

Patterns of Changes in Arterial PO₂ During One-Lung Ventilation: A Comparison Between Patients With Severe Pulmonary Emphysema and Patients With Preserved Lung Function

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Objectives: One-lung ventilation (OLV) during thoracoscopic surgery is associated with a significant decline in arterial PO₂ in patients with severe pulmonary emphysema and patients with preserved lung function. The authors hypothesized that patterns of arterial PO₂ changes are different in these 2 patient groups.

Design: Prospective nonrandomized study.

Setting: University hospital.

Participants: Twenty-five patients undergoing thoracoscopic interventions: 16 with severe pulmonary emphysema and 9 patients without emphysema.

Interventions: Continuous arterial blood gas measurement (PaO₂, PaCO₂, pHa) during OLV of the left lung in left lateral position using the Paratrend 7 blood gas monitoring system (PT7; Pfizer Hospital Products Group, High Wycombe, UK).

Main Results: The decrease of PaO₂ was delayed in patients with severe emphysema. Steady state (defined as $\Delta\text{PaO}_2 < 7.5\text{mmHg/min}$) was reached after 18 ± 4 minutes

compared with 11 ± 3 minutes (mean \pm standard deviation) in patients with normal lung function ($p = 0.0002$). PaO₂ values at steady state were comparable ($p = 0.49$); the pattern of changes in PaO₂ for the first 15 minutes of left-sided OLV was significantly different between the groups ($p = 0.0004$). The difference of predicted versus measured PaO₂ at steady state was -48 ± 160 mmHg for patients with emphysema and -51 ± 60 mmHg for patients with normal lung function ($p = 0.019$).

Conclusion: During OLV, oxygenation is better preserved for a longer period of time in patients with severe pulmonary emphysema as compared with patients with normal lung function. In contrast to patients without emphysema, prediction of oxygenation during OLV for the individual patient with emphysema is unreliable because of large inter-individual differences.

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KEY WORDS: anesthesia, one-lung ventilation, emphysema, arterial PO₂, Paratrend

VIDEO-ASSISTED THORACOSCOPIC surgery is used in an increasing number of therapeutic and palliative procedures. One-lung ventilation (OLV) of the dependent lung, with a collapsed nondependent lung and lateral positioning of the patient are required to enable surgical access to the thoracic cavity. OLV with a thoracoscopic surgical approach has been used successfully to perform resections of bullae and wedge resections of hyperinflated lung tissue in patients with severe pulmonary emphysema.¹⁻⁴ Adequate oxygenation during OLV in these patients remains a major concern, but, according to the authors' clinical experience, sufficient oxygenation can often be maintained during OLV. This observation correlates with the findings of higher PaO₂ in patients with reduced preoperative forced expiratory volume in 1 second (FEV₁) in previous studies.^{5,6} However, a considerable number of patients with end-stage pulmonary disease develop a low PaO₂ in the course of OLV. Possible mechanisms of the PaO₂ course in these patients include the delayed development of atelectasis of the nondependent lung serving as an oxygen reservoir and concomitant delayed intrapulmonary right-to-left shunt, increased functional residual capacity of the dependent lung during OLV because of development of intrinsic positive end-expiratory pressure,⁷ kinking of pulmonary vessels of the atelectatic lung due to loss of elastic recoil,⁵ and altered hypoxic pulmonary vasoconstriction (HPV) in the presence of chronic, irreversible disease in the pulmonary vessels rendering vessels incapable of a normal HPV response.^{8,9} Under normal conditions, HPV plays an important role in reducing the perfusion to the nondependent, atelectatic lung, and, hence, preserving adequate arterial oxygen tension with lateral positioning during OLV; a possible beneficial effect regarding oxygenation, as compared with supine positioning.^{10,11}

The aim of this prospective study was to compare changes in PaO₂ associated with left-sided OLV in left lateral position

between a group of patients with end-stage pulmonary disease (ie, severe pulmonary emphysema scheduled for thoracoscopic lung volume reduction surgery) and a group of patients with a normal lung function (scheduled for elective thoracoscopic surgery) and to predict the lowest PaO₂ in both patient groups.

MATERIAL AND METHODS

With ethics committee approval and written informed consent, 25 adult patients undergoing elective thoracoscopic surgery were enrolled in the study. Sample size was selected according to previous studies.^{3,4,12} Nine patients without known lung or heart disease and without a preexisting intracardiac right-to-left shunt were included in the control group (sympathectomy, $n = 2$; mediastinal tumor resection, $n = 3$; pleural abrasion, $n = 3$; lung biopsy, $n = 1$). Sixteen patients with end-stage pulmonary emphysema scheduled for lung-volume reduction surgery (LVRS) were included in the emphysema group. Emphysema patients underwent lung perfusion scanning preoperatively to identify regions of maximal ventilation-perfusion mismatch for targeting the areas of surgical resection. Therefore, the preoperative ventilation-to-perfusion ratios of the right and left lungs were known in these patients.

Patients with preserved lung function received oral midazolam, 3.75 to 7.5 mg, 1 hour before induction of anesthesia; whereas the emphysema patients were not premedicated to prevent respiratory depression.

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1053-0770/05/1904-0011\$30.00/0

doi:10.1053/j.jvca.2005.05.005

Table 1. Patient Characteristics and Preoperative Lung Function Parameters

	Severe Emphysema (n = 16)	No Emphysema (n = 9)	<i>p</i>
Female/male ratio	5/11	3/6	
Age (y)	62 ± 11 (43, 78)	50 ± 21 (16, 82)	0.007
Body weight (kg)	56 ± 14 (43, 74)	74 ± 17 (46, 98)	<0.001
BMI (kg/m ²)	19 ± 4 (14, 26)	23 ± 4 (19, 30)	0.012
FVC (L)	2.2 ± 0.3 (1.7, 2.6)	3.4 ± 1.6 (2.2, 6.6)	0.006
(%)	65 ± 17 (43, 118)	103 ± 26 (62, 136)	<0.001
FEV ₁ (L)	0.7 ± 0.4 (0.5, 1)	2.9 ± 1.2 (1.5, 5.6)	<0.001
(%)	27 ± 4 (20, 42)	96 ± 24 (64, 162)	<0.001
FEV ₁ /FVC	34 ± 5 (28, 43)	84 ± 13 (58, 95)	<0.001
(%)	44 ± 9 (31, 57)	123 ± 10 (106, 136)	<0.001
PEF (L/min)	2.7 ± 0.8 (1.3, 4.2)	6.6 ± 2.1 (3.7, 12)	<0.001
(%)	38 ± 12 (19, 68)	88 ± 18 (58, 130)	<0.001

NOTE. Data are presented as mean ± SD (range: min, max).

Abbreviations: BMI, body mass index; FVC, forced vital capacity; FEV₁, forced expiratory volume during the first second; FEV₁%, percentage of expected FEV₁ reached; PEF, peak expiratory flow rate; PEF%, percentage of expected PEF reached.

After application of routine monitoring according to institutional standards (pulse oximetry, 5-lead electrocardiogram and noninvasive blood pressure monitoring) and insertion of a peripheral intravenous catheter, the left radial artery was cannulated under local anesthesia using a 20-G catheter. In patients undergoing LVRS, a thoracic epidural catheter was placed at the level of T₄-T₇. A test dose of 2 mL of lidocaine 2% with epinephrine 1:200,000 was given and bupivacaine 0.5% at a rate of 3 to 5 mL/h was infused during the surgical procedure. Total intravenous anesthesia was induced using fentanyl (0.05-0.1 mg), intravenous lidocaine 1% (100 mg), and propofol (1-2.5 mg/kg). Rocuronium (0.6 mg/kg) or atracurium (0.5 mg/kg) was given for muscle relaxation after loss of eyelash reflex and was followed by endotracheal intubation. A left-sided double-lumen tube (SHER-I-BRONCH; Sheridan Catheter Corp, Argyle, NY) was placed in the trachea, and correct tube position was verified by fiberoptic bronchoscopy after patient positioning in the left lateral position. Anesthesia was maintained with an intravenous propofol infusion of 3 to 8 mg/kg/h and additional fentanyl (0.05-0.1 mg). All hemodynamic and respiratory measurements (pulse oximetry, fraction of inspired oxygen [F_IO₂], end-tidal carbon dioxide concentration) were recorded by Hellige Monitoring VICOM-smSMU 612 PPG (Hellige, Freiburg, Germany).

The blood gas monitoring system Paratrend 7 (PT7; Pfizer Hospital Products Group, High Wycombe, UK) was calibrated in vitro and introduced through the radial artery cannula for continuous blood gas monitoring. No in vivo recalibration was performed. The PT7 system incorporates 4 different sensors to measure PaO₂, PaCO₂, pHa, and blood temperature simultaneously and continuously. A Clark electrode is used to measure PaO₂, optodes (absorbance sensors) are used to determine PaCO₂ and pHa, and a thermocouple allows temperature correction of blood gas values. Measured values are displayed on the PT7 monitor as a digital readout of the actual values and as trend curves of PaO₂, PaCO₂, and pHa over a period of time. The system has been shown to provide reliable results over a wide range of arterial blood gas values during thoracoscopic surgery.³

Fifteen minutes before and during left-sided OLV, F_IO₂ was set to 1.0. Ventilator settings (including the use of pressure-limited or -controlled mode) were adjusted during surgery to the individual requirements of the patient according to previously described guidelines.^{2,4,12} Tidal volume (10-12 mL/kg), respiratory rate (usually 12-14 breaths/min), inspiration/expiration ratio (25%-33%), and peak inspiratory pressure ≤30 cmH₂O to prevent barotrauma were adjusted as guided by end-tidal carbon dioxide and PaCO₂ (35-40 mmHg). No positive end-expiratory pressure was used. OLV was started with the patient in the left lateral position before the introduction of the trocars through the

intercostal spaces. The OLV period was to end at a PaO₂ value ≤45 mmHg (need for apneic oxygen insufflation, reventilation of the non-dependent lung) or with the termination of the surgical procedure. Steady state during OLV was defined as a PaO₂ change of less than 7.5 mmHg in 1 minute.

Data were collected via an RS232 port of the PT7 blood gas monitor by a commercial personal computer to a Microsoft Access 97 database (Microsoft Corp, Redmond, WA). The sample rate was 1/min; the beginning and end of OLV periods as well as any other event that might potentially influence oxygenation during the procedure were registered by the attending anesthesiologist. Data were analyzed using Stat View 4.57 (SAS Institute Inc, Cary, NC) and SuperANOVA (Abacus Concepts, Inc, Berkeley, CA). ANOVA for repeated measures with Greenhouse-Geisser correction was used to compare the course of blood gases over time (analysis within factors) and between patients (analysis between factors).

Predicted minimal PaO₂ values during OLV were calculated for each patient according to Marshall and Marshall¹³ and Benatar et al.¹⁴ Perfusion ratios as determined by preoperative lung perfusion scanning were used in patients with severe emphysema. For patients with normal lung function, a perfusion ratio of 45% of cardiac output to the left lung was assumed.¹⁵ Gravitational blood shift because of left lateral decubitus positioning was assumed to cause an additional increase of 10% of the cardiac output to the left side.¹⁶ Linear correlation between predicted and observed PaO₂ was established for both groups. Mean difference of predicted and measured PaO₂ was compared using the *t* test; significance of the variance between the 2 patient groups was determined using the *F* test. Data are presented as mean ± standard deviation (SD [range]). A *p* value <0.05 was considered to be statistically significant.

RESULTS

The mean age of the 16 patients with emphysema was significantly higher, and their body mass index was significantly lower as compared with the 9 patients with preserved pulmonary function; there was a significant difference of lung function parameters between the 2 groups (Table 1). Lung perfusion scanning of the patients undergoing LVRS showed similar mean perfusion ratios for the right and left lungs (52% ± 12% v 48% ± 12% of cardiac output, *p* = 0.38) with large interindividual differences (range, 28%-68% for perfusion of the right lung).

Table 2. Measured Parameters Related to One-Lung Ventilation

	Severe Emphysema (n = 16)	No Emphysema (n = 9)	p
Duration of OLV (min)	26 ± 12 (16, 55)	39 ± 13 (15, 93)	0.042
Time to steady state (min)	18 ± 4 (12, 27)	11 ± 3 (7, 15)	<0.001
PaO ₂ at t ₁ (mmHg)	465 ± 88 (300, 577)	387 ± 93 (242,295)	0.044
PaO ₂ at t ₅ (mmHg)	420 ± 152 (206,557)	253 ± 69 (100,394)	<0.001
PaO ₂ at t ₁₀ (mmHg)	329 ± 112 (115,482)	149 ± 78 (74,279)	<0.001
PaO ₂ at t ₁₄ (mmHg)	217 ± 116 (62,419)	131 ± 66 (64,253)	0.059
PaO ₂ at t ₁₅ (mmHg)	198 ± 120 (49,388)	129 ± 66 (62,246)	0.122
PaO ₂ at steady state (mmHg)	163 ± 112 (39, 389)	135 ± 66 (73, 253)	0.500
PaCO ₂ at steady state (mmHg)	49 ± 8 (36, 62)	40 ± 3 (34, 50)	0.008

NOTE. Steady state during OLV = PaO₂-change <7.5 mmHg/min. t_{1,5,10,14,15} = time points 1-15 minutes after start of OLV. Data are presented as mean ± SD (range: min, max).

OLV periods were significantly shorter for thoracoscopic lung volume reduction surgery compared with other thoracoscopic procedures because of surgical considerations (Table 2). OLV of the left lung was associated with a significant decrease in PaO₂ in both patient groups. PaO₂ decreased following a delay in patients with severe emphysema. The time to reach steady state was significantly longer in patients with emphysema compared to patients with preserved pulmonary function. A PaO₂ ≤45 mmHg with the need for rescue maneuvers (study end-point) was reached in only 1 patient in the emphysema group (PaO₂ = 39 mmHg). There was a statistically significant

difference in PaO₂ between the 2 groups before the start of OLV, and patterns of PaO₂ changes during the first 15 minutes of OLV of the left lung were different in patients with preserved lung function as compared with patients with emphysema (Fig 1, Table 2). After 15 minutes of OLV, PaO₂ was trending higher in patients with emphysema as compared to patients with preserved lung function. However, this difference did not reach statistical significance. Analysis of PaO₂ patterns during OLV revealed a significant difference between the groups (p < 0.001) as well as for the interaction with time (p = 0.008).

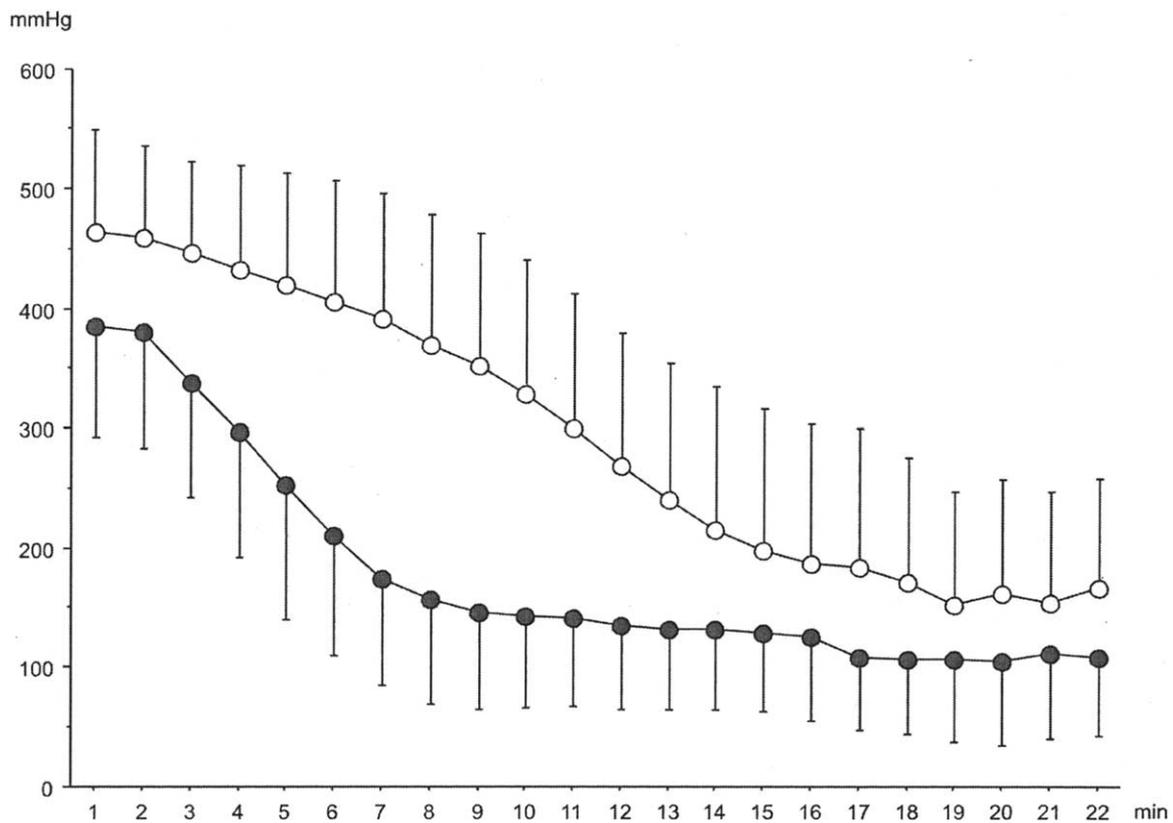


Fig 1. Arterial PO₂ during the first 22 minutes of left OLV in patients with (white circles, n = 16) and without (dark gray circles, n = 9) severe pulmonary emphysema.

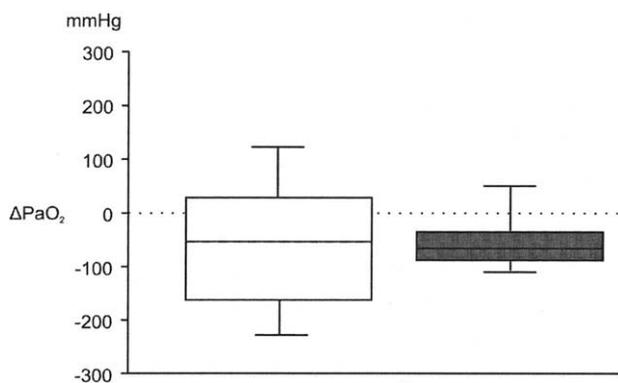


Fig 2. The difference between the predicted and the measured PaO_2 values in steady-state during OLV for patients with (white box plot) and without (dark gray box plot) severe emphysema. (Hinges indicate 25th and 75th percentile; whiskers indicate the 10th and 90th percentile).

For patients with severe emphysema, no significant correlation between estimated and measured PaO_2 values at steady state during OLV could be established ($r^2 = 0.187$, $p = 0.090$). The mean difference of predicted and measured PaO_2 values was -48 mmHg and interindividual variability was considerable ($\text{SD} = \pm 160$ mmHg) (Fig 2). Thus, prediction of minimal PaO_2 values for the individual patient with severe emphysema was unreliable.

In patients with preserved pulmonary function, a significant correlation was found ($r^2 = 0.402$, $p = 0.007$). Overall difference for PaO_2 of -51 mmHg was comparable to the observed value in patients with severe emphysema, but variability between individuals was significantly smaller ($\text{SD} = \pm 60$ mmHg, $p = 0.019$). Therefore, prediction of PaO_2 in these patients was more reliable.

DISCUSSION

During OLV of the left lung, PaO_2 significantly decreased to a similar extent in patients with preserved lung function and in patients with severe pulmonary emphysema. However, the pattern of changes in PaO_2 after the onset of OLV was significantly different between the 2 groups. Oxygenation was better preserved for a longer period of time in patients with end-stage pulmonary disease as compared with the group with normal lung function. On the other hand, larger interindividual differences in oxygenation were observed in patients with emphysema, rendering prediction of their individual minimal PaO_2 values during OLV unreliable.

Intrapulmonary right-to-left shunt occurs with the beginning of lung collapse during OLV (ie, as soon as parts of the nonventilated lung become atelectatic). Pulmonary emphysema is characterized by alveolar wall destruction associated with loss of elastic recoil and hence decreased expiratory flow rates.¹ As a result, air trapping, progressive hyperinflation, and increased deadspace ventilation are typical characteristics of patients with end-stage pulmonary emphysema. Lung volumes, primarily total lung volume and residual volume, may be severely enlarged. As a consequence, these increased lung volumes of both the dependent and the independent lung, if filled

with oxygen, may serve as a reservoir for oxygen. Lung collapse is considerably delayed, and it may even remain incomplete long after OLV has been initiated.^{5,7} Significantly higher PaO_2 values before OLV in patients with severe pulmonary emphysema, a major predictor of low PaO_2 during OLV,¹⁷ may support this hypothesis. The kinking of pulmonary vessels of the nondependent lung during OLV diverting the blood flow to the dependent, ventilated lung⁵ and a redistribution of perfusion because of altered HPV in the presence of chronic, irreversible disease in the pulmonary vessels⁷ may be another mechanism of this beneficial effect observed in patients with end-stage pulmonary disease.

In contrast, patients without severe emphysema show an earlier and steeper decline in PaO_2 with OLV. HPV plays an important role in this case, early after OLV initiation. Alveolar oxygen tension (PAO_2) and mixed venous oxygen tension (PvO_2) are known to be stimuli for this HPV reflex mechanism.¹⁸ The threshold is estimated to be around 125 mmHg and the effect to be maximal at 40 mmHg.¹⁹ Soon after onset of OLV in patients with normal lung function, PAO_2 approaches PvO_2 in the collapsing lung regions (eg, a PvO_2 at 125 mmHg may trigger HPV). PvO_2 was not measured in the present study. However, during OLV, the group of patients with healthy lungs reached a mean PaO_2 value of 149 ± 22 mmHg after 10 minutes and 131 ± 22 mmHg after 14 minutes, whereas the emphysema group remained at 329 ± 28 mmHg at 10 minutes and 217 ± 29 mmHg at 14 minutes, respectively (Table 2). Comparisons with previous studies investigating the changes of PaO_2 during OLV are possible with some reservations based on different study designs, ventilator settings, anesthetic techniques, and surgical interventions. Despite these limitations, Katz et al⁵ and Guenoun et al¹⁷ reported a course of PaO_2 during OLV comparable to the present patients without emphysema. Not surprisingly, preoperative mean FEV_1 (percentage of predicted) in their patient groups was $71\% \pm 20\%$ and $80\% \pm 11\%$ compared with $96\% \pm 24\%$ in the present patients without emphysema. The current patients with a preoperative FEV_1 of $27\% \pm 4\%$ scheduled for LVRS represent a significantly different patient group.

The prediction of the lowest PaO_2 during OLV for this patient group would be clinically desirable. Relative perfusion to the operative lung assessed by perfusion scans is thought to be the best predictor for PaO_2 during OLV.²⁰ These scans are routinely available for patients undergoing LVRS. Perfusion of a healthy left lung usually is 45% and perfusion of the right lung 55% of the cardiac output in the supine position. The influence of general anesthesia on the distribution of perfusion is minimal.²¹ However, positioning of the patient significantly influences this relation due to gravity; in the left lateral decubitus position, blood flow to the dependent (left) lung is increased by 10%, hence resulting in a 45% perfusion ratio to the nondependent right lung.^{15,16} Therefore, during OLV of the left lung (ie, right lung collapse in this position), a right-to-left shunt of 45% would theoretically be induced. According to calculations by Marshall and Marshall,¹³ however, HPV reduces perfusion to the atelectatic lung by 43%, resulting in a shunt fraction of 26%. Using isoshunt diagrams,^{14,22} the expected PaO_2 at steady state with $\text{F}_i\text{O}_2 = 1.0$ would be 165 mmHg. The PaO_2 of 135 ± 22 mmHg measured in the present

patients with normal lung function at a steady state of 11 ± 3 minutes after initiation of OLV (Table 2) was relatively close to this calculated predicted, but theoretical, value. The difference may account for additional shunting in the dependent ventilated lung^{14,15,23,24} and/or indicate impaired HPV mechanisms. Furthermore, it is difficult to assess PaO₂ steady state in the given clinical situation, or steady state may be unachievable in fact. For study purposes, it was defined empirically as a change in PaO₂ of less than 7.5 mmHg (1 kPa) per minute. In contrast, the response to OLV of the individual patient with emphysema was not predictable (Fig 2). Shunt formulas assume a hypoxia-induced constriction of pulmonary blood vessels to 74.9% of their initial diameter.¹³ However, hypoxic vasoconstriction in patients with emphysema may vary depending on the stage and pattern of pulmonary disease.¹⁶ The presence of chronic irreversible disease may even render these vessels incapable of an HPV response^{8,9} and also of pharmacologic vasodilation.²⁵ Therefore, in clinical practice, frequently repeated blood gas assessment is mandatory during OLV and thoracoscopy in these patients.¹²

There are several limitations to this clinical study, and the results should be interpreted cautiously. Both patient characteristics (Table 1) and anesthesia management were different between the 2 groups of patients. Severe pulmonary emphysema is inherently found in a more elderly population, and patients with normal lung function scheduled for minor thoracoscopic surgery belonged to a younger age group. Age has been shown to have a negative effect on arterial PO₂, relationship of ventilation/perfusion, and impairment of gas exchange.^{26,27} In the present study, however, oxygenation

was better in the elderly population with emphysema. In contrast, CO₂ elimination was impaired in these patients during OLV because of the underlying pathophysiology of emphysema. Hypercapnia, in theory, could contribute to an increase in right-to-left shunt. All patients with emphysema, as a part of the routine clinical protocol in the authors' institution, received combined general and thoracic epidural anesthesia with local anesthetics. In contrast, the group of patients with normal lung function had general anesthesia only. The effects on gas exchange of the anesthesia technique per se (ie, combined anesthesia using thoracic epidural anesthesia v general anesthesia alone) are controversial. Thoracic epidural anesthesia has been found to negatively influence HPV (ie, increased right-to-left shunt size was reported in patients anesthetized with combined v general anesthesia by Garutti et al).²⁸ In contrast, ventilation-perfusion relationship was not affected by thoracic epidural anesthesia in a study by Hachenberg et al.²⁹ Furthermore, like many other factors, anesthetic technique alone is unlikely to be a major determinant of oxygenation in this complex clinical situation.

In conclusion, OLV can safely be used in patients with severe end-stage pulmonary emphysema. Oxygenation was better preserved for a longer period of time in a group of patients with emphysema as compared with a group of patients with normal lung function. In patients with emphysema, however, large interindividual differences were observed, rendering prediction of minimum PaO₂ during OLV for the individual patient impossible.

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