

## Changes in the Distribution of Ventilation and Perfusion Associated with Separation from Mechanical Ventilation in Patients with Obstructive Pulmonary Disease

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A trial of separation from mechanical ventilation may induce an abnormal respiratory pattern and a maldistribution of ventilation-to-perfusion ratios ( $\dot{V}_A/\dot{Q}$ ), especially in patients with chronic obstructive pulmonary disease. This study was designed to assess the effects of three different modes of ventilation on the distribution of global and also regional  $\dot{V}_A/\dot{Q}$  in eight patients with chronic obstructive pulmonary disease recovering from acute respiratory failure who remained dependent on mechanical ventilation after more than 5 days of attempted separation from the ventilator.  $\dot{V}_A/\dot{Q}$  distribution was assessed using the multiple inert gas and isotopic scanning methods after 30 min each of controlled mechanical ventilation (CMV), 10 cmH<sub>2</sub>O inspiratory pressure support, and spontaneous breathing (SB). Controlled ventilation was provided at a respiratory rate ranging from 12 to 18 breaths per min and a tidal volume of 8 ml · kg<sup>-1</sup>. In comparison to CMV, SB resulted in a decrease in tidal volume (from 512 ± 144 to 301 ± 102 ml,  $P < 0.01$ ), and an increase in respiratory rate (from 15.5 ± 3.2 to 27.3 ± 15.0 breaths per min,  $P < 0.05$ ), which increased dead space (+7.1% of minute ventilation), cardiac output (+36%), and the perfusion to areas of low  $\dot{V}_A/\dot{Q}$  (+8.9% of cardiac output) ( $P < 0.05$ ,  $P < 0.001$ , and  $P < 0.05$ , respectively). Isotopic scans revealed a horizontal craniocaudal difference of  $\dot{V}_A/\dot{Q}$  in all modes, with the lowest  $\dot{V}_A/\dot{Q}$  zones at the basal part of the lungs (mean basal  $\dot{V}_A/\dot{Q}$  0.58 in SB and 1.05 in CMV). During SB, this craniocaudal difference of  $\dot{V}_A/\dot{Q}$  was highly correlated to the dispersion of perfusion (dispersion around the mean [log SD<sub>Q</sub>],  $r = 0.87$ ,  $P < 0.01$ ). Moreover, the patients with the smallest tidal volume during SB showed the lowest caudal  $\dot{V}_A/\dot{Q}$  ratios ( $r = 0.88$ ,  $P < 0.01$ ), the largest craniocaudal gradient in  $\dot{V}_A/\dot{Q}$  ( $r = 0.77$ ,  $P < 0.05$ ), and the largest amount of perfusion in the areas of low  $\dot{V}_A/\dot{Q}$  ratios ( $r = -0.71$ ,  $P < 0.05$ ). We conclude that in our patients, the change from CMV to SB, induced an abnormal breathing pattern with small tidal volumes. This resulted in a maldistribution of  $\dot{V}_A/\dot{Q}$  ratios that was not improved by pressure support at a level of 10 cmH<sub>2</sub>O. (Key words: Critical care. Lung, function: ventilation-perfusion ratios; respiratory failure. Ventilation: mechanical; inspiratory pressure support; spontaneous breathing.)

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SEPARATION FROM MECHANICAL VENTILATION may be difficult in patients with chronic obstructive pulmonary disease (COPD) recovering from acute respiratory failure. Factors such as increased airway resistance and increased dead space<sup>1</sup> can induce respiratory muscular fatigue, resulting in decreased tidal volume ( $V_T$ ) and inefficient ventilation.<sup>2</sup> These conditions intensify the work of breathing,<sup>3</sup> increase its metabolic cost, and increase the patient's cardiac output.<sup>4</sup> Torres *et al.*<sup>5</sup> investigated the consequences of the separation from controlled mechanical ventilation (CMV) in patients with COPD and reported changes in the distribution of ventilation. Inspiratory pressure support (IPS) is now commonly provided to ease the transition from mechanical to spontaneous breathing (SB). This mode acts by exerting an adjustable level of positive pressure to the airways during inspiration. IPS increases minute ventilation and decreases cardiac output.<sup>6,7</sup>

The aim of this study was to evaluate pulmonary gas exchange abnormalities at the time of discontinuation of mechanical ventilation in patients with COPD, using two different methods of measuring ventilation-to-perfusion ratios ( $\dot{V}_A/\dot{Q}$ ): the conventional inert gas technique,<sup>8</sup> which quantifies the changes in  $\dot{V}_A/\dot{Q}$  distributions, and an isotopic scanning method.<sup>9</sup> It was expected that the isotopic method would help localize the regions of the lungs responsible for the  $\dot{V}_A/\dot{Q}$  abnormalities.

### Materials and Methods

We studied patients with COPD (table 1) in our intensive care unit who were recovering from an acute respiratory failure and in whom either tracheal intubation or tracheostomy had been performed. Included in the study were eight consecutive patients meeting the following criteria: the existence of an obstructive disease documented by lung function tests or a history of a heavy smoking (> 50 pack-years) with lung distention on the chest roentgenogram. At the time of the study, these patients remained dependent upon mechanical ventilation after more than 5 days of attempted separation from the ventilator but could sustain at least 1–3-h periods of SB.

Our protocol was approved by our local ethics committee, and informed consent was obtained in all cases.

TABLE 1. Clinical Characteristics of Patients

Patient	Age (yr)	Sex	Size (cm)	Weight (kg)	Etiology of Failure	FEV <sub>1</sub> /FVC	P <sub>aCO<sub>2</sub></sub> (mmHg)	P <sub>aO<sub>2</sub></sub> (mmHg)	Duration of Ventilation after the Study (days)
1	76	F	149	65	Pneumonia	65	41	81	7
2	76	F	147	83	Cardiac failure	64	39	77	9
3	68	M	171	66	Postoperative	51	45	71	8
4	72	F	160	51	Pneumonia	—	—	—	5
5	61	M	170	68	Postoperative	52	49	60	6
6	70	F	156	41	Pneumonia	48	50	55	6
7	77	M	178	64	Postoperative	49	50	58	5
8	67	M	169	70	Pneumonia	—	—	—	6

A dash indicates that basal lung function tests were not available. Nevertheless, these two patients had an history of previous respiratory failures with artificial ventilation, and a typical lung distension was

observable on the chest x-ray at the time of the study. These findings strongly support the diagnosis of chronic obstructive pulmonary disease.

FEV<sub>1</sub> = forced expiratory volume in 1 s; FVC = forced vital capacity.

All patients had indwelling pulmonary artery (7-Fr, Edwards) and radial arterial catheters. They were monitored by electrocardiography (ECG). Hemodynamic and ECG data were continuously displayed on an oscilloscope (Hewlett Packard 78352A). At the time of the study, seven patients had a clear chest roentgenogram and one had a residual opacity in the left lung.

#### MODES OF VENTILATION

We compared the effects of CMV, IPS, and spontaneous ventilation (without positive end-expiratory pressure) on pulmonary gas exchange and on cardiac output, with respect to  $\dot{V}_A/\dot{Q}$ . We used a conventional volume-cycled ventilator (Servo 900C, Siemens) including a filter-humidifier device at the Y piece (Ultipor<sup>®</sup>, Pall Laboratories). The flowmeters of the ventilator were calibrated prior to the study. We kept the fractional inspired oxygen concentration constant (range, 0.30–0.45) to maintain an arterial oxygen tension greater than 100 mmHg, as measured by blood gas analysis (ABL 30, Radiometer, Copenhagen). CMV was characterized by a respiratory rate ranging from 12 to 18 breaths per min, a ratio of the duration of inspiration to the duration of the total respiratory cycle of 33%, and a V<sub>T</sub> of 8 ml · kg<sup>-1</sup>. IPS was provided at a level of 10 cmH<sub>2</sub>O, with the minimal trigger level available (– 1 cmH<sub>2</sub>O). This level of pressure support has been reported to eliminate efficiently the resistance of the endotracheal tube and to decrease slightly the work of breathing.<sup>10</sup> SB and pressure support ventilation were studied in random order, and controlled ventilation was studied last, and served as the control mode.

V<sub>T</sub> was recorded on a paper chart recorder (Gould ES1000) from the analog signal of the ventilator and was averaged over 2 min during a period of steady-state ventilation. Minute ventilation during each mode was calculated as the product of V<sub>T</sub> and respiratory rate. Arterial and mixed venous blood samples were collected for standard blood gas analysis. Cardiac output was determined using the thermodilution technique. The distribution of

ventilation and of perfusion ( $\dot{V}_A/\dot{Q}$  ratios) and the percent shunt or dead space during each ventilatory mode were determined using the inert gas<sup>8</sup> and isotopic scanning<sup>9</sup> techniques. Each mode was studied for 30 min, followed by a 30-min period of rest during CMV before study of the next mode. The same sequence of ventilation was followed during the isotopic study performed 4 h later.

#### INERT GAS STUDY

For practical considerations, we performed the inert gas study before isotopic scanning. Patients lay supine when we determined the  $\dot{V}_A/\dot{Q}$  distribution during each ventilatory mode. Therefore we used the six-inert-gas technique described by Wagner *et al.*<sup>11</sup> In brief, after achieving a stable condition where V<sub>T</sub> did not vary more than 15% in the selected mode, we infused six inert gases (sulfur hexafluoride, ethane, cyclopropane, enflurane, diethyl ether, and acetone) dissolved in isotonic sodium chloride into a large peripheral vein of the patient's arm at a constant rate of 4 ml · min<sup>-1</sup>. After 30 min of infusion and under steady-state conditions, arterial and mixed venous blood samples were drawn and transported to the laboratory for immediate analysis. Mixed expired gases were collected from the expiratory port of the ventilator by means of a heated mixing box. The expiratory tubing and valve were heated by a heating coil wrapped around these components. The concentrations of inert gases in the blood and expired gas samples were measured using gas chromatography (models 427 and 489, Packard).

#### ISOTOPIC STUDY

The isotopic study was performed 4 h after the inert gas study. Between these two periods the patients' lungs were ventilated with CMV. The isotopic imaging was performed in the Nuclear Medicine Department. Patients lay supine, their backs facing a  $\gamma$  camera detector (Compagnie Générale de Radiologie, Paris, France) equipped with a medium-energy collimator and linked to a com-

puter (Sophia, Paris, France) for image processing. Regional  $\dot{V}_A/\dot{Q}$  ratios during each mode were measured for both lungs by two sequential scintigrams. The first provided a map of ventilation using  $^{81m}\text{Kr}$  according to the method of Amis and Jones.<sup>9</sup>  $^{81m}\text{Kr}$ , a short-lived radionuclide ( $t_{1/2} = 13$  s;  $\gamma$ -emission energy = 190 keV), was produced by a  $^{81m}\text{Rb}$  generator and pumped to the inspiratory limb of the ventilator at a constant rate of 300 ml  $\cdot$  min<sup>-1</sup>. The second scintigram provided the perfusion scan via  $^{99m}\text{Tc}$ -labeled albumin macroaggregates. The  $^{99m}\text{Tc}$  was injected into a peripheral vein of the patient's arm in gradually increased doses for three trials (1, 2, and 4 mCi). Just before the second and third  $^{99m}\text{Tc}$  injection, we recorded regional background  $\gamma$  emission by performing a blank acquisition. The background emission was subtracted from the subsequent  $^{99m}\text{Tc}$  scan. Scintigraphy of each mode was followed by a 30-min period of rest during CMV.

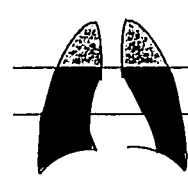
For each study, at least 200,000 corrected counts of the posterior view were collected into the computer memory in a 64  $\times$  64 matrix and stored on magnetic tape. Because the energy of the  $\gamma$  emission is different for each isotope ( $^{81m}\text{Kr} = 190$  keV;  $^{99m}\text{Tc} = 140$  keV), we applied a 20% window to each energy spectrum peak to separate one isotope emission from another. The scans were displayed on a video monitor after background emission subtraction.

The boundaries of the lungs were then drawn electronically under visual control to determine the regions of interest. Each scan was normalized to its corresponding flow (*i.e.*, ventilation or perfusion). The 64  $\times$  64 matrices were then contracted into 32  $\times$  32 matrices to improve statistical analysis. Each entry in the matrix of the  $^{81m}\text{Kr}$  scan was divided by that of the corresponding  $^{99m}\text{Tc}$  scan to provide a  $\dot{V}_A/\dot{Q}$  map of each ventilatory mode.

The view of the two lungs was then divided into three compartments of the same height along the craniocaudal axis. The mean  $\dot{V}_A/\dot{Q}$  in each of the three zones (apical, mid-, and basal) was calculated (fig. 1). In order to evaluate the craniocaudal gradient of  $\dot{V}_A/\dot{Q}$ , we computed the difference between the apical and the basal mean  $\dot{V}_A/\dot{Q}$  for each patient.

#### STATISTICAL ANALYSIS

All results are expressed as the mean  $\pm$  the standard deviation. The overall difference between mean values of gas exchange parameters and inert gas data were compared using a two-way analysis of variance in order to separate the mode effect from the patient effect. The differences in isotopic regional mean  $\dot{V}_A/\dot{Q}$  were assessed by a three-way analysis of variance to separate between the patients the effect of the mode of ventilation and that of the differences between regional distribution. Internal comparisons between means were performed in all cases



	$0.79 \pm 0.28$	$0.90 \pm 0.28$	$1.23 \pm 0.48$
	$0.72 \pm 0.28$	$0.82 \pm 0.25$	$1.11 \pm 0.44$
	$0.58 \pm 0.24$	$0.67 \pm 0.26$	$1.05 \pm 0.42$
	SB	IPS	CMV

FIG. 1. The mean isotopic  $\dot{V}_A/\dot{Q}$  ratio  $\pm$  SD for apical (dotted), mid- (crossed), and lower (solid) lung regions with spontaneous ventilation (SB), inspiratory pressure support (IPS), and controlled mechanical ventilation (CMV).

by Tukey's tests for repeated measurements.<sup>12</sup> Linear regressions by the least-squares method were used to assess linear relationship between pairs of variables.

#### Results

##### VENTILATION, BLOOD GASES, AND CARDIAC OUTPUT

The effects of SB and IPS on respiratory variables, arterial, and mixed-venous blood gas tensions and cardiac output were significantly different from those of CMV for all variables except minute ventilation (table 2).  $V_T$  during SB was on average 41% less ( $301 \pm 102$  vs.  $512 \pm 144$  ml,  $P < 0.01$ ) and respiratory rate 76% greater ( $27.3 \pm 15.0$  vs.  $15.5 \pm 3.2$  breaths per min,  $P < 0.05$ ) than during controlled ventilation. Despite a minute ventilation in spontaneous mode equal to that in the controlled mode, the corresponding alveolar ventilation was reduced presumably because of a 18% increase in dead space-to- $V_T$  ratio (dead space ventilation [ $V_D/V_T$ ]) (table 3). IPS led to results similar to those of SB. Slight changes in arterial oxygen tension occurred among the three modes, whereas arterial carbon dioxide tension significantly increased, by 18% from CMV to SB (from  $41.4 \pm 10.5$  to  $48.7 \pm 10.7$  mmHg,  $P < 0.05$ ) and by 13% from CMV to IPS (from  $41.4 \pm 10.5$  to  $46.9 \pm 10.5$  mmHg,  $P < 0.05$ ). Oxygen consumption and cardiac output were 20 and 36% greater ( $P < 0.001$ ) and the arteriovenous difference in oxygen content 15% less ( $P < 0.05$ ) during spontaneous ventilation than during controlled ventilation. IPS yielded values of oxygen consumption and cardiac output similar to those of SB. When data from all three modes of ventilation were pooled, significant correlations were found between cardiac output and arteriovenous difference in oxygen content ( $r = -0.44$ ,  $P < 0.05$ ) and between cardiac output and oxygen consumption ( $r = 0.63$ ,  $P < 0.001$ ).

##### INERT GAS STUDY

During the calculation of the  $\dot{V}_A/\dot{Q}$  distribution, the residual sum of squares value below which 50 and 90%

TABLE 2. Gas Exchange, Cardiac Output, and Ventilation

Mode	Row	PaO <sub>2</sub> (mmHg)	PaCO <sub>2</sub> (mmHg)	C(a-v)O <sub>2</sub> (vol · 100 ml <sup>-1</sup> )	$\dot{V}_{O_2}$ (ml · min <sup>-1</sup> )	$\dot{Q}_T$ (l · min <sup>-1</sup> )	V <sub>T</sub> (ml)	RR (breaths per min)	$\dot{V}_E$ (l · min <sup>-1</sup> )
SB	1	96.4 ± 21.8	48.7 ± 10.7	4.46 ± 0.79	269 ± 55	5.81 ± 0.85	301 ± 102	27.3 ± 15.0	7.08 ± 1.40
IPS	2	101.3 ± 24.9	46.9 ± 10.5	4.66 ± 0.82	265 ± 52	5.55 ± 1.06	349 ± 78	24.5 ± 10.1	7.87 ± 1.88
CMV	3	103.2 ± 26.6	41.4 ± 10.5	5.26 ± 1.20	224 ± 43	4.27 ± 0.76	512 ± 144	15.5 ± 3.2	7.44 ± 1.79
Statistical comparisons between rows (mode effect)		NS	* 1-3 2-3	* 1-3 2-3	† 1-3 2-3	‡ 1-3 2-3	† 1-3 2-3	* 1-3 2-3	NS
Patient effect		‡	‡	‡	‡	‡	†	*	‡

SB = spontaneous breathing; IPS = inspiratory pressure support ventilation; CMV = controlled mechanical ventilation; NS = not significant.  
\* P < 0.05.

† P < 0.01.  
‡ P < 0.001.

of sets laid were 3 and 9, respectively. Moreover, the residual sum of squares was less than 10 for each ventilatory mode in all but one patient, in whom it reached 23 during CMV. This outlying sum of squares was not perfectly stable during CMV, contrary to those of all other subjects studied.

*Distribution of Ventilation*

The transformation of the retention and excretion of the six gases into a continuous distribution showed that the ventilation was distributed primarily in the range of  $\dot{V}_A/\dot{Q}$  between 0.1 and 10 and did not vary significantly between modes of ventilation in this central range of  $\dot{V}_A/\dot{Q}$  ratios (table 3). However, the distribution of ventilation in regions of  $\dot{V}_A/\dot{Q}$  above 100, i.e., V<sub>D</sub>/V<sub>T</sub>, differed significantly by mode. V<sub>D</sub>/V<sub>T</sub> was high during all three modes but still 18% greater during SB and IPS than during CMV (on average 45.7 ± 7.1 and 45.5 ± 7.2% vs. 38.6 ± 8.2%, respectively, of total ventilation, P < 0.05, table 3). Nevertheless, the differences in V<sub>D</sub>/V<sub>T</sub> across modes apparently were not large enough to induce significant differences in either the mean  $\dot{V}_A/\dot{Q}$  for venti-

lation or the dispersion around the mean (log SD<sub>v</sub>). Looking at individual values, we found a positive relationship between V<sub>D</sub>/V<sub>T</sub> obtained in CMV and that observed in SB (r = 0.73, P < 0.05). A similar correlation was found between log SD<sub>v</sub> measured in CMV and log SD<sub>v</sub> measured in SB (r = 0.83, P < 0.01). Hence, the patients who experienced the largest abnormalities in V<sub>D</sub>/V<sub>T</sub> and the widest distribution of ventilation when they were changed to spontaneous mode were those who already had the largest dead space during the preceding period of controlled ventilation.

*Distribution of Perfusion*

Changes in the distribution of perfusion were more striking than those of ventilation (table 4). During SB and IPS, one patient had a unimodal distribution of perfusion limited to the central zone of  $\dot{V}_A/\dot{Q}$  ratios (0.1 <  $\dot{V}_A/\dot{Q}$  < 10). Another showed a unimodal distribution that included mainly the central zone of the  $\dot{V}_A/\dot{Q}$  scale but also partially overlapped into the region of low  $\dot{V}_A/\dot{Q}$  ratios. The six other patients had a bimodal distribution of perfusion, where more than 5% of the perfusion was directed

TABLE 3. Inert Gas Results: Ventilation Distribution

Mode	Row	Mean $\dot{V}_A/\dot{Q}$	Log SD <sub>v</sub>	0.1 < $\dot{V}_A/\dot{Q}$ < 10 (%)	10 < $\dot{V}_A/\dot{Q}$ < 100 (%)	V <sub>D</sub> /V <sub>T</sub> (%)
SB	1	1.59 ± 0.68	0.71 ± 0.23	53.4 ± 7.1	1.80 ± 4.58	45.7 ± 7.1
IPS	2	1.39 ± 0.40	0.65 ± 0.22	53.5 ± 7.7	0.65 ± 1.18	45.5 ± 7.2
CMV	3	1.80 ± 0.87	0.75 ± 0.35	58.0 ± 11.7	3.09 ± 4.92	38.6 ± 8.2
Statistical comparisons between rows (mode effect)		NS	NS	NS	NS	*1-3
Patient effect		†	‡	‡	NS	‡

Mean  $\dot{V}_A/\dot{Q}$  and distribution (log SD<sub>v</sub>) of ventilation and their partitioning to different  $\dot{V}_A/\dot{Q}$  ranges.

SB = spontaneous breathing; IPS = inspiratory pressure support ventilation; CMV = controlled mechanical ventilation; NS = not sig-

nificant.  
\* P < 0.05.  
† P < 0.01.  
‡ P < 0.001.

TABLE 4. Inert Gas Results: Perfusion Distribution

Mode	Row	Mean $\dot{V}_A/\dot{Q}$	Log $SD_Q$	$Q_s/\dot{Q}_T$ (%)	$0.005 < \dot{V}_A/\dot{Q} < 0.1$ (%)	$0.1 < \dot{V}_A/\dot{Q} < 10$ (%)
SB	1	$0.45 \pm 0.25$	$1.42 \pm 0.43$	$7.50 \pm 8.93$	$15.0 \pm 10.6$	$77.2 \pm 14.5$
IPS	2	$0.51 \pm 0.16$	$1.20 \pm 0.31$	$7.28 \pm 8.75$	$8.9 \pm 8.5$	$82.3 \pm 0.97$
CMV	3	$0.76 \pm 0.27$	$1.00 \pm 0.47$	$7.35 \pm 7.47$	$6.1 \pm 8.4$	$87.4 \pm 9.5$
Statistical comparisons between rows (mode effect)		† 1-3 2-3	$P = 0.09$	NS	* 1-2 1-3	NS
Patient effect		*	*	‡	†	†

Mean  $\dot{V}_A/\dot{Q}$  and distribution (log  $SD_Q$ ) of perfusion and their partitioning to different  $\dot{V}_A/\dot{Q}$  ranges.

SB = spontaneous breathing; IPS = inspiratory pressure support ventilation; CMV = controlled mechanical ventilation; NS = not sig-

nificant.

\*  $P < 0.05$ .

†  $P < 0.01$ .

‡  $P < 0.001$ .

to regions characterized by low  $\dot{V}_A/\dot{Q}$  ratios ( $0.005 < \dot{V}_A/\dot{Q} < 0.1$ ). In these patients, a clear demarcation centered around the  $\dot{V}_A/\dot{Q}$  boundary of 0.1 was observed. The lower limit for low  $\dot{V}_A/\dot{Q}$  regions was set at 0.005.

The amount of perfusion in the regions of low  $\dot{V}_A/\dot{Q}$  was higher during spontaneous ventilation ( $15.0 \pm 10.6\%$ ) than during CMV ( $6.1 \pm 8.4\%$ ) or IPS ( $8.9 \pm 8.5\%$ ,  $P < 0.05$ ) (see example in fig. 2). The changes in perfusion within the low  $\dot{V}_A/\dot{Q}$  regions also were reflected in a significantly lower mean  $\dot{V}_A/\dot{Q}$  for perfusion during SB and IPS than during CMV ( $0.45 \pm 0.25$  and  $0.51 \pm 0.16$  vs.  $0.76 \pm 0.27$ , respectively,  $P < 0.01$ ). In contrast, the average changes in the dispersion of perfusion (log  $SD_Q$ ) between modes that included the whole range of  $\dot{V}_A/\dot{Q}$  did not reach significance ( $P = 0.09$ ). Nonetheless, considering individual values, we found a good relationship between the amount of perfusion in the low  $\dot{V}_A/\dot{Q}$  range ( $0.005 < \dot{V}_A/\dot{Q} < 0.1$ ) and log  $SD_Q$  ( $r = 0.90$ ,  $P < 0.01$ ).

This suggests that the increased perfusion to low  $\dot{V}_A/\dot{Q}$  regions is accompanied by an increase in the dispersion of perfusion and therefore is due not only to an overall shift of the perfusion on the  $\dot{V}_A/\dot{Q}$  diagram. Of note, while breathing spontaneously, the patients with the smallest  $V_T$  had the most abnormal distribution of  $\dot{V}_A/\dot{Q}$ . This is shown in figure 3 by the significant negative correlation ( $r = -0.71$ ,  $P < 0.05$ ) between the amount

of perfusion in the range of low  $\dot{V}_A/\dot{Q}$  ratios and  $V_T$ . Shunt, in contrast, remained low and similar in the three modes. We found no correlation between values of perfusion in the low  $\dot{V}_A/\dot{Q}$  regions during CMV and the corresponding values obtained in SB. Similarly, no correlations were found between these two modes of ventilation for individual values of log  $SD_Q$ .

ISOTOPE STUDY

The mean  $\dot{V}_A/\dot{Q}$  ratios of each lung region (apical, mid-, and basal) were significantly lower during SB than during IPS and significantly lower during IPS than during CMV ( $P < 0.001$ ) (fig. 1). For instance, the  $\dot{V}_A/\dot{Q}$  ratio in the basal region during SB was nearly half that observed for the same region during the CMV. A significant trend ( $P < 0.001$ ) also appeared in the spatial partition of  $\dot{V}_A/\dot{Q}$  along the craniocaudal axis with all three modes: the  $\dot{V}_A/\dot{Q}$  ratios significantly decreased from the apex to the base of the lung. Furthermore, as figure 3 shows, the  $\dot{V}_A/\dot{Q}$  of the bases was highly and positively dependent on the size of the  $V_T$  during SB. A clear relationship was found also between the size of the  $V_T$  and both the magnitude of the craniocaudal gradient in  $\dot{V}_A/\dot{Q}$  ( $r = -0.77$ ,  $P < 0.05$ ) and the magnitude of the caudal  $\dot{V}_A/\dot{Q}$  ratio ( $r = 0.88$ ,  $P < 0.001$ ).

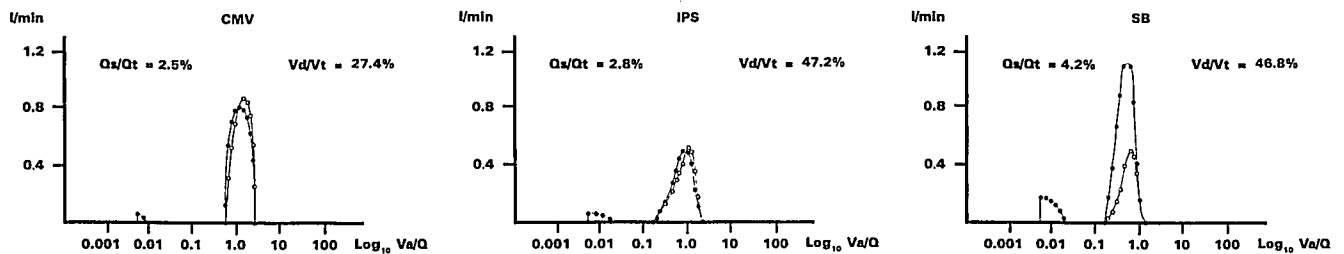


FIG. 2. Example of ventilation (open circles) and perfusion (closed circles) distribution by inert gases in one patient, for the three ventilatory modes.

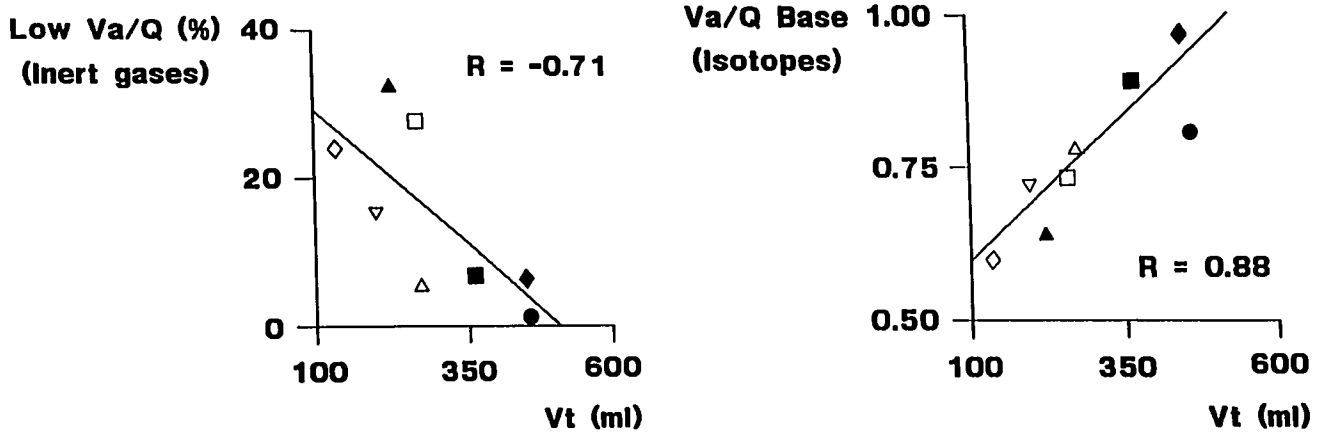


FIG. 3. Linear regression of pulmonary blood flow to regions with low  $\dot{V}_A/\dot{Q}$  ( $0.005 < \dot{V}_A/\dot{Q} < 0.1$ ) versus  $V_T$  ( $P < 0.05$ ) (left) and of  $\dot{V}_A/\dot{Q}$  base versus  $V_T$  ( $P < 0.01$ ) (right), using individual values from the eight patients in spontaneous breathing. Inert gas method: Low  $\dot{V}_A/\dot{Q}$  = percentage of the perfusion distributed in units with  $\dot{V}_A/\dot{Q}$  comprised between 0.005 and 0.1. Isotopes:  $\dot{V}_A/\dot{Q}$  base = basal  $\dot{V}_A/\dot{Q}$  expressed as a ratio to the overall  $\dot{V}_A/\dot{Q}$  of the lung.  $V_T$  = tidal volume.

COMPARISON BETWEEN THE INERT GAS AND THE ISOTOPE RESULTS

We compared the perfusion in the low- $\dot{V}_A/\dot{Q}$  units obtained from the inert gas method to the regional heterogeneity of  $\dot{V}_A/\dot{Q}$  ratios by plotting the craniocaudal difference in  $\dot{V}_A/\dot{Q}$  against the log  $SD_Q$  ( $r = 0.87, P < 0.01$ ). Figure 4 shows a significant correlation between these two parameters during SB. Moreover, during SB, we found a good correlation between the isotopic  $\dot{V}_A/\dot{Q}$  of the bases versus the perfusion of the low  $\dot{V}_A/\dot{Q}$  units by the inert gas technique ( $r = -0.82, P < 0.05$ ) (fig. 4). This suggests that low  $\dot{V}_A/\dot{Q}$  units identified by the inert gas technique were located at the bases.

Discussion

Our study was designed to evaluate the changes in ventilation and perfusion distribution under three different modes of ventilation. We added an isotopic scanning method to the inert gas technique in order to localize the  $\dot{V}_A/\dot{Q}$  abnormalities during spontaneous ventilation. When changing from controlled to spontaneous ventilation, our patients developed a shallow breathing pattern with an increased respiratory rate and a low  $V_T$ . Concomitantly, they increased cardiac output. Considering average values for the eight patients, the distribution of perfusion was significantly shifted toward lower values. Moreover, during SB, isotopic dispersion of  $\dot{V}_A/\dot{Q}$  cor-

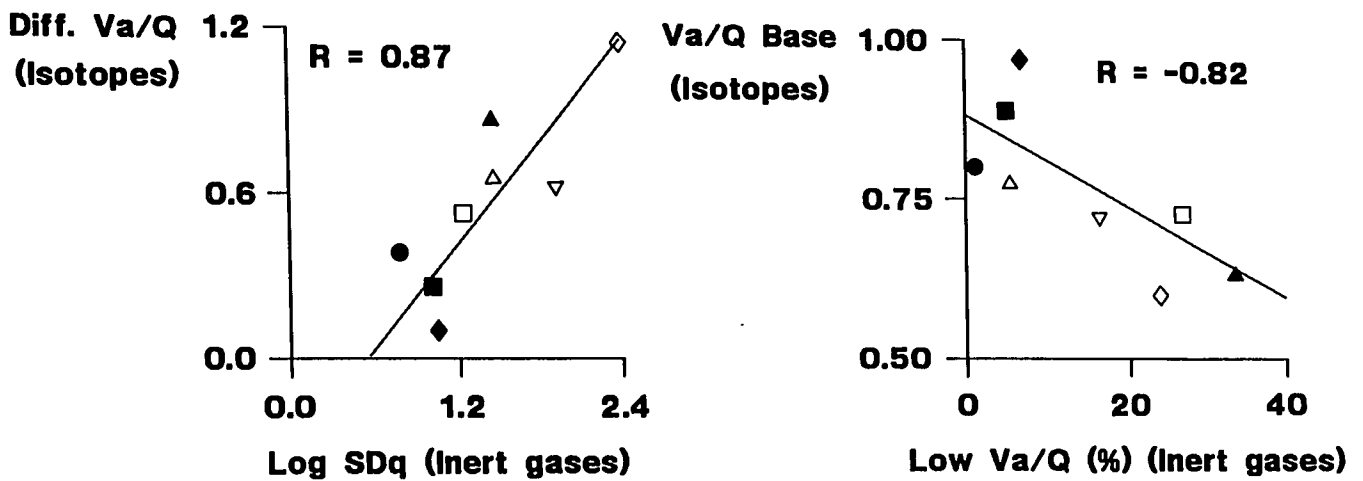


FIG. 4. Linear regression of diff.  $\dot{V}_A/\dot{Q}$  versus log  $SD_Q$  ( $P < 0.01$ ) (left) and of  $\dot{V}_A/\dot{Q}$  base versus low  $\dot{V}_A/\dot{Q}$  ( $P < 0.05$ ) (right), using individual values from the eight patients in spontaneous breathing. Isotopes: Diff.  $\dot{V}_A/\dot{Q}$  = algebraic difference between the mean isotopic  $\dot{V}_A/\dot{Q}$  of the apices and that of the bases.  $\dot{V}_A/\dot{Q}$  base = basal  $\dot{V}_A/\dot{Q}$  expressed as a ratio to the overall  $\dot{V}_A/\dot{Q}$  of the lung. Inert gas method: Low  $\dot{V}_A/\dot{Q}$  = percentage of the perfusion distributed in units with  $\dot{V}_A/\dot{Q}$  comprised between 0.005 and 0.1. Log  $SD_Q$  = Log of standard deviation for perfusion.

related with  $\log SD_Q$  from the inert gas technique. The regions with a low  $\dot{V}_A/\dot{Q}$  were located at the bases of the lungs (fig. 1). The size of the  $V_T$  was the major determinant for these changes and correlated with perfusion in the low  $\dot{V}_A/\dot{Q}$  range, the decrease of basal  $\dot{V}_A/\dot{Q}$  ratios, and the widening of the isotopic craniocaudal gradient. Hence, an abnormal respiratory pattern in SB probably accounts for the  $\dot{V}_A/\dot{Q}$  heterogeneities in this mode.

Changes in breathing pattern and pulmonary gas exchange during the removal of assisted ventilation are common.<sup>13</sup> Gilbert *et al.*<sup>14</sup> showed that shallow breathing occurred in patients with COPD within the first 30 min of being disconnected from the ventilator. They reported spirometric and blood gas values similar to those we report and found their patients unable to sustain increased respiratory work. Brochard *et al.*<sup>15</sup> also observed that blood gas and spirometric findings were abnormal in the same type of patients during disconnection from the ventilator. They reported that increasing levels of pressure support increased the  $V_T$ , normalizing the respiratory pattern.

In our study, IPS yielded results close to those for SB. This could be due to the relatively low level of pressure support (10 cmH<sub>2</sub>O) we used. Indeed, the  $V_T$  achieved during IPS was only 16% higher than that observed under SB. Fiastro *et al.*<sup>10</sup> reported that an IPS ranging from 4 to 6 cmH<sub>2</sub>O is needed to cancel the resistances of the endotracheal tube. Consequently, we chose an IPS level 10 cmH<sub>2</sub>O, expecting this supplementary positive pressure to be able to relieve our patients from the resistive load of the endotracheal tube and partly to relieve them from their intrinsic resistive and elastic respiratory charges. We chose a similar level of IPS for all patients in order to standardize this parameter throughout the study. This level appeared to be insufficient to efficiently improve spontaneous ventilation. Nevertheless, if a higher level of IPS had been used, one may suppose that  $V_T$  and perhaps  $\dot{V}_A/\dot{Q}$  distributions would have been closer or even equal to those observed under controlled ventilation, thereby suppressing any difference between these two modes. This highlights the problem of choosing the adequate IPS level in such a comparative protocol. Due to these methodologic restrictions, most of the results we discuss here will consider SB and IPS together.

Several mechanisms may explain the changes in the distribution of  $\dot{V}_A/\dot{Q}$  we observed during both spontaneous and IPS ventilation. First,  $V_D/V_T$  was significantly larger during SB and IPS compared to that during CMV. Consequently, the distending effect of large  $V_T$ s on airways reported under controlled ventilation, which should have increased dead space<sup>16</sup> in our patients, was probably overwhelmed during spontaneous ventilation by the deleterious effects of shallow breathing, which reduced  $V_T$  and increased the  $V_D/V_T$ . Interestingly, individual profiles could be identified for the parameters describing the

distribution of ventilation by inert gases ( $\log SD_V$  and  $V_D/V_T$ ). Indeed, the patients who had the largest abnormalities in CMV were those who were the most abnormal for these parameters in SB. Because all patients suffered from relatively severe COPD (table 1), one may postulate that they showed the hallmarks of a disturbed distribution of ventilation even during CMV.

Second, combined with the regional changes in ventilation, the increase in cardiac output during the spontaneous mode which was correlated with an increase in oxygen consumption and a decrease in arteriovenous oxygen content difference is likely to have amplified the changes in distribution of  $\dot{V}_A/\dot{Q}$ , by overperfusing zones of low  $\dot{V}_A/\dot{Q}$ . The shunt perfusion (in regions of  $\dot{V}_A/\dot{Q}$  under 0.005) did not rise as did perfusion in areas of low  $\dot{V}_A/\dot{Q}$  (between 0.005 and 0.1) during SB or IPS. In fact, the dependence of shunt on cardiac output has been reported for higher values of shunt than those we obtained.<sup>17</sup>

The distribution of both ventilation and perfusion were larger than normal ( $\log SD > 0.5$ )<sup>8</sup> in our patients but were consistent with those reported by Wagner *et al.*<sup>18</sup> in patients with COPD. Changes in  $\dot{V}_A/\dot{Q}$  distribution from one ventilatory mode to another also have been studied by Dantzer *et al.*<sup>19</sup> in awake patients being disconnected from mechanical ventilation after coronary artery bypass graft surgery. During intermittent pressure ventilation, they found a consistent shunt and a variable degree of  $\dot{V}_A/\dot{Q}$  inequality by the inert gas technique, while SB resulted in a lower mean  $\dot{V}_A/\dot{Q}$  ratio without any change in shunt or  $\dot{V}_A/\dot{Q}$  dispersion. Because cardiac output remained stable, they attributed these changes to the predominant effect of hypoventilation.

These findings need to be compared to those of Torres *et al.*,<sup>5</sup> who studied eight patients with COPD during the separation from mechanical ventilation. Part of their study was conducted at a maintenance fractional inspired oxygen concentration of 0.4, as was ours. The change from controlled to SB induced a marked reduction of  $V_T$ , an increase in respiratory rate, and an increase in  $\dot{Q}_T$ . This resulted in increased perfusion of the regions of low  $\dot{V}_A/\dot{Q}$  and a lower mean  $\dot{V}_A/\dot{Q}$  for perfusion without significant increase in  $\log SD_Q$ . At the same time, the mean  $\dot{V}_A/\dot{Q}$  for ventilation decreased and  $\log SD_V$  increased. Hence the results of both studies are close to ours for perfusion but demonstrated marked changes in the dispersion of ventilation from CMV to SB.

In our patients, the absence of significant differences in the dispersion of  $\dot{V}_A/\dot{Q}$  for perfusion ( $\log SD_Q$ ) and ventilation ( $\log SD_V$ ) between CMV and SB could be due to a large interpatient scatter, especially in SB. Nevertheless, these apparent large interpatient differences, at least for  $\log SD_Q$ , may be explained during SB by the size of the  $V_T$ . Indeed, there was a strong correlation between  $\log SD_Q$  and  $V_T$  and also between the craniocaudal gra-

dient in  $\dot{V}_A/\dot{Q}$  and  $V_T$ . Using the isotopic scanning technique to localize the regions of low  $\dot{V}_A/\dot{Q}$ , we found a clear gradient in  $\dot{V}_A/\dot{Q}$  from the apex to the bases of each lung (figure 1). In addition, the mean  $\dot{V}_A/\dot{Q}$  ratios of the apical, mid and basal zones of the lung were significantly lower during SB than during CMV. When SB was investigated further, we found the excess in perfusion of the low  $\dot{V}_A/\dot{Q}$  units to be located at the bases of the lungs and to correlate with the size of the  $V_T$ .

The problem of the spatial partition of abnormal  $\dot{V}_A/\dot{Q}$  during the separation from mechanical ventilation has to our knowledge never been assessed previously. Only one study, by Parsons *et al.*,<sup>20</sup> has compared the topographic distribution of  $\dot{V}_A/\dot{Q}$  in different modes of assisted ventilation. However, these authors used <sup>133</sup>Xe to study healthy seated patients during spontaneous, continuous positive-pressure, and intermittent positive-pressure ventilation. They found no significant difference in the distribution of  $\dot{V}_A/\dot{Q}$  for the three modes. In addition to the obvious differences in study population and scanning technique, their patients were seated, which would make it difficult to distinguish changes in gradient due to  $\dot{V}_A/\dot{Q}$  abnormalities from the physiologic and gravity-related major vertical gradient in  $\dot{V}_A/\dot{Q}$  normally observed. In contrast, the isotopic method we used allowed us to attribute the increase in low  $\dot{V}_A/\dot{Q}$  in the caudal part of the lungs to a low  $V_T$  in SB.

A plausible explanation is that impaired diaphragmatic function in our patients with COPD would result in an inability to support the weight of the abdomen<sup>21</sup> in the supine position, perhaps favoring these low basal  $\dot{V}_A/\dot{Q}$  values. In addition, a possible cranial shift of the diaphragm could lead to a reduction in functional residual capacity<sup>22</sup> below closing capacity. This would result in intermittent airway closure phenomena in the more caudal parts of the lungs, enhancing low  $\dot{V}_A/\dot{Q}$ .<sup>23</sup> Basal airway closure could also increase local airway resistances, inducing a redistribution of inspiratory flow to the apex.<sup>24</sup> These physiopathologic hypothesis are supported by the experimental findings of Engel and Prefaut.<sup>25</sup> These authors, in an isotopic study of the spatial distribution of  $\dot{V}_A/\dot{Q}$  ratios in supine volunteers, proved the existence of a craniocaudal gradient in  $\dot{V}_A/\dot{Q}$  ratios. They also demonstrated that changes in the distribution of  $\dot{V}_A/\dot{Q}$  ratios could be attributed to airway closure phenomena occurring at low lung volume. Indeed, their subjects who had a closing capacity greater than FRC had a craniocaudal gradient in  $\dot{V}_A/\dot{Q}$  as high as that observed in our patients during SB. This gradient faded out when lung volume was greater than FRC plus 20% of the total lung capacity. In contrast, when closing capacity was lower than FRC, the craniocaudal gradient was always minimal and did not show consistent change with lung volume.

A methodologic limitation may apply to our isotopic

method. Since the bases of the lungs are larger than the apices, the isotopic emission from the most anterior parts of the lungs (the furthest from the camera) may have not been fully detected as a consequence of the attenuation occurring in the lung parenchyma. This theoretical limitation would have favored the analysis of the most posterior basal segments, those closest to the camera. These segments of the lung bases are known to have lower  $\dot{V}_A/\dot{Q}$  than regions that are less dependent upon gravity, *i.e.*, the anterior parts of the bases. Accordingly, the craniocaudal gradient in  $\dot{V}_A/\dot{Q}$  would have been magnified. Nevertheless, we used high-energy isotopes, and the absolute lung volume differences between CMV and SB were small. Therefore, we believe that such an attenuation effect, if any, would be comparable in all modes studied and should not explain all the high regional differences in  $\dot{V}_A/\dot{Q}$  we found.

We conclude that in patients with COPD, the major determinants for the worsening in  $\dot{V}_A/\dot{Q}$  distribution during SB resulted from a critical alteration of the ventilation pattern due to an increase in respiratory rate and a decrease in  $V_T$ . This led to development of basal regions with very low  $\dot{V}_A/\dot{Q}$ .

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