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Chronic obstructive pulmonary disease and anaesthesia: formation of atelectasis and gas exchange impairment

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ABSTRACT: Gas exchange impairment and the development of atelectasis during enflurane anaesthesia were studied in 10 patients (mean age 70 yrs) with chronic obstructive pulmonary disease (COPD). Awake, no patient displayed atelectasis as assessed by computed X-ray tomography. The ventilation/perfusion distribution ($\dot{V}_A/\dot{Q}$), studied by the multiple inert gas elimination technique, displayed an increased dispersion of $\dot{V}_A/\dot{Q}$ ratios (the logarithmic standard deviation of the perfusion distribution, mean log Q SD 0.99; upper 95% confidence limit of normal subject: 0.60), and increased perfusion of regions with low $\dot{V}_A/\dot{Q}$ ratios ($0.005<\dot{V}_A/\dot{Q}<0.1$: 5.4% of cardiac output). Shunt was negligible (mean 0.6%). Computed chest tomography showed significantly larger cross-sectional thoracic areas than previously seen in subjects with healthy lungs ($p<0.01$). No atelectasis was seen in any patient.

During anaesthesia there was a further worsening of the $\dot{V}_A/\dot{Q}$ mismatch with significantly increased log Q SD (1.29, $p<0.05$) but no increase in shunt (mean 1%). Minor atelectatic areas were noted in three patients, the others displayed no atelectasis at all. Chest dimensions were reduced by no more than 3% during anaesthesia, suggesting an unchanged or only minimally affected functional residual capacity.

These findings contrast with those seen in patients with healthy lungs in whom atelectasis and shunt regularly develop during anaesthesia.
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Pulmonary gas exchange is impaired during anaesthesia and sometimes arterial hypoxaemia may develop despite supplemental oxygen in the inspired gas [1, 2]. Studies on ventilation/perfusion distributions $\dot{V}_A/\dot{Q}$, as assessed by multiple inert gas elimination technique [3], have shown the appearance of shunt and varying but mostly minor increase in the dispersion of $\dot{V}_A/\dot{Q}$ ratios [4–7]. In recent studies we have demonstrated prompt development of atelectasis on induction of anaesthesia [8]. The magnitude of shunt correlated to the size of the atelectasis [9, 10]. Thus, a major cause of gas exchange impairment during anaesthesia has been identified.

Patients with chronic obstructive pulmonary disease (COPD) have an impaired gas exchange already in the awake state [3, 11, 12], and there is a further worsening of their gas exchange impairment during anaesthesia [2–4]. COPD patients also have a higher incidence of postoperative complications than patients with healthy lungs [4, 13–16].

We addressed the question of whether COPD patients develop their more severe gas exchange impairment during anaesthesia because of larger formation of atelectasis than in anaesthetized subjects with healthy lungs, or whether they develop a qualitatively different pulmonary dysfunction. The purpose of the present study was, therefore, to study gas exchange and ventilation/perfusion distributions with the multiple inert gas elimination technique in patients with severe chronic obstructive pulmonary disease, and to correlate the findings with atelectasis formation, if any, as assessed by computed chest tomography.

Patients and methods

Ten patients scheduled for elective abdominal or vascular reconstructive surgery were studied, awake, immediately before, and during general anaesthesia. Seven were men and three women, their ages ranging from 57–77 yrs (mean 70 yrs) (table 1). All patients were, or had been, heavy smokers and all patients suffered from chronic bronchitis according to the definition of the British Medical Research Council (productive cough for at least 3 months per year during the last 3 years). Spirometry before the investigation showed increased functional residual capacity (FRC) and/or residual volume (RV), and reduced expiratory flow to less than 80% of the expected value in all patients (table 1). Most of the patients received medication both

Table 1. – Subject data

No.	Sex	Age	Height	Weight	Smoking free	habits pack	TLC	FRC	VC	RV/TLC	FEV_1/FVC	Pao_2 awake	$Paco_2$ awake	Surgical diagnosis	Medication
	M/F	yrs	m	kg	yrs	yrs	%pred	%pred	%pred	%	%	kPa	kPa		
1	M	77	1.80	60	6	25	96	124	85	54	44	10.8	4.1	Sigmoid cancer	Furosemide
2	F	70	1.45	41	0.5	12	140	156	75	63	40	8.1	5.9	Stenosis of the femoral artery	Salbutamol, nifedipine, furosemide
3	M	72	1.74	70	8	30	104	131	112	48	38	7.9	5.2	Aortic aneurysm	Terbutaline, salbutamol, becotide, theophylline
4	M	74	1.75	74	10	40	107	130	98	46	34	10.7	3.7	Aortic aneurysm	Salbutamol, beclomethasone
5	M	65	1.74	77	2	40	116	144	102	47	50	10.3	5.5	Renal artery stenosis	Digoxine, nifedipine, enalapril, prazosin
6	M	57	1.78	87	-	42	97	72	89	40	55	9.6	5.3	Rectal cancer	Metaprolol, hydralazine, bendroflumethiazide
7	M	75	1.78	56	10	22	80	75	76	45	60	9.6	5.3	Sigmoid cancer	Theophylline
8	M	67	1.76	49	-	39	103	147	81	55	50	12.0	4.8	Rectal cancer	Theophylline, digoxin
9	F	69	1.52	44	0.3	25	111	119	92	58	57	9.0	6.5	Aortic, iliacal emboli	Theophylline, terbutaline, beclomethasone
10	F	77	1.74	70	2	55	111	163	67	68	45	8.5	6.2	Aortic aneurysm	Theophylline, bromhexine bendroflumethiazide, sodium cromoglycate
Mean		70	1.72	63			107	126	88	52	47	9.7	5.6		
SD		±7.9	±0.11	±17.4			±15.5	±31.0	±13.6	±8.8	±8.6	±1.3	±0.7		

TLC: total lung capacity; FRC: functional residual capacity; VC: vital capacity; RV: residual volume; FEV_1: forced expiratory volume in one second; FVC: forced vital capacity; Pao_2 and $Paco_2$: arterial oxygen and carbon dioxide tension, respectively.

for COPD and coexistent cardiovascular disease, consisting of theophylline, β_2-agonists, digitalis and diuretics. The patients did not receive any bronchodilator therapy for at least 12 h prior to the study and none of the patients needed bronchodilator treatment during the investigation. The patients were studied in the awake state and after 15 min of general anaesthesia. Five of the patients were randomly selected and studied after an additional 30 min of anaesthesia.

Informed consent was obtained from each patient and the study was approved by the Ethics Committee of Huddinge University Hospital. All patients were ventilated postoperatively until circulation was stable and body temperature normal. The postoperative ventilator period lasted less than 6 h in all patients except in patient no. 9. She was reoperated twice due to bleeding and eventually died two days later. No other postoperative complications were noted.

Anaesthesia

All patients received atropine 0.5 mg *i.v.* before induction of anaesthesia. No other premedication was given. Anaesthesia was induced with thiopental 300–400 mg and fentanyl 0.10 mg *i.v.*, and was maintained with enflurane (0.6–1.0%) in oxygen/nitrogen with an inspired oxygen fraction of 0.4. To facilitate intubation the patients received suxamethonium 75–100 mg *i.v.* To maintain muscle paralysis a priming dose of 6–8 mg pancuronium bromide was given *i.v.*, and intermittent doses of 2 mg *i.v.* were given when needed. After intubation the patients were ventilated mechanically at a rate of 12 breaths·min^{-1} (Servo 900 C Ventilator, Siemens) equipped with an infra-red carbon dioxide analyser (CO_2 Analyzer 930, Siemens). The minute ventilation was adjusted to maintain an end-tidal CO_2 concentration of approximately 4%. Ventilatory volumes and airway pressures were read on the ventilator.

Catheterization

A triple-lumen thermistor-tipped catheter, Swan-Ganz 7 F (Edward's Laboratories), was introduced percutaneously by a sleeve technique into a medial cubital vein. The catheter was advanced to the pulmonary artery under radiographic guidance. Pulmonary vascular pressures relative to atmospheric pressure were recorded, and mixed venous blood was drawn for gas analyses (see below). The brachial artery was cannulated for pressure recordings and blood sampling, and an additional venous catheter was inserted into the opposite arm for infusion of inert gases (see below).

Cardiac output was determined by thermodilution. Ten ml of ice-cold glucose 5% was manually injected into the right atrium at random during the respiratory cycle, and the dilution curve was analysed by a cardiac output computer (model 9250 A, Edward's Laboratories). Under each investigated condition 3 to 4 measurements of cardiac output were made and the mean value was calculated. Systemic (SVR) and pulmonary (PVR) vascular resistances were calculated as SVR=(systemic mean arterial pressure-right atrial pressure)/cardiac output and PVR=(pulmonary artery mean pressure-pulmonary capillary wedge pressure)/cardiac output, respectively.

Ventilation perfusion ratios

Six gases (sulphur hexafluoride, ethane, cyclopropane, halothane, diethyl ether and acetone) were dissolved in isotonic saline and infused into a vein at a rate of 3 ml·min^{-1}. After 40 min of infusion, under steady-state conditions, arterial and mixed venous blood samples were taken and mixed expired gas was collected for analysis by gas chromatography (Sigma 3, Perkin-Elmer). Technical details have been reported previously, [17]. Blood-gas-partition coefficients were determined by a two-step procedure [18]. Arterial/mixed venous and mixed expired/mixed venous gas concentration ratios (retention and excretion, respectively) were plotted against blood gas partition coefficients. By formal mathematical analysis with enforced smoothing, these relationships were transformed into a multicompartmental plot of blood flow and ventilation against $\dot{V}_A/\dot{Q}$ [19, 20]. From the $\dot{V}_A/\dot{Q}$ distributions, we present data for the mean and standard deviation of the blood flow log distribution (Q_M and log SD Q, respectively), shunt (perfusion of lung regions with $\dot{V}_A/\dot{Q}$ ratios <0.005), "low $\dot{V}_A/\dot{Q}$" (perfusion of lung regions with 0.005 <$\dot{V}_A/\dot{Q}$ ratios <0.1), the mean and standard deviation of the ventilation log distribution (V_M and log SD V, respectively), "high $\dot{V}_A/\dot{Q}$" (ventilation of lung regions with 10<$\dot{V}_A/\dot{Q}$ ratios <100), and deadspace (V_D; ventilation of lung regions with $\dot{V}_A/\dot{Q}$ ratios >100). All subdivisions of blood flow and ventilation are expressed in percentage of cardiac output and expired minute ventilation, respectively.

Additional gas analysis

Arterial oxygen tension (Pao_2), mixed venous oxygen tension ($P\bar{v}o_2$) and arterial carbon dioxide tension ($Paco_2$,) were measured by standard techniques (blood-gas analyser: ABL2, Radiometer). Samples of inspiratory gas were analysed for oxygen by mass spectrometry (Centronics, MGA 200).

Computed tomography (CT) of the chest

The transverse lung area and the structure and density of the lungs were studied by CT scanning. The subject lay supine on the tomograph table (Somatom 2, Siemens). A frontal scout view covering the chest was initially obtained. Two CT scans in the transverse plane were then performed, the lowermost at a level just above the top of the diaphragm and the other 5 cm cephalad to the first one. The same scan levels, relative to the spine, were used during the succeeding measurements during anaesthesia. The scan time was 5 s, at 115 mAs

and 125 kV, slice thickness 8 mm, and centre/window setting ±0/512.

The transverse area of the thorax was calculated from the images. To calculate the dense area a magnified image (2×) was made of the dorsal portion of the CT scan with an image from both the right and left lungs. The border between the thoracic wall and the dense area can be identified on the magnified image, although the attenuations of the dense area and of the soft tissues of the chest wall did not differ by more than 30–40 Hounsfield units (HU). A manual delineation of the dorsal border of the dense area was made. The ventral border of the dense area is recognized by the high contrast in the CT scan between the air-filled and dense lung parenchyma. The ventral border was encircled at some distance so that, together with the dorsal border, a region of interest was created. Within this region, atelectasis was defined as picture elements (pixels) with an attenuation value between -100 and +100 HU. The atelectatic area was calculated by the computer. The amount of atelectasis in the lungs was expressed in percentage of the total transverse area of the thoracic cavity. The variability in duplicate measurements of the manually delineated areas was 5%.

Procedure

The catheters were introduced at the catheterization laboratory, and the infusion of the inert gases was started. The patient was then moved to the X-ray department and after 20 min of complete rest (40 min of infusion) recordings of central haemodynamic and gas exchange variables were made while the patient was breathing air. CT scans were then obtained and the patient was anaesthetized. After 15 min of enflurane anaesthesia in oxygen/nitrogen, the haemodynamic and gas exchange variables were recorded and the CT scans repeated. In five patients new measurements were made after an additional 30 min (total 45 min) of anaesthesia.

After the study the patient, while still anaesthetized, was moved to the operating room. All recordings, awake and during anaesthesia, were made with the patient in the supine position.

Statistics

Mean values and standard deviations (SD) were calculated. The significance of a difference between the awake state and the condition of anaesthesia, as well as between 15 and 45 min of anaesthesia, were tested by Wilcoxon signed rank's test and Friedman two-way analysis of variance by ranks.

Results

Awake

Before induction of anaesthesia, minute ventilation, cardiac output, and central systemic and pulmonary vascular pressures were within normal limits in all subjects, but pulmonary vascular resistance (PVR) was increased [21] (tables 2 and 3). No correlation between impairment of spirometry and impairment of gas exchange could be found.

Retention and excretion data of the measured inert gases resulted in technically good $\dot{V}_A/\dot{Q}$ distributions. The fit of the $\dot{V}_A/\dot{Q}$ data expressed as the remaining sum of squares (RSS) averaged 3.1 and was less than 6 in all but two patients (table 3) [22]. The ventilation/perfusion distribution was abnormal in all patients with: 1) perfusion of regions with low $\dot{V}_A/\dot{Q}$ ratios (patients no. 6–10); 2) ventilation of regions with high $\dot{V}_A/\dot{Q}$ ratios (patient no. 2), or a combination of both (patients no. 3–5); or 3) broadening of the main mode (increased log SD Q: 0.99; upper 95% confidence limit of normal: 0.60 [23]) (patient no. 1) (fig. 1). The perfusion of regions with low $\dot{V}_A/\dot{Q}$ ratios averaged 5.4% of cardiac output and the ventilation of regions with high $\dot{V}_A/\dot{Q}$ ratios was 2.2% of the total minute ventilation. Only a small shunt was seen, with a mean of 0.6%. For data on $\dot{V}_A/\dot{Q}$ distributions, see table 3. Six patients had a Pa_{O_2} below 10.0 kPa, the lower normal limit at our laboratory, see also [24]. Pa_{CO_2} averaged 5.3 kPa (table 3). $P\bar{v}_{O_2}$ was 5.1 kPa awake.

The cross-sectional thoracic area averaged 398 cm^2 in the caudal CT scan and 375 cm^2 in the cranial CT scan, which was significantly larger at both scan levels than in previously studied subjects with healthy lungs (areas: scan 1: 377±41 and scan 2: 335±45 cm^2, n=45, $p<0.01$ at both scan levels, own unpublished data) (fig. 2). For comparison with a subject with healthy lungs, see fig 3. No atelectasis was seen in any of the patients (table 4). No correlation between cross-sectional thoracic area and pulmonary function tests was found.

Anaesthesia. (table 2 and 3)

The first recordings were made after approximately 15 min of enflurane anaesthesia during mechanical ventilation and muscle paralysis. Cardiac output and systemic arterial blood pressure were reduced to approximately 65–80% of the awake level. Heart rate tended to increase. Minor changes in right atrial, pulmonary arterial mean and wedge pressures were seen however, the PVR was not altered compared to the awake state. Tidal volume (and minute ventilation) was deliberately reduced to about 3/4 of the awake level to maintain an end-tidal CO_2 level of approximately 4%. End-inspiratory airway pressure, measured in the ventilator tubings, averaged 11 cmH_2O.

RSS averaged 2.4 during the anaesthesia measurements, and exceeded 6 in only one of the 15 recordings made during anaesthesia. There was an increased dispersion of ratios (increased log SD Q) after 15 min of anaesthesia, indicating a worsening of the mismatch, and a slight right shift of the distribution of the ventilation curves towards higher $\dot{V}_A/\dot{Q}$ ratios (increased V_M). The common finding in all patients was that the pattern of $\dot{V}_A/\dot{Q}$ mismatch that was seen when awake was

Table 2. – Central circulation and ventilation, awake and during anasthesia

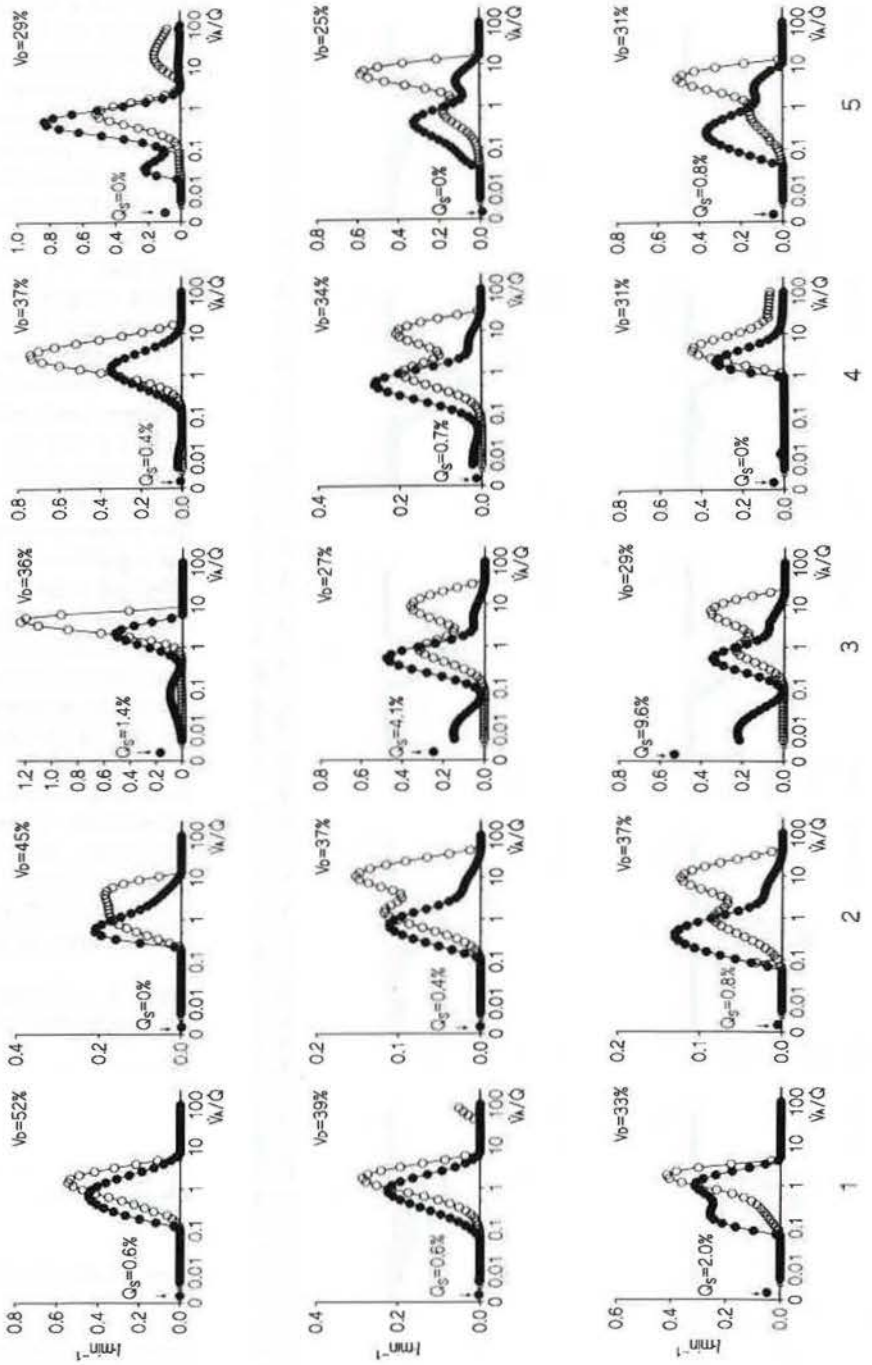
	CO	HR	Vascular mean pressures				SVR	PVR	$\dot{V}_E$	V_T	Respiratory	End-inspiratory airway pressure
			Syst	Pulm	Wedge	RA						
	$l \cdot min^{-1}$	$b \cdot min^{-1}$	mmHg	mmHg	mmHg	mmHg	$mmHg \cdot l^{-1} \cdot min$		$l \cdot min^{-1}$	ml	$breath \cdot min^{-1}$	cmH_2O
Awake (n=10)												
	5.0	68	94	18	7	5	19.1	2.31	8.0	646	13	0
	±1.3	±6	±21	±4	±3	±4	±5.3	±0.83	±2.4	±211	±0.3	±0
Anaesthesia 15 min (n=10)												
	3.8*	73	62*	15	6	5	15.7	2.27	5.8*	480*	12	11*
	±0.9	±14	±10	±3	±3	±3	±3.8	±0.98	±1.6	±77	±0.0	±4
Anaesthesia 45 min (n=5)												
	3.8*	75	69	17	7	6	16.7	2.60	5.8*	475*	12	9*
	±1.2	±14	±23	±3	±3	±2	±4.3	±1.10	±0.4	±59	±0.0	±2
Percentage of anaesth. 15 min#												
	106	103	113	113	117	120	99	100	100	100	100	100

Data are presented as mean±SD. CO: cardiac output; HR: heart rate; syst: systemic; pulm: pulmonary artery; wedge: pulmonary capillary wedge; RA: right atrial; SVR and PVR: systemic and pulmonary vasculary resistance, respectively; $\dot{V}_E$: minute ventilation; V_T: tidal volume. #the percentage values in the bottom line of the table show the change in cardiovascular data from 15 to 45 min of anaesthesia in the five subjects studied on both occasions. *: significantly different from awake, $p<0.05$.

Table 3. – Gas exchange awake and during anaesthesia

	Shunt	Low $\dot{V}_A/\dot{Q}$	high $\dot{V}_A/\dot{Q}$	V_D	QM	log SD Q	V_M	log SD V	FIO_2	Pao_2	$Paco_2$	$P\bar{v}o_2$
	% CO	% CO	% $\dot{V}_E$	% $\dot{V}_E$								
Awake (n=10)												
	0.6	5.4	2.2	39.8	0.71	0.99	1.61	0.78	0.21	9.16	5.3	5.1
	±0.4	±5.9	±5.6	±7.8	±0.28	±0.30	±0.68	±0.29	±0.00	±1.3	±0.9	±0.7
Anaesthesia 15 min (n=10)												
	1.0	8.5	6.1	34.7	0.62	1.29*	2.33*	1.00	0.38	16.8	5.2	5.1
	±1.1	±7.4	±7.8	±5.9	±0.18	±0.31	±0.85	±0.29	±0.02	±6.1	±0.5	±0.8
Anaesthesia 45 min (n=5)												
	2.6	9.6	8.9	32.1	0.85	1.26	2.93	1.11	0.39	18.0	5.4	5.0
	±4.0	±2.5	±7.2	±3.6	±1.00	±0.48	±1.54	±0.24	±0.01	±8.1	±0.4	±0.9
Percentage of anaesth. 15 min#												
	217	126	73	100	144	102	103	90	100	97	102	98

Data are presented as mean±SD. Shunt and low $\dot{V}_A/\dot{Q}$: perfusion of non-ventilated ($\dot{V}_A/\dot{Q}$ <0.005) and poorly ventilated (0.005<$\dot{V}_A/\dot{Q}$<0.1) regions, respectively; high $\dot{V}_A/\dot{Q}$ and V_D: ventilation of poorly perfused regions (10<$\dot{V}_A/\dot{Q}$<100) and deadspace ($\dot{V}_A/\dot{Q}$>100), respectively; Q_M, log SD Q, V_M and log SD V: mean and log SD of perfusion and ventilation respectively; FIO_2: inspired oxygen fraction; $P\bar{v}o_2$: mixed venous oxygen tension. For other abbreviations see legends to tables 1 and 2. # see explanation in legend to table 2; *: significantly different from awake, $p<0.05$.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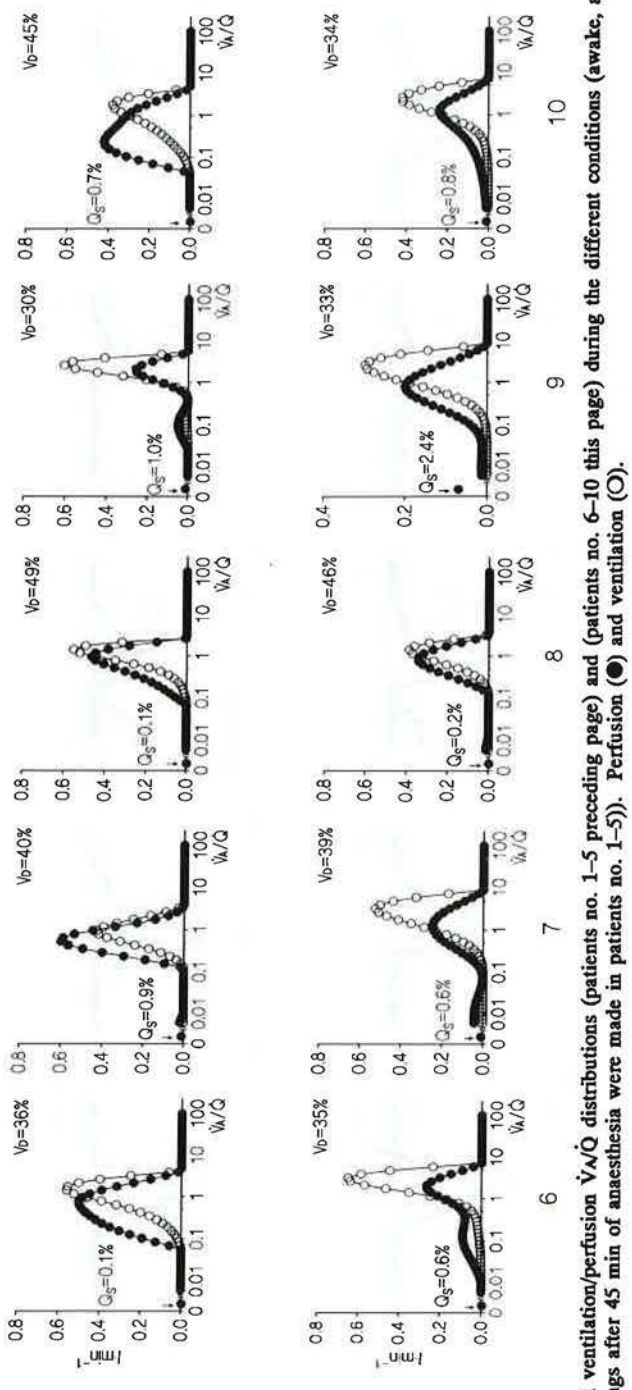

Fig. 1. – Individual ventilation/perfusion $\dot{V}_A/\dot{Q}$ distributions (patients no. 1–5 preceding page) and (patients no. 6–10 this page) during the different conditions (awake, after 15 and 45 min of anaesthesia (recordings after 45 min of anaesthesia were made in patients no. 1–5)). Perfusion (●) and ventilation (○).

exaggerated during anaesthesia. Thus, all patients who showed perfusion of regions with low $\dot{V}_A/\dot{Q}$ ratios awake (patients no. 3–10), increased their perfusion to such regions during anaesthesia. The patients who had ventilation of regions with high $\dot{V}_A/\dot{Q}$ ratios awake (patients no. 2–5), also increased their ventilation of high $\dot{V}_A/\dot{Q}$ regions during anaesthesia. Patient no. 1, who had a broad unimodal $\dot{V}_A/\dot{Q}$ distribution awake, widened his $\dot{V}_A/\dot{Q}$ mode further during anaesthesia, so that it included regions with both high and low $\dot{V}_A/\dot{Q}$ ratios. However, due to the interindividual differences in response to anaesthesia the changes in perfusion of low $\dot{V}_A/\dot{Q}$ regions and ventilation of high regions were not significant for the material as a whole. Only two patients had a shunt above 2% (patients no. 3: 4.1% and no. 9: 2.4%). In the remaining patients the shunt was less than 1% or was absent. Due to the increased inspired oxygen fraction during anaesthesia, Pa_{O_2} increased to a mean of 16.8 kPa. Pa_{CO_2} and $P\bar{v}_{O_2}$ remained stable at the same level as in the awake state (table 3).

After another 30 min of anaesthesia, no significant changes were noted in any variable (patients no. 1–5) (tables 2 and 3). However, in patient no. 3, who had the largest shunt after 15 min of anaesthesia, a further increase in shunt to 9.6% was noted (fig. 1).

The cross-sectional area at the two CT scan levels was not significantly altered, after induction of anaesthesia, although a small mean reduction of 2–3% was shown (table 4). During anaesthesia the diaphragm was seen in the caudal CT scan in two patients (nos 2 and 3), the scan level relative to the spine being the same as during the awake recordings. Awake, this level was just above the top of the dome of the diaphragm (approximately 0.5 cm above). This suggests that the diaphragm had been displaced cranially in 2 of the 10 patients during anaesthesia, whereas in the other eight patients no, or only minor, displacement of the diaphragm had occurred. Small atelectatic areas were shown in two patients in the caudal CT scan (patient no. 1: 0.2% and no. 9: 0.8%), while in another three patients atelectases were

Table 4. – Computed tomography (CT) cross-sectional and atelectatic areas, awake and during anaesthesia

	Cross-sectional area		Atelectasis	
	Scan 1	Scan 2	Scan 1	Scan 2
	cm^2	cm^2	% of intrathoracic area	
Awake (n=10)				
	398	375	0.00	0.00
	±69	±48	±0.00	±0.00
Anaesthesia 15 min (n=10)				
	391	365	0.10	0.21
	±69	±53	±0.27	±0.37
Anaesthesia 45 min (n=5)				
	397	381	0.04	0.26
	±95	±64	±0.09	±0.36
Percentage of anaesth. 15 min#				
	99	100	100	115

Data are presented as mean±SD. Scan 1 and Scan 2: caudal and cranial CT scan, respectively. #: see explanation in table 2.

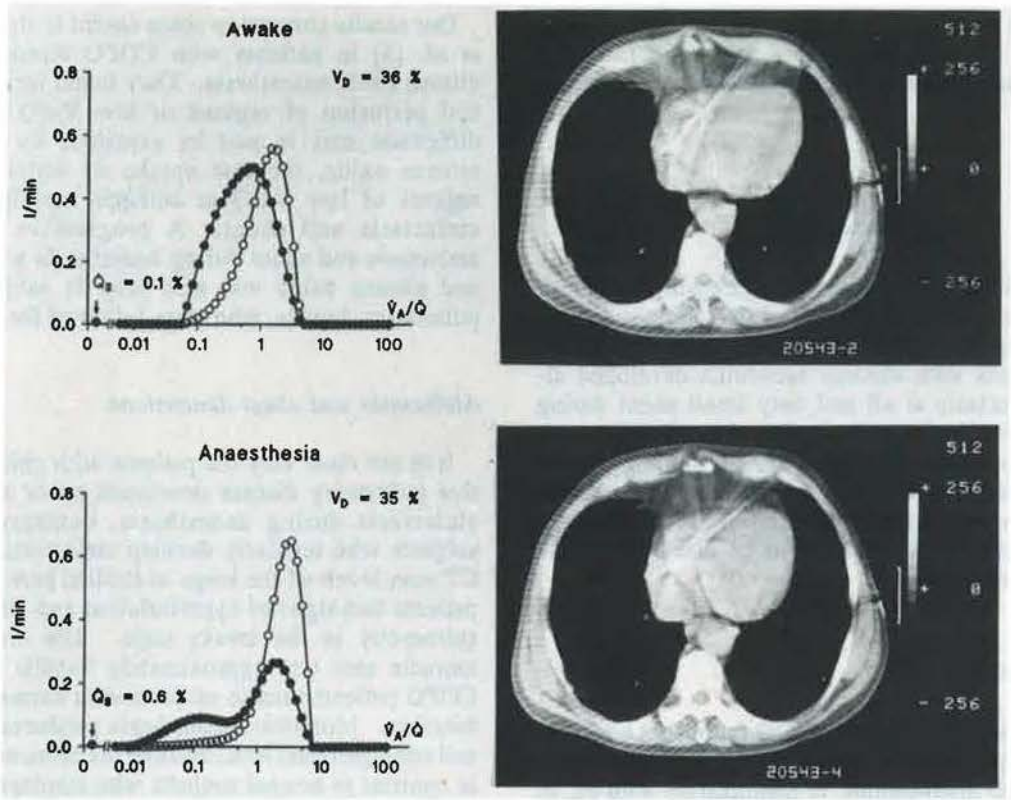

Fig 2. – Ventilation perfusion ($\dot{V}A/\dot{Q}$) distribution and computed tomography (CT) scans in patient no. 6 awake and during enflurane anaesthesia. Perfusion (●) and ventilation (○). Note the large transverse lung area, suggestive of hyperinflation, in comparison with a lung healthy subject (fig. 3).

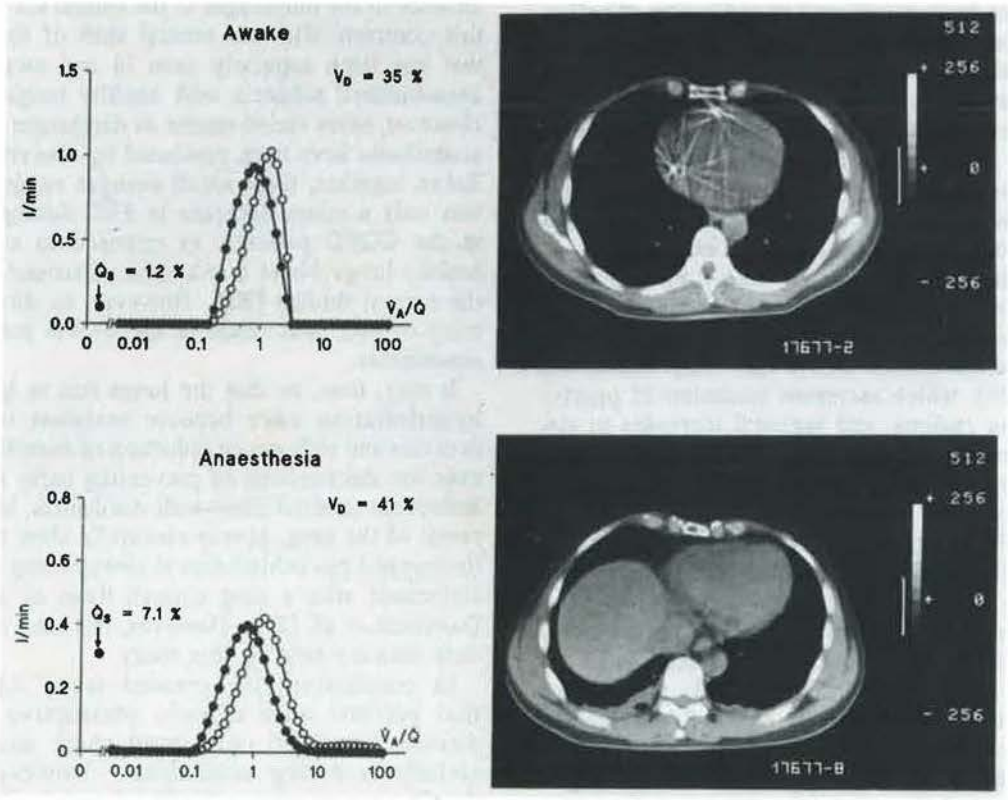

Fig 3. – Ventilation perfusion ($\dot{V}A/\dot{Q}$) distribution and computed tomography (CT) scans in a subject with healthy lungs awake and during enflurane anaesthesia. Perfusion (●) and ventilation (○). The subject participated in the study by GUNNARSSON *et al.* [10], his individual data have not been published previously.

shown in the cranial CT scan (patient no. 3: 1.1%, no. 5: 0.4% and no 6: 0.6%) (table 4, and fig. 2). There was no further increase in the atelectatic area during anaesthesia.

Discussion

In previous studies on patients with healthy lungs we have shown prompt development of atelectasis and shunt on induction of anaesthesia [1–5]. The presently studied patients with chronic bronchitis developed almost no atelectasis at all and only small shunt during anaesthesia, but the large dispersion of $\dot{V}_A/\dot{Q}$ ratios, seen already when awake, increased further during anaesthesia. Mechanisms that may explain the difference in reaction between patients with chronic bronchitis and patients without lung disease will be discussed in the following paragraphs.

Gas exchange

The increased dispersion of $\dot{V}_A/\dot{Q}$ ratios that was seen in all patients, and the presence of bimodal or even trimodal $\dot{V}_A/\dot{Q}$ distributions, in combination with no, or only minor, shunt are similar to what has been reported earlier in patients with chronic obstructive pulmonary disease [3, 12, 25, 26]. In asthmatic patients, the absence of shunt and presence of perfusion of low $\dot{V}_A/\dot{Q}$ regions have been considered an indication of collateral ventilation, maintaining a certain gas exchange in lung units behind occluded airways [27]. Hypoxic pulmonary vasoconstriction (HPV) is another mechanism to reduce shunt, by diverting blood flow away from poorly- or non-ventilated lung regions. The moderate hypoxaemia that was seen in most patients should have stimulated the HPV response, according to the dose-response curves by BARER *et al.* [28].

The major effect of anaesthesia was a further increase in the $\dot{V}_A/\dot{Q}$ mismatch with widened perfusion distribution, as indicated by an increased log Q SD. Possible causes may be attenuation of the HPV response by the anaesthetic [29], which increases perfusion of poorly-ventilated lung regions, and regional increases in airway resistance [30], and more widespread airway closure [31], which reduce ventilation in relation to blood flow.

Interestingly, shunt was virtually absent in the anaesthetized COPD patient, with one exception, in striking difference to the findings in anaesthetized subjects with healthy lungs who develop large shunts [6–10]. The shunt in the anaesthetized normal subject is more likely to be explained by the formation of atelectasis in dependent lung regions [8, 9], and similarly the absence of shunt in the COPD patient is reasonably explained by the absence of atelectasis. The only patient with large shunt in the present study also had the largest atelectasis although the atelectatic area was still smaller than normally seen in subjects with healthy lungs during anaesthesia [8–10].

Our results contrast to some extent to those of DUECK *et al.* [5] in patients with COPD during halothane/nitrous oxide anaesthesia. They found increasing shunt and perfusion of regions of low $\dot{V}_A/\dot{Q}$ ratios. The difference may in part be explained by their use of nitrous oxide, the fast uptake of which may force regions of low $\dot{V}_A/\dot{Q}$ to collapse rapidly, producing atelectasis and shunt. A progressive increase in atelectasis and shunt during anaesthesia with enflurane and nitrous oxide was also seen in subjects without pulmonary disease, who were followed for 90 min [10].

Atelectasis and chest dimensions

It is not clear why the patients with chronic obstructive pulmonary disease developed no or only minimal atelectasis during anaesthesia, contrary to normal subjects who regularly develop atelectasis at the same CT scan levels of the lungs as studied here [1, 3]. Most patients had signs of hyperinflation and air trapping on spirometry in the awake state. The cross-sectional thoracic area was approximately 5–10% larger in the COPD patients than in subjects with normal pulmonary function. Moreover, anaesthesia produced only minor and nonsignificant reductions of the cross-sectional area, in contrast to normal subjects who displayed larger and significant decreases [32]. Also, the position of the diaphragm was almost unaltered, or shifted cranially to a very minor extent, in the anaesthetized COPD patient, as inferred from the maintained diaphragm area, or absence of the diaphragm in the caudal CT scan. Again this contrasts with the cranial shift of the diaphragm that has been regularly seen in our own studies on anaesthetized subjects with healthy lungs [8–10, 33]. However, more varied results on diaphragm shape during anaesthesia have been presented by KRAYER *et al.* [34]. Taken together, these small changes suggest that there was only a minor decrease in FRC during anaesthesia in the COPD patients, as opposed to subjects with healthy lungs where a reduction of around 0.4–0.5 *l* is the normal finding [33]. However, no direct measurement of FRC was made in the COPD patients during anaesthesia.

It may, thus, be that the lungs due to long-standing hyperinflation have become resistant to a volume decrease and collapse on induction of anaesthesia. Whatever the mechanisms of preventing early formation of atelectasis (altered chest-wall mechanics, loss of elastic recoil of the lung, airway closure?), slow resorption of the trapped gas behind closed airways may still produce atelectasis after a long enough time, as discussed by DANTZKER *et al.* [35]. However, this may take a longer time than covered by this study.

In conclusion, the present study demonstrated that patients with chronic obstructive pulmonary disease developed only small shunt and almost no atelectasis during anaesthesia. However, they did develop a more severe $\dot{V}_A/\dot{Q}$ mismatch with increased log Q SD. It may be, that long-standing hyperinflation of the lungs makes them resistant to early collapse, and/or

that airway closure prevents gas from leaving the alveoli (gas trapping).

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References

1. Marshall BE, Wyche MQ Jr. – Hypoxemia during and after anesthesia. *Anesthesiology,* 1972, 37, 178–209.
2. Nunn JF, Milledge JS, Chen D, Dore C. – Respiratory criteria for fitness for surgery and anaesthesia. *Anaesthesia,* 1988, 43, 543–551.
3. Wagner PD, Dantzker DR, Dueck R, Clausen JL, West JB. – Ventilation-perfusion inequality in chronic obstructive pulmonary disease. *J Clin Invest,* 1977, 59, 203–216.
4. Rehder, K, Knopp, TJ, Sessler, AD, Didier, PE. – Ventilation-perfusion relationship in young healthy awake and anesthetized-paralyzed man. *J Appl Physiol,* 1979, 47, 745–753.
5. Dueck R, Young I, Clausen J, Wagner PD. – Altered distribution of pulmonary ventilation and blood flow following induction of inhalational anesthesia. *Anesthesiology,* 1980, 52, 113–125.
6. Prutow RJ, Dueck R, Davies NJH, Clausen J. – Shunt development in young adult surgical patients due to inhalational anesthesia. *Anesthesiology,* 1982, 57, A477.
7. Bindslev L, Hedenstierna G, Santesson J, Gottlieb I, Carvallhas A. – Ventilation-perfusion distribution during inhalational anaesthesia. Effect of spontaneous breathing, mechanical ventilation and positive end-expiratory pressure. *Acta Anaesth Scand,* 1981, 25, 360–371.
8. Brismar B, Hedenstierna G, Lundquist H, Strandberg Å, Svensson L, Tokics L. – Pulmonary densities during anesthesia with muscular relaxation – a proposal of atelectasis. *Anesthesiology,* 1985, 62, 422–428.
9. Tokics L, Hedenstierna G, Strandberg Å, Brismar B, Lundquist H. – Lung collapse and gas exchange during general anesthesia - effects of spontaneous breathing, muscle paralysis and positive end-expiratory pressure. *Anesthesiology,* 1987, 66, 157–167.
10. Gunnarsson L, Strandberg Å, Brismar B, Tokics L, Lundquist H, Hedenstiema G. – Atelectasis and gas exchange impairment during enflurane/nitrous oxide anaesthesia. *Acta Anaesthesiol Scand,* 1989, 33, 629–637.
11. Briscoe WA, Cree EM, Filler S, Houssay HEJ, Cournand A. – Lung volume, alveolar ventilation and perfusion interrelationships in chronic pulmonary emphysema. *J Appl Physiol,* 1960, 15, 785–795.
12. Marthan R, Castaing Y, Manier G, Guénard H. – Gas exchange alterations in patients with chronic obstructive lung disease. *Chest,* 1985, 87, 470–475.
13. Fowkes FGR, Lunn JN, Farrow SC, Robertson IB, Samuel P. – Epidemiology in anaesthesia. III: Mortality risk in patients with coexisting physical disease. *Br J Anaesth,* 1982, 54, 819–825.
14. Tarhan S, Moffit EA, Sessler A, Douglas WW, Taylor WF. – Risk of anesthesia and surgery in patients with chronic bronchitis and chronic obstructive pulmonary disease. *Surgery,* 1973, 74, 720–726.
15. Gass GD, Olsen GN. – Preoperative pulmonary function testing to predict postoperative morbidity and mortality. *Chest,* 1986, 89, 127–135.
16. Tisi GM. – Preoperative evaluation of pulmonary function. *Am Rev Respir Dis,* 1979, 119, 293–310.
17. Hedenstierna G, Lundh R, Johansson H. – Alveolar stability during anaesthesia for reconstructive vascular surgery of the leg. *Acta Anaesth Scand,* 1983, 27, 26–34.
18. Wagner PD, Naumann PF, Lavaruso RB. – Simultaneous measurement of eight foreign gases in blood by gas chromatography. *J Appl Physiol,* 1974, 36, 600–605.
19. Wagner PD, Saltzman HA, West JB. – Measurement of continuous distribution of ventilation-perfusion ratios. Theory. *J Appl Physiol,* 1974, 36, 588–599.
20. Evans JW, Wagner PD. – Limits of $\dot{V}_A/\dot{Q}$ distributions from analysis of experimental inert gas elimination. *J Appl Physiol,* 1977, 42, 889–898.
21. Ekelund LG, Holmgren A. – Central hemodynamics during exercise. *Circ Res,* 1967, 20 (suppl. 1), 33–43.
22. Wagner PD, West JB. – Continuous distributions of ventilation-perfusion relationships. *In:* Pulmonary gas exchange, vol 1. J.B. West ed., Academic Press, New York, 1980, pp. 233–235.
23. Wagner PD, Hedenstierna G, Bylin G. – Ventilation-perfusion inequality in chronic asthma. *Am Rev Respir Dis,* 1987, 136, 605–612.
24. Raine JM, Bishop JM. – A-a difference in O_2 tension and physiological deadspace in normal man. *J Appl Physiol,* 1963, 18, 284–288.
25. Torres A, Reyes A, Roca J, Wagner PD, Rodriguez-Roisin R. – Ventilation-perfusion mismatching in chronic obstructive pulmonary disease during ventilator weaning. *Am Rev Respir Dis,* 1989, 140, 1246–1250.
26. Freyshuss U, Hedlin G, Hedenstierna G. – Ventilation-perfusion relationships during exercise-induced asthma in children. *Am Rev Respir Dis,* 1984, 130, 888–894.
27. Wagner PD, Dantzker DR, Iacovoni VE, Tomlin WC, West JB. – Ventilation-perfusion inequality in asymptomatic asthma. *Am Rev Respir Dis,* 1978, 118, 511–524.
28. Barer GR, Howard P, Shaw JW. – Stimulus-response curves for the pulmonary vascular bed to hypoxia and hypercapnia. *J Physiol,* 1970, 211, 139–155.
29. Marshall C, Lindgren L, Marshall BE. – Effects of halothane, enflurane and isoflurane in rat lungs *in vitro*. *Anesthesiology,* 1984, 60, 304–308.
30. Broseghini C, Brandolese R, Poggi R, Polese G, Manzin E, Milic-Emili J, Rossi A. – Respiratory mechanics during the first day of mechanical ventilation in patients with pulmonary edema and chronic airway obstruction. *Am Rev Respir Dis,* 1988, 138, 355–361.
31. von Mieding G, Löllgren H, Smidt U, Linde H. – Simultaneous washout of helium and sulphur hexafluoride in healthy subjects and patients with chronic bronchitis, bronchial asthma, and emphysema. *Am Rev Respir Dis,* 1977, 116, 649–660.
32. Hedenstiema G, Strandberg Å, Brismar B, Lundquist H, Svensson L, Tokics L. – Functional residual capacity, thoracoabdominal dimensions, and central blood volume during general anesthesia with muscle paralysis and mechanical ventilation. *Anesthesiology,* 1985, 62, 247–254.
33. Rehder K, Sessler AD, Marsch HM. – Lung disease. State of art, general anesthesia and the lung. *Am Rev Respir Dis,* 1975, 112, 541–563.
34. Krayer S, Rehder K, Vetterman J, Didier EP, Ritman EL. – Position and motion of the human diaphragm during anesthesia-paralysis. *Anesthesiology,* 1989, 70, 891–898.
35. Dantzker DR, Wagner PD, West JB. – Instability of lung units with low $\dot{V}_A/\dot{Q}$ ratios during O_2 breathing. *J Appl Physiol,* 1975, 38, 886–895.

Maladie pulmonaire obstructive chronique et anesthésie - Formation d'atélectasies et troubles des échanges gazeux. L. Gunnarsson, L. Tokics, H. Lundquist, B. Brismar, Å. Strandberg, B. Berg, G. Hedenstierna.

RÉSUMÉ: Les troubles des echanges gazeux et le développement d'atélectasies au cours d'une anesthésie à l'enflurane ont été étudiés chez 10 patients (âge moyen: 70 ans) atteints de maladie pulmonaire chronique obstructive (COPD). A l'état d'éveil, aucun patient n'a développé d'atélectasie après étude au moyen de la tomographie computée. La distribution de la ventilation et de la perfusion ($\dot{V}_A/\dot{Q}$), étudiée par la technique d'élimination de gaz multiples inertes, a montré une dispersion accrue des relations $\dot{V}_A/\dot{Q}$ (la déviation standard logarithmique de la distribution de la perfusion, logarithme moyen Q SD 0.99; intervalle de confiance supérieur à 95% chez un sujet normal: 0.60), ainsi qu'une augmentation de la perfusion des régions dont les rapports $\dot{V}_A/\dot{Q}$ sont bas ($0.005 < \dot{V}_A/\dot{Q} < 0.1$: 5.4% du débit cardique). Le shunt est négligeable (moyenne 0.6%). La tomographie computée du thorax a montré des zones transversales thoraciques plus grandes qu'elles n'avaient été décelées antérieurement chez les sujets à poumons sains ($p<0.01$). Aucune atélectasie n'a été décelée chez aucun patient.

Au cours de l'anesthésie, l'on a noté une aggravation plus marquée du manque de congruence entre $\dot{V}_A$ et $\dot{Q}$, avec une augmentation significative de log Q SD (1.29, $p<0.05$), mais pas d'augmentation du shunt (moyenne 1%). Des zones atélectasiques minimes ont été notées chez trois patients, les autres n'ayant aucune atélectasie. Les dimensions du thorax n'ont pas été réduites de plus de 3% au cours de l'anesthésie, ce qui suggère que la capacité résiduelle fonctionnelle n'a pas été modifiée, ou seulement affectée de façon minime.

Ces observations contrastent avec ce qui se produit chez des patients dont les poumons sont sains, et chez lesquels l'atélactasie et les shunts se développent régulièrement au cours de l'anesthésie.

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