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Effects of Intravenous Anesthesia on $\dot{V}_A/\dot{Q}$ Distribution:

A Study Performed during Ventilation with Air and with 50% Oxygen, Supine and in the Lateral Position

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Distribution of ventilation and perfusion in relation to ventilation–perfusion ratio ($\dot{V}_A/\dot{Q}$) were studied in 14 patients, with a mean age of 59 yr, before elective lung surgery, in the supine position when awake, during intravenous anesthesia and mechanical ventilation with air, after increasing the fraction of inspired oxygen ($F_{I_{O_2}}$) to 0.5, and in the lateral position. Before anesthesia, small inert gas shunts and perfusion of low $\dot{V}_A/\dot{Q}$ regions, indicating some degree of $\dot{V}_A/\dot{Q}$ mismatch, were observed in several patients. After induction, $F_{I_{O_2}}$ = 0.21, the major changes were a significant decrease in cardiac output and an increase in log SD for perfusion from 0.77 ± 0.45 (SD) to 1.13 ± 0.50 (SD), while the shunt remained low at 1% of cardiac output and arterial oxygen tension (Pa_{O_2}) was unchanged. An increase to $F_{I_{O_2}}$ = 0.5 induced only small changes with a shunt of 2.5% of cardiac output. In the lateral position, the shunt was 4.0% and increases in ventilation to high $\dot{V}_A/\dot{Q}$ regions were observed. The lack of marked changes in the $\dot{V}_A/\dot{Q}$ distribution after induction either could be a result of only minor alterations in the distribution of ventilation and perfusion or an effective vascular response to alveolar hypoxia (hypoxic pulmonary vasoconstriction, HPV). (Key words: Anesthetics, intravenous: diazepam; fentanyl; thiopental. Lung: hypoxic pulmonary vasoconstriction; shunting; ventilation–perfusion ratio. Oxygen. Ventilation: mechanical; ventilation–perfusion ratio.)

ABBREVIATIONS

- BSA = body surface area
- BTPS = body temperature and pressure, saturated
- bw = body weight
- Ca_{O_2} = oxygen content in arterial blood
- $C(a\text{-}\bar{v})_{O_2}$ = arterio-venous oxygen content difference
- $FEV_{1.0}$ = forced expiratory volume in one second
- FRC = functional residual capacity
- HPV = hypoxic pulmonary vasoconstriction
- HR = heart rate
- MVV_{40} = maximal voluntary ventilation, 40 breaths · min^{-1}
- P_{50} = tension at which 50% saturation of the haemoglobin occurs
- $P(A\text{-}a)_{O_2}$ = alveolar–arterial oxygen tension difference
- PA_{O_2} = alveolar oxygen tension
- Pa_{CO_2} = arterial carbon dioxide tension
- Pa_{O_2} = arterial oxygen tension
- $\bar{P}art$ = mean radial arterial pressure
- Paw = airway pressure, end-inspiratory
- $\bar{P}_{PA}$ = mean pulmonary arterial pressure
- $P\bar{v}_{O_2}$ = mixed venous oxygen tension
- PVR = pulmonary vascular resistance
- $\bar{P}_W$ = mean pulmonary wedge pressure
- $\dot{Q}$ = cardiac output
- $\dot{Q}_{SH}/\dot{Q}_T$ = shunt fraction
- $\dot{Q}_{VA}/\dot{Q}_T$ = venous admixture
- SF_6 = sulfur hexafluoride
- SV = stroke volume
- $\dot{V}_A/\dot{Q}$ = ventilation–perfusion ratio
- VC = vital capacity
- V_D/V_T = deadspace to tidal volume ratio
- $\dot{V}_E$ = minute expired ventilation
- $\dot{V}O_2$ = oxygen uptake
- Wsl = symptom limited work capacity, determined as the highest work load performed on a bicycle ergometer and limited by symptoms such as angina, fatigue, dyspnea, ECG changes

IT GENERALLY IS ACCEPTED that pulmonary gas exchange is impaired during anesthesia with mechanical ventilation. This is evident from a large number of studies, based on measurements of gas concentrations and tensions in arterial and mixed venous blood,[1,2] as well as from recent investigations using the inert gas elimination technique.[3–6] Although the underlying mechanisms are not understood completely, there is general agreement that functional residual capacity (FRC) decreases during anesthesia[7] and that the distribution of ventilation is shifted toward nondependent regions of the lung.[8] Earlier studies have shown this to be due to changed shape and motion of the chest wall[9] with airway closure in dependent parts of the lung.[10,11] The

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TABLE 1. Preoperative Data for Fourteen Patients Scheduled for Lung Surgery (Spirometry data are given in per cent of predicted)

Patient No.	Sex	Age (yr)	Height (M)	Weight (kg)	Smokers	Type of Disease	Wsl. (watts)	VC (% pred)	$FEV_{1.0}$ (% pred)	MVV_{40} (% pred)
1	M	72	1.63	52	Yes	Carcinoma	80	84	90	68
2	M	71	1.71	67	No (ex)	Carcinoma	100	51	41	44
3	M	56	1.71	66	Yes	Carcinoma	90	71	63	51
4	M	64	1.83	80	Yes	Carcinoma	150	99	103	109
5	F	33	1.69	57	No (ex)	Bronchiectasis	120	86	81	65
6	M	65	1.72	69	No (ex)	Carcinoma	—	80	81	82
7	M	53	1.76	79	Yes	Carcinoma	120	112	88	97
8	F	47	1.65	69	Yes	Carcinoma	120	106	81	90
9	F	58	1.63	67	No	Bronchial cyst	110	75	73	79
10	M	45	1.70	72	Yes	Carcinoma	140	78	78	78
11	F	62	1.62	74	Yes	Carcinoma	80	70	60	81
12	M	68	1.81	88	No (ex)	Carcinoma	140	109	108	117
13	M	65	1.72	74	Yes	Carcinoma	100	80	68	80
14	M	46	1.79	82	Yes	Bronchiectasis	170	104	100	—
$\bar{X}$		57.5	1.71	71.1			116.9	86.0	79.6	80.0
s.d.		11.4	0.07	9.7			27.5	17.7	18.1	20.6

normal adaptation of pulmonary blood flow to ventilation, hypoxic pulmonary vasoconstriction (HPV),[12] seems to be inhibited during anesthesia.[13–15] This effect may be more marked in elderly subjects,[5,6] especially with lung disease,[4] than in young healthy volunteers.[3] A preferential distribution of blood flow to dependent regions also could be exaggerated passively due to increased, transmural pressures in the vessels of the nondependent alveoli brought about by mechanical ventilation.[16]

A common factor in most earlier studies was the combination of general anesthesia and an increased fraction of inspired oxygen ($F_{I_{O_2}}$). The aim of the present investigation was to determine the role of the commonly used $F_{I_{O_2}}$ of 0.5 in the reported impairment of pulmonary gas exchange in elderly subjects, since it has been demonstrated that O_2 can increase the shunt fraction by inhibiting HPV and/or by creating absorption atelectasis.[17] For the purpose of the investigation, general anesthesia therefore was induced during ventilation with air, and intravenous agents were used for anesthesia.

Methods

Patients and Anesthesia

Fourteen patients, 10 men and four women, with a mean age of 59 yr (range 33–72 yr), were investigated. Nine patients were smokers, one never smoked, and four had stopped smoking more than 6 months earlier. The patients were accepted for surgery due to pulmonary carcinoma (n = 11) bronchiectasis (n = 2) and a bronchial cyst (n = 1). One patients (patient 2) with carcinoma of the left lung had surgery for stenosis of the left subclavian artery 4 years previously and had paresis of the left diaphragm postoperatively. His preoperative vital capacity was decreased to 51% of predicted and his forced expiratory flow also was decreased. However, the impaired lung function was mainly localized to the left lung, which received only 33% of total blood flow with perfusion scintigraphy, and he therefore was accepted for surgery. Another patient had a mitral valve replacement 6 months previously with an uneventful recovery. Clinical data, including dynamic spirometry, are given in table 1. Informed consent was obtained from each patient, and the study protocol was approved by the Ethical Committée of the Karolinska Hospital.

Measurements were performed before thoracotomy on four occasions: 1) patient awake in supine position about 1.5 h after premedication; 2) during intravenous anesthesia, 30 min after intubation, $F_{I_{O_2}} = 0.21$, and with mechanical ventilation with zero end-expiratory pressure (supine position); 3) 30 min after $F_{I_{O_2}}$ was increased to 0.5 (supine position); 4) 30 min after the patient was placed in the lateral position with his diseased lung uppermost as for lung surgery ($F_{I_{O_2}} = 0.5$).

For premedication morphine, 7.5–15 mg, and scopolamine, 0.3–0.6 mg, depending on age and weight, were used. Anesthesia was induced and intubation was performed during ventilation with air, using thiopentone, 125–250 mg, diazepam, 5–10 mg, and fentanyl, 0.1–0.2 mg, followed by pancuronium bromide, 0.1 $mg \cdot kg^{-1}$ bw, before endotracheal intubation. Anesthesia was maintained with incremental doses of diazepam and fentanyl. Ventilation (Servo-ventilator® 900, Siemens Elema, Solna, Sweden) was set at 15 or 20 $breaths \cdot min^{-1}$ and with a minute volume intended to result in normoventilation.

Catheterization

A balloon-tipped, fluid-directed, single-lumen catheter was inserted percutaneously via the right basilic vein, and its correct position in the right pulmonary artery was determined by x-ray and pressure tracing. The

catheter was used for monitoring mean pulmonary artery ($\bar{P}_{PA}$) and mean pulmonary wedge ($\bar{P}_W$) pressures, and for sampling mixed venous blood. A 1.0-mm plastic cannula was inserted into the left radial artery following the usual routine during lung surgery and was used for monitoring mean arterial pressure ($\bar{P}art$) and for collection of arterial blood. The ECG was recorded with a CR_5 lead, and pressure recordings were carried out with equipment from Siemens Elema.

Ventilation–perfusion Ratio

Representative distributions of perfusion ($\dot{Q}$) and ventilation ($\dot{V}_E$) in relation to the ventilation–perfusion ratio ($\dot{V}_A/\dot{Q}$) were determined according to Wagner *et al.*[17–20] with the following minor modifications. Inert gas analysis was performed with a Perkin-Elmer® gas chromatograph (F22) equipped with an electron capture detector (ECD) for SF_6 and halothane and a flame ionization detector (FID) for ethane, cyclopropane, ether, and acetone. The 1.5-m column, made of nickel, was packed with Poropac Q-S®, 50/80 mesh. An oven temperature of 65° C was used for SF_6 and increased to 140–150° C for the remaining gases. This gave a better separation between SF_6 and CO_2. Carrier gas flow was 20 ml · min^{-1} of N_2. Blood gas partition coefficients for the six gases were taken from Evans and Wagner.[20,**] The compatibility between the distributions of perfusion and ventilation in relation to $\dot{V}_A/\dot{Q}$, and the inert gas data was tested by using least-squares analysis. The residual sum of squares was 5.5 ± 5.2 (SD) for all measurements, indicating acceptable fits.[21] The distributions also were used to calculate arterial blood gas tensions that were compared with the values actually measured. The differences were not significant for either Pa_{O_2} or Pa_{CO_2} under the four study conditions.

Blood Gases and Minute Ventilation

Blood samples were anticoagulated with heparin or EDTA and stored in ice water until analyzed, usually within 5 min. Gas tensions and *p*H were determined with an IL-autoanalyzer (model 613, Instrumentation Laboratory, Inc.). The oxygen saturation of blood was determined spectrophotometrically with a CO-oximeter (model 282, Instrumentation Laboratory, Inc.) and corrected for dissolved oxygen. P_{50} was determined according to Aberman *et al.*[22] The blood buffer line was established with the microequilibration technique of Siggard-Andersen *et al.*[23] Minute expired ventilation ($\dot{V}_E$) was measured with a ventilation monitor (model LS75, Bourns, Inc.). Inspired and expired air were analyzed for O_2, CO_2, and N_2 with a mass spectrometer (model 200 MGA, 20th Century Electronics Ltd., England).

Calculations

Cardiac output ($\dot{Q}$) was calculated using the direct Fick method from the oxygen uptake ($\dot{V}_{O_2}$) and the arteriovenous oxygen content difference ($C(a\text{-}\bar{v})_{O_2}$). Pulmonary vascular resistance (PVR), in mmHg · l^{-1} · min · m^2, was calculated from the formula: $(\bar{P}_{PA} - \bar{P}_W) \cdot \dot{Q}^{-1} \cdot BSA$. Venous admixture ($\dot{Q}_{VA}/\dot{Q}_T$) was calculated using the shunt equation, where the oxygen contents were calculated from the formula: 1.34 · Hb · % saturation + $P_{O_2} \cdot 0.0031$. Alveolar–arterial oxygen tension difference ($P(A\text{-}a)_{O_2}$) in mmHg, was calculated from the formula: $PA_{O_2} - Pa_{O_2}$, where PA_{O_2} was derived from the alveolar gas equation. Dead space to tidal volume ratio (V_D/V_T) was determined according to the Enghoff modification of the Bohr equation and included patient and apparatus dead space.

Statistics

The data were analyzed by analysis of variance, followed by the Studentized range test for multiple comparisons.[24] For nonnormal distributions Friedman's two-way analysis of variance was used. $P < 0.05$ was considered significant. The results are presented as mean ± SD.

Results

$\dot{Q}$, $\dot{V}_{O_2}$, and $\bar{P}_W$ are presented as mean ± SD for the patients ventilated with 15 (n = 7 and 20 (n = 7 breaths · min^{-1}, as there were small differences in the time course of these variables (table 2). The remaining results are presented as means for all 14 patients (tables 2 and 3). Individual $\dot{V}_A/\dot{Q}$ distributions are shown in figs. 1 and 2.

Control, FI_{O_2} = 0.21 (I)

Central Hemodynamics. In the premedicated supine patients, $\dot{Q}$ was normal in relation to $\dot{V}_{O_2}$. Pulmonary vascular resistance was slightly increased in four patients, although the mean value for all was within the normal range.

Gas Exchange. Several patients had increased retentions of the less soluble gases. Decreased excretion of the more soluble gases was observed in one patient. Transformation of these data to continuous distributions of $\dot{V}_A/\dot{Q}$ ratios indicated the existence of small shunts with a mean value for all of 2% of cardiac output. In several patients (more pronounced in two) there was also perfusion to units with $\dot{V}_A/\dot{Q}$ between 0.005 and 0.1 (mean

** The computer program kindly was supplied by Drs. Wagner and West.

TABLE 2. Circulatory and Gas Exchange Data (Abbreviations according to text. $Pa_{O_{2m}}$ and $Pa_{CO_{2m}}$ are measured, while $Pa_{O_{2c}}$ and $Pa_{CO_{2c}}$ are calculated from the inert gas data)

Variables		Awake Supine (I) (n = 14)	Anesthesia Supine (II) (n = 14)	Anesthesia Supine (III) (n = 13)	Anesthesia Lateral (IV) (n = 12)
FI_{O_2}		0.21	0.21	0.51 ± 0.02*·†	0.51 ± 0.03*
$\dot{Q}$	$(l \cdot min^{-1})$ f = 15	6.5 ± 1.0	3.8 ± 1.0*·†	4.6 ± 1.0*	4.7 ± 0.8*
	f = 20	5.4 ± 0.9	3.8 ± 0.4‡·§	4.9 ± 1.2	5.3 ± 1.5
$C(a-\bar{v})_{O_2}$	$(ml \cdot l^{-1})$	40 ± 5	47 ± 6*·†	45 ± 7	41 ± 6
HR	$(beats \cdot min^{-1})$	76 ± 12	74 ± 10	69 ± 9	69 ± 10¶
SV	(ml)	80 ± 18	53 ± 15*·†	70 ± 16§·¶	74 ± 22
$\dot{V}_E$	$(l\ BTPS \cdot min^{-1})$	7.7 ± 2.1	6.5 ± 1.0*·†	6.2 ± 1.0*	6.2 ± 1.0*
$\dot{V}O_2$	$(mmol \cdot min^{-1})$ f = 15	11.0 ± 1.8	7.8 ± 1.1*·†	8.7 ± 1.2*	8.2 ± 1.2*
	f = 20	10.1 ± 1.2	7.8 ± 0.8*·†	9.9 ± 20§	10.0 ± 2.0
$\bar{P}_{PA}$	(mmHg)	19 ± 5	16 ± 3**	17 ± 2¶	16 ± 2‡
$\bar{P}_W$	(mmHg) f = 15	7.7 ± 3.2	8.7 ± 2.9	9.9 ± 2.7	10.4 ± 4.3
	f = 20	11.6 ± 2.6	9.7 ± 3.0	9.6 ± 2.6	9.7 ± 2.9
PVR	$(mmHg \cdot l^{-1}pdmin \cdot m^2)$	3.1 ± 1.3	3.4 ± 1	2.7 ± 0.9	2.1 ± 1.0
$\bar{P}art$	(mmHg)	95 ± 13	70 ± 10*·†	74 ± 8*	78 ± 11*
$Pa_{O_{2m}}$	(mmHg)	76 ± 13	76 ± 14	200 ± 47*·†	209 ± 41*
$Pa_{O_{2c}}$	(mmHg)	76 ± 16	76 ± 17	199 ± 61*·†	203 ± 48*
$Pa_{CO_{2m}}$	(mmHg)	42 ± 4	37 ± 3*·†	39 ± 4	41 ± 5
$Pa_{CO_{2c}}$	(mmHg)	42 ± 4	37 ± 3*·†	39 ± 3	41 ± 5
$P\bar{v}_{O_2}$	(mmHg)	42 ± 4	37 ± 4*·†	43 ± 5†	45 ± 4¶
$\dot{Q}_{VA}/\dot{Q}_T$	(%)	13.2 ± 8.3	9.9 ± 5.2¶·**	6.9 ± 2.6*	6.7 ± 2.6*
$\dot{Q}_{SH}/\dot{Q}_T$	(%)	2.0 ± 2.3	1.0 ± 1.6	2.6 ± 2.2	4.0 ± 2.2
$P(A-a)_{O_2}$	(mmHg)	23 ± 11	32 ± 13¶	105 ± 43*·†	102 ± 40*
P_{aw}	(mmHg)		8.8 ± 2.7	8.7 ± 2.6	9.4 ± 2.1
V_D/V_T		0.46 ± 0.10	0.45 ± 0.07	0.48 ± 0.07	0.53 ± 0.08‡·§

Means ± SD are given.
* Significantly different from the awake value, $P < 0.001$.
† Significantly different from previous value, $P < 0.001$.
‡ Significantly different from the awake value, $P < 0.01$.
§ Significantly different from previous value, $P < 0.01$.
¶ Significantly different from the awake value, $P < 0.05$.
** Significantly different from previous value, $P < 0.05$.

value 4.1% of $\dot{Q}$, range 0–26.7%), and in one patient a high mode (peak ratio at $\dot{V}_A/\dot{Q} = 14$) was observed.

Pa_{O_2} was less than normal in six patients (<75 mmHg), the lowest being 56 mmHg (patient 2). Pa_{CO_2} was above normal, 50 mmHg, in one patient.

ANESTHESIA, FI_{O_2} = 0.21 (II)

Central Hemodynamics. Cardiac output decreased from 6.5 to 3.8 $l \cdot min^{-1}$ ($P < 0.001$) (f = 15) and 5.4 to 3.8 $l \cdot min^{-1}$ ($P < 0.01$) (f = 20). These decreases were due

TABLE 3. Relative Perfusion ($\dot{Q}/\dot{Q}_T$), Per Cent, and Relative Ventilation ($\dot{V}/\dot{V}_E$), Per Cent, for Five Intervals of $\dot{V}_A/\dot{Q}$ (upper part), and Mean $\dot{V}_A/\dot{Q}$ for the Distributions of Perfusion and Ventilation with Mean Values for the Log Standard Deviations of those Distributions (lower part)

	$\dot{Q}/\dot{Q}_T \times 100$				$\dot{V}/\dot{V}_E \times 100$			
$\dot{V}_A/\dot{Q}$ Range	Awake Supine FI_{O_2} = 0.21 (n = 14)	Anaesthesia Supine FI_{O_2} = 0.21 (n = 14)	Anaesthesia Supine FI_{O_2} = 0.51 (n = 13)	Anaesthesia Lateral FI_{O_2} = 0.51 (n = 12)	Awake Supine FI_{O_2} = 0.21 (n = 14)	Anaesthesia Supine FI_{O_2} = 0.21 (n = 14)	Anaesthesia Supine FI_{O_2} = 0.51 (n = 13)	Anaesthesia Lateral FI_{O_2} = 0.51 (n = 12)
0	2.0 ± 2.3	1.0 ± 1.6	2.5 ± 2.2	4.0 ± 2.2	0	0	0	0
0.005–0.1	4.1 ± 8.1	7.5 ± 8.7	6.7 ± 6.5	6.8 ± 5.3	0	0.1 ± 0.2	0.1 ± 0.2	0.1 ± 0.3
0.1–10	93.8 ± 8.4	91.2 ± 8.3	90.6 ± 6.0	88.7 ± 5.8	57.1 ± 10.9	64.6 ± 6.9*·†	63.8 ± 6.7*	58.2 ± 8.1‡
10–100	0.1 ± 0.3	0.3 ± 0.5	0.2 ± 0.5	0.5 ± 0.7	1.1 ± 4.1	2.3 ± 4.0	2.4 ± 3.9	4.9 ± 7.5
>100	0	0	0	0	41.8 ± 10.5	33.0 ± 7.2*·†	33.7 ± 6.8*	36.8 ± 6.8*
	$\dot{Q}$				$\dot{V}$			
$\overline{\dot{V}_A/\dot{Q}}$	0.54 ± 0.18	0.71 ± 0.23‡·§	0.57 ± 0.14	0.53 ± 0.17	0.87 ± 0.27	1.51 ± 0.52*·†	1.45 ± 0.56*	1.57 ± 0.71*
±log SD	0.77 ± 0.45	1.13 ± 0.50¶·**	1.19 ± 0.38¶	1.14 ± 0.22§	0.58 ± 0.32	0.69 ± 0.29	0.82 ± 0.28§	0.95 ± 0.39¶

Means ± SD are given.
* 3 Significantly different from awake value, $P < 0.001$.
† 6 Significantly different from previous value, $P < 0.001$.
‡ 4 Significantly different from previous value, $P < 0.05$.
§ 1 Significantly different from awake value, $P < 0.05$.
¶ 2 Significantly different from awake value, $P < 0.01$.
** 5 Significantly different from previous value, $P < 0.01$.

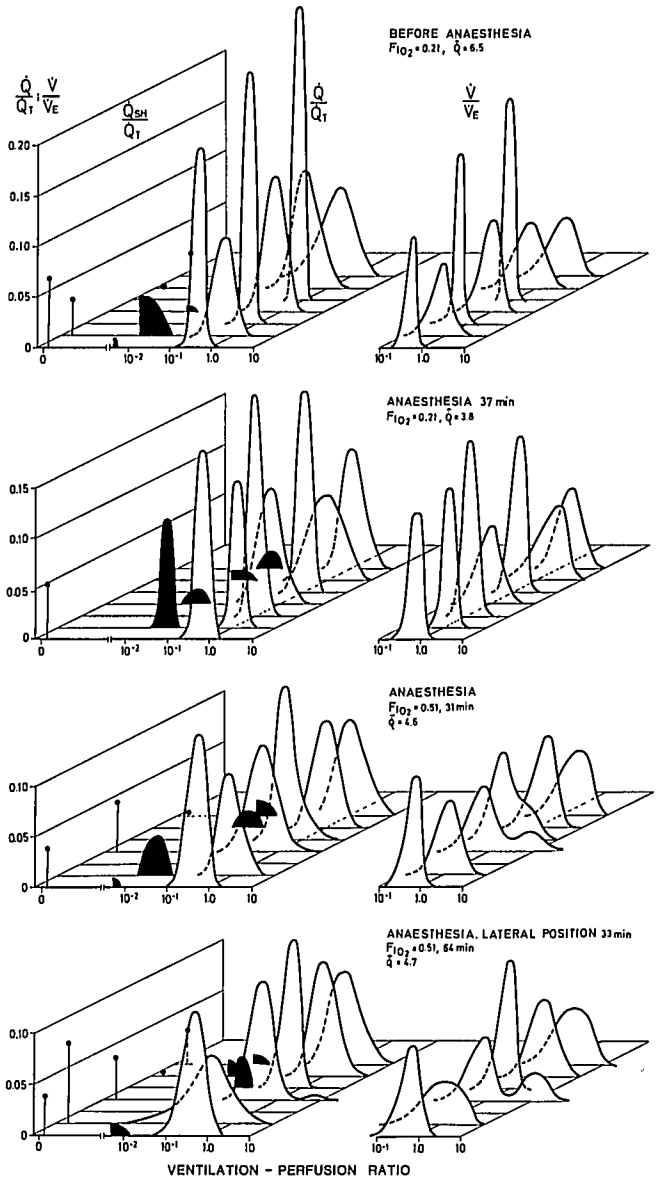

FIG. 1. $\dot{V}_A/\dot{Q}$ in patients with pulmonary tumors, effect of anesthesia (f = 15). Relative perfusion, $\dot{Q}/\dot{Q}_T$ (*left*), and ventilation, $\dot{V}/\dot{V}_E$ (*right*) (y-axis), as a function of $\dot{V}_A/\dot{Q}$ (x-axis) in a 50-compartment lung model before and during iv anesthesia, $F_{I_{O_2}}$ = 0.21 and 0.51, in seven patients, supine and in the lateral position, before lung surgery. Filled circles with vertical lines indicate shunt, $\dot{Q}_{SH}/\dot{Q}_T$, and shaded areas indicate modes of perfusion of compartments with low $\dot{V}_A/\dot{Q}$ (0.005–0.1). During anesthesia, mechanical ventilation was set at 15 breaths·min^{-1}. The patients (patients 1–7) are numbered from front.

to decreased stroke volumes (SV) and were accompanied by an increase in $C(a\text{-}\bar{v})_{O_2}$, although $\dot{V}_{O_2}$ also decreased ($P < 0.001$, f = 15 and 20). There also were decreases in $\bar{P}art$ from 95 to 70 mmHg ($P < 0.001$) and in $\bar{P}_{PA}$ from 19 to 16 mmHg ($P < 0.05$), although $\bar{P}_W$ and PVR remained unchanged.

Gas Exchange. A decrease or disappearance of the shunt was observed in 10 patients. The mean value was unchanged, however. The mode within the low $\dot{V}_A/\dot{Q}$ range increased in 10 patients, although this increase was not significant for the whole group. There was, however, an increase in log standard deviation for the perfusion distribution from 0.77 to 1.13 ($P < 0.01$). Mean $\dot{V}_A/\dot{Q}$ for the distribution was shifted to the right, as could be expected with a decrease in $\dot{Q}$. Mean $\dot{V}_A/\dot{Q}$ for ventilation, $\dot{V}_E$, also was increased from 0.87

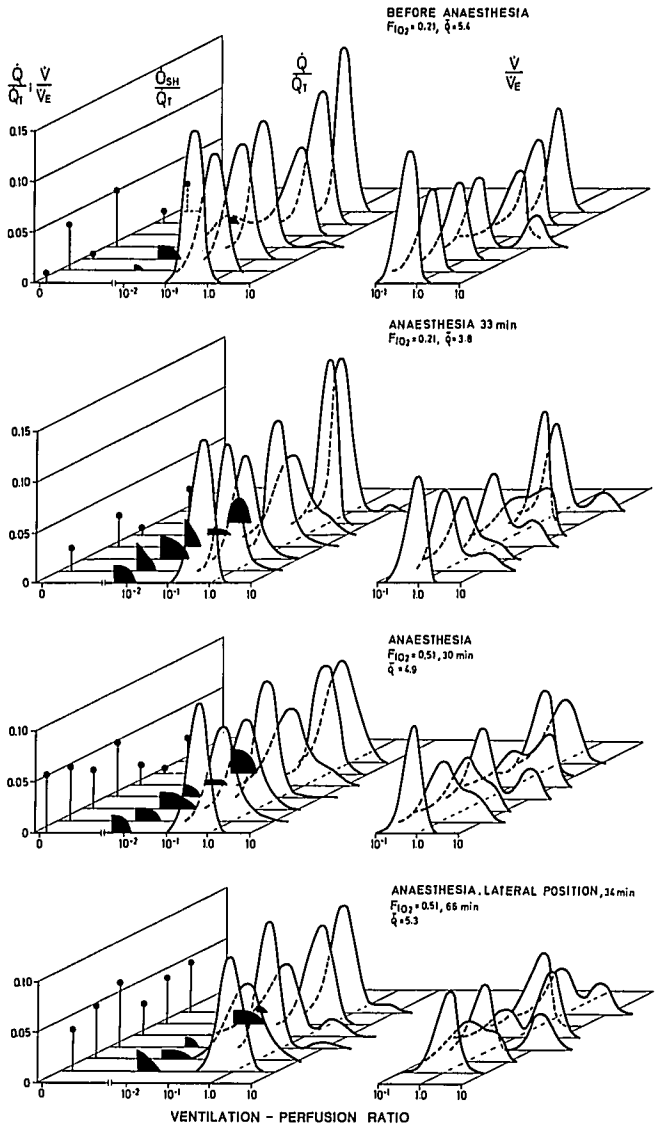

FIG. 2. $\dot{V}_A/\dot{Q}$ in patients with pulmonary tumors, effect of anesthesia (f = 20). Relative perfusion, $\dot{Q}/\dot{Q}_T$ (*left*), and ventilation, $\dot{V}/\dot{V}_E$ (*right*) (y-axis), as a function of $\dot{V}_A/\dot{Q}$ (x-axis) in a 50-compartment lung model before and during iv anesthesia, $F_{I_{O_2}}$ = 0.21 and 0.51, in seven patients, supine and in the lateral position, before lung surgery. Filled circles with vertical lines indicate shunt, $\dot{Q}_{SH}/\dot{Q}_T$, and shaded areas indicate modes of perfusion of compartments with low $\dot{V}_A/\dot{Q}$ (0.005–0.1). During anesthesia, mechanical ventilation was set at 20 breaths·min^{-1}. The patients (patients 8–14) are numbered from front.

to 1.51 ($P < 0.001$). Although there were no significant differences between the two groups, more patients ventilated with 20 breaths · min^{-1} developed modes in the high $\dot{V}_A/\dot{Q}$ range. Mean dead space ($\dot{V}_A/\dot{Q} > 100$) decreased from 42 to 33% of $\dot{V}_E$ ($P < 0.001$).

Pa_{O_2} remained unchanged 30 min after induction, $FI_{O_2} = 0.21$. Pa_{CO_2} decreased from 42 to 37 mmHg ($P < 0.001$). $P(A\text{-}a)_{O_2}$ increased slightly, but not significantly, from 23 to 32 mmHg. $\dot{Q}_{VA}/\dot{Q}_T$ decreased slightly from 13.2 to 9.9% of cardiac output (<0.05).

Anesthesia, $FI_{O_2} = 0.51$ (III)

Central Hemodynamics. Thirty minutes after increasing FI_{O_2} to 0.51, only small nonsignificant increases in $\dot{Q}$ and $\dot{V}_{O_2}$ were observed. The pressures in the systemic and pulmonary vascular bed remained unchanged from measurement II.

Gas Exchange. There were only minor changes in the distribution of $\dot{Q}$ with development of small shunts, especially in the group ventilated with 20 breaths · min^{-1}. There were, however, no significant differences between the groups and the mean value for all patients amounted to 2.5%, which was not significantly different from the preanesthetic level. The mean $\dot{V}_A/\dot{Q}$ decreased to the value observed before anesthesia. The distribution of $\dot{V}$ remained unchanged from measurement II. The increase in FI_{O_2} caused increases in Pa_{O_2} to 200 mmHg ($P < 0.001$) and in $P(A\text{-}a)_{O_2}$ from 32 to 105 mmHg ($P < 0.001$). Pa_{CO_2} and $\dot{V}_D/\dot{V}_T$, remained unchanged from II.

Lateral Position, $FI_{O_2} = 0.51$ (IV)

Cardiac output and $\dot{V}_{O_2}$ as well as pulmonary vascular pressures and resistance were unchanged from previous measurement.

Gas Exchange. Small shunts were observed in nearly all patients, and the mean value amounted to 4.0% of $\dot{Q}$, which, however, was not significantly different from previous measurements. There were no further changes in the perfusion distribution. Ventilation, however, was shifted to regions with higher $\dot{V}_A/\dot{Q}$, as expressed by an increase in mean $\dot{V}_A/\dot{Q}$ to 1.57 ($P < 0.001$) compared with the preanesthetic level of 0.87.

Pa_{O_2}, Pa_{CO_2}, and $P(A\text{-}a)_{O_2}$ remained at the same level as during stage III, but V_D/V_T increased significantly to 0.53 ($P < 0.01$).

Discussion

This study has demonstrated a rather well-maintained matching between ventilation and perfusion during iv anesthesia and mechanical ventilation with air in elderly patients undergoing elective lung surgery. Before anesthesia, they had $\dot{V}_A/\dot{Q}$ patterns similar to that generally found in patients of this age,[5,6,17] *i.e.*, insignificant shunts and broad main modes, sometimes accompanied by a small mode within the low $\dot{V}_A/\dot{Q}$ range, indicating some degree of $\dot{V}_A/\dot{Q}$ mismatch. Nearly all were smokers or had been smokers, some had moderately impaired lung function, and Pa_{O_2} was slightly decreased, which also could be an effect of premedication and the supine position. Three patients had a $\dot{V}_A/\dot{Q}$ pattern compatible with chronic bronchitis and/or emphysema.[25]

Although the changes induced by iv anesthesia and mechanical ventilation with air were remarkably small, there was a significant increase in the dispersion of $\dot{V}_A/\dot{Q}$ ratios. In the majority of the patients there were increases in perfusion of low $\dot{V}_A/\dot{Q}$ units, but no increase in shunt. The latter could have been attenuated, however, by the simultaneous decrease in cardiac output, as parallel changes in shunt fraction and cardiac output have earlier been observed in humans.[26–28] The observed decrease in inert gas dead space ($\dot{V}_A/\dot{Q} > 100$) can be calculated to 54 ml per breath and could well have been due to smaller anatomic dead space caused by endotracheal intubation. The physiologic dead space, calculated from the Enghoff modification of the Bohr equation, however, remained unchanged. This dead space also includes dead-space–like effects of lung units below $\dot{V}_A/\dot{Q} = 100$. Therefore, an increase in the number of such units is plausible. This is supported by the finding of a marked increase in the mean value for the $\dot{V}_A/\dot{Q}$ ratios between 0.005 and 100. Part of this increase, however, is explained by the decrease in cardiac output.

Recently, several studies have been reported on the effects of inhalation anesthesia and mechanical ventilation using the multiple inert gas technique. Our findings are similar to the observations made by Rehder *et al.*[3] on healthy young volunteers. They found a significant increase in the dispersion of $\dot{V}_A/\dot{Q}$ ratios but only small shunts during anesthesia–paralysis with methoxyflurane and air–oxygen mixture, $FI_{O_2} = 0.3$ or 0.4.

In elderly patients, however, more dramatic changes in inert gas excretion and retention have been observed. Dueck *et al.* found a striking increase in shunt and/or low $\dot{V}_A/\dot{Q}$ units, often amounting to 40% of cardiac output, in humans after induction with halothane in nitrous oxide and oxygen. Most of their patients had advanced pulmonary disease. Two of them had preoperative pulmonary function tests within the range of the test of the patients in this study and they also developed marked shunts (16 and 21% of cardiac output). One reason for the differing results could be the absence of N_2O in the present study, as N_2O could increase the tendency of units with critically low $\dot{V}_A/\dot{Q}$ to collapse.[29] However, two of the patients in Dueck's study did not

receive N_2O and still developed marked shunts and low $\dot{V}_A/\dot{Q}$ units.

Other investigators, not using N_2O for anesthesia, have reported conversion of low $\dot{V}_A/\dot{Q}$ units to shunt units, ranging from 4.5 to 16.5% of $\dot{Q}$,[5] and marked increases in the dispersion of $\dot{V}_A/\dot{Q}$ ratios[6] in elderly patients anesthetized with halothane, $F_{I_{O_2}} = 0.30$ or 0.40. In the latter study, the shunt remained low (2% of $\dot{Q}$).

Thus, the expected impairment in $\dot{V}_A/\dot{Q}$ matching was less obvious in this study. One reason could be a more effective matching of blood flow to the altered distribution of ventilation, which commonly is found in connection with anesthesia and mechanical ventilation,[8] *i.e.*, hypoxic pulmonary vasoconstriction. The anesthetic agents used, diazepam, thiopentone, and fentanyl, have been shown not to influence HPV in an isolated lung model.[15] In contrast, inhibition of the vasoconstrictor response has been reported for most inhalation agents in similar models[13,14] and for ether and halothane in humans.[30] Preservation of HPV during halothane anesthesia also has been observed in intact dog lung.[31,32]

The use of large tidal volumes during mechanical ventilation has been advocated.[1] Large tidal volumes possibly could increase ventilation and decrease perfusion of nondependent lung regions, resulting in an increase of alveolar dead space. Ventilation of regions with high $\dot{V}_A/\dot{Q}$ ratios also was more pronounced in the previously mentioned studies employing the inert gas technique, where higher tidal volumes were used, than in the present study. However, formation of atelectasis and shunts have been reported to occur when small tidal volumes are used.[33]

One purpose of this study was to investigate how the level of $F_{I_{O_2}}$ generally used during lung surgery would influence $\dot{V}_A/\dot{Q}$ distribution, as it has been shown that O_2 breathing can increase shunting by formation of resorbtion atelectasis and/or by inhibiting HPV.[29] The patients therefore were ventilated with air during induction. Repeated analysis did not reveal significant hypoxemia, and at 30 min after induction Pa_{O_2} remained unchanged, which is compatible with the $\dot{V}_A/\dot{Q}$ pattern. Increasing $F_{I_{O_2}}$ to 0.5 caused only minor changes in the $\dot{V}_A/\dot{Q}$ distribution with development of small shunts, never exceeding 5% of cardiac output. Lundh and Hedenstierna[34] reported no change in the distribution pattern on increasing $F_{I_{O_2}}$ from 0.29 to 0.53 during inhalation anesthesia in elderly patients. A further increase to 0.85 caused an increase in shunt from 7 to 10% of cardiac output.[34] A moderate increase of $F_{I_{O_2}}$ (≤ 0.5) therefore seems to be of minor importance for the development of gas exchange abnormalities during anesthesia and mechanical ventilation lasting for the period of time investigated here. Substituting N_2 for a more soluble gas like N_2O could, however, increase the tendency of low $\dot{V}_A/\dot{Q}$ units to collapse.[29] Whether this increases the ventilation–perfusion mismatch during anesthesia in humans remains to be answered.

An important question is also whether the commonly used technique of ventilating the lungs with 100% oxygen in connection with endotracheal intubation could increase shunting. A decrease in FRC with impaired ventilation in the dependent part of the lung probably occurs immediately on induction.[35] Using pure O_2 in this situation probably contributes to the inadequate adjustment of blood flow to the changed distribution of inspired gas, *i.e.*, inhibition of HPV. According to Dantzker *et al.*, collapse of units with low $\dot{V}_A/\dot{Q}$ theoretically could occur within 6 min of ventilation with 100% oxygen, at a pulmonary blood flow of 6 $l \cdot min^{-1}$ and FRC of 3 l. The rate of collapse might even be greater in the dependent parts of the lung where the ratio of blood flow to end-expired volume is greater.[29] This is important, as using nondepolarising muscle relaxants and new techniques with high doses of opiates involve longer periods of assisted ventilation, generally with 100% O_2, before endotracheal intubation can be performed.

The $\dot{V}_A/\dot{Q}$ pattern in the lateral position was characterized by the existence of shunts, although never exceeding 8% of cardiac output, and a further increase in the number of units with $\dot{V}_A/\dot{Q} > 10$ with a simultaneous increase in the dispersion of $\dot{V}_A/\dot{Q}$ ratios. This was specially evident in the group ventilated with 20 breaths $\cdot min^{-1}$, indicating an increase in dead space. The results confirm earlier studies using pulmonary N_2 clearance,[36] ^{133}Xe[37] and the multiple inert gas technique[3] and can be explained by increased ventilation to nondependent poorly perfused lung regions, airway closure in the dependent regions, where closing capacity exceeds FRC,[11] and inadequate HPV.

In conclusion, this study has shown only a modest increase in the dispersion of $\dot{V}_A/\dot{Q}$ ratios and no development of intrapulmonary shunt after induction of iv anesthesia and mechanical ventilation with air, although most of the patients were elderly and had pulmonary dysfunction. Ventilation with 50% oxygen does not, alone, seem to be of importance for the reported gas exchange abnormalities during anesthesia lasting 1 h. Therefore, other factors, such as the use of 100% oxygen during induction and certain inhalation agents, appear to have more influence on gas exchange. The $\dot{V}_A/\dot{Q}$ pattern in the lateral position with increased $\dot{V}_A/\dot{Q}$ mismatch confirms earlier observations.

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