

Ventilatory Protective Strategies during Thoracic Surgery

Effects of Alveolar Recruitment Maneuver and Low-tidal Volume Ventilation on Lung Density Distribution

Alf Kozian, M.D., Ph.D.,* Thomas Schilling, M.D., Ph.D., D.E.A.A.,* Hartmut Schütze, Ph.D.,† Mert Senturk, M.D.,‡ Thomas Hachenberg, M.D., Ph.D.,§ Göran Hedenstierna, M.D., Ph.D.||

ABSTRACT

Background: The increased tidal volume (V_T) applied to the ventilated lung during one-lung ventilation (OLV) enhances cyclic alveolar recruitment and mechanical stress. It is unknown whether alveolar recruitment maneuvers (ARMs) and reduced V_T may influence tidal recruitment and lung density. Therefore, the effects of ARM and OLV with different V_T on pulmonary gas/tissue distribution are examined.

Methods: Eight anesthetized piglets were mechanically ventilated ($V_T = 10$ ml/kg). A defined ARM was applied to the whole lung (40 cm H_2O for 10 s). Spiral computed tomographic lung scans were acquired before and after ARM. Thereafter, the lungs were separated with an endobronchial

* Assistant Professor in Cardiac and Thoracic Anesthesia, ‡ Assistant Professor in Anesthesia, § Professor of Anesthesia and Chair, Department of Anesthesiology and Intensive Care Medicine, Otto-von-Guericke-University Magdeburg, Magdeburg, Germany. † Research Biologist, Institute of Cognitive Neurology and Dementia Research, Otto-von-Guericke-University Magdeburg. || Professor in Clinical Physiology and Head of the Research Department of Clinical Physiology, Department of Medical Sciences, Uppsala University, Uppsala, Sweden.

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Address correspondence to Dr. Schilling: Department of Anesthesiology and Intensive Care Medicine, Otto-von-Guericke-University Magdeburg, Leipziger Strasse 44, D-39120 Magdeburg, Germany. thomas.schilling@med.ovgu.de. Information on purchasing reprints may be found at www.anesthesiology.org or on the masthead page at the beginning of this issue. ANESTHESIOLOGY's articles are made freely accessible to all readers, for personal use only, 6 months from the cover date of the issue.

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What We Already Know about This Topic

- One-lung ventilation (OLV) may be associated with increased mechanical stress and hypoxemia.

What This Article Tells Us That Is New

- A single recruitment maneuver before OLV and ventilation with 5 ml/kg during OLV has beneficial effects on aeration of the ventilated lung.

blocker. The pigs were randomized to receive OLV in the dependent lung with a V_T of either 5 or 10 ml/kg. Computed tomography was repeated during and after OLV. The voxels were categorized by density intervals (*i.e.*, atelectasis, poorly aerated, normally aerated, or overaerated). *Tidal recruitment* was defined as the addition of gas to collapsed lung regions.

Results: The dependent lung contained atelectatic (56 ± 10 ml), poorly aerated (183 ± 10 ml), and normally aerated (187 ± 29 ml) regions before ARM. After ARM, lung volume and aeration increased (426 ± 35 vs. 526 ± 69 ml). Respiratory compliance enhanced, and tidal recruitment decreased (95% vs. 79% of the whole end-expiratory lung volume). OLV with 10 ml/kg further increased aeration (atelectasis, 15 ± 2 ml; poorly aerated, 94 ± 24 ml; normally aerated, 580 ± 98 ml) and tidal recruitment (81% of the dependent lung). OLV with 5 ml/kg did not affect tidal recruitment or lung density distribution. (Data are given as mean \pm SD.)

Conclusions: The ARM improves aeration and respiratory mechanics. In contrast to OLV with high V_T , OLV with reduced V_T does not reinforce tidal recruitment, indicating decreased mechanical stress.

- ◆ This article is accompanied by an Editorial View. Please see: Alfille PH: Using recruitment maneuvers to decrease tidal volumes during one-lung ventilation. ANESTHESIOLOGY 2011; 114:1009-10.

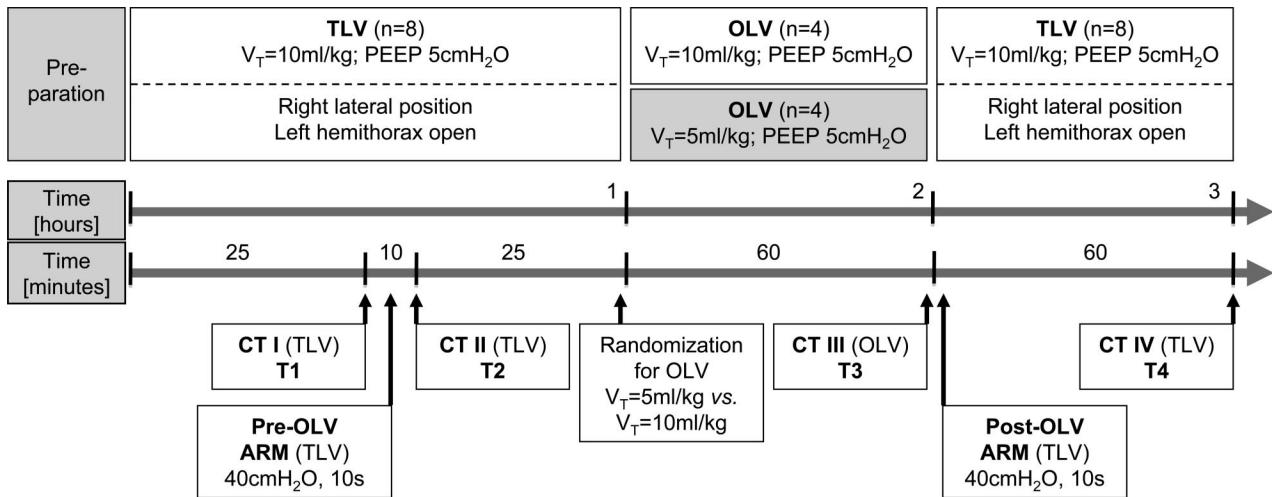


Fig. 1. Experimental work flow, which is closely related to the standard anesthetic management for thoracic surgery. The figure presents ventilation setup, position, and status of the left hemithorax and timing of different procedures, interventions, and computed tomographic (CT) scans. The pig was placed into the right lateral decubitus position after preparation. Thereafter, the left upper nondependent hemithorax was opened. The position of the animal was not changed throughout the study. The alveolar recruitment maneuvers (ARMs) were performed during two-lung ventilation (TLV) before and after one-lung ventilation (OLV). PEEP = positive end-expiratory pressure; T = time point; V_T = tidal volume.

LUNG resection surgery commonly requires exclusion of the nondependent lung from ventilation (one-lung ventilation [OLV]) to improve surgical conditions.¹ However, OLV is associated with an increased intrapulmonary shunt that results from residual perfusion in the nondependent collapsed lung and from insufficient oxygenation of blood in atelectatic and poorly ventilated regions of the dependent ventilated lung.² As a result, hypoxemia is observed in approximately 10% of patients despite the use of high inspiratory fractions of oxygen (FiO_2) during OLV.³

Different ventilation approaches may overcome OLV-induced hypoxemia.⁴ In addition to the application of continuous positive airway pressure and pure oxygen insufflations into the nonventilated lung, relatively high tidal volumes ($V_T > 10\text{ ml/kg}$) with zero end-expiratory pressure have been used to recruit poorly aerated alveoli in the ventilated lung and to avoid blood shift to the nondependent lung during OLV.⁵ This strategy may reinforce airway pressure,^{6,7} alveolar stretching, and shearing secondary to cyclic recruitment/derecruitment of alveoli. Consequently, OLV results in significant diffuse alveolar damage.⁸ However, OLV with reduced V_T ($V_T = 5\text{ ml/kg}$) has decreased the expression of alveolar proinflammatory mediators in a clinical setting⁹ and has reduced the risk of postpneumonectomy respiratory failure.¹⁰ Nevertheless, the simple reduction of V_T seems to be insufficient to completely abolish OLV-induced lung injury.

A more rational approach to avoid alveolar collapse and to improve oxygenation during OLV may include application of repetitive alveolar recruitment maneuvers (ARMs)^{11,12} and reduced V_T and positive end-expiratory airway pressure (PEEP) to minimize atelectasis and cyclic tidal recruitment. An effect of ARM lasting 30–40 min may be anticipated if subsequent ventilation is provided with moderate inspired oxygen concentra-

tions of approximately 40%¹³ or even with a higher FiO_2 if sufficient PEEP is applied to the ventilated lung.¹⁴

Therefore, this randomized computed tomographic (CT) study was undertaken to establish the effects of ARM and subsequent OLV with a V_T of 5 or 10 ml/kg on pulmonary gas/tissue distribution in a porcine model of thoracic surgery. The change in aeration of previously collapsed lung regions was defined as the primary variable that characterizes the radiologic effects of ARM and tidal recruitment/derecruitment.¹⁵ The following null hypothesis was tested: ARM and OLV with different V_T did not affect cyclic recruitment and the distribution of overaerated, normally aerated, poorly aerated, and atelectatic lung regions in the ventilated lung.

Materials and Methods

The study was conducted as a prospective randomized animal experiment. The Institutional Committee on Care and Use of Animals at Uppsala University, Uppsala, Sweden, approved the experimental protocol.

Animals and Randomization

Two-month-old piglets ($n = 8$; mean \pm SD weight, $28 \pm 2.4\text{ kg}$) of the Hampshire, Yorkshire, and Swedish country breeds, which fasted overnight with free access to water, were examined.

After preparation and baseline two-lung ventilation (TLV), pre-OLV-ARM and measurement algorithms including CT scans (1 and 2), the animals were randomly assigned to two groups (random number list generated by EXCEL [Microsoft Corp, Redmond, WA]): the first group ($n = 4$) underwent OLV with a V_T of 10 ml/kg, and the second group ($n = 4$) underwent OLV with a V_T of 5 ml/kg. Figure 1 presents the experimental protocol.

General Procedures

All pigs received an intramuscular injection of xylazine (2.2 mg/kg; Bayer, Leverkusen, Germany), tiletamine-zolazepam (6 mg/kg; Virbac, Carros, France), and atropine (0.04 mg/kg; NM Pharma, Stockholm, Sweden). The pigs were placed in a supine position, and 18-gauge catheters (Becton Dickinson, Heidelberg, Germany) were placed in both ear veins. Anesthesia was maintained by continuous administration of fentanyl ($5 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$; Janssen-Cilag AB, Sollentuna, Sweden), pancuronium ($0.24 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$; Organon, Oss, The Netherlands), ketamine ($25 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$; Intervet, Boxmeer, The Netherlands), and propofol ($3 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$; Astra, Södertälje, Sweden). The animals received $3 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ of isotonic sodium chloride solution (Fresenius Kabi AB, Halden, Norway).

After loss of the hind limb flexion reflexes and corneal reflex responses, which reflected adequate depth of anesthesia, the trachea was intubated (ID 7.0 mm; Mallinckrodt, Athlone, Ireland). The endotracheal tube was replaced with another tube (ID 8.5 mm; Mallinckrodt) by median tracheotomy. A bronchial blocker (9.0 French Arndt-Endobronchial Blocker Set; COOK®, Bjaeverskov, Denmark) was placed in the left main bronchus. The correct endobronchial blocker position was confirmed by fiberoptic bronchoscopy (EF-B 14L; Xion Medical Ltd., Berlin, Germany).

Invasive hemodynamic monitoring included a carotid arterial catheter (20 gauge; Becton-Dickinson Critical Care Systems, Yishun, Singapore), a central venous catheter (4.0 French; Becton-Dickinson Critical Care Systems), a flow-directed pulmonary artery catheter (7.0 French Swan-Ganz thermodilution catheter; Baxter, Irvine, CA), and a suprapubic urinary catheter (Sympakath®; Ruesch, St Gallen, Switzerland). Body temperature was monitored continuously.

Thereafter, the animals were placed into the right lateral decubitus position. This position was kept throughout the study (fig. 1).

The left thoracic cavity was opened by lateral thoracotomy, cranial of the diaphragm. The pigs were allowed to stabilize for 30 min after instrumentation and preparation procedures.

After final measurement, the animals were killed by an intravenous bolus injection of potassium chloride (150 mEq).

Ventilation Management and ARM

Mechanical ventilation started after tracheal intubation (baseline TLV: $V_T = 10 \text{ ml/kg}$, $F_{\text{IO}_2} = 0.40$, $\text{PEEP} = 5 \text{ cm H}_2\text{O}$, and inspiration/expiratory ratio = 1:2) using a ventilator (Servo I; Maquet Critical Care, Solna, Sweden). Respiratory rates were adjusted to maintain the PACO_2 at approximately 40 mmHg. After right lateral positioning and stabilization, measurement of cardiopulmonary variables (time 1) and first CT scan were performed (fig. 1).

The lungs were recruited using the integrated inspiratory-hold function of the ventilator (Servo I) in a standardized manner. A constant airway pressure of 40 cm H_2O was applied to the whole lung for 10 s (ARM)¹⁶ during TLV.

One-lung Ventilation

OLV was started by inflation of the left-sided bronchial blocker for 60 min. The V_T was set to either 5 or 10 ml/kg on the basis of the randomization protocol. The respiratory rates were adjusted to maintain normal PACO_2 . PEEP, inspiration/expiratory ratio, and F_{IO_2} were not changed during OLV ($\text{PEEP} = 5 \text{ cm H}_2\text{O}$; inspiration/expiratory ratio = 1:2; $F_{\text{IO}_2} = 0.40$). The left nondependent lung collapsed without any application of continuous positive airway pressure. The lung collapse was verified by inspection and by CT scout scans.

After OLV, the nondependent lung was reinflated by ARM as described. Thereafter, TLV was reestablished ($V_T = 10 \text{ ml/kg}$; $F_{\text{IO}_2} = 0.40$; and $\text{PEEP} = 5 \text{ cm H}_2\text{O}$).

Measurements

Hemodynamic variables (*e.g.*, cardiac index, heart rate, mean arterial pressure, and central venous pressure) and ventilation and gas exchange data (arterial and mixed venous blood gases) were assessed at defined points (time 1–time 4). The dynamic respiratory compliance was continuously recorded using the ventilator-integrated function. The quasi-static respiratory compliance was calculated on the basis of differences in airway pressure after 5 s of end-inspiratory and end-expiratory hold maneuvers.

CT Acquisition and Analysis

The CT images were acquired *via* a scanner (Somatom Sensation 16CT; Siemens Medical Systems; Erlangen, Germany) in a standardized manner: expiration-hold and subsequent inspiration-hold maneuvers were performed using the ventilator-integrated functions without disconnecting the closed breathing circuit. Transverse CT scans were acquired with the following settings: 120 kV; 100 mA; rotation time, 0.5 s; collimation, $16 \times 1.5 \text{ mm}$; pitch, 1.05; and slice thickness, 5 mm. This algorithm resulted in a scan time of 7 s.

The images were reconstructed and analyzed as follows: Raw image data files from the CT scanner were converted into the Analyze format (1995, Biomedical Imaging Resource, Mayo Foundation, Jacksonville, FL) by the Dicom2Analyze script (V 1.33; Matthew Robson, Ph.D., John Radcliffe Hospital, Headington, Oxford, United Kingdom). The original image metadata and voxel intensities (dimensions and scaling Hounsfield units) were preserved. Regions of interest that followed the boundaries of the lungs along the ribs and the mediastinal organs were drawn manually in each CT image. Voxels that covered the trachea, main bronchi, and large blood vessels were excluded. The regions of interest were defined in the CT images using software (MRICO, V 1.40 build 1; Chris Rorden, Ph.D., Georgia State University/Georgia Institute of Technology Center for Advanced Brain Imaging, Atlanta, GA). The processing and analysis of CT data were conducted by an investigator (H.S.) blinded to the experimental protocol and randomization.

Image Analysis

CT images were filtered with the regions of interest using scripts (MATLAB® V 7.0; MathWorks Inc., Natick, MA) that used statistical parametric mapping functions (2002 Wellcome Department of Cognitive Neurology, University College London, London, United Kingdom). The gray values of all voxels of each slice were classified by counting the voxels falling into the intensity windows of the four compartments (Hounsfield units in parentheses): atelectatic (from 100 to -100), poorly aerated (from -100 to -500), normally aerated (from -500 to -900), and overaerated (from -900 to -1000). As a result, the size of the four compartments could be estimated, either relative to the whole lung volume or in relation to the actual slice.

The distribution of the lung density was normalized to a common length of 100 points without changing the value magnitude to compare lungs of different dimensions. Therefore, all spatial distributions provide the size of the four compartments at certain percentages of the total lung length in craniocaudal orientation.

Cyclic tidal recruitment/derecruitment was defined as the difference in the amount of collapsed lung tissue (atelectatic and poorly aerated, Hounsfield units from 100 to -500) during the ventilatory cycle, with atelectasis/poorly aerated regions decreasing during inspiration and increasing during expiration.

Statistical Analysis

With reference to a previous study,¹⁷ power calculations on the basis of a two-sided design at a significance level of 5% ($\alpha = 0.05$) and a probability of 80% ($\beta = 0.20$) revealed that at least four pigs were needed to detect a difference of 35% in the distribution of different lung compartments between TLV and OLV. The change in aeration of collapsed lung tissue (the sum of atelectasis and poorly aerated regions) was defined as the primary variable.

The data were tested for normal distribution with the Shapiro–Wilks W test. After confirmation of normal distribution, the results were presented as mean \pm SD (circulatory, ventilation, and gas exchange variables and data from CT scans). Hemodynamic and ventilation data were analyzed by a repeated-measures one-way ANOVA with *post hoc* Bonferroni correction. The CT data were assessed by a repeated-measures two-way ANOVA with the independent variables “group” and “slice.” *Post hoc* multiple comparisons were performed by the Bonferroni procedure to compare the groups at different slices. No data were lost during the experiment or were missed in the statistical analysis.

$P < 0.05$ was considered significant for all procedures. The statistical calculations were performed using computer software (SPSS® V. 17; SPSS Inc., Chicago, IL).

Results

TLV before ARM

The end-expiratory dependent lung volume consisted of a small fraction of normally aerated tissue (15 ± 9 ml) during

baseline TLV (CT 1). The dependent lung had mainly poorly aerated (213 ± 13 ml) and atelectatic (90 ± 16 ml) lung regions before ARM. Atelectasis was observed in the most dependent, caudal, and paradiaphragmatic regions (fig. 2). The apical lung zones contained exclusively normally and poorly aerated lung tissue; no overaerated regions were seen.

Inspiration increased the dependent lung volume (table 1). It was associated with reduced atelectatic (56 ± 10 ml) and poorly aerated (183 ± 10 ml) compartments, in favor of normally aerated regions (187 ± 29 ml), which indicated tidal recruitment (table 1; fig. 2).

The density of the nondependent lung was distributed in the same way: atelectatic lung tissue (inspiration/expiration, 18 ± 8 ml/ 21 ± 9 ml), poorly aerated (inspiration/expiration, 62 ± 11 ml/ 100 ± 14 ml), and normally aerated regions (inspiration/expiration, 438 ± 74 ml/ 275 ± 55 ml), without any signs of overaeration (table 1).

Hemodynamic, ventilation, and gas exchange data reflected normal values for pigs that underwent mechanical TLV (table 2 and table 3).

TLV after ARM

The mean end-expiratory lung volume was increased by 36% after ARM ($P < 0.001$, fig. 2). The amount of atelectasis was reduced to 41 ± 12 ml. Normally aerated lung compartments were increased to 57 ± 18 ml of the dependent lung volume, which reflected the recruitment of collapsed lung tissue. The volume of poorly aerated compartments was unchanged (table 1).

Inspiration after ARM further increased normally aerated regions up to 355 ± 49 ml of the dependent lung volume (table 1). Non-aerated and poorly aerated regions became smaller (26 ± 9 ml and 144 ± 33 ml, respectively) in favor of normally aerated lung tissue. The change in aeration of previously atelectatic and poorly aerated lung regions by the ARM was significant ($P < 0.001$). There was no evidence of overaeration (lower than 1% of the dependent lung volume after ARM).

Cyclic recruitment/derecruitment included 95% of the end-expiratory dependent lung volume before ARM but only 79% after ARM ($P < 0.001$).

As a result of ARM, the PAO_2 ($P = 0.02$) and respiratory compliance ($P = 0.018$) were enhanced (tables 2 and 3).

Dependent Lung Density Distribution during and after OLV

OLV with $V_T = 10$ ml/kg reinforced the dependent lung volume and shifted the inspiratory density spectrum toward compartments with a lower density (fig. 3; table 1). This was accompanied by reduced poorly aerated (305 ± 66 vs. 94 ± 24 ml; $P < 0.001$) and atelectatic (27 ± 2 vs. 15 ± 2 ml; $P = 0.005$) regions and by increased normally aerated lung compartments (76 ± 9 vs. 580 ± 98 ml; $P < 0.001$) during the ventilatory cycle. The overaerated lung volume covered an insignificant fraction.

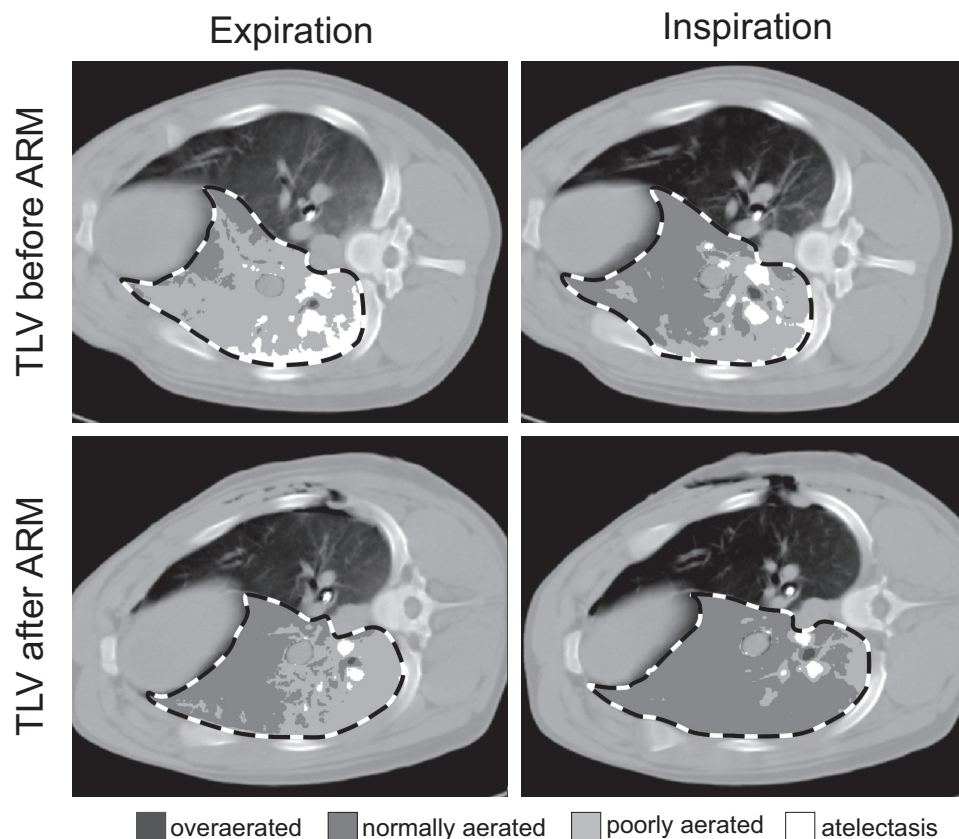


Fig. 2. The juxtadiaphragmatic lung computed tomographic images of representative pigs were acquired during two-lung ventilation (TLV) before and after alveolar recruitment. In each image, the region of interest is marked by a dashed line (Hounsfield units in parentheses): overaerated (from -1000 to -900), normally aerated (from -900 to -500), poorly aerated (from -500 to -100), and atelectatic (from -100 to 100) lung regions. The regions are coded by gray scale. There was a decrease or even elimination of consolidated lung tissue. ARM = alveolar recruitment maneuver.

In contrast, OLV with $V_T = 5$ ml/kg did not change the lung density distribution compared with TLV after ARM, neither at end-expiration nor at end-inspiration (fig. 3; table 1). As a result, the cyclic change in lung volume was smaller during OLV with $V_T = 5$ ml/kg compared with $V_T = 10$ ml/kg. The difference of atelectasis and poorly aerated tissue between expiration and inspiration (cyclic recruitment/derecruitment) was 65% of the dependent lung volume in the high V_T group and 42% in the low V_T group ($P = 0.008$, table 1).

After resuming TLV, the distribution of poorly aerated lung regions differed between the groups, which were ventilated with a V_T of either 5 or 10 ml/kg. The poorly aerated lung volume was increased after OLV with the higher V_T (fig. 4).

Spatial Density Distribution in the Dependent Lung

Figure 5 displays the spatial distribution of normally, poorly aerated, and atelectatic regions in the dependent lung. The use of different V_T values during OLV did not affect the distribution of normally aerated lung regions in any stage of the experiment (*i.e.*, after ARM, during OLV, and during TLV; fig. 5, A–C, respectively). The distribution of poorly aerated areas did not change after ARM (fig. 5D), but the use of high or low V_T resulted in a different amount of poorly aerated tissue during OLV (fig. 5E) and during TLV after

OLV (fig. 5F). OLV with a V_T of 10 ml/kg decreased poorly aerated paradiaphragmatic lung areas compared with OLV with a V_T of 5 ml/kg (fig. 5E: slices 60–100), whereas the distribution was reversed 60 min thereafter during TLV. Poorly aerated compartments were increased in pigs subjected to a V_T of 10 ml/kg (fig. 5F: slices 10–80). The spatial distribution of atelectatic regions was unchanged in all pigs throughout the experiment (fig. 5, G–I).

Hemodynamic and Gas Exchange Data during and after OLV

OLV with a V_T of 10 ml/kg increased peak, plateau, and mean airway pressures compared with TLV before OLV. The intrapulmonary shunt increased in all animals without differences between OLV groups. OLV with a V_T of 5 ml/kg resulted in lower PAO_2 ($P = 0.03$) and respiratory compliance ($P = 0.001$) than OLV with a V_T of 10 ml/kg (tables 2 and 3).

After restoration of TLV, airway pressures, lung compliance, and arterial oxygenation returned to the values before OLV in all animals.

Discussion

The main finding of this study is that the combination of a lung recruitment maneuver before OLV and ventilation with a V_T of

Table 1. Changes in Radiological Density Distribution in Differently Aerated Regions of the Dependent Lung from Expiration to Inspiration

Variables	TLV before ARM Expiration	TLV before ARM Inspiration	Difference between Expiration and Inspiration	TLV after ARM Expiration	TLV after ARM Inspiration	Difference between Expiration and Inspiration
TLV Data						
Dependent Lung Volume, ml	318 ± 34	426 ± 35	108 ± 34	379 ± 41	526 ± 69	147 ± 55*
Atelectasis, %	28 ± 3	13 ± 1	-15 ± 6	10 ± 3*	5 ± 2*	-5 ± 4*
Poorly Aerated, %	67 ± 4	43 ± 1	-24 ± 11	69 ± 4*	27 ± 4*	-42 ± 13*
Normally Aerated, %	5 ± 2	44 ± 2	39 ± 16	21 ± 6*	68 ± 4*	47 ± 14
Variables	OLV 5 ml/kg Expiration	OLV 5 ml/kg Inspiration	Difference Expiration-Inspiration	OLV 10 ml/kg Expiration	OLV 10 ml/kg Inspiration	Difference Expiration-Inspiration
Dependent Lung Volume, ml	382 ± 38†	521 ± 20‡	137 ± 30	409 ± 73§	690 ± 99	281 ± 87#
Atelectasis, %	8 ± 3†	4 ± 1‡	-4 ± 3	7 ± 2§	2 ± 1	-5 ± 3
Poorly Aerated, %	72 ± 1†	34 ± 10‡	-38 ± 17	74 ± 3§	14 ± 4 #	-60 ± 23#
Normally Aerated, %	19 ± 2†	63 ± 10‡	44 ± 11	19 ± 1§	84 ± 4 #	65 ± 16#

Data are given as mean ± SD. The ARM caused an alveolar opening that included the expiratory lung tissue distribution. The effects of different V_T values (5 or 10 ml/kg) on lung density distribution during OLV was detected only during inspiration, but the difference between expiration and inspiration is significant.

* $P < 0.05$ before vs. after ARM. † Data are given for OLV, 5 ml/kg expiration. ‡ Data are given for OLV, 5 ml/kg inspiration. § Data are given for OLV, 10 ml/kg expiration. || Data are given for OLV, 10 ml/kg inspiration. # $P < 0.05$ for expiration vs. inspiration.

ARM = alveolar recruitment maneuver; OLV = one-lung ventilation; TLV = two-lung ventilation; V_T = tidal volume.

5 ml/kg during OLV is associated with a more homogeneous distribution of lung tissue in the dependent ventilated lung. The ARM results in an increased fraction of normally aerated areas; therefore, the ratio of poorly aerated and atelectatic regions remains low during and after OLV, independent from V_T . Although there is a further increase in normally aerated regions during OLV with a V_T of 10 ml/kg, this effect is limited to the

end-inspiratory lung density distribution, without any difference between a V_T of 10 and 5 ml/kg at end-expiration.

Different experimental and clinical studies¹⁸ have established that mechanical ventilation with a large V_T results in diffuse lung injury. Consequently, a protective approach of mechanical ventilation is advocated in patients with acute lung injury.¹⁹ However, studies^{20,21} that

Table 2. Hemodynamic and Gas Exchange Data at Different Points: During Two-lung Ventilation before and after Alveolar Recruitment, during One-lung Ventilation with Different V_T Values, and 60 min Later

Variables	TLV at $V_T = 10$ ml/kg		OLV		TLV after OLV ($V_T = 10$ ml/kg)	
	Before ARM	After ARM	$V_T = 5$ ml/kg	$V_T = 10$ ml/kg	OLV- $V_T = 5$ ml/kg	OLV- $V_T = 10$ ml/kg
HR/min	99 ± 9	91 ± 6	92 ± 5	95 ± 7	93 ± 6	95 ± 8
MAP, mmHg	79 ± 11	77 ± 8	76 ± 9	79 ± 5	78 ± 9	77 ± 5
CVP, mmHg	6 ± 1	6 ± 1	8 ± 1	9 ± 1	7 ± 1	6 ± 1
CI, $l \cdot \text{min}^{-1} \cdot \text{m}^{-2}$	3.7 ± 0.9	3.8 ± 0.6	3.6 ± 0.7	4.1 ± 0.6	3.9 ± 0.5	3.9 ± 0.5
PAO ₂ , mmHg	138 ± 38	191 ± 18*	139 ± 15†	164 ± 22‡	194 ± 22	193 ± 18
PACO ₂ , mmHg	42 ± 3	43 ± 2	47 ± 2†	41 ± 2	44 ± 2	43 ± 2
Qs/Qt, %	4.6 ± 2.2	3.6 ± 1.7	6.4 ± 2.6†	5.8 ± 3.0†	3.2 ± 1.9	3.6 ± 1.8

Data are given as mean ± SD.

* TLV after vs. before ARM ($P = 0.02$). † OLV vs. TLV after ARM ($P = 0.04$). ‡ $V_T = 5$ vs. 10 ml/kg during OLV ($P = 0.03$).

ARM = alveolar recruitment maneuver; CI = cardiac index; CVP = central venous pressure; HR = heart rate; MAP = mean arterial pressure; OLV = one-lung ventilation; Qs/Qt = venous admixture/intrapulmonary shunt; TLV = two-lung ventilation; V_T = tidal volume.

Table 3. Ventilation Data during Two-lung Ventilation before and after Alveolar Recruitment, during One-lung Ventilation with Different V_T Values, and 60 min after One-lung Ventilation

Variables	TLV at $V_T = 10$ ml/kg		OLV		TLV after OLV ($V_T = 10$ ml/kg)	
	Before ARM	After ARM	$V_T = 5$ ml/kg	$V_T = 10$ ml/kg	OLV- $V_T = 5$ ml/kg	OLV- $V_T = 10$ ml/kg
MV, l/min	6.2 ± 0.6	6.3 ± 0.6	6.5 ± 0.6	6.5 ± 0.6	6.2 ± 0.5	6.3 ± 0.7
RR/min	22 ± 3	21 ± 2	44 ± 4*	23 ± 2†	22 ± 2	22 ± 2
V_T , ml/kg	10.1 ± 0.1	10.3 ± 0.4	5.2 ± 0.2*	10.2 ± 0.2†	10.3 ± 0.3	10.2 ± 0.2
P_{AW} , cm H ₂ O						
Peak	27 ± 4	25 ± 4	25 ± 4	31 ± 3*†	26 ± 3	26 ± 4
Plateau	21 ± 3	20 ± 3	19 ± 3	25 ± 3*†	21 ± 3	20 ± 3
Mean	9 ± 2	10 ± 1	10 ± 1	13 ± 1	10 ± 1	10 ± 1
Effective	16 ± 3	15 ± 3	14 ± 3	20 ± 3*†	16 ± 3	15 ± 3
PEEP, cm H ₂ O	5 ± 0	5 ± 0	5 ± 0	5 ± 0	5 ± 0	5 ± 0
C_{stat} , ml/cm H ₂ O	19.2 ± 2.4	23.3 ± 2.7‡	12.1 ± 1.7*	16.9 ± 2.5*	21.0 ± 2.4	22.2 ± 3.6
C_{dyn} , ml/cm H ₂ O	17.1 ± 3.1	20.0 ± 3.5‡	10.0 ± 1.5*	14.9 ± 2.7*	18.3 ± 2.5	19.2 ± 2.1

Data are given as mean ± SD.

* OLV vs. TLV after ARM ($P < 0.05$). † OLV with $V_T = 5$ vs. 10 ml/kg ($P < 0.05$). ‡ TLV after vs. before ARM ($P = 0.04$).

ARM = alveolar recruitment maneuver; C_{dyn} = dynamic compliance; C_{stat} = static compliance; MV = minute ventilation; OLV = one-lung ventilation; P_{AW} = airway pressure; PEEP = positive end-expiratory pressure; RR = respiratory rate; TLV = two-lung ventilation; V_T = tidal volume.

address the effects of a V_T of 10 ml/kg or greater during OLV report controversial results. The application of a relatively high V_T may prevent atelectasis during OLV and achieves better oxygenation and reduced lung injury.⁵

On the other hand, a V_T of 10 ml/kg or greater during OLV is associated with increased alveolar damage and enhanced expression of proinflammatory cytokines in the bronchoalveolar lavage fluid.^{9,20–22}

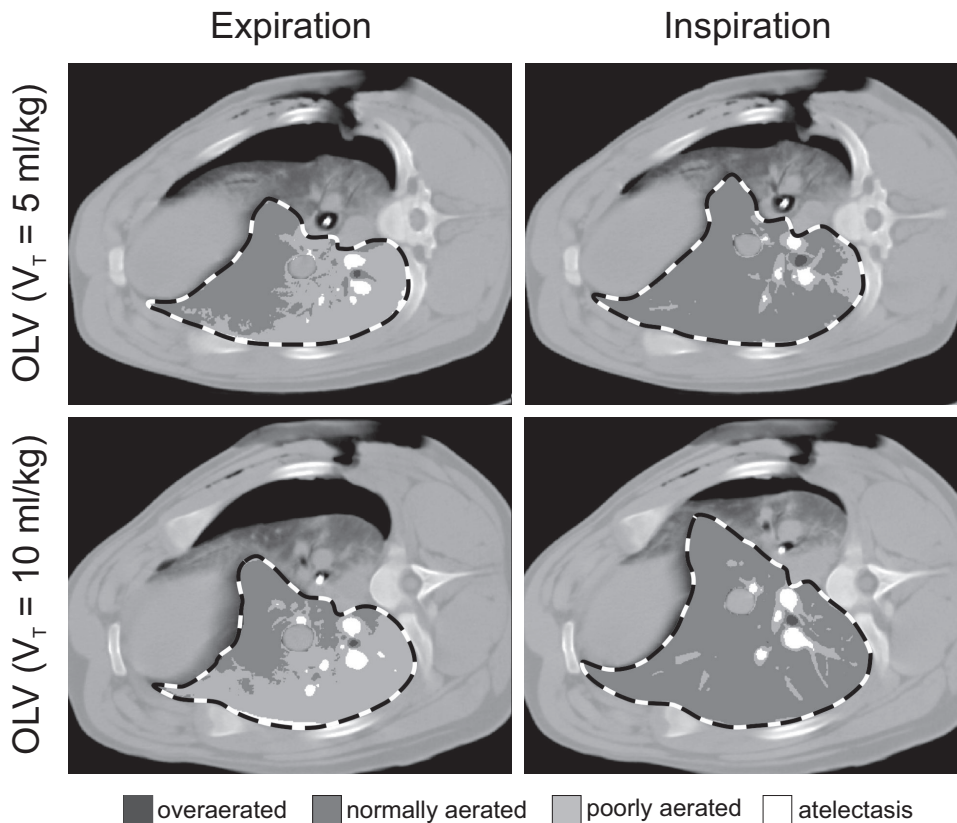


Fig. 3. Juxtadiaphragmatic lung computed tomographic scans of pigs during one-lung ventilation (OLV) with a tidal volume (V_T) of 5 or 10 ml/kg. In each image, the region of interest includes the following (Hounsfield units in parentheses): overaerated (from -1000 to -900), normally aerated (from -900 to -500), poorly aerated (from -500 to -100), and atelectatic (from -100 to 100) lung areas. The regions are coded by gray scale. There were differences in lung density during ventilation with high or low V_T values at inspiration.

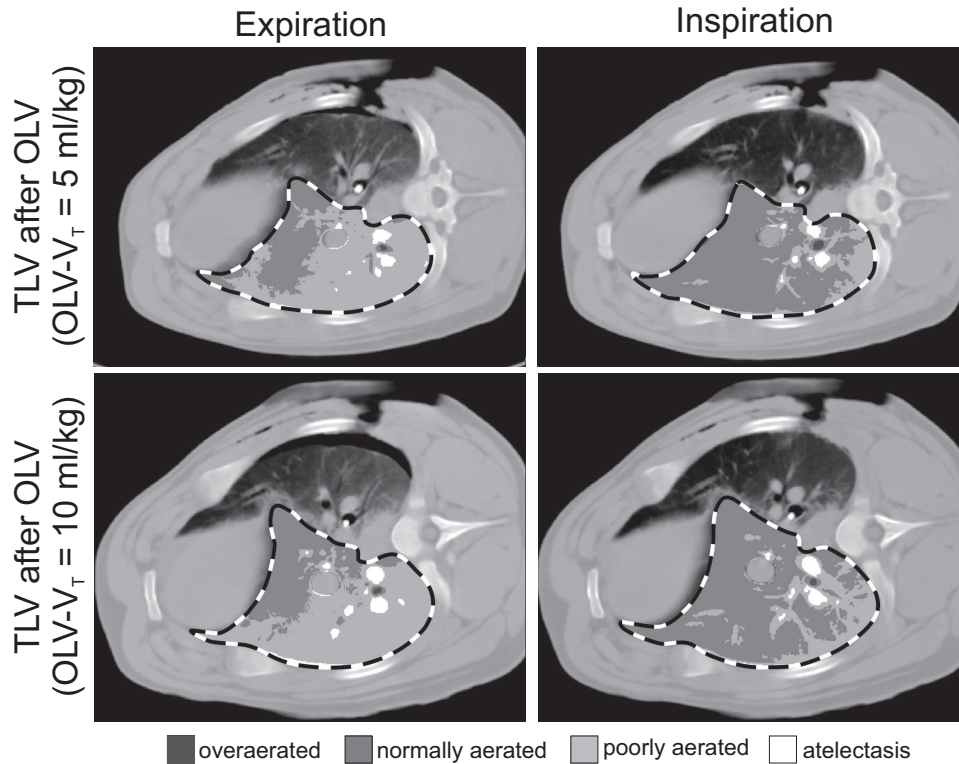


Fig. 4. The images were acquired during two-lung ventilation (TLV) (tidal volume [V_T] = 10 ml/kg) after one-lung ventilation (OLV) with a V_T of 5 or 10 ml/kg. In each image, the dashed line marks (Hounsfield units in parentheses): overaerated (from -1000 to -900), normally aerated (from -900 to -500), poorly aerated (from -500 to -100), and atelectatic (from -100 to 100) lung regions. V_T = tidal volume.

The data of the current study may explain this discrepancy. Mechanical ventilation with a V_T of 10 ml/kg is associated with expanded normally aerated lung regions at end-inspiration but not at end-expiration. In fact, there is an increase in the cyclic transitional area, which suggests alveolar collapse and reopening during each expiration and inspiration. These cyclic changes during mechanical ventilation induce diffuse inflammation in normally aerated regions.^{23,24} In addition, alveolar damage can also occur at the boundaries of atelectatic, poorly aerated, and normally aerated tissue.²⁵ Thus, the increase of normally aerated regions during inspiration seems to be harmful rather than beneficial, during both TLV and OLV.

The current results indicate that ARM of the whole lung before OLV provides sustained effects that extend to OLV. The first CT scan confirms the presence of atelectatic and poorly aerated lung regions after induction of anesthesia.²⁶ The recruitment maneuver enhances aeration and reduces cyclic recruitment during inspiration and during the entire cycle of ventilation, irrespective of whether OLV is continued with a V_T of 5 or 10 ml/kg. In addition, improved aeration and reduced cyclic recruitment/derecruitment of alveoli are responsible for changes in respiratory compliance and oxygenation.

The CT images of healthy pig lungs demonstrate at most only minor overaeration, even during OLV with a V_T of 10 ml/kg, which confirms the results of a previous study.¹⁷

These data disagree with findings in patients with acute respiratory distress syndrome, in whom mechanical ventilation with a large V_T results in overinflation of the lung.^{27,28} Although speculative, open lung conditions may allow a more even distribution of ventilation, with less distension of non-dependent regions. However, distribution of almost the entire perfusion to the dependent lung during OLV²¹ may have influenced X-ray attenuation and may shift voxels toward a higher density, thereby masking overaeration.²⁹ In addition, the lack of overaerated regions in CT scans does not imply that the ventilation is protective. Consequently, OLV can induce an acute pulmonary inflammatory response, even if lung-protective strategies are applied.⁹

The reduction of V_T preserves the lung density distribution resulting from ARM during OLV. Based on the redistribution of lung density from collapse to aeration by ARM, OLV with a V_T of 5 ml/kg does not change the global density distribution and does not increase tidal recruitment. Most important, OLV with a V_T of 5 ml/kg is not associated with increased atelectasis formation if it is combined with a PEEP of 5 cm H₂O; this may confirm recent CT data during TLV.³⁰

In contrast, OLV with a V_T of 10 ml/kg expands the poorly aerated lung tissue, especially in paradiaphragmatic regions. This may increase the amount of poorly aerated tissue in exactly these lung areas after OLV, and it may be attributed to the repetitive reopening of collapsed alveoli.³¹ In addition, high V_T ventilation and sequential inflation to total lung capacity³² have

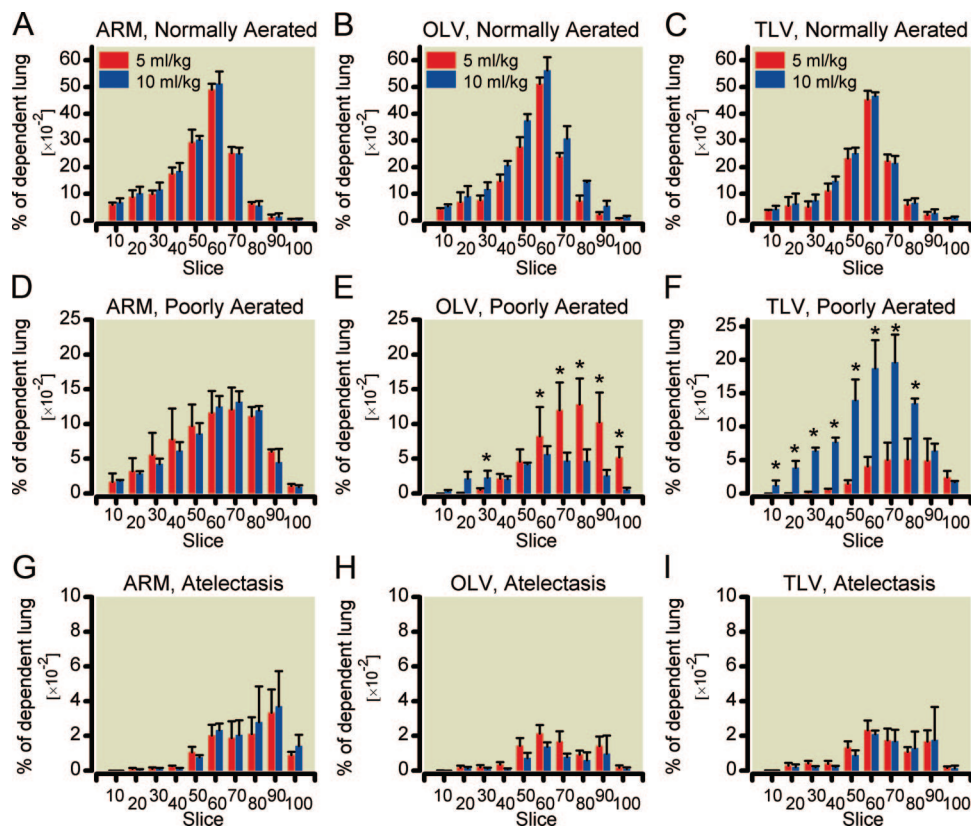


Fig. 5. Distributions of (Hounsfield units in parentheses) normally aerated (from -900 to -500 ; A–C), poorly aerated (from -100 to 100 ; D–F), and atelectatic (from -100 to 100 ; G–I) areas in craniocaudal direction (slice 1–100) according to voxel density at inspiration after alveolar recruitment, during one-lung ventilation (OLV) and during two-lung ventilation (TLV) thereafter. Data are summarized in blocks of 10 slices of the dependent lung and presented as means and SDs. They are grouped related to the use of different tidal volumes (V_T) values during OLV (* $P < 0.05$: 5 vs. 10 ml/kg). ARM = alveolar recruitment maneuver.

been demonstrated to inhibit surfactant production,³³ which, in turn, affects alveolar recoil forces.

Therefore, protective ventilation approaches should consider the increased mechanical stress during OLV. The incidence of acute lung failure is significantly reduced by the use of lower V_T values during OLV.^{10,20} However, the reduction of V_T does not completely abolish alveolar inflammation,⁹ suggesting the existence of persistent shear forces in the lung induced by cyclic opening and collapse of lung tissue. These forces may occur even at low inspiratory pressures and low inspiratory volumes.^{23,34,35} The avoidance of cyclic recruitment and alveolar overdistention seems to be a key factor of lung-protective mechanical ventilation and may be achieved by a combination of ARM, sufficient PEEP, and reduced V_T .^{36,37}

The most significant limitations of this study are the short postoperative observation period and the lack of a control group for the effects of ARM before OLV. Therefore, it is unclear whether the OLV effects with different V_T on lung tissue are similar to conditions in which OLV is applied without preceding ARM. However, ARM is a key component in lung-protective ventilation and was, therefore, included to analyze the more important effects of different V_T during OLV. It is commonly held that the change from poor to normal aeration by ARM would be beneficial; however,

the optimal ratio of this change has not been defined. Therefore, this study reports only relative differences with low and high V_T values before and after OLV.

Furthermore, the experimental setup does not include data demonstrating that cyclic recruitment during OLV with a higher V_T has increased lung injury (e.g., by measurement of proinflammatory mediators). However, possible deleterious effects of either ARM³⁸ or mechanical ventilation^{8,21} have been well established during OLV and in various experimental³⁹ and clinical⁴⁰ studies. In fact, histologic examination findings of the lungs of pigs that underwent a similar experimental setup have demonstrated that an OLV with a V_T of 10 ml/kg induces significant diffuse alveolar damage.⁸

In conclusion, a single ARM before OLV has persistent effects on aeration of the dependent lung tissue. In addition, it improves respiratory compliance and enhances arterial oxygenation. OLV with a V_T of 10 ml/kg results in a higher ratio of normally aerated lung regions and increases PAO_2 . These changes are less pronounced during OLV with a V_T of 5 ml/kg after ARM. However, the improved oxygenation by a higher V_T results in inhomogeneous distribution of aeration and increased mechanical stress that predisposes the lungs to postoperative lung injury.⁸ Therefore, a protective

ventilation strategy with preceding ARM,^{11,12} reduced V_T ,^{9,10} and sufficient PEEP³⁶ ensures oxygenation during OLV and may decrease mechanical stress in the lung by reduced cyclic alveolar collapse. The positive effects of this ventilatory setup on lung injury and outcome after OLV need to be confirmed in further clinical studies.

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