

Klinik Çalışma

Effects of Non-Dependent Lung Oxygen Insufflation on Oxygenation and Respiratory Mechanics During One-Lung Ventilation in Patients with Stage II COPD

Tülün ÖZTÜRK*, Demet AYDIN*, Sadık YALDIZ**, Gökhan YUNCU***, Aynur ATAY****, Serdar SAVACI*****

SUMMARY

Introduction: The aim of this study was to investigate the changes on oxygenation, shunt ratio and respiratory mechanics of 6 L/min oxygen insufflation to the non-dependent lung, while extrinsic PEEP (PEEPe, equivalent to the patient's PEEPi) was being applied to the dependent lung in patients undergoing lung surgery.

Material and Methods: Patients with stage II COPD undergoing elective lung surgery (n=22) were intubated with a double-lumen endobronchial tube and performed a PA catheterization. One lung ventilation settings were: tidal volume 6 ml/kg, 12 breaths/min, and I: E ratio 1: 2. Procedure was performed in four sequential periods (each period continued for 15 minutes): After first stabilization period (PEEP0-1), PEEPe (at the level of intrinsic PEEP, PEEPi) was applied in the dependent lung while the non-dependent lung was exposed to air. After second stabilization period (PEEP0-2), the non-dependent lung received 6 L/min oxygen (O₂) through a catheter placed into the tube while PEEPe (at the level of PEEPi) was applied in the dependent lung (PEEPe+O₂). At the end of each 15 minute period, haemodynamic data, lung compliance (C), airway resistance (R), and PEEPi were recorded and blood gas samples were obtained.

Results: PaO₂ was significantly higher during the PEEPe+O₂ period (p<0.001), while Qs/Qt was significantly lower in the PEEPe+O₂ period when compared with the PEEPe period (p<0.0001). Compliance increased significantly during PEEPe compared to PEEP0-1 (p<0.05).

Discussion and Conclusion: The insufflation of oxygen to the non-dependent lung with application of PEEPe- equivalent to the patient's PEEPi -to the dependent lung increased oxygenation and decreased Qs/Qt in patients with moderate COPD. We recommend this simple and useful method which does not need extra equipment.

Key words: one lung ventilation, oxygen insufflation, PEEP

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* Celal Bayar Üniversitesi Tıp Fakültesi Anesteziyoloji ve Reanimasyon Anabilim Dalı

** Celal Bayar Üniversitesi Tıp Fakültesi Göğüs Cerrahisi Anabilim Dalı

*** Pamukkale Üniversitesi Tıp Fakültesi Göğüs Cerrahisi Anabilim Dalı

**** İzmir Atatürk Eğitim ve Araştırma Hastanesi Anesteziyoloji ve Reanimasyon Kliniği

Yazışma adresi: Doç. Dr. Tülün Öztürk, Celal Bayar Üniversitesi Tıp Fakültesi Merkez Mah. 45020 Manisa

e-mail: ozturktulun@yahoo.com

ÖZET

Evre II KOAH'lı Hastalarda Tek Akciğer Ventilasyonu Sırasında Bağımsız Akciğere Oksijen İnsüflasyonunun Oksijenasyon ve Solunum Mekanikleri Üzerine Etkileri

Giriş: Bu çalışmanın amacı akciğer cerrahisi geçiren hastalarda, dependent akciğere ekstrensek PEEP (PEEPe; hastanın PEEPi'ne eşit) uygularken, ventile edilmeyen akciğere 6 L/dk. oksijen sunumunun; oksijenasyon, şant oranı ve solunum mekanikleri üzerindeki değişikliklerini araştırmaktır.

Gereç ve Yöntem: Elektif akciğer cerrahisi geçirecek, stage II kronik obstrüktif akciğer hastalıklı hastalar (n=22), çift lümenli endobronşial tüp ile entübe edildi ve pulmoner arter kateteri uygulandı. Tek akciğer ventilasyon ayarları: 6 mL/kg tidal volüm, 12 soluk/dk., ve I: E oranı 1: 2 olarak yapıldı. Çalışma ardışık 4 periyoddan oluştu (her period 15 dk. sürdü): İlk stabilizasyon periyodu (PEEP0-1: no PEEP) sonrası, non-dependent akciğer havaya açıkken dependent akciğere ekstrensek PEEP (PEEPe; intrinsic PEEP seviyesinde) uygulandı. İkinci stabilizasyon periyodu (PEEP0-2: no PEEP:) sonrasında, dependent akciğere PEEPe uygulanırken, non-dependent akciğere tüp içine yerleştirilen kanül aracılığı ile 6 L/dk. oksijen (O₂) sunuldu (PEEPe+O₂). Her bir 15 dk.'lı periyodun sonunda hemodinamik veriler, akciğer kompliyansı (C), hava yolu rezistansı (R) ve PEEPi kaydedildi ve kan gazı örnekleri alındı.

Bulgular: PEEPe+ O₂ periyodunda PEEPe periyodu ile karşılaştırıldığında, Qs/Qt anlamlı olarak düşük iken (p<0.0001), PaO₂ anlamlı olarak daha yüksek (p<0.001) idi. PEEPe'deki kompliyans, PEEP0 ile karşılaştırıldığında anlamlı olarak artmıştı (p<0.05).

Tartışma ve Sonuç: Ventile akciğere hastanın PEEPi'ne eşdeğer ekstrensek PEEPe ile non-ventile akciğere oksijen insüflasyonu, oksijenasyonu artırdı ve Qs/Qt oranını azalttı. Bu ekstra donanım gerektirmeyen basit ve yararlı metodu önermekteyiz.

Anahtar kelimeler: tek akciğer ventilasyonu, oksijen sunumu, PEEP

INTRODUCTION

Hypoxemia (PaO₂<60 mmHg) is a serious problem during one-lung ventilation (OLV) in patients undergoing thoracic surgery which occurs in up to 10% of the patients [1,2]. Ventilation-perfusion mismatch-

ing in the ventilated lung and continued perfusion of the non-ventilated lung are the most important causes of hypoxemia during OLV^[2-4]. Other causes include various degrees of lung hyperinflation (an increase in PEEPi) and endothelial injury in the pulmonary vasculature due to preexisting chronic obstructive lung disease^[1-5].

In this setting, various ventilatory strategies are used to improve oxygenation. External PEEP (5-10 cm H₂O) is routinely applied to the dependent lung in thoracic surgery cases because this manoeuvre improves oxygenation by increasing compliance, opening collapsed alveoli^[6-9].

To decrease the amount of blood shunted from the collapsed lung during OLV, CPAP^[9-11] or continuous oxygen insufflation^[12,13] is applied to the non-ventilated lung. Continuous oxygen insufflation to the non-ventilated lung during OLV without the application of external PEEP to the dependent lung has been found to decrease the incidence of arterial oxygen desaturation in one study^[12], and fail to improve arterial oxygen saturation in another^[13].

The aim of this prospective sequential trial was to investigate the effect of insufflation of 6 L/min oxygen to the non-dependent lung while extrinsic PEEP (PEEPe, equivalent to the patient's PEEPi) is applied to the dependent lung in patients with moderate COPD undergoing elective thoracic surgery. Primary outcomes were changes in PaO₂ and shunt ratio (Qs/Qt), while secondary outcomes were effects on lung compliance (C), airway resistance (R), and PEEPi.

MATERIALS and METHODS

After institutional ethics committee approval and written informed consent were obtained from patients, 27 consecutive adult patients scheduled for elective lobectomy were included in the study. After giving consent for initial evaluation, an anamnesis and physical examination were performed, along with screening blood tests. Patients with active pulmonary infection (n=2), renal insufficiency (creatinine >1.5 mg/dL; n=1), hepatic insufficiency (SGOT or SGPT >40 U/L; n=1), severe heart disease (as determined by clinical and echocardiographic data), and those having contraindications to the use of double-lumen

endobronchial tube (DLT) (n=1) were excluded from the study. In the remaining patients (n=22), pulmonary function [percentage of expected forced expired volume during the first second (FEV1%), the ratio of FEV1/FVC% (percentage of expected forced vital capacity to FEV1)] were measured once during the three days prior to surgery. Patients with FEV1 between 30 and 80%, and FEV1/FVC ratio of <70% were defined as "stage II, moderate COPD" by the Global Initiative for Chronic Obstructive Lung Disease classification scheme^[14], and their written informed consent forms were obtained for the enrolment in the study (n=21). Patients received diazepam (5 mg PO) the night before the operation and midazolam (5 mg IM) approximately 30 min before the induction of anaesthesia. An epidural catheter was placed at the T7 or T8 level. After bolus doses, epidural anaesthesia was maintained with a continuous epidural infusion of 0.1% bupivacaine and 0.1 mg morphine per mL (2-5 mL/hour) administered throughout the operation.

Anaesthesia was induced with 3 µg/kg fentanyl and 3-5 mg/kg thiopental, and maintained with inhaled sevoflurane and air in oxygen targeting a BIS value of 40. After adequate muscle relaxation was achieved with cis-atracurium, the bronchus of the dependent lung was intubated with a left or right-side double-lumen endobronchial tube (Ruschelit® Bronchopart®, Willy Rusch AG, Kernen, Germany). The size varied from 37F to 39F, depending on the patient's height (37F for <1.7 m and 39F for >1.7 m). After placing the patient in the lateral decubitus position, the correct position of the tube was confirmed with a fiberoptic bronchoscope. A pulmonary artery catheter was inserted for the haemodynamic measurements via the right internal jugular vein.

After thoracotomy incision and opening of the pleura, OLV was begun with 100% oxygen using an Aestiva 3000 ventilator (Datex-Ohmeda Inc. Madison, USA) with a tidal volume of 6 mL/kg at a rate of 12 breaths/min, and an I:E ratio of 1:2. The ventilatory pattern remained the same throughout the operation. In summary, the procedure was performed in four phases of fifteen minutes:

- a) **Stabilization period (PEEP0-1):** The dependent lung was ventilated as described above, but no PEEP was applied (PEEP0). The non-dependent lung was exposed to air.

- b) PEEPe period (PEEPe):** The dependent lung was ventilated with PEEP applied at the level of PEEPi. The non-dependent lung was exposed to air, but an oxygen cannula (inside diameter 2.8 mm) was advanced 20 cm into the tracheal lumen of the endobronchial tube. Oxygen was not delivered yet.
- c) Stabilization period (PEEPO-2):** PEEP was not applied to the dependent lung at second stabilization period. The non-dependent lung was exposed to air, with the oxygen cannula in place.
- d) PEEPe + oxygen insufflation period (PEEPe + oxygen):** PEEPe was applied to the dependent lung. The non-dependent lung received 6 L/min oxygen through the oxygen cannula in the tracheal lumen of the endobronchial tube (approximate $FiO_2=0.5$).

Measurements

Arterial blood gas and mixed-venous blood gas samples were obtained at the end of the each period. Mean arterial pressure (MAP), central venous pressure (CVP), mean pulmonary arterial pressure (MPAP) and pulmonary arterial occlusion pressures (PAOP) were measured. Cardiac index (CI) was estimated by thermodilution. Pulmonary shunt was calculated as follows [15]:

$$Qs/Qt = CcO_2 - CaO_2 / CcO_2 - CvO_2$$

$$CaO_2 = (PaO_2 \times 0.03) + (Hb \times 1.39 \times SaO_2)$$

$$CvO_2 = (PvO_2 \times 0.03) + (Hb \times 1.39 \times SvO_2)$$

$$CcO_2 = (PAO_2 \times 0.03) + (Hb \times 1.39)$$

$$PAO_2 = [(760 - 47) \times FiO_2] - PaCO_2$$

[Qs/Qt, pulmonary shunt fraction; CaO_2 , arterial oxygen content; CvO_2 , mixed venous oxygen content; CcO_2 , end capillary oxygen content; PAO_2 , partial alveolar oxygen pressure; PaO_2 , partial arterial oxygen pressure; Hb, hemoglobin; SaO_2 , arterial oxygen saturation; SvO_2 , venouse oxygen saturation].

Because hemodynamic parameters may vary after ligation of the pulmonary vessels, all measurements were completed before any attempt at lung resection, while waiting for the frozen section results of lymph node sampling for intraoperative staging.

MAP was maintained within 30% of the value measured after premedication and before induction. Central venous pressure was maintained between 0-4 cm H₂O. Volume treatment was continued with infusion of crystalloid (Isolyte S®, Eczacıbaşı, Istanbul, Turkey) solution and Gelofusine 4% (Braun Melsungen, Melsungen, Germany) and blood (as needed, Ht<30%). Hemodynamic instability was defined as heart rate less than 60 beats/min and/or MAP less than 75 mmHg. In order to improve hemodynamic stability infusion of dobutamine or dopamine (PAOP ≥ 18 mmHg and/or CVP > 15 mmHg) was applied. If MAP rose above 30% of its initial value, a nitroglycerin infusion was started. Data of patients receiving nitroglycerin or any inotropic agent(s) were excluded from the analysis because of their known effects on pulmonary vasculature and Qs/Qt.

Before the study commenced, the volume-controlled ventilator was tested and calibrated for accuracy. Compliance (C), airway resistance (Raw) and total PEEP (PEEPt), PIP (peak inspiratory pressure) were continuously determined by the ventilator's integrated electronic spirometer (Datex-Ohmeda Captmac Ultima® monitor, M-CAiOV model, Madison, USA) during dynamic conditions and also recorded at the end of each period. PEEPt, which was measured at the end of the stabilization period, was assessed as PEEPi.

Statistical analysis: Data were analyzed using Statistics for Windows® v6.0 (StatSoft Inc., Tulsa, USA) computer software package program. Dependent Student's t test for dependent variables was utilized to compare hemodynamic parameters (PEEPO vs PEEPe and PEEPO vs PEEPe+oxygen). Independent Student's t test was utilized to compare data in the two ventilation periods (PEEPe vs PEEPe+oxygen). A p value of less than 0.05 was considered to be statistically significant.

RESULTS

Demographic and clinical features of the patients are shown in Table 1. Individual changes in PaO₂ and pulmonary shunting during the different periods of OLV are shown in Table 2.

The mean PEEPi was 4.5 ± 0.6 (range 3-5) and 4.6 ± 0.7

(range3-5) cm H2O during the first and second stabilization periods, respectively (p=0.6). Compared to the PEEP0-1 period, PaO2 and Qs/Qt were not significantly different during the PEEPe period (p>0.05; see Table 3). However, during the PEEPe+oxygen period, PaO2 was significantly higher and Qs/Qt was significantly lower (p<0.001 and p<0.05, respectively) when compared to the PEEP0-2 period (Table 3). Similarly, PaO2 was significantly higher (p<0.001) and Qs/Qt was significantly lower (p<0.01) during the PEEPe+oxygen period compared to the PEEPe-2 period (Table 3). PEEPi and PIP were significantly higher during the PEEPe and PEEPe+oxygen peri-

Table 1. Demographic and clinical features of the 20 patients.

Clinical Features	Mean±SD (Min.-Max.)
Age (year)	58±3 (52-64)
Male / Female	20/0
BSA (m2)	1.8±0.1 (1.7-2.0)
EF (%)	56.9±2.1 (52-62)
FEV1 (%)	59±6.4 (51-74)
FEV1/FVC (%)	58.8±4.2 (52- 68)
Left Lobectomy / Right Lobectomy	11 / 9
Duration of the operation (hours)	4.6±0.5

BSA: Body Surface Area, EF: Ejection Fraction, FEV₁: Force Expiratory Volume in the first second, FVC: Forced Ventilatory Capacity

Table 3. Hemodynamic and pulmonary gas exchange parameters during the different modes of single lung ventilation (mean±SD).

	PEEP ₀ -1	PEEP _e	PEEP ₀ -2	PEEP _e +O ₂	p
PaO ₂ (mmHg)	144±35	147±31	150±36	192±37	<0.001** <0.001#
PaCO ₂ (mmHg)	44±4	45±7	42±3	43±8	<0.01#
HR (bpm)	80±7	81±9	79±6	80±10	ns
MAP (mmHg)	88±9	88±8	86±8	85±8	ns
MPAP (mmHg)	22±4	22±4	21±3	21±4	ns
LVEDP (mmHg)	13±2	14±3	13±2	14±2	ns
CVP (mmHg)	8±2	9±2	8±2	9±2	ns
CI (L/min/m ²)	2.6±0.6	2.6±0.6	2.4±0.5	2.5±0.6	ns
SvO ₂ (%)	84±5	85±5	82±4	87±6	<0.01** <0.05**
Qs/Qt (%)	32±7	34±3	32±8	27±4	<0.01# <0.01*
PEEPi (mmHg)	4.5±0.6	5.1±1.0	4.6±0.7	5.1±0.9	<0.05** <0.001**
PIP (cmH ₂ O)	18±2	20±2	17±3	20±3	<0.01**
C (ml/cmH ₂ O)	26±9	29±7	26±8	28±10	<0.05*
R (cmH ₂ O/L/min)	26±10	22±6	25±8	23±9	ns

PEEP₀: The non-dependent lung was open to room air and no PEEP was applied to the dependent lung.

PPEP_e: The non-dependent lung was open to room air and extrinsic PEEP equivalent to the patient's PEEPi was applied to the dependent lung.

PEEP_e+O₂: Oxygen was applied to the non-dependent lung oxygen catheter and extrinsic PEEP equivalent to the patient's PEEPi was applied to the dependent lung.

Dependent Student's t-test: *PEEP₀-1 vs PEEP_e **PEEP₀-2 vs PEEP_e+O₂

Independent Student's t-test: #PEEP_e+O₂ vs PEEP_e

Table 2. The changes in PaO₂ and pulmonary shunt on an individual basis (n=20) during one-lung ventilation.

Patient No:	PaO ₂				Qs/Qt			
	PEEP ₀ -1	PEEP _e	PEEP ₀ -2	PEEP _e +O ₂	PEEP ₀ -1	PEEP _e	PEEP ₀ -2	PEEP _e +O ₂
1	145.2	170.6	134.7	235.5	41	38	39	31
2	136.1	141.7	151.0	161.9	18	31	14	24
3	94.5	114.4	102.3	129.9	37	33	41	21
4	134.5	168.6	142.6	276.6	34	34	32	27
5	198.8	180.0	201.0	215.4	16	39	19	32
6	189.9	161.7	176.3	219.7	38	33	34	28
7	181.4	163.5	189.21	222.8	28	29	31	25
8	92.5	104.9	87.0	179.2	35	37	38	27
9	131.6	139.4	124.2	171.8	35	35	36	27
10	179.2	202.0	180.0	242.4	28	33	23	21
11	122.1	134.2	133.3	161.4	34	37	33	22
12	172.1	114.8	155.5	165.7	35	33	35	29
13	90.9	88.4	111.5	174.7	35	39	37	33
14	116.0	129.4	114.0	207.1	34	35	34	26
15	144.2	152.2	133.1	155.0	35	34	37	27
16	172.2	166.0	176.2	199.1	36	30	38	25
17	172.9	189.3	167.9	198.2	35	32	36	31
18	166.9	178.1	172.1	201.4	31	33	30	28
19	144.9	110.4	152.2	179.1	18	38	22	30
20	87.5	119.2	101.1	143.2	31	33	27	25

Abbreviations: PaO₂, partial pressure of arterial oxygen; QS/QT (%), shunt ratio

PEEP₀: The non-dependent lung was open to room air and no PEEP was applied to the dependent lung.

PPEP_e: The non-dependent lung was open to room air and extrinsic PEEP equivalent to the patient's PEEPi was applied to the dependent lung.

PEEP_e+O₂: Oxygen was applied to the non-dependent lung oxygen catheter and extrinsic PEEP equivalent to the patient's PEEPi was applied to the dependent lung.

ods, compared to PEEP0 ($p < 0.05$, Table 3). Compliance increased significantly during PEEPe compared to PEEP0-1 ($p < 0.05$). Resistance during PEEPe did not drop significantly compared to the PEEP0-1 ($p = 0.4$, Table 2). The lowest PaO₂ during OLV was 87.0 mmHg. With insufflation of additional oxygen, PaO₂ increased to 179 mmHg and Qs/Qt decreased from 38 to 27.

Data from two patients were excluded from analysis because one with hypertension requiring nitroglycerin infusion and another experienced over-distension of the non-dependent lung during oxygen insufflation (SaO₂ did not drop below 92%, and the position of the endobronchial tube was verified with a fiberoptic bronchoscope).

DISCUSSION

The fall in PaO₂ occurring during OLV results primarily from the pulmonary shunt of deoxygenated blood through the non-dependent lung and secondarily from ventilation-perfusion mismatch within the ventilated lung^[10]. The insufflation of oxygen, which creates alveolar hyperinflation and a positive pressure in the non-dependent lung, limits the volume of shunt. We found that PaO₂ increased in proportion to the decrease in Qs/Qt when oxygen was insufflated to the non-dependent lung while PEEPe was applied to the ventilated lung in patients with moderate COPD scheduled for lobectomy. Our outcomes were similar to those of Rees and Wansbrough^[12], who showed that continuous oxygen insufflation to the non-ventilated lung during periods of OLV reduces Qs/Qt and minimizes arterial oxygen desaturation. In contrast, Slimani and colleagues^[13] did not find any significant change in arterial oxygenation when oxygen was given through an oxygen reservoir to the non-ventilated lung. Our study was different from their study. Indeed, all of our patients had stage II COPD, and that PEEP was applied to the dependent lung, while the oxygen was insufflated to the non-dependent lung.

We found that insufflation of additional oxygen increased PaO₂ and lowered Qs/Qt. The method in this study was not tested directly on hypoxemic patients during OLV. However, this intervention was found to be also useful to improve oxygen saturation in severely hypoxic patients during OLV^[16-18]. Sanchez-Lorente

and colleagues^[16] have shown that oxygen flow of 5-10 L min⁻¹ administered by a paediatric intra-field catheter placed in the distal bronchi during circular bronchial anastomosis of the spared lobe(s) successfully improved oxygenation in patients who had decreased peripheral oxygen saturation (SaO₂ lower than 90%) during one-lung ventilation. Ku and colleagues^[17] indicated that selective ipsilateral segmental insufflation of oxygen via fiberoptic bronchoscope (FOB) improved oxygenation in patients with very poor respiratory function (FEV1 < 40% of predicted) during one-lung ventilation in video-assisted thoracoscopic surgery (VATS). Russell WJ^[18] slowly delivered 2 L/min of oxygen into the non-ventilated lung for two seconds to manage hypoxemia (SaO₂ < 95%) during one-lung anaesthesia, and repeated this procedure every 10 seconds for five minutes. They found that all patients had an increase in oxygen saturation and the mean oxygen tension. All authors advocated this simple, useful and beneficial technique, which does not need extra equipment and is free of side effects and significant impairment of the operation field.

In previous studies, application of 5-10 cm H₂O of PEEPe significantly improved PaO₂ and decreased compliance of the dependent hemithorax, but these improvements were observed only in patients who had a FEV1 above 72%^[4,7,19]. In keeping with the recommendations of previous studies regarding the optimum level of PEEP to be used during OLV, we applied external PEEP at a level which was equal to the PEEPi measured at the beginning of OLV (3-5 cm H₂O)^[20,21]. We found that compliance and PaO₂ increased significantly during the PEEPe period (compared to PEEP0) while Qs/Qt decreased. Thus we thought that PEEP of 5 cm H₂O was a reasonable level to use in our patients.

Ishikawa, et al. reported that mean PaO₂ decreased rapidly after starting OLV, but increased gradually afterwards^[22]. Oxygenation may improve after 20-30 min of OLV^[23,24] and peak after one hour^[22] during OLV. We assessed oxygenation after only 15 min of OLV, but we achieved a return to baseline with a second stabilization period. Although a cross-over design for this study would have been ideal, the two stabilization periods that were incorporated in our study design allowed for a return to baseline between periods of PEEP applied with and without oxygen.

In our study, an insufflation rate of 6 L/min was used to obtain an approximate FiO₂ of 0.5 to prevent both atelectasia and overdistension developing with high FiO₂ levels. Overdistension (as determined by clinical exam, not by any measurement of hyperinflation) of the non-dependent lung during oxygen insufflation occurred in one patient, even though an open airway had been visualized beforehand with a fiberoptic bronchoscope. The problem was solved by lowering the insufflation rate. In order to prevent this complication, we recommend fine-tuning of the insufflation rate on an individual basis and using a larger endobronchial tube, after the tube position and patency have been verified. The catheter size relative to the diameter of the lumen and the location of the catheter in the bronchial tube were standardized, since any variations in these parameters would influence downstream pressure and the efficiency of oxygenation. The oxygen catheter was placed during the PEEPe period because the catheter may have affected the rate of expiration from the non-dependent lung.

Limitations of our study include leaving the bronchial tube exposed to air in the PEEPO period, whereas insufflation of air at 6 L/min could have been delivered. In addition, all of our patients were male, thus these results may not be valid in female patients.

In conclusion, insufflation of 6 L/min oxygen to the non-dependent lung with application of PEEPe (at a level equal to the patient's PEEPi) to the ventilated lung increased oxygenation and decreased Qs/Qt ratio in patients with moderate COPD. To prevent overinflation of the non-dependent lung, the insufflation rate must be adjusted individually. We recommend this simple and useful method which does not need extra equipment.

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