than on the effects of HPV. However, their study was performed in COPD patients, who could develop comorbidities due to pulmonary vasculature remodeling. In addition, they measured only $PaO_2$ as a surrogate for intra-pulmonary shunt fraction.

The change in PVBF assessed by using echocardiography and that in intra-pulmonary shunt assessed by using blood gas analysis during OLV showed a strong correlation. Consequently, assessment of PVBF by using TEE is considered as a good modality for real-time estimation of the severity of hypoxemia caused by intra-pulmonary shunt instead of SPECT or venous blood gas analysis for intra-pulmonary shunt fraction. The strength of our study was a comprehensive examination of cardiopulmonary interaction according to positional changes and HPV during OLV on echocardiography. In particular, none of the existing studies obtained serial measurements of positional and HPV changes during OLV. In addition, our study proved that assessment of changes in PVBF on echocardiography is a clinically relevant modality that predicts intra-pulmonary shunt determined by using blood gas analysis and simultaneously showed cardiac function during OLV. Although some previous studies [18, 25] also assessed the effects on PVBF during OLV, they did not simultaneously show both components that gravitation and HPV effect on lung isolation, as was confirmed in our study. Gong et al [25] found a significant change in PVBF during OLV with echocardiography. However, their study was conducted in supine position. Wang et al [18] stated that intra-pulmonary shunt fraction measured by TEE was significantly correlated with $PaO_2$. However, they performed only in lateral position to assess the HPV effect during lung isolation. We maintained the cardiac output stably during OLV, they couldn't thus failed to exclude the influence of increased cardiac output on PVBF. More crucially, they did not estimate intra-pulmonary shunt fraction by performing blood gas analyses.

In terms of changes in cardiac performance after lung resection, pulmonary arterial pressure, RV diastolic diameter, and RV systolic pressure are known to increase [9, 10]. Furthermore, during thoracic surgery, structural and functional changes of lung can affect acute RV function. Because the heart is located in the left hemithorax, left lateral decubitus position shifts the axis of the heart through hydrostatic pressure [26] and can increase intracardiac pressure [27]. In addition, left lateral decubitus position distorts the mediastinum to the left side owing to the weight of the heart. In relation to RV systolic function, Wilkinson et al [28] interpreted the increase in RVEDA and RVESA immediately after OLV as an increase in pre-

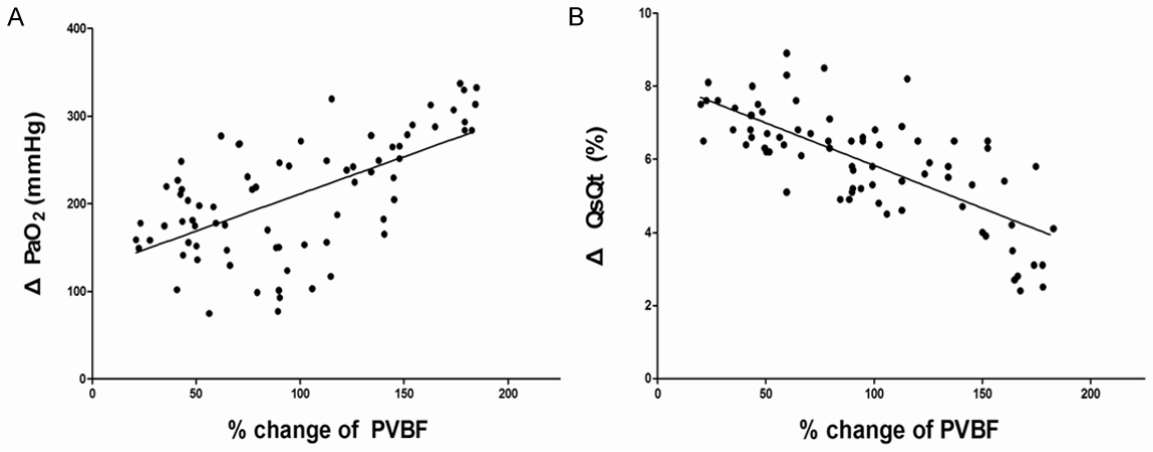


**Figure 3.** The correlation between pulmonary venous blood flow and intra-pulmonary shunt. A. There were significant correlations between percent change in pulmonary venous blood flow (PVBF) and change in arterial oxygen tension ($PaO_2$) during one-lung ventilation. The correlation coefficient ($r^2$) was 0.4 ($P$<0.0001). B. There were inverse correlations between percent change in PVBF and change in intra-pulmonary shunt fraction (Qs/Qt) during one-lung ventilation. The correlation coefficient ($r^2$) was 0.5 ($P$<0.0001).

load reserve to compensate for the increase in ventricular afterload. Matyal et al [29] reported an acute functional change in RV at 10 min after lung isolation. In this study, RV DT was prolonged temporarily, until within its normal range, only in the early phase of OLV. Because tissue Doppler indices that are independent of SV or preload were not changed during OLV, RV function was not impaired. In this study, the systolic indices of FAC, EF, s' and TAPSE remained unchanged during TLV and OLV in lateral decubitus position. In addition, the systolic function was not significantly affected by the positional change to the lateral decubitus position or OLV. In relation to LV systolic and diastolic functions, OLV seemed not to affect cardiac performance in patients with normal cardiac function.

This study has several limitations. First, this study was performed in patient with normal lung function. When pulmonary vasculature remodeling was induced, as in chronic obstructive pulmonary disease [30], or when the disease dimension was large, changes in perfusion might have occurred because the "shunted away" lesion was chronically located. Pulmonary flow redistribution may differ in such patient groups. Second, we examined only blood flow of left upper pulmonary vein. Because the upper pulmonary veins are more easily seen than the lower pulmonary veins and are most parallel to the Doppler beam [31]. However we cannot assure that left upper pulmonary blood flow may represent the change of blood flow in the entire pulmonary vasculature including pulmonary artery during OLV. Third, this study excluded patients who had undergone thoracic surgery in the right lateral decubitus position. Normally, the left lung receives 10% less CO than the right lung [32]. The mediastinum was distorted in left lateral position due to the weight of the heart, decreasing the left lung volume and increasing pulmonary vascular resistance [33]. Therefore, gravitational variations on the left side are prominent. Ultimately, blood flow distribution and total ventilation are lower and the ventilation/perfusion ratio is larger in left-sided than in right-sided OLV [33]. Therefore, including the right lung in this study may have result in different findings. Fourth, because this study included only the patients without cardiovascular disease, prediction of results in patients with heart failure would be different [34, 35]. Therefore, further studies targeting patients with cardiovascular disease are needed in the future. Fifth, because this study limited the OLV duration to 30 min, it was conducted in relatively short operative periods. Lumb et al [36] stated that HPV reflex is biphasic and that the second phase becomes reactive again 1 hour after hypoxia. Therefore, this study may not be applicable to prolonged OLV.

In summary, the change of PVBF was quantified by using echocardiography during OLV in lateral decubitus position. Our findings demonstrated redistribution of the pulmonary perfusion relevant to gravitational effect and HPV during OLV by using echocardiography. The pattern of PVBF changes was proven to have a significant correlation with intra-pulmonary shunt and oxygenation during OLV, while the response of HPV to the intra-pulmonary shunt appeared to start and become established relatively early phase of OLV. However, lung isolation itself did not cause cardiac impairment.

## Disclosure of conflict of interest

None.

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## References

[1] Slinger P, Triolet W and Wilson J. Improving arterial oxygenation during one-lung ventilation. Anesthesiology 1988; 68: 291-295.

[2] Schwarzkopf K, Klein U, Schreiber T, Preussetaler NP, Bloos F, Helfritsch H, Sauer F and Karzai W. Oxygenation during one-lung ventilation: the effects of inhaled nitric oxide and increasing levels of inspired fraction of oxygen. Anesth Analg 2001; 92: 842-847.

[3] Slinger P, Suissa S and Triolet W. Predicting arterial oxygenation during one-lung anaesthesia. Can J Anaesth 1992; 39: 1030-1035.

[4] Szegedi LL, D'Hollander AA, Vermassen FE, Deryck F and Wouters PF. Gravity is an important determinant of oxygenation during one-lung ventilation. Acta Anaesthesiol Scand 2010; 54: 744-750.

[5] Bardoczky GI, Szegedi LL, d'Hollander AA, Moures JM, de Francquen P and Yernault JC. Two-lung and one-lung ventilation in patients with chronic obstructive pulmonary disease: the effects of position and $FiO_2$. Anesth Analg 2000; 90: 35-41.

[6] Benumof JL. One-lung ventilation and hypoxic pulmonary vasoconstriction: implications for anesthetic management. Anesth Analg 1985; 64: 821-833.

[7] Glenny RW. Determinants of regional ventilation and blood flow in the lung. Intensive Care Med 2009; 35: 1833-1842.

[8] Mure M, Domino KB, Robertson T, Hlastala MP and Glenny RW. Pulmonary blood flow does not redistribute in dogs with reposition from supine to left lateral position. Anesthesiology 1998; 89: 483-492.

[9] Smulders SA, Holverda S, Vonk-Noordegraaf A, van den Bosch HC, Post JC, Marcus JT, Smeenk FW and Postmus PE. Cardiac function and position more than 5 years after pneumonectomy. Ann Thorac Surg 2007; 83: 1986-1992.

[10] Venuta F, Sciomer S, Andreetti C, Anile M, De Giacomo T, Rolla M, Fedele F and Coloni GF. Long-term Doppler echocardiographic evaluation of the right heart after major lung resections. Eur J Cardiothorac Surg 2007; 32: 787-790.

[11] Foroulis CN, Kotoulas CS, Kakouros S, Evangelatos G, Chassapis C, Konstantinou M and Lioulias AG. Study on the late effect of pneumonectomy on right heart pressures using Doppler echocardiography. Eur J Cardiothorac Surg 2004; 26: 508-514.

[12] Barber RL and Fletcher SN. A review of echocardiography in anaesthetic and peri-operative practice. Part 1: impact and utility. Anaesthesia 2014; 69: 764-776.

[13] Stavrakis S, Madden GW, Stoner JA and Sivaram CA. Transesophageal echocardiography for the diagnosis of pulmonary vein stenosis after catheter ablation of atrial fibrillation: a systematic review. Echocardiography 2010; 27: 1141-1146.

[14] Boyd SY, Sako EY, Trinkle JK, O'Rourke RA and Zabalgoitia M. Calculation of lung flow differential after single-lung transplantation: a transesophageal echocardiographic study. Am J Cardiol 2001; 87: 1170-1173.

[15] Rivera IR, Mendonca MA, Andrade JL, Moises V, Campos O, Silva CC and Carvalho AC. Pulmonary venous flow index as a predictor of pulmonary vascular resistance variability in congenital heart disease with increased pulmonary flow: a comparative study before and after oxygen inhalation. Echocardiography 2013; 30: 952-960.

[16] Stavrakis S, Madden G, Pokharel D, Po SS, Nakagawa H, Jackman WM and Sivaram CA. Transesophageal echocardiographic assessment of pulmonary veins and left atrium in patients undergoing atrial fibrillation ablation. Echocardiography 2011; 28: 775-781.

[17] Czepizak CA, O'Callaghan JM and Venus B. Evaluation of formulas for optimal positioning of central venous catheters. Chest 1995; 107: 1662-1664.

[18] Wang M, Gong Q and Wei W. Estimation of shunt fraction by transesophageal echocardiography during one-lung ventilation. J Clin Monit Comput 2015; 29: 307-11.

[19] Walther SM, Domino KB, Glenny RW, Polissar NL and Hlastala MP. Pulmonary blood flow dis-

tribution has a hilar-to-peripheral gradient in awake, prone sheep. J Appl Physiol 1997; 82: 678-685.
[20] Walther SM, Domino KB, Glenny RW and Hlastala MP. Pulmonary blood flow distribution in sheep: effects of anesthesia, mechanical ventilation, and change in posture. Anesthesiology 1997; 87: 335-342.
[21] Hakim TS, Dean GW and Lisbona R. Effect of body posture on spatial distribution of pulmonary blood flow. J Appl Physiol 1988; 64: 1160-1170.
[22] Domino KB, Chen L, Alexander CM, Williams JJ, Marshall C and Marshall BE. Time course and responses of sustained hypoxic pulmonary vasoconstriction in the dog. Anesthesiology 1984; 60: 562-566.
[23] Carlsson AJ, Bindslev L, Santesson J, Gottlieb I and Hedenstierna G. Hypoxic pulmonary vasoconstriction in the human lung: the effect of prolonged unilateral hypoxic challenge during anaesthesia. Acta Anaesthesiol Scand 1985; 29: 346-351.
[24] Marshall BE and Marshall C. Continuity of response to hypoxic pulmonary vasoconstriction. J Appl Physiol Respir Environ Exerc Physiol 1980; 49: 189-196.
[25] Gong Q, Yang Z and Wei W. The changes of pulmonary blood flow in non-ventilated lung during one lung ventilation. J Clin Monit Comput 2010; 24: 407-412.
[26] Fujise K, Shingu K, Matsumoto S, Nagata A, Mikami O and Matsuda T. The effects of the lateral position on cardiopulmonary function during laparoscopic urological surgery. Anesth Analg 1998; 87: 925-930.
[27] Nakao S, Come PC, Miller MJ, Momomura S, Sahagian P, Ransil BJ and Grossman W. Effects of supine and lateral positions on cardiac output and intracardiac pressures: an experimental study. Circulation 1986; 73: 579-585.
[28] Wilkinson JN, Scanlan M, Skinner H and Malik M. Right heart function during one-lung ventilation--observations using transoesophageal echocardiography. Anaesthesia 2009; 64: 1387-1388.
[29] Matyal R, Mahmood F, Hess P, Zhao X, Mitchell J, Maslow A, Gangadharan S and Decamp M. Right ventricular echocardiographic predictors of postoperative supraventricular arrhythmias after thoracic surgery: a pilot study. Ann Thorac Surg 2010; 90: 1080-1086.
[30] Barbera JA, Riverola A, Roca J, Ramirez J, Wagner PD, Ros D, Wiggs BR and Rodriguez-Roisin R. Pulmonary vascular abnormalities and ventilation-perfusion relationships in mild chronic obstructive pulmonary disease. Am J Respir Crit Care Med 1994; 149: 423-429.
[31] Shanewise JS, Cheung AT, Aronson S, Stewart WJ, Weiss RL, Mark JB, Savage RM, Sears-Rogan P, Mathew JP, Quinones MA, Cahalan MK and Savino JS. ASE/SCA guidelines for performing a comprehensive intraoperative multiplane transesophageal echocardiography examination: recommendations of the American Society of Echocardiography Council for Intraoperative Echocardiography and the Society of Cardiovascular Anesthesiologists Task Force for Certification in Perioperative Transesophageal Echocardiography. Anesth Analg 1999; 89: 870-884.
[32] Slinger P, Suissa S, Adam J and Triolet W. Predicting arterial oxygenation during one-lung ventilation with continuous positive airway pressure to the nonventilated lung. J Cardiothorac Anesth 1990; 4: 436-440.
[33] Chang H, Lai-Fook SJ, Domino KB, Schimmel C, Hildebrandt J, Robertson HT, Glenny RW and Hlastala MP. Spatial distribution of ventilation and perfusion in anesthetized dogs in lateral postures. J Appl Physiol 2002; 92: 745-762.
[34] Berensztein CS, Pineiro D, Luis JF, Iavicoli O and Lerman J. Effect of left and right lateral decubitus positions on Doppler mitral flow patterns in patients with severe congestive heart failure. J Am Soc Echocardiogr 1996; 9: 86-90.
[35] Tanabe K, Ishibashi Y, Ohta T, Oyake N, Shimada T, Murakami R, Morioka S and Moriyama K. Effect of left and right lateral decubitus positions on mitral flow pattern by Doppler echocardiography in congestive heart failure. Am J Cardiol 1993; 71: 751-753.
[36] Lumb AB and Slinger P. Hypoxic Pulmonary Vasoconstriction: Physiology and Anesthetic Implications. Anesthesiology 2015; 122: 932-946.