One-lung ventilation induces hyperperfusion and alveolar damage in the ventilated lung: an experimental study


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Background. One-lung ventilation (OLV) increases mechanical stress in the lung and affects ventilation and perfusion (V, Q). There are no data on the effects of OLV on postoperative V/Q matching. Thus, this controlled study evaluates the influence of OLV on V/Q distribution in a pig model using a gamma camera technique [single-photon emission computed tomography (SPECT)] and relates these findings to lung histopathology after OLV.

Methods. Eleven anaesthetized and ventilated pigs (VT=10 ml kg⁻¹, Fio₂=0.40, PEEP=5 cm H₂O) were studied. After lung separation, OLV and thoracotomy were performed in seven pigs (OLV group). During OLV and in a two-lung ventilation (TLV), control group (n=4) ventilation settings remained unchanged. SPECT with ⁸¹mKr (ventilation) and ⁹⁹mTc-labelled macro-aggregated albumin (perfusion) was performed before, during, and 90 min after OLV/TLV. Finally, lung tissue samples were harvested and examined for alveolar damage.

Results. OLV affected ventilation and haemodynamic variables, but there were no differences between the OLV group and the control group before and after OLV/TLV. SPECT revealed an increase of perfusion in the dependent lung compared with baseline (49–56%), and a corresponding reduction of perfusion (51–44%) in non-dependent lungs after OLV. No perfusion changes were observed in the control group. This resulted in increased low V/Q regions and a shift of V/Q areas to 0.3–0.5 (10⁻⁰.⁵–10⁻⁰.³) in dependent lungs of OLV pigs and was associated with an increased diffuse alveolar damage score.

Conclusions. OLV in pigs results in a substantial V/Q mismatch, hyperperfusion, and alveolar damage in the dependent lung and may thus contribute to gas exchange impairment after thoracic surgery.

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One-lung ventilation (OLV) during thoracic surgery can cause injury in terms of increased mechanical stress, alveolar cell stretch and overdistension, shear forces secondary to repeated tidal collapse and reopening of alveolar units, compression of alveolar vessels, and increased pulmonary vascular resistance.¹ ² Despite the consequences of an extensively decreased ventilated lung volume, tidal volumes of 8–10 ml kg⁻¹ and zero end-expiratory pressure are recommended during OLV to limit shunt, avoid atelectasis, and preserve arterial oxygenation and carbon dioxide elimination.³

A protective ventilation approach to prevent lung injury during OLV by reduction of tidal volumes and application of PEEP did not completely inhibit thromboxane B₂ formation in isolated rabbit lungs⁴ or the enhanced alveolar proinflammatory response in rats.⁵ Likewise, OLV with...
tidal volumes of 5 ml kg\(^{-1}\) decreased only partially the expression of proinflammatory IL8, TNFα, and neutrophil infiltration in patients undergoing thoracic surgery and OLV.\(^6\)

Consequently, mechanical ventilation might not be the only variable affecting alveolar integrity during and after OLV. However, there are currently no data addressing distribution of pulmonary blood flow and ventilation/perfusion (\(V/Q\)) ratios during and after OLV and their relationship to diffuse alveolar damage (DAD).

The present experimental study investigated the effects of OLV on \(V/Q\) distribution by single-photon emission computed tomography (SPECT) in a pig model of thoracic surgery. The null hypothesis (H\(_0\)) was tested that OLV may have no effects on postoperative distribution of pulmonary perfusion and ventilation and on alveolar histomorphology.\(^7\,^8\)

Methods
The study was conducted as a prospective animal experiment and the study protocol was approved by the Animal Ethics Committee of Uppsala University (Sweden).

Animals
Eleven piglets of the Hampshire, Yorkshire, and Swedish country breeds obtained from a local breeder were used in the study. The animals fasted overnight with free access to water. Seven pigs were assigned to the OLV group; in the control group (\(n=4\)) standard two-lung ventilation (TLV) was performed throughout the study. All pigs underwent the same study algorithm (anaesthesia, preparation, measurements, tissue sampling; Fig. 1).

Anaesthetic and surgical management
The pigs were anaesthetized by an i.m. injection of xylazine (2.2 mg kg\(^{-1}\), Rompun\(^\circledR\); Bayer, Leverkusen, Germany), tiletamine/zolazepam (6 mg kg\(^{-1}\), Zoletil\(^\circledR\); Virbac, Carros, France), and atropine (0.04 mg kg\(^{-1}\), NM Pharma, Stockholm, Sweden). The trachea was intubated with an ID 7.0 mm cuffed endotracheal tube (Mallinkrodt, Athlone, Ireland).

Anaesthesia was maintained by continuous infusions of fentanyl (5 μg kg\(^{-1}\) h\(^{-1}\), Leptanal\(^\circledR\); Janssen-Cilag AB, Sweden), pancuronium (0.3 mg kg\(^{-1}\) h\(^{-1}\), Pavulon\(^\circledR\); Organon, Oss, The Netherlands), ketamine (25 mg kg\(^{-1}\) h\(^{-1}\), Ketaminol vet\(^\circledR\); Intervet, Boxmeer, The Netherlands), and propofol (3 mg kg\(^{-1}\) h\(^{-1}\), Diprivan\(^\circledR\); Astra, Södertälje, Sweden) via 18 G catheters (Becton Dickinson, Heidelberg, Germany) placed in an ear vein.

After intubation, animals were mechanically ventilated with intermittent positive pressure ventilation (IPPV) with an \(F_{1O_2}\) of 0.40 and PEEP of 5 cm H\(_2\)O provided by a Servo I ventilator (Maquet Critical Care, Solna, Sweden). The tidal volume was set to 10 ml kg\(^{-1}\), respiratory frequencies were adjusted to achieve a normal arterial \(P_{CO_2}\) of 40–45 mm Hg.

Gas flow and airway pressures were measured at the proximal end of the endotracheal tube with a standard monitor for ventilation and haemodynamic measurements (SC 9000 XL, Siemens, Erlangen, Germany).

A median tracheotomy was performed, and the orotracheal tube was replaced by an ID 8.5 mm cuffed endotracheal tube (Mallinkrodt). A left-sided bronchial blocker (9.0 French Arndt-Endobronchial Blocker Set, COOK\(^\circledR\); Bjaæverskov, Denmark) was fixed in the left main bronchus under bronchoscopic control (EF-B 14L, Xion medical, Berlin, Germany).

A flow-directed pulmonary artery catheter (PAC, 7.0 French, Swan-Ganz thermodilution catheter, Baxter, Irvine, CA, USA) and a single lumen central venous catheter (4.0 French, Becton-Dickinson Critical Care Systems, Singapore) were inserted via the left external jugular vein. The balloon tip of the PAC was located in wedge position for cardiac output measurements and mixed venous blood sampling. PAC was replaced before each measurement to ensure that the tip was always located in regions with highest pulmonary blood flow.

All pigs received a left carotid arterial catheter for continuous arterial pressure measurements and arterial blood sampling (20 G; Becton-Dickinson Critical Care Systems). Blood gas analysis was performed immediately after blood sampling, with standard blood gas electrodes (ABL 500; Radiometer, Copenhagen, Denmark).

Finally, a suprapubic urinary catheter (Sympakath\(^\circledR\); Ruesch AG, St Gallen, Switzerland) was placed for monitoring of urine output.

After 30 min stabilization, pigs were then placed in the right lateral position. In the OLV group, ventilation of the non-dependent left lung was discontinued by bronchoscopically controlled inflation of the bronchus blocker for 90 min. OLV of the dependent, right lung was started, and a typical left-sided lateral thoracotomy of about 10 cm was performed. Left lung collapse was confirmed by visual control via thoracotomy, low-resolution CT, and distribution of ventilation in SPECT. The left lung collapsed completely in all OLV pigs.

A surgical procedure was simulated by handling the collapsed left lung for 15 min.

During OLV and in the control group, ventilation settings remained constant: \(V_1=10\) ml kg\(^{-1}\), respiratory frequency adjusted to a \(P_{aCO_2}\) of 40–45 mm Hg, \(F_{1O_2}=0.4\), PEEP=5 cm H\(_2\)O. The bronchial blocker was removed immediately after second SPECT, and the non-dependent lung was re-inflated by repetitive vital capacity manoeuvres. After re-inflation, TLV was re-established.

All pigs received 8–10 ml kg\(^{-1}\) h\(^{-1}\) of isotonic saline solution (Fresenius Kabi AB, Halden, Norway) during the study period in order to maintain urine output at 2–4 ml kg\(^{-1}\) h\(^{-1}\) and to keep arterial pressure and haemoglobin
concentration stable. Body temperature was monitored and was kept constant by thermoconvection.

Study protocol
The workflow of the experimental protocol is presented in Figure 1.

Baseline
After 30 min of stabilization, baseline haemodynamic, ventilation, and gas exchange data were assessed in the right lateral position and the first SPECT and computerized tomography (CT) were performed.

Haemodynamic, ventilation, and gas exchange variables
The following cardiopulmonary and respiratory variables were recorded at $T_1$, $T_2$, $T_3$, and $T_4$: cardiac output, heart rate (HR), mean arterial pressure (MAP), and mean pulmonary artery pressure (MPAP), central venous pressure (CVP), pulmonary artery occlusion pressure (PAOP), arterial and mixed venous blood gases. Systemic vascular resistance, pulmonary vascular resistance, pulmonary capillary pressure, oxygen delivery (DO$_2$), oxygen consumption (VO$_2$), and venous admixture were calculated according to the standard formulae.

Single-photon emission computed tomography
Pulmonary blood flow distribution was assessed by i.v. injection of $^{99m}$Tc-labelled macro-aggregated albumin ($^{99m}$Tc-MAA, Pulmocis; CISbiointernational, Gif sur Yvette, France); ventilation was studied by continuous inhalation of Krypton ($^{81m}$Kr), produced by a Rubidium generator on site (Mallinkrodt; The Netherlands). Three SPECT-measurements were performed: (I) baseline (TLV), (II) after 45 min of OLV (OLV group) or TLV (control group), and (III) 45 min after OLV/TLV.

Sub-baseline SPECT scans were performed before SPECT (II) and (III) in order to subtract the remaining technetium activity from the previous scan since the shape of the lungs had changed.

A CT scan (covering the same volume as the SPECT) was performed immediately after each SPECT and used for attenuation correction.

Images were acquired using a SPECT/CT dual-head gamma camera (Millennium; General Electric Systems, Milwaukee, WI, USA) with an all-purpose medium-energy collimator. Acquisition was performed in two separate energy windows, one at 140 ($\pm$10) keV for $^{99m}$Tc and the other at 190 ($\pm$10) keV for $^{81m}$Kr. SPECT acquisition was made in 60 projections (30 per head) and stored in a 128 by 128 matrix, resulting in a pixel size of (4.42 mm). The acquisition time was 60 s per projection. This rather long time resulted from the comparatively low activity of $^{81m}$Kr. The overall scan time for SPECT and CT was approximately 42 min.

Data were reconstructed first on an eNTEGRA workstation and later on a Xeleris workstation (Millennium; General Electric Systems). The reconstruction was performed with an iterative model (OSEM, four iterations and eight subsets) and a Hann filter (cut-off 0.85) for the post-reconstruction filtering on both workstations. The reconstructed transverse slices were corrected for radiation spill-over and for baseline subtraction using a HERMES workstation (Hermes Medical Solution, Stockholm, Sweden).

For each reconstructed slice, in apex–base and anterior–posterior directions, the contents were analysed by specially written software. Before calculating activity distribution, a background subtraction of 10% of the global maximum was performed.

After evaluation of the lung borders assessed by CT, the left and the right lungs were separated by drawing the external boundaries of the lungs along the inside of the ribs and the internal boundaries along the mediastinal organs. The lungs were divided into 40 equally thick
slices in the inferior (dependent, right lung) to superior (non-dependent, left lung) direction, to assess vertical distribution of krypton and technetium.

Tissue samples

After completion of measurements, the pigs were killed by an i.v. bolus injection of potassium chloride. A bilateral thoracotomy was performed and both lungs were removed and dissected. Tissue samples (approximately 1×1×0.5 cm) at the level of the lungs largest diameter were harvested from the peripheral right and left lower lobe for histological staining. The tissue samples were immediately placed in a 4% phosphate buffered formaldehyde (Formalin; Apoteket AB, Göteborg, Sweden) and stored at 20°C.

Three independent representative sections of each lung were immersed in the fixative for at least 72 h, embedded in paraffin, sectioned (2–3 μm slices), and stained with haematoxylin and eosin (H&E) for light-microscopic analysis. The slides were evaluated by a blinded pathologist (C.R.). The severity of injury was scored based on the DAD score.

DAD score

The characteristics of alveolar injury (alveolar oedema, interstitial oedema, microhaemorrhage, inflammatory infiltration, microatelectasis, and alveolar overdistension) were estimated in the H&E stained sections by light microscopy (Model CHK; Olympus, Taiwan) using magnifications of ×40, ×100, and ×400. In three different sections of each lung, four separate non-overlapping fields of view were analysed.

Values from 0 to 3 represent the severity of the feature, as follows: 0 normal appearance; 1 slight effect; 2 intermediate effect; and 3 severe effect. The extent of damage in each sector is described as follows: 0 no damage; 1 up to 25%; 2 25–50%; 3 50–75%; 4 75% to almost complete; and 5 complete. For each feature evaluated, severity was multiplied by the extent, leading to values in the range of 0–15. Values for all sectors per lung (n=12) were averaged. The sum corresponded to the DAD score.

Statistical analysis

For calculation of V/Q ratios, proprietary interfile format files were converted to Analyze™ format (1995, Biomedical Imaging Resource, Mayo Foundation) by header file parsing without changing the binary image data. Regions of interest (ROI) of the upper and lower lungs were manually defined in the CT images using the MRICO software (V 1.40, 2005). These ROI were applied to the SPECT data images using SPM functions (Wellcome Department of Cognitive Neuroscience, University College, London, UK) in MATLAB (V 7.0, MathWorks Inc.), thus reading the 81mKr and 99mTc (SP) counter values for each voxel in each lung. Voxels outside the ROI were ignored. For estimation of absolute ventilation and perfusion, counts per voxel were summarized separately for each lung and normalized to individual maximum activity. For V/Q relationships, logarithmic V/Q ratios were calculated by: $\log_{10} (81mKr activity/99mTc activity)$. The results were plotted as V/Q distributions over the whole lung.

Statistical analysis was performed using SPSS (Chicago, IL, USA). Power calculations using a two-sided design at a significance level of 5% (α=0.05) and a probability of 80% (β=0.20) to detect a difference in perfusion between both lungs after OLV showed that a minimum of four pigs would be needed in the OLV group.

Data were tested for normal distribution using the Shapiro–Wilks W-test. Normally distributed data are presented as mean (SD) (cardiopulmonary, ventilation, and gas exchange variables) or as mean (SEM) (SPECT data). These data were analysed by a repeated measures one-way analysis of variance with post hoc Bonferroni correction. SPECT data were filtered for time, lung, and subject and selectively grouped. Two-sample t-tests were performed to establish differences between lungs, subjects, and controls.

Non-normally distributed variables (alveolar damage) are given as median and inter-quartile range (P25–75). Alveolar damage scores were compared using the Mann–Whitney U-test. Differences were considered to be statistically significant for all procedures if P<0.05.

Results

Animals

Eleven 2-month-old pigs [mean weight 28.1 (2.9) kg] were used in the study. Biological variables and administered radioactivity were not different in the OLV group (n=7) and the control group (n=4). The mean injected activity of 99mTc-MAA was increased from 24.7 (2.4) MBq (first SPECT scan) to 65.9 (11.5) MBq (second SPECT scan) to 128.1 (16.4) MBq (third SPECT scan).

Haemodynamic, ventilation, and gas exchange

Mean haemodynamic values, ventilation, and gas exchange data are presented in Tables 1–3. In comparison with baseline, OLV resulted in an increase in airway pressures, MPAP, PAOP, and CVP and a decrease in Pao2.

Cardiac index decreased from 4.5 (0.7) to 3.5 (0.8) litre min−1 m−2 (P<0.05) after 45 min of ongoing OLV but returned to baseline after OLV.

In the control group, there were no differences in ventilation and haemodynamics throughout the study.
Table 1 Haemodynamic data at the beginning of the study (baseline, right lateral position, T1), during OLV/TLV (after 45 min, T2), during TLV (45 min after OLV/TLV, T3), and at the end of the study (90 min TLV after OLV/TLV, T4). Data are presented as mean (SD) (*P<0.05 vs baseline, OLV group; #P<0.05 OLV group vs control group).

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<td>18 (3)</td>
<td>18 (3)</td>
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<td>8 (2)</td>
<td>13 (4)*</td>
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<td>PAOP (mm Hg)</td>
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<td>8 (2)</td>
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<td>Aw plateau (cm H₂O)</td>
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<td>PaO₂ (mm Hg)</td>
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<td>PaO₂ (mm Hg)</td>
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Table 2 Ventilation data [mean (SD)] at the beginning of the study (baseline, right lateral position, T1), during OLV/TLV (after 45 min, T2), during TLV (45 min after OLV/TLV, T3), and at the end of the study (90 min TLV after OLV/TLV, T4) (*P<0.05 vs baseline, OLV group; #P<0.05 OLV group vs control group).

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Table 3 Gas exchange data [mean (SD)] at the beginning of the study (baseline, right lateral position, T1), during OLV/TLV (after 45 min, T2), during TLV (45 min after OLV/TLV, T3), and at the end of the study (90 min TLV after OLV/TLV, T4) (*P<0.05 vs baseline, OLV group; #P<0.05 OLV group vs control group).

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<td>141 (16)</td>
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<td>Qu/Qt (%)</td>
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Ventilation and perfusion SPECT

Distribution of ventilation and perfusion to the left, non-dependent lung and the right, dependent lung in the OLV group is depicted in Figures 2 and 3. At baseline, ventilation was primarily distributed to the non-dependent lung [67.5 (5.5)% vs 32.5 (6.7)%]. During OLV, tidal volume was delivered solely to the right lung, which resulted in an upward shift of the mediastinum of about 10 slices (Fig. 3, OLV), and the accessory lobe of the right lung became more apparent (Fig. 2, OLV).

After resuming TLV, ventilation distribution returned to baseline TLV values [67.3 (7.4)% vs 32.6 (7.5)%]. In the control group, distribution of ventilation did not differ between SPECT scans I, II, and III. Additionally, ventilation distribution in the control group was not different in comparison with the OLV group before and after OLV.

Perfusion distribution between the two lungs was comparable in all pigs, with 48% delivered to the upper lung and 52% delivered to the lower lung during baseline TLV.
Only a minimal percentage of whole perfusion passed through the upper, non-ventilated lung during OLV. After resuming TLV in OLV pigs, pulmonary blood flow was distributed 56.2% to the dependent lung and 43.8% to the non-dependent lung \((P<0.01,\) compared with baseline, Fig. 3: TLV after OLV), despite the normalization of cardiac index and ventilatory parameters.

In the control group, perfusion was evenly distributed to the upper and lower lung throughout the study period. Differences in perfusion distribution between SPECT I and III were <2%.

**Distribution of V/Q ratios**

Regions with low V/Q ratios increased in the dependent lungs after OLV. Likewise, the V/Q shift was significant in the range of V/Q \([\log_{10}]\approx-0.5\) to 0.1 compared with baseline (Fig. 4). These effects were not observed in the control group.

**Diffuse alveolar damage**

Data on alveolar damage of tissue samples from the right dependent lungs and left non-dependent lung of all pigs are depicted in Figures 5 and 6.

Alveolar and interstitial oedema, haemorrhage, neutrophil infiltration, and microatelectasis were increased in the right dependent ventilated lung compared with the left non-dependent lung in OLV pigs. The degree of alveolar overdistension did not differ between the lungs (Figs 5 and 6) after OLV. Thus, the highest DAD score was seen in the right, dependent lungs of OLV pigs.

In the control group, diffuse alveolar damage was minor and there were no differences between left and right lung tissue samples.

**Discussion**

These experimental data suggest that OLV of the dependent lung and surgical manipulation of the non-dependent lung is followed by a substantial V/Q mismatch secondary to hyperperfusion in the previously ventilated lung and hypoperfusion of the manipulated lung. Likewise, low V/Q regions increased in the dependent lung after OLV. The V/Q mismatch developed, despite normalization of haemodynamic and ventilatory variables after OLV. Histopathological examination exposed signs of DAD which were significantly more prominent in the dependent lung of OLV pigs.

Although gravity influences the V/Q relationship, pulmonary blood flow follows principally the pulmonary artery tree. The pulmonary vascular structure has been shown to be the dominant factor in determining perfusion distribution as assessed by injection of coloured microspheres and post-mortem analysis. Recent experiments using aerosol deposition revealed similar ventilation heterogeneities closely related to perfusion. These studies also confirmed that positioning has only a minor effect on pulmonary blood flow in pigs and dogs.

Simultaneous lung perfusion and ventilation scintigraphy is the primary and only validated tool for repeated in vivo V/Q measurements. The combination of SPECT and CT and the subsequent fusion of images facilitate...
Fig 3 Hyperperfusion in the dependent lung and hypoperfusion in the non-dependent lung in pigs after OLV: ventilation and perfusion [mean (SEM)] derived from SPECT scans in transverse planes from OLV pigs before (TLV, baseline, SPECT I), during (SPECT II), and after OLV (TLV, SPECT III). The mediastinum is located in slices 19–23 (SPECT I, III); OLV resulted in an upward shift to slices 29–33 (SPECT II). Perfusion (99mTc-MAA activity) and ventilation (81mKr-activity) was calculated as percentage of individual maximal ventilation and perfusion (*P<0.05 TLV vs baseline).
correlations of time-dependent functional parameters with anatomical structures. The existence of an additional lobus accessorius pulmonis dexter in pigs, however, made the accurate separation of lungs by CT in this species difficult.

The use of radioisotopes allows repeated tracer administration during different conditions, for example, ventilator settings or OLV. Previously administered $^{99m}$Tc-MAA remained fixed in the lung tissue, thus later imaging of tracer distribution corresponds to distribution at administration. After subtraction, repetitive manoeuvres and interventions can therefore be assessed.

The distribution of radioisotopes in the reconstructed transverse slices is not only affected by radiation scatter and partial volume effect (which are different for the two isotopes used) but also by the reconstruction technique. Further, time required for image acquisition is longer when compared with MRI or CT.

Spatial resolution of SPECT is approximately 15 mm. The present SPECT acquisitions with $^{81m}$Kr and $^{99m}$Tc isotopes resulted in a voxel size of (4.42 mm). Alternatively, perfusion distribution can be assessed by coloured microspheres. The resolution level of the microsphere technique attainable using a destructive approach is a function of the cut piece size with a standard of about 2 cm$^3$ in large laboratory animals. Measurement of ventilation distribution by coloured microspheres, however, has not been validated, thus calculation of $V/Q$ ratios may be unreliable. The technique has further disadvantages: it lacks in the time dimension and animals need to be killed to obtain experimental data.

Baseline SPECT (TLV) revealed an almost even distribution of perfusion over both halves of the lung in OLV and control pigs. Ventilation was primarily distributed to the non-dependent lung, similar to preferential ventilation of upper lung regions and perfusion of dependent regions in anaesthetized human patients in the supine position.

Perfusion distribution is only marginally affected by gravitation; additionally, even PEEP or the lateral decubitus position had no influence on pulmonary blood flow.

Initiation of OLV generally results in characteristic haemodynamic and ventilatory changes. In the OLV group, cardiac indices decreased during OLV, attributable

Fig 4 OLV increased low $V/Q$ regions in the dependent lung of pigs: distributions of $V/Q$ ratios (mean) in non-dependent and dependent lungs separately in the OLV group and in the control group at baseline (SPECT I) and after OLV/TLV (SPECT III). $V/Q$ ratios were calculated in transverse planes, gated separately for the non-dependent and dependent lungs, in all pigs (*$P$<0.05, SPECT III vs I).
to the increased right ventricular afterload augmented by increased airway pressures. However, CI normalized after OLV in comparison with baseline, suggesting that cardiac output per se may not have affected the distribution of pulmonary blood flow before and after OLV.

During OLV, only a minimal fraction of pulmonary blood flow passed through the non-ventilated lung, reflecting efficient hypoxic pulmonary vasoconstriction in pigs. This may explain the insignificant increase of intrapulmonary shunt in the OLV group.

After OLV, vasoconstriction in the upper lung induced by microatelectasis and hypoxic exposure may result in a continuous decrease of blood flow. Previously collapsed lung tissue is more prone to formation of atelectasis due to alterations of surfactant even after complete reexpansion by repetitive vital capacity manoeuvres.

In addition, OLV may induce a proinflammatory response preferably in the ventilated lung indicated by increased neutrophil infiltration in the dependent lung of OLV pigs. Mechanical stretch alters alveolar type II cell mediator release towards a proinflammatory pattern. Most immune mediators act as vasodilators; therefore, cytokine-induced direct vasodilatation may have resulted in a shift of perfusion to the dependent lung in the OLV group.

It should be emphasized that signs of alveolar damage were mostly present in the dependent lung of OLV pigs, suggesting that OLV was worse than a period of complete lung collapse and manipulation. Lung tissue damage can thus be attributed to hyperperfusion and hyperinflation of the ventilated lung during OLV. The findings of epithelial damage in the non-ventilated collapsed lung reflect the impact of surgical manipulation and confirm data of previous studies.

Limitations of the present study included the size of the study group, the fixed ventilation setup, and the short postoperative observation period. Nevertheless, the study protocol is closely related to a typical thoracic surgical procedure. Moreover, SPECT is also used as a clinical diagnostic tool; therefore, the present data may reflect the conditions in humans.

In conclusion, hyperperfusion and hyperinflation of the ventilated lung during OLV initiates diffuse damage in the alveolar compartment. In patients undergoing thoracic surgery, reductions of tidal volumes and subsequently decreased peak airway pressures had significant effects on the alveolar inflammatory response after OLV and in the postoperative course. Whether this approach is also associated with a decrease in \( V/Q \) mismatch and less severe histopathological alterations remains to be investigated.
Fig 6 Representative lung histology (haematoxylin–eosin staining) of the dependent, ventilated right lung and non-dependent non-ventilated surgically manipulated left lung in a control pig with TLV and in a pig after OLV: (A) normal lung tissue, control pig 1 (×10). OLV pig 4: (B) interstitial oedema (×10), (C) microhaemorrhage (×10), (D) alveolar overdistension (×10), and (E) neutrophil infiltration (×40).
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