EXPERIMENTAL

Rolf Dembinski
Martin Max
Ralf Bensberg
Johannes Bickenbach
Ralf Kuhlen
Rolf Rossaint

High-frequency oscillatory ventilation in experimental lung injury: effects on gas exchange

R. Dembinski (✉) · M. Max · R. Bensberg
J. Bickenbach · R. Kuhlen · R. Rossaint
Klinik fuer Anaesthesiologie,
Universitaetsklinikum der RWTH Aachen,
Pauwelsstrasse 30,
52074 Aachen, Germany
e-mail:
Rolf.Dembinski@post.rwth-aachen.de
Tel.: +49-241-8088179
Fax: +49-241-8888406

Abstract *Objective:* To compare ventilation-perfusion ($\dot{V}_A/\dot{Q}$) distributions during improvement of oxygenation caused by high-frequency oscillatory ventilation (HFOV) and pressure-controlled mechanical ventilation with high PEEP levels (CMV) in experimental acute lung injury (ALI). *Design:* Prospective, controlled animal study. *Setting:* Animal research facility of a university hospital. *Interventions:* Twelve pigs with oleic acid-induced ALI were randomised to HFOV (n=6) or to CMV (n=6) with a PEEP of 15 mbar for 1 h. The mean airway pressure was adjusted in both groups to achieve comparable improvements in arterial oxygen partial pressure (PaO_2) and to avoid clinically relevant impairments of cardiac output, as assured by adequate mixed venous oxygen saturation and lactate levels. $\dot{V}_A/\dot{Q}$ distributions were determined by the multiple inert gas elimination technique (MIGET). *Measurements and results:* Arterial oxygen partial pressure improved during CMV with a mean airway pressure of 20 mbar ($p<0.05$) whereas HFOV revealed comparable improvements with a mean airway pressure of 40 mbar ($p<0.05$). Shunt decreased and blood flow to normal $\dot{V}_A/\dot{Q}$ areas increased due to CMV and HFOV ($p<0.05$). The perfusion of low $\dot{V}_A/\dot{Q}$ areas remained unchanged. Statistical analysis did not reveal differences of PaO_2, shunt or blood flow to low $\dot{V}_A/\dot{Q}$ areas between the groups. *Conclusions:* In this model of acute lung injury CMV and HFOV improved gas exchange due to similar changes in $\dot{V}_A/\dot{Q}$ distribution. However, mean airway pressure had to be adjusted twofold higher during HFOV then during CMV to achieve comparable improvements in gas exchange.

Keywords Oscillation, high frequency · Exchange, pulmonary gas · Injury, acute lung · Experimental model

Introduction

In acute lung injury (ALI) pulmonary gas exchange is characterised by hypoxaemia due to pulmonary ventilation-perfusion ($\dot{V}_A/\dot{Q}$) inequality [1]. Large fractions of pulmonary blood flow are diverted towards poorly ventilated areas or non-ventilated atelectatic regions. Hypoxaemia is usually present, therefore, despite high inspiratory oxygen fractions.

The application of high PEEP levels ranging from 10 to 20 mbar during controlled mechanical ventilation (CMV) has been demonstrated to increase oxygenation by an improvement of $\dot{V}_A/\dot{Q}$ inequality [1, 2, 3, 4]. Thus, shunt and perfusion of the lung areas with a low $\dot{V}_A/\dot{Q}$ ratio decrease, while the perfusion of regions with a normal $\dot{V}_A/\dot{Q}$ ratio increases. Thereby, the recruitment of collapsed lung areas is supposed to be the most important mechanism by which high PEEP levels improve $\dot{V}_A/\dot{Q}$ distribution. High-frequency oscillatory ventilation (HFOV) may also improve gas exchange in experimental and clinical ALI [5, 6, 7, 8, 9]. However, the underlying

effects of HFOV on $\dot{V}_A/\dot{Q}$ distribution in ALI remain unclear.

Using the multiple inert gas elimination technique (MIGET), the distribution of ventilation and perfusion has been described for HFOV in healthy subjects [10], during experimental hypoxic gas ventilation [11] and in animals with experimentally induced extensive $\dot{V}_A/\dot{Q}$ mismatch but only little intrapulmonary shunt [12]. However, in ALI $\dot{V}_A/\dot{Q}$ distribution is mainly characterised by large amounts of pure shunt [1]. Similar findings can be obtained after the intrapulmonary infusion of oleic acid, a commonly used method to induce experimental ALI in animals comparable to clinical ALI [13]. Thus, this study was performed to compare $\dot{V}_A/\dot{Q}$ distribution in pigs with oleic acid-induced ALI in which oxygen partial pressure was increased by CMV with high PEEP levels and HFOV. We hypothesised that HFOV may improve gas exchange due to similar changes in $\dot{V}_A/\dot{Q}$ distribution as has been described for ventilation with high PEEP levels during CMV.

Materials and methods

Animal preparation

The experimental protocol was approved by the appropriate governmental institution and the study was performed according to the Helsinki convention for the use and care of animals.

In 12 female pigs weighing 30 ± 1 kg (mean ± SD) anaesthesia was induced with 5 mg/kg thiopental and maintained with continuous infusion of 5–10 mg/kg per h thiopental and 8–12 μg/kg per h fentanyl. Muscle relaxation was achieved with 0.2–0.4 mg/kg per h pancuronium. The animals were positioned supine, intubated with a 8.0–9.0 mm ID endotracheal tube (Mallinckroth, Athlone, Ireland) and submitted to pressure-controlled mechanical ventilation (Servo 300 A Ventilator, Siemens Elema, Lund, Sweden) set to achieve a tidal volume of 8 ml/kg with a respiratory rate of 20/min, an inspiratory:expiratory time ratio of 1:2 and a PEEP of 5 mbar. Inspiratory oxygen fraction (FIO_2) was 1.0. A 16 G arterial catheter (Vygon, Ecouen, France) and a 8.5 Fr venous sheath (Arrow Deutschland, Erding, Germany) were inserted percutaneously into femoral vessels. A right heart catheter (model AH-05050–7.5 F, Arrow Deutschland, Erding, Germany) was positioned in a pulmonary artery under transduced pressure guidance. The blood temperature, determined by means of the pulmonary artery catheter, was maintained at 36.7 ± 0.9°C during the experiment, using an infrared warming lamp and a warming pad. Before baseline measurement, 500 ml balanced electrolyte infusion was administered to substitute the fluid demand of the fasting period. A continuous infusion of 4–5 ml/kg per h of a balanced electrolyte solution was administered for adequate hydration over the entire study period.

Data acquisition

All haemodynamic measurements were taken in the supine position with zero reference level at the mid chest. Central venous pressure (CVP), mean arterial pressure (MAP), mean pulmonary artery pressure (MPAP) and pulmonary capillary wedge pressure (PCWP) were transduced (pvb, Medizintechnik, Kirchseeon, Germany) and recorded (AS/3 Compact, Datex-Ohmeda, Achim, Germany). Cardiac output (CO) was measured using standard thermodilution techniques and expressed as the mean of three measurements. Heart rate (HR) was traced by the blood pressure curve.

Blood samples were collected simultaneously in duplicate and analysis of arterial and mixed venous blood gases (PO_2, PCO_2), haemoglobin (Hb) and oxygen saturation (SO_2) was performed immediately. Blood gases were determined using standard blood gas electrodes (ABL 510, Radiometer Copenhagen, Denmark). The parameters Hb, SaO_2 and SvO_2 were measured via species-specific spectroscopy (OSM 3, Radiometer Copenhagen, Denmark). Lactate concentrations were measured by a lactate electrode system (EML 105 Radiometer Copenhagen, Denmark). Venous admixture ($\dot{Q}_{VA}/\dot{Q}_T$) was calculated using the secondary parameters arterial (CaO_2), mixed venous (CvO_2) and arterial capillary oxygen content (CcO_2), as described previously [14]. Oxygen delivery (DO_2) and consumption (VO_2) were determined using the usual formulas: $DO_2 = CO \times CaO_2 \times 10$ and $VO_2 = CO \times (CaO_2\text{-}CaO_2) \times 10$. The data are presented as the mean of each measurement taken in duplicate.

Ventilation-perfusion distributions were analysed using the MIGET [15]: briefly, 45 min before the first blood sampling an isotonic saline solution equilibrated with six inert gases (sulphur hexaflouride, ethane, cyclopropane, enflurane, ether and acetone) was infused into a peripheral vein at a constant rate of 4 ml/min. Samples of arterial and mixed venous blood and mixed expired gas were collected simultaneously at each study point during several respiratory cycles and analysed immediately by gas chromatography. The expiratory tubing and the mixing box for the expired gas samples were heated above body temperature to avoid a loss of the more soluble gases in condensed vapour. During HFOV, expiratory gas samples were collected from the downstream limb of the bias flow system. Expiratory bias flow was also taken to be the minute ventilation during HFOV for calculation of $\dot{V}_A/\dot{Q}$ distribution [10]. All samples were taken in duplicate. For each inert gas retention (the ratio of the gas concentration in arterial, to that in mixed venous, blood) and excretion (the ratio of the gas concentration in expired gas to that in mixed venous blood) were calculated and $\dot{V}_A/\dot{Q}$ distributions were estimated retention-weighted. The duplicate samples were processed separately resulting in two $\dot{V}_A/\dot{Q}$ distributions for each condition investigated in this study. The data presented are the mean values of $\dot{V}_A/\dot{Q}$ distributions taken in duplicate.

Shunt ($\dot{Q}_S/\dot{V}_T$) was defined as the fraction of pulmonary blood flow ($\dot{Q}_T$) perfusing lung areas with a $\dot{V}_A/\dot{Q}$ less than 0.005. Low $\dot{V}_A/\dot{Q}$ regions were defined as those with $\dot{V}_A/\dot{Q}$ ratios between 0.005 and 0.1 and normal $\dot{V}_A/\dot{Q}$ regions as those with $\dot{V}_A/\dot{Q}$ ratios between 0.1 and 10. Data for perfusion distribution are presented in percent of the total pulmonary blood flow and expressed as $\dot{Q}_{low}$ and $\dot{Q}_{normal}$. The position of the distributions is also described by the mean $\dot{V}_A/\dot{Q}$ ratio for perfusion (mean $\dot{V}$) and their dispersion by the log standard deviation of perfusion (log $\dot{Q}$). Quality control was performed by calculating the remaining sum of squares (RSS) between the measured and calculated $\dot{V}_A/\dot{Q}$ distributions and the differences between predicted and measured PaO_2 based on perfusion distribution.

Experimental protocol

After animal preparation, a baseline measurement of all values was performed. ALI was induced with oleic acid ($C_{18}H_{34}O_2$, Sigma-Aldrich, Taufkirchen, Germany) dissolved in heparinised blood and infused via the right heart catheter. Values for ALI were collected after the PaO_2 remained persistently below 100 mmHg for 1 h without additional oleic acid infusion. Subsequently, the animals were randomised to HFOV (Sensor Medics 3100 A – Respirator, Sensor Medics, Bilthoven, Netherlands) or to CMV.

High-frequency oscillatory ventilation was performed with a bias flow of 20 l/min, a respiratory rate of 4.5 Hz, an inspirato-

ry:expiratory time ratio of 1:2 and an oscillatory pressure amplitude of 50 mbar (*n*=6). CMV was performed pressure-controlled with a respiratory rate of 20/min, an inspiratory:expiratory time ratio of 1:2 and a PEEP of 15 mbar (*n*=6). Mean airway pressure was adjusted in both groups with two major goals: first, to achieve comparable improvements in PaO_2 and, second, to avoid clinically relevant impairments of CO as assured by adequate SvO_2 and lactate levels.

After 1 h a new measurement was performed. At the end of the study, all animals were killed with intravenous potassium chloride in deep sedation.

Statistical analyses

All values are expressed as means ± SD. Statistical analyses were performed using the SigmaStat for Windows 5.0 (Jandel, San Rafael, USA) software package. Each parameter was analysed by two-way analysis of variance for repeated measures (ANOVA) within and between the groups. Statistical analyses were followed by the Student-Newman-Keuls test for all pairwise comparison when ANOVA revealed significant results. Probability values less than 0.05 were considered significant.

Results

All animals survived the entire study period. Examination of all animals by a veterinary surgeon prior to the study confirmed the absence of any sign of infection or pulmonary disease and haemodynamic, gas exchange and MIGET data measured at baseline were within normal ranges. Statistical analyses did not reveal differences in any parameter determined at baseline and ALI when compared between the two groups. Total Hb remained unchanged throughout the study.

A mean of 1.0±0.3 ml/kg oleic acid had to be infused to obtain a stable ALI with a decrease of PaO_2 from 552±26 to 69±13 mmHg. During CMV with a PEEP of 15 mbar a mean airway pressure of 20 mbar had been adjusted, resulting in a mean tidal volume of 244±59 ml and an increase of PaO_2 from 63±15 to 299±139 mmHg (*p*<0.05). Mean airway pressure during HFOV had to be set at 40 mbar to achieve a comparable improvement in PaO_2 from 75±4 to 340±127 mmHg (*p*<0.05).

Haemodynamics are presented in Table 1. In both groups the experimental interventions resulted in a decrease of CO after 1 h (*p*<0.05). CMV also caused a decrease in MPAP (*p*<0.05). Other haemodynamic parameters remained unchanged.

Conventional gas exchange parameters are presented in Table 2. In both groups statistical analyses revealed an increase in PaO_2, PvO_2 and SvO_2 after 1 h (*p*<0.05). Additionally, $\dot{Q}_{VA}/\dot{Q}_T$ decreased during CMV and HFOV (*p*<0.05). No statistical differences were revealed for the comparison of PaO_2, PvO_2 or $\dot{Q}_{VA}/\dot{V}_T$ between the groups. Other gas exchange parameters and lactate concentrations remained unchanged.

Multiple inert gas elimination technique data are presented in Table 3. MIGET revealed an improvement in

Table 1 Haemodynamics (mean ± SD). High-frequency oscillatory ventilation (*HFOV*, *n*=6) versus controlled mechanical ventilation (*CMV*, *n*=6) 1 h after induction of experimental acute lung injury (*ALI*) (*HR* heart rate, *MAP* mean arterial pressure, *CO* cardiac output, *CVP* central venous pressure, *MPAP* mean pulmonary artery pressure, *PCWP* pulmonary capillary wedge pressure)

		Baseline	ALI	1 h
HR (per min)	CMV	98±13	105±24	96±21
	HFOV	85±18	91±13	95±10
MAP (mmHg)	CMV	105±10	100±14	100±14
	HFOV	110±9	104±21	90±12
CO (l/min)	CMV	5.6±0.6	4±0.7	3.4±0.6[a]
	HFOV	5.7±1.8	3.7±0.7	3.1±0.4[a]
CVP (mmHg)	CMV	10±4	11±3	11±4
	HFOV	12±4	13±4	13±4
MPAP (mmHg)	CMV	22±2	44±4	37±4[a,b]
	HFOV	22±1	47±4	49±4[b]
PCWP (mmHg)	CMV	9±4	10±4	10±3
	HFOV	11±4	10±3	10±3

[a] *p*<0.05 for comparison of ALI and 1 h within the group
[b] *p*<0.05 for comparison between the groups

Table 2 Conventional gas exchange (mean ± SD). High-frequency oscillatory ventilation (*HFOV*, *n*=6) versus controlled mechanical ventilation (*CMV*, *n*=6) 1 h after induction of experimental acute lung injury (*ALI*). (*PaO₂* arterial oxygen partial pressure, *PvO₂* venous oxygen partial pressure, *SvO₂* mixed venous oxygen saturation, *PaCO₂* arterial carbon dioxide partial pressure, *DO₂* oxygen delivery, *V̇O₂* oxygen consumption, *Q̇_VA/Q̇_T* venous admixture)

		Baseline	ALI	1 h
PaO₂ (mmHg)	CMV	547±29	63±15	299±139[a]
	HFOV	559±22	75±4	340±127[a]
PvO₂ (mmHg)	CMV	58±5	32±7	50±9[a]
	HFOV	69±11	41±3	51±8[a]
SvO₂ (%)	CMV	89±3	33±15	58±10[a]
	HFOV	93±4	45±7	54±17[a]
Lactate (mmol/l)	CMV	1.4±1.0	1.8±1.4	0.9±0.4
	HFOV	1.3±1.0	1.0±0.9	0.7±0.3
PaCO₂ (mmHg)	CMV	31±3	54±4	57±17
	HFOV	33±3	59±9	57±5
DO₂ (ml/min)	CMV	675±66	299±65	371±83
	HFOV	657±148	314±41	334±71
VO₂ (ml/min)	CMV	147±25	168±9	161±9
	HFOV	122±15	151±16	162±38
Q̇_VA/Q̇_T (%)	CMV	11±4	47±14	17±8[a]
	HFOV	12±5	42±2	15±6[a]

[a] *p*<0.05 for comparison of ALI and 1 h within the group

the distribution of pulmonary perfusion due to CMV and HFOV. Thus, shunt decreased and $\dot{Q}_{normal}$ increased in both groups (*p*<0.05) while $\dot{Q}_{low}$ remained unchanged. No statistical differences were revealed for the comparison of shunt, $\dot{Q}_{low}$ or $\dot{Q}_{normal}$ between the groups.

Table 3 Multiple inert gas elimination technique data (mean ± SD). High-frequency oscillatory ventilation (*HFOV*, *n*=6) versus controlled mechanical ventilation (*CMV*, *n*=6) 1 h after induction of experimental acute lung injury (*ALI*) (*RSS* remaining sum of squares, *PaO$_2$ (p-m)* predicted – measured arterial oxygen partial pressure, $\dot{Q}_S/\dot{Q}_T$ shunt, $\dot{Q}_{low}$ blood flow to regions with low (0.005–0.1) $\dot{V}_A/\dot{Q}$ ratio, $\dot{Q}_{normal}$ blood flow to regions normal (0.1–10) $\dot{V}_A/\dot{Q}$ ratio, *mean $\dot{Q}$* mean $\dot{V}_A/\dot{Q}$ ratio of perfusion, *log SD$\dot{Q}$* logarithmic standard deviation of perfusion)

		Baseline	ALI	1 h
RSS	CMV	3±2	4±4	1±0
	HFOV	2±1	1±1	1±0
P$_a$O$_2$ (p-m) measured (mmHg)	CMV	78±32	8±13	53±93
	HFOV	93±31	1±8	43±100
$\dot{Q}_S/\dot{Q}_T$ (% $\dot{Q}_T$)	CMV	7±4	48±14	15±11[a]
	HFOV	3±6	48±4	13±6[a]
$\dot{Q}_{low}$ (%$\dot{Q}_T$)	CMV	5±7	8±6	9±7
	HFOV	6±8	4±5	6±6
$\dot{Q}_{normal}$ (% $\dot{Q}_T$)	CMV	87±8	44±16	75±16[a]
	HFOV	90±7	48±6	76±7[a]
Mean $\dot{Q}$	CMV	0.7±0.2	1.1±0.4	0.7±0.3
	HFOV	0.5±0.1	1.0±0.4	0.9±0.4
log SD$\dot{Q}$	CMV	1±0.4	1.9±0.7	1.5±0.5
	HFOV	0.9±0.5	1.2±0.7	1.5±0.3

[a] *p*<0.05 for comparison of ALI and 1 h within the group

Discussion

The aim of this study was to describe $\dot{V}_A/\dot{Q}$ distributions during HFOV in comparison to CMV with high PEEP levels. Our major finding was that HFOV and CMV equally improved oxygenation, due to a decrease of shunt and increase of $\dot{Q}_{normal}$. However, it is worth noting that equal improvements in gas exchange required a twofold higher mean airway pressure with HFOV when compared to CMV.

Ventilation distribution was calculated as well, but the mean data are not presented in this study because of their lack of information. As previously revealed by McEvoy and co-workers, the determination of ventilation distribution during HFOV by inert gas elimination has certain limitations [10]: first, during HFOV gas transport through the conducting airways is different, depending on the solubility of each gas. Thus, it has been shown that for the most soluble gases, acetone and ether, gas flux from the lung may be up to twice that of the other gases sulphur hexaflouride, ethane, cyclopropane and enflurane. A possible explanation given by the authors is an increased gas exchange of highly soluble gases with the wet luminal surface of the conducting airways, which may facilitate gas transport during small oscillatory flows. As a consequence, higher excretion values for acetone and ether result in the calculation of large amounts of dead space and high $\dot{V}_A/\dot{Q}$ regions during HFOV. Second, the measurement of minute ventilation analogous to conventional minute ventilation during
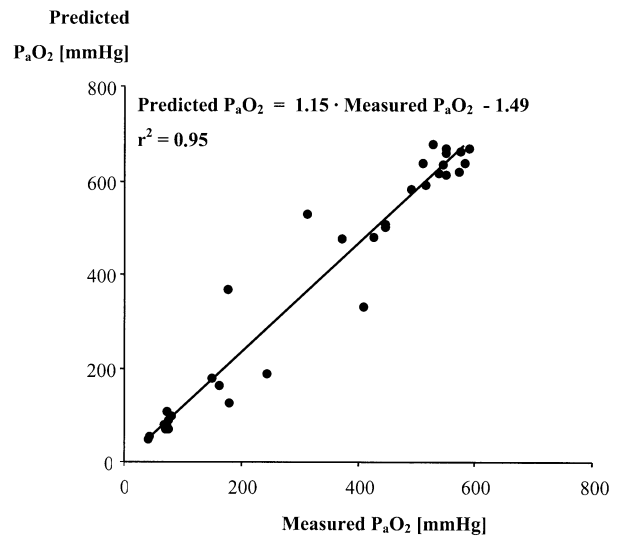
Predicted

P$_a$O$_2$ [mmHg]

Fig. 1 Predicted – measured arterial oxygen partial pressure. Predicted PaO$_2$ calculated by the multiple inert gas elimination technique (MIGET) versus measured PaO$_2$

CMV is usually not possible during HFOV. Thus, bias flow has to be measured instead and used for the calculation of ventilation distribution during HFOV. Therefore, the validity of excretion values and the analysis of corresponding ventilation distribution may be further reduced. In conclusion, the calculation of $\dot{V}_A/\dot{Q}$ distributions during HFOV must result in unreliably high amounts of ventilation and perfusion in areas with high $\dot{V}_A/\dot{Q}$ ratios greater than 10.

However, in ARDS $\dot{V}_A/\dot{Q}$ mismatching is mainly characterised by the presence of pulmonary shunt and perfusion of low $\dot{V}_A/\dot{Q}$ regions [1]. Accordingly, this study was designed to focus on changes of perfusion distribution due to HFOV and the presentation of the MIGET data was limited to the mean values of blood flow distribution in normal $\dot{V}_A/\dot{Q}$, low $\dot{V}_A/\dot{Q}$ and shunt areas. Additionally, calculations of $\dot{V}_A/\dot{Q}$ distributions were performed retention-weighted and the remaining sum of squares (RSS) and the differences between predicted and measured PaO$_2$ were calculated based on perfusion distribution.

To confirm an acceptable quality of the $\dot{V}_A/\dot{Q}$ distribution data, it has been suggested that the RSS should be 5.348 or less in at least 50%, or 10.645 or less in at least 90%, of all experimental runs [16]. In the present study the RSS was less than 5.348 in 92% and less than 10.645 in 97% of all experimental runs. Additionally, the quality of the MIGET data in this study was analysed by the differences between predicted and measured PaO$_2$, which were comparable to those presented by Neumann et al. for pigs with oleic acid-induced lung injury [13]: thus, in the present study measured and predicted PaO$_2$ correlated with r^2=0.95 (Fig. 1). According to Bland et al. [17],
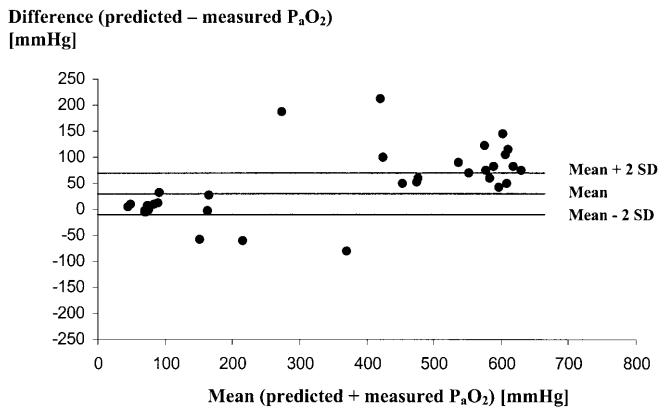
Fig. 2 Predicted – measured arterial oxygen partial pressure. Mean values of predicted PaO_2 (calculated by the multiple inert gas elimination technique) and measured PaO_2 versus the difference between predicted PaO_2 and measured PaO_2

the mean value of predicted and measured PaO_2 is plotted against the difference between predicted and measured PaO_2 in Fig. 2. Both figures revealed that the differences between predicted and measured PaO_2 increased at high PaO_2 levels. As Neumann et al. pointed out, this may be due to the fact that the precision of blood gas analysis usually decreases with an increase of PaO_2 [13]. However, the RSS provide acceptable quality of the MIGET data.

Induction of ALI caused $\dot{V}_A/\dot{Q}$ mismatching comparable to other studies using oleic acid lung injury models and to clinical ARDS as well [1, 13]. Thus, hypoxaemia was mainly caused by shunt, while small amounts of $\dot{Q}_{low}$ impaired oxygenation additionally. Haemodynamics were characterised by elevated MPAP due to the induction of ALI.

Ventilation with high PEEP levels (CMV) resulted in an improvement of blood flow distribution with a decreased shunt and increased normal $\dot{V}_A/\dot{Q}$ regions, as has been demonstrated recently [3]. The perfusion of low $\dot{V}_A/\dot{Q}$ regions and log $SD\dot{Q}$ remained unchanged. We conclude that the changes of blood flow distribution are probably the result of a recruitment of atelectatic lung regions. The distribution of ventilation and perfusion during CMV is demonstrated for one representative animal (Fig. 3).

Perfusion distribution during HFOV was almost identical to CMV: following HFOV, shunt decreased for the benefit of blood flow to normal $\dot{V}_A/\dot{Q}$ areas while perfusion of low $\dot{V}_A/\dot{Q}$ regions and log $SD\dot{Q}$ remained unchanged. We therefore proposed that, similarly to CMV, pulmonary recruitment is the main mechanism of improved gas exchange during HFOV. However, the correlation between shunt reduction and recruitment of atelectatic areas is estimated by analysis of $\dot{V}_A/\dot{Q}$ distribution but can be proved only by other diagnostic methods, such as computer tomography. The distribution of venti-
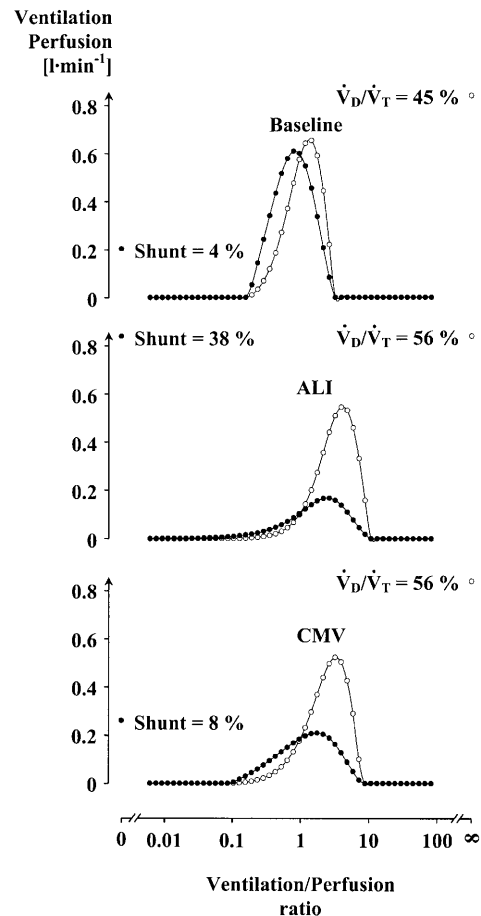

Fig. 3 Ventilation-perfusion distribution during controlled mechanical ventilation (*CMV*). Ventilation (white dots) – perfusion (black dots) distribution from one representative animal calculated by the multiple inert gas elimination technique (*MIGET*) at baseline, oleic acid-induced acute lung injury (*ALI*) and CMV ($\dot{V}_D/\dot{V}_T$ dead space ventilation)

lation and perfusion during HFOV is demonstrated for one representative animal (Fig. 4).

The finding that $\dot{Q}_{low}$ remained unchanged during HFOV in our investigation is in accordance with the results of Kaiser and co-workers [12]. They demonstrated that high frequency ventilation is not effective in blood flow redistribution in a canine model of lung disease characterised by large amounts of $\dot{Q}_{low}$. In contrast to Kaiser et al., we aimed to determine $\dot{V}_A/\dot{Q}$ distribution during HFOV and CMV in an oleic acid lung injury model with high amounts of pure shunt comparable to clinical ALI. Previously, Thompson and co-workers had demonstrated equal improvements of oxygenation during HFOV and CMV in dogs with oleic acid-induced lung injury [18], while a prospective clinical trial recently presented by Mehta and co-workers revealed improved oxygenation during HFOV in comparison to CMV in patients with acute lung injury [19]. However, analyses of
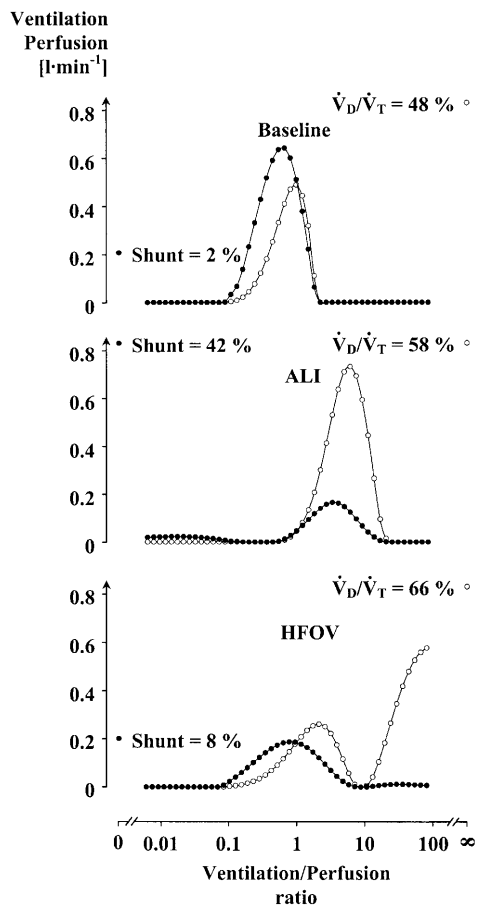
Fig. 4 Ventilation-perfusion distribution during high-frequency oscillatory ventilation (*HFOV*). Ventilation (white dots) – perfusion (black dots) distribution from one representative animal calculated by the multiple inert gas elimination technique (*MIGET*) at baseline, oleic acid-induced acute lung injury (*ALI*) and HFOV ($\dot{V}_D/\dot{V}_T$ dead space ventilation)

$\dot{V}_A/\dot{Q}$ distributions were not performed in either study. Our results reveal that the improved oxygenation during HFOV and CMV with high PEEP is caused by a comparable decrease of pulmonary shunt.

In both groups, CO decreased due to the experimental procedure. With regard to a simultaneous increase in PvO_2, we hypothesised that this was the result of increased oxygenation and does not necessarily reflect im-paired venous return due to increased thoracic pressure. Furthermore, SvO_2 increased while normal lactate levels were measured during both experimental interventions, demonstrating that the decrease in CO did not cause tissue hypoxia due to impaired DO_2. During CMV a decrease in MPAP was revealed, probably due to increased oxygenation resulting in decreased hypoxic pulmonary vasoconstriction. In contrast, MPAP remained unchanged during HFOV although PvO_2 increased in both groups and hypoxic pulmonary vasoconstriction should decrease equally. Possibly, vascular compression due to a higher mean intrathoracic pressure during HFOV also contributed to the increased MPAP. However, it has been demonstrated that pulmonary artery pressure may increase during HFOV, in comparison to CMV, without an increase of airway pressure [11].

In the present study, airway pressures were not measured with an intratracheal catheter but derived from the pressure-control devices inside the ventilators. We are aware of the fact that this method, especially during HFOV, does not reflect real intratracheal pressures. However, our aim was to describe mechanisms of $\dot{V}_A/\dot{Q}$ distribution during different ventilator modes with ventilator settings that cause a comparable improvement of oxygenation without major impairment of haemodynamics. Thereby, the measurement of intratracheal pressures might have been helpful, but is not necessary to analyse $\dot{V}_A/\dot{Q}$ distributions.

The increase of oxygenation during both ventilatory strategies in our study was achieved with different airway pressures, which is, to a moderate extent, a common finding in other investigations [19]. In contrast, Thompson et al. found no differences of gas exchange at equal transpulmonary pressures measured with an oesophageal catheter [18]. These different results reflect the problem of the measurement and evaluation of airway pressures during HFOV because neither ventilator settings nor oesophageal- or intratracheal catheter-derived pressures reflect real intra-alveolar pressures. However, the point should be made that mean airway pressure in the present study had to be adjusted twofold higher during HFOV than during CMV to achieve comparable improvements in gas exchange. Therefore, further investigations are needed to validate HFOV as a ventilatory strategy in ALI.

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