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Ventilation-Perfusion Distribution and Shunt Fraction during One-Lung Ventilation: Effect of Different Inhaled Oxygen Levels

Jane-Yi Hsu[1], Wei-Teing Chen[2, 3], Chung-Cheng Kao[4], Shih Jun Lee[5], and Hung Chang[5, 6]

[1]*Division of Thoracic Surgery, Department of Surgery*
Armed Forces Kao-hsiung General Hospital
[2]*Division of Pulmonary and Critical Care Medicine*
Department of Medicine, Tri-Service General Hospital
[3]*Respiratory Care Ward*
Hsiao Chung-Cheng Hospital
[4]*Department of Emergency*
Taoyuan Armed Forces General Hospital
Taoyuan
[5]*Division of Thoracic Surgery*
Department of Surgery Tri-Service General Hospital
Taipei
and
[6]*Department of Physiology and Biophysics*
National Defense Medical Center
Taipei, Taiwan, Republic of China

Abstract

Ventilation with higher fraction of inspired oxygen (F_IO_2) is one of the commonly-chosen strategies executed for treatment of hypoxemia during one lung ventilation (OLV) for thoracic surgery. In this study, we investigated the effect of F_IO_2 on pulmonary ventilation-perfusion ($\dot{V}A/\dot{Q}$) distribution during OLV. Six pigs, weighing 27 to 34 kg, were selected for this study. Following by a steady-state period, randomized administrations of F_IO_2 with 0.4, 0.6 and 1.0 were performed for 30 minutes at the right lateral decubitus position during OLV, while hemodynamic data and lung mechanics were simultaneously monitored. The $\dot{V}A/\dot{Q}$ distributions of the lung(s) were assessed by the multiple inert gas elimination technique (MIGET). PaO_2 at F_IO_2 of 100% was significantly reduced in OLV compared with two-lung ventilation (TLV) (522 ± 104 *vs*. 653 ± 21 mmHg; $P < 0.001$) at right lateral decubitus position. MIGET algorithms demonstrated a wider $\dot{V}A/\dot{Q}$ distribution during OLV at F_IO_2 of 40%, as compared with distribution during TLV at F_IO_2 of 100%, but a bimodal perfusion distribution shifted to lower $\dot{V}A/\dot{Q}$ component during OLV at F_IO_2 of 100%. There was an increase of pulmonary shunting in OLV, as compared with TLV at F_IO_2 of 100% (1.94 ±2.2% *vs*. 9.5 ±9.7%; $P < 0.01$). In addition, OLV caused a significant increase in the dispersion of perfusion at F_IO_2 of 100% (0.62 ± 0.20 *vs*. 0.44 ±0.23; $P < 0.01$), but ventilation showed no denoting changes (1.06 ± 0.20 *vs*. 0.98 ±0.35; $P > 0.01$). During OLV with right lateral decubitus position, there were no significant changes in the pulmonary shunt, the dispersion of perfusion and ventilation at different F_IO_2. OLV resulted in an increase in pulmonary shunting and heterogeneity compared with TLV. Furthermore, the PaO_2 decreased during OLV regardless of the postural changes. At different F_IO_2, there were no significant changes in the pulmonary shunt, the dispersion of perfusion and ventilation during OLV with right lateral decubitus posture.

Key Words: one lung ventilation, hypoxic pulmonary vasoconstriction (HPV), oxygenation, pulmonary gas exchange, multiple inert gas elimination technique

Corresponding author: Hung Chang, MD, Ph.D., Division of Thoracic Surgery, Department of Surgery, Tri-Service General Hospital, Rm 6318, No. 161, MinChuan E. Road, Sec. 6, Taipei 114, Taiwan, ROC.
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Introduction

In complex procedures of unilateral thoracic operations, one-lung ventilation (OLV) was widely used to provide better surgical exposures and more delicate lung resection. Postural changes during OLV may augment the dynamic changes of ventilation and perfusion ($\dot{V}A/\dot{Q}$) distribution of lungs (4). Patients with OLV, hypoxemia was prone to occur at the ipsilateral decubitus posture (5, 8). Ventilation with higher fraction of inspired oxygen (F_IO_2) is one of the commonly-chosen strategies executed for treatment of hypoxemia during OLV for thoracic surgery (9, 11). The question of whether the alteration of F_IO_2 has impacts on $\dot{V}A/\dot{Q}$ distribution of lungs during OLV merits further study and discussion.

Multiple inert gas elimination technique (MIGET), using six inert gases for tracing fifty compartments, allows assessment of entire distinction of $\dot{V}A/\dot{Q}$ distribution and gas exchange physiology (17, 18). It could provide values of shunt, dead space, mean and standard deviation of $\dot{V}A/\dot{Q}$ (18, 19). The $\dot{V}A/\dot{Q}$ relationships ranging from zero (shunt) to infinite (dead space) were used to indicate the efficiency of gas exchange (18). The $\dot{V}A/\dot{Q}$ value away from 1.0 represents inefficient gas exchange. To mimic the OLV for the surgical condition, the animals were anesthetized and prepared with right lung intubation at right lateral decubitus posture. In the study, MIGET was applied to assess dynamic $\dot{V}A/\dot{Q}$ distribution with different F_IO_2 during OLV.

Materials and Methods

Animal Preparation

This study was approved by the National Defense Medical Center Animal Care Committee. Pigs (n = 6, 25-30 kg) were selected to be the experimental models, they were anesthetized with pentobarbital sodium (30 mg/kg, intravenous injection) and anesthesia was maintained by adding extra doses (25-50 mg/h). (3)

A modified double-lumen endotracheal tube (broncho-Cath, left; Mallinckrodt Medical, Inc. Pleasanton, CA, USA) was placed *via* a subcricoid tracheotomy. The position of the bronchus blocker was verified by fiber-optic bronchoscopy (BF-N20, Olympus, Tokyo, Japan) prior to each experimental phase. The animals were then mechanically ventilated with a constant-volume ventilator (Harvard Instruments, South Natick, MA, USA). They were ventilated with the tidal volume of 10-15 ml/kg and the respiratory rate adjusted for maintaining end-tidal CO_2 of 35-45 mmHg. The tidal volumes were measured by spirometry. The animals received intermittent two deep inflations with 1.5 times of the predetermined tidal volume per 15 min and 30 sec before measurements. Body temperature was kept at 37.2 ±0.9 °C with heating pads.

Through a catheter inserted through the femoral artery, systemic arterial blood pressure and heart rate were continuously monitored (Power Lab, AD Instruments Pty Ltd, Colorado Springs, CO, USA). Cardiac output was measured in triplicate through a pulmonary arterial catheter by thermodilution (Edwards COM 2; Baxter Edwards, Irvine, CA, USA). Arterial and mixed venous blood gases were analyzed with blood gas analyzer (Rapidlab 845 with COOX, Bayer, Holliston, MA, USA).

Experimental Protocol

All animals with OLV of right lung and TLV were studied in supine at 100% of F_IO_2, and in right lateral decubitus posture at randomized sequential inhalations of 100%, 60% or 40% of F_IO_2. During OLV, the tidal volume was adjusted to be 60% of that used at TLV. The interval between any two assessments was 30 to 40 minutes to allow stay in steady state. Hemodynamic and physiological data were measured.

Assessment of $\dot{V}A/\dot{Q}$ by MIGET

The continuous $\dot{V}A/\dot{Q}$ distributions were assessed by MIGET as described by Wagner and his coworkers (18, 19). In brief, six inert gases (SF6, ethane, cyclopropane, halothane, diethyl ether, and acetone), dissolved in normal saline, and were continuously infused at a rate of 0.5 ml/min. After an equilibration period of 30 min, 10 ml of whole blood was simultaneously drawn with heparinized syringes from both pulmonary artery and femoral vein. An equivalent of 50-ml exhaled gas sample was then collected from the heated expiration gas-mixing chamber. In a separate study, partition coefficient for each inert gas in blood were measured with the double-dilution method (17). Extraction of the dissolved gas in blood was carried out by equilibration with nitrogen in a shaking water bath at 37°C.

The concentrations of equilibrated inert gas phases of blood sample, as well as the exhaled gases were analyzed by gas chromatography (5890 GC, Agilent, Foster City, CA, USA) equipped with a flame ionization detector and an electron capture detector. Retention and excretion data and measured inert-gas solubility were transformed into $\dot{V}A/\dot{Q}$ distributions on a logarithmic scale derived by Evans and Wagner (6). The distribution curves were illustrated by calculating the mean $\dot{V}A/\dot{Q}$ ratio of perfusion and ventilation on a logarithmic scale by use of 50-compartment model. The dispersions of both perfusion and ventilation were calculated by their logarithmic standard deviation (log $SD\dot{Q}$; log $SD\dot{V}A$).

Table 1. Blood gas analysis and physiological data at right lateral decubitus posture. (n = 6)

	TLV F_IO_2 = 1.0	OLV F_IO_2 = 1.0	OLV F_IO_2 = 0.6	OLV F_IO_2 = 0.4
Blood Gases				
pH	7.54 ± 0.06	7.49 ± 0.05	7.51 ± 0.05	7.53 ± 0.05
PaO_2 (mm Hg)	653 ± 21	522 ± 104*	268 ± 83*†	163 ± 41*†‡
$PaCO_2$ (mm Hg)	38 ± 3	42 ± 4	41 ± 5	37 ± 4†‡
$P\bar{V}O_2$ (mm Hg)	56 ± 6	52 ± 7*	44 ± 5*†	42 ± 5*†‡
$P(A\text{-}a)O_2$ (mm Hg)	20 ± 11	139 ± 103*	123 ± 72*†	76 ± 38*†‡
FRC (ml)	428 ± 138	251 ± 68*	288 ± 173*	264 ± 110*
Hemodynamic				
HR (min^{-1})	99 ± 18	96 ± 10	98 ± 12	99 ± 12
MBP (mm Hg)	96 ± 20	93 ± 23	90 ± 23	91 ± 22
MPAP (mm Hg)	21 ± 8	21 ± 10	21 ± 8	22 ± 8
Pw (mm Hg)	7.2 ± 6.3	6.0 ± 6.7	6.6 ± 6.6	7.0 ± 6.4
CO (l/min)	3.4 ± 0.8	3.4 ± 0.8	3.5 ± 0.7	3.6 ± 0.6
Mechanic				
V_T (ml)	359 ± 37	251 ± 21*	246 ± 22*	249 ± 23*
RR (min^{-1})	11 ± 2	18 ± 3*	19 ± 4*	20 ± 3*
MV (l)	4.1 ± 1.0	4.7 ± 0.8*	4.6 ± 1.2*	4.9 ± 1.0*
ET_{CO_2} (mm Hg)	34 ± 11	34 ± 10	34 ± 11	33 ± 10
AWP (cmH_2O)	6.1 ± 2.5	5.5 ± 2.1	5.9 ± 1.7	6.2 ± 2.2

TLV: two-lung ventilation, OLV: one-lung ventilation
*P < 0.05 compared with TLV (within group comparisons)
†P < 0.05 compared with OLV F_IO_2 = 1.0
‡P < 0.05 compared with OLV F_IO_2 = 0.6
CO = cardiac output; HR = heart rate; MAP = mean arterial blood pressure; MPAP = mean pulmonary arterial pressure. Pw = wedge pressure; MBP = mean blood pressure; V_T = tidal volume; RR = respiration rate; MV = minute volume; $ETCO_2$ = end-tidal CO_2; AWP = airway pressure; $P\bar{V}O_2$ = mixed venous O_2 tension; $P(A\text{-}a)O_2$: difference in alveolar and arterial oxygen tension; FRC = functional residual capacity

Calculations and Statistics

FRC was calculated as FRC = Vi (Hei/Hefin) – Vi, where Vi is the initial volume of the helium mixture, and Hei is the initial concentration of helium. Hefin is the final concentration of helium. $(A\text{-}a)PO_2$ was also calculated using the alveolar gas equation (17) with a respiratory quotient of 0.8.

All data are presented as mean ± SD. *P* less than 0.05 was considered statistically significant. Comparison of experimental data among groups (> 3 groups) was performed using repeated measures analysis of variance (repeated ANOVA) and Tukey-Kramer Multiple Comparisons Test for post hoc comparisons.

Results

Physiological Data

Physiological data and blood gas analyses are shown in Table 1. During OLV, the ventilator was set with tidal volume of 250 ± 21 ml, and respiratory rate of 18 ±3 breaths/min. Throughout the whole experiment, there was no significant difference in hemodynamic change. On the other hand, PaO_2 at F_IO_2 of 100% has significantly reduced in OLV, as compared with TLV (522 ± 104 *vs*. 653 ± 21 mmHg; P < 0.001) at right lateral decubitus posture.

MIGET Data

In one example of our study at F_IO_2 of 100% and supine posture, MIGET algorithms demonstrate a uni-model ventilation and perfusion distribution with a wider $\dot{V}A/\dot{Q}$ component in OLV, compared with TLV (Fig. 1). To mimic the surgical condition at OLV, the right side bronchi of the animals were intubated concomitantly with the right lateral decubitus posture. MIGET algorithms demonstrated a wider ventilation and perfusion distribution during OLV at F_IO_2 of 40%,

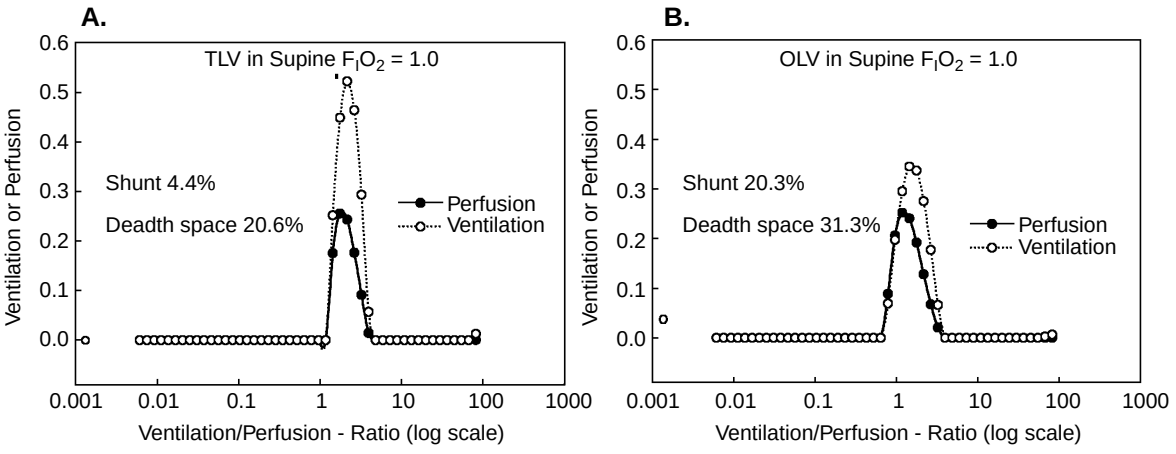

Fig. 1. MIGET algorithms during two-lung and one-lung ventilation in a representative animal. A. An animal prepared in supine posture received F_IO_2 of 100% with two lung ventilation. B. the same animal, during one lung ventilation. TLV: two lung ventilation. OLV: one lung ventilation. F_IO_2: fraction of inspired oxygen.

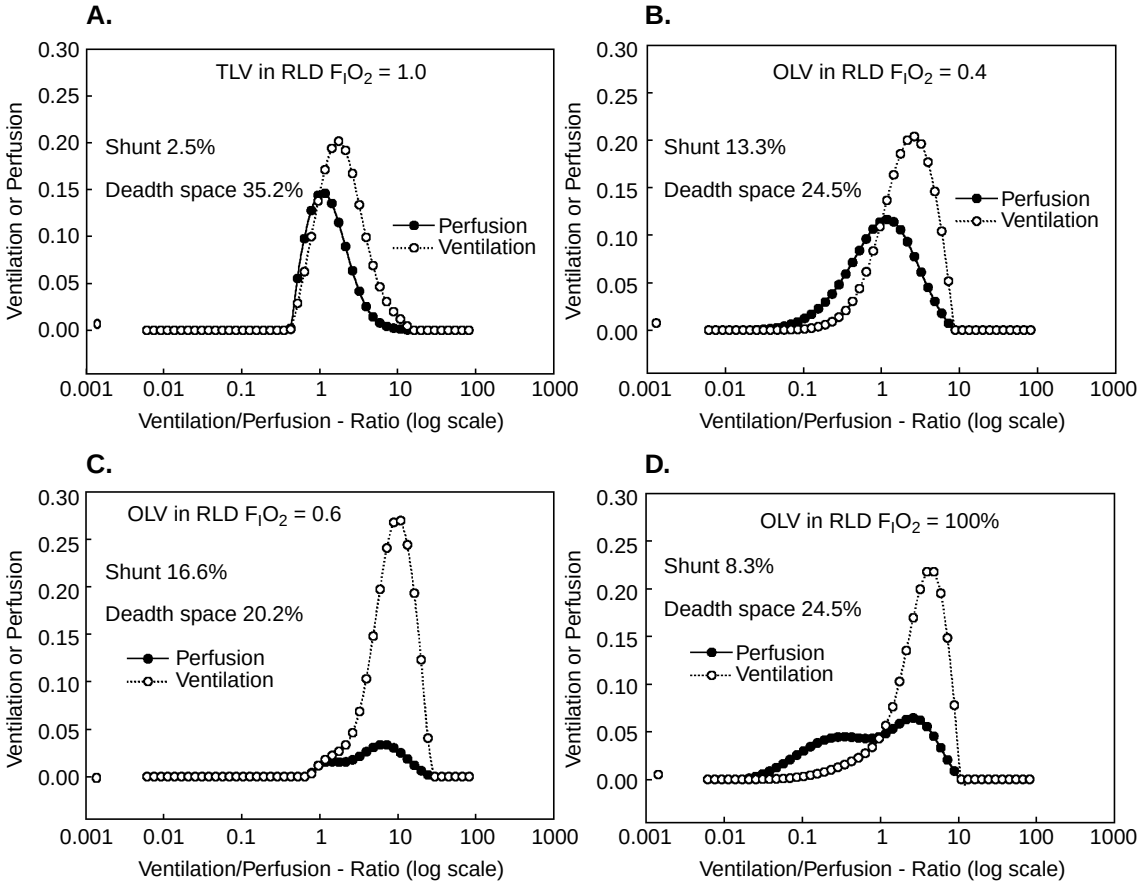

Fig. 2. MIGET algorithms in right lateral decubitus posture during one-lung and two-lung ventilation in a representative animal. A. A pig received F_IO_2 of 100% with two-lung ventilation. B. The same animal received F_IO_2 of 40% with one-lung ventilation. C. The same animal received F_IO_2 of 60% with one-lung ventilation. D. The same animal received F_IO_2 of 100% with one-lung ventilation. RLD: right lateral decubitus posture

as compared with that during TLV at F_IO_2 of 100%, but bimodal perfusion distribution shifts to lower $\dot{V}A/\dot{Q}$ component during OLV at F_IO_2 of 100% (Fig. 2). MIGET data are shown in Table 2. Pulmonary shunting increased at OLV, as compared with TLV at F_IO_2 of 100% (1.94 ±2.2 *vs*. 9.5 ±9.7; $P < 0.01$). In

Table 2. MIGET data at right lateral decubitus posture

	TLV F_IO_2 = 1.0	OLV F_IO_2 = 1.0	OLV F_IO_2 = 0.6	OLV F_IO_2 = 0.4
Shunt (%$\dot{Q}$)	1.94 ± 2.2	9.5 ± 9.7*	11.3 ± 6.3*	9.6 ± 6.9*
Low $\dot{V}A/\dot{Q}$ (%$\dot{Q}$)	0.03 ± 0.01	1.8 ± 4.5	0.02 ± 0.01	0.8 ± 1.9
$\dot{Q}_{mean}$	1.33 ± 1.06	0.98 ± 0.26	1.59 ± 1.51	2.71 ± 3.01
Log SD$\dot{Q}$	0.44 ± 0.23	0.62 ± 0.20*	0.64 ± 0.20*	0.80 ± 0.24*
Dead Space	30.5 ± 21.8	39.4 ± 13.0	42.9 ± 18.9	39.1 ± 21.1
High $\dot{V}A/\dot{Q}$ (%$\dot{V}A$)	0.11 ± 0.08	0.16 ± 0.17	0.13 ± 0.13	0.13 ± 0.18
$\dot{V}A_{mean}$	3.01 ± 1.93	2.40 ± 0.83	3.13 ± 2.58	4.76 ± 4.17
Log SD$\dot{V}A$	1.06 ± 0.20	0.98 ± 0.35	1.01 ± 0.30	0.78 ± 0.29

Values are mean ± SD

TLV = two-lung ventilation, OLV = one-lung ventilation

*P < 0.05 compared with TLV (within group comparisons)

Shunt = intrapulmonary shunt flow (% from total blood flow); Low $\dot{V}A/\dot{Q}$ = blood flow to poorly ventilated regions (% from total blood flow); $\dot{Q}_{mean}$ = mean blood flow (calculated on a logarithmic scale); Log SD$\dot{Q}$ = dispersion of pulmonary blood flow (calculated as the SD from mean blood flow on a logarithmic scale); Dead space = ventilation of area with a ventilation-perfusion ratio higher than 100 (% from total ventilation); $\dot{V}A_{mean}$ = mean ventilation (calculated on a logarithmic scale); Log SD$\dot{V}A$ = dispersion of ventilation (calculated as the SD from mean ventilation)

addition, the OLV had caused a significant increment in the dispersion of perfusion at F_IO_2 of 100% (0.62 ±0.20 *vs*. 0.44 ±0.23; P < 0.01), but ventilation showed no denoting changes (1.06 ±0.20 *vs*. 0.98 ±0.35; P > 0.01). During OLV with right lateral decubitus posture, there were no significantly changes in the pulmonary shunt, the dispersion of perfusion and ventilation at different F_IO_2. A quantitative estimation of the general experimental error in the evaluation of $\dot{V}A/\dot{Q}$ distributions by the residual sum of squares (mean: 3.4 ±1.4; range: 0.12 to 5.42; data not shown) indicated the quality control of inert gas measurements.

Discussion

During OLV, hypoxemia was often detected at the instant of operation (10). Atelectasis in the dependent lung during OLV impairs arterial oxygenation and increases dead space (11, 16). Thus, the application of low positive end-expiratory pressure (PEEP) had been shown to increase the partial pressure of arterial oxygen during OLV through the effects of expiratory and inspiratory pulmonary recruitment (1, 12, 15). In the study, 5-cmH_2O PEEP was applied to improve gas exchange within lung and attenuate the heterogeneity of regional pulmonary perfusion (8, 14).

In comparison with the TLV, OLV had been shown to result in the PaO_2 decrease regardless of the postural change. A previous study had revealed that the decrease in PaO_2 was less in the lateral, compared with the supine posture with OLV (2). During OLV, the degree of transpulmonary shunt and the role of hypoxic pulmonary vasoconstriction (HPV) have been shown to maintain arterial oxygenation(4). At the right lateral decubitus posture, gravity and vascular structure might augment the redistribution of perfusion as a result of HPV compared with the supine posture, which explains the higher PaO_2 during OLV(2, 7, 13).

MIGET allows entire assessment of $\dot{V}A/\dot{Q}$ distribution and gas exchange physiology. However, discrimination between the right and left lung during two-lung ventilation is not possible. Compared with TLV, OLV with right lateral decubitus posture caused the increase in the pulmonary shunting and the dispersion of perfusion (Log SD$\dot{Q}$ around 0.6 ~ 0.8). During OLV with right lateral decubitus posture, there were no significantly changes in the pulmonary shunt, the dispersion of perfusion and ventilation at different F_IO_2.

Our data demonstrated that OLV resulted in increases in pulmonary shunting and heterogeneity, compared with TLV. Furthermore, the PaO_2 decreased during OLV regardless of the postural changes. At different F_IO_2, there were no significant changes in the pulmonary shunt, the dispersion of perfusion and ventilation during OLV with right lateral decubitus posture.

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