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Alternating versus synchronous ventilation of left and right lungs in piglets

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Abstract *Objective:* We tested whether alternating ventilation (AV) of each lung (i. e. with a phase difference of half a ventilatory cycle) would decrease central venous pressure and so increase cardiac output when compared with simultaneous ventilation (SV) of both lungs.
Theory: If, during AV, the inflated lung expands partly via compression of the opposite lung, mean lung volume will be smaller during AV than SV. As a consequence, mean intrathoracic pressure (as cited in the literature), and therefore, central venous pressure will be smaller.
Design: The experiments were performed in seven anaesthetized and paralyzed piglets using a double-piston ventilator. Minute ventilation was the same during AV and SV. Starting at SV, we alternated three times between AV and SV for periods of 10 min.
Results: During AV, central venous pressure was decreased by 0.7 mmHg and cardiac output was increased by 10±4.4% (mean, ±SD) compared with SV. AV also resulted in increased arterial pressure. During one-sided inflation with closed outlet of the opposite lung, a pressure rise occurred in the opposite lung, indicating compression.
Conclusion: The higher cardiac output during AV than SV can be explained by the fact that central venous pressure is lower during AV. This lower central venous pressure is very probably due to the lower mean intrathoracic pressure caused by compression of the opposite lung during unilateral inflation.

Key words Alternating ventilation · Cardiac output · Central venous pressure

Introduction

In 1972, Seed and Sykes [1] used a tracheal divider to permit independent ventilation of each lung in an attempt to match ventilation to perfusion in the lateral position. This technique, which they called differential ventilation (DV), has subsequently been used to enable different ventilatory patterns to be applied to each lung in patients with unilateral and bilateral lung disease [2–5]. DV, applied either synchronously (SV) or asynchronously [6, 7], did not decrease cardiac output below that with conventional, common ventilation of both lungs. In 1983, Muneyuki et al. [8] studied alternating ventilation, in which one lung is inflated whilst the other is being deflated. In 22 mongrel dogs, they found no difference in cardiac output and central venous pressure between synchronous and alternating ventilation (AV), whereas oesophageal pressure, as a substitute of intrathoracic pressure, was significantly lower during AV. Thus, these results implied a rise in transmural central venous pressure, as a substitute of right ventricular filling pressure (pre-load), at constant cardiac output. If AV reduces intrathoracic pressure, one would expect that central venous pressure would also decrease.

In our observations of the changes that take place during the ventilatory cycle, we always noted that during inflation, a rise in intrathoracic pressure coincides with a slightly smaller rise in central venous pressure, resulting in decreased cardiac output and decreased transmural central venous pressure. During expiration all the same variables changed in the opposite direction [9, 10]. The decrease in mean intrathoracic pressure during AV with respect to SV [8] is very probably due to decreased mean lung volume, which causes less thoracic recoil forces [11]. The lower lung volume might be attributable to a lower end-expiratory volume of the opposite lung by some compression and expiration during unilateral inflation. We studied in piglets whether central venous pressure was lower and cardiac output higher during AV than SV under the same conditions of minute ventilation. In addition, we performed heart beat-to-beat analyses of haemodynamic variables during AV and SV to compare the changes during the ventilatory cycles. To minimize the jeopardizing effects of non-physiological conditions, we performed the study under conditions of intact chest and circulation but for the insertion sites of the catheters.

Methods

Surgery

Seven young pigs of 9.9±0.6 kg (mean, ±SD) body weight (BW) were each anaesthetized with an intraperitoneal injection of 30 mg pentobarbital-sodium (Abbott/Sanofi, Maassluis, The Netherlands) per kg BW. The study was approved by the Committee for Animal Research of our university.

The animals were placed in the supine position on a thermo-controlled operation table to maintain a body temperature of 38–39 °C. An ear vein was cannulated to infuse pentobarbital-sodium continuously (8.5 $mg \cdot h^{-1} \cdot kg^{-1}$) during surgery.

Needle electrodes were placed subcutaneously in the right leg and xyphoid region to record the ECG. A tracheostomy was performed and a Y-shaped cannula inserted. Airway pressure was measured via a small side tube in the Y-shaped cannula. The two limbs of the cannula were connected to the two pistons of our computer-controlled ventilator [12], which were driven independently but synchronously, each delivering half the tidal volume. Tidal volume was adjusted to an arterial P_{CO2} of 40±3 mmHg. Ventilation was performed at a frequency of 10 beats/min with an inspiratory time (I) of 2.4 s, an end-inspiratory pause (IP) of 0.6 s and an expiratory time (E) of 3 s. The inspired gas was 60% O_2 and 40% N_2. Except for the delivery of tidal volume by each piston, all ventilatory settings were maintained at constant levels throughout the experiment.

An arterial catheter was inserted into the aortic arch via the right common carotid artery to measure aortic pressure and to sample arterial blood. Two catheters were inserted via the right external jugular vein: a Swan-Ganz catheter, with a thermistor near the tip to measure pulmonary artery pressure and blood temperature, respectively; and a four-lumen catheter, which served to measure central venous pressure and to infuse pentobarbital-sodium (again 8.5 $mg\,h^{-1}\,kg^{-1}$) and pancuronium bromide (0.2 $mg\,h^{-1}\,kg^{-1}$, Pavulon, Organon Teknika, Boxtel, The Netherlands) after surgery.

Urine flow was measured by exposing the interior of the bladder transabdominally and then passing a catheter downstream through the urethra. The inner end of the catheter was funnel-shaped and had several side-holes. The bladder and abdominal wall were tightly sutured after insertion.

Measurements and calculated variables

ECG and aortic, pulmonary artery, central venous and airway pressures were recorded continuously on a chart recorder (Gould, RS 3800) with the use of amplifiers for the ECG (HP 8811 B) and pressures (HP 8805 B). Heart rate was calculated from the R-R interval. In addition, data sampling was done by computer (PC-AT) at a rate of 250 Hz. Samples were stored on disk for data analysis.

Blood gases and haemoglobin concentration were analysed with a blood gas analyser (type ABL 510, Radiometer) and O_2 and CO_2 gas concentrations, by a mass spectrometer (type 1200, Perkin-Elmer). Cardiac output was always determined as the mean of two estimates. We used the direct Fick method for oxygen [13], based on the oxygen mass equation. This equation implies equality between oxygen uptake from the ventilatory air and oxygen uptake into the pulmonary blood. Thus, we determined oxygen consumption and arterial-to-venous difference in oxygen content. Oxygen consumption and RQ did not change throughout the experimets. We also estimated physiological dead space [14] and right-to-left shunt (Q'_{sh}) in percentage of cardiac output (Q'_T) [15].

To determine the ideal oxygen saturation in the lung capillaries, the parameters in the equation of the human oyygen saturation curve [16] were fitted for the pig's oxygen saturation curve, based on pig blood data from other experiments in our laboratory. This oxygen saturation curve was similar to the curve described by Bartels and Harms [17].

From the seven observation periods in the seven pigs, we obtained 49 paired estimates of cardiac output using the Fick method. We tested the reproducibility by determining the differences between the first and second estimates as a percentage of the mean, which was −0.8±4.1% (SD) and not significantly different from zero ($p = 0.18$), indicating no bias between the first and second estimate.

The *zero level* of the blood pressures was established by connecting the pressure transducers (type Uniflow, Baxter) to a reservoir filled with saline. The surface of the saline was set at the height of the right atrioventricular valve. This height was found by transversal radiographic examination, the straight part of the Swan-Ganz catheter just before its loop in the right ventricle being taken as an indicator of the level of the valve.

Calibration of the blood pressure transducers was performed during application of pressure to the fluid level in the reservoir by comparison with a mercury manometer. Cardiac output, which was determined by the Fick method, was used to calibrate the area of the arterial pulse contour curves as described in a previous paper [18]. In that paper was also demonstrated the identity with a high correlation coefficient ($r = 0.996$) between LV output determined with the pulse contour method and LV output determined with an electromagnetic blood flow meter, where both methods were calibrated with the Fick method. Areas of the pulse contour curves of aortic pressure have been divided by the calibration factor into area units per millilitre to obtain stroke volume of the left ventricle (LV). We calculated mean LV output per cardiac cycle from LV stroke volume divided by the R-R interval in the ECG. The pulse contour wave was recalibrated after each change of ventilatory mode.

Separate ventilation of left and right lung

When surgery had been completed, the tracheal cannula was replaced by another Y-shaped cannula with an endobronchial tube in-

corporated in one limb. It took 30–40 s to effect this exchange, during which time the animals were apnoeic. The cannula was similar to that used by Moens et al. [19] in horses and was chosen because the right cranial (upper) lung lobe in the pig is ventilated via a bronchus that originates in the trachea 22–25 mm cephalad from the carina. The junction between the trachea and the cannula was made airtight by a ligature around the trachea. The endobronchial tube was guided into the left main bronchus under radiographic control. The tube was sealed into one limb of the tracheostomy cannula by means of a silicone rubber collar and vaseline. The seal in the left main bronchus was achieved with a circumferential balloon, which was inflated to a pressure of 100–150 mmHg throughout the experiment.

The right lung was ventilated via the other limb of the tracheal cannula. Pressures in the left and right airways were measured in the endobronchial tube and the tracheal cannula, respectively, via side tubes with the use of air-filled transducers (type uniflow, Baxter, Anaheim, Ca, USA). These transducers were balanced against ambient air pressure and calibrated by a water manometer.

When SV was established, each lung received half of the tidal volume. Since this resulted in a lower airway pressure in the right and a higher airway pressure in the left lung than the preceding airway pressure during the combined ventilation of both lungs, we decreased the tidal volume to the left lung and increased the tidal volume to the right lung until both airway pressures, measured at the end of the end-inspiratory pause, were equal, the total V_T remaining at 16.4 ± 1.2 ml kg^{-1} BW (mean, ±SD, $n = 7$). The ratio of tidal volume between right and left lungs was 1.30 ± 0.11 (mean, ±SD).

The total respiratory compliance during SV and AV was calculated for each lung separately on the basis of its tidal volume divided by the difference between its airway pressure at the end of the inspiratory pause and the end-expiratory pressure.

We checked airtightness between the endobronchial tube and the wall of the left main bronchus by one-sided inflation of the right and left lungs, respectively (Fig. 1), while the outlet of the opposite lung was closed. Pressure increased in the inflated lung and, to a small extent, also in the opposite lung due to compression by the volume increase at the inflated side. A leakage would have caused a progressive pressure rise in the opposite, non-inflated lung.

In all of the animals, we checked the position of the endobronchial tube during the autopsy following the experiments. The location of the cuff was between the carina and the first side branch in the left main bronchus, going to the left cranial lobe (in the human, the left upper lobe). The distance between the carina and the first side branch in the left main bronchus was 13–17 mm. The left cranial lobe showed no signs of atelectasis.

Protocol

We studied SV and AV alternately and consecutively during seven 10-min periods: three periods of AV in between four periods of SV, as shown in Fig. 2. Five minutes after the start of a period, we stored haemodynamic data on the computer hard disc for 72 s (12 ventilatory cycles) for off-line analysis. We then sampled arterial and mixed venous blood and measured inspiratory and mixed expiratory gas concentrations to estimate cardiac output, right-to-left shunt, physiological dead space, oxygen consumption and the respiratory quotient (RQ). During each observation period, we performed these measurements of blood and ventilatory gas concentrations twice and averaged the data. We calculated systemic vascular flow resistance from the difference between aortic and central venous pressures and cardiac output. Blood pressures and heart rate were averaged over a period of four ventilatory cycles.

We analysed the haemodynamic events during the first three ventilatory cycles beat-to-beat by calculating the mean values per cardiac cycle of left ventricular output and aortic, pulmonary arteri-

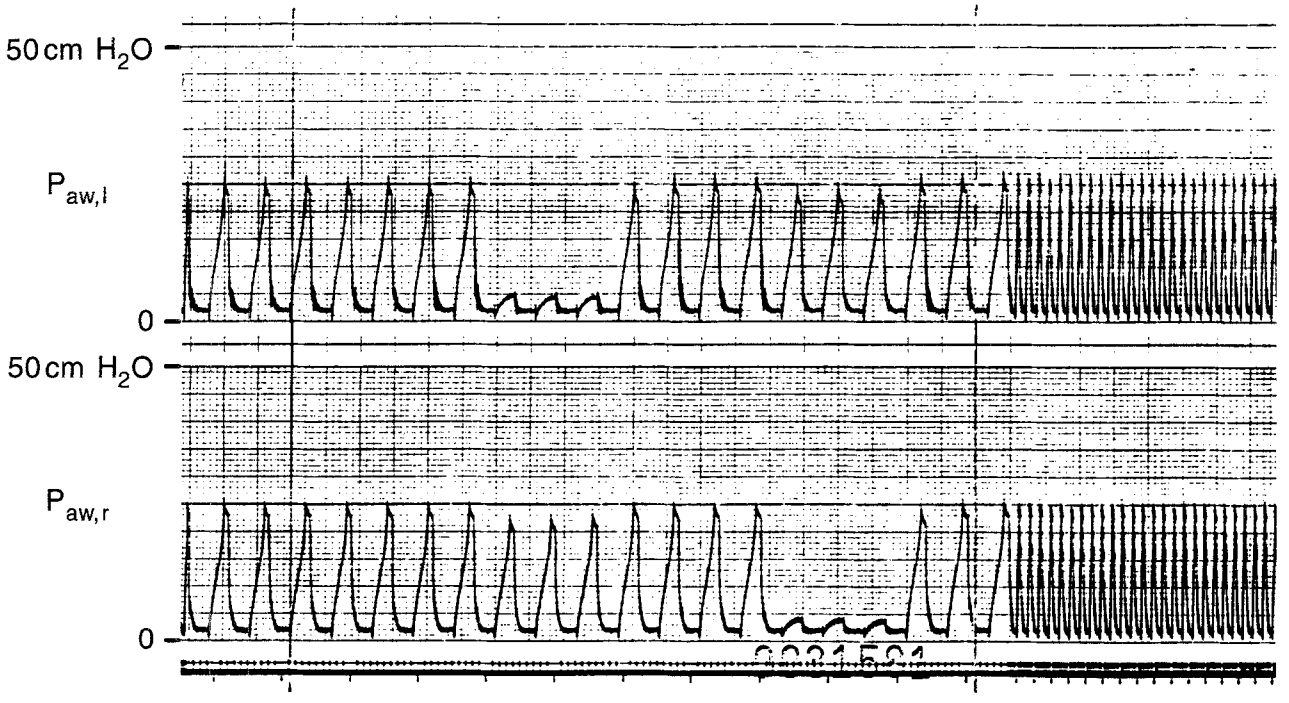


Fig. 1 Check of airtightness of position of endobronchial tube in the left lung. The *upper* and *lower recordings* are airway pressure in left (P_{aw}) and right lungs ($P_{aw,r}$), respectively. During the end-inspiratory pause after one-sided inflation, no rise occurred in the much lower pressure plateau of the opposite lung

al and central venous pressures. If a premature heart beat occurred in the first series, we used the second series of three ventilatory cycles.

Statistical analysis

The data from an AV period were tested against the mean of the data of the SV periods immediately before and after the AV period. In all seven experiments, we obtained three values for each variable during both ventilatory modes. We used a paired Student's *t*-test (one-sample analysis) to determine the *p* value of differences between the 21 individual sets of AV and SV data.

Results

Differences between AV and SV

An individual example of data obtained during successive periods of SV and AV is presented in Fig. 2. Cardiac output and aortic pressure were greater during AV than SV, whereas central venous pressure was lower and physiological dead space smaller. In Table 1 we present the mean values of all data as well as the differences between AV and SV ($n = 21$). During AV, cardiac output was 10% higher, central venous pressure was 0.7 mmHg lower, arterial pressure was higher and physiological dead space was smaller when compared to the value obtained during SV. Pulmonary arterial pressure was 0.5 mmHg lower during AV than during SV, which was not significantly different from the decrease in central venous pressure ($p = 0.44$, paired testing of the individual differences). Systemic blood flow resistance was slightly, but nevertheless significantly, smaller during AV than during SV. No differences in heart rate were found.

Total respiratory compliance of the right lung was larger than that of the left during AV as well as during SV, which we attributed to the larger volume of the right lung. During AV, total respiratory compliances of left and right lungs were larger than the corresponding values during SV.

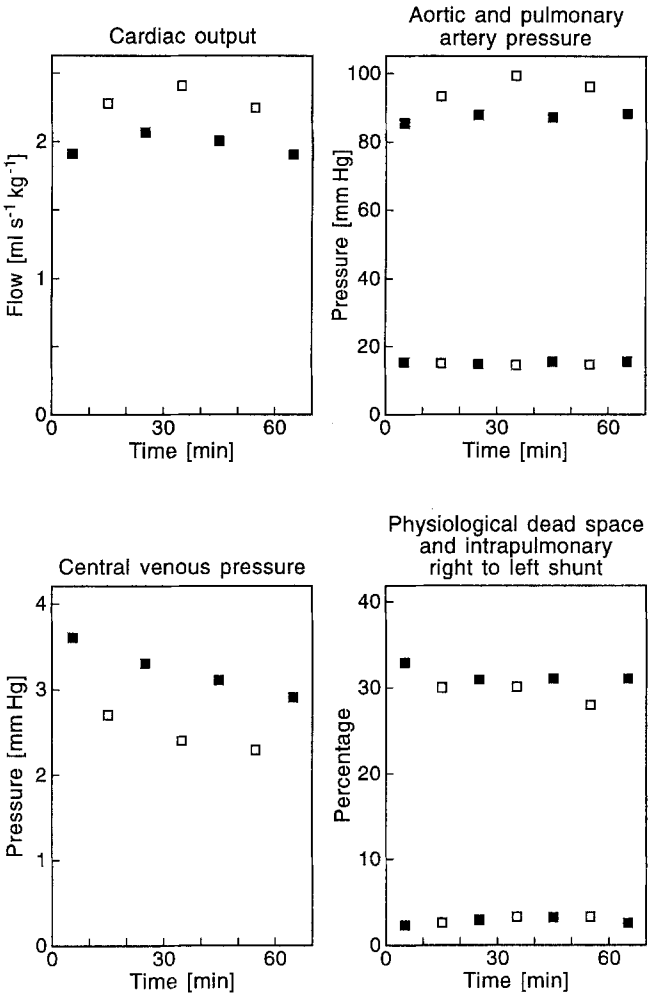


Fig. 2 An individual example of mean values of cardiac output, blood pressures, physiological dead space and right-to-left shunt during AV and SV. □, AV (alternating ventilation); ■, SV (simultaneous ventilation). Values were obtained during sequential periods of 10 min SV and AV. Physiological dead space is given as a percentage of tidal volume and intrapulmonary right-to-left shunt, as a percentage of cardiac output

Table 1 Haemodynamic and ventilatory data during alternating and simultaneous ventilation (*AV* alternating ventilation, *SV* simultaneous ventilation), *Difference* differences between the variables during AV and SV. Q'_T cardiac output (ml s^{-1} kg^{-1}) determined with the Fick method, P_{cv} central venous pressure (mmHg), P_{ao} aortic pressure (mmHg), P_{pa} pulmonary arterial pressure, R_s systemic vascular flow resistance (mmHg s ml^{-1}), Q'_{sh} right-to-left shunt flow in the pulmonary circulation or right-to-left shunt (% of Q'_T), $V_{D,phys}$ physiological dead space (% of V_T); F_H heart rate (beats min^{-1}), $C_{tot,l}$ total compliance of the left lung (ml cmH_2O^{-1}), $C_{tot,r}$ total compliance of the right lung (ml cmH_2O^{-1}), $C_{tot,l} < C_{tot,r}$ during both AV and SV. $p \ll 0.001$ for both differences

	AV		SV		Difference		*p*-value
	Mean ($n = 21$)	SD	Mean ($n = 21$)	SD	Mean ($n = 21$)	SD	
Q'_T	2.07	0.32	1.88	0.30	0.19	0.09	<0.001
P_{cv}	1.8	1.1	2.4	1.3	−0.66	0.31	<0.001
P_{ao}	102	7	96	7	6.4	3.7	<0.001
P_{pa}	13.8	2.2	14.4	2.0	−0.52	0.60	0.001
R_s	5.0	0.6	5.1	0.6	−0.11	0.14	<0.01
Q'_{sh}	4.8	3.3	4.5	3.2	0.37	0.45	<0.001
$V_{D,phys}$	32.0	4.0	34.2	3.7	−2.2	2.1	<0.001
F_H	150	26	148	26	2.5	12	0.34
$C_{tot,l}$	6.4	0.28	4.3	0.51	2.15	0.86	<0.001
$C_{tot,r}$	8.3	1.83	5.7	0.98	2.59	0.92	<0.001

Changes during the ventilatory cycles during AV and SV

The beat-to-beat changes in left ventricular output and central venous, aortic and pulmonary arterial pressure during SV and AV are illustrated in Fig. 3.

During SV, central venous pressure increased during inflation, attained its peak value at peak inflation and during the inspiratory pause, and decreased again during expiration to an end-expiratory plateau. LV output began to decrease several beats after the start of inflation and reached its lowest value in early expiration. In contrast to our previous results [9, 10], there was usually no end-expiratory plateau of left ventricular output. The cyclic changes in aortic pressure corresponded to those of left ventricular output. The pattern of changes in pulmonary arterial pressure was similar.

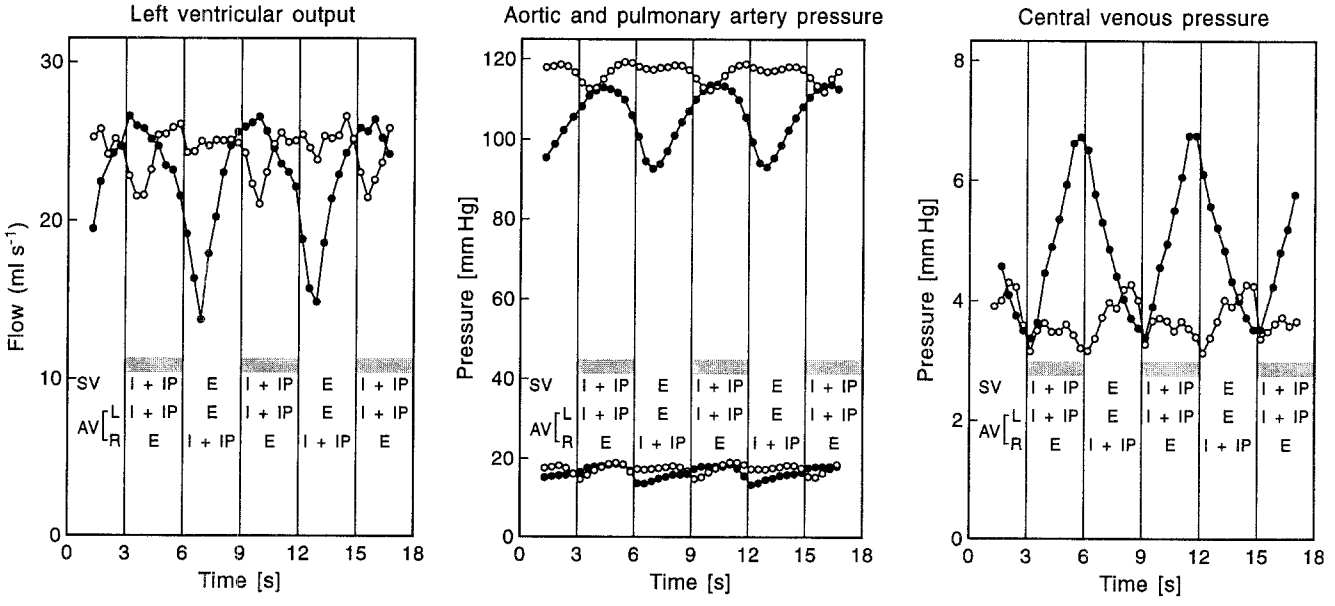
The cyclic changes of all variables had a smaller amplitude during AV than SV and occurred at twice the rate of the cyclic changes during SV. Inflation of the right lung caused greater fluctuations than inflation of the left.

Discussion

Events during the ventilatory cycle

The smaller amplitude of changes during AV when compared with SV was caused by the coincidence of inflation of one lung and deflation of the other. There were no characteristic differences between the pattern during SV and AV except that the frequency of changes were doubled and the amplitude was much smaller during AV. The changes during inflation of the right lung were larger than those occurring during inflation of the left lung and were probably due to the larger tidal volume delivered to the right. The larger (on average 1.3 times) tidal volume to the right than to the left lung for the same rise in airway pressure strongly indicates that the right lung volume is on average 1.3 times larger than the left lung volume. Because of the larger right lung volume, expansion of the left lung during one-sided inflation might coincide with right lung compression for a relatively larger part of the left tidal volume than the reverse. As a consequence, thoracic wall expansion relative to tidal volume is smaller during left lung than right lung inflation, which could explain the smaller increase in central venous pressure during left lung inflation than during inflation of the right lung. In previous studies [9, 10], where we ventilated with an I : E ratio = 2.4 : 3.6, the tidal decrease in LV output averaged over the total period of the ventilatory cycle was approximately 10% of end-expiratory flow. This percentage thus represents the difference between mean cardiac output during the ventilatory cycle and end-expiratory flow. In the present study, we were unable to estimate the tidal decrease in flow relative to end-expiratory flow from the beat-to-beat changes in LV output accurately, as frequently no end-expiratory plateau in output was present to serve as a baseline value for calculation of the tidal decrease. The shorter expiratory time caused by the insertion of a inspiratory plateau was the main reason for the lack of a period of constant flow at end expiration. Very probably, the tidal decrease in flow during SV in the present study was a few percent greater than the 10% of end-

Fig. 3 Individual example of cyclic events during AV and SV. □, AV; ■, SV. All values are averaged per cardiac cycle and plotted on the *y*-axis. During SV: I+IP inflation and end-inspiratory pause of both lungs, *E* expiration. During AV: from 3 s to 6 s, I+IP of left lung (*L*) and *E* of right lung (*R*); the reverse occurs during the next 3 s, and so on



expiratory flow observed in previous studies, because of the longer period during which the lungs remained in an inflated state. If, then cardiac output is about 10% higher during AV than during SV, we may conclude that a large part of the tidal fall during SV is prevented by AV.

Cardiac output and central venous pressure changes

The tidal decrease in LV output during AV was considerably less than that during SV (Fig. 3). This is in agreement with the estimates of mean cardiac output, which on average were 10% higher during AV than SV (Table 1). As heart rate did not change, we assume that nervous and humoral control activity did not change either. This assumption is supported by the fact that there was no significant physiological change in systemic flow resistance, in spite of a statistical significancy. We concluded that the differences in cardiac output between both ventilatory modes were due mainly to the differences in central venous pressure, which were very probably themselves the result of the mechanical factors mentioned earlier, including the smaller thoracic expansion during AV caused by compression of the opposite lung. Because peripheral resistance hardly changed, the higher mean arterial pressure during AV can be attributed to the higher cardiac output.

The decreased intrathoracic pressure during AV than SV observed by Menyuki et al. [8] implies an even larger increase in transmural aortic pressure in our experiments. If we regard this pressure as a substitute for afterload of the left ventricle, we certainly cannot attribute the increase in cardiac output during AV to this small rise in afterload.

An increase in cardiac output will also cause an increase in transmural central venous pressure and transmural pulmonary arterial pressure. If intrathoracic pressure had been constant, the result would have been an increase in both pressures relative to ambient air pressure. However, that there were similar decreases in pulmonary arterial and central venous pressure during AV, which point to the suggestion that both resulted from a reduction in mean intrathoracic pressure due to a smaller thoracic extension. The decrease in intrathoracic pressure was probably slightly larger [8–10]. Therefore, it is very likely that a slight rise in transmural pulmonary arterial pressure occurred during AV, as compared with SV. A slight rise in transmural pulmonary arterial pressure will certainly not increase cardiac output. We reject the possibility that the rise in cardiac output can be attributed to the observed decrease in pulmonary arterial pressure relative to ambient air pressure. Moreover, a moderate change in pulmonary arterial pressure does not affect cardiac output [19, 20].

Total respiratory compliance of each lung increased nearly 50% during AV compared with SV (Table 1) due to a decrease in intrapulmonary pressure of each lung to almost half its value, whereas tidal volume to each lung was kept constant. If no compression of the opposite lung had occurred during one-sided inflation, we would have predicted similar pressure rises in the inflated lung during AV and during SV. Furthermore, during one-sided inflation with closed outlet of the opposite lung, a small pressure rise occurred in the opposite lung (Fig. 1). These data indicate that a volume expansion of one lung during AV causes a compression and expiration of the non-inflated opposite lung. This supports our supposition that the lower intrathoracic pressure [8] during AV is due to expansion of the inflated lung partly at the expense of a volume decrease in the opposite lung.

We could not find an explanation for the discrepancy between our haemodynamic results and those of Muneyuki et al. [8]. During mechanical ventilation, estimations of cardiac output on the basis of thermodilution imply a wide spread of data unless three or four determinations are performed at equal intervals in the ventilatory cycles [12]. Although Muneyuki et al. used the thermodilution technique without a special protocol, we do not believe this is enough to explain the discrepancy. If that were the case, they would presumably have reported a lower central venous and a higher arterial pressure during AV than during SV.

Additional effects

As ventilation was constant, the decrease in physiological dead space during AV compared to SV can be explained by the increase in cardiac output and resultant decrease in the overall ventilation-perfusion ratio in the lungs. Right-to-left shunt was slightly greater during AV than it was during SV. Presumably a slight redistribution of blood flow occurred from the inflated lung to less well-ventilated areas of the noninflated lung during AV.

Concluding comment

Our results are in agreement with the supposition that the increase in cardiac output during AV compared to SV will be due to a reduction in mean central venous pressure. This reduction has been attributed to a lower intrathoracic pressure and, therefore, smaller mean thoracic volume. In conclusion, although AV has been shown to have some beneficial effects, its use in patients cannot be recommended without further studies on its effects in the presence of lung disease.

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